An ERP investigation of premotor sensory activity and response control in adults with
Developmental Coordination Disorder.

Duncan Brown

A thesis submitted to the University of London for the degree of Doctor of Philosophy

Goldsmiths, University of London
New Cross, London, SE14 6NW

Declaration

I, Duncan Brown, confirm that the work presented in this thesis is my own. Where information has been derived from other sources, I confirm that this has been indicated in the thesis.

Signed:

Date:

Acknowledgements

Abstract

Within the Developmental Coordination Disorder (DCD) literature the primary research focus has been directed towards children with DCD. Little has been investigated regarding the long term prognosis of these individuals with regards to the impact of the disorder in later life. Also, previous investigations and resulting suggestions of underlying aetiology have been based on behavioural data of poor performance with few studies examining the underlying biological considerations. Thus, the research within this thesis had two key aims. The first being to examine underlying processes associated with adaptive and goal directed movement in a sample of adults with DCD. The second aim was to provide biological evidence for the continued difficulties of adults with DCD.

Previous work in the area of cognitive psychology has identified distinct sensory and motor control functions as hallmarks of efficient and adaptive movement. This thesis explores the underlying sensory and motor control abilities of adults with DCD. There were two key aspects of this thesis with the first consisting of an investigation into the manner in which adults with DCD utilize sensory functions as a consequence of movement preparation. The secondary portion of this thesis focused on two key aspects of response modulation, the ability to effectively activate cortical regions underpinning effector response and response inhibition. Both aspects of the thesis drew methodological influences from the field of electroencephalography. This approach provided direct biological measurement of both sensory and response related activity.

The data obtained within this thesis provides evidence that adults with DCD do in fact demonstrate both atypical behavioural and biological functions during manual response activity. Chapter 4 highlighted key behavioural findings identifying that the DCD group demonstrates continued difficulty with accurate movement compared to typically developing peers. Chapters 5 and 6 focused on sensory activity as a consequence of movement preparation. The findings from these chapters suggest that adults with DCD present with maladaptive early sensory processing functions required for accurate movement output. Findings from the later chapters investigating response related activity suggest that adults with DCD experience difficulty with both measures of response activation and inhibition.

In summary, these findings suggest that adults with DCD experience an array of sensorimotor and response related difficulties vital to adaptive goal directed movement. Importantly, the findings presented within this thesis are the first to present direct biological based evidence for continued difficulties in a sample of adults with DCD. Conclusions are discussed in relation to previous research along with the possible influences these findings have in behaviour. The limitations of the current research and suggestions for future work are also considered.

Table of Contents

List of Tables

List of Figures

List of Abbreviations

ACC= Anterior cingulate cortex

ADAN= Anterior directing attention negativity

ADHD= Attention deficit hyperactivity disorder

ASRS= Adult ADHD Self-report Scale

DCD= Developmental coordination disorder

DTI= Diffusion tensor imaging

EDAN= Early directing attention negativity

EEG= Electroencephalography

ERP= Event related potential

fMRI= Functional magnetic resonance imagine

IQ= Intelligence quotient

PFC= Prefrontal Cortex

LDAP= Late directing attention positivity

LRP= Lateralised Readiness Potential

M-ABC- Movement assessment battery for children

Ms= Milliseconds

MT=Movement time

RT= Reaction time

Chapter 1

Introduction to Developmental Coordination Disorder

Outline

The first part of this chapter will provide an overview of Developmental Coordination Disorder (DCD). A summary of diagnostic features and general characteristics will be provided along with an overview of previous research investigating the performance difficulties faced by individuals with DCD. A brief discussion of the possible atypical sensory and motor subsystems that may underlie the observed performance difficulties will be included. The second part of this chapter will consider the manner in which the sensory and cognitive control processes examined in the current thesis influence adaptive motor output and link to DCD. Finally, the key aims and structure of the thesis will be outlined.

Diagnostic features

Developmental coordination disorder (DCD) is a neurodevelopmental disorder diagnosed on the basis of motor coordination dysfunction. According to the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV-TR; American Psychiatric Association (APA; 2000)), the term DCD incorporates a spectrum of motor related difficulties resulting in a decreased ability to learn and perform coordinated motor skills (see Table 1.1 for the four criteria that must be met in order for a diagnosis of DCD to be given).

Table 1.1.

Diagnostic Criteria for DCD (APA, 2000, pg 58)

_____

A) Performance in daily activities that require motor coordination is significantly below

expected given the individual's chronological age and calculated intelligence. These

performance difficulties may present as marked delays in developmental motor activity

(crawling, walking, and sitting) or degradation of performance in activities such as

handwriting.

B) The observed disruption in criterion A must also present significant interference with

academic achievement or activities of daily living (ADLs). Activities of daily living refer

to daily tasks that include any activity for self-care such as feeding, bathing, dressing,

grooming, vocational tasks, homemaking, and leisure.

C) The coordination disturbance is not attributable to a general medical condition and

does not meet the criteria for Pervasive Developmental Disorder.

D) If mental retardation is present, the motor difficulties are in excess of those usually

associated with it.

Historical observations and terminology

The observation of less than optimal coordination abilities in children is not a modern one.

As early as 1925 children described as motorically deficient were observed (e.g., Dupre,

1925), with Orton (1937) describing a sample of children demonstrating motor difficulties as

"clumsy".   More recent labels have included sensory integration disorder (e.g., Ayres, 1972),

clumsy child syndrome (e.g., Gubbay, 1975), developmental dyspraxia (Denckla, 1984),

physical awkwardness (Polatajko et al., 1995), disorder of attention and motor perception

(DAMP) (Gillberg et al., 1986) and the World Health Organization's label of Specific

Developmental Disorder of Motor Function (SDDMF; ICD-10, 1992). The inclusion of the term Developmental Coordination Disorder in the Diagnostic and Statistical Manual for Mental Disorders of the American Psychiatric Association (DSM-III, 1987) was the first point at which the disorder was clearly separated from other motor related conditions. In 1994, the term 'clumsy child syndrome' was substituted with Developmental Coordination Disorder (DCD) in the DSM-IV (APA, 1994). In the same year the term DCD was adopted at a consensus meeting of the world's leading clinicians and researchers as the term (among the many in usage) that should be used consistently when referring to the condition (Polatajko, Fox, & Missiuna, 1995). The use of terminology to describe the disorder still fluctuates between geographic region and professions, although the term DCD is used most widely and continues to be recommended by international experts (Sugden, 2006). The term DCD will be used throughout this thesis.

Diagnostic procedures/materials

Parents and teachers of children with DCD recognise the problems they encounter in their physical interactions with the world around them. These are generally identified as the child having difficulty learning the physical skills that other children acquire almost without effort. These may include difficulties with managing tools, such as crayons, scissors, or cutlery. Difficulties with tasks such as throwing/kicking balls, tying shoelaces and fastening buttons are also generally seen.

In light of these observations a referral (via a GP or SENCO) to a school based occupational therapist or paediatric clinic may be suggested. A series of checklists may be used to identify patterns of coordination commensurate with criterion A of the DSM diagnostic standards. These checklists include the Movement ABC-2 (Henderson, Sugden, & Barnett, 2007) and/or

the Developmental Coordination Disorder Questionnaire (DCD-Q) (Wilson et al., 2000). If the information obtained from these checklists suggests coordination difficulty is present, then follow-up motor based assessments would be performed to determine whether criterion A is satisfied. Standardized motor assessments such as the Movement Assessment Battery for Children (M-ABC2) (Henderson et al. 2007) or the Bruininks Oseretsky Test of Motor Proficiency (BOT2) (Bruininks & Bruininks, 2005) would be performed. These assessments focus on the relationship between skilled motor performance (Gross/Fine) and chronological age. In order to investigate criterion B, the therapist should perform an assessment of ADL proficiency by administering a clinical interview to establish the impact of the motor impairment on daily activities and academic achievement. If the therapist believes that DCD is present, a paediatrician should perform neurological and physical assessments to establish that criterion C is met (no presence of additional biological/medical condition). Furthermore, psychological testing by a clinical/educational psychologist would provide additional information regarding social-emotional status and cognitive abilities such as intelligence quotient. In light of a diagnosis of DCD, ideally a dynamic multidisciplinary approach to intervention would take place with occupational therapists, physical therapists, speech-language pathologists, and the child's physician all involved. In reality, in the UK, much of this intervention would be presented through information sheets given to parents suggesting ways of supporting their child's motor development needs.

Unfortunately, a similar diagnostic approach is not present for adults or individuals that have left the educational system. Often, adults that have not received a diagnosis earlier in life find it difficult to obtain formal diagnoses based on lack of knowledge regarding the presentation of DCD in adults. Another difficulty with diagnosing DCD in adults is the availability of a standardized motor assessment that contains normative data for adults. The

most recent edition of the Bruininks Oseretsky Test of Motor Proficiency (BOT-2) (Bruininks & Bruininks, 2005) provides standardized data for individual up to the age of 21, while the M-ABC2 (Henderson et al., 2007) provides standardized data for individuals up to the age of 16 years 11 months. There are no standardized motor assessments for individuals over these age limits, thus it is difficult to assess motor ability above these ages for either clinical or research purposes. Although, it is difficult to obtain a normative motor assessment for adults, these adults often report difficulty commensurate with criteria A and B of the DSM criteria (See below "Studies of DCD in adulthood").

Population prevalence and general characteristics

The scant studies examining population prevalence identify differing percentages of DCD in the child population. The DSM states that around 5% of children meet the criteria for a diagnosis of DCD (APA, 2000), whereas a more recent population based study reported a prevalence of 1.7% (labeled "severe DCD") with a prevalence of 3.2% of children when children considered as having "probable Developmental Coordination Disorder" were included in the figures (Lingam et al., 2009). A significant portion of children diagnosed with DCD continue to display motor coordination deficits through adolescence into adulthood (Cousins & Smyth, 2003; Rasmussen & Gillberg 2000; Visser, 2003).   DCD is reported in a larger proportion (2:1) of males than females (Sugden & Chambers, 1998) and presents similarly across all races and socioeconomic backgrounds (Sugden, 2006). Causality is as yet unknown and it is likely that there will be a complex combination of factors leading to DCD. Although studies are limited, low birth weight and premature birth have been cited as potential risk factors (e.g., Sugden & Chambers, 2001; Visser, 2003), and DCD is also reported in many (but by no means all) individuals with other neurodevelopmental disorders such as autism spectrum disorder (e.g., Mari et al., 2003),

specific language impairment (e.g., Hill, 2001) and attention deficit hyperactivity disorder (e.g., Fliers et al., 2008).

Secondary issues to coordination difficulty

In addition to motor impairments, children and adolescents with DCD experience socio-emotional difficulties including low self perception (e.g., Cantell et al., 1994), increased risk of anxiety (e.g., Pratt & Hill, 2011) and emotional and behavioural difficulties (e.g., Green et al., 2006) suggesting low self-esteem and peer isolation. In adult life low quality of life satisfaction has been reported by adults with DCD compared to their peers (Hill et al., 2011), and higher then expected rates of depression and anxiety are also evident (Hill & Brown, under review). This suggests that the negative psychosocial outcomes observed in children with DCD transcend into adulthood, though the nature and specific impact of these psychosocial difficulties is yet to be determined.

Studies of DCD in adulthood

The overwhelming majority of DCD research has been directed towards children, with few studies examining DCD in adolescence or beyond. Losse and colleagues (1991) reported significant problems with motor coordination, low self esteem, and compromised academic abilities in the majority of the children aged 16 who had been diagnosed with DCD at age ten. This study thus pointed to the view that continuing difficulties exist for those with a DCD diagnosis. Given this, it is, therefore, surprising that studies that explicitly examine adults are rare. Recently researchers have confirmed that the impact of motor skill dysfunction does not dissipate as the individual matures through adolescence and adulthood. A pivotal study by Cousins and Smyth (2003) examined adults that had received a diagnosis of DCD, or had reported having motor difficulties consistent with a history of DCD, and revealed that these

individuals did in fact demonstrate decreased motor performance into adulthood, with a significant impact on daily function and well-being being reported. Cousins and Smyth reported that adults with coordination impairments provided lower scores than their typical peers on a self-rating skills checklist including topics such as motor ability in the domains of obstacle avoidance, balance, manual dexterity, interception, handwriting and construction, together with their reading ability. The DCD group members also performed significantly worse on motor measures assessed during a test session, including manual dexterity tasks, ball catching tasks, and measures of balance.

A more recent study by de Oliveira and Wann (2010) investigating virtual driving characteristics of adults with DCD found the group displayed difficulty with adjustment of speed/position and poorer hazard adjustment in comparison to age matched controls. This study is the first to examine ADL performance of an adult DCD group and provides further support for specific difficulties in the adult DCD population. Although the research explicitly examining adult performance is limited, it is apparent from these studies, as well as anecdotal reports, that difficulties with motor function continue into adulthood for the majority of those diagnosed with DCD in childhood. In conjunction with continued motor difficulty there appears to be a knock on effect on emotional well being which may in fact impact these individuals later in life more severely than their movement difficulties. More detailed investigations are required to present a precise view of the prognosis in this disorder with respect to both performance and psychosocial contexts. Such studies will provide invaluable information that may influence both intervention methods and adaptive measures to improve motor function and overall well-being across the lifespan.

<u>Descriptive studies of DCD</u>

A collection of symptoms have been outlined among groups of individuals with DCD. These may not all be seen in all individuals or within the same individual over a long period of time. A brief overview of the profile of difficulties will be presented below.

Gross/Fine motor observations

Gross and fine motor deficits are seen consistently in DCD. Gross motor difficulties include poor balance modulation, falling, running deficits, and body position awareness (Smyth, 1992). Bimanual limb modulation has been shown to be slow and variable in children with DCD, mostly during ball catching tasks (Utley, 2007; van Waelvelde et al., 2004). Rodgers and colleagues (2003) employed the fine motor subsets of the Peabody Developmental Motor Scales (PDMS) (Case-Smith, 1995) to show that children with DCD performed significantly worse than typically developing controls on a variety of measures including hand use, grasp, eye hand coordination, and manual dexterity.

Fine motor skills have also been shown to be less sophisticated in DCD, including handwriting and other graphomotor tasks (such as tracing) (Henderson & Henderson, 2002; Schoemaker et al., 2001). Handwriting difficulties are the most commonly reported difficulties faced by children with DCD once the child has entered the educational system and is often the reason for referral to occupational and physical therapy (Malloy-Miller et al., 1995; Peters et al., 2004). As such this performance factor is a key measure during intervention strategies (Dunford, 2004). From another perspective, a recent study by Missiuna and colleagues (2005) reported that a significant proportion of children referred to therapy for handwriting difficulty met the diagnostic criteria for DCD. Furthermore, it appears that handwriting difficulty continues into adulthood for those with DCD (Cousins

& Smyth, 2003). It is obvious that general difficulties with gross and fine motor applications would have a continued negative influence on a range of tasks, and particularly ADLs. These difficulties will be discussed below.

Activities of daily living

Activities of daily living refer to the things we do throughout daily life and require the incorporation of appropriate motor skills for successful completion. These can include activities such as feeding, bathing dressing, occupational tasks, homemaking, and leisure activities.   As mentioned above the collection of difficulties faced by individuals with DCD would ultimately impact performance across ADLs, since these require gross and fine motor skill as well as the integration and planning of these. Although the diagnostic criteria explicitly state that DCD must have a significant impact on the performance of these activities, knowledge regarding the development of ADL performance in children with and without DCD is limited. Although this performance characteristic is explicitly linked to the diagnostic criteria, a recent investigation by Magalhaes and colleagues (2011) revealed that only 14.4% of studies presented any data related to activity or participation issues.

Previous research has reported that children with DCD have difficulties with daily living skills including dressing, personal hygiene, and eating (Mandich et al., 2003; Missiuna et al., 2007). A study by Summers and colleagues (2008) expanded upon this and investigated individuals' ADL skills via parent interviews. It was reported that children with DCD experience difficulties with a varying collection of ADLs including dressing, personal hygiene (bathing, hair brushing, hand washing, nail care, toilet hygiene) and eating. Although limited, the research into the ADL implications of DCD presents a varied collection

of deficits that hinder participation and successful completion of a range of daily tasks. This has not been investigated in adults with DCD using age relevant tasks.

Academic performance

The majority of longitudinal studies of DCD report some degree of educational underachievement in adolescents with early diagnosed motor problems (Hellgren et al., 1993; Losse et al., 1991). A few studies have employed questionnaires and interviews to investigate the social functioning of adolescents with DCD. Four studies have used questionnaires with a multidimensional perspective to study self perception (Cantell, Smyth, & Ahonen, 1994; Larkin & Parker, 1997; Losse et al., 1991; Skinner & Piek, 2000). Adolescents with DCD were found to perceive themselves as less competent in several domains, including academic competence. Other studies have reported that children with DCD experience reading comprehension difficulties in comparison to age matched controls (Dewey et al., 2002; Kadesjo & Gillberg, 1999). These studies highlight the association between atypical motor development and academic performance.

Balance/Postural control-strength

Information about postural muscle function in children with DCD is limited which is surprising given the direct influence a difficulty in this area would have on activity performance. Steele (1994) recorded postural muscle activity from muscles of the legs and trunk as children performed a rapid voluntary arm movement. Children with DCD presented atypical timing of muscle activation compared to typically developing children, while altered activity in postural muscles has been shown in children with DCD during a reaching study performed while standing (Johnston et al., 2002). In particular, shoulder muscles and posterior trunk muscles demonstrated early activation. Furthermore, children with DCD

demonstrated delayed trunk muscle activation as compared to their typically developing peers. Johnston and colleagues suggest atypical postural muscle activity may contribute to poor proximal stability and consequently the poor arm movement control observed in children with DCD.

During a static balance task Wann and colleagues (1998) found that when children with DCD stood upright with eyes closed they showed a significantly greater amount of standing sway than age matched controls. Geuze (2003) reported that children with DCD did not perform significantly worse than normal children when standing on two legs with eyes open or closed. However, he identified that children with DCD showed increased sway in more difficult conditions such as standing on the non-preferred leg with eyes closed. Geuze (2005) reported that a group of children with DCD showed weaker coupling between electromyography (EMG) recordings from the muscles and corrective force compared with control children, indicating decreased balance control in those with DCD. Finally, studies investigating symptom subgroupings of children with DCD have identified subgroups with a static balance deficit (Hoare, 1994; MacNab et al., 2001).

Although limited, the physical strength of children with DCD has also been investigated via EMG coactivation of lower limb activity. Raynor (2001) reported that children with DCD produced lower levels of maximal strength and power during knee flexion tasks when compared with age-matched peers. They also reported that children with DCD showed higher levels of coactivation, which is suggested to be a major contributor to decreased strength and power. A more recent study comparing physical fitness in children with DCD by reported that children with DCD showed decreased hand strength and aerobic power (Tsiotra et al., 2009). The atypical balance, postural control, and strength difficulties observed in those with

DCD would have an impact on ADL achievement, as these abilities are integral for accurate performance and underpin both gross and fine motor activity.

Atypical subsystems in DCD

Given the breadth of motor difficulties reported in DCD (outlined briefly above), the question often posed concerns what the underlying mechanisms supporting these difficulties might be? The literature concerning DCD has focused primarily on investigating behavioural deficits believed to indicate atypicality of sensory-motor system function.   As summarized by Geuze and colleagues (2001), these measures have revealed that individuals with DCD exhibit decreased performance in areas that include poor kinesthetic acuity, poor visual perception, poor static balance, postural control, decreased attentional control, reduced strength, enhanced spatial and temporal variability, and slow movement preparation.   The varying symptoms and co-morbidity factors also help obscure the delineation between independent neurological mechanisms and their association with motor skill production and the dynamic interaction of sensory and cognitive subsystems that may be responsible for performance difficulties observed within the DCD cohort.

A primary approach to the understanding of DCD has involved the investigation of difficulties of perception and movement impairment (see chapters in Sugden & Chambers, 2005; in particular for the purposes of the current thesis the chapter by Hill, 2005, in that volume). This information-processing approach has attempted to identify atypical performance that may be suggestive of underlying deficits that impact the observed movement problems seen in individuals with DCD. Previous investigations have focused on visual and kinaesthetic perception, however the cross modal interaction of these two

perceptual abilities has also been investigated. An overview of findings within the DCD literature will be presented below.

Visual perception

Visual perceptual difficulties have been noted frequently within the DCD literature and these difficulties are not due to occulomotor/ophthalmic deficits (Mon-Williams et al., 1994). In the early 1980's Hulme and colleagues initially described a specific deficit with visuospatial perception particularly with visuospatial memory and visual feedback mechanisms when children with DCD were required to assess line length in visual and kinaesthetic modalities (Hulme et al., 1982). Further studies expanded these findings to difficulty with size consistency estimations and the discrimination of area, slope, line length, and spatial positioning (Hulme & Lord 1987). However, Schoemaker and colleagues (2003) reported that the perceptual difficulties of children with DCD during spatial position and figure completion tasks were apparent only when a motor component was integrated into the task (tracing/trail drawing). From this study, it would appear that when perceptual abilities involve a motor component there is a degradation of perceptual abilities. However, the visuospatial deficits observed in individuals with DCD have yet to be attributed consistently with their atypical motor output.

Wilson and colleagues (1997) and Wilson and Maruff (1999) investigated visuospatial attention in children with DCD using a covert orienting of visual-spatial attention task which is a version of the Posner Paradigm (1980). Participants were required to respond manually to the presence of a stimulus in one of two peripheral locations which was preceded by a spatial cue that directed a participant's attention either to the target location (valid cue) or away from the target location (invalid cue). After an invalid cue, participants had to

disengage their attention from the incorrect target location and orient it to the correct target location. The paradigm utilized by Wilson and Maruff examined two forms of attentional orienting: endogenous and exogenous. Exogenous cues are thought to attract attention automatically whilst endogenous cues elicit voluntary attentional processes. The findings of both studies identified that children with DCD took significantly longer to shift attention following invalid endogenous cueing compared to controls suggesting a difficulty with attention disengagement.

A recent ERP study employing a Posner spatial cueing paradigm and reporting both behavioural performance measures (RT) and electrophysiological effects, identified significantly longer reaction times and a deficit in inhibitory response capacity in children with DCD when compared to typically developing children (Tsai et al., 2009). The ERP analysis revealed that children with DCD demonstrated deficits with attentional orienting, anticipatory mechanisms, and cognitive-to-motor transfer as evident by longer cue-P3 and target-N1 component latency, smaller target-P3 amplitude, an elongated interval between N2 and the motor response, and small areas on contingent negative variation (CNV) (Tsai, et al, 2009). The combined analyses of behavioural performance and ERP data suggested that children with DCD are slower in target identification, interhemispheric and cognitive-to-motor transfer speed than their peers, as well as showing decreased anticipatory and executive processes. This latter finding supports the findings reported by Wilson and colleagues (1997), outlined above.

Visuospatial orientation deficits may have further implications for motor control, since mechanisms involved in shifting of voluntary attention could also be involved in allocation of processing abilities to task relevant locations for which action is required. This profile meshes with an earlier meta-

analysis performed by Wilson and McKenzie (1998), which revealed that visuo-perceptual deficits were the most apparent difficulty faced by individuals with DCD whether or not a motor response was involved. In the aforementioned studies by Wilson and colleagues the child participants were required to provide a manual response upon detection of stimuli presented at locations on the screen. Although Wilson and colleagues suggest that the delayed responses of the DCD children underlie possible attentional orienting difficulties, this leaves open to question the response abilities of those with DCD. As mentioned earlier, children with DCD are slow to respond across a collection of modalities. This may be due to a general difficulty in response preparation or a difficulty with stimulus response programming in individuals with DCD leading to generally slower responses. Thus, in Wilson's work, it is difficult to confirm whether those with DCD do indeed have a greater difficulty with covertly orienting attention to locations since a motor response is used as an indicator of attentional orienting to stimuli. However, a recent ERP study provides support for Wilson et al.'s view. Tsai et al. (2009) considered ERP correlates of visual spatial attention (visual N1) during the task utilized by Wilson and colleagues. This allowed consideration of whether poor performance reported by Wilson arose from difficulties producing a motor response per se, or difficulties covertly orienting attention to locations since ERPs are not influenced by the response process and provide a direct online neurological measurement of perceptual processing and attention orienting. . Analyses of ERP component characteristics suggested that children with DCD exhibit longer attention orienting processing time and delayed internal processing, indexed by latent visual N1 peak amplitudes in the DCD group compared to typically developing peers. As the component was elicted by modulation of attention to the occurrence of the stimuli it was independent of a manual response. Thus, the N1 component was a valid indicator of attentional modulation within the environment. These findings provide valuable support to Wilson and colleagues earlier findings of atypical attentional modulation in children with DCD.

These limited findings are important as they demonstrate that individuals with DCD may experience orientation deficits of visuospatial processing in conjunction with low level judgments of spatial parameters.   However, while the measures employed in these studies examine cue-induced attentional modulations of sensory processing, they do not afford the investigation of a naturally occurring process that is recruited during movement preparation. Given that movement preparation is vital for efficient motor output, it will be crucial to investigate visuospatial processing and its interaction with motor preparation. The influence of visuospatial processing on movement production will be discussed later in this chapter.

Kinaesthetic perception

Another perceptual subsystem examined to some degree in children with DCD involves kinesthetic ability. Kinaesthesis, or the ability to judge body position, movement velocity, and force, is integral to coordinated and controlled movement and the information relayed by this system is utilized throughout all levels of motor output (Fitts & Posner, 1967). An effective motor action requires on- line afferent influences and, thus, it is kinesthetic feedback coupled with visual feedback that facilitates a good match between the motor plan and motor execution. Clearly kinaesthetic ability is required for optimal acquisition and development of motor skills (Lazlo & Bairstow, 1983; Luria; 1966).

The kinaesthetic ability of children with DCD has been measured primarily through the administration of the Kinesthetic Sensitivity Test (KST; Laszlo & Bairstow, 1985). The KST is comprised of two parts that measure acuity and perception and memory. These assessments require the participant to identify which arm is higher after the two arms have been moved passively up two ramps. The perceptual and memory subtest requires the individual to correct an altered pattern after the object has been traced by the participant without vision and the

object has been moved. Individuals with DCD have demonstrated difficulty with these tasks requiring static kinesthetic performance (Laszlo & Bairstow, 1983; Kaufman, 2007; Piek & Coleman-Carmen, 1995), although replication studies have not always reported similar findings (Hoare & Larkin, 1991; Lord & Hulme, 1987a). Smyth and Mason (2008) found that the KST did not predict differences in motor skills. Although children with DCD have demonstrated difficulties with tasks involving kinaesthetic perception, the nature of this difficulty has yet to be attributed fully to coordination deficits (but see Sims et al, 1996a; 1996b; Sims & Morton, 1998 for studies showing motor skill improvement after a short kinaesthetic training intervention). Again, this may be due to the heterogeneous collection of difficulties inherent in the DCD population and further investigation of the relationship between kinaesthetic ability and motor function is warranted.

While the mechanism by which a putative kinaesthetic processing deficit is unclear, Laszlo and Sainsbury (1993) reported kinaesthetic training including spatial and temporal programming/handwriting, led to improvements in kinesthetic perception and motor performance in a group of children aged 6 classified as having "perceptual motor dysfunction." Laszlo and Sainsbury argued that this improvement was effected by the training having facilitated use of kinesthetic inputs for further actions. Furthermore, the effectiveness of a kinaesthetic training programme put forth by Laszlo was investigated by Sims and colleagues (1996a/b). An initial investigation comparing improvement between two groups of children with DCD matched pairwise for age, IQ, sex, degree of kinaesthetic and motor impairment was performed. Administration of assessments of kinaesthetic ability and assessment of motor competence post intervention revealed an improvement in both groups although no effect of training was discovered. The improvements were immediate in the balance skills category of the Test of Motor Impairment (TOMI; Stott, Moyes & Henderson,

1984; the precursor to the MABC), however 3 months after training improvements in the manual dexterity and ball skills subsections of TOMI were observed.

The research investigating kinesthesia suggests that individuals with DCD experience difficulty with interpreting limb position/biomechanical constraints. Difficulty with sensory modalities regarding limb position would ultimately impact severely as these processes are vital for afferent somatic pathways carrying information regarding limb location and movement (Burke et al., 1976; Ribot-Ciscar & Roll, 1998). Such links between limb perception and visual interpretation of environment pose the question of how this interaction might be impacted in DCD. Indeed cross modal interactions will be discussed below.

Cross modal perceptual processing-Vision and proprioceptive performance

The cross modal interaction of vision and proprioception has also been investigated in the DCD population. Proprioception in this sense means the information about body position integrated via receptors located in the muscles, joints, and tendons. Cross modal mapping or the ability to calculate positioning of a limb to a visual location must incorporate information regarding visual coordinates and limb location via proprioceptive information termed visual proprioceptive mapping (Wann, 1991). This method of cross modal perception has been investigated by means of an experimental paradigm developed by von Hofsten and Rösblad (1988). The task involves placing a pin under the table at the point which matches the location of a pin on the tabletop. Mapping was investigated under three situations in which a seen hand identifies the location above the table (visual-proprioceptive mapping condition), the participant can see but not touch the tabletop (vision only), and the participant can touch the unseen location above the table (proprioception only). von Hofsten and Rösblad reported that typically developing children produced significantly less errors in the

visual-proprioceptive matching condition in comparison to children with DCD suggesting an advantage for visual guidance during proprioceptive tasks. Studies utilizing this paradigm in DCD have reported that children with DCD perform poorly compared to age matched controls in all three task conditions (Smyth & Mason, 1998; Sigmundsson, 1999). Mon-Williams and colleagues (1999) also confirmed that children with DCD made more errors than age matched controls in these spatial limb matching tasks and did not gain an advantage of visual influences for spatial limb locations in the same manner as control children. These results suggest that those with DCD have greater difficulty incorporating cross modal perceptual activity during the performance of manual tasks. It is possible that an atypical interaction of the visuomotor system is responsible for the observed deficits. Interestingly, a recent study of visual activation during reaching tasks has revealed that neural activation in the visual association cortex contributed to kinetic processing. This finding supports the importance of higher visual processing for limb movement during guided reaching movements, suggesting that kinaesthesia and visual processing co-occur during encoding for task relevant location (Darling et al., 2006). Such links between limb perception and visual interpretation of environment pose the question of how this interaction might be impacted in individuals with DCD, a group that clearly displays difficulty with perceptual capacities. It would seem appropriate to suggest that when both perceptual deficits are coupled together this would lead to deficient processing abilities with the knock on effect being increased movement variability and inaccuracy. These performance shortcomings may stem from an inadequate ability to incorporate information from both modalities or in establishing a functional relationship between the two perceptual capacities.

Force timing and control

 Force control and timing are also essential components of skilled movement that are required for control and coordinated action (Jordan et al., 1994; Wolpert et al., 1995).   In a set of studies reported by Hill and Wing (1998; 1999), children with DCD exhibited variable performance compared to control children with regards to controlling grip force in upward and downward vertical movements. This finding led to the suggestion that those with DCD may have difficulty with establishing and predicting initial force load during a movement (Hill & Wing, 1998). The ability to modulate patterns of grip force are indicative of acquiring knowledge of the environment and task constraints and again indicate that children with DCD experience difficulties in their planning and execution of movements.

Observable timing differences tend to manifest themselves during synchronization tasks in which the individual is expected to perform finger tapping skills in unison with a timing cue. Children with DCD demonstrate increased variability and inconsistency with movement time and tapping intervals (Williams et al., 1992; Hill & Wing, 1999). With reference to performance on such tasks by patients with known damage to the cerebellum or basal ganglia, Williams and colleagues postulated that the functional locus for timing control lies in the cerebellum, with influences from the basal ganglia. In a similar vein, de Castelnau and colleagues (2007) asked children with DCD to perform a continuous attention task in which individuals were to flex one finger in syncopation to visual stimuli whose frequency was altered in a stepwise fashion to assess synchronization ability. The children with DCD demonstrated enhanced variability on measures including error rate and reaction time with increased synchronization variability (de Castelnau et al., 2007). Based on their data, these researchers concluded that this synchronization dysfunction may underlie poor coordination skills. However attentional performance did not correlate with timing ability and thus the two modes were considered separate.

Response selection

Early studies of children with DCD showed that these children showed increased reaction and movement times (e.g., Henderson, Rose, & Henderson, 1992). Henderson and colleagues (1992) suggested that the increased response patterns observed in children with DCD may constitute a difficulty with stimulus response mapping suggesting a degradation of the planning of action. In line with these observed slower reaction and movement times, Van Dellen and Geuze (1988) reported that when more complex patterns of stimulus and response conditions were present during a choice reaction time task, children with DCD showed increased (i.e., slower) response selection onset. Missiuna (1994) showed that during an aiming task children with DCD performed more poorly when task and response complexity were modulated. These studies suggest that those with DCD show greater performance difficulty with complex tasks, which may indicate that they have difficulty with adapting to task requirements when stimulus response complexity is increased.

One tool to investigate the role of response selection in a task is through the provision of advance information (precue) which has the potential to produce faster RTs. In other words, increasing the precue information allows the appropriate action to be selected more quickly.   Precue manipulation during choice reaction time tasks have been reported by van Dellen and Geuze (1988/1990). These studies identified that although children with DCD showed increased RT and MT relative to their peers, both groups benefited from precue information in a similar fashion. During an aiming to target task with four precuing conditions, Pettit and colleagues (2008) reported that children with DCD showed a decrease in RT as the quality of an advance precue increased (none, low,

moderate, and high quality). The precue provided staggered information pertaining to location of forthcoming reach target on the screen. For example, the quality of the precues consisted of reducing the number of circles that indicated the possible location of the forthcoming target.   The effect of decreased RT in response to precue quality was observed primarily between the moderate and high quality cue when possible targets were reduced from two to one. These studies further suggest that stimulus response compatibility may be affected in those with DCD and that individuals with DCD require greater information to complete a task as efficiently as their typically developing peers.

The ability to modulate and control online movements has also been investigated in the DCD cohort. Hyde and Wilson (2011) recently investigated online control employing chronometric analysis of a reaching task during which jump trials to peripheral targets were present. In jump trials, the intended goal location was switched following movement onset and the new goal was located peripherally from the originally cued goal. Children with DCD were more disadvantaged by target jumps as evidenced by slower movements and increased performance errors on jump trials compared with typically developing children. Online correction is thought to be implemented by integrating predictive (or feedforward) and feedback based mechanisms efficiently (Williams et al., 2006; Wilson et al., 2004). Hyde and Wilson argue that the slower and less accurate double-step reaching during the jump trials in those with DCD may reflect a difficulty using forward models to update movement plans. Theories of motor programming have suggested that an internal aspect of effective movement production involves an accurate representation of the movement. This view proposes that action representation is a component of an internal forward model that replicates the behavior in reaction to environmental contexts (Wolpert, 1997). This theory argues that internal models incorporate predictive parameters of the external environment and are integral to the

planning and execution of action. Wilson and colleagues suggest that an internal modeling

deficit provides an interpretation of the results obtained when performing tasks investigating

DCD performance across a range of cognitive control processes, including motor imagery.

Previous research employing motor imagery has also been investigated as a possible

underlying procedural difficulty that may influence the movement difficulties observed in

individuals with DCD. Motor imagery is defined as the state in which an individual mentally

simulates an action which consists of the temporal programming constraints and

biomechanical process required to make that movement, although the execution of the

movement is not pursued (Jeannerod, 1994). In studies by Maruff and colleagues (1999) as

well as Wilson et al. (2001), children with DCD demonstrated similar speed and accuracy

patterns as the control group while displaying unique difficulties with the ability to perform

imagined versus pursued behaviors during a visually guided pointing task between two points

(Maruff et al., 1999; Wilson et al. 2001). Wilson and colleagues (2004) performed a follow-

up mental rotation task in which children with DCD were required to identify handedness at

various rotation presentations. It was reported that while mental rotation accuracy was

relatively preserved in participants with DCD, the pattern of response times in accordance

with rotation angle differed between groups. Responses of the control children were similar

to the typical pattern of mental rotation in that a moderate trade off between response time

and angle of rotation was identified. The response pattern for the DCD group was less

typical, with a small trade off function between response time and rotation angle. Wilson and

colleagues suggest that this effect represents a reduced ability to use motor imagery when

making judgments about handedness. Because accuracy was relatively preserved it seems that

these children were using an alternative strategy than their typically developing peers.

Wilson and colleagues proposed that these effects may represent a compromised ability to

accurately incorporate visuospatial coordinates into the internal feedforward movement model. They argued that these results provide further support for an internal modeling deficit. It must be mentioned that a study performed by Lust and colleagues (2006) in which EEG measures of a mental rotation task were employed failed to replicate Wilson et al.'s earlier findings. Lust and colleagues had their child participants take part in a training session before experimental testing began which might account for the non significant group differences. It is also possible that only a subgroup of children with DCD shows an internal modeling deficit. Interestingly a study by Snow and colleagues (1991) found that children with DCD demonstrated adequate proficiency with visual rotation tasks involving shape identification. This complicates the view put forward by Wilson and colleagues, as it would be expected that those with DCD would have similar difficulties with an object rotation task if a general difficulty with internal modeling was present in the disorder. Nevertheless, the studies by Wilson and colleagues imply that individuals with DCD show a unique pattern of perceptual processing that may rely on differing strategies from a typically developing group and that this altered approach to programming may be constructed upon a malfunctioning feedforward or internal modeling procedure. Although these imagery studies provide valuable links between perceptual function and motor programming, it is still unclear whether the underlying process proposed as an explanation does, indeed, underpin the functional difficulties observed in DCD. It is important that future research builds upon the internal modeling theory, particularly because replication of its proponent findings has been difficult and has only been evident during rotation tasks consisting of body parts (hands).

Motor planning

Motor planning has also been studied within those with DCD as a probable deficit that contributes to the observed difficulties of individuals with DCD. One aspect of planning

investigated has involved microscopic contributions to movement planning (that is planning occurring at half a millisecond or less (Hill & Wing, 1999)). These measures include grip force parameters on a finite time scale during the initiation or termination of a movement. Hill and Wing (1998) showed that a child with DCD increased his grip force earlier than typically developing control child when making downward movements but not upwards movements. In a secondary study, the child with DCD showed an earlier onset of grip force when performing both upward and downward movements (Hill & Wing, 1999). Furthermore, the child performed poorly on timing measures during a tapping task. No difference between the child with DCD and the control child was discovered with regards to grip force and movement onset when required to lift and hold and object above the tabletop. The authors propose that the observed deficits reflect an inability to incorporate feed forward models more specifically the internal prediction of the movement requirements.

Movement planning has also been investigated via grasping tasks that examine initial grasp profile in relation to primary and endpoint position of the hand. Smyth and Mason (1997) used Rosenbaum and colleagues' (1992) handle task, performance on which suggests that participants plan for end state comfort when reaching out to grasp and turn a bar. Children aged 4-8 years with reported coordination difficulties and children that were reported to have normally developed coordination completed this task. The DCD group was not composed of clinically diagnosed children, but of a population based sample of children for whom teachers endorsed significant numbers of movement difficulties on a motor checklist. While young children grasped the handle in a way that led to uncomfortable end states after rotation, no difference was seen in the performance of the DCD and typically developing groups. Since the DCD group was comprised of non- clinically assessed children it is difficult to comment on whether or not this area of planning is atypical in children with DCD. A pilot study

performed by Hill (personal communication) employing the identical task outlined above did in fact identify group differences in performance during the grasping task between a group of children with DCD and controls between the ages of 5 and 8 matched for age, IQ, and gender. A further study by van Swieten et al. (2010) investigated the reach and grasp of a cylinder in one of two orientations before turning it clockwise or anticlockwise. On half the trials, the turning condition led to a comfortable final posture at the cost of making a more difficult initial grasp action. Results showed that children with DCD were more likely to choose an easier initial grasp profile regardless of end state comfort. The authors of this study proposed that children selected an easier primary grasp in accordance with their intrinsic knowledge of their movement difficulties. A more recent study by Biancotto and colleagues (2011) reported that children with DCD showed normal patterns of reaching and grasping movements in terms of proximal to distal action but their grasping trajectory was wider than that of controls, particularly when vision was not allowed. In addition, the performance of children with DCD was slower, more dependent on vision, and more variable than that of controls. The atypical performance of the children with DCD could be explained by a deficit in the internal construction of movement for a forward model. In sum, then, the majority of the results from the studies above suggest a planning deficit in DCD (although, note the exception of the Smyth and Mason study although this study did not contain clinically diagnosed children with DCD). Clearly, further research is required to expand atypical planning to other tasks.

Executive control

Finally and also of particular relevance to the aims of the current thesis is the question of whether executive functions are impaired in DCD. Executive function refers to a higher order control system that manages novel situations and includes planning/decision making, error correction, working memory, set shifting and adaptive sequencing (Sergeant, 2000; Shallice,

1988). Rather little has been investigated on this topic in those with DCD although anecdotal reports of poor organization in those with DCD, as well as motor planning characteristics noted above, suggest that this would be an important line of enquiry. The results of the few studies conducted to date suggest that executive functioning may be compromised in DCD. Children with DCD often experience difficulty with more complex tasks (Piek & Coleman-Carman, 1995) as well as with cross modal integration (Wilson & McKenzie, 1998). In addition, error detection (Lord & Hulme, 1988) and working memory (Alloway, 2007) have been shown to be poor in children with DCD. These tasks all contain performance processes that fall under the umbrella of executive functions, thus it could be suggested that executive functioning is less than optimal in those with DCD.

Response inhibition is another aspect of executive functioning. Since this is required for adapted goal directed behaviour, it will be a key focus of this thesis. Findings of the limited studies to-date involving manual response inhibition in children with DCD have demonstrated that this group produced significantly more errors of response inhibition than their peers (Mandich et al., 2002; Piek et al., 2007). This result is consistent with earlier findings pointing to an inhibitory deficit for children with DCD (Maruff et al., 2003) although the conclusions from that study were attributed retrospectively to poor inhibition. In light of the available evidence suggesting impaired inhibition, future research would benefit from investigating the particular parameters under which difficulties with inhibition impact motor performance in DCD. A difficulty with response inhibition would greatly impact an individual's ability to modulate performance in response to environmental/task requirements. Examples of poor response inhibition could include failing to raise one's hand before answering a question in class, failing to wait for one's turn to play in a game or to speak during a conversation, and an inability to ignore distractions while working on homework.

When response inhibition is active in an effective manner it can include stopping oneself from entering a busy road upon detection of an approaching car, concentrating on long multi-step tasks, or reading directions before starting an assignment.

Summary of collective difficulties in those with DCD

Based on the collection of research surrounding DCD and the associated performance difficulties it is quite evident that there is a vast array of sensory- perceptual and cognitive based procedural deficits present within the DCD population. These difficulties have been reported overwhelmingly in children with DCD although the limited adult studies undertaken show continued significant motor difficulties. The independent manner in which each unique performance capacity affects motor skill coordination is yet to be determined. The disparate collection of difficulties presents researchers with a difficult task to collectively interpret results and make inferences about the aetiology of DCD and its prognosis.   The debate continues on whether or not the underlying aetiology is attributable to an isolated modal/unisensory deficit or multi sensory/cross modal performance or whether more psycho physiological deficits underlie the disorder. It is also unclear at what stage of processing or planning the difficulties occur, particularly since the putative difficulties with underlying sensory processing would be expected to impinge on the ability to formulate appropriate response selection parameters.

Sensory and motor control approaches present in the current thesis

As outlined above, a range of cognitive and perceptual processes have been considered with reference to DCD. However, a number of considerations in the approaches used and understanding developed remain with regards to causality of the observed performance difficulties of the DCD cohort. Two aspects of this are relevant to the current thesis. The first is the lack of a directed, theoretically driven programme of research into the coordination difficulties seen in DCD. In the current thesis, the approach is to draw upon an established literature that relates to sensory and motor control processing in the context of action. It is proposed that previous studies of typically developing individuals and the associated literature can be used to provide a focused investigation and subsequent improved understanding of DCD in relation to the central component of this disorder, coordination. The second aspect of the current thesis that is particularly lacking in previous research is the consideration of an adult sample of individuals with DCD. The first of these points will be considered in relation to the typical literature in the following section, the second has been considered in the previous part of the current chapter.

Hierarchical organisation of movement planning

Movement planning is comprised of a complex collection of processes that requires communication between stimulus and control processes. Movement planning takes place in a top down fashion with levels of sensory processing (Connelly, 1970). The resulting processing stages involve stimulus integration, internal control mechanisms, and interaction of these two processes with expectant outcomes of the forthcoming movement. A key body of literature has focused on goal directed action; making a movement relating to a specific goal, such as reaching to pick up a coffee cup, or

turning a glass in which you will pour wine. Since the focus of the current thesis is on

goal directed action, it is this literature that will be summarised here. Research has

shown that goal directed action is organized hierarchically, involving a series of

sensory and motor control transformations that must occur prior to the onset of the

desired behaviour. Imagine a classic experimental set-up where the participant must

reach to a target following a starting cue or, to take a naturalistic example, reach

towards a glass of water on the tabletop. Reaching to a target involves an initial

cognitive representation of the goal directed behaviour, as well as of the object (or

goal) to which the behaviour shall be directed (Jeannerod, 1999; Gallese, 2000). This

initial phase affords an organisation of the different actions required (Lestou et al.,

2008). In our example the individual would define the motor strategies, the objectives

of the movement and the behaviours to be applied to reach and grasp the glass.

Action planning continues with spatial and temporal characteristics being evaluated.

These characteristics include the distance between effector and object/goal location as

well as consideration of the trajectory and velocity of the desired movement

(Desmurget & Grafton, 2000; Kawato, 1999). This results in an overarching

spatiotemporal plan being made in order to achieve the required goal directed

movement. This plan is made in the so called task space coordinate system which is a

direct effect of movement planning (Kelso et al. 1986; Saltzman, 1979). The task

space and goal direction movement parameters are broken down into movements for

all effectors (such as a bimanual task of holding a mug with one hand to pour milk

into with the other). This forms a central motor program of action including

coordination of all neuromuscular control signals required by the effectors involved in

the performance of the upcoming action. Continuing with our example, the actor

would have determined the appropriate direction and trajectory towards the glass

based on the spatial configuration of the end state in relation to effector location. The location of the glass would be converted into a set of intrinsic coordinates for which the adjustment of movement angles is applied. The motor programme must be closely related to spatial planning as well as known effector specific constraints since movement parameters are given in specific coordinate systems dependent upon end location of effector with regards to goal location (Saltzman, 1979; Sober & Sabes, 2003). The inclusion of spatial parameters is a key aspect of the motor planning stage and is required for fluid and accurate transition to the final stage of the motor plan.

The final level in the hierarchy of action representation is action execution. The motor commands for effectors coordinated by the central motor programme become activated and lead to temporally coordinated neuromuscular activation and to coordinated movements of all effectors involved in the goal-directed action (Jeannerod 1999; Saltzman & Munhall, 1989). The resulting movements can be monitored from visual, auditory, and somatosensory feedback (Sober & Sabes 2005), with appropriate adaptations to the motor programme being implemented during action execution. The actor would commence the reach task to the glass and receive constant feedback during the movement. For example, if the glass shifted slightly on an uneven surface, the individual may adjust end effector state to accommodate the new position. Thus an intact sensorimotor system is able to efficiently incorporate these sensory integration formulations to refine movement plans on-line, indicating the use of both feedforward and feedback systems in motor planning and execution (Jeannerod, 1997; Munzert, Lorey, & Zentgraf, 2009). A corruption at any one of these stages would ultimately lead to an inefficient motor plan resulting in variable

performance and the ability to adapt responses in accordance to dynamic environmental influences.

Motor preparation and sensory control/processing

Another key characteristic of motor production is the integration of sensory information with motor components during the preparation of a movement. Gibson (1950) argued that perception of one's environment is a required property of viable action, without which behaviour would be directionless and erratic. As mentioned above, the integration of environmental information via various sensory processing networks is a vital building block for which movement is constructed. The brain is often characterized as a sensorimotor interface for the selection of sensory parameters and the transformation of this information into goal directed behaviour. The relationship between sensory integration and motor production is composed of a dynamic interaction between environment and behavioural goals.

Theories and research surrounding the interaction of motor control and sensory processing have often been formulated on the assumption that isolated control systems remain functionally separated (Posner & Peterson, 1990; Posner & Dehaene, 1994). Recent psychophysiological studies have changed our understanding of this traditional view and have presented networks that demonstrate overlap between motor and sensory control procedures (Anderson & Bueno, 2002: Eimer et al., 2006; Snyder, Batista, & Anderson, 1997). These findings suggest that the relationship between preparatory sensory modulation and motor activity may not be isolated but rather that may be closely linked. Evidence for this relationship will be discussed below.

Motor preparation and visuospatial processing

Much of our behaviour is controlled by an internal model of the environment in which we interact, and this model is influenced by sensory information. The representational systems that interface sensory information within the brain allow humans to model the world and to establish a causal relation between response preparation and the environment for which action is required. One sensory system that has been shown to be highly central to movement preparation is vision (Desmurget et al., 1998). Adaptive goal-directed behaviour in humans must depend on a successful integration of the complementary visual control contributions. Much research has shown that the preparation of goal directed action is influenced by visual processing as well as top-down signals that weight visual information at early processing stages. Actions also rely on selection processes to include motor related spatial parameters that involve the extraction of the visuospatial parameters relevant for the movement (Neumann, 1987). As discussed above, visual parameters must be defined within some coordinate frame of reference with regards to the environmental movement parameters. These control processes are thought to reflect the prioritizing of areas for action and are considered a vital processing stage in response preparation (Baldauf & Deubel, 2010; Deubel & Schneider, 1996; Findlay & Blythe, 2009).

The close relationship between the adaptation of visual resources and response preparation has received support with studies suggesting a forthcoming movement results in enhanced visuospatial processing being distributed to locations in external space of the action related to goals (Deubel et al., 1998). Recent behavioural research has discovered enhanced processing at goal location prior to forthcoming movements in typically developing individuals. Deubel and colleagues (1998) used perceptual

discrimination of letters as an index of processing performance at intended goal location and reported that visuospatial processing was deployed to goal location prior to movement. Similar enhanced performance of letter discrimination has also been found to occur at both goal locations in sequenced reaching tasks to more than one goal location (Baldauf, Wolf, & Deubel, 2006). In a similar vein, Schiegg and colleagues (2003) used letter discrimination to investigate processing at areas when grasping a cross. It was reported that increased letter discrimination occurred when letters were presented to intended (i.e., grasp) vs. unintended contact points. In a follow up study employing ERP measures, Baldauf and Deubel (2009) measured visually evoked potentials in response to visual stimuli flashed at various locations in the visual field prior to a sequenced pointing task. Enhanced visual evoked ERP components were identified in response to visual stimuli at goal locations in comparison to task irrelevant locations (Baldauf & Deubel, 2009). Furthermore, Hayhoe and colleagues (2003) reported that during a reaching task participants' tended to fixate most of the time at the goal of the motor action being performed. To add further support for the importance of vision, Adam and colleagues (1995) reported increased error rates when vision was occluded whilst reaching to targets. Clearly visual processing of end point areas of a forthcoming action result in enhanced processing of the location and appears to represent a tightly coupled effect of movement preparation during reaching tasks. In other words when preparing a movement to goal locations, visuospatial processing of the goal area is prioritized compared to other irrelevant locations.

Although much of the research examining visual processing and movement preparation has investigated goal related effects, recently ERP studies have presented

data that suggests processing of effector location also occurs prior to response onset. Van Velzen and colleagues identified enhancement of early visual evoked potentials in response to task irrelevant visual probes places near cued hand and concluded that visuospatial processing faculties may be directed towards the effector locations prior to forthcoming manual movement (Van Velzen, Gherri, & Eimer, 2006). This collection of studies examining processing enhancement at goal and effector locations suggest that modulation of visual processing is significantly influenced by control processes during the preparation of a response.   It is as yet unknown if both goal location and effector are processed in unison or if these areas are processed over a differing timecourse prior to movement onset. Nevertheless, it is evident from these studies that motor preparation elicits visuospatial processing activity for locations for which action is directed.

In summary, visuospatial processing underpins motor preparation, allowing the preparation of effective movement strategies. This, in turn, reflects a top down information feedback structure that contributes to action planning and in turn affects sensory processing. The complex spatial arrangements of the environment is determined by selection processes that are present during the response preparation phase and appear to be dependent upon the requirements of the upcoming response (Allport, 1987).   In order to adopt appropriate parameters for a forthcoming reach the system must establish parameters to include position in space, size, and consistency of objects thus effector movements are contingent upon visual information which appears to be specific for body/effector location and endpoint of the desired behaviour. Thus, an inability to organize spatial parameters with effective time course modulation and distribution would present difficulty across a range of tasks.

<u>Preparatory effects of selective sensory control</u>

Whereas the effects of movement and spatially selective processing of visual stimuli have been studied in some detail, research investigating the control processes that underpin selective processing has only begun to emerge more recently. ERPs have provided a useful tool in uncovering the time course and topographic distribution of control processes that follow the presentation of a spatial cue. The initial investigation of these early ERP effects was presented by Harter and colleagues (1989) using a modified Posner paradigm. A central arrow instructed the typically developing child participants to shift attention to a peripheral location. During 75% of the trials a target stimulus occurred at the cued location requiring the children to respond. Harter and colleagues identified an early negativity contralateral to shifts of attention, labelled EDAN (Early directing attention negativity), and a secondary effect labelled LDAP (Late directing attention positivity). The earlier EDAN effect was suggested to underlie an initial control process that led to an attentional shift towards cued target, whereas the later occurring LDAP reflected the modulation of contralateral areas involved during visual processing underlying information processing at the target location.

These effects have been replicated, particularly during spatial cuing paradigms (Eimer et al., 2002; Eimer, Van Velzen, Forster, & Driver, 2003; Nobre, Sebesyten & Miniussi, 2000). Furthermore, a third effect has been identified. This is termed ADAN (Anterior directing attention negativity), a negativity component contralateral to the direction of attention shift and most visible at lateral frontal electrodes (Hopf & Mangun, 2000).   Of particular importance to the current thesis is the finding that ADAN/LDAP effects are also elicited during the preparatory period of a unimanual

movement. Eimer and colleagues have shown consistently that during the time following a visual cue indicating which finger to lift similar ADAN and LDAP components were present (Eimer et al., 2005; Eimer et al., 2006; Eimer & van Velzen, 2006). In a follow up study, Gherri and colleagues (2007) used the same paradigm, but required participants to make larger reaching movements (of the hand) to target locations. Again, ADAN and LDAP features were identified following the initial cue and preceding the movement cue. It appears that ADAN/LDAP effects appear during attentional task paradigms and during the preparatory time window of simple manual movements. This suggests selective sensory control processes are present when both movement preparation and shifts of attention in space are required.

These ERP studies offer an exciting avenue for research within the movement preparation realm as they provide direct support for the view that preparatory control processes underpin selective processing, particularly in response to movement preparation. Indeed, studies of brain activation during spatial attention shifts and motor preparation have revealed similar enhancement of neurological structures. Based on the time course and topographical distribution of effects observed during attention shifts, it is strongly suggested that a frontoparietal network is explicitly involved in the control of attention and of motor processes that code space as a function of motor requirements (Corbetta et al., 1998; Praamstra et al. 2005). These control processes are suggested to be responsible for the allocation of attention processes but also have been implicated as primary effects of sensory processing in action (Townsend et al., 1996). The similar neurological activity identified during the two tasks is suggestive of a shared selective sensory mechanism. This top down controlled mechanism is a fundamental stage of sensory control during goal directed

activity and is suggested to facilitate movement to include initial direction and trajectory along the frontoparietal network (Filimon et al., 2007; Beurze et al., 2009). These sensory relationships ultimately influence the perception of the environment as well as one's behaviour, particularly in terms of movement preparation as these control mechanisms are suggested to establish the appropriate allocation of visuospatial processing resources that are essential for accurate response formation (Kato et al., 2001). Importantly the findings from the aforementioned ERP studies provide support for the premotor theory of attention (Rizzolatti, 1994). This theory postulates that processes involved in the control of selective spatial attention and spatially directed motor responses are implemented by common neurological areas. The premotor theory was based on observations in neurological patients and originally explained links between shifts of attention and eye movements, however studies of movement preparation have revealed similar frontoparietal effects. The appearance of these effects provides support for the close relationship between movement preparation and early selective sensory processing. The premotor theory will be elaborated upon in Chapters 5 and 6 where ERP data reflecting the processes mentioned above are presented.

<u>Summary of motor preparation and sensory processing</u>

The preparatory control and sensory processing mechanisms mentioned above underlie a preferred effect of sensory processing attributed to action. The presence of these two processes suggests that the initial effects of response programming involve the recruitment of early control processes that establish spatial parameters for which a response programme is structured. The relationship between these two aforementioned sensory processing and control procedures has yet to be establised

although it may be implied that these procedures work with one another to formulate spatial inferences of our surroundings that infleunce the movement preparation phase. Overall, the processes discussed above represent a collection of fundamental aspects of movement preparation that must be active in order to formulate accurate motor plans. Ultimately if these mechanisms are not in place, maladaptive motor programs would be produced, resulting in poor motor performance. In addition to the aforementioned sensory and motor control processes, the current thesis will investigate cognitive control mechanisms that monitor adaptable movement output in response to environmental influences. These include the activation of cortical areas underpinning activation of response hand prior to movement onset and response inhibition.

Response inhibition

In addition to the motor planning and associated sensory processes mentioned above, response selection also includes cognitive monitoring strategies that select appropriate behaviour in relation to contextual and environmental requirements. Adaptive and flexible goal directed behaviour requires cognitive control mechanisms that are able to appropriately select information for organisation and optimization of processing pathways that structure goal directed behaviour. This requires an ability to monitor ongoing procedures and performance outcomes with internal goals. Executive control is a high order cognitive function for orchestrating multiple cognitive and behavioural processes that are adaptive and instrumental to achieve equilibrium between behavioural goals and environmental influences (Barkley, 1997; Miller & Cohen, 2001). It is regarded as a top down effect and is especially integral when novel action

plans are integrated and responses must be sequenced and selected to accommodate task requirements (Robbins, 1998).

An essential control process required for adaptive response modulation involves the ability to quickly adapt behaviours to prioritize actions and elicit informed responses dependent upon the suppression of actions that are no longer required or that are inappropriate. This process, termed response inhibition, supports flexible goal-directed behaviour in ever-changing environments. Control of inhibition is essential across all aspects of performance, including attention, movement, intelligence, and memory as it affords the individual an adaptable time course for which more appropriate cognitive occurrences may occur (Kochanska et al., 1996). Essentially, inhibitory control is the ability to suppress the processing or expression of information that would disrupt the efficient completion of the task at hand (Dempster, 1992). One established model of response inhibition has been outlined by Logan and Cowen (1984). The "horse race model of inhibition" proposes the existence of two response phases. One constitutes the 'go' processes while the other controls inhibition processes. According to this model, the two processes (essentially, stop and go) are programmed in unison and compete against each other for activation. The response that is activated (overt/withheld) is dependent upon the time course of each response programme and completion in accordance with cognitive control mechanisms. Recently the prefrontal cortex has been described as the area where associations with stimuli, action, and constraints are formed in relation to inhibitory processes (Aron, Robbins, & Poldrack, 2004; Ridderinkhof, 2004). Activity of this area is most evident when actions compete and cognitive control is required for the timely inhibition of the selected response (Miller & Cohen, 2001). Ultimately response

inhibition is the elimination of an inappropriate response and is vital for the evaluation and successful implementation of behavioural adjustments. Humans adopt response inhibition in a variety of daily tasks. For example an individual approaching a busy street may need to stop themselves from leaving the curb in response to an approaching car. Also, stopping oneself from reaching towards a hot item removed from the oven or withhold raising one's arm in class to answer a question are daily examples of response inhibition. Thus response inhibition is a necessary control process that is the hallmark of adaptive behaviour and it could be argued that it is responsible for safe and adaptable interactions with daily tasks.

<u>Neurobiology of motor preparation</u>

As the disruption of motor performance observed in DCD is suggested to be caused by a corruption at some neurological level, an overview of typical motor related neurological activity is necessary. The preparation and activation of cortical areas for movement have been thoroughly investigated by brain imaging. These studies have identified the time course and distribution of activity across different regions of the brain during the preparation and activation of a movement. A brief summary of this process will be discussed below.

Scherwin (2010) provides an excellent overview of the neuroanatomical structures involved in the production of movement and the sequence of cortical activation. During the preparation phase of movement the parietal and frontal lobes (premotor cortex) become active with contributions from the subcortical structures that underlie alertness and sensory information. The prefrontal cortex is responsible for planning the movement in conjunction with the frontal cortex which receives projections from

the parietal cortex. The posterior parietal cortex is involved in transforming visual information into motor commands. The posterior parietal areas project this information to the premotor cortex and the supplementary motor area. During this time, body position in relation to movement parameters is established for which the basal ganglia provide information. At this point past motor experiences and learned motor programs are consulted to help determine the amplitude, direction, and force of the movement. During the next phase of motor programming the premotor area and the supplementary motor area interact with the cerebellum to formulate the sequenced activation of the muscles that are required to complete the chosen movement. The primary motor cortex calculates the force requirements for each muscle and projects this information through the spinal motor neurons to generate the movement. The duration and force of the movement are constructed upon sensory information from learned movements and upon feedback of the current task.

Imaging studies examining neurological activity during the preparation of a movement have elucidated the sequence and distribution of neuroanatomical activation. Due to the limited movement constraints inherent to fMRI, investigation on the majority of these studies has focused on small limb movements. Nevertheless, a collection of studies has identified increased activation in the premotor cortex, supplementary motor cortex, and the superior parietal association cortex during response preparation (D'Esposito et al., 2000, Deiber et al., 1991, Lee et al., 1999). Motor programming takes place in a well organised hierarchical fashion that encompasses a unique and dynamic interaction between neurological structures. It is quite obvious that if an area or process is corrupted it would have a severe knock on effect on programming strategies downstream. It is yet to be determined at which

individual or collective programming stage those with DCD exhibit difficulty however further by studies of brain imaging during motor tasks can only help to elucidate the area of dysfunction.

Possible neurobiology of Developmental Coordination Disorder

Very little is known about the neurobiology of DCD. Historically, assumptions about likely foci were made by implication from similarities in the behavioural components of movement between those with DCD and patients with known brain lesions / brain involvement such as acquired brain pathology and degenerative motor conditions such as Parkinson's disease. More recently a small number of studies have focused on neuroimaging techniques such as fMRI and EEG. These implicate a range of possible underlying areas in DCD and point to a range of crucial areas of investigation. Given the psychobiological nature of the focus of the current thesis, likely neuroanatomical involvement is overviewed here.

Cerebellum involvement

The cerebellum has often been referred to as a distinct area involved in the coordination of motor control particularly with the control of sequencing, timing of muscular activity, postural control, and force control (Barlow, 2002; Ghez & Thach, 2000). Research supporting cerebellum involvement in children with DCD stems from behavioural measures of timing and rapid movements of the hand which have been shown to be less sophisticated than control children (Geuze & Kalverboer, 1994; Hill & Wing, 1999; Lundy-Elkman et al. 1991; Piek & Skinner, 1999). In addition, postural control difficulties observed in children with DCD have also provided support for cerebellum involvement (Johnston, 2002; Geuze, 2005; Wann, 1988).

A collection of studies by Kagerer and colleagues (2004; 2006) investigating visuomotor adaptation in children with DCD reported that during a drawing task in which varying degrees of visual distortion to endpoint target were imposed, children with DCD were less affected by these distortions than typically developing children. This finding was suggested to arise from an inadequately defined internal model of movement under visual manipulations in DCD, reflecting atypical cerebellar involvement. However, general adaptive ability when ball throwing in a prism adaptive task was reported to be similar in DCD vs. typically developing children, leading Cantin and colleagues (2007) to argue against a cerebellar deficit in this group. In terms of the cerebellum, then, results are ambiguous and it is likely that a complex relationship between key areas of the motor system as well as other connected areas (e.g., frontal cortex; cf. Diamond, 2000) will be at play in DCD.

Parietal lobe involvement

The other neuroanatomical area that has received much attention within the DCD literature is the parietal region. Results from studies investigating motor imagery in children with DCD by Wilson and colleagues (2001) suggest the difficulty may underlie an inability to incorporate efferent somatosensory copies which has been suggested to originate in the parietal lobe (Blakemore & Sirigu, 2003). In line with Wilson's original findings regarding motor imagery, Katschmarsky and colleagues (2001) showed that children with DCD have difficulties in generating secondary saccades during a sequenced saccade task compared to typically developing individuals. These researchers suggest that parietal lobe involvement and processing of efference copy signals could underlie motor clumsiness in the majority of children with DCD. These results leave little support for a direct neuroanatomical influence

for DCD as cerebellum activity has been observed during motor imagery tasks and visuospatial calculations (Parsons et al., 1995; Ryding et al., 1993). Visuospatial deficits have consistently been suggested in the DCD literature (see above) which again provides viable support for parietal lobe involvement as this area has primary involvement with integration of visual spatial information processing (Wilson & McKenzie, 1998).

Slowly, the involvement of individuals with DCD in neuroimaging studies has become evident, providing clearer pointers of likely neuroanatomical contributors. Taken together, these studies highlight a collection of atypical neurological activity within the DCD population to include parietal involvement. Kashiwagi and colleagues (2009), using fMRI measures, identified decreased left posterior parietal cortex and left postcentral gyrus activity in children with DCD compared to typically developing children during a continuous tracking task. A similar finding of atypical neurologic activity was reported by Zwicker and colleagues (2011) who examined neurologic activity during a fine motor trail tracing task in children with DCD. Compared to aged matched controls, activation patterns suggest that the children with DCD show decreased activation of the cerebellar–parietal and cerebellar–prefrontal networks representative of visuospatial faculties during the tracing task (Zwicker et al., 2011). De Castelnau and colleagues (2008) reported an EEG spectral coherence analysis during a finger syncopation task to visual stimuli with alternating stimulus frequency. Data obtained from this task revealed that coupling between frontal and central regions increased with task difficulty compared that seen in control children. This suggests that children with DCD demonstrate an increased reliance on the frontal cortex for motor programming, thus reducing the input of posterior perceptual

mechanisms (De Castelnau et al., 2008). Although contributions from behavioural

and neuroimaging studies do suggest atypical parietal lobe involvement in those with

DCD, it is yet to be confirmed as a primary neurological locus underlying difficulties.

Basal ganglia

The contribution of the corpus callosum and basal ganglia have been suggested, but

not thoroughly investigated, in DCD. Lundy-Ekman and colleagues (1991) divided a

group of so-called clumsy children into those who showed mild signs of cerebellar

dysfunction and those with mild signs of basal ganglia damage (based on soft

neurological signs) and compared their performance on a continuous tapping task

with age-matched controls. They found that the cerebellar group displayed increased

inter-tap interval and force variability compared to the basal ganglia group whose

timing variance was within normal limits compared to typically developing children.

In contrast, the basal ganglia group displayed increased force variance compared to

the cerebellar group. Although not followed up further, these findings suggest that

cerebellar or basal ganglia involvement may be implicated in subgroups of individuals

with DCD.

The case for evaluating DCD using motor preparation paradigms

It is apparent that despite the evidence for localized atypical neurological affliction in

the DCD population (see above), there is still no consensus as to the distinctive area

that is responsible for the observable deficits in DCD. It seems likely that a more

broad regional relationship is affected in DCD and the difficulties faced by the group

cannot be attributed to one specific area, since sensorimotor and other cognitive

control transformations span numerous neurological areas. The heterogeneous

collection of symptoms within the DCD cohort also presents difficulty with prescribing an isolated neurological region as the main area underpinning DCD. It seems that further work and replication of neuroimaging studies across tasks and age groups is required to support atypical neurological influences that contribute to the difficulties observed in the DCD cohort. It is questionable that atypical involvement of one region strictly underlies the performance difficulties observed in DCD. It is more likely that a network of neuroanatomical regions contribute to the difficulties observed in individuals with DCD. As the current thesis will be examining ERP correlates related to neurologic activity, it will help to provide support for previous atypical neurological activation patterns observed in the DCD cohort.

As mentioned above, a large amount of research investigating typically developing individuals has identified sensorimotor and motor control processes that underpin adaptable and efficient motor output. Specifically these studies have demonstrated that movement preparation is coupled with sensory processes that occur during the preparatory period of a movement and reflect key stages of motor control organisation. More importantly these findings have been theoretically driven and support postulated interactions of action and perception indexed by performance measures and neurological activation (e.g., Rizzolatti, 1994). Further discussion of the premotor theory will be presented in Chapters 5 and 6 when ERP data related to perception and action are presented. As will be mentioned in the methods and ERP chapters, the paradigm employed throughout this thesis and the accompanying ERP measurements will allow consideration of the processes outlined above and their precise contribution to the motor preparation and control process. Although ERP measures do not isolate activity to specific neurological regions, the data obtained will

afford an initial investigation into the processes that can be attributed to specific neurological regions and influences to motor control. To this end, the current aims of the thesis with regards to aforementioned sensory and cognitive control processes will be discussed.

Aims of the current research 1: Integrating sensorimotor and motor control approaches with DCD

The research outlined in this introductory chapter highlights the performance difficulties faced by individuals with DCD across sensory and cognitive domains. Information reviewed in this chapter also highlights the integration of sensory and motor control strategies that are required for efficient goal-directed behaviour, an area that may be particularly problematic for those with DCD. The purpose of the current research was, therefore, to draw on the literature identifying overlapping sensory processing and motor preparation mechanisms, and to use an *a priori*, theoretical approach to investigating a key aspect of the *coordination* difficulties apparent in this coordination disorder, collecting cognitive behavioural and biological data from a goal directed movement task. To collect these data, ERPs reflecting the aforementioned motor control and sensory processes will be measured. ERP measures allow a direct measurement over very discrete temporal resolution, thus the preparatory and control measures of interest can be investigated in conjunction with a goal directed movement task. Finally, while previous research in the DCD population has focused on children, the current project considers the performance of *adults* with DCD on the paradigm of interest.

Visuospatial processing

As mentioned previously, perceptual difficulties have been consistently presented in the DCD literature to include visuospatial difficulties (Hulme et al., 1982; Schoemaker et al., 2003; Wilson et al., 1997; Wilson & Mckenzie, 1998; Wilson & Maruff, 1999). From the literature investigating cross modal (visual/prioprioceptive) performance, children with DCD have difficulty incorporating cross modal abilities during reaching tasks (Smyth & Mason, 1998; Sigmundsson, 1999; Mon-Williams et al., 1999). This collection of studies implies that DCD children have difficulty utilizing visuospatial parameters across a range of tasks. More importantly it appears the children with motor impairments are relatively more dependent on visual information about the target for end-point accuracy. It is suggested that children with DCD have deficits in temporal and spatial parameterization of movement. As a result many children with DCD seem to experience more disturbances in movement parameterization, including visuospatial influences.

Although important to the body of knowledge concerning DCD, there is yet to be a study that examines visuospatial processing as an effect of movement preparation. As the modulation of visuospatial enhancement has been shown to have unique distribution characteristics to goal locations and cued effectors, it appears that it is a vital aspect to movement preparation and establishes task space coordinate parameters. These enhanced location effects have been demonstrated consistently in typically developing individuals and emphasize the explicit coupling of movement preparation and visuospatial processing. As visuospatial abilities are a vital step in the motor control process, it is important to investigate this process in individuals with DCD as atypical modulation of visuospatial processing would impede the integration

of spatial components into the motor programme. In Chapter 5, data that examines visuospatial processing and movement preparation will be presented. This will enable an investigation into the distribution of visuospatial processing during the preparation of a movement to examine if adults with DCD modulate processing parameters as effectively as typically developing peers.

Selective sensory control

It appears that the distinction between the processes involved in sensory control and those involved in motor preparation are no longer as separable as previously thought. The collection of ERP findings supports inferences from the premotor theory of attention (e.g., Rizzolatti, 1994) that response programming and early sensory control processes are based on shared control mechanisms. The previously mentioned results and their relation to movement provide a theoretically validated measure of movement preparation and associated sensory activities which has been lacking in the DCD literature. These studies have consistently recorded effects that underpin sensory control processes crucial for adaptive behaviour, it seems a logical direction to direct these measures towards the investigation of individuals who display difficulties that are suggestive of atypical movement preparation. As mentioned above, early selection control processes appear to facilitate spatial processing following cue to shift spatial attention and more recently during the preparation of a unimanual movement. Failure to incorporate initial selective control stages would impede overt movement applications as the forthcoming motor plan would be reliant upon poorly established spatial control parameters. The manner in which those with DCD employ flexible control resources is yet to be fully investigated however, a maladaptive transformation of these processes would impede adaptive behaviour and is a possible

conduit for observed difficulties. This initial sensory control process has primarily

been investigated through attentional paradigms however these effects have also

presented during the preperation of manaul movements. Indeed children with DCD

have presented with atypical response patterns during spatial cueing paradigms,

suggesting a difficulty with the primary selective sensory control procedure (Wilson

& Maruff, 1997; Mandich et al., 2002; Tsai et al., 2009). These studies suggest that

individuals with DCD demonstrate difficulty with early selective sensory processes.

As mentioned above these ERP effects (ADAN/LDAP) have been presented in ERP

studies during movement preparation and shifts of attention and appear to reflect a

cross modal sensory control process in typically developing idnviduals.   In Chapter 6,

the current thesis will investigate this initial sensory control process in adults with

DCD.

Cortical activation of a response effector

Within the DCD literature there is a vast collection of atypical sensory shortcomings

that would suggest a corruption at one of the processing or integration stages is likely

ultimately leading to atypical motor execution. It is still unclear as to the processing

stage at which the disruption occurs in DCD or the manner in which sensory

shortcomings directly influence stages of response programming. Difficulties with

response selection have been evident throughout the DCD literature (van Dellen &

Geuze, 1988; Henderson et al., 1992; Hyde & Wilson; 2011; Petit et al., 2008).

Several experimental studies have been carried out in an attempt to identify the

underlying response selection/programming mechanisms of DCD, yet relatively few

studies have investigated the critical aspect of effector activation. One aim of the

current thesis is to examine the endpoint of the motor planning stage in the form of

the timecourse and distribution of neural activation underpinning effector activation over the motor cortices. This will be performed for simple and complex movements. It is also intended to provide direct neurophysiologic evidence for an information processing deficit regarding motor planning and subsequently provide support for continued difficulties into adulthood. In chapter 8, this will be performed by examining the response locked lateralised readiness potential (LRP) which is a direct neurological marker of cortical activity that is present prior to the onset of a limb movement and indicates how close one is to the response threshold (Coles, 1989; De Jong et al., 1988). By examining the LRP we will be able to investigate if effector activation is involved in the response selection difficulties observed in DCD individuals. Specific theoretical and experimental information regarding the LRP will be discussed in the forthcoming chapter dedicated to event related potentials (ERPs) and in chapter 8 in which LRP data from the current study is presented.

Response inhbition

Although the research explicitly examining executive functioning, specifically response inhibition, in individuals with DCD is limited, there are a few studies that suggest executive functioning shortcomings in DCD individuals (Alloway & Archibald, 2008; Mandich et al., 2002; Piek et al., 2004). Difficulty with the organisation and integration of this cognitive control mechanism would significantly impact successful adaptation of daily task performance. Recently, Querne and colleagues (2008) examined fMRI connectivity during a go/no-go task and reported that children with DCD showed significantly stronger anterior cingulated activity and weaker prefrontal activity in comparison to their typically developing peers; two key areas for response inhibition and error detection.   One aim of the current thesis is to

examine the time course and distribution of ERP inhibitory activity following an instruction to withhold a manual response during both simple and more complex movements in adults with DCD. This will be done by utilizing ERP measures of response inhibition. These measures will be discussed in detail in the forthcoming ERP chapter (Chapter 2) as well as within Chapters 4 and 8 when the inhibition data from the current thesis is presented (behavioural and biological data, respectively).

Aims of the current research 2: Specific research questions

The principal goal of the current thesis is to examine underlying sensory and motor control procedures upon which goal-directed movements are built, and to establish if these underlying abilities are intact in adults with DCD. Whereas the DCD literature has focused on behavioural measures that are suggested to represent atypical integration of these processes, ERP analysis of these measures will afford a direct investigation into the time course and distribution of these effects.

The main questions of the current thesis are:

(i) Do adults with DCD present with the same distribution of enhanced visuospatial processing at task relevant locations during the preparation of simple and complex movements as typically developing individuals?

(ii) Do adults with DCD activate initial selective sensory control mechanisms during the preparation of a limb movement in a similar fashion to their typically developing peers?

(iii) Do adults with DCD present with similar time course and scale of effector activation at cortical areas as typically developing individuals?

(iv)   Do adults with DCD recruit the active inhibitory mechanisms required to adapt responses and monitor response selection strategies as effectively as their typically developing peers?

Justification for a singular experimental approach throughout the thesis

As mentioned above the processes of movement preparation and response execution involve varying aspects of sensory and response related cognitive functions imperative to adaptive and goal directed movement. Although one experimental task was employed in the current thesis (see Chapter 3 for details), the task itself afforded the investigation of a multitude of sensory and response related functions indicative of processes that subserve the overall movement process. As will be mentioned in Chapter 2 as well as in the forthcoming experimental chapters (5-8) each of the ERP components considered is representative of specific processes that must occur in order to appropriately determine environmental influences that impact movement planning and the subsequent response. The early sensory components examined in Chapters 5 and 6 underpin activity following movement intention and subsequent movement cue and have been shown to be vital aspects to the movement planning stage. These early sensory processes afford the establishment of environmental aspects upon which movement parameters are computed. Furthermore, as will be discussed in detail in Chapters 7 and 8 the task consisted of instructions to pursue the planned movement or withhold the movement (Go/No go). These two characteristics rely heavily upon cognitive approaches underpinning collective response preparation. In summary, although a singular experiment was used throughout the thesis the ERP methodology and associated components allow for a detailed examination of sensory and response related activity along the continuum of movement preparation and execution. Thus within the singular experiment various aspects of early and later processes relating to movement

preparation and execution could be drawn out and investigated within the same task. The focus on using this paradigm with those with DCD relates to the reported difficulties of this population in terms of goal directed movement and the processes that underlie efficient movement production.

Furthermore, from a practical perspective, the clinical group identified for investigation and the central concern of the thesis is a very unique group. As mentioned above obtaining a diagnosis of DCD is very problematic for children and as for adults a consistent and applicable diagnostic approach is almost non-existent. Thus, the recruitment effort was quite robust yet yielded relatively low numbers of potential participants that fit the diagnostic criteria (see Chapter 3). In this respect a singular experiment that afforded a multitude of sensory and response related processes in the same sample was ideal and would provide valuable information regarding the performance of the adult DCD group.

Structure of the thesis

Early sensory processing and control measures are fundamental components of goal directed movement and appear to co-occur during the preparation of movement. These aspects of movement preparation form the basis of the investigations presented within this thesis. In addition to these early sensory functions, two additional aspects of goal directed activity were included; effector activation and response inhibition. These were investigated in a group of adults with DCD in comparison to a group of well-matched typically developing peers. The experimental task consisted of a choice reaction time reaching task with Go/Nogo conditions for reaches towards goal locations on the same side of the body as cued effector or reaching across midline to cued goal location. Please refer to Chapter 3 for specific methodological information.

In Chapter 2, a historical and theoretical discussion of the event related potentials (ERPs) investigated throughout the current thesis will be presented. These measures have been employed consistently in various research contexts and paradigms to investigate the processes described in the current chapter. ERP measures have proven themselves to be reliable indicators of sensory/cognitive control performance in typically developing individuals. The specific ERP components isolated for examination will be discussed in terms of underlying sensory and response related functions. Previous research and interpretations surrounding the cognitive functions that the ERP components represent will be considered. Further detailed descriptions of their use within the experimental task will be provided in Chapters 5-8.

Moving onto the research phase of the current project, adults with and without DCD took part in the ERP paradigm which is the focus of the current study. All measures reported were collected in the same testing session and thus all participants provided the data reported across all chapters in the thesis. Group selection criteria and assessment procedures for the DCD and typically developing participants are outlined in Chapter 3, along with the experimental paradigm. General EEG recording methods will be presented at this point, with the isolated aspects of analyses for each ERP investigation presented in the individual experimental chapters (Chapters 5-8).

In Chapter 4, the behavioural data obtained from the study are presented, specifically reaction time, movement time, effector selection errors and response inhibition errors. These measures will be used as indices of continued movement difficulties and particular difficulty with the experimental task. Although the measures presented within this chapter have been

examined within the child DCD literature, this is not the case in adults with DCD. It is essential that these measures are investigated in an adult sample. The chapters then move onto focus on individual ERP components calculated from the EEG data recorded.

In Chapter 5, the N1 data will be presented. This ERP component describes visuospatial processing at task relevant locations and is believed to be an index of early task relevant visuospatial processing of the movement environment during the preparation of a reach to goal. This chapter will provide a detailed investigation into the ability of adults with DCD, in comparison to their peers, to prioritise locations within the movement environment during the preparation of a straight or midline crossing unimanual reach to goal providing evidence for early sensory processing associated with manual response preparation.

In Chapter 6, early selective sensory processing measures (ADAN/LDAP) that appear following cue for movement direction will be presented. These early frontoparietal distributed components have been suggested to underpin shifts of attention that are activated during response preparation implying that the control of both goal directed movements and of attention are executed by common neural mechanisms required for movement preparation (Rizzolatti et al., 1994). These early frontoparietal activations are suggested to contribute to computations of the movement environment, establishing parameters such as movement trajectory and goal location. Within this chapter comparisons of the distribution and activation of these components will be compared between the two groups in order to identify if those adults with DCD activate similar frontoparietal networks as their typically developing peers.

Chapter 7 will address the manner in which adults with DCD recruit neurological areas that reflect effector activation for a forthcoming movement based on an ERP measure of motor cortical activation. The lateralised readiness potential (LRP) reflects the preparation of motor activity on one side of the body, in this case effector activation for a reach to goal. This motor related component provides a direct measurement of the motor cortical area activation prior to movement onset and will allow a detailed investigation into the manner in which adults with DCD engage these motor areas prior to movement onset, in comparison to their peers.

In Chapter 8, activation of cortical areas associated with manual response inhibition will be examined in order to investigate the manner in which adults with DCD recruit cognitive control mechanisms for adaptive control of behaviour, in comparison to their peers. As will be outlined in Chapter 2, inhibitory components N200 and P300 have been used as indices of response inhibition since these components demonstrate differing characteristics between a withheld and pursued response. The investigation of the N200 and P300 component will afford an investigation into the recruitment of the underlying neurological processes and regions directly associated with response modulation.

Finally, Chapter 9 will present a general discussion of the key findings of the research, as well as their implications for understanding of the nature of sensory and motor control difficulties in DCD. Proposed models of difficulty will be presented relating to the difficulties that those with DCD may experience both in the sensory realm, whilst preparing a movement, and with response related activity. Limitations of the current thesis and future directions will also be discussed.

Chapter 2

Introduction to Event-Related Brain Potentials

<u>Outline</u>

This chapter will provide an overview of Electroencephalography (EEG) and Event Related Potentials (ERPs) with particular focus on ERP correlates of the sensorimotor and cognitive control processes described in Chapter 1.   This will include a short introduction to the methods and procedures associated with this form of psychophysiological investigation. In addition, a brief literature review of the ERPs investigated throughout the current thesis will be presented.

<u>Electroencephalography and Event-Related Potentials</u>

Electroencephalography (EEG) was first reported by Hans Berger in 1929 as measured electrical activity of the human brain by placing electrodes on the scalp and isolating the fluctuations in voltages over time (Berger, 1929). Berger's findings were first thought of as simple physiological muscle activity however this view was soon reconsidered as EEG was shown to indicate underlying cognitive and sensory activity. Event-related potentials (ERPs) began to come to the forefront of EEG research in the mid 1960's with the discovery of the contingent negative variation (CNV) component (Walter, 1964) and the P300 component (Sutton et al., 1965). During the 1970's and 1980's there was a vast expansion of EEG/ERP practices that sought to increase the information base surrounding the existence of ERPs and the specific neurological strategies underlying their production (Luck, 2005).

EEG signal activity reflects the activity of a large collection of neurons associated with the occurrence of a physical or mental/cognitive event in response to an internal or external stimulus (Picton et al., 2000). This signal is a collection of a large number of neurons that can include populations as large as 1 billion (Nunez & Srinvasan, 2006; Ward, 2006). Although it is difficult to extrapolate the exact neural generator of activity utilizing EEG methods, it is possible to extract discrete cognitive, motor, and sensory activity from the overall EEG signal by averaging large conditional effects to isolate activity attributed to the cognitive or behavioural processes being investigated (Luck, 2005). Conventional neuroimaging techniques such as functional Magnetic Resonance Imaging (fMRI) and Diffusion Tensor Imaging (DTI) isolate hemodynamic (blood) and water diffusion across biological tissue. These methods produce a greater spatial representation of activity compared to the EEG/ERP, which is much more effective at measuring changes with extremely accurate temporal resolution.

In order to appropriately derive an ERP as a direct result of the physical, sensory, or cognitive process in question one must average together a large number of trials isolating the process being investigated. A large portion of continuous EEG will contain activity not related to this underlying process (this is often referred to as background EEG). By averaging a large collection of trials it is possible to isolate the activity that represents the functional process of interest that remains constant across conditional parameters (Ward, 2006). This averaging procedure allows any spurious activity that occurs at random from trial to trial to be cancelled out leaving the ERP in question isolated, independent of spurious system noise. ERP components are always presented relative to a baseline period, normally averaged in reference to a specified

stimulus onset with a predetermined time epoch prior to the stimulus used as baseline (see Figure 2.1). A baseline correction is employed to isolate the specific afferent waveform and remove any artefactual abnormalities that may occur between conditions to ensure that the ERP obtained is similar in enhancement for the prescribed conditions and is devoid of physiological interference.

Because voltage ultimately is the measurement of the current potential between two locations, EEG is always recorded as the potential for current to pass between electrodes. The ERP in fact represents the difference between active and reference sites. Since there is no neutral point reference site, the ERP represents contributions from both the active and reference sites. The overall EEG measurement is the relative value of activity that corresponds to a particular reference point. Reference points may include physiological locations such as the bony protrudance area of the mastoids, the earlobes, and nose. In addition, the EEG may be referenced to an average of all the scalp electrodes. Practices of preferred referencing locations tend to vary between labs and researchers. It is important to maintain consistency with utilizing a reference point between experiments and participants. A lack of consistency between participants and experimental manipulations can lead to improper conclusions being made regarding the distribution of EEG topography and experimental effects (Picton et al., 2000).

ERP components are often discussed with reference to the experimental manipulations regarding functional relevance and underling neurological sources (Otten & Rugg, 2004). The ERP waveform is representative of the component summation indicating various cognitive processes that take place during the

completion of the experimental task, thus ERP components are often investigated by comparison between differing experimental conditions rather than investigating independent raw ERP activity during isolated conditions (Luck, 2005; Otten & Rugg, 2004). The key method of isolating underlying processes with regards to ERP effects stems from cognitive subtraction or the ability to compare particular cognitive processes (e.g., Donders, 1869). This requires an experimental condition to be contrasted with a control condition that is intended to elicit all of the cognitive processes present in the experimental task except for the one of interest. Under this assumption any difference in neural activity between the two conditions can be attributed to the process of interest. In other words, a comparison between experimental task requirements is necessary to support differing processes in relation to task constraints. This factor presents further support for an experimental design that incorporates differing conditions in order to isolate the ERP effect in question.

ERP nomenclature

Most identifiable ERP components are referred to by the letter indicting its polarity, negative or positive (N or P), followed by a numerical descriptive referring to the sequential order for which they appear post stimulus. For example the P1 followed by N1 component describes the first positive peak followed by the first negative peak (See figure 2.1). ERPs may also be named based on their timecourse post stimulus such as somatosensory component N140 which presents negatively approximately one-hundred and forty milliseconds post stimulus. ERP components can also be referred to as acronyms such as Anterior Directing Attention Negativity (ADAN), although traditionally most components follow the nomenclature guidelines discussed earlier. The component latencies are not static in occurrence and can vary with

experimental task manipulations or between groups and are quite often variable with

regards to timecourse and distribution effects post stimulus. ERP components can also

be classified as exogenous or endogenous. Exogenous ERP components are

determined by external stimulus where as endogenous components are elicited by the

participant's intentions and capacity for action. Exogenous components are usually

static in response to a stimulus as compared to endogenous components which

demonstrate characteristics that are behaviour dependent.   Detailed characteristics of

component activity will be described in further detail in subsequent paragraphs and

experimental chapters.
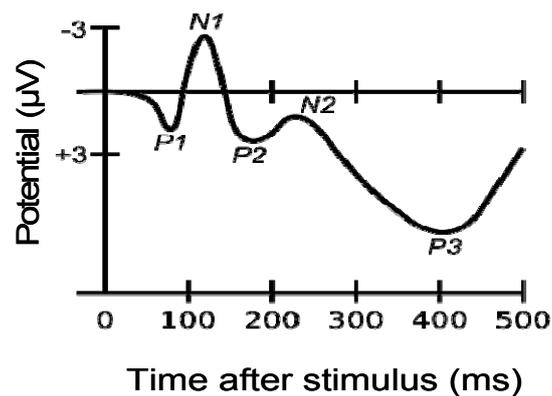
Figure 2.1. Example of ERP waveform. Note waveform deflection (+/-) and descriptive of waveform presentation. For example, P1 and N1 being the first positive and negative deflection of the waveform following stimulus. Figure adopted from Nieuwenhuis et al. (2003).

Presentation of ERP waveforms

Graphically, ERP waveforms are usually presented with the x axis reflecting time (msecs) and the y axis reflecting the amplitude of the waveform in microvolts (uV) (See figure 2.1). Furthermore the waveforms can be plotted with either the negative or positive potential in the upwards direction. As there is no consensus amongst researchers regarding presentation criteria, it is important to be mindful of this when interpreting ERP waveform graphs. In the current thesis, ERP waveform graphs are presented with negative potential in the upwards direction. In conjunction to isolated waveform presentations, the distribution of the activity within a given time window along the scalp in topographical or current-source density maps will be presented. This affords comparison of component distributions that have been examined in the previous literature and provides consistency amongst component findings with regards to experimental and methodological manipulations influencing scalp distribution of effects.

ERP components

This section will provide a short review of the literature pertaining to ERPs that were examined as part of the current thesis. The historical background, supporting empirical evidence and procedures, as well as current practices and findings will be presented in order to justify the validity and relevance of the use of each measure of the underlying performance factors investigated in this thesis. Further discussion of the methodology and examination of the specific ERPs with regards to their measurement in this thesis will be discussed in greater detail in the appropriate experimental chapters.

ERPs as an index of visuospatial processing

Visual ERPs are elicited whenever a participant is presented with some variation of visual stimulus and are considered to reflect a primary visual response (Wang et al., 2001). The early visual ERP component C1 is considered to reflect activity in the primary visual cortex and typically appears 50-80 milliseconds following presentation of visual stimulus (Clark, Fan, & Hillyard, 1995). The subsequent ERP components (P1, N1) have been linked to activity in extrastriate cortex and can be modulated by spatial processing (Di Russo et al., 2002). This modulation of the later occurring visual ERP components is suggested to underlie enhanced sensory modulation towards pertinent locations in space with enhanced processing of sensory/spatial information at specified locations that are task-relevant (Mangun et al, 1987). Lateralisation of the N1 is dependent upon the location of the visual stimulus presentation at with the amplitude of these components demonstrating greater enhancement at electrode sites contralateral to stimulus (Clark & Hillyard, 1996). Enhancement has been shown to be modulated by luminance scale and angle of presentation (Mangun et al. 1991).

As compared with conditions that simply require a response, the N1 component is enhanced in conditions that require a differentiation between classes of visual stimuli (Anllo-Vento & Hillyard, 1996). Callaway and Halliday (1982) reported that modulation of N1 was directly related to task difficulty suggesting that greater active attention or effort influenced the N1 activity. In addition, Fort and colleagues (2005) reported that N1 onset latency varied in response to stimulus motion and detection thus supporting perceptual influence on this visual component. A vast body of literature provides evidence that the amplitude of the N1 component is enhanced

when the eliciting stimulus occurred at an attended location in space (Eimer et al., 2002; Heinze et al, 1994; Van Voorhis & Hillyard, 1977).

The exact functional significance of the N1 component has long been debated The task location related N1 enhancement patterns are interpreted as reflecting early visuospatial selection and discrimination processes (Luck, 1995). Even though the N1 component is classified as a visual evoked potential its appearance and characteristics are manipulated by additional influences including attention resources, sensory gating, and spatial-perceptual factors. These findings are suggestive of perceptual properties being selected for further processing/activity which inherently involve a form of discrimination within the locus of attention.

ERP components associated with preparatory control processes- ADAN/LDAP

As mentioned in the previous chapter, past studies of the areas of attention and movement preparation have been examined independently of one another without consideration of the links between them. With the advancement of neuroimaging techniques and applied methods the links between early selective processing and action have been established (Anderson & Bueno, 2002; Eimer & Van Velzen, 2006). Findings have supported theoretical inferences that motor action and sensory processing are coupled together forming significant functional overlaps.

The most common experimental paradigm used to study visuospatial attention is the Posner paradigm (1980) with slight variations to elucidate different pathways of attentional activation. This experimental task revolves around cued visuospatial orientation that requires attentional activation. Participants staring at a fixation point

are usually presented with a cue that guides the individual toward a particular spatial location or object shape. This prepares the attentional system of the individual to anticipate and respond specifically to the corresponding target following the guided cue. The cue and target are usually separated by longer intervals so that neural activation of attention can be assessed in the presence and absence of visual stimuli. This helps elucidate the neural mechanisms associated with early selective processing versus direct visual activation.

The most consistent ERP effects associated with these processing shifts are recorded over frontocentral and occipitotemporal areas in the form of voltage differences between the hemispheres ipsilateral and contralateral to the attended hemifield (Eimer, 1995; Eimer & Van Velzen, 2002; Harter et al., 1989). Frontoparietal areas have been suggested to be involved with sensorimotor activity related to saccades and reaching (Verleger et al., 2000). These effects are observed in response to a cue directing attention, and before the imperative stimulus is presented are described as anterior directing-attention negativity (ADAN) and late directing-attention positivity (LDAP).

Praamstra and colleagues (2006) have suggested that the origins of the ADAN component include the lateral prefrontal cortex and the lateral and medial premotor cortex. The LDAP component origins may include the posterior parietal cortex and the ventral occipital cortex (Praamstra et al, 2005). Of pivotal importance to the current thesis, is that recent research has identified similar early effects during the covert preparation of a movement post response cue (Eimer et al., 2006; Praamstra, 2006; Gherri & Eimer, 2010). The occurrence of these early ERP effects during cued

shifts of attention and movement preparation suggests that overlapping frontoparietal network subserve the control of attention and movement preparation. This finding signals strong support for the aforementioned Premotor Theory of Attention, most importantly that movement initiates early selective processing to space. These components are suggested to reflect frontoparietal cortical networks for early selective processing that directs processing capacities and eye activity to task relevant visual locations in space.

<u>Neural correlates of motor inhibition</u>

The most commonly reported ERP components of inhibitory activity are the Nogo N200 and P300. The exploration of these correlates typically results from using a Go/Nogo, or delayed response paradigm requiring participants to respond to a selected stimulus whilst withholding a response upon appearance of another stimulus form (Pfefferbaum et al., 1985). The predominant components isolated during the interval in which participants are withholding a response are the Nogo N200 and P300 which have been shown to differ between tasks requiring a response and those when an overt response must be withheld (Bruin & Wijers, 2002). In recent years, the functional interpretations of both Nogo N200 and P300 have been under debate.

In recent times, the Nogo N200 ERP component has been studied in isolation from the P300 component and used as a marker for comprehending the nature and procedural onset of movement inhibition strategies. A large literature collection has emerged focusing on the role of anterior Nogo N200 in the monitoring or regulating of strategy and processing of feedback during response selection. Some researchers argue that the Nogo N200 component reflects a top down inhibitory process which

suppresses an incorrect response at the processing stage (Kaiser et al., 2003; Kim et al., 2007), and that the Nogo N200 reflects conflict resolution within the motor program when determining an appropriate response (Donkers & van Boxtel, 2004). One argument in favour of the inhibition hypothesis is the existence of enhanced Nogo N200 amplitudes in Go/Nogo tasks when Go and Nogo trials occur with an equal frequency (Eimer, 1993). In contrast, Nieuwenhuis and colleagues (2003) argued that the Nogo N200 reflects conflict arising from competition between the execution (Go trials) and the inhibition (Nogo trials) of overt motor responses based on the appearance of the N200 during less frequent Go trials in comparisons to Nogo trials.

The Nogo N200 effect has been studied through both auditory and visual modalities with interesting results. Falkenstein and colleagues (1999) suggest that the different enhancement of the N200 during visual and auditory modalities may reflect specific neural generators that are modality specific prior to motor programming. This may be true on a biological level as the visual modality Nogo N200 has been shown to be generated in the caudal principal sulcus whilst the auditory Nogo N200 originates in the dorsal bank of the principal sulcus (Gamba & Sasaki, 1990). In a more recent study involving both children and adults, the medial frontal cortex (near ACC) was shown to be involved in the generation of Nogo N200 activity (Jonkman et al., 2007). The Nogo N200 complex has also been shown to be larger in individuals with a high false alarm rate (i.e., responding to Nogo trials) which may be suggestive of a relationship between enhancement and success of response inhibition (Falkenstein et al, 1999). A further study reported that the stop-signal N200 was reduced over right inferior frontal electrodes in children with attention-deficit-hyperactivity disorder

(ADHD) relative to normal controls (Brandeis et al., 2003). This was true for both successful and unsuccessful stop trials. Over these same electrodes, N200 amplitude was correlated with percentage of successful inhibitions in both normal and ADHD children. If the N200 does in fact reflect inhibition, it is not likely that this reflects motor inhibition per se, but rather a premotor inhibition process such as the decision to withhold the response. The inhibition process in the prefrontal cortex is consistent with further literature pertaining to the prefrontal lobe being the locus of control for executive processes, conflict resolution, and the control of inappropriate goal directed responses (Ridderinkhof et al., 2004).

The P300 component has also undergone some interpretational difficulties although it is also frequently investigated in tasks requiring a form of response inhibition. Researchers have hypothesized this component to reflect sensorimotor inhibition with greater amplitude for successful inhibition as compared to failed attempts (Liotti et al., 2005; Roberts et al., 1994). This component has also shown diminished amplitude in participants with ADHD, and having its origins in the anterior cingulate cortex (Liotti et al., 2005). Lansbergen and colleagues (2008) reported decreased inhibitory P300 components in participants scoring high relative to low on self-reported impulsivity. Researchers have argued that the NoGo P300 may present too late to reflect inhibition, suggesting that this component may reflect the closure of a preceding inhibition process (Falkenstein, 1999). Verleger and colleagues (2005) reported that the amplitude of the P300 component was the same for both response and stimulus locked segmentation, which may reflect the transition from stimulus processing to response processing or monitoring to action.

In summary, these two components (N200 and P300) commonly extracted when required to withhold a forthcoming response have been linked to inhibitory control mechanisms. While the exact functional significance of these components requires further clarification, it is clear that the Nogo N200/P300 complex reflects activity related to inhibitory mechanisms.

Motor Preparation-Lateralised Readiness Potential (LRP)

The Lateralised Readiness Potential (LRP) is a measure of motor preparation and is typically found whenever participants are required to execute a movement of the extremities. This LRP is based on the movement related readiness potential first presented by Kornhuber and Deecke (1965) that appeared as a central negativity several hundred milliseconds prior to a voluntary movement. Historically, this component was examined using cueing paradigms indicating response hand, although it is also present during forced choice response tasks. The LRP is considered to reflect the on-line activation of response related processes (Coles, 1989; De Jong et al., 1988).

It is not yet fully known what exact process or stage of information integration the LRP may reflect. Differing subcomponents of the readiness potential have been identified (Shibasaki & Hallet, 2006) that can be allocated into early and late properties. Another factor that obscures the functional relativity of the LRP is that it overlaps with the Contingent Negative Variation (CNV) which is another negativity that reflects preparedness for an upcoming event or stimulus (Kutas & Donchin, 1980). Overall a significant collection of studies have isolated the readiness potential to the contralateral side of the cued effectors which appears to be motor specific.

Ulrich and colleagues (1998) reported LRP enhancement only for conditions that included precue information regarding force level, direction, and response hand suggesting that force and movement direction parameters must be integrated before a movement plan can move forward.

The LRP component is obtained by recording ERPs from above the motor cortices in tasks that require left and right handed manual responses (Coles, 1989). This pronounced component is regarded as a useful tool in the study of human information processing as it is generally considered a measure of response activation. The LRP is suggested to reflect a measure of the duration of premotor responses including perceptual ability and response selection (Kutas & Donchin, 1980; Gratton et al., 1988; Sanders, 1980). Factors such as movement complexity, precueing validity, and force control velocity have been shown to influence the LRP (Gratton et al., 1990; Hackley & Miller, 1995). Increased LRP amplitudes have also been identified during more complex movements as compared to movements involving simplistic parameters and with the quantity of movement parameter information during precuing tasks (Hackley & Miller, 1995; Leuthold et al., 1996; Stief et al., 1998). The effects of stimulus response compatibility and stimulus characteristics suggest that the LRP represents a post perceptual processing stage and the succeeding response selection. Furthermore, studies examining the lateralised distribution of the LRP during tasks consisting of incompatible stimuli corresponding to correct responses have shown this component to present with a reversal of positive activity preceding the negativity shift typically observed prior to correct response onset. It is suggested that the positive reversal observed during these tasks underlies the cancellation of the incorrect response activation for one hand and response activation of the correct hand. The

inappropriate activation may be cancelled first and replaced by the correct activation suggesting that the conflicting responses are integrated in the premotor cortex where information regarding the response is transmitted to the correct and incorrect response hand (Verleger et al., 2009).

LRPs may be isolated in two manners. The stimulus-locked method requires the LRP to be segmented with respect to the moment the eliciting stimulus appears. This method reflects the premotor process including response selection/integration and response selection. Response-locked segmentation involves isolating the component with respect to the moment the subject initiated the motor activity required. This measure requires the experimenter to use a method of monitoring movement onset in relation to the EEG recording. This secondary method reflects an online measure of the actual motor process (Osman et al., 1995).

Coles (1989) was the initial researcher to formulate a calculation to segregate motor activity in the form of the LRP. Coles suggested a formula to average the lateralised activity over the motor cortices in relation to hand activation (see Chapter 7). Any spurious activity not related to motor activity is cancelled out as the formula averages the difference between the two hemispheres for right and left handed activity (Coles, 1989). Prior to this form of LRP, isolated raw data from the contralateral hemisphere to the cued hand was examined (Kutas & Donchin, 1980).

The LRP has been studied in great detail with regards to differing experimental parameters and information processing, mostly dependent upon theories surrounding perceptual processing and response related stages. For the purpose of the current

thesis the LRP will be discussed in terms of indexing processing response stages that precede effector activation.

<u>Summary</u>

In sum, this brief introduction to electroencephalography and Event-Related Potentials is intended to give a general overview of the components examined throughout the current thesis. More detailed explanations of the experimental measures adopted in this thesis and the interaction of experimental parameters with these components will be presented in the appropriate experimental chapters. It is to the experimental task that we now turn.

Chapter 3

General Methods

Outline

This chapter will detail the methodologies adopted in this thesis. Participant information, including the methods utilized for recruitment and clinical group identification and assessment will be outlined. In addition, the behavioural and EEG experimental task and associated materials/procedures will be described in detail. Participant performance on background and matching variables will be presented, alongside group analyses of motor proficiency, co- morbid inattention assessment, and intelligence.

Participant recruitment

Adult participants

Adult DCD participants (N=14) were recruited through support groups located within the Greater London area and Home Counties whose membership comprised adults that were diagnosed with DCD or reported a history of coordination difficulties. Initial identification of support groups involved an internet search for appropriate groups that stated motor coordination dysfunction as a primary concern. The services of these groups were overwhelmingly directed towards children with DCD, however some of the groups did have individuals that had been involved in the program from adolescence. Nevertheless, in order to expand our participant search, recruitment information was sent to groups who expressed an interest in the distribution of recruitment information to adults who had an association with the group. The primary group accessed in this way was a London based adult support group whose

membership was comprised of adults with neurodevelopmental disorders, and with coordination difficulties more specifically. It was fortunate that a large collection of these members had received a previous diagnosis of DCD during childhood. It was the goal of the primary investigator to obtain participants with DCD that had previously received a formal diagnosis through appropriate channels (e.g., paediatrician, educational psychologist). The primary investigator attended local support group meetings in order to distribute information about the study, and to evaluate the likelihood of DSM diagnostic criteria being met, particularly given the difficulty in obtaining a diagnosis of DCD in adulthood (see diagnostic discussion in chapter 1). Given the lack of adult motor assessments or guidelines, the investigator focused particularly on two key inclusion and one exclusion criteria: (i) demonstration of continued coordination difficulties commensurate with an earlier obtained diagnosis of DCD; (ii) a profile of motor difficulty and general ability compatible with DSM diagnostic criteria (to include IQ within the normal range (>84); and (iii) a profile of deficits that were beyond the scope of a motor coordination disorder, suggesting an alternate diagnosis (exclusion criterion; and in part meeting DSM criterion C). At these initial meetings an informative recruitment flyer was distributed and recipients were instructed to contact the primary investigator for a secondary meeting at which time diagnostic records could be reviewed and an interview performed detailing symptom presentation and specific difficulties. A total of 21 individuals expressed an interest in the study through this route, with 10 (47.62%) of these being recruited and participating in the current EEG study. The remaining 11 did not reply to follow up contact or were unable to schedule a convenient time to come into the university to take part in the study.

In addition to attending adult support groups, recruitment information was placed on a social networking site (Facebook) that contained an adult support group whose members included adults diagnosed with DCD. An informative summary of the study was placed on the message board of the forum instructing potential participants to contact the primary investigator for further information and to discuss their history of coordination difficulties and subsequent diagnoses. For both methods of recruitment (support group; facebook) if an individual possessed a diagnosis s/he was asked to bring accompanying material confirming that diagnosis for review by the primary investigator. For individuals who were not in possession of a formal diagnosis (n=1) and were classified as self reporting, a detailed interview regarding their history of coordination deficits was performed.

In all cases, an information email or packet was posted to the participant containing material that provided information regarding the goals of the study and methods/materials to be utilized. This information pack described in detail the tasks that would be performed by the participants, including the assessment and experimental tasks. In total, the internet forum method of recruitment elicited seven people who requested further information, of which four (57.14%) consented to participate in the project and were seen at the university to participate. Clinical group members did not receive any monetary compensation for their participation although they were offered travel reimbursement. None of the participants reported additional neurological afflictions and/or diagnoses. An upper age limit of 40 was adopted in order to make recruitment of control participants easier and to obtain age matched samples.

Only one of the 14 clinical group participants did not possess a prior diagnosis, although his/her status was fully investigated through an in-depth interview examining difficulties commensurate with DCD. This individual demonstrated poor motor skills and obtained IQ scores that were within normal limits. Furthermore his/her daily life experiences were commensurate with a DCD diagnosis and s/he was in the process of obtaining a diagnosis through their university. Taken together, this information was deemed supportive of a diagnosis and therefore this participant was included in the DCD group reported in this, and subsequent, chapters.

Control group members (N=14) were recruited through informative flyers distributed around the university campus. Control group members were matched for age, gender, and years in education to those in the DCD group (see Table 3.3 below). A general medical questionnaire was administered to each control group member in order to check for abnormal medical or psychological diagnoses. None of the control participants reported a history of coordination difficulties or developmental/psychotic disorders. A monetary amount of 15 pounds was offered to control group participants.

All participants had normal or corrected to normal vision and all were right handed except for two members of the DCD group. Participants were only included if they had a measured IQ within the normal range (>84), were aged between 18 and 40 years and did not endorse an ADHD checklist at clinically significant levels (see below for more detail on assessments used). Ethical approval was obtained from the Department of Psychology's Research Ethics Committee. All research practices were performed

in accordance to guidelines set forth by the British Psychological Society's Standards

of Research (Ethics Committee of the British Psychological Society, 2009).

Assessment of group background characteristics

Background information

In order to confirm the appropriateness of clinical group membership (focusing on the

DSM-IV criteria for DCD) and to characterize the current motor profile of those in the

DCD group, along with that of the control group, all participants provided information

about their history of difficulties (if any) through a brief informal interview with the

primary investigator. Topics covered during this time included a brief discussion of

how any motor coordination difficulties impacted daily activities and of other tasks

that a participant felt s/he performed in a less than optimal manner (DSM Criterion

B). Interestingly a majority of the adults with DCD did not drive and described

disorganization and avoidance of leisure activities/sports as primary concerns. A

majority of the diagnoses (10; 71.43%) had been obtained when the individuals were

in primary/secondary school and the remaining participants (3; 21.43%) obtained

diagnoses when at further or higher education institutions such as Sixth Form College

or university. A single participant from the clinical group had not yet received a

diagnosis, although this individual was undergoing assessment of their difficulties at

their current educational institution.   This participant's symptom presentation and

associated deficits were commensurate with a diagnosis of DCD, which was

confirmed through the assessments conducted to validate diagnoses in all participants

(see below), and thus s/he was included in the sample. Of particular interest were the

motor skills, and these are presented below in Table 3.1. In addition to the modified

motor assessment, an adult ADHD checklist was administered to both groups, and a

measure of IQ was obtained for all participants. These measures will be discussed

below.

Table 3.1

 Summary of assessment battery

Daily life experiences (past/present)
Semi structured interview

Adult ADHD Self-report Scale (ASRS; Kessler et al., 2005)

IQ (WAIS-III; Wechsler, 1997)

Motor Assessment
       Finger thumb opposition (Denckla, 1973)
       Clap catch (Gubbay, 1975)
       M-ABC2 (Henderson et al., 2007; Upper age band subtests)
              Pegboard turning
              Peg placement
              Triangle construction
              Ball aiming task
              Catch with one hand return
              Dynamic balance
              Static balance
              Zig-zag hopping

ADHD symptomatology

All DCD group members completed the Adult ADHD Self Report Scale (ASRS)

(Kessler et al., 2005) in order to confirm if symptoms consistent with a diagnosis of

ADHD were present.   This assessment is a validated self report measure and was

employed to obtain a sample of individuals with DCD that did not exhibit co- morbid

inattentive difficulties since a link between inattentive symptomology and motor

ability has been reported (Piek et al., 1999). Indeed the DSM-IV suggests that the

motor skills observed in ADHD may be attributed to distractibility and impulsiveness

and not to a general motor impairment. As there is yet to be a definitive relationship established between inattention difficulty and motor performance, it was our goal to obtain as pure a sample as possible in order to isolate performance specifically to the DCD group (see Chapter 1 for information pertaining to prevalence of co-morbidity). It was deemed essential to perform a measurement of ADHD symptom presentation in all participants in order to (i) maximize the likelihood that DCD participants did not have any overlapping disorders that might influence the sensory/cognitive processes under examination, (ii) make any relevant findings explicit to groups that displayed motor coordination difficulties independent of additional co-morbid difficulties that may result from a dual diagnosis, and (iii) ensure the control participants did not show signs of ADHD.

Materials

Adult ADHD Self-Report Scale (ASRS-v1.1) Symptom Checklist

The ASRS is a self-report screening scale of attention-deficit hyperactivity disorder (ADHD) developed in conjunction with the WHO Composite International Diagnostic Interview (CIDI) (WHO, CIDI, 1990). The ASRS contains 18 questions regarding frequency of recent DSM-IV Criterion A symptoms of adult ADHD. The ASRS screener consists of six out of these 18 questions, selected based on stepwise logistic regression to optimize concordance with the clinical classification (Kessler, 2005). Each of the symptom measures was significantly related to clinical symptom presentation and the screening tool is useful in clinical outreach programs and case studies. A follow up study by Kessler and colleagues (2007) based on a large population (n=668) revealed significant test-retest reliability (Pearson correlations) in the range of 0.58-0.77 and strong concordance with clinician diagnoses.

Administration

In line with the published instructions, participants were required to complete both Part A and Part B of the Symptom Checklist by marking an X in the box that most closely represents the frequency of occurrence of each of the symptoms. Response options are: never, rarely, sometimes, often, and very often. Participants were asked to answer the questions using a 6-month recall period. If four or more marks are made in the darkly shaded boxes within Part A, then the patient has symptoms highly consistent with ADHD in adults. In this case, the frequency scores on Part B provide additional cues and can serve as further probes into the patient's symptoms. The six questions shown in Part A of the ASRS can be seen in Table 3.2.

Table 3.2

Part A questions: Adult ADHD Self-Report Scale (ASRS; Kessler et al., 2005).

Response options: never, rarely, sometimes, often, and very often.

1. How often do you have trouble wrapping up the final details of a project, once the challenging parts have been done?
2. How often do you have difficulty getting things in order when you have to do a task that requires organization?
3. How often do you have problems remembering appointments or obligations?
4. When you have a task that requires a lot of thought, how often do you avoid or delay getting started?
5. How often do you fidget or squirm with your hands or feet when you have to sit down for a long time?
6. How often do you feel overly active and compelled to do things, like you were driven by a motor?

None of the clinical or control group members obtained scores that predict the presence of ADHD symptoms or would warrant a diagnosis (see Table 3.3). The two groups did not differ statistically with regards to scores obtained on the ADHD scale [$F(1,26)=.964$, $p=335$]. Therefore, nobody was excluded from the study on the basis of this criterion.

Intelligence

To ensure that DSM-IV's Criterion A ("motor coordination is substantially below that expected given the individual's chronological age and calculated intelligence" APA, 2000, p.58), Intelligence Quotient (IQ) was measured using a short form of the Wechsler Adult Intelligence Scale-Third Edition (WAIS-III; Wechsler, 1997). Verbal and performance subtests were included. Verbal subtests comprised vocabulary, similarities, arithmetic, and digit span tasks. Performance subtests were picture completion, block design, and matrix reasoning. Verbal and performance IQ, as well as full scale IQ scores were calculated by prorating from the short form scores. Participants were included in the study provided they scored in the normal range for IQ (85+; see Table 3.3). No participant was excluded on the basis of performance on this task.

Table 3.3

Participant characteristics

	DCD (n=14)	Control (n=14)
Gender: Male (Female)	12 (2)	12 (2)
Handedness: RH (LH)	12 (2)	14 (0)
Age (years)		
Mean (SD)	24.3 (7.8)	24.9 (7.2)
Range	19-36	18.5-35
Education level (years)		
Mean (SD)	17.2 (1.3)	18.5 (1.7)
Range	15-19	16-20
ASRS		
Mean (SD)	2.2 (.97)	1.85 (.95)
Range	0-3	0-3
IQ		
Verbal IQ		
Mean (SD)	111.2 (3.9)	112.0 (3.8)
Range	105-117	106-121
Performance IQ		
Mean (SD)	104.6 (4.9)	116.9 (5.8)
Range	99-113	107-130
Full scale IQ		
Mean (SD)	109.3 (3.5)	115.2 (4.6)
Range	103-115	109-128

Motor Assessments

Motor assessments were performed in order to confirm the continued presence of coordination difficulties and to provide evidence for placement of individuals into the DCD group. At present, no standardized motor assessment battery containing normative data across an adult sample exists. Although not appropriate for the diagnosis of DCD in adults, the Movement Assessment Battery for Children (MABC-2; Henderson, Sugden, & Barnett, 2007) was adopted for the current study since it is the most widely used test of motor proficiency in the UK. The MABC-2 assessment battery yields both normative and qualitative measures of movement proficiency by examining manual dexterity, ball skills, static and dynamic balance through a series of tasks. Although norms are available only for individuals up to the age of 16.11 years it was deemed suitable as a component of the motor assessment completed by the study participants, in terms of the tasks used. While test performance would usually be coded in terms of scaled scores (indexing impairment), motor skill in the current sample was analysed in terms of the raw data collected (timing or accuracy). As mentioned previously, a study by Cousins and Smyth (2003) examining the motor performance of adults with DCD utilized similar measures of motor proficiency to evaluate DCD group inclusion criteria. These motor measures proved useful in identifying adults with coordination difficulties. In terms of the current study, it was also deemed appropriate to consider the sensitivity of the use of raw data collected from the Movement ABC in future adult studies of DCD.

Given the lack of assessment materials that examine individuals over the age of 18, a unique assessment battery was constructed for the current study. This included all subtests of age band 3 of the M-ABC-2 as well as two additional motor tests; finger

thumb opposition and clap/catch (see Table 3.1). These measures were performed to support the assignment of individuals with coordination difficulties to the DCD group and to document the continued nature and range of motor difficulties into adulthood within the selected sample. The specific tasks completed are described below.

Manual Dexterity

Peg placement, peg turning, and triangle construction tasks from the MABC-2 were administered according to the test manual. An additional sequential finger tapping task (Denckla, 1973), commonly used in neurological assessments, was also included. In each of these tasks, the participant sat at a desk.

Peg Placing:

Participants placed 12 pegs into a board as quickly as possible. A peg board was placed at the participant's body midline on the desktop surface, at a distance of 2.5 cm from the edge. A peg receptacle was placed in a lateral midline body position corresponding to the bottom edge of the pegboard adjacent to the non-preferred hand. This was reversed when the preferred hand was tested. Participants were instructed to hold the peg receptacle containing the pegs stationary with the untested hand and place the other hand on the mat prior to the trial commencement signal. Upon a verbal GO cue, the participant was to retrieve the pegs from the receptacle one at a time and insert them into the board as quickly as possible. Timing (Sec) began when the hand left the mat to remove the first peg, and finished when the last peg was inserted into the pegboard. The task and placement of hands was demonstrated to the participant prior to beginning the task. Participants were reminded not to pick up more than one peg at a time, change hands, stabilize pegs with body or on desktop, and

avoid dropping any peg. Participants initiated the first trial with preferred hand and performed two trials per hand. The mean time to complete the task was calculated for the two trials for each hand separately.

Peg Turning:

Participants turned each of 12 pegs that were placed in a board, as quickly as possible. The pegboard was positioned at the participant's body midline at a distance of 2.5cm from the desktop edge. Participants were instructed to steady the pegboard with their non-active hand whilst they picked up the pegs one at a time and replaced them into the hole so that the opposite colour was showing. Timing (Sec) commenced once the hand being used left the desktop and ended when the last peg was reinserted into the board. This procedure was performed for both the preferred and non preferred hand with a total of two trials per hand. The mean time to complete the task was calculated for the two trials for each hand separately.

Triangle Construction:

The construction components required to build the triangle (3 bars/3 nuts/3 bolts) were placed at the participant's body midline, in front of the participant with the completed model positioned above. The three yellow sides were placed in horizontal rows on the mat. The three bolts and nuts were placed above the yellow sides. With both hands on the desktop participants were instructed to construct the triangle in any order with their arms in any position. Once an item is lifted from the mat the item should not be rested against the desktop or body for stabilisation. Each participant was given one practice trial followed by two recorded trials. If a participant joined the sides together in the wrong arrangement, rested any items on table or body, or

103

dropped any item, the trial was recorded as a fail. Upon a verbal GO signal, timing commenced when both hands left the tabletop and terminated once the last nut was screwed into the last bolt. The mean time (Sec) taken to complete the two trials was calculated.

Finger Thumb Opposition:

This task was adopted from earlier studies of adolescents with DCD as it was found to discriminate between adolescents and adults with DCD (Cantell et al., 1994). Cousins and Smyth (2003) also found this an efficient measure to discriminate between adults with DCD and typically developing peers. Participants started the task with the preferred hand and were instructed to move each finger in succession to the thumb beginning with the index finger and moving in order to the little finger. This sequence was repeated five times. Each participant received a demonstration from the examiner and was allowed one practice trial. Each participant was timed (Secs) performing the sequence for five consecutive attempts using both preferred and non preferred hands. Two trials were performed for each hand. The mean time to complete the sequence for each hand separately was calculated.

<u>Ball skills</u>

Aiming and ball catching tasks from the MABC-2 were performed using the instructions recorded in the test manual. A clap and catch task was adopted from a similar motor assessment battery performed by Cousins and Smyth (2003) in their study of adults with coordination difficulties. This clap-catch task was originally utilized by Gubbay (1975) and was one of the tasks that showed continued differences in performance for children with DCD retested at age 18 (Knuckey & Gubbay, 1983).

Aiming task:

A circular target (25cm disk) was placed at a distance of 3 meters with the lower edge of the circular target at approximately the same height as a participant's forehead. Participants were instructed to stand behind a line on the floor at all times and using their preferred throwing method (overarm/underarm) to hit the target with a tennis ball. Each participant received three practice trials. The number of accurate throws that hit the target out of ten was recorded for the preferred throwing hand.

Clap-and-catch task:

For the clap-and-catch task, participants were required to throw the ball up and catch it with the same hand. They were required to perform a hand-clap in between the time the ball left the throwing hand and returned for a catch. The number of claps increased over trials to a maximum of four with the maximum number of claps achieved on the final trial recorded. Each hand was tested, commencing with the preferred hand.

Catching with one hand-return:

Participants stood at a distance of 2.5 meters from a bare wall in a clear space away from obstacles. The participant was to throw the ball at the wall from the marked distance and catch the returning ball with one hand. This was repeated for the non preferred and preferred hands. Participants were reminded to catch the ball before it touched the ground and not to trap the ball between clothing or their body. The correct number of catches out of ten was recorded with one point awarded for each catch made.

Gross Motor/Balance

Gross motor performance and balance were evaluated using measures from the
MABC-2 and following the instructions recorded in the test manual.

Dynamic Balance:

Participants were asked to walk heel-to-toe backwards along a 4.5 metre taped line for
15 steps.   The number of correct consecutive steps was recorded. Correct steps
included steps made from the beginning point on the line without stepping off the
line, regaining balance by touching opposite foot to floor, or leaving a large space
between the two feet when planting the foot. If the participant reached the end of the
line without any errors the participant received a maximum score of 15.

Static Balance:

Participants were instructed to balance heel-to-toe on the MABC-2 balance board for
up to 30 seconds. Once the participant achieved the balance position, timing
commenced.   Timing (Secs) stopped when an error occurred, including lifting one's
foot, touching the floor with one's foot, or touching the base of the boards with the
sides of the shoes. Participants performed two trials. The mean of the two trials was
calculated and included for analysis.

Zig Zag Hopping:

Floor tiles were placed in a zig zag row formation 4.5 meters in length. Participants
started the trial by standing on one foot on the beginning floor tile. From this position
the participant was to make five continuous hops in diagonal fashion from one mat to
the next mat. A trial was considered a fail if the participant hopped outside the area of

the mat, hopped twice on a mat, let the opposite foot touch the floor, stopped on any

mat before reaching the end mat, or lost balance on the end mat. Error rates were

recorded for the total amount of trial errors out of five per leg.

Results of the modified motor assessment

Performance on each movement task is shown in Table 3.3 for each group and

measurement separately. Group performance was compared for each task separately

using either a one way ANOVA (with group as the between subject variable and task

score as the dependent variable) or, in cases where performance was recorded for each

hand or leg separately, with a mixed ANOVA (group; limb (hand/leg)). Group

comparisons are reported in Table 3.3 below. It is clear from the table that the DCD

group performed significantly worse on each motor task than their typical peers. This

is particularly striking given that these tasks are included in a test battery that is not

designed for use with adults. For tasks where the main effect of limb and the

interaction of this with group were considered, no significant main effect of limb or

interactions between this and group were identified.

Table 3.3

Mean (SD) scores for each group on each motor task. F values are shown

_____

	DCD	Control	F- Ratio (1,26)
	Mean SD	Mean SD	
Fine Motor-Manual Dexterity tasks			
Peg Placing (sec)			
Preferred Hand	31.30 (3.48)	24.95 (2.89)	F= 31.96, P<.001
Non-Preferred hand	31.49 (3.03)	25.71 (3.58)	F= 23.24, P<.001
Peg Turning (sec) Preferred Hand	32.07 (4.49)	24.58 (3.11)	F= 26.24, P<.001
Non-Preferred hand	32.14 (4.27)	24.96 (3.61)	F= 22.71, P<.001
Finger- Thumb Opposition (sec)			
Preferred Hand	11.45 (.99)	9.91 (.99)	F= 20.52, P<.001
Non-Preferred hand	11.63 (1.01)	9.84 (.92)	F= 23.62, P<.001
Triangle Construction (Sec)	45.43 (11.81)	33.27 (7.15)	F= 11.27, P=.002
Ball Skills			
Aim Target/10	7.42 (1.39)	9.28 (.91)	F= 23.63, P<.001
Clap-Catch/4			
Preferred Hand	2.51 (.65)	3.28 (.61)	F= 10.84, P=.003

Non-Preferred hand	2.51 (.65)	3.07 (.73)	F= 4.78, P=.038
Catch-wall return/10			
Preferred Hand	8.07 (1.26)	9.64 (.63)	F= 17.19, P<.001
Non-Preferred hand	7.57 (.85)	9.57 (.51)	F= 56.63, P<.001
<u>Gross Motor</u>			
Static-two-board balance	16.57 (3.34)	23.5 (2.44)	F= 39.18, P<.001
Dynamic walking	13.78 (1.21)	11.50 (1.99)	F= 14.01, P=.001
Zig-Zag Hopping/5			
Right	4.42 (.51)	5 (0)	F= 19.11, P<.001
Left	4.28 (.61)	5 (0)	F= 17.33, P<.001

_____

<u>General procedure with timeline</u>

Prior to commencing with the EEG setup and acquisition phase of the experiment, participants reviewed an information sheet containing general information explaining aspects of the study and associated EEG requirements. The primary investigator encouraged participants to ask for clarification if any of the experimental information was unclear. Participants were also given an introduction to the EEG lab and the materials that would be used throughout the experiment (i.e., setup materials including EEG cap, electrodes, and procedure of applying cap to scalp). Following this introduction participants were required to complete a consent form confirming their full understanding of the study and requirements as a participant. In addition participants completed a brief medical history form in order to identify any possible co-occurring medical/psychological conditions that might affect their participation in

the study and associated experimental tasks. The questionnaire contained questions pertaining to any medications, physical constrictions, mental illness, or medical devices that would hinder further participation. The introduction and completion of associated forms took approximately 20 minutes.

Next, a modified motor assessment was performed comprised of gross and fine motor tasks (see above for task descriptions). This took participants approximately 20 minutes to complete in its entirety. After completion of the motor assessment, each participant completed a short form version of the Wechsler Adult Intelligence Scale-Third Edition (WAIS-III; Wechsler, 1997), taking around 20 minutes. In addition to the motor and IQ assessment each participant completed the Adult ADHD Self-Report Scale (ASRS; Kessler et al., 2005).

Following the introduction to the testing area, information review, medical questionnaire, consent form completion, behavioural assessments and completion of the self-report scale the EEG set-up commenced. A cap with 64 electrodes (BioSemi) was fitted. Reference electrodes were placed onto the earlobes (linked earlobe reference) and HEOG electrodes on the outside canthi of each eye. The attachment of the EEG materials to the participant took approximately 20 minutes to complete. Participants were then led into a dimly illuminated sound attenuated cabin, viewing a computer screen placed at a distance of 70cm from which stimuli would be presented at a central location. The experimental task was presented using a C++ program. A refresh rate of 60 hz was set for the computer screen. Participants were instructed to keep movements to a minimum during the experiment except for when required to

initiate a movement response and to try and reduce the amount of blinks during the time between response cue and GO/STOP signal.

The primary investigator gave an overview of the experimental task before the practice blocks. Participants completed two practice blocks for each movement condition (straight; midline). Following the practice blocks the experimental trials commenced. There were a total of 16 experimental blocks consisting of 60 trials per block (8 straight movement blocks; 8 midline crossing blocks). Each block took around six minutes to complete. The entire EEG portion of the testing session lasted approximately two hours with participants encouraged to take as many breaks as possible to avoid fatigue. Following the completion of the EEG portion of the study, participants were led out of the testing room and seated adjacent to the room. The cap and electrodes were removed and the participant was able to wash their hair to remove the electrode gel in an adjacent wash area. In total each participant spent a total of four hours at the university.

Experimental Task

Participants were instructed to focus on the central fixation point present on the stimulus monitor at all times during the experiment. Instructions displayed prior to block commencement provided participants with information regarding response cue implications for movement effector and direction to target button for each movement condition; straight and midline crossing. For example, in the straight movement condition a green square presentation would indicate the participant was to move their right hand up to the target button on the straight side of the cued effector. For the

midline movement, the presentation of a green square indicated that the participant should perform a movement from the right home position to the left side target button in a diagonal fashion across the body midline (see Figure 3,2, 3.3, and 3.4). Instructions were presented to each participant prior to each block but with differing task implications for the appearance of a red or green square (response). Counterbalancing techniques altered response cue significance (left/right for green or red square) and block order (straight/midline) between participants and groups in an even distribution. Prior to experimental blocks each participant performed 10 practice trials of each condition.

Trial Outline

Instructions presented on the stimulus monitor prior to each block provided the participants with the response cues implication (green/red square) for differing movement conditions (straight/midline). Participants were informed of the block order during the instructions presented prior to commencement of experimental trials. Each trial commenced with the presentation of a fixation cross at the central screen location for 1000 msec followed by replacement of the fixation cross by a visual response cue (coloured square) indicating effector and goal location that was present for 200 msec.   Following the response cue, a fixation cross reappeared for 900 ms. At the end of this 900 msec interval a task irrelevant visual probe flashed in one of four locations on the response console at locations adjacent to cued hand, opposite cued hand, adjacent to cued target, opposite cued target. Two hundred msec post probe onset a visual cue appeared at central screen replacing central fixation cross with either the word GO or STOP.   In 80% of the trials a GO signal appeared and

with the remaining 20% a STOP stimulus occurred. Once the participant completed

the trial by performing the desired movement to target and returning their action hand

to the home position or withholding the movement, there was a 1000 msec delay

during which fixation cross reappeared at central location before the appearance of

another response cue square. A new trial would not commence until the participant's

hand was returned to the home position or a successful inhibition was recorded. The

order of blocks (straight/midline) and response cue (green square/red square) were

counterbalanced equally between participants and groups. There were 16 blocks (8

straight/8 midline) in total with each block containing 60 trials (total=960 trials).
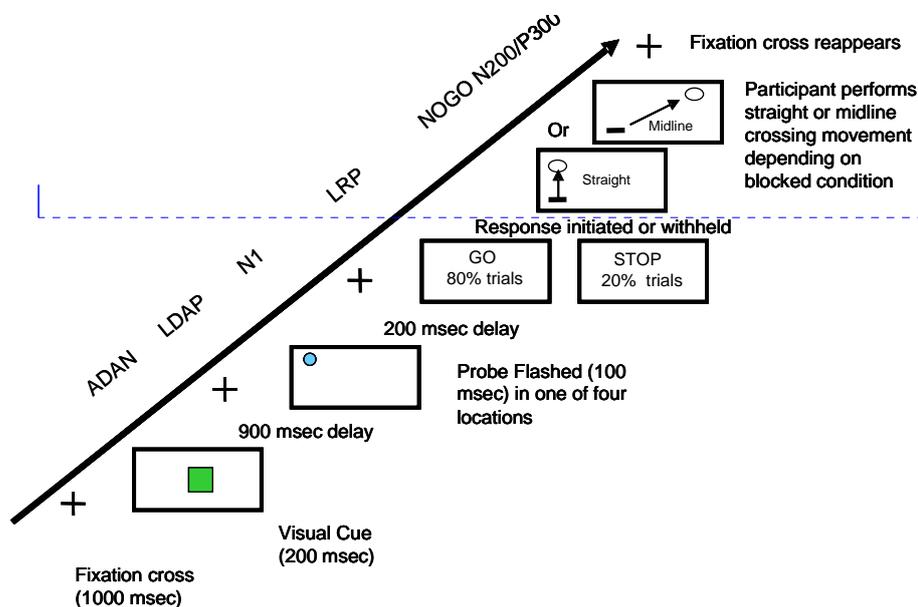
Figure 3.1: Outline schematic of experimental trial. Participant fixated on a central cross with hands placed on home sensor/buttons on the testing console (See figure 3.2). After 1000 msec a green or red square (response cue) is seen for 200 msec, followed by a fixation cross for 900 msec. Then a probe is flashed in one of four locations (cued/uncued effector; cued/uncued goal) for 100msec, followed after 200 msec by a stop or go signal replacing central fixation cross at center of screen. In the 80% of go trials, the participant then initiated a response and moved to the target button. Note the secondary line above with general component segmentation in relation to experimental time points/stimuli presentation. Specific component segmentation will be discussed in forthcoming experimental chapters. Movement conditions were blocked and the participant knew whether the green or red square indicated right or left effector cue in advance of a block of trials.

<u>Midline Crossing Approach</u>

In the current experimental approach movements to goal location were performed under two movement conditions; moving one's hand to goal locations in the same hemisphere as the cued effector (straight movement condition) or moving one's hand across body midline to the goal location in the hemisphere opposite the initial effector location (midline crossing movement condition). Several studies have shown that the preference to reach across the body midline in order to manipulate objects with the dominant hand develops through childhood (Carlier et al., 2006; Hill & Khadem, 2009), suggesting development of motor dominance (van Hof et al., 2002). Differences in preference to reach across the midline with the dominant hand have been identified between children with developmental disabilities and their typically developing peers (Cermack & Ayres, 1984; Hill & Bishop, 1998; Woodard & Surburg, 1999).

Consistently when individuals perform a reaching or aiming motion towards targets on the same side of the body as the active effector there are observed advantages including shorter reaction and movement time and greater accuracy of the movement required (Cermak et al., 1980; Screws et al., 1998). As a general point, two factors appear to have the most influence on preparation of reach: (1) motor dominance and (2) attentional information related to task demands (Gabbard & Helbig, 2004). While motor dominance may be the primary factor in the programming and execution of reaching movements at the midline and dominant side of hemispace, attentional information appears to override this factor to influence the programming of movements to contralateral space.

To date, the research examining the differing components of sensory processing associated with making a straight vs. midline movement is scant. It has been suggested that the observed

114

midline reaching performance characteristics are dependent upon increased attentional demands of the stimulus response compatibility complex. It has also been suggested that the hemisphere connectivity processing plays a role. For reaching into ipsilateral hemispace the hemisphere that processes the goal is responsible for the motor output whereas during preparation of a midline reach this hemispheric relationship seems to be effected with slower processing speeds. When the task demands involve increased spatial accuracy then the individual will need to scale the spatial relations between their effector and the target in a refined manner (Fisk & Goodale, 1989). In this instance the target location becomes another spatial constraint to be considered during the preparation of the reach. Previous theories of midline crossing performance have suggested that this movement requires a greater influence of the corticospinal tract and corpus collosum, with greater reliance upon computational processes regarding the spatial information required for this movement trajectory (Colby & Duhamel, 1991). Furthermore, lesion studies have revealed that the right hemisphere is important for motor behaviours that explore the contralateral side of egocentric space (Gentilini et al., 1989; Farne et al., 2003; Karnath et al., 1996). Indeed, studies have identified a unique distribution of brain activity between hemispheres receiving visual input (e.g., target location) to the hemisphere emitting the motor output (e.g., reach to target) (Jakobson et al., 1994). More specifically, reformulating this in relation to the present experiment, the right hemisphere contributes to the processing of visuomotor information that is necessary for executing actions with the effector for which a movement into contralateral hemispace is required. Studies examining the attentional requirements of movements into contralateral hemispace are limited. Recent studies, primarily involving child participants, have identified the attentional requirements relating to object location and task complexity in the contralateral locations suggesting differing sensory aspects of the intended movement. Movement parameters related to the end state and object location can

affect the hand selection in the contralateral hemispace (Leconte & Fagard, 2004). Given that studies have focused almost entirely on child samples, the question arises of whether the effect of these factors is restricted to childhood or whether they impact upon movement selection choices made across the lifespan. This would be relevant particularly in a group that demonstrates delayed movement performance. Considering different features of children and adults with DCD in the process of reaching and hand selection, and in view of the limited background of studies about these factors comparing adults to children, the research proposed here is intended to study the effects of task complexity and object location on the sensory and motor related activity of body midline crossing movements. One focus was on the impact of reaching trajectory upon early sensory processing and response modulation in accordance with task complexity in a group of adults with DCD.

There also appears to be some biomechanical influence on the contralateral reach compared to ipsilateral reach trajectories. Grey and colleagues (1996) proposed that the performance degradation associated with reaching across the body midline may be due to increased activation of muscular mass incorporated into controlling a midline movement compared to an ipsilateral one. Reaching across midline is less biomechanically efficient than reaching in an ipsilateral trajectory to a goal location and incorporates increased degrees of freedom. For example, using the right hand to reaching into far left hemispace is arguably less biomechanically efficient than reaching ipsilaterally with the closer left hand (Gabbard & Helbig, 2004). Mark et al. (1997) have suggested than an individual's choice of reaching is driven primarily by postural dynamics.

In summary, the adoption of a midline crossing condition in the experimental paradigm aimed to investigate the sensory and response differences between a straightforward

ipsilateral response (effector and target on the same side of the body) and a more difficult

midline crossing reaching response (effector and target on different sides of the body). This

is of particular importance as the clinical group of interest has demonstrated difficulty with

complex task completion, as well as atypical midline crossing performance. The addition of

a more spatially and biomechanically restrictive parameters of the midline crossing

movement vs. the ipsilateral reach to goal allow for a comparison between those with and

without DCD in terms of the ability to modulate sensory and response related processes in

accordance with task demands.

Materials

Response console

The response console consisted of two home sensors comprised of infrared break

beams using matching pairs of IR emitting diodes and IR sensitive phototransistors 25

cm to the left and right of the body midline where participants placed their hands prior

to the onset of the cued movements. A secondary set of response buttons were

custom made using microswitches as the switching element with turned plastic

actuators riding on polished 6.35 mm diameter metal rods placed in a vertical line 25

cm from the home sensors. The response console was angled with approximately 15

degrees from the home sensors to the response buttons. Visual probes consisted of 1

cm diameter LEDs positioned in locations 3 cm above each home sensor and response

button (see Figure 3.2). The LEDs were driven using Darlington power transistors

switched by signals from the PC parallel port. The experiment code was written in

house using the C++ programming language and ran under Windows XP. Interfacing

was via a pair of standard parallel ports, tests indicating that the overall timing

resolution for both input and output was better than 0.1 milliseconds.

Participant arrangement during experimental task

Straight movement condition

Midline movement condition
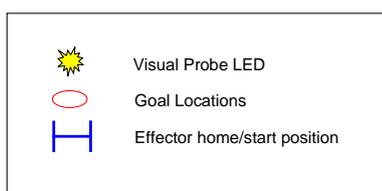
Figure 3.2. Photograph of response console and example of responses for both straight (Panel A) and midline crossing (Panel B) movement conditions. The example provided is for a right handed movement to goal location. Also note the position of task irrelevant visual probes in relation to effector home position and target button location

EEG Recording and Data Acquisition

EEG was DC-recorded from 64 Ag-AgCl electrodes relative to a linked earlobe reference (all impedances below 5 kΩ; 500 Hz sampling rate; 40 Hz upper cut-off frequency) using the BioSemi Active Two system. EEG was digitally re-referenced to the average of the left and right earlobe. The specific epochs of interest will be described in more detail during the experimental chapters to follow. Data were recorded unreferenced and unfiltered at a digitization rate or 512Hz. All data were referenced to both reference electrodes and filtered offline with a 0.3 Hz high pass filter and a 30Hz low pass filter. Trials with eyeblinks (exceeding ±80 μV relative to baseline), horizontal eye movements (HEOG exceeding ±30 μV relative to baseline), or other artifacts (a voltage exceeding ±80 μV at any electrode location relative to baseline) were excluded prior to analyses of ERP components. Electrodes were placed in accordance to the international 10-20 system. EEG pre-processing was performed using Brain Vision Analyzer. Please refer to individual experimental chapters for details regarding epoch segmentation for components of interest.

119

Chapter 4

Behavioural results of the experimental task: Timing and error responses

<u>**Outline**</u>

This chapter will present behavioural data recorded during the performance of the experimental task (See Chapter 3). Reaction time (RT) and movement time (MT) following GO cue as well as percentage of effector selection errors and unsuccessful inhibitions following the stop signal were compared between the two groups. The findings were in line with previous studies investigating individuals with DCD: The DCD group showed significantly greater RT and MT as well as more effector selection and inhibitory errors than their typically developing peers.

<u>**Introduction and Hypotheses**</u>

While the focus of the current thesis is primarily on ERP recordings in adults with DCD, it is important to consider the behavioural performance of adult participants on the experimental task. Since these behavioural measures have been studied fairly extensively within populations of children with DCD, it will be possible to consider the likely developmental profile of these characteristics across the lifespan in DCD (although note that longitudinal studies are required for truly *developmental* study). Past studies have consistently shown that DCD children have slower RT and MT in comparison to their peers as well as increased response selection and inhibition errors (e.g., Henderson et al., 1992; Mandich et al., 2002; Petit et al., 1998; Plumb et al., 2008; Raynor, 1998). It is hypothesized that in line with past research with children as well as the motor proficiency findings reported in Chapter 3, the slowed reaction

and movement times as well as increased error profiles observed in children with DCD will be seen in the current sample of adults with DCD (in both straight and midline crossing conditions). Furthermore, previous studies have identified that when response and task complexity are manipulated, children with DCD often show performance degradation (Missiuna et al., 1994; van Dellen & Geuze, 1988). It is therefore predicted that the adult DCD group will show a larger difference of RT/MT and errors in the arguably more complex midline crossing condition. Given the paucity of data available relating to the performance of an adult DCD group, hypotheses are based on the limited experimental data from this population, and more directly on the performance profiles of children with DCD.

<u>Methods</u>

Please refer to Chapter 3 for specifics regarding the experimental task. Figure 4.1 below presents the experimental task outline per trial with consideration of the measures presented within this chapter.
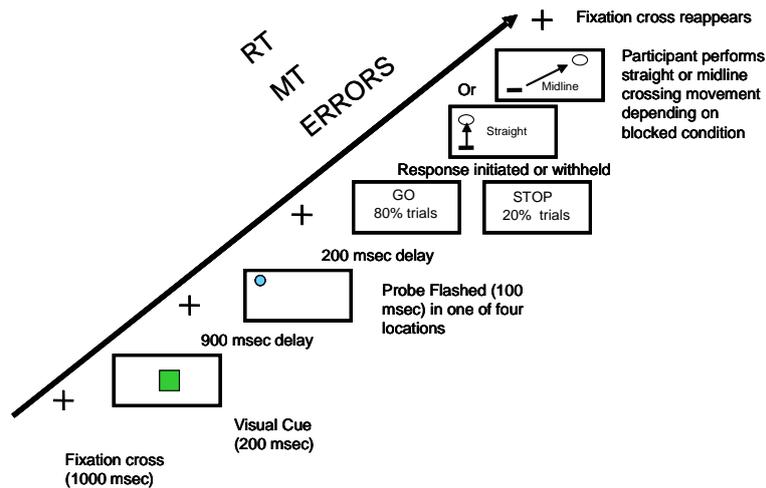
Figure 4.1: Outline schematic of trial. Participant fixates on a central cross, after 1000 msec a green or red square is seen for 200 msec, followed by a fixation cross for 900 msec. Then a probe is flashed in one of four locations (cued/uncued effector; cued/uncued goal) for 100 msec, followed after 200 msec by a stop or go signal replacing the central fixation cross at central screen location. In the 80% of go trials, the participant then initiated a response and moved to the target. Movement conditions were blocked and the participant knew whether the green or red square indicated right or left effector cue in advance of a block of trials. Note the areas of behavioural measurements (RT, MT, and Errors) in relation to stimuli and task requirements.

Results

Please refer to Table 4.1 for mean, standard deviation, and range data for each group on RT, MT, and error values.

Reaction Time

Reaction time (in msec) was defined as the time recorded between the appearance of the GO response cue and disruption of the infrared beam at the cued effector location, indicating a response had been initiated to the goal location.

A mixed ANOVA with one between subject factor (group: DCD, control) and two within subject factors (hand; preferred, non preferred; movement condition; straight, midline) was applied to the RT data. As expected, a significant main effect of group

123

was found [F(1,26) = 11.48, p=.002], with the control group producing faster RTs overall (M=514.50, SD=57.78) than the DCD group (M=596.58, SD=69.79). A significant main effect of condition was found [F(1,26)= 195.54, p<.001], with RTs to midline movements (M=589.45, SD=78.72) being slower than RTs to straight movements(M= 521.64, SD=74.69). The group x condition interaction was significant [F(1,26) =4.83, p =.037] indicating a different pattern of RTs between the groups in response to movement conditions. During the straight movement condition the control group produced faster RTs (M=485.93, SD=64.23) as compared to the DCD group (M=557.35, SD=68.67); [t(26)= -2.84, p=.009]. The same trend for shorter RT's for the control group (M=543.07, SD=52.670 was also identified during the midline crossing condition as compared to the DCD group (M=636.82, SD=73.92); [t(26)= -3.82, p=.001]. In order to further investigate the group x condition interaction, a follow up (unpaired) t-test was performed on the mean RT difference between conditions with group as the between subject factor.   A significant group difference was identified [t(26)= -2.19, p=.037] with the DCD group showing a significantly greater RT difference between conditions (M=78.46, SD=29.55) as compared to the control group (M=57.14, SD=21.04), indicating that the DCD group was particularly affected by the more complex movement condition. Moving back to the original ANOVA, a significant main effect of hand was found [F(1,26)= 55.68, p<.001], with reaction times for the preferred hand (M=543.14, SD=72.12) being significantly faster than those of the non-preferred hand (M=567.94, SD=79.93). In addition, a significant interaction of hand x group was also found [F(1,26)= 4.83, p=.037]. Follow up t-tests collapsing across conditions identified that the control group had significantly faster reaction times for preferred hand movements (M=506.50, SD=58.15) as compared to movements with the non-preferred hand

(M=522.50, SD=59.34) [t (13)= -4.12, p=.001]. This pattern was also found within the DCD group, with RT for preferred hand movements (M=579.78, SD=67.30) being significantly faster overall than non preferred hand movements (M=613.39, SD=73.60); [t(13)=-6.22, p<.001]. To further investigate the hand x group interaction follow up analysis compared the mean RT difference between hands with group as a between subject factor. This comparison identified that the control group showed a significantly smaller mean RT difference between hands (M=16.01, SD= 14.53) compared to the DCD group (M=33.61, SD=20.19); [t(26)=-2.65, p=.014], indicating that the DCD group showed a greater RT difference between preferred and non-preferred hand. Neither the condition x hand [F(1,26)=.268, p=.609] nor the group x condition x hand interaction [F(1,26)=2.47, p=.128] reached significance. Thus, the same pattern of RT results was identified for both groups, however the adults with DCD were slower than controls, and particularly more so during the midline crossing condition.

Movement Time

Movement time (in msec) was recorded as the total time window beginning when the cued effector sensors were triggered due to response onset and terminated when the goal button was depressed signalling the movement had been completed.

A mixed ANOVA with one between subject factor (group: DCD, control) and two within subject factors (hand; preferred, non preferred; and movement condition; straight, midline) was applied to the MT data. As expected, a significant main effect of group [F(1,26) = 11.93, p=.002] was found, with the control group producing significantly faster MTs than the DCD group. A main effect of condition [F(1,26) =

65.68, p<.001] showed that straight movements to goal (M= 926.12, SD=114.97) were shorter than movements to goals when moving across midline (M=1094.91, SD=125.57). The distance between goal location and effector home position (see Chapter 3) was slightly larger for the midline movement thus this effect was to be expected. A non significant interaction of condition x group [F(1,26)=1.67, p=.207] indicated that both groups followed similar patterns of increased MT between movement conditions. A main effect of hand was present [F(1,26)= 23.42, p<.001] indicating that the preferred hand (M=994.91, SD=106.17) moved to goal more efficiently than the non-preferred hand (M=1096.90, SD=125.57). The condition x hand interaction [F(1,26) =4.32, p = .048] was significant, although the condition x hand x group interaction was not [F(1,26)=.616, p=.440]. Follow up t-tests comparing preferred vs. non preferred hand for movement condition revealed that movements to goal were faster during the straight movement condition for the preferred hand (M=916.42, SD=117.67) as compared to the preferred hand during the midline crossing movement condition (M=1073.39, SD=125.13); [t(27)=-7.04, p<.001] The same comparison for non preferred hand use identified that non preferred hand movements to goal were shorter in the straight movement condition (M=935.82, SD=114.55) compared to the midline crossing movement (M=1116.43, SD=131.94); [t(27)=-8.46, p<.001]. To further investigate this interaction, the mean difference between preferred and non preferred hand for MT was compared between conditions. The greatest mean difference for preferred vs. non preferred hand MT was identified during the midline movement (M=43.03, SD=55.32) as compared to the straight movement condition (M=19.39, SD=32.55) [t(27)=-2.09, p=.046], indicating that participants showed an increased benefit of preferred hand usage during the midline movement condition compared to the straight condition.

Inhibitory Error Analyses

Successful inhibition was classified as the ability to withhold a response upon the appearance of a STOP signal and was expressed as a percentage.

A mixed ANOVA with one between subject factor (group: DCD, control) and two within subject factors (hand; preferred, non- preferred; and movement condition; straight, midline) was applied to the inhibitory error data. As expected, a significant main effect of group [$F(1,26)= 22.16$, $p<.001$] was found with the DCD group producing a significantly greater percentage of errors (M=2.84%, SD=.63) compared to the control group (M=1.74%, SD=.60). A significant main effect of condition [$F(1,26)=19.07$, $p=.001$] indicated less inhibitory errors during the straight condition (M=2.09%, SD=.69) than the midline movement condition (M=2.48%, SD=1.01) A significant main effect of hand [$F(1,26) = 29.14$, $p<.001$] indicated that fewer errors were made with the preferred hand (M=1.95%, SD=.78) than the non-preferred hand (M=2.63%, SD=.98). Furthermore, a non significant hand x group interaction [$F(1,26)= .595$, $p=.448$] was identified. A significant condition x group interaction was identified [$F(1,26) = 10.08$ $p=.004$]. During the straight movement condition the DCD group (M=2.50, SD=.54) made more inhibitory errors than the control group (M=1.68, SD=.61); t(26)=-3.77, $p=.001$]. Similar comparison of the midline crossing condition also revealed that the DCD group made more errors (M=3.17, SD=.85) during the midline crossing condition as compared to the control group (M=1.79, SD=.61); [t(26)=-4.94, $p<.001$]This conditional error effect was not found for the control group where inhibitory error rates were similar across movement conditions

[t(13) =-1.21, p=.244]. Non significant interactions of hand x condition [F(1,26)=2.62, p=.117] and hand x condition x group [F(1,26)=1.33, p=.258] were identified.

Effector Selection Error Analyses

Error measures were recorded when a participant utilized the incorrect response hand to produce a movement to target (effector selection error), and were expressed as a percentage.

A mixed ANOVA with one between subject factor (group: DCD, control) and two within subject factors (hand; preferred, non preferred; movement condition; straight, midline) was applied to the effector selection error data. As expected, a significant main effect of group was found [F(1,26) = 12.59, p=.001] highlighting significantly fewer effector selection errors committed by the control group (M=2.47%, SD=.81) compared to the DCD group (M=4.20%, SD=1.64). A main effect of condition [F(1,26) = 24.14, p< .001] was identified with a higher percentage of errors occurring during the midline condition (M=3.57 %, SD=1.50) than the straight movement condition (M=3.09%, SD=1.64). The main effect of hand [F(1,26) = 16.84, p<.001)] identified that more errors were committed when the non-preferred hand (M=3.72%, SD=1.73) was recruited for an upcoming movement as opposed to the preferred hand (M= 2.95%, SD=1.49). A significant group x condition interaction [F(1,26) = 10.42, p =.003] was identified with follow up tests revealing that the DCD group made more errors during the midline movement (M=4.61%, SD=1.70) than the straight movement condition (M=3.79%, SD=1.62); [t(13)= -5.92 p<.001]. The control group showed less errors than the DCD group during the straight movement condition (M=2.38, SD=.99) compared to the DCD group (M=3.79, SD=1.62); [t(26)= -2.77,

p=.010). Similar analysis of the midline movement condition between groups

identified a similar trend with the control group showing less effector selection errors

(M=2.55, SD=.66) during the midline crossing condition than the DCD group

(M=4.61, p=1.70); [t(26)=-4.22, p<.001)]. The control group did not show any

movement condition effects with regards to effector selection error rates [t(13)=-1.16,

p=.266]. Non significant interactions of hand x condition [F(1,26)= .399, p=.533] and

hand x condition x group [F(1,26)=2.64, p=.116] indicated that error rates for

preferred hand vs. non preferred hand remained consistent between movement

conditions for both groups.

Table 4.1

Mean, SD and range for reaction time, movement time, inhibitory errors, and effector selection errors for preferred hand and non-preferred hand for both the DCD and the control group.

	DCD			Control		
	Mean	SD	Range	Mean	SD	Range
Reaction time (Msec)						
Straight Movement						
Overall	557.3	68.6	434.0-687.0	485.9	64.2	353.0-643.0
Preferred	538.5	63.3	423.0-657.0	478.9	61.8	350.0-620.0
Non-Preferred	576.1	75.4	446.0-717.0	492.9	67.3	357.0-667.0
Midline Movement						
Overall	635.8	73.9	477.0-765.0	543.0	52.6	436.0-671.0
Preferred	621.0	73.5	456.0-750.0	534.0	55.3	415.0-664.0
Non-Preferred	650.6	75.9	498.0-780.0	552.1	51.6	458.0-679.0

Movement Time

(Msec)

Straight Movement						
Overall	998.6	132.4	775.0-1237.0	853.8	109.7	608.0-986.0
Preferred	987.5	60.4	898.0-1100.0	845.2	119.1	586.0-986.0
Non-Preferred	1009.1	73.3	830.0-1101.0	862.5	101.4	630.0-986.0
Midline Movement						
Overall	1140.2	103.0	988.0-1294.0	1049.6	132.5	775.0-1239.0
Preferred	1113.1	99.54	942.0-1290.0	1033.6	138.6	740.0-1200.0
Non-Preferred	1167.2	118.3	1009.0-1359.0	1065.5	128.7	810.0-1274.0

Inhibitory Errors (%)

Straight Movement						
Overall	2.5	0.5	1.5-3.2	1.6	0.6	1.0-2.5
Preferred	2.2	0.6	1.0-3.0	1.4	0.5	1.0 -2.0
Non-Preferred	2.7	0.8	1.5-4.5	1.9	0.7	1.0-3.0
Midline Movement						
Overall	3.1	0.8	2.0-5.0	1.7	0.6	1.0-2.5
Preferred	2.6	0.9	1.0-5.0	1.4	0.5	1.0-2.0
Non-Preferred	3.6	0.9	2.5-6.0	2.1	0.8	1.0-3.0

Effector Selection

Error (%)

Straight Movement						
Overall	3.7	1.6	2.0-7.5	2.3	0.9	1.0-5.0
Preferred	3.4	1.7	1.0-8.0	2.0	0.7	1.0-3.0
Non-Preferred	4.1	1.8	2.0-9.0	2.7	1.4	1.0-7.0
Midline Movement						
Overall	4.6	1.7	2.5-8.0	2.5	0.6	1.5-4.0
Preferred	4.0	1.7	2.0-8.0	2.3	0.7	1.0-4.0
Non-Preferred	5.2	1.8	3.0-9.0	2.7	0.6	2.0-4.0

Panel A
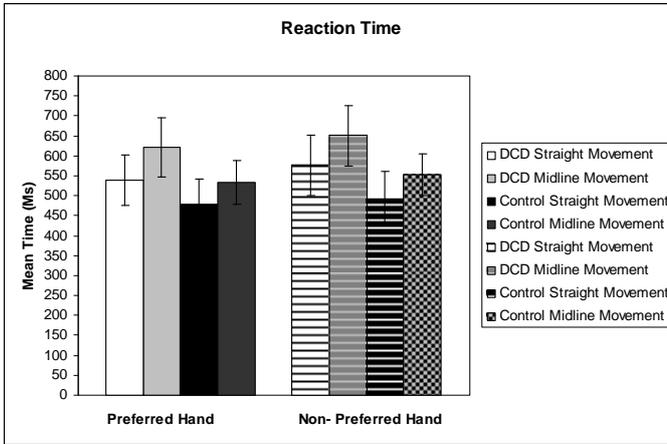
Panel B
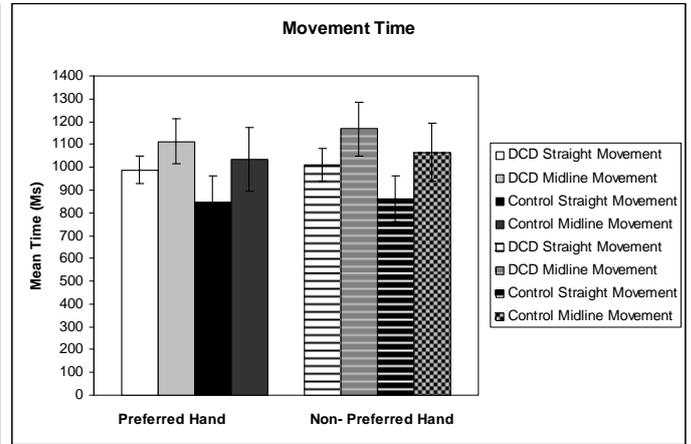
Panel C
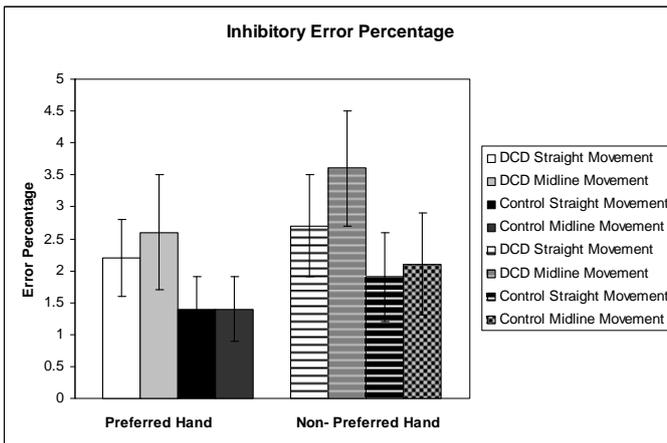
Panel D
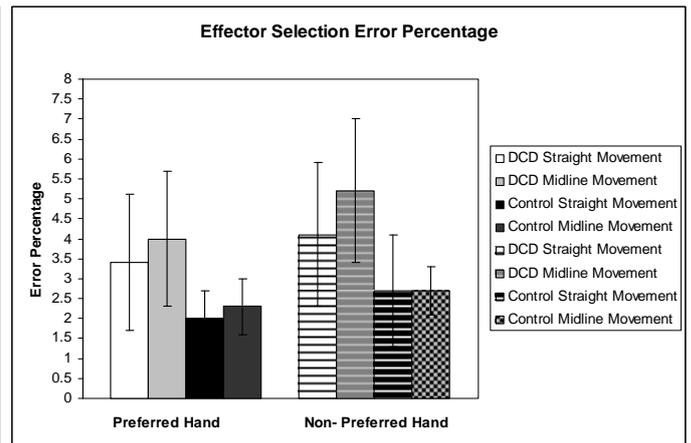
Figure 4.2. Behavioural measures obtained from the experimental task for both groups and movement conditions. Reaction time (Panel A) and Movement time (Panel B) data for preferred and non-preferred effector. Error percentages for inhibitory (Panel C) and effector selection errors (Panel D) for preferred and non-preferred effector.

The analysis of behavioural responses on the experimental task highlights key areas of difficulty encountered by adults with DCD during a manual response task. The reaction time, movement time, effector selection and inhibitory error rates clearly show that these adults with DCD showed atypical performance during a motor task in comparison to their typically developing peers. In addition the DCD group showed greater difficulty with the midline crossing condition as compared to the straight movement condition as evident by increased error rates between movement conditions. Although these performance difficulties have been consistently shown in the child DCD literature, the results obtained above provide evidence for a clear continuation of difficulties into adulthood.

Discussion

As predicted, these results support the existing literature relating to movement timing and error performance in children with DCD. Moreover, they confirm a continued difficulty with crucial components of movement production in adults with DCD. In summary, the DCD group showed increased reaction and movement time to goal than the control group for both straight and midline crossing movement conditions. Although both groups showed increased RT and MT during the midline movement conditions, the DCD group showed a greater mean difference between the two conditions for these measures. In addition, the DCD group produced significantly more effector selection and inhibitory errors than the control group. The DCD group also showed a condition by error interaction for both forms of errors (effector selection/inhibition) arising from a greater number of errors during the midline crossing as opposed to the straight movement condition. This interaction was not present in the control group where error rates were consistent between conditions. Critically, these results support one of the premises of this thesis, that adults with

DCD demonstrate difficulty with response preparation and require a prolonged duration in order to move an effector (e.g., hand) to a cued goal location when compared to their typically developing peers. While clearly a lab task, this set-up has obvious parallels to reaching for items in everyday life. The experimental results support adults' comments about day-to-day difficulties in these kinds of activities. Interestingly, the DCD group produced greater errors during the task requiring movement across midline. This suggests that those in the adult DCD group were hindered by increasing task parameters, in this case movement across body midline and modulating response onset (inhibition). Overall, then, the findings of the behavioural analysis of the experimental task support the existence of wide reaching difficulties in daily life activities in adults with DCD, resembling those seen in children. In the following chapters the biological components of the dataset will be considered in order to probe further the key focus of this thesis, to investigate the interaction of sensorimotor and response parameters during a reaching task.

Chapter 5

An ERP investigation of visuospatial processing and movement preparation in adults with Developmental Coordination Disorder

Abstract

This chapter will investigate the manner in which adults with DCD deploy early visuospatial processing capacities prior to the onset of a unimanual movement to goal location. Visuospatial processing at different locations in action space will be investigated by examining the brain activity elicited by task-irrelevant visual probe stimuli presented near the starting location of the effector that will perform the movement as well as near the goal location of the movement. Brain activity in response to these visual probes will be compared to activity elicited by probe stimuli presented at locations that are not relevant in the context of the movement being prepared. The enhancement of these visual components reflects a distinct method of spatial discrimination and thus provides a measure of processing attenuation at task relevant locations during manual response preparation. Results indicate that the DCD group activated similar processing abilities as the control group at cued effector and goal locations when performing a straight movement to goal. However, when required to move across the body midline, the DCD group showed reduced visuospatial processing at cued effector and goal locations.

Introduction

Perception and action are functionally and neurologically linked. The brain is often referred to as an interface that processes sensory information from the environment and uses this information to formulate adaptive and goal directed behaviour. Vision is a key aspect of this functional relationship and a range of studies have highlighted the importance of processing visual information at task relevant locations in everyday activities such as walking (Turano et al., 2004), steering a car (de Oliviera & Wann, 2010; Land, 1998), and ADL activities such as food preparation (Land, Mennie & Rusted, 1999; Hayhoe, Shrivastava, Mruczek & Pelz, 2003). Much of our behaviour is clearly controlled by an internal model of the environment in which we interact. The representational systems that interface within the brain allow humans to model the world and to establish a causal relation to response preparation (Milner & Goodale, 1995). The system must establish parameters to include position in space, size, and consistency of objects thus effector movements are contingent upon visual information specific for body/effector location and endpoint of the desired behaviour (Allport, 1987). Selective sensory processing procedures are employed during response preparation and establish profiles upon which the individual can formulate actions. One aspect of this sensory processing ability involves the modulation of processing at task relevant locations required for the preparation and control of manual reaching and grasping movements (Castiello, 1996). These sensory control processes are thought to reflect the prioritizing of areas for action and are considered a vital processing stage in response preparation (Deubel & Schneider, 1996; Findlay & Blythe, 2009).

The close relationship between the adaptation of visual resources and manual response preparation has received support with studies suggesting that a forthcoming movement results in enhanced visual processing being distributed to action relevant locations. As mentioned in

Chapter 1, a collection of behavioural and ERP studies have identified increased visuospatial discrimination at the intended goal location of a forthcoming reach movement (Baldauf & Deubel, 2008a, 2008b; Deubel et al., 1998; Riek et al, 2003; Schiegg et al., 2003). Although the research into visuospatial processing during the preparation of a movement has presented data clearly supporting goal related activity, research has also examined sensory processing at cued effector locations prior to movement onset. An ERP study by Van Velzen and colleagues has identified larger early components in the visual ERPs in response to task-irrelevant visual probes placed near the start position of the left or right hand during the programming of a forthcoming movement (Van Velzen, Gherri, & Eimer, 2006). It was concluded that these enhanced early visual ERPs elicited by the visual probes suggest that during the covert preparation of reaching movements, spatial attention shifts to the starting location of the cued hand and not to the goal location. A further study by Forster and Eimer (2007) examined ERPs in response to task irrelevant tactile probes that were presented while participants prepared to move one hand towards the index finger of the other hand. In this study the somatosensory N140 component was enhanced when probes were presented to the effector in comparison to the goal hand. These results strongly suggest that processing shifts are directed to the effector prior to movement onset.

The collection of studies examining sensory processing and response preparation suggest visuospatial processing is modulated at locations that are relevant in the context of the movement that is being prepared. It is still unclear as to the timecourse effects of these sensory processing mechanisms as such it is yet to be determined if processing is directed towards hand or goal location in sequential order, however the evidence thus far suggests increased processing in action related areas relating to endpoint and possibly effector locations. A key focus of the current chapter is to examine spatially separate locations that are

action-relevant and need to be considered in the movement planning phase. One consequence of this is that an inability to organize spatial parameters would present as difficulties across a range of tasks since these parameters are specific for the required action (Neumann, 1987).

Given the evidence for the tight coupling of perception and action, as well as for the influence of early sensory processing on motor preparation, atypical development in these areas would be expected to lead to significant daily life difficulties. Considering the clinical group that is the focus of the current thesis, at least a proportion of the difficulties of those with DCD might be attributed to poor visuospatial processing and/or motor planning, and there is some literature on this (see Chapter 1). However, as was apparent in Chapter 1, it is as yet unclear whether the visuospatial impairments that have been reported in individuals with DCD are by-products of a motor difficulty per se or are the consequence of deficits in other areas or of poor integration of information from two or more systems. Here, a brief overview of the literature suggesting atypical visuospatial processing in those with DCD will be presented with a view to providing the basis for the importance of the use of the paradigm adopted in the current study. At this point, it should be noted that all of the studies on this topic have involved children, and not adults with DCD despite adults with DCD continuing to experience difficulties commensurate with visuospatial processing and motor planning explanations of the disorder.

As mentioned in Chapter 1, children with DCD have demonstrated difficulty with a varied collection of tasks involving visuospatial abilities. Early studies conducted by Lord and Hulme (1987a; 1987b) reported that children with DCD show low level visuospatial difficulties including size consistency estimations and the discrimination of area, slope, line

length, and spatial positioning. A study by Mon-Williams and colleagues (1994) did not identify any ophthalmic abnormalities that could explain visual perceptual difficulties in DCD children thus it appears that atypical performance in this area is due to a processing difficulty rather than an isolated biological disruption. A meta-analysis performed by Wilson and McKenzie (1998) to identify information processing factors that characterise children with DCD revealed the greatest difficulties were related to visuospatial processing, irrespective of whether a task did / did not involve a motor component. In a separate strand of study, the use of visual information during tabletop matching tasks has also been investigated in children with DCD. Using the paradigm developed by Von Hofsten and Rösblad (1988), participants are required to match the location of a pin on the tabletop with a pin that they place in the corresponding location under the tabletop. The child is able to see or feel the pin on the tabletop before placing a pin in the corresponding matching location. Children with DCD performed poorly on both visual and proprioceptive measures of this task (Sigmundsson, 1999; Smyth & Mason, 1998). Smyth and Mason compared performance between conditions, showing the greatest difficulty in the proprioceptive condition. In a similar vein, Mon-Williams and colleagues (1999) performed a series of cross-modal matching studies requiring children with DCD to use visual information to guide proprioceptive judgements of limb positioning. It was identified that children with DCD had greater difficulty in making cross-modal judgements that required the use of visual information to guide proprioceptive judgements of limb position. These studies provide further support that children with DCD demonstrate difficulty incorporating visuospatial processing into accurate movement output.

Although there is clear evidence of atypical visuospatial processing in children with DCD, the nature of the relationship between visuospatial performance and movement in those with

DCD remains unclear, although there is some suggestion of an association between the two (Van Waelvelde et al., 2004). Clearly, though, a dysfunction at some level of visual processing could greatly impact motor output. Using a more dynamic performance-based measure of visuospatial processing that involved a manual response, Wilmut and colleagues (2006) used a double-step target pointing task and demonstrated that children with DCD performed similarly to their typically developing peers when producing simple aiming movements but were slower when producing a second movement to a secondary target in a sequence. Importantly in the latter condition, the children with DCD presented with a unique pattern of look-then-move suggesting a difficulty with gaze shift and accompanying hand coordination to *sequential* goal locations. This finding is important as it suggests that children with DCD place increased reliance upon visual information and demonstrate a difficulty with visuospatial orientation during the completion of arguably more difficult tasks to include sequential reaching. Related to this, Baldauf and colleagues (2006) reported that typically developing adults show significantly enhanced discrimination performance at both the primary and secondary goal of a planned movement sequence, which suggests that the entire movement sequence is pre-planned before the first movement is made. Considered along with Wilmut et al.'s findings, Baldauf et al.'s finding provides further support for the view that children with DCD have difficulty sequencing visual processing in order to configure a full movement plan to both sequential targets prior to movement onset.

Other studies have examined the modulation of visuospatial orientation to locations in children with DCD. The covert orienting visuospatial task (COVAT) is an attentional cueing paradigm that measures deployment of visual attention to locations in both the endogenous (following directional cue) or exogenous (detection of novel stimuli in the periphery) realm. Studies utilizing this experimental paradigm have revealed that while children with DCD

have greater difficulty with shifting visual attention to peripheral locations from central fixation, they do not demonstrate difficulty with exogenous orienting to stimuli at peripheral locations (Wilson & Maruff, 1999; Wilson et al., 1997). Thus, while children with DCD were able to detect novel peripheral stimuli (exogenous) as efficiently as their typically developing peers, they took longer to disengage attention from central fixation to cued stimuli presented in peripheral locations (endogenous). Consistent with this observed difficulty, a recent ERP study also utilizing an attentional cueing paradigm identified ERP correlates of atypical attentional control, as indexed by longer cue P3 and target N1 component latencies in children with DCD, suggesting that children with DCD take longer to identify a target and have slower attentional modulation of visual processing to stimuli in the periphery than age matched typically developing controls (Tsai et al., 2009). The results from the attentional cueing paradigm are pivotal as they implicate a difficulty with the attentional modulation of visual processing at task-relevant locations in external space. Although these locations were not action related in the sense of requiring a manual response, the findings suggest that a general delay of visuospatial orientation is present in those with DCD. In line with Wilmut and colleagues' study mentioned above it appears that a general delay in visuospatial orientation is present in those with DCD during low level orientation tasks as well as in more complex tasks requiring manual responses. A more recent ADL related study examining visual processing in adults with DCD whilst driving in a virtual reality simulator revealed that those with DCD failed to detect visual information in the form of pedestrians entering the driving field suggesting less than optimal mappings between environmental visual input and vehicle control (de Oliviera & Wann, 2011). This study exemplifies the knock on effect that poor visuospatial processing can have on everyday tasks and more importantly provides data that directly support the impact on life skills that adults with DCD may encounter.

Cognitive and perceptual processing atypicalities in visuospatial processing and motor preparation have, therefore, been suggested in experimental studies of DCD although very few studies have examined underlying neurological activity. Examples of atypical neurological connectivity have been suggested by neuroimaging studies in those with DCD. Kashiwagi and colleagues (2009) reported atypical parietal activation in children with DCD compared to typically developing children during a continuous tracking task. De Castelnau and colleagues (2008) reported an EEG spectral coherence analysis during a finger syncopation task to visual stimuli with alternating stimulus frequency. Data obtained from this task revealed that coupling between frontal and central regions increased with task difficulty in children with DCD vs. controls. This unique pattern of enhancement was not evident in the control group with increased task difficulty. This suggests that children with DCD demonstrate an increased reliance on the frontal cortex for motor programming as compared to typically developing individuals. De Castelnau and colleagues suggest that the increased reliance upon frontal structures may reduce the input of posterior perceptual mechanisms during motor preparation. As frontal sites are related to motor planning the results may suggest that children with DCD require increased pre-programming to compensate for difficulties with the perceptual-motor aspects of coordination that are intrinsic to their disorder (De Castelnau et al., 2008). A similar finding of atypical neurologic activity was reported by Zwicker and colleagues (2011) who examined neurological activity during a fine motor trail tracing task in children with DCD. Compared to aged matched controls, fMRI activation patterns showed decreased activation of the cerebellar–parietal and cerebellar–prefrontal networks in children with DCD. It is suggested that these areas are involved in visuospatial processing during the tracing task and may imply decreased ability on the part of the DCD children to actively recruit these areas for visuospatial planning (Zwicker et al., 2011).

Overall the few behavioural and psycho-physiological studies examining spatial processing in those with DCD elicit interesting findings that suggest atypicalities related to the relationship between visual perceptual and motor processing. It is also not known whether or not the visuospatial difficulties seen in DCD are influenced by task difficulty or the modulation of task parameters affecting the time course and distribution effects of cognitive mechanisms that underlie sensorimotor processes. There is good evidence that more complex motor patterns/task requirements present greater challenges for those with DCD than for their peers, as evident by studies in which the DCD group performed similarly to control participants with actions consisting of simple spatial demands, but performed more poorly when response complexity was increased (e.g., Missiuna, 1994; Wilmut et al., 2006), as well as during choice reaction time tasks where stimulus and response complexity were manipulated (e.g., Van Dellen & Geuze, 1988). This suggests that task complexity has an effect on underlying sensory control mechanisms. It is still not clear if the degradation in performance observed in DCD is due to a systematic corruption or is attributable to a unisensory deficit during complex tasks. An inability to organize spatial components with an effective time course modulation and distribution parameters would be expected to lead to difficulties across a broad range of tasks, and these are consistent with a good proportion of the difficulties observed in DCD. However, rather little is understood about the mechanisms underlying these difficulties. A valuable contribution to improving our understanding of the causes of these difficulties will include examining the neurological correlates of sensory processing during tasks consisting of simple and complex spatial parameters. Research into the role of visuospatial processing in movement preparation in DCD is still in its infancy and further research is required to establish the manner in which individuals with DCD employ sensory processing capabilities, including visuospatial processing, as this is a compulsory requirement for adaptive and goal directed behaviour.

It is clear, then, that despite the relevance of the role of visuospatial processing in movement preparation in DCD, research in this domain is still in its infancy. The current study sets out to plug this gap by examining how individuals with DCD modulate visuospatial sensory processing during the preparatory phase of a unimanual limb movement towards targets in line with cued effectors or across the body midline. As previously mentioned, there is substantial evidence that enhanced sensory processing at task relevant locations occurs prior to movement onset in typically developing adults. Based on previous behavioural and neuroimaging research it is apparent that individuals with DCD have difficulty with spatial perceptual tasks as well as with orientating visuospatial faculties towards targets. To this end, the paradigm adapted by Eimer and colleagues (2006) will be used to examine visuospatial processing that precedes a unimanual movement to a goal location (see Chapter 3 for detailed method). In summary the experimental task involves a delayed response choice reaction time task in which participants are cued to prepare a unimanual response to goal location and to initiate or withhold the movement upon appearance of a response cue (Go/Stop). Critically, visual probe stimuli were presented at task relevant locations adjacent to cued and uncued effector and goal locations. These visual probes afford the investigation of covert visuospatial processing of task relevant locations indexed by the modulation of the N1 visual evoked potential. As mentioned previously (see Chapters 1 & 2) the N1 component demonstrates enhancement in response to visual stimuli presented at a location that is relevant in the context of an attention or motor task. (Refer to Chapter 2 for a review of visual potential N1 component characteristics.) This attribute allows for an investigation of the enhancement of spatially important locations during the preparation of a movement (Eimer et al., 2006; Hillyard & Mangun., 1991; Hillyard & Mangun, 1987). As such it provides a unique method in which to investigate the modulation of visuospatial processing within reaching space, providing behavioural and biological data within the same paradigm.

<u>Hypotheses</u>

This study is the first of its kind to examine sensory modulation functions in adults with DCD. Given the paucity of data available relating to the performance of this group, hypotheses are based on the limited experimental data from this population, and more directly on the performance profiles of children with DCD, typical developing individuals, and reports of daily living skills of adults with DCD. Note that the findings and hypotheses relating to the behavioural results of the paradigm have been reported in the previous chapter (Chapter 4). Herein the focus is on predictions relating to the biological (ERP) data. There are two key hypotheses:

1. Visuospatial processing during response preparation in the DCD group will differ from that of a well-matched typically developing control group. This effect will present as decreased visually evoked potential N1 enhancement between cued and uncued effector/goal locations suggesting an reduced ability to prioritise areas of action in an effective manner indexed by reduced effects of sensory processing distribution to task relevant locations.

2. The DCD group will show further degradation of visuospatial prioritisation of effector and goal locations during the midline movement. This would be suggestive of a difficulty with employing visuospatial processing mechanisms during complex movements and provide continued support to the argument that this arises from insufficient coherence between sensory control capacities and motor structures, particularly during complex movements.

Materials and Methods

Participants

Please refer to Chapter 3 for a detailed description of group member characteristics. For the

analysis of the effector related N1 data, the data from two members of the control group were

removed. The DCD group contained the full 14 members. During the analysis of the goal

related N1 data, the data from five members of the control group were removed resulting in 9

control group participants. The entire DCD group's data (n=14) were used for the analysis.

Stimuli and Procedure

Please refer to Chapter 3 for a detailed description of the experimental task and associated

materials. Below, a schematic of an experimental trial is shown (Figure 5.1)
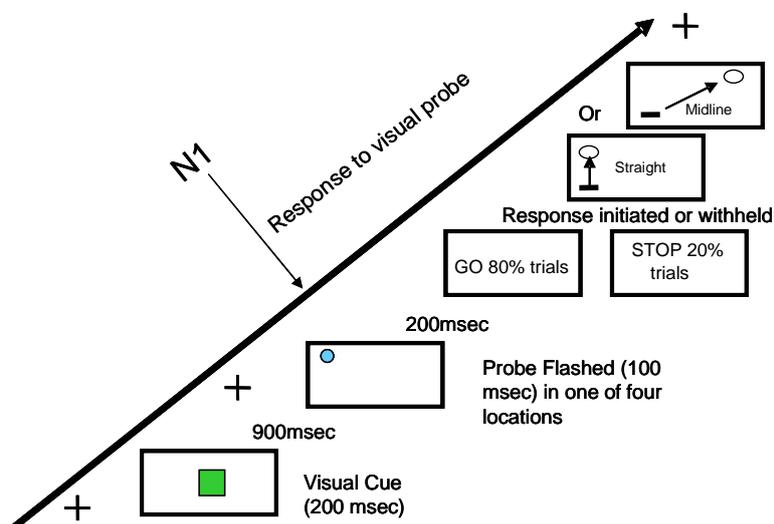
Figure 5.1. Outline schematic of trial. Participant fixates on a central cross, after 1000 msec a green or red square is seen for 200 msec, followed by a fixation cross for 900 msec. Then a probe is flashed in one of four locations (cued/uncued effector; cued/uncued goal) for 100 msec, followed after 200 msec by a stop or go signal replacing central fixation cross. In the 80% of go trials, the participant then initiated a response and moved to the target. Movement conditions were blocked and the participant knew whether the green or red square indicated right or left effector cue in advance of a block of trials. Note the N1 appearance in relation to trial outline and visual probe.

Electrophysiological (EEG) recording and analyses

Please refer to Chapter 3 for specific information regarding EEG recording procedures. The visual ERP N1 elicited in response to each task irrelevant probe stimulus was computed relative to a 100 msec pre- stimulus baseline to 500 msec post stimulus. Separate mean peak N1 amplitudes were computed for all permutations of movement condition, cue, and probe location in relation to effector and goal locations (for straight and midline movements separately, adjacent to relevant effector/goal; in opposite hemifield to relevant effector/goal). Mean peak amplitudes were computed within latency windows centred on the peak amplitudes of visual N1 component post-stimulus (180-300msec). Analyses were performed separately for effector and goal related ERP data. Specifically regional electrode pairs were as follows: Posterior-P3/P4, P5/P6, PO3/PO4; Central-C1/C2, C3/C4, C5/C6; Frontal-F1/F2, F3/F4, FC1/FC2.

Results

Behavioural findings

Please refer to Chapter 4 for a full review of the behavioural results (reaction time, movement time, and error rates). The focus of the current chapter is on the electrophysiological data. Note that, for the most part, only significant analyses are reported.

EEG Results

Visual ERPs elicited by task-irrelevant probe stimuli presented near the hand

An initial repeated measures ANOVA was performed containing within subject factors of Movement Condition (straight, midline movement), Cue (probe presented adjacent to cued

effector vs. presented in hemifield opposite the cued effector), Region (frontal, central, posterior), Electrodes within region (frontal, central, posterior), Hemisphere of recording relative to probe stimulus location (ipsilateral, contralateral), Hand (right/left) and with Group as the between subject factor. Interactions that violated sphericity are reported using Greenhouse-Geisser correction values. Please refer to Figures 5.2 and 5.3 for the topographical scalp distribution of the N1 ERP in response to visual probes presented adjacent to cued effector and uncued effector for the movement conditions. Figures 5.4 and 5.5 reflect the grand average N1 ERPs in response to cued vs. uncued effector for both movement conditions. Of interest in this first set of analyses were the effects/interactions of cue, condition, region, and lateralisation of N1 distribution in response to visual probes at cued and uncued effector location. Interactions containing the electrode and hand factors will be analysed in subsequent analyses examining specific region and group effects. No main effects of Group [$F(1,24)=4.19$, $p=.052$], Movement Condition [$F(1,24)=2.24$, $p=.147$], or Hemisphere [$F(1,24)=1.87$, $p=.184$] were identified. A main effect of Cue was identified [$F(1,24)=12.87$, $p=.001$] showing the presence of increased N1 activity in response to visual probes adjacent to cued effector. A main effect of Region was identified [$F(2,48)=5.35$, $p=.008$] in addition to a significant interaction of Region x Group [$F(2,48)=5.31$, $p=.008$] showing that distribution of the N1 differed between regions of interest and within groups. Overall this initial statistical examination of the data shows that the N1 response was dissimilar between cueing conditions in response to visual probe location (uncued vs. cued effector), as well as across regions. Further analysis is required to understand the distribution of N1 enhancement in response to task relevant locations for both regions and groups.

Following the initial analysis, a secondary repeated measures ANOVA was applied to the data for each region separately, with within subject variables of Movement Condition

(straight/midline), Cue (cued effector/uncued effector), Electrodes with region (frontal, central, posterior), Hemisphere of recording relative to probe stimulus location (ipsilateral, contralateral), Hand (right,left) and with Group as the between subject factor. Effects and interactions of interest included the presence of significant main effects of movement condition and cue, as well as significant group differences for the individual regions. Also of importance are any lateralised effects seen within the regions analysed and conditional differences regarding enhancement indicating differing topographic distribution of enhancement in response to visual probes. Not all interactions are reported at this level. Only interactions suggesting enhanced N1 activity in response to visual probes will be reported.

The results of the frontal region analysis revealed no main effect of Group [$F(1,24)=2.06$, $p=.164$], Movement Condition [$F(1,24)=1.76$, $p=.196$], or Hemisphere [$F(1,24)= .861$, $p=.363$]. A main effect of Cue was identified [$F(1,24)=8.76$, $p=.007$] showing that over frontal regions increased enhancement of the N1 was present in response to visual probes placed adjacent to cued effector. A significant interaction of Cue x Hemisphere x Group [$F(1,24)=5.59$, $p=.026$] identified a lateralised distribution of N1 enhancement in response to visual probes for one of the groups. Comparison of pooled frontal activity in response to cued vs. uncued effector visual probes identified greater enhancement in response to probes adjacent to cued effector (M=-2.84, SD=.82) compared to uncued effector location (M=-2.51, SD=.76); [$t(20)=-2.09$, $p=.049$].

Over the central region no main effects of Group [$F(1,24)= 1.38$, $p=.251$] or Movement Condition [$F(1,24)=2.75$, $p=.110$] were identified. A main effect of Cue [$F(1,24)=7.47$, $p=.012$] showed that over central regions enhanced N1 ERPs were present in response to cued effector visual probes. No further interactions were identified suggesting that both

groups displayed similar distribution of the N1 over the frontal region in response to visual probes. Thus, over central regions both groups showed similar patterns of enhancement in response to visual probes placed adjacent to cued effector location. This was confirmed by a follow up comparison of central activity in response to cued vs. uncued visual effector probes. N1 ERPs were larger in response to cued effector probes (M=-3.17, SD=.84) compared to probes adjacent to uncued effector (M=-2.92, SD=.82); [t(24)=-2.69, p=.012].

Analysis of the posterior region identified a main effect of Group [F(1,24)=9.04, p=.006]. No main effect of Movement Condition [F(1,24)=.694, p=.413] or significant interaction of Movement Condition x Group [F(1,24)= .046, p=.832] was identified showing that movement condition did not have an effect on N1 enhancement over the posterior region. A main effect of Cue was identified [F(1,24)=7.61, p=.011] showing that N1 enhancement over the posterior region was greater in response to visual probes placed adjacent to cued effector locations. Comparison of pooled posterior enhancement revealed that the DCD group (M=-3.17, SD=.79) showed greater posterior activity as compared to the control group (M=-2.30, SD=.65); [t(24)=3.01, p=.006].

Further analyses will focus on the posterior region. Specifically, these analyses removed group as a factor and examined within group performance between movement conditions for posterior region enhancement in response to both cued and uncued effector probes. Interactions containing the hand factor will be mentioned if this factor presents an interaction with the cue factor, indicating that for a specific hand the N1 ERP was enhanced for processing at that location.

Control group

Over the posterior region a significant main effect of Cue was identified [$F(1,11)=23.79$, $p<.001$] identifying increased N1 amplitudes in response to visual probes adjacent to cued effector. A non significant main effect of Movement Condition [$F(1,11)=.148$, $p=.708$] indicated that the increased response to visual probes was constant between movement conditions. No further interactions were identified that would suggest the distribution of the N1 was dissimilar between movement conditions in response to visual probes presented at cued effector locations. Comparison of pooled posterior electrodes in response to cued vs. uncued effector probes identified that over posterior regions the control group showed increased N1 enhancement (M=-2.44, SD=.69) in response to visual probes adjacent to cued effector compared to uncued effector (M=-1.81, SD=.63); [$t(11)=-2.27$, $p=.044$].

DCD group

Analysis of the DCD group's data identified a significant interaction of Movement Condition x Cue [$F(1,13)=8.65$, $p=.011$] indicating that N1 effects in response to visual probes differed between movement conditions. A significant interaction of Cue x Hemisphere x Hand [$F(1,14)=22.43$, $p<.001$] identified that lateralised distribution of enhanced N1 was present for visual probes presented at one of the cued effector locations. Follow up comparisons of pooled contralateral and ipsilateral posterior hemispheres revealed that the DCD group showed enhanced N1 ERPs in the ipsilateral hemisphere (M=-3.43, SD=1.35) to cued effector probes as compared to to uncued effector probes in that hemisphere (M=-2.35, SD=1.06) when the left hand was cued for the upcoming movement [$t(13)=-4.39$, $p=.001$]. The analyses above identified that both groups displayed similar patterns of enhancement for cued vs. uncued effector location with both groups demonstrating increased N1 in response to cued effector location during the straight movement condition. The control group

demonstrated greater breadth of posterior enhancement in response to cued effector visual

probes than the DCD group. However, the DCD group did demonstrate a similar pattern of

enhancement at cued effector location all be it for a cued hand. The next stage of analysis

will examine N1 enhancement in response to visual probes placed adjacent to cued and

uncued goal locations for both movement conditions.
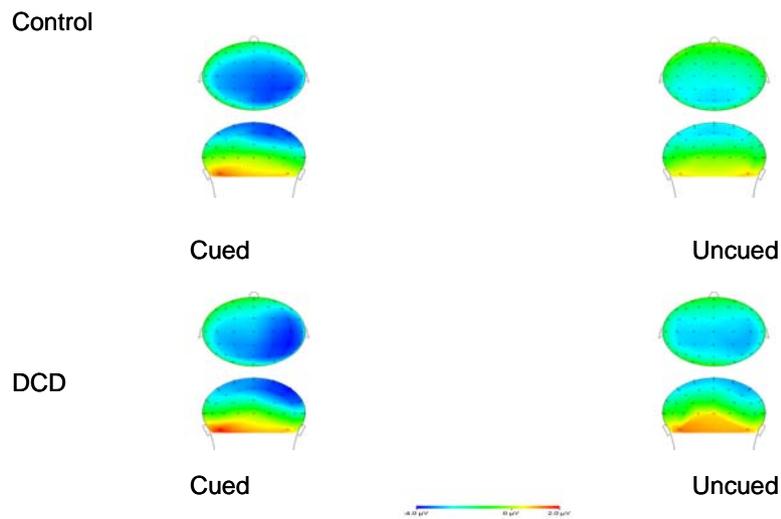
Figure 5.2. Topographic scalp maps of the N1 distribution in response to cued vs uncued
effector visual probes during the straight movement condition.
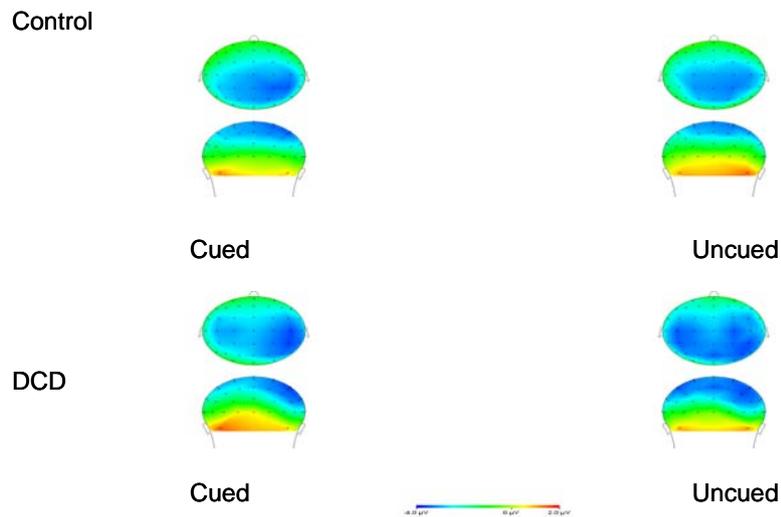
Figure 5.3. Topographic scalp maps of the N1 distribution for cued vs uncued effector visual
probes during the midline movement condition.

N1-Cued Effector vs. Uncued Effector-Straight Movement.

Legend:
- Un-cued effector control (red)
- Cued effector control (black)
- Un-cued effector DCD (blue)
- Cued effector DCD (green)
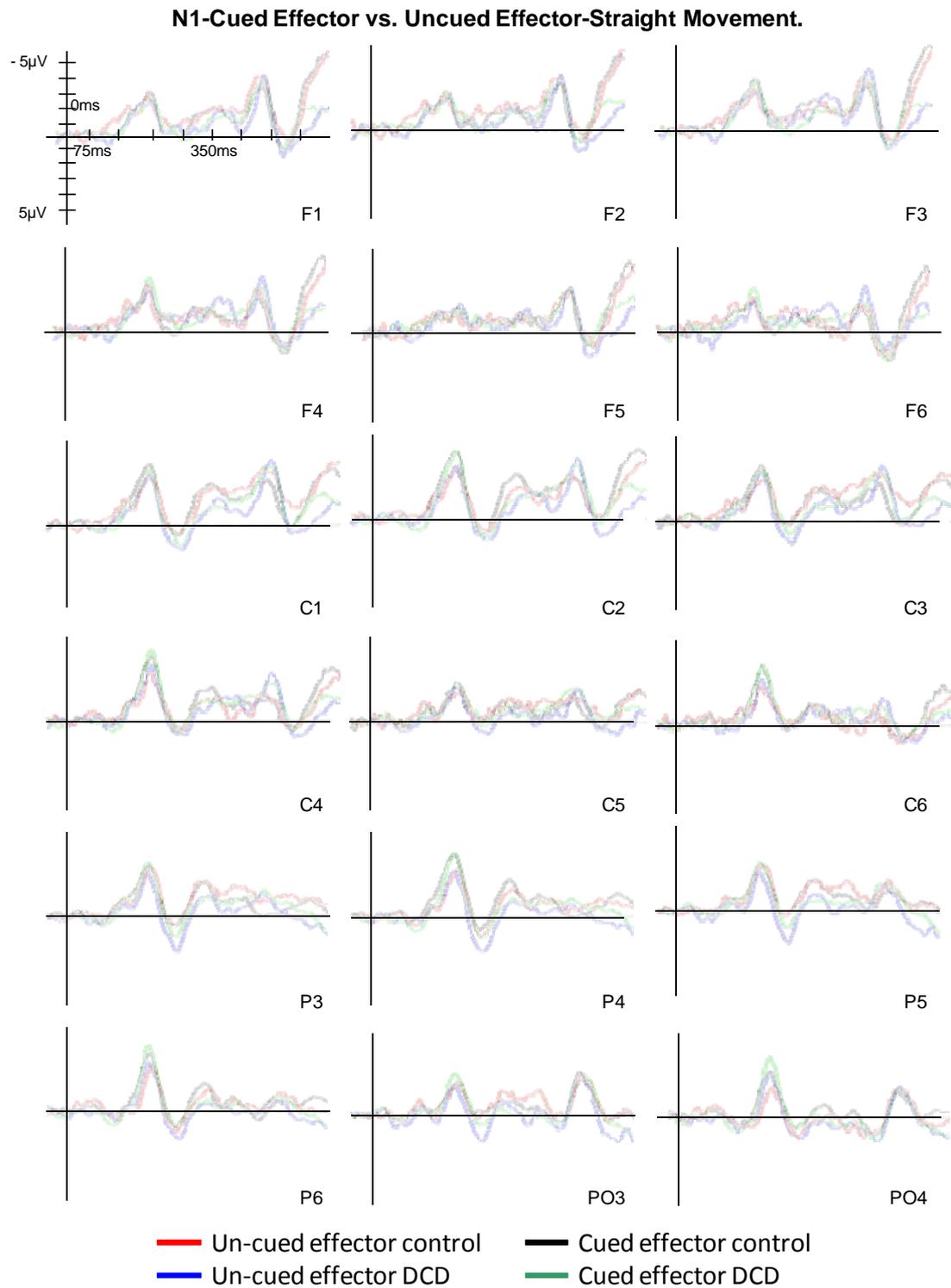
Figure 5.4. Grand average N1 waveforms collapsed across effectors in response to visual probes presented at uncued vs. cued effector location during the straight movement condition. Note that the amplitudes for N1 waveforms in response to probes delivered adjacent to cued effector were generally larger than N1 amplitudes for uncued locations. Both groups showed similar patterns of enhancement for cued effector visual probes adjacent to cued effector.

153
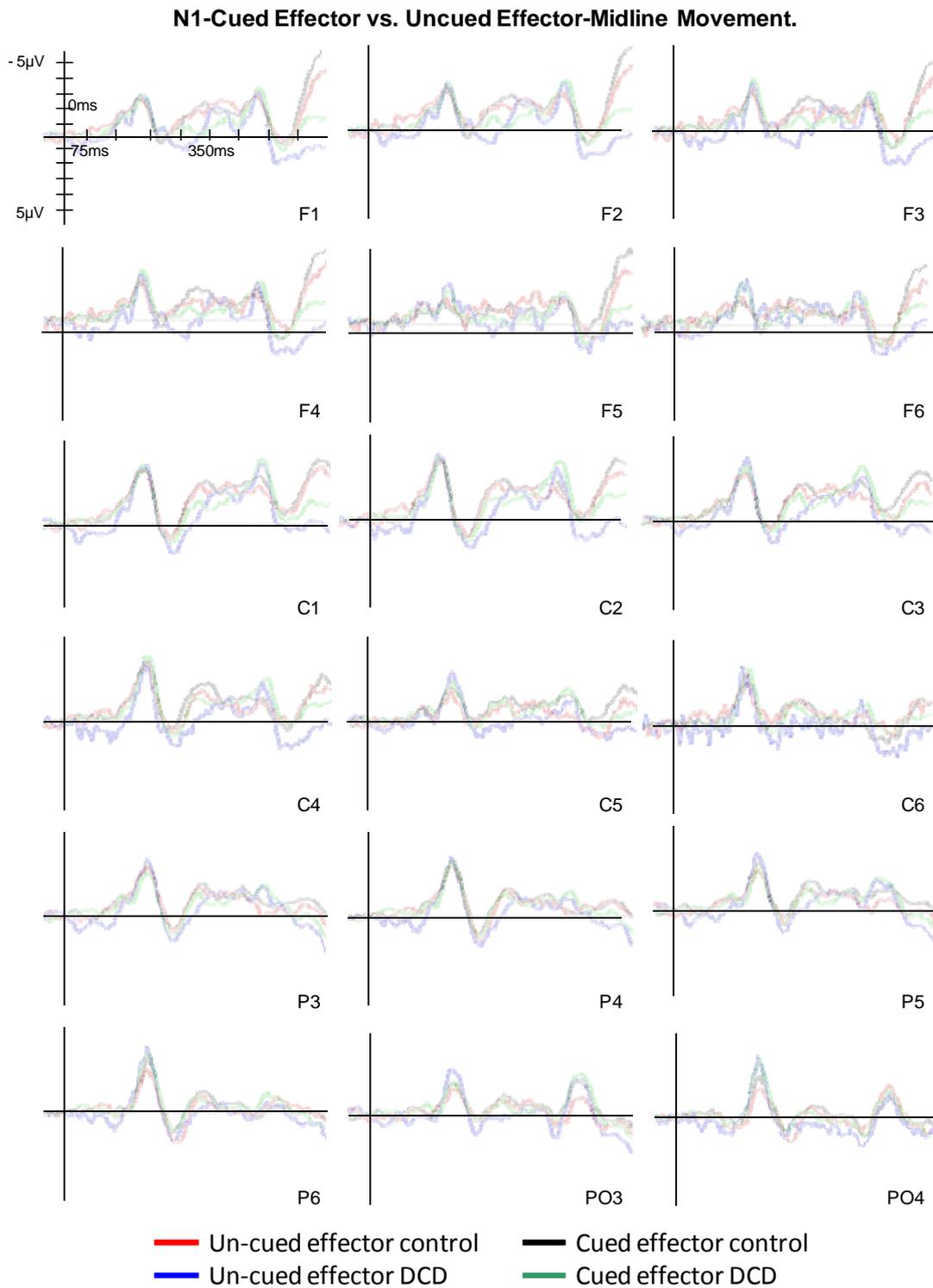
Figure 5.5. Grand average N1 waveforms collapsed across effectors in response to visual probes presented at uncued vs. cued effector location during the midline movement condition. Note that the amplitudes for N1 waveforms in response to probes delivered adjacent to cued effector were generally larger than N1 amplitudes for uncued locations. Both groups showed similar patterns of enhancement for cued effector visual probes adjacent to cued effector.

The analyses above identified that both groups displayed similar patterns of enhancement for cued vs. uncued effector location with both groups demonstrating increased N1 in response to cued effector location during the straight movement condition. The control group demonstrated greater breadth of posterior enhancement in response to cued effector visual probes than the DCD group. However, the DCD group did demonstrate a similar pattern of enhancement at cued effector location all be it for a cued hand. The next stage of analysis will examine N1 enhancement in response to visual probes placed adjacent to cued and uncued goal locations for both movement conditions.

Visual ERPs elicited by task-irrelevant probe stimuli presented near the goal

The analyses procedure follows a similar structure to that for the effector probe stimulus presented above. An initial repeated measure ANOVA was performed containing within subject factors of Movement Condition (straight, midline movement), Cue (probe presented near to cued goal vs. uncued goal), Region (frontal, central, posterior), Electrodes within region (frontal, centra, posterior), Hemisphere of recording relative to probe stimulus location (ipsilateral hemisphere, contralateral), Goal (right, left) and Group as the between subject factor. Please refer to Figures 5.6 and 5.7 show the topographic scalp distribution of the N1 in response to visual probes presented at goal locations for the two movement conditions. Figures 5.8 and 5.9 show the grand average N1 ERPs in response to visual probes at goal locations for the two movement conditions Of interest in this first set of analyses were the effects of cue, movement condition, region, and any interactions identifying regional and hemispheric distribution of the N1 in response to goal located visual probes. Further analyses will investigate within regional effects to goal cues between movement conditions and groups. A main effect of Group $[F_{(1,21)}=10.68, p=.004]$ was identified, however no main effects of Movement Condition $[F_{(1,21)}=.162, p=.692]$ or Cue $[F_{(1,8)}=1.18, p=.289]$ were

present. A significant Movement Condition x Cue x Hemisphere x Group interaction [F(1,21)=5.18, p=.033] indicated that movement condition had an effect on the lateralised distribution of the N1 within groups. A significant interaction of Cue x Region x Group [F(2,42)=10.13, p<.001] showed that enhanced N1 in response to visual probes differed for a group across a region, Overall, this initial statistical examination of the data showed the presence of an enhanced N1 effect with regards to perceptual processing of the visual probe at goal locations prior to movement onset. It also shows that the N1 response was dissimilar between cueing conditions in response to visual probes presented at cued vs. uncued goal locations, as well as across regions. Further analysis is required to understand the distribution of N1 enhancement in response to task relevant locations for both regions and groups. Individual regional effects will be examined in the analyses presented below.

Following the initial analysis, a repeated measures ANOVA was applied to the data for each region separately, with within subject factors of Movement Condition (straight, midline), Cue (cued, uncued goal), Region (frontal, central, posterior), Hemisphere Lateralisation (contralateral, ipsilateral) to cued effector, Goal (right, left) with Group as the between subject factor. Effects and interactions of interest included the presence of significant main effects of movement condition and cue, as well as significant group differences. Also of importance are any lateralised effects seen within the regions analysed and conditional differences regarding enhancement between regions indicating differing topographic distribution of enhancement in response to visual probes. Interactions with the goal factor are reported only if this factor demonstrated an interaction with the cue factor since this suggests that N1 enhancement was present for a specific cued goal.

Over the frontal region there was a main effect of Group [F(1,21)=6.09, p=.022], but no main effects of Movement Condition [F(1,21)=.006, p=.937] or Cue [F(1,21)=.837, p=.371]. No further interactions were present that would suggest either group showed increased frontal N1 in response to visual probes at cued vs. uncued goal location for the two movement conditions over the frontal region. Follow up analysis examining the main effect of group involved comparing pooled frontal electrodes between the two groups. Over the frontal region the DCD group (M=-3.14, SD=.79) showed greater frontal activity than the control group (M=-2.36, SD=.63) [t(21)=2.46, p=.022].

Analysis of the central region revealed a main effect of Group [F(1,21)=4.70, p=.042] but no main effects of Movement Condition [F(1,21)=.196, p=.662] or Cue [F(1,21)=2.15, p=.152]. A significant interaction of Movement Condition x Hemisphere x Group [F(1,21)=5.71, p=.026] was seen suggesting that movement condition had an effect on the N1 distribution over the central region within the groups. In order to investigate this effect, pairwise t-tests were performed comparing hemispheric enhancement between movement conditions for the two groups. Analysis of the control group revealed a marginal difference between contralateral hemisphere activity (M=-2.46, SD=.76) during the straight movement compared to contralateral hemisphere activity during the midline movement (M=-2.71, SD=.58) [t(9)=-2.64, p=.050]. Similar comparison of the DCD group's data revealed greater activity contralateral to cued goal (M=-3.46, SD=1.33) compared to activity present within the contralateral hemisphere to uncued goal location (M=-2.74, SD=1.03) [t(13)= 3.03, p=.010]. Comparison of pooled central activity revealed the DCD group (M=-3.16, SD=.82) showed greater activity over this region as compared to the control group (M=-2.45, SD=.66) [t(21)=2.17, p=.042].

Analysis of the posterior region identified a main effect of Group [$F(1,21)=17.51$, $p=.001$] however no main effects of Cue [$F(1,21)= .422$, $p=.523$] or Movement Condition [$F(1,21)= .430$, $p=.519$] were identified. A significant interaction of Condition x Cue x Hemisphere x Group [$F(1,21)=5.69$, $p=.027$] indicated that within the groups, the cueing effects in the two movement conditions were differently distributed over the posterior region. In order to investigate the main effect of group, pooled posterior activity was compared between the groups. This revealed that the DCD group ($M=-3.12$, $SD=.64$) showed significantly greater posterior activity than the control group ($M=-2.03$, $SD=.55$) [$t(21)=4.18$, $p<.001$]. The significant interactions mentioned above will be examined further in subsequent analyses examining individual group performance across the posterior region.

Specifically, these analyses removed group as a factor and examined within group performance between movement conditions for enhancement within the posterior region in response to probes delivered at cued and uncued goal locations.

Control group

Within the posterior region the control group did not display a significant main effect of Movement Condition [$F(1,8)=.069$, $p=.800$] however, as expected, a main effect of Cue was found [$F(1,8)=23.20$, $p=.001$], supporting increased enhancement of N1 at cued goal locations as compared to uncued goal locations. A main effect of Hemisphere was not identified [$F(1,8)=3.58$, $p=.095$] suggesting similar hemispheric distribution of the N1 over posterior regions for the control group. No further interactions were significant, suggesting that posterior enhancement remained constant for the control group between conditions for goal locations regardless of location from cued effector.

DCD Group

Similar analysis applied to the posterior data of the DCD group did not identify main effects of Movement Condition [$F_{(1,13)}=.509$, $p=.488$] or Cue [$F_{(1,13)}=1.01$, $p=.332$]. However, an interaction of Movement Condition x Cue x Hemisphere was present [$F_{(1,13)}=7.11$, $p=.019$] showing that movement condition had an effect on the lateralised distribution of the N1 in response to visual probes at the goal location. In order to investigate the cueing effect described in the interaction above further analysis will investigate each movement condition separately for the DCD group over the posterior region.

Analysis of posterior activity during the straight movement condition revealed a significant interaction of Cue x Hemisphere x Electrode [$F_{(1,13)}=5.94$, $p=.007$] indicating that cue did have an effect on electrode activity within a hemisphere. In order to investigate this interaction pairwise t-tests were performed over posterior electrodes comparing enhancement effects in response to visual probes. This revealed that only electrode PO4 demonstrated increased enhancement in response to visual probes at cued goal locations (M=-3.47, SD=.83) as compared to uncued goal location (M=-2.41, SD=1.11) [$t(13)=-3.82$, $p=.002$] during the straight movement condition. A similar comparison for electrode PO3 approached significance (p=.70) for cued vs. uncued goal location. It appears that there was a small enhancement over the posterior region for the DCD group at goal locations during the straight movement; however this was limited to a single electrode. Nevertheless this finding suggests that the DCD group demonstrated a similar pattern of enhancement in response to cued goal location probes during the straight movement condition compared to uncued goal location. Although the DCD group showed increased posterior enhancement compared to the control group, it appears that the enhancement of the N1 was not as robust as that seen in their typically developing peers in response to visual probes presented at cued goal location.

Analysis of the posterior region during the midline movement identified a significant interaction of Cue x Hemisphere x Goal [F(1,13)=11.97, p=.004] and a significant interaction of Cue x Hemisphere x Goal x Electrode [F(1,13)=12.29, p<.001] indicating that increased activity was seen at an electrode within a hemisphere in response to visual probes presented at cued vs. uncued goal locations. Follow up pairwise t-tests were performed on lateralised electrode pairs over the posterior regions within the contralateral hemisphere to cued and uncued probe locations. This revealed that the DCD group demonstrated increased enhancement for uncued probes for electrode pairings P3/P4 (M=-3.8, SD=1.24) as compared to cued probes at goal location (M=-3.21, SD=.86) [t(13)=-2.34, p=.035]. See Figure 5.9 for grand average N1 ERPs in response to visual probes at cued and uncued goal locations during the midline crossing condition. Figures 5.10 provides schematics of regional enhancement in response to visual probes both at effect for goal locations for both groups and movement conditions.

160
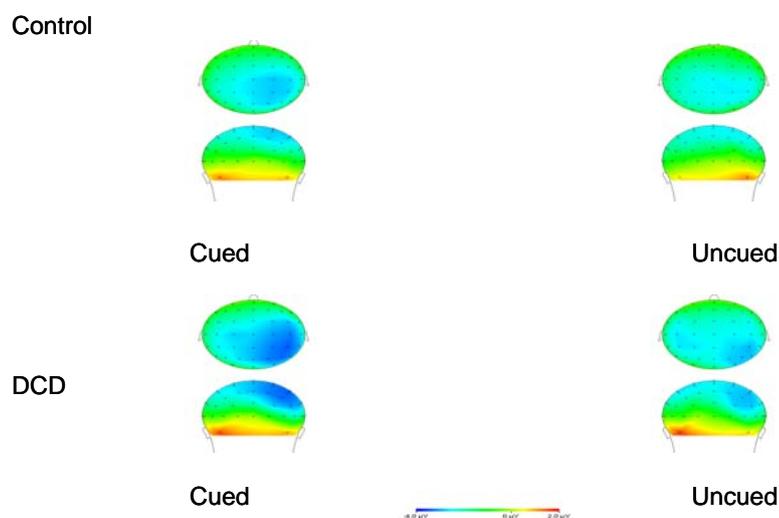
Figure 5.6. Topographic scalp maps of the N1 distribution for cued vs uncued goal visual probes during the straight movement condition.

Control

Cued   Uncued

DCD

Cued   Uncued
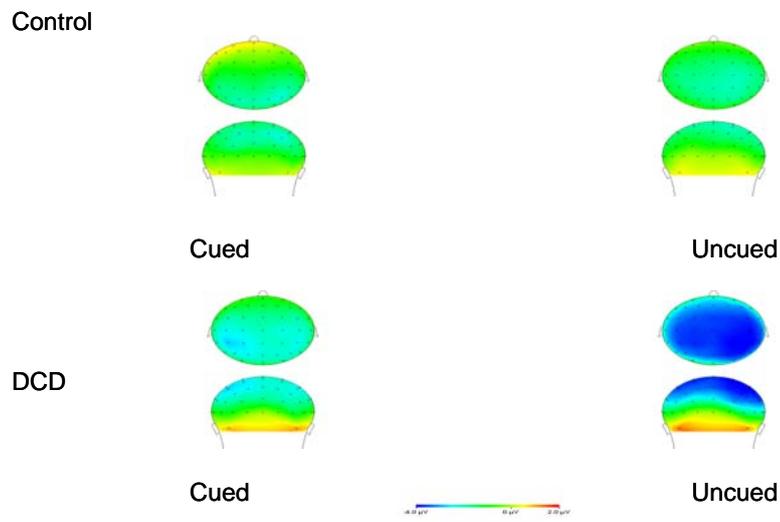
Figure 5.7. Topographic scalp maps of the N1 distribution for cued vs uncued goal visual probes during the midline movement condition.

N1-Cued Goal vs. Uncued Goal-Straight Movement.
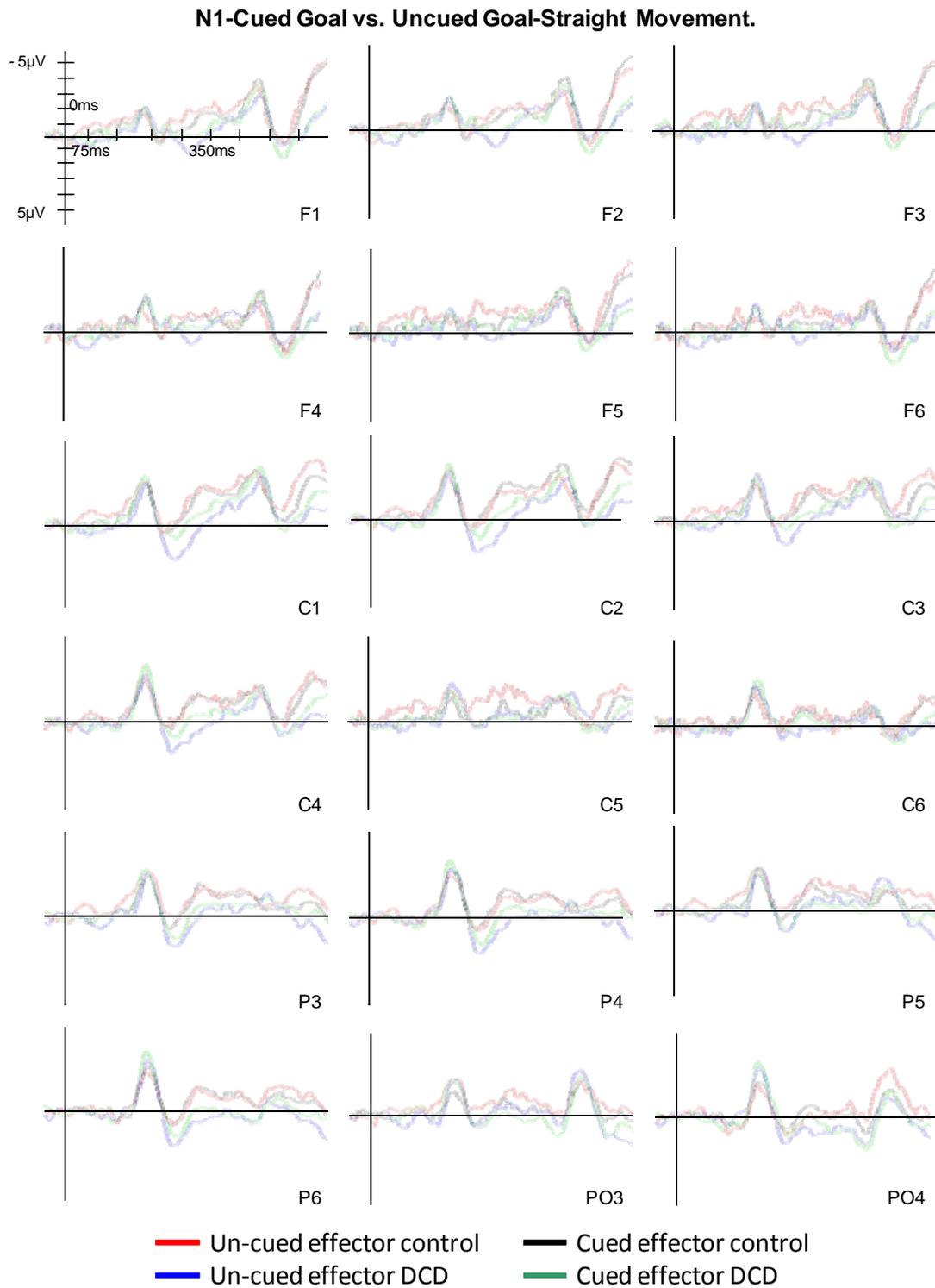
Figure 5.8. Grand average N1 waveforms collapsed across effectors in response to visual probes presented at uncued vs. cued effector location during the straight movement condition. Note that the amplitudes for N1 waveforms in response to probes delivered adjacent to cued effector were generally larger than N1 amplitudes for uncued locations. Both groups showed similar patterns of enhancement for cued effector visual probes adjacent to cued effector.

N1-Cued Goal vs. Uncued Goal-Midline Movement.

Legend:
— Un-cued effector control   — Cued effector control
— Un-cued effector DCD   — Cued effector DCD
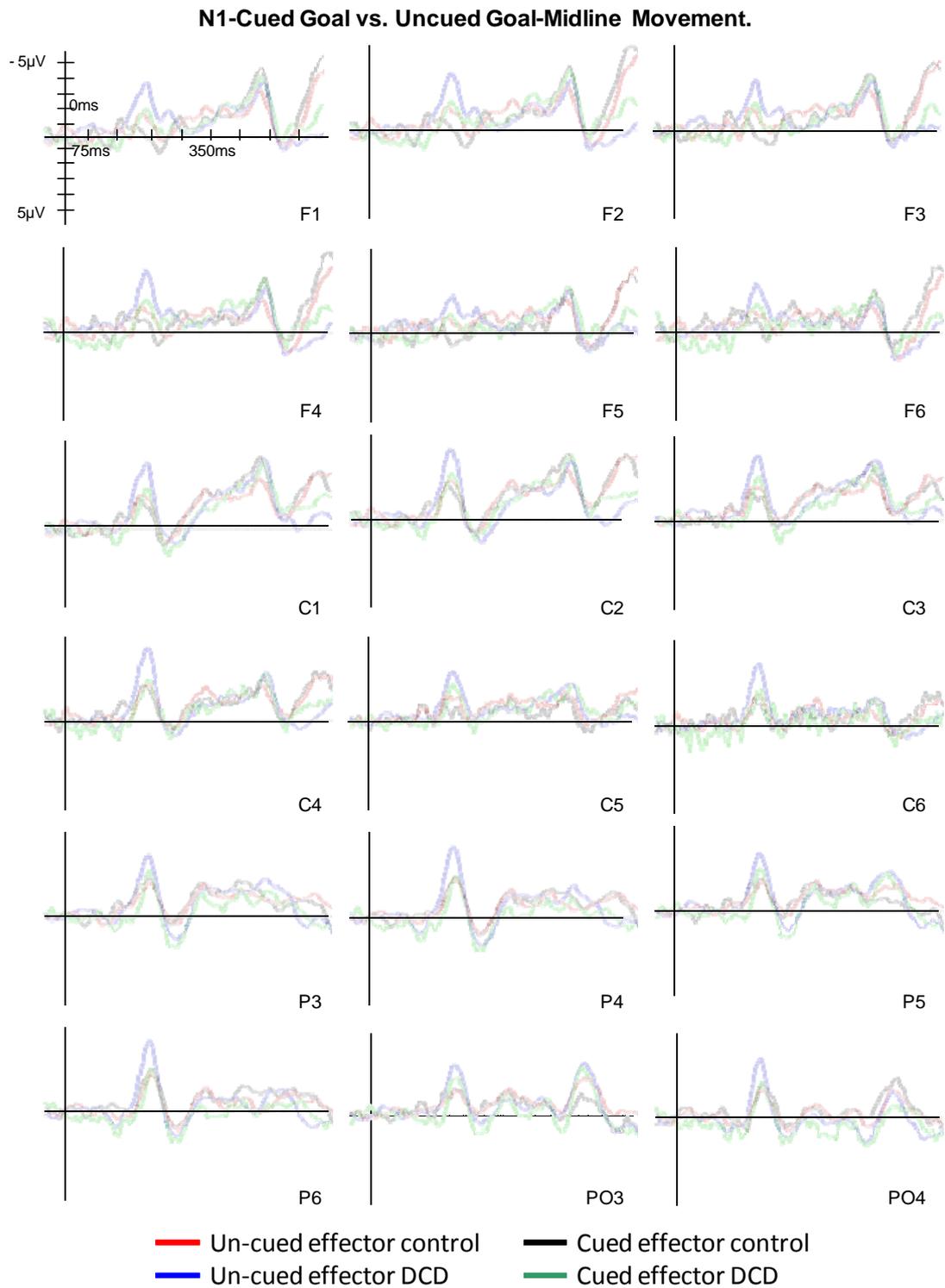
Figure 5.9. Grand average N1 waveforms collapsed across effectors in response to visual probes presented at uncued vs. cued effector location during the straight movement condition. Note that the amplitudes for N1 waveforms in response to probes delivered adjacent to cued effector were generally larger than N1 amplitudes for uncued locations. Both groups showed similar patterns of enhancement for cued effector visual probes adjacent to cued effector

In this chapter, the focus was on enhanced visuospatial attention processing of the movement environment at cued effector and goal locations, believed to reflect early preparatory sensory activity as a direct consequence of movement preparation. Both the control and DCD groups demonstrated similar patterns of location prioritisation within the movement space of a reach during simple straight movements to goal, showing enhanced visuospatial processing at cued effector and goal locations. However, when reaching towards a goal across the body midline the DCD group showed enhanced visual processing (reflected in an increased N1 ERP) in response to un-cued goal locations. In contrast, the control group showed enhanced processing at the cued goal location. These results suggest that adults with DCD may have difficulties modulating visuospatial attention towards goal locations when required to make a spatially more complex movement (i.e., across midline) to goal locations from initial effector location. The possible implications will be discussed below.
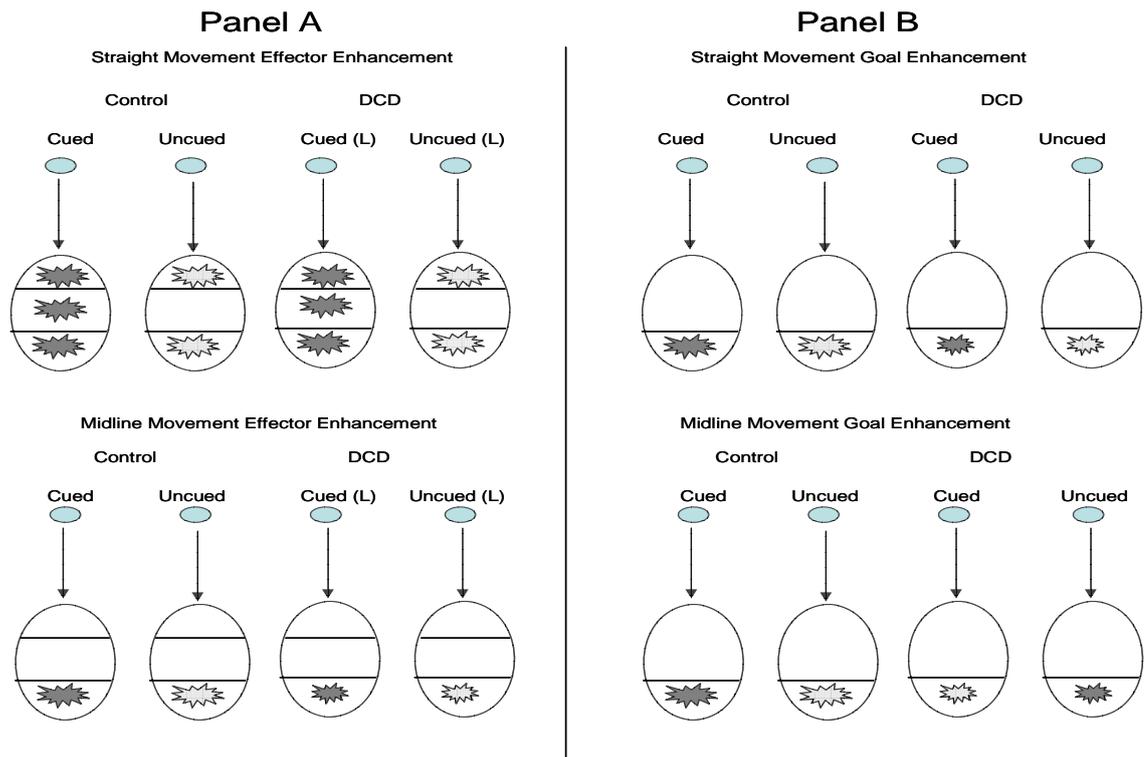
Figure 5.10. Panel A. Schematic of enhancement in response to task irrelevant visual probes presented at cued and uncued effector locations. The control and DCD group presented with increased frontal, central, and posterior N1 ERPs in response to visual probes adjacent to cued effector during the straight movement condition. However, the DCD group only demonstrated increased enhancement of the N1 for probes delivered near the left hand for both movement conditions. During the midline movement condition the control group only showed increased posterior enhancement of the N1 to visual probes adjacent to cued effector location. Panel B. Goal related enhancement of the N1. During the straight movement both groups presented with enhanced N1 over the posterior region however for the DCD group this was limited to a single electrode. For the movement across midline the control group showed a similar enhanced N1 at goal location as the straight movement. The DCD group showed an increased enhancement to uncued goal locations over a single electrode pair.

Discussion

This study was designed to examine whether adults with DCD demonstrate unique visuospatial processing of task relevant locations during the preparatory period of an overt unimanual movement. This was achieved through the use of event related potential (ERP) measurements sensitive to visuospatial processing and which are known to show enhanced processing at task relevant locations during the preparation of a unimanual response. Within

the DCD literature the focus has been on the putative cognitive subsystems that underlie behavioural performance. However, the manner in which these deficits influence movement planning has yet to be investigated rigorously. By combining movement performance with direct ERP analyses of visuospatial processing we have been able to embark on an initial investigation of the manner in which adults with DCD modulate visual processing activity prior to movement onset. Overall it was hypothesized that the DCD group would demonstrate less efficient prioritisation of visuospatial processing indexed by decreased enhancement of visual evoked potential N1 in response to task irrelevant probes presented at cued effector and goal locations. It was further hypothesized that a continued degradation of visuospatial prioritisation would be present during the more complex movement condition indicating that movement complexity has an effect on the ability of DCD adults to prioritise areas for action.

Primary analyses were conducted on the posterior region where the enhancement effect in response to task irrelevant probes was greatest. Initial results indicated that an increased N1 amplitude for probes presented near the cued effector was observed during the movement condition requiring participants to manoeuvre from a starting point straight to a goal location in the same hemifield as the cued effector,. The enhanced N1 amplitude was larger for cued effector locations for both the DCD and control groups demonstrating increased visuospatial processing at cued effector locations during the straight movement condition and midline crossing condition. Thus, adults with DCD and well-matched controls showed similar patterns of visuospatial prioritisation in response to visual probes adjacent to cued effectors, as compared to when the probe was presented at the opposite cued hand location.

Analyses of N1 enhancement at intended goal locations during the straight movement revealed that both groups demonstrated increased visuospatial processing at task relevant goal locations. The control group displayed no difference in the level of enhanced modulation at goal location for the two movement conditions in response to probe stimuli at cued goal locations. The most revealing findings came from the analysis of the N1 data in response to goal location probes particularly during the midline crossing condition. During the straight movement condition, the DCD group showed an increased amplitude of the N1 in response to cue target locations. However, during the more complex midline movement condition the DCD group showed an increased N1 amplitude in response to uncued goal locations (see Figure 5.9). This was a surprising result as it revealed that for a particular electrode pair the DCD group demonstrated an increased visual response to uncued goal locations within the same hemifield as the cued effector in the condition in which the intended goal is across the body midline. These collective results for enhancement at effector and goal locations partially support the initial hypothesis that the DCD group would present with decreased ability to prioritise visuospatial processing at task relevant locations. However, this atypical level of processing was only evident at goal locations during the the more complex midline movement. (See Figure 5.10 and 5.11 for schematics of visuospatial processing enhancement patterns for both groups and movement conditions.)

Error! Bookmark not defined.
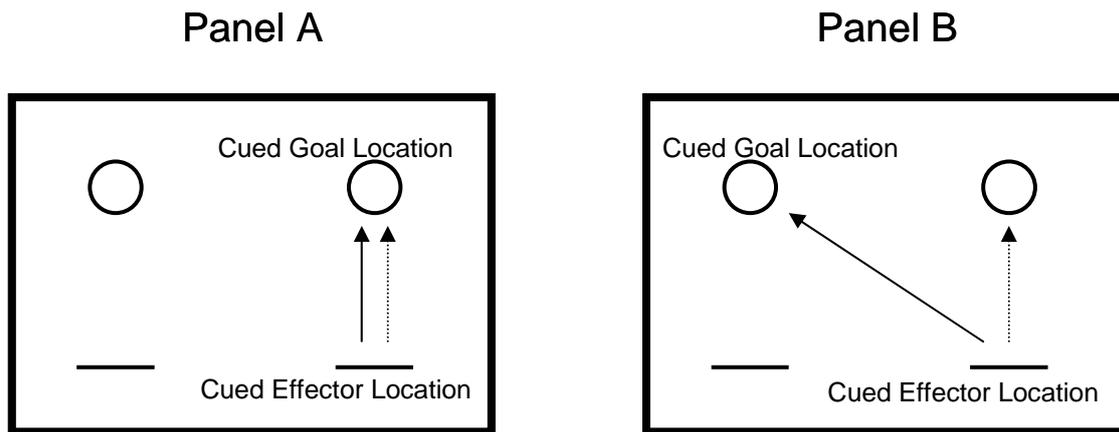
Figure 5.11. Schematic representing visual processing of task relevant locations for both control (solid line) and DCD (dashed line) collapsed across effector/goal locations during: A. Straight movement condition and B. Movement across midline. During the straight movement the two groups demonstrated similar enhancement at cued effector and goal location. During the movement across midline the enhancement at cued effector was similar between the groups. However the enhancement towards cued goal was greater at locations opposite the intended goal for the DCD group.

By utilizing an experimental procedure incorporating an ERP measure of visual processing during manual response preparation we were able to examine the coupling of motor preparation and visuospatial processing during the preparatory window of unimanual movements. Importantly the data presented here replicated prior ERP findings in which enhanced visuospatial processing was present at action relevant locations during the preparation of a manual response (Baldauf & Deubel, 2009; Eimer et al., 2006). Importantly this study adds further support to previous studies showing that goal directed hand movement facilitates visuospatial processing at task relevant locations for which that action is directed (Van Velzen et al., 2006). Subsequently the results here suggest that visuospatial enhancement of goal location is present regardless of initial hand location, particularly in the typically developing group. The cued effector and goal related enhancements provide further support to the findings of the existing literature for evidence of early selective processing stages involved in establishing environmental movement parameters. Furthermore these

results exemplify the close relationship between the adaptation of visual resources and response preparation.

In terms of DCD, visuospatial processing has been at the forefront of studies into the difficulties faced by children with DCD. However the extent to which these sensory control processes are involved during movement preparation is yet to be fully examined within the DCD population. Other studies suggest that those with DCD fail to incorporate visuospatial influences in a typical way and propose that the deficient motor actions stem from a corruption of feedforward models (Wilson et al., 1997). The sensory gating of attended locations within visual perception is a precursor to the efficient development of controlled movement (Rizzolatti et al., 1994), which is consistent with the study findings presented here. Thus, it may be that individuals with DCD are unable to correctly interpret the spatial requirements of intended movement trajectories, resulting in the development and/or implementation of movement plans that lack accurate spatial parameters. Our findings suggest that adults with DCD show atypical discrimination of goal locations during both simple and arguably more complex movements. This may represent an insufficient approach when organizing the spatial parameters required for forthcoming movements and the translation of spatial parameters into accurate motor plans. It appears that this deficit may be exacerbated by increasing task constraints or spatial demands as evident by decreased processing enhancement at intended goal locations during midline crossing. It is unclear, however, at this time whether or not the atypical visual processing identified here represents a discrete planning difficulty or could be representative of maladaptive or delayed feedback processes.

As mentioned previously, research strongly supports early visuospatial processing during the preparation of a goal directed movement (Baldauf & Deubel, 2008a, 2008b; Deubel et al., 1998; Eimer et al., 2006). An fMRI study by Beurze and colleagues (2009) provides evidence that regardless of the type of information conveyed by the cue, spatial parameters are activated prior to effector selection. During their task, typically developing adults were instructed to prepare either a saccade or a reach following two consecutive visual instruction cues, presented in either order. One cue indicated which effector to use (eyes, right hand), whilst the other signalled the goal (left/ right target location) of the movement. It was reported that during the initial phase of movement preparation after cueing either goal or effector, activity was found along the parietofrontal network responsible for spatial configurations. Beurze and colleagues (2009) suggest this order of activity underpins the initial processing of goals, followed by effector information being added to the movement composition. Although the study presented within the current chapter contained both effector and goal location information within the cue, it could be suggested that based on the results obtained in the current study the DCD group was unable to initially incorporate spatial parameters into movement preparation, particularly when the movement contained more complex spatial arrangements. In this case, and following data from the neuroimaging study mentioned above, determining effector profiles for action would be compromised as primary visuospatial coordinates that precede effector activation may be insufficient, potentially resulting in the observed movement difficulties. This could explain the increase in errors and slowed reaction times in the more complex midline crossing condition reported in Chapter 4. Furthermore, it could underlie the poor incorporation of spatial parameters of a more complex movement in movement planning. Although the results presented here suggest that movements containing conflicting spatial codes may be difficult for those with DCD, these findings are in line with studies that have reported immature hand preference in midline

crossing tasks in children with DCD (e.g., Cermak et al., 1990; Hill & Bishop, 1998) as well as poor motor planning in this group (Hill & Wing, 1998; 1999). It is important to note that based on the behavioural results of the study presented here (Chapter 4) this difficulty continues into adulthood and may be suggestive of continued developmental immaturity.

During the sequencing of reaching tasks, visual processing has been shown to isolate end points in an efficient manner. It appears that typically developing individuals are able to examine movement environments over a very precise time course and this processing effect is not limited to singular goals but can be adapted for multiple sequenced goal locations (Deubel & Baldouf 2006; Ricker at al., 1999). Interpreting visual space for action requires the continued monitoring of space for relevant items for which action is built around. This distinction may also help describe the differing effect for the DCD group during the midline crossing movement. Although only one goal was present in this study, it may be that the current updating of the space for action involves a suppression of task irrelevant locations and the observed enhancement at uncued goal represents a discriminatory process that the adult DCD group relies more heavily upon during discrimination of possible goal locations during more complex reaching tasks. The control group may be able to suspend this discrimination task or complete it much more efficiently than the DCD group thus explaining the significant enhancement at cued effector and goal locations for both movement conditions. Work by Tereo and colleagues (2002) investigated gaze control whilst isolating several targets for pointing movements in typically developing individuals. This group discovered that participants were able to prepare a reach to several locations without adjusting gaze to goals. This suggests that processing is distributed temporally in parallel to several locations thus spatially coding several locations in unison. The DCD group may not be able to apply this spatial coding as efficiently as the control group and it may be that during the time course

analysed during the midline crossing condition the DCD group had not yet completed the spatial coding of locations.

Regarding the experiment here sensory processing also needs to be controlled temporally so that action towards space can be prepared accurately and efficiently. The probes were placed at a time point of 200 milliseconds preceding the response stimulus, thus capturing covert processing at effector and goal locations during similar time frames prior to the motor response. Results from this study appear to support previous work suggesting that covert visuospatial attention can capture characteristics of numerous task relevant locations (Baldauf & Deubel, 2008a, 2009b). Based on the observed pattern of N1 modulations in this study, it appears that the DCD group may have difficulty with visual processing at various locations on a similar time course as the control group. Those with DCD may require increased information or more time to isolate goal locations during this preparatory time in order to carry out an accurate movement. Zoia and colleagues (2005) analysed movement trajectories and deceleration times by manipulating visual feedback in children with DCD. Children with DCD demonstrated atypical trajectories and extended deceleration times suggesting insufficient visual feedback as compared to typically developing peers. Wilmut and colleagues (2006) also suggested that those with DCD take longer to utilize online visual feedback information for the generation and control of actions. It may be possible that the enhanced processing observed at uncued goal location in the current study reflects an atypical use of the visual system to establish movement parameters on the part of the adults with DCD.

The distinct underlying neurological area from which atypical sensory processing may arise is yet to be established. However, parietal regions, as well as frontoparietal networks have

been implicated in movement preparation in typical individuals (Anderson & Bueno., 2002; Connolly et al., 2003). While the extent to which atypicality in the parietal region may underlie performance in the DCD population is unknown, researchers have postulated that the region most likely to underlie DCD is the posterior parietal region. This view emerged intially from evidence of difficulties with motor imagery in DCD children (Maruff et al., 1999; Wilson et al., 2001). It is argued that since efference copies of this process are believed to originate in the parietal region (e.g Sirigu et al., 1996), atypicality of this region may be implicated in DCD. Certainly, the parietal area is often referred to as the location where sensory information is integrated and as such represents a plausible candidate for future study (Goodale & Milner, 1992; Jeannerod, 1994). Importantly for the current study, damage to the parietal region has been shown to result in severe problems in the modulation of spatial attention (Baylis et al., 2001; Heilman et al., 1985). Movement coding for spatial goals has also been localised to the posterior parietal cortex (PPC) from movement intentions of effectors (Anderson & Buneo, 2002). Moreover, Matelli and colleagues (1998) suggested that the premotor and supplementary motor areas organise the spatial coordinates of intended movements which are then projected to visual areas for selection of location. Finally, parietal regions have been identified as being responsible for the representation of eye and hand motor space directed towards the contralateral workspace (Battaglia-Mayer et al., 2005). Certainly consideration of past data, as well as the findings of the current study, suggests atypical parietal involvement would be an area worthy of investigation. It must be mentioned that analysis of regional activity during the goal related analysis revealed that the DCD group showed increased activity over all regions including the parietal region compared to the control group. Thus, it is difficult to comment on activation strength and parietal function at this stage as it would be expected that decreased parietal activity would go hand in hand with the observed atypical enhancement particularly during the acquisition of midline goal

location. As mentioned previously, a limited number of neuroimaging studies have been conducted in DCD. However, those that have been reported, alongside data from cognitive behavioural studies, suggest atypical neurological activity within regions that are responsible for sensory processing. Thus it is likely that visuospatial processing may be affected in those with DCD. Indeed, the next chapter will investigate further aspects of parietal processing closely linked with early selective processing involved in motor preparation.

Regarding developmental aspects of visuospatial processing, studies of development and visual processing although quite limited, suggest that adults make more efficient use of spatial information to program their movements (Gabbard et al., 1998). However this is yet to be measured during midline crossing (Pryde et al., 2000). It is likely that as children mature their spatial processing abilities develop to include more refined midline processing capacities and thus older children may employ similar functions to those observed in the adult control group. In a developmental study, Schwiensburg and colleagues (2005) reported a positive correlation between age and bilateral activity of the posterior parietal cortex for participants aged 12-17 during a spatial working memory task. It was concluded that the areas responsible for spatial processing continue to develop during adolescence and into adulthood. Furthermore, Clements-Stephens and colleagues (2009) performed an fMRI study of line discrimination in children between the ages of 7 and 15 comparing activity for age and sex. Older males engaged regions associated with visuomotor activity whilst older females utilized areas indicated in spatial attention and working memory. The implication of developmental maturity and visuospatial processing for the current findings is not well established, however the limited number of studies examining age related visuospatial processing suggest that as we age neuroanatomical regions active during visuospatial tasks develop. The influence of these neuroanatomical changes is yet to be determined and it

would be speculative to comment on the developmental trend of performance measurements examined in this initial investigation. It is, however, plausible that the adult DCD group continues to demonstrate a developmental delay regarding the efficiency of visuospatial processing and recruitment of neurological areas required for effective modulation of visuospatial processing. As mentioned previously, neuroimaging studies involving DCD children has demonstrated atypical activation of areas involved in visuospatial processing. It remains to be seen if this atypical neural activation patterns continue into adulthood via neuroimaging methods. Further research examining visuospatial processes over various age groups is required to substantiate a developmental influence on visuospatial processing abilities.

In a transition from experimental outcomes to real life performance, the task utilized here represents everyday interactions that require reaching for objects during both simplistic movements and complex spatial arrangements. It is easy to see how such a difficulty would have a constant and significant impact on activities of daily living, education and employment. The manner in which humans employ sensory processing procedures is a prerequisite occurrence for successful completion of everyday tasks. Imagine an individual with DCD preparing a meal on the kitchen countertop, where items such as ingredients and cutlery may be placed in areas that are not spatially compatible with initial hand location. Say for instance the individual must reach across midline to pick up a container of ingredients. During this specific task those with DCD may have difficulty deploying visual selective processes to identify characteristics of the reaching area and formulate a forthcoming reach built upon an accurate awareness of the containers position. The reach towards the container may be inaccurate and lead to spillage of the contents. Another example could involve household maintenance tasks. Say for instance the individual is

attempting to nail an object into a wall. The incorporation of visuospatial parameters and the motor activity could lead to degraded performance and thus less than optimal completion of the task. This is likely to be the case in complex tasks. While at this point it is difficult to comment on the direct manner in which task complexity might influence visuospatial processing in the DCD group, an overall difficulty with complex movements and visuospatial processing capabilities appears to be compromised in the adult DCD cohort.

Conclusions

Difficulties in visuospatial processing and the interrelationship with motor preparation is a potential explanation for a range of difficulties experienced by those with DCD. However, the examination of these processes in DCD is rather limited. This is particularly true in an adult sample. To this end, the current study presents the first detailed consideration of this topic by drawing on a well researched paradigm from the cognitive neuroscience literature and focusing on a well-matched adult sample. The findings of this study partially support the hypothesis that the DCD group would demonstrate decreased modulation of visuospatial attention (indexed by reduced N1 enhancement) to task relevant locations during the preparatory phase of a speeded unimanual movement. This decreased processing modulation was only evident during the midline crossing movement suggesting that the DCD group experiences difficulty with visuospatial processing during complex (but not simple) movement tasks. The findings of the current study provide an initial glimpse into sensory control processes that may contribute to these difficulties. This small, but expanding body of evidence highlights significant and continued motor difficulties in the adult DCD cohort (Cousins & Smyth, 2003; de Olivera & Wann; 2011). These, along with reports of reduced quality of life satisfaction, high levels of depression and anxiety and functional difficulties with activities of daily living and employment (Hill et al., 2011; Hill & Brown, under review;

Kirby et al., 2011), highlight the fact that DCD is a lifelong, debilitating condition that may stem from a specific difficulty (in this thesis the focus is on sensory processing / motor preparation as a source of atypical performance), but that is likely to have widespread, downstream consequences in terms of cognitive, behavioural and functional effects. To fully understand the manner in which adults with DCD utilise visuospatial processing prior to movement onset, and to substantiate the findings presented here, replication of the current study is vital. Further manipulations should include varying the probe presentation prior to movement onset and placing goals in novel locations. These would reveal information regarding spatial thresholds of atypical visual processing for varying movement complexities. In the next chapter more direct preparatory control processes of movement facilitation will be examined to provide a broader picture of the extent and nature of the apparent atypical ERP responses of those with DCD relative to well-matched peers at the preparatory stage of a unimanual response.

Chapter 6

An ERP investigation of the neural mechanisms underpinning response preparation in adults with Developmental Coordination Disorder

Abstract

This experimental chapter aims to investigate the manner in which adults with Developmental Coordination Disorder (DCD) employ early selective sensory processing faculties during the preparation of a unimanual response. This will be achieved by examining lateralised ERP effects present during the interval between visual response cue – indicating effector/goal location and the appearance of the visual go/nogo stimulus – requiring participants to execute or withhold the desired unimanual movement to goal location. Results indicate that overall the DCD group showed much greater activity over all regions of interest whilst preparing for a forthcoming reach to goal. The lateralised components ADAN/LDAP reflecting frontoparietal activity were discovered much later for the DCD group suggesting delayed activation of the mechanisms required for early selective control processes.

Introduction

The ability to actively recruit early selective processing mechanisms for goal directed behaviour is an essential process required to engage with one's environment. As mentioned previously in Chapter 1, the motor planning hierarchy is comprised of sensory processing and selection stages that must be intact in order to create an adaptive and efficient movement. These early sensory control mechanisms enable the actor to infer environmental characteristics to formulate adaptable and goal directed movement based upon the establishment of pragmatic spatial maps. Without such early control mechanisms output would be reliant upon poor environmental information resulting in variable and erratic

movement profiles. Imagine a typical movement; say for instance a reach towards a glass of water on the tabletop. Although a simple task, this activity is comprised of a number of processing stages that must occur in a serial fashion. Initial aspects of the glass, such as its location, shape, circumference and distance from body must be established. Early sensory control stages afford an initial representation of the current task sensory information and is a precursor to motor control mechanisms that select, program, and execute motor responses. Returning to our example, the initial selective processing stage allows the actor to modulate processing capacities to the glass in order to establish the spatial and object characteristics upon which the forthcoming movement is formulated. As such these spatial locations are a crucial feature for the establishment of spatial maps for which future movements are built upon. As a result of having spatial locations identified, there seems to be an effect on sensory processing with enhanced processing of these locations.

The support for effects of motor preparation on sensory processing has arisen through behavioural and psychophysiological studies where participants were required to prepare and perform a goal directed response and identify stimuli adjacent to intended movement target or at different locations in visual field. At a behavioural level, initial studies have identified increased discrimination performance when visual events occur at predetermined saccade locations (Deubel & Schneider, 1996, 2003; Irwin & Gordon, 1998). Discrimination performance has also been shown to be enhanced at the goal location of a manual reaching task (Deubel & Schneider, 2003; Deubel, Schneider, & Paprotta, 1998; Schiegg et al., 2006). These studies suggest that selective processing faculties are in place when preparing a response and provide support for the effects of response preparation on sensory processing. It has been recognized in previous studies that the attentional modulation of visuospatial processing may require the activation of motor control pathways within the brain (Craighero

et al., 1999; Klein, 1980). As mentioned in Chapters 1 and 2, recent ERP studies have provided valuable information pertaining to activity in overlapping brain areas during both shifts of attention and movement preparation (Corbetta et al., 2000). In studies using attentional cueing paradigms similar to the one mentioned above, ERPs (ADAN/LDAP) reflecting these preparatory attention processes have been recorded over frontocentral and posterior areas in the form of voltage differences between the hemispheres ipsilateral and contralateral to the attended hemifield (Harter et al., 1989; Eimer, 1995). More recently, and of importance to the current thesis, similar ERP effects have been observed during the preparation of a manual response (Eimer & Van Velzen, 2002; Eimer et al. 2006; Gherri & Eimer, 2010; Praamstra et al., 2005). Furthermore, a study by Gherri and colleagues (2007) investigating the ADAN and LDAP components during spatially incongruent movements suggests the link between these early sensory control processes and directed manual response preparation is complex. In their study participants were required to move the hand inward towards the body midline. During this incongruent movement task the ADAN component was not identified and the LDAP component was greatly reduced during this movement condition as compared to a spatially congruent movement. These findings suggest that movement complexity contributes to these components. Gherri and colleagues suggest that the diminished ADAN/LDAP effects identified may underlie simultaneous shifts of attention in opposite direction when preparing a movement in the contralateral hemisphere from intended goal location. Important to the analysis presented within this thesis chapter is the distribution of these lateralised effects between the groups during a similar spatially conflicting reaching task where the hand is prepared for action in the contralateral hemisphere from intended goal location. Although the work examining ADAN/LDAP under differing spatial task parameters is limited, it is suggested that the null findings discussed above underpin a congruent relationship between effector and movement direction selection

processes and that conflicting spatial codes have an effect on the ability to recruit frontoparietal mechanisms involved in early sensory control processes. Nevertheless it appears that ADAN/LDAP effects appear during attentional task paradigms and during the preparatory time window of simple manual movements. This suggests selective sensory control processes are present when both movement preparation and shifts of attention in space are required.

Importantly these studies suggest that action and perception are tightly coupled and provide support for previously established theories that suggest early selective sensory processing and response preparation are functionally related. A number of theories have emerged that address the links between attention and motor control (Klein, 1980; Rizzolatti, 1994; Allport; 1989). Perhaps the most widely known theory is the Premotor Theory of Attention (Rizzolatti, 1994). Specifically the Premotor Theory of Attention presents anatomical and physiological considerations of the organization of the neurological circuits involved in sensorimotor transformations. According to this theory spatial attention is related to activation in specific movement related spatial maps as a result of a frontoparietal network accompanying behaviour towards specified spatial locations. The behavioural and ERP studies discussed in Chapters 1 and 2 have provided support for the main attribute of this theory, that is that the modulations of visuospatial processing result from the activity of the frontoparietal circuits, rather than a distinct attentional mechanism. Enhanced visuospatial processing at attended locations extends from activity in any of the pragmatic maps and links to effector systems required for action. Furthermore, while the primary incorporation of the premotor theory concerned shifts of attention that are linked to oculomotor activity, recent evidence has provided strong support for early selective effects during the preparation of manual activity.

The neurological regions that underlie spatial attention have also been investigated. Early studies of lesion patients have implied that frontal and parietal brain areas were responsible for the control of selective spatial processing resulting in neglect to shift processing capacities to contralateral hemispheres from lesion (Mesulam, 1981). With the advancement of neuroimaging techniques a wealth of information regarding the associations between motor processing and attention have been established. Based on distribution of activity these studies showed activity in overlapping areas in the frontal and parietal cortex in both motor processing and attention. (Anderson & Bueno, 2002; Astafiev et al., 2003; Corbetta et al., 2000). The ERPs of interest for the current thesis have also been localised to originate in a frontoparietal network showing a link between motor processing and attention (Praamstra et al., 2005). These converging results suggest that frontal and parietal areas are actively recruited during the top-down modulation of early selective attention regardless of effector to include both ocular and manual movements.

This presence of frontoparietal activity (ADAN/LDAP) during both shifts of attention and motor preparation provide strong evidence for a frontoparietal network that is recruited when a manual or eye movement is being prepared. It has been suggested that activity in this network leads to enhanced processing at the goal of a prepared movement. This finding signals strong support for the Premotor Theory of Attention, and most importantly that during movement preparation sensory processing at task relevant locations is enhanced as a result of activity in the frontoparietal network.

The performance difficulties of the DCD group described in Chapter 1, suggest that at some level this population experiences a corruption with the underlying sensorimotor processes

that precede goal directed movement (Piek & Dyck, 2004). The exact stage or stages at which this disruption occurs has yet to be determined, however it is possible that atypical prioritisation of processing at task-relevant locations that occurs as a function of movement preparation may influence observed movement difficulties observed in those with DCD. The limited number of studies investigating early selective processing via attentional cueing paradigms does propose some difficulty with this ability in those with DCD.

The ability of individuals with DCD to incorporate task relevant spatial parameters has not been examined in great detail, particularly in relation to movement preparation. As reviewed in Chapter 1, studies examining the performance of DCD children during a modified attentional cueing paradigm have identified some difficulty with spatial orientation in those with DCD. Across a number of studies DCD groups have displayed orienting deficits for endogenous condition requiring disengagement from central fixation to stimuli in the periphery as compared to typically developing peers (Wilson et al, 1997; Wilson et al. 2003; Mandich et al., 2002; Tsai et al., 2009). Although this performance difficulty is an important finding, it poses the question of whether this selective processing difficulty is evident as a consequence of movement preparation. In a recent study Wilmut and colleagues (2007) adopted a similar attentional cueing paradigm involving a motor component. Children were seated in front of a central fixation point and six peripheral targets. Saccade and hand movement latencies were recorded as the children were asked to look at or hit targets when illuminated. Children with DCD were not slower than controls to disengage attention during the look condition. However, during the look- hit condition the children with DCD showed a prolonged saccade disengagement period as compared to typically developing children. This suggests that children with DCD have difficulty with the allocation of attention for action and the recruitment of early selective processing faculties. Early selective mechanisms are

believed to integrate expectations and goals to voluntarily decide where to shift attention. Thus, the collection of studies presented above suggests that children with DCD may have difficulty recruiting early selective processing mechanisms during the preparation an ocular or manual response.

In addition to these measures of early selective processing, a large collection of studies have suggested that individuals with DCD exhibit difficulties with visual perceptual and perceptual motor activity (Bonifacci, 2004; Sigmundsson et al., 2003; Wilson & Mckenzie, 1998). Individuals with DCD have also presented with low level visuospatial perceptual (Hulme et al, 1983; Lord & Hulme, 1987), and visual feedback difficulties (Geuze & Kalverboer, 1987). Overall, visuospatial deficits are the most common difficulty reported in children with DCD although the relation between these difficulties and overall movement production is not known (Wilson & McKenzie, 1998).   Deficits in selecting and processing visual parameters might be linked to problems incorporating essential environmental attributes such as pragmatic spatial maps and object characteristics into appropriate movement planning, on-line movement correction, and feedback control. Based on the collective visuospatial difficulties observed in the DCD group, it may also be suggested that an inability to modulate sensory processing at movement task-relevant locations is present resulting in less than optimal visuospatial processing of the environment for which action is required.

Indeed the limited number of neuroimaging studies performed in those with DCD also points to neuroanatomical areas that may underlie this difficulty. As mentioned in Chapter 1, these studies have in fact demonstrated atypical neuroanatomical activation of areas, primarily in the parietal lobe (De Castelnau et al., 2008; Kashiwagi et al., 2009; Zwicker et al., 2011). Important to the development of research in the area of DCD is to prescribe to theoretically

driven research paradigms that combine motor programming and sensorimotor performance. As the functional links suggested by previous theories of action and perception have been validated and replicated in the typically developing population they allow for an examination of clinical groups in order to investigate if atypical incorporation of these processes may underlie the observable motor difficulties of the DCD cohort.

<u>Hypotheses</u>

Although the empirical work surrounding the underlying abilities of the DCD population is limited, there is strong evidence that the observed difficulties may be attributable to the incorporation of early selective control mechanisms into motor processes, although the specific disruption is yet to be isolated. This study is the first of its kind to examine preparatory cortical control processes that are active during response preparation in adults with DCD. Given the lack of data available relating to the performance of this group, hypotheses are based on the performance profiles of typical developing individuals, and reports of similar attentional investigation in children with DCD. The two key hypotheses are:

1. Based on observed difficulties in those with DCD to include slow movement preparation, it is hypothesized that a deficit with the preparatory control processes following a response cue will be problematic for the DCD group during motor preparation, evidenced by atypical timecourse and distribution effects of the ADAN/LDAP complexes in comparison to typically developing peers.

2. It is also hypothesized that the DCD group will demonstrate a difficulty in modulating preparatory control processes between movement conditions. This atypical task adaptation is expected when more complex movements are prepared and will manifest as a

reduction of these preparatory ERP components (ADAN/LDAP) for movement instruction

containing spatially incongruent task constraints for goal location and effector selection.

Participants

Please see methods chapter for a review of participants. The data from three members of

each experimental group were removed from analyses as inspection revealed their data to

contain a large amount of artifactual interference during the time window analysed for ERPs

of interest and yielded low amounts of acceptable trials for averaging procedures. The data

from 11 members of each group were included in the analysis.

Experimental Procedure

Please refer to Chapter 3 for a detailed description of the experimental procedure and

associated materials. Figure 6.1 below presents a schematic of the experimental trial outline.

Please note the area above the arrow as this reflects the appearance of the ADAN/LDAP

complex in relation to experimental task outline.

ADAN
300-500 msec

LDAP
600-800 msec

Or

Midline

Straight

Response initiated or withheld

GO/STOP

200msec

Probe Flashed (100 msec) in one of four locations

900msec

Visual Cue (200 msec)

Fixation Cross(1000msec)
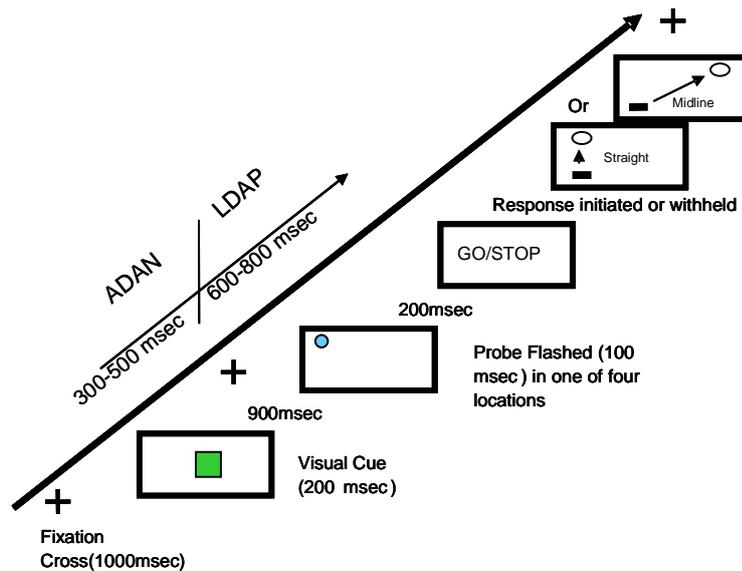
Figure 6.1. Outline schematic of trial. Participant fixates on a central cross, after 1000 msec a green or red square is seen for 200 msec, followed by a fixation cross for 900 msec. Then a probe is flashed in one of four locations (relevant/irrelevant effector; relevant/irrelevant target) for 100msec, followed after 200 msec by a stop or go signal. In the 80% of go trials, the participant then initiated a response and moved to the target. Movement conditions were blocked and the participant knew whether the green or red square indicated right or left effector cue in advance of a block of trials. Note the segmentation of the two components of interest post visual response cue in line with the experimental timeline.

EEG Data Recording and Acquisition

Please refer to methods Chapter 3 for specific EEG recording procedures. For the current investigation, trials containing left and right cues for both movement conditions were averaged for each participant. Statistical analyses were based on mean amplitudes obtained within two post cue latency windows of 300-500 ms (ADAN presentation) and between 600-800ms (LDAP presentation). Prior to statistical analyses, horizontal/vertical eye movement activity was statistically compared between groups to ensure that frontal effects were not influenced by ocular motor activity or movement related physiological occurrences. No difference was found between the groups for amplitude values for horizontal/vertical eye movement electrodes.

Results

Analyses of the two ERP components (ADAN/LDAP) were performed separately for the

mean amplitude of electrodes during epochs following the presentation of visual response

cue, and are reported separately below.

ADAN component (300-500 msec post cue stimulus)

A repeated measures ANOVA was performed with the following factors: Movement

Condition (straight, midline movement), Cue (left, right), Region (frontal, central, posterior),

Electrodes within region (frontal AF7/AF8, F5/F6, F7/F8, central C1/C2, C3/C4, C5/C6,

posterior P9/P10, TP7/TP8, PO3/PO4), Hemisphere (ipsilateral/contralateral to cue), and

Group as the between subjects factor. The purpose of this initial ANOVA was to examine if

any lateralised effects, regional or movement condition differences were present between

groups. Interactions containing the electrode factor will be investigated when individual

regional analysis is performed for each group. Please refer to Table 6.1 for a summary of

results from the ADAN analysis presented below. Figures 6.2 provides topographic scalp

distributions of activity during the early time window examined. Figure 6.3 shows non-

lateralised regional activity for the groups during the early time window analysed. Figures 6.4

and 6.5 provide difference waveforms between electrode pairs during the interval between

visual response cue – indicating effector/goal location and the appearance of the visual

go/nogo stimulus for both movement conditions. A main effect of Group was identified

[$F(1,20)=9.54$, $p=.006$]. Differing regional enhancement was evident from a main effect of

Region [$F(2,40)= 12.46$, $p>.001$] along with a Cue x Region x Group interaction $F(2,40)=$

6.11, $p=.005$] indicating that the cue had an effect on regional enhancement for the groups.

This analysis revealed that the distribution over the scalp op the cueing effects differed

between the two. These regional effects will be examined in subsequent analyses in order to

identify if specific localised lateralised effects were observed over individual regions during the early ADAN time window.

ADAN analysis by region

The secondary analyses involved a repeated measure ANOVA with the region factor removed to examine isolated regional characteristics between groups and conditions. The ANOVA contained the following factors: Movement Condition (straight, midline movement), Cue (left, right), Electrodes within region (frontal AF7/AF8, F5/F6, F7/F8 - central C1/C2, C3/C4, C5/C6 - posterior P9/P10, TP7/TP8, PO3/PO4), Hemisphere (ipsilateral, contralateral to cue) with Group as the between subjects factor. The results of this analysis are reported below, for each region separately in order to examine the regional effects of the ADAN distribution.

Frontal

Within the frontal region a main effect of Group was identified [$F_{(1,20)}= 4.68$, p=.043]. However, a significant interaction of Cue x Hemisphere x Electrode [$F_{(2,40)}=5.70$, p=.007] identified a lateralised effect for a particular electrode pairing.

A secondary ANOVA was applied to the frontal data removing the group and movement condition factors in order to identify the movement condition for which a lateralised effect was present. Control group data will be presented first. During the straight movement condition there was a significant interaction of Cue x Hemisphere x Electrode [$F_{(2,20)}=5.49$, p=.013] identified a lateralised effect for a frontal electrode pair during the straight movement. Analysis of the frontal region during the midline crossing condition did not identify a significant Cue x Hemisphere interaction [$F_{(1,10)}=.013$, p=.912] nor a significant

interaction of Cue x Hemisphere x Electrode [F(2,20)=.613, p=.551]. To confirm that the lateralised distribution observed during the straight movement was indeed an ADAN component double subtractions were performed between frontal electrodes. This revealed that electrode pair F5/6 demonstrated a negative lateralisation (M=-.13, SD=.40) however the other frontal electrode pairs of AF7/8 and F7/8 did not show anterior negativity (See Figures 6.2 and 6.4). Thus, an anterior negative lateralised effect (ADAN) was identified for the control group over a singular electrode pair for the frontal region. Similar analysis of the DCD group's data revealed that no frontal lateralised distribution was present during the straight movement or during the midline crossing movement. It was confirmed that the control group showed lateralised distribution over the frontal region during the straight movement condition whereas the DCD group did not show any lateralised distribution for either movement condition. Comparison of pooled frontal data between groups confirmed that the DCD group showed significantly greater frontal activity that the control group; [t(20)=-2.16, p=.043]. See Figure 6.3 for pooled activity over the frontal region for the groups.

Central

Analysis of the central region revealed a main effect of Group [F(1,20)=16.82, p=.001]. A significant interaction of Cue x Hemisphere x Electrode x Group [F(2,40)=3.51, p=.039] identified a lateralisation for a particular electrode pair for one of the groups.

In a similar procedure performed for the frontal region, an ANOVA was performed removing the condition and region factors to investigate central activity individually for each group and movement condition. Analysis of the control group's data did not identify any significant interactions that would suggest lateralised activity over the central region for the control

group during the straight movement condition. Analysis of the midline crossing condition identified a significant interaction of Cue x Hemisphere x Electrode [F(2,20)= 4.81, p=.020] showing that lateralised effects were expressed differently at the electrode pairs included in the analysis. Double subtraction computations of central electrodes during the midline movement revealed that the lateralised activity was positive for electrodes C1/2 (M=.12, SD=.13) and C3/4 (M=.13, SD=.21) suggesting that the lateralised effect observed over the central region may be a positive distribution (LDAP) following on from the negative effects observed over the frontal region (See Figures 6.2 and 6.4). A similar comparison for the DCD group did not identify lateralised effects during both the straight or midline movements over the central region. In order to examine the group difference, comparison of pooled central activity between groups was performed. This confirmed that the DCD group showed significantly greater central activation during this early time window compared to the control group; [t(20)=-4.10, p=.001]. See Figure 6.3 for pooled activity over the central region for the groups.

<u>Posterior</u>

Analysis of the posterior region identified a main effect of Group [F(1,20)=5.14, p=.035]. A significant interaction of Cue x Hemisphere x Electrode [F(2,40)=12.91, p<.001] and a significant interaction of Cue x Hemisphere x Electrode x Group [F(2,40)=6.41, p=.004] identified a posterior lateralised distribution for a particular electrode pair within the groups.

A secondary ANOVA was performed removing the condition and region factor to investigate posterior activity individually for each group and movement condition. Analysis of the control group's data during the straight movement condition did not identified a significant interaction of Cue x Hemisphere x Electrode [F(2,20)= 12.65, p<.001] was present, indicating

a lateralised effect over the posterior region for the control group. Analysis of the midline

crossing condition did not identified a significant interaction of Cue x Electrode x

Hemisphere was identified [F(2,20)= 33.01 , p<.001]. Analysis of the DCD group's data

over the posterior region did not identify any interactions that would suggest a lateralised

effect over the posterior region for both movement conditions. Thus it appears that only the

control group showed lateralised distribution over the posterior region. In order to investigate

the direction of the lateralised effect double subtractions between electrodes were performed

for each movement condition. These double subtractions revealed that the lateralised

distribution was in the positive direction (LDAP) for electrode pair PO3/4 during both the

straight (M=.34, SD=.30) and midline crossing movement conditions (M=.49, SD=.85).

Follow-up analysis comparing these lateralised effects between movement conditions did not

identify a difference between movement conditions [t(10)= -.502, p=.627] for the control

group (See Figures 6.3 and 6.4). Comparison of overall posterior activity identified that the

DCD group showed increased posterior activity compared to the control group; [t(20)=-2.26,

p=.035]. See Figure 6.3 below for pooled activity over the posterior region for the groups.
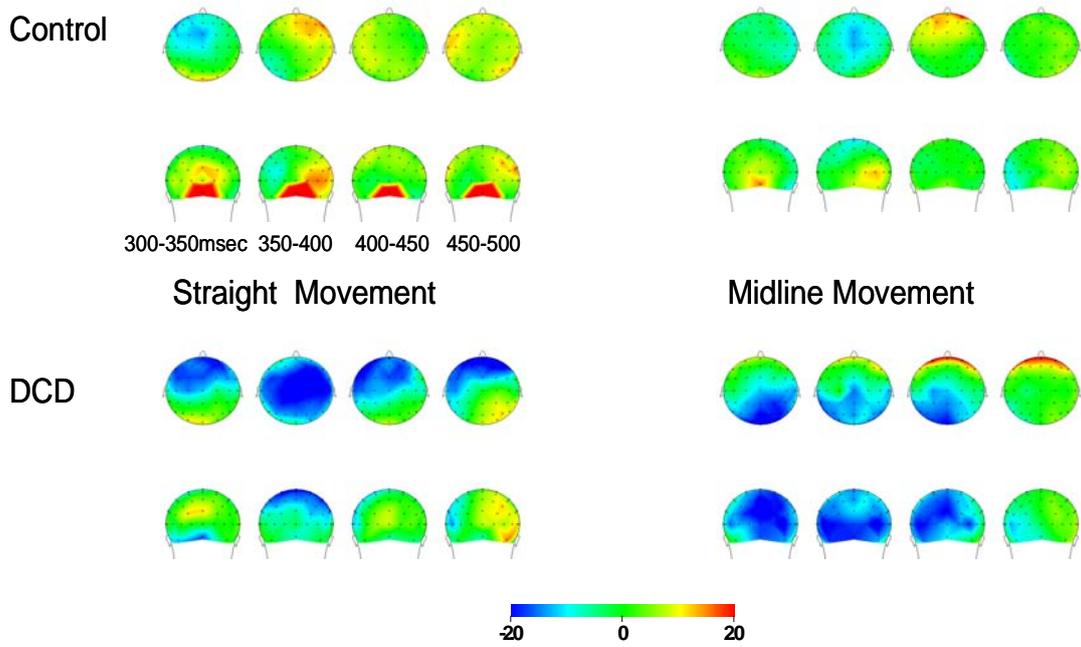
Figure 6.2. Topographic scalp distribution of activity for both groups and movement conditions during the 300-500 msec time window post cue. Note the lateralised activity over the frontal region for the control group during the straight movement and the posterior positive lateralisations present for the control group over central and posterior regions.
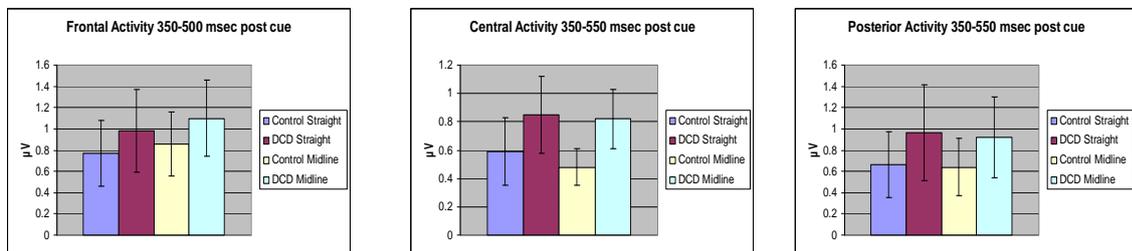
Figure 6.3. Pooled regional activity for the groups during the early ADAN time window.
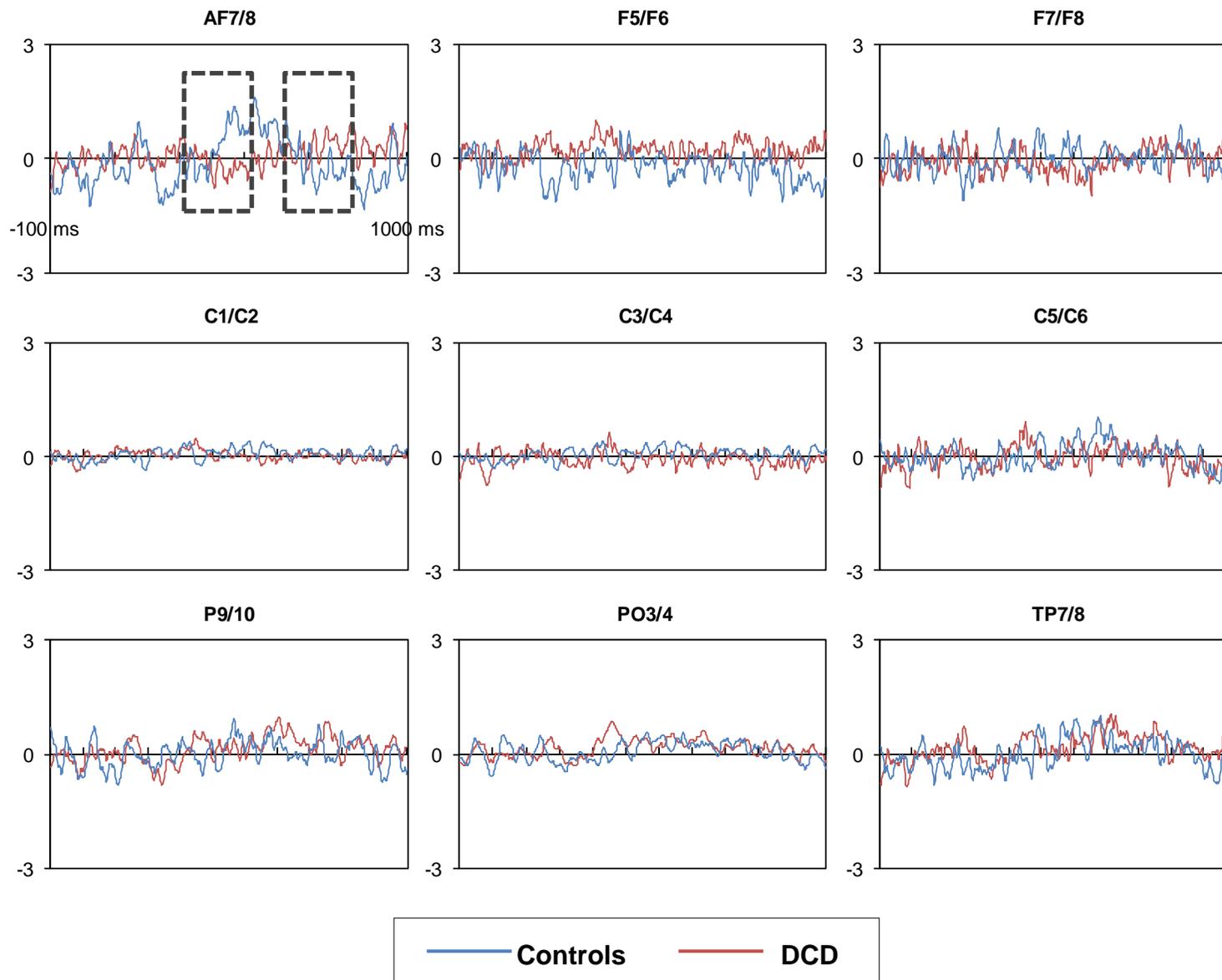
Figure 6.4. Difference waveforms showing lateralisation between electrode pairs/hemispheres during preparation of the straight movement condition. The grey boxes represent the time intervals examined for the ADAN (300-500 msec) and LDAP (600-800 msec) components.
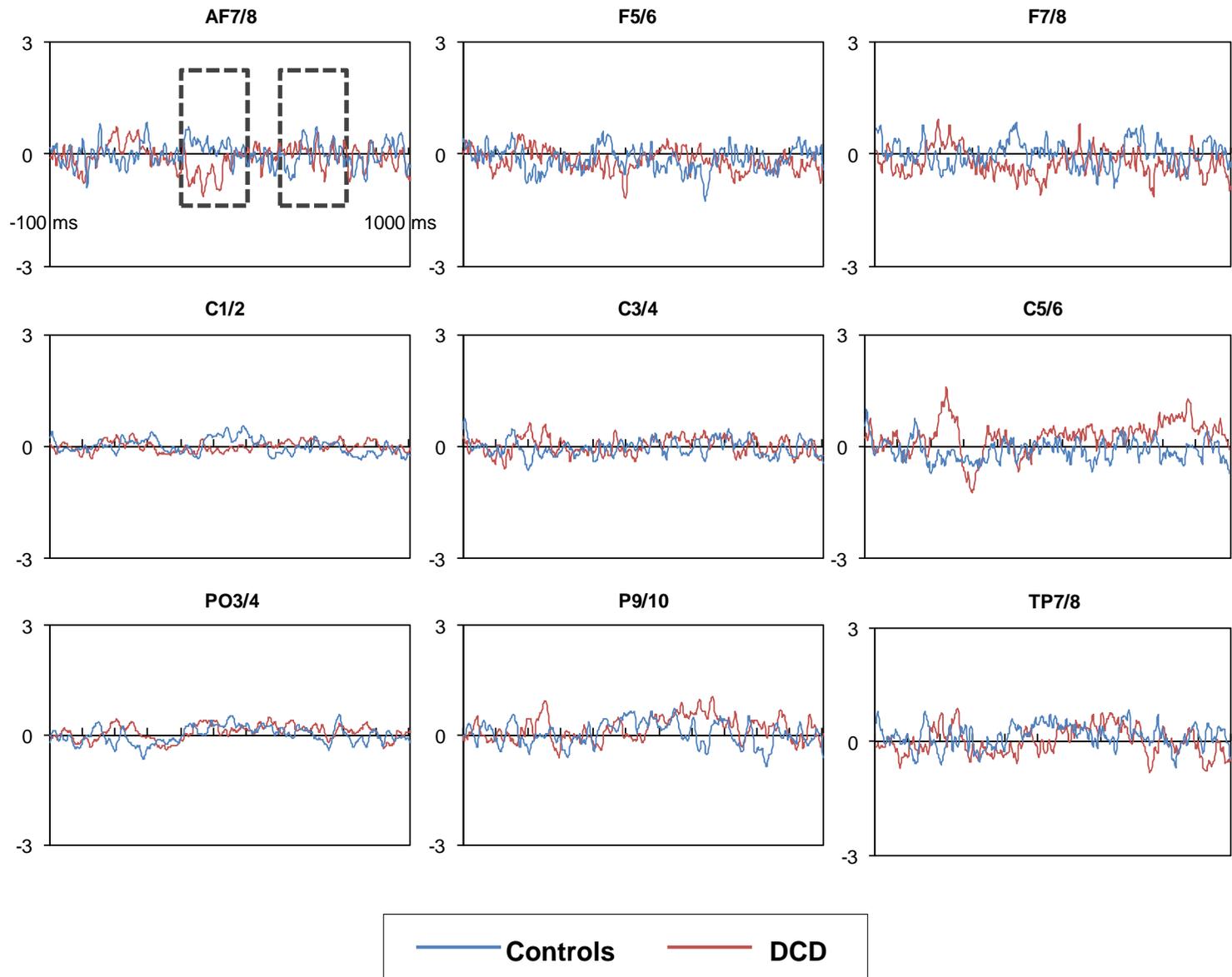
Figure 6.5. Difference waveforms showing lateralisation between electrode pairs/hemispheres during preparation of the midline movement condition. The grey boxes represent the time intervals examined for the ADAN (300-500 msec) and LDAP (600-800 msec) components.

Table 6.1.

Summary of results from analysis of ADAN component

Frontal Region	- Main effect of group.
	- ADAN identified for control group during straight movement over single electrode pair.
	-No main effect of condition on frontal activity.
	-DCD group significantly more frontal activity than control group (pooled effects analysis).
Central Region	-Main effect of group.
	-DCD group elicited same activity (non lateralised) between conditions.
	-Control group showed central lateralised activity (LDAP) during the midline crossing condition.
	-DCD group significantly more central activity than the control group (pooled effects analysis).
Posterior	-Main effect of group.
	-Control group showed lateralisation (LDAP) during straight movement and midline crossing condition.
	-DCD group showed no lateralised effects over posterior regions.
	-DCD group showed greater posterior activity compared to control group (pooled effects analysis).

LDAP component (600-800 msec post cue stimulus)

A repeated measures ANOVA was performed with the following factors: Movement Condition (straight, midline movement), Cue (left, right), Region (frontal, central, posterior), Electrodes within regions (frontal AF7/AF8, F5/F6, F7/F8- central C1/C2, C3/C4, C5/C6 posterior P9/P10, TP7/TP8, PO3/PO4), Hemisphere (ipsilateral, contralateral to cue) with group as the between subject factor. This first set of analyses was performed to establish any regional effects of lateralisation (Cue x Hemisphere interactions) during which the LDAP component appears post visual response stimulus. Please refer to Table 6.2 for summary of the LDAP analysis results. Figures 6.4 and 6.5 above provide difference waveforms between electrode pairs during the interval between visual response cue and the appearance of the visual go/nogo stimulus for both movement conditions. Figure 6.6 shows the topographic scalp distribution of activity during the 600-800 msec time window post cue for both groups and conditions. Figure 6.7 shows pooled regional activity for the groups during this later time window. A main effect of group was identified [$F(1,20)=7.68$, $p<.012$]. Differing regional distribution of the effects was evidenced by a main effect of Region [$F(2,40)= 12.55$, $p<.001$] however the non significant Region x Group interaction [$F(2,40)=1.21$, $p=.308$] showed that both groups demonstrated similar regional distribution of enhancement during this time window. A significant interaction of Cue x Hemisphere x Electrode [$F(2,40)=3.31$, $p=.047$] identified that for an electrode pair lateralisation was present during the later time window. This initial analysis reveals that during the late time window, lateralised effects were present, however these were limited to a particular electrode pair. Specified regional effects and group differences will be reported in subsequent analysis in addition to any electrode interactions that were present.

LDAP analysis by region

A secondary set of analyses were conducted using the repeated measures ANOVA reported above with the region factor removed to examine isolated regional characteristics between groups and conditions. Factors were Movement Condition (straight, midline movement), Cue (left, right), Electrodes with region (frontal AF7/AF8, F5/F6, F7/F8 , central C1/C2, C3/C4, C5/C6 posterior P9/P10, TP7/TP8, PO3/PO4) Hemisphere (ipsilateral,contralateral to cue), with Group as the between subjects factor.

Frontal Region

The results of this analysis showed a main effect of Group [$F_{(1,20)}$= 4.80, p=.040] however no main effects of Movement Condition [$F_{(1,20)}$= 1.22, p=.281] or Cue [$F_{(1,20)}$= .026, p=.875] were identified. No further interactions were present that would suggest lateralised effects were present for either group over the frontal region for both movement conditions. This analysis identifies that over frontal regions during the 600-800 msec time window, no lateralised effects were present for either group. It was confirmed that the DCD group showed significantly increased frontal activity compared to the control group; [t(20)=-2.19, p=.040]. See Figure 6.7 for pooled activity over the frontal region for the groups.

Central Region

A main effect of Group was identified [$F_{(1,20)}$= 4.38, p=.050] however no main effects of Movement Condition [$F_{(1,20)}$= .005, p=.945] or Cue were present [$F_{(1,20)}$= .057, p=.814]. A non significant interaction of Movement Condition x

Group [F(1,20)=1.21, p=.283] was identified. A Cue x Group interaction [F(1,20)=6.24, p=.021] highlighted that a group showed increased central activity for one of the cues. There was a significant interaction of Movement Condition x Cue x Hemisphere x Group [F(1,20)= 4.93, p=.038] identifying that for one of the conditions central lateralised distribution was present within the groups.

In order to identify the movement condition for which a central lateralised activity was present a repeated measures ANOVA was performed with group and movement condition factors removed thus each movement condition was examined individually for each group. Control group data will be presented first. Analysis of central region data during both movement conditions did not identify any interactions that would suggest lateralised effects over the central region for the control group. Similar analysis of the DCD group's data identified a significant interaction of Cue x Hemisphere x Electrode [F(2,20)= 4.99, p=.015] showing that a lateralised effect was present for an electrode pair during the straight movement condition. Analysis of the midline movement data did not identify any significant interactions that would suggest lateralised effects during the midline crossing condition for the DCD group. In order to investigate the direction of the lateralisation for the DCD group, double subtractions were computed over the central region during the straight movement. The mean lateralisation values obtained from the double subtraction revealed that the lateralisations for electrode pair C5/C6 (M=.11, SD=.31) were in the positive direction suggesting a central distribution of the LDAP component (See Figures 6.4 and 6.5) for the DCD group. In order to investigate the main effect of group a comparison of pooled central activity was performed. This analysis confirmed that the DCD group showed significantly increased activity over the central region

compared to the control group; [t(20)= -2.08, p=.050]. See Figure 6.7 for pooled activity over the central region for the groups.

Posterior Region

A main effect of Group was identified [F(1,20)= 11.52, p=.003] however no main effect of Movement Condition [F(1,20)=.520, p=.479] was present. A main effect of Cue [F(1,20)= 7.05, p=.015] was identified in addition to a significant Cue x Group interaction [F(1,20)= 6.42, p=.020]. A significant interaction of Movement Condition x Cue x Hemisphere x Group [F(1,20)= 7.65, p=.012] showed that lateralised effects were present over the posterior region. Furthermore, a significant interaction of Cue x Hemisphere x Electrode [F(2,40)=4.79, p=.014] identified a lateralised distribution over the posterior region for an electrode pair.

A secondary ANOVA was performed removing the condition and group factors to identify the specific movement condition for which lateralised activity was present for the groups. Analysis of the control group's data did not identify significant interactions showing that for the straight movement the control group did not show any posterior lateralised activity. Analysis of the midline movement for the control group revealed a significant interaction of Cue x Hemisphere [F(1,10)= 7.27, p=.022]. Analysis of double subtractions performed over the posterior electrodes revealed PO3/4 (M=.17, SD=.17), P9/10 (M=.15, SD=.29), and TP7/8 (M=.03, SD=.18) demonstrated positive lateralisation over the posterior region (See Figures 6.4 and 6.5). Analysis of the DCD group's posterior data identified a Cue x Hemisphere x Electrode [F(2,20)= 8.11, p=.002] interaction showing a lateralised effect for a particular electrode pair during the straight movement condition. Analysis of the

direction of the lateralisations via double subtractions identified positive

lateralisations for electrode pairings PO3/O4 (M=.15, SD=.22) and P9/10 (M=.08,

SD=.47) showing the presence of a posterior LDAP component.   Analysis of the

midline movement condition did not identify ademonstrating that lateralised activity

was not present over the posterior region during the midline crossing condition. In

both groups the observed posterior lateralisations were in the positive direction

supporting the presence of an LDAP component.

 In order to investigate the main effect of group a comparison of pooled posterior

activity between groups was performed. This analysis confirmed that the DCD group

showed increased activity over the posterior region compared to the control group;

[t(20)= -3.39, p=.003]. See Figure 6.7 for pooled activity over the posterior region for

the groups.   Follow-up analysis of the Cue factor revealed greater posterior activity

when a participant was cued to move the right hand (M=.66, SD=.35) as compared to

the left hand (M=.55, SD=.22); [t(20)= 2.37, p=.028]. Investigation of the Cue x

Group interaction revealed that the DCD group showed greater posterior activity in

response to right cues (M=.87, SD=.37) compared to left cues (M=.66, SD=.22);

[t(10)= 2.77, p=.020].
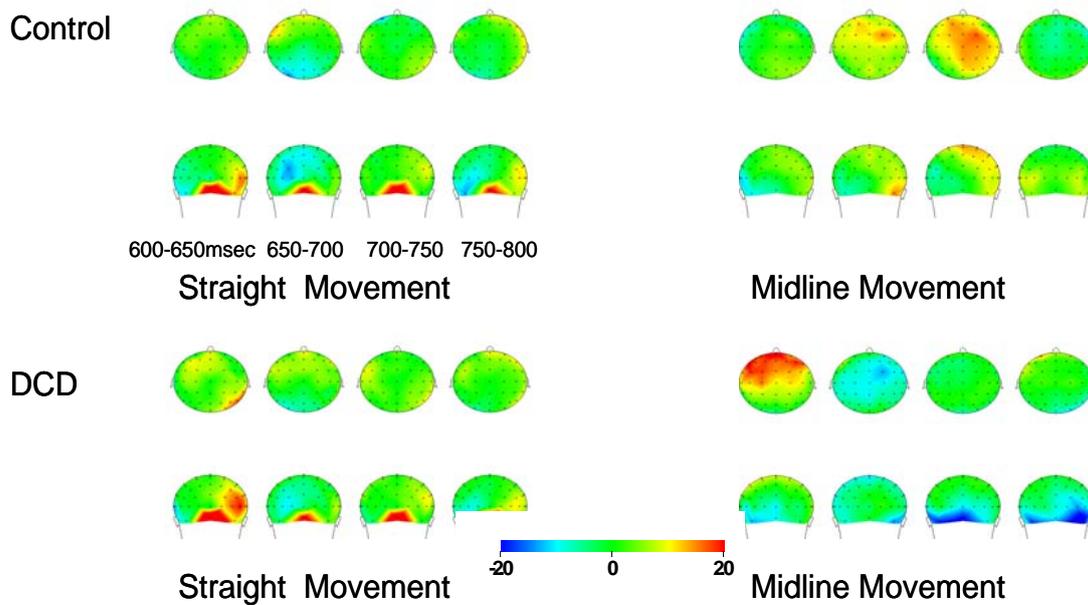
Figure 6.6. Topographic scalp distribution of activity for both groups and movement conditions during the 600-800 msec time window post cue. Note the lateralised activity (LDAP) over the central region for the DCD group during the straight movement condition for electrodes C5/6. Over the posterior region the DCD group showed an LDAP during the straight movement condition for electrode pairs PO3/4-P9/10 whilst the control group showed LDAP activity during the midline movement condition over posterior electrode pairs.
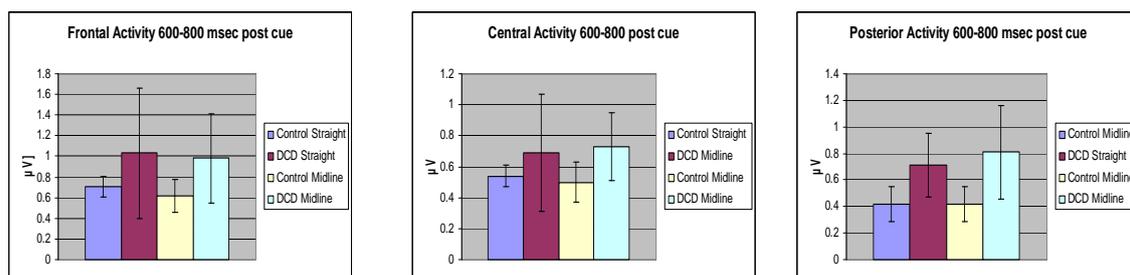
Figure 6.7. Pooled regional activity for the groups during the later LDAP time window.

Table 6.2.

Summary of results from analysis of LDAP component

Frontal Region	-Main effect of group.
	-No lateralised activity for either group.
	-No group differences regarding enhancement between movement conditions.
	-DCD group showed greater frontal activity than control group.
Central Region	- Main effect of group.
	-Control group did not show any lateralised activity for both movement conditions.
	- DCD group showed lateralised activity (LDAP) during midline crossing condition but not straight movement condition.
	-DCD group expressed greater central activity.
Posterior Region	-Main effect of group.
	-Control group showed lateralised activity (LDAP) during midline crossing condition.
	- DCD group showed lateralised (LDAP) activity during straight movement condition.
	- DCD group expressed greater posterior activity.

The aim of the investigation presented within this chapter was to examine ERP correlates of frontoparietal activity associated with attentional modulation during the preparation of a manual response. Results indicate that adults with DCD showed delayed coupling and activity of the early frontal and posterior lateralised ERP components compared to their typically developing peers. These components are suggested to reflect a sensory consequence of movement preparation underpinning examination of the movement environment. The potential consequences of the findings will be discussed below.

Discussion

Previous research has demonstrated that attentional control mechanisms and motor preparation are functionally linked and are implemented by overlapping neurological mechanisms. The present study aimed to investigate if a group of adults with DCD employs similar preparatory control processes as their typically developing peers active during motor preparation of a unimanual response to a goal . This investigation also aimed to replicate previous findings in typically developing adults that have identified preparatory sensory components ADAN/LDAP and their appearance during covert unimanual response preparation. Additionally, any differences between the two participant groups would provide support for the continued presence of discrete neurological difficulties into adulthood for those with DCD and more importantly identify atypical integration of early selective processing as a key underlying difficulty in those with DCD.

Electrophysiological studies have identified two distinct neurological markers (ADAN/LDAP) during cue-target intervals for both shifts of spatial attention and movement preparation (Harter et al, 1989; Eimer at al., 2006; Hopf & Mangun, 1994;

Yamaguchi et al., 1994).   In typical individuals, these two components are suggested to reflect activity in a frontoparietal brain network responsible for modulation of sensory processing during response preparation. As mentioned above, ERP studies have elaborated on the interaction of motor preparation and selective sensory processes predicted by the Premotor Theory of Attention (Rizzolatti, 1994). This theory concludes that the processes involved in the control of selective attention and motor responses are implemented by common neural mechanisms. Although limited, previous studies examining selective processes in DCD have identified those children with DCD have difficulty with early selective visuospatial orientation difficulties suggesting a general difficulty with early selective processing capacities.

This study is the first of its kind to examine preparatory control processes related to response preparation in adults with DCD. Given the paucity of data available relating to the performance of this group, hypotheses are based on the limited experimental data from this population, and more directly on the performance profiles of children with DCD and results obtained from typical developing individuals. In the current investigation, it was hypothesized that the DCD group would show atypical timecourse and distribution effects of the ADAN and LDAP complexes thus suggesting an overall difficulty with activating the appropriate control mechanisms during the preparation of a unimanual movement. It was further proposed that the arguably more difficult midline crossing movement condition would lead to decreased ADAN/LDAP enhancements in the DCD group suggesting that task complexity or conflicting spatial parameters affects the ability of those with DCD to recruit early frontoparietal control mechanisms.

As predicted, lateralised effects were observed during the ADAN time window in the current study. This early lateralised effect (ADAN) was identified over the frontal region but only for the control group during the straight movement condition. In addition the control group demonstrated early onset of the LDAP component over central and posterior regions during this early time window whereas the DCD group did not show any lateralised activity over the frontal, central, or posterior regions (See Figures 6.4 and 6.5). This finding does add support to previous ERP investigations where lateralised activity has been observed primarily over frontal regions following a visual response cue prior to a forthcoming manual response (Eimer et al., 2005; Gherri & Eimer, 2010). In addition, overall activity across the three regions was much greater for the DCD group during this time window compared to the control group for both movement conditions.

Although the results obtained here do support the initially hypothesized identification of frontal lateralised effects, these lateralisations were only identified for the control group. Although the DCD group did not show frontal lateralised effects, this group did show greater frontal activity than their typically developing peers. Thus, it is plausible that the DCD group demonstrates greater dependence upon frontal regions as opposed to the control group although those with DCD do not appear to show typical lateralised frontal effects in comparison to their typically developing peers. Such an interpretation is in line with the findings of Zwicker et al.'s (2010) fMRI study conducted with children with and without DCD. Results from this imaging study suggest that children with DCD rely more upon frontal regions for motor control thus reducing the integration of more posterior attention mechanisms.

Analysis of the central and posterior regions during the early time window identified lateralised activity for the control group. These lateralised distributions were confirmed to be positive deflections suggesting an earlier distribution of the LDAP component for the control group compared to the DCD group. Although the DCD group showed increased central activity compared to the control group, a lateralised distribution was not identified suggesting that the DCD group may not show a similar distribution of activity over the frontoparietal network as the control group. In addition only the control group showed lateralised activity over the posterior region (LDAP) during the early time window. This provides additional support for earlier recruitment of the parietal aspect of the early sensory processing network for the control group compared to the DCD group as the LDAP was identified during the early time window (300-500msec). As was the case with the frontal and central regions, the DCD group showed increased posterior activity compared to the control group. Interestingly this posterior effect (LDAP) has been observed at later time intervals than the time window probed for the ADAN component and was predicted to be identified in the later 600-800 msec time window. The earlier posterior effects observed for the control group suggest that the typically developing group is considerably more efficient at recruiting posterior regions during response preparation compared to the DCD group.

Lateralised effects in the 600-800 msec time window post visual response stimulus representing the LDAP component were also compared between the two groups and movement conditions. Based on previous ERP studies this lateralised positivity is concentrated over posterior regions and is found to follow anterior negativity lateralisation over frontal structures. Over the central region the only lateralised

distributions (LDAP) that were identified were for the DCD group during the midline crossing condition. No central effects were identified for the control group. Over the posterior regions lateralised distribution (LDAP) was observed for the control group during the midline crossing and for the DCD group during the straight movement condition. As was the case throughout the entire analysis, the DCD group continued to demonstrate increased activity over both central and posterior regions compared to the control group. The increased lateralised activity over the central and posterior regions for the DCD group observed during this late time window may suggest a delayed recruitment of the posterior aspects of the frontoparietal network as these lateralised effects were identified much earlier for the control group during the 300-500 msec interval. Central lateralised effects were only identified during the later LDAP time window for the straight movement and not for the midline crossing movement for the DCD group. This may also provide support for complexity of movement parameters delaying effective coherence between frontoparietal areas involved in early selective processing required during movement preparation. It may be that the increased activity identified for the DCD group suggests later transition of frontal to posterior activity suggesting a reduced coherence between frontoparietal structures involved in response related sensory processing.

The impact of differing movement conditions on the presentation of lateralised effects was of interest during this analysis. The behavioural results obtained from the current study do in fact demonstrate greater error rates and increased reaction time/movement time during the midline crossing condition, particularly for the DCD group (see Chapter 4). As mentioned previously, ADAN and LDAP components have been shown to be reduced during a reaching task where incongruent spatial parameters

were present (Gherr & Eimer, 2007). The results obtained in the current study, though inconclusive, do demonstrate a similar trend for diminished lateralised effects when tasks constraints involve spatially incongruent parameters. This was mostly evident for the ADAN component identified in the control group as this component was not observed during the spatially incongruent midline movement for the control group. In addition the LDAP component identified in the control group showed similar lateralised activity between movement conditions. This finding is not in line with Gherri and Eimers (2007) observation of reduced LDAP activity for spatially incongruent movement patterns thus it is difficult to comment at this stage on how movement incongruence influences the LDAP component and subsequent sensory control mechanisms. Movement condition did not appear to effect overall activity as similar regional enhancement was observed between movement conditions for both groups. It was predicted that the DCD group would show decreased ADAN and LDAP components in response to the arguably more complex midline crossing condition. It is difficult to comment on the effect of movement condition on these ERP components as the distribution was not consistent between movement conditions over the regions of interest for comparison. Although, during the early time window the DCD group did not show activity suggestive of lateralised components of interest during the midline crossing condition, During the later time window the DCD group did in fact show lateralised distribution over the posterior region however this was only during the straight movement condition. This could suggest that complexity of movement may impact those with DCD and their ability to actively recruit those neurological areas associated with sensory processing.

Another interesting finding of the current study was the increased activity over all regions for the DCD as compared to the control group. Previous studies examining frontoparietal activity in the elderly have identified differential brain activation with motor tasks including increased activation of brain areas (Goble et al., 2010; Heuninckx et al., 2008; Ward & Frackowiak, 2003). These patterns of enhanced brain activity are suggested to reflect increased motor task preparation underlying an increased reliance upon selective attention for the incorporation of task-relevant information. In addition, recent imaging studies have shown that individuals with autism demonstrate increased brain activity during visuospatial tasks in comprison to age matched typically developing peers (Sahyoun et al., 2010). It is reasonable to suggest that brain activity is more prominent in the DCD group because of the increased neural recruitment required for task execution, and specifically with sensory feedback processing during the preparation of a forthcoming movement. However, the enhanced activity does not seem to involve enhanced lateralised distribution of activity.

Conclusion

Overall, it appears that the DCD group experience much stronger activation over all regions compared to their typically developing peers during the response planning stage of a reaching task. However, they appear to show atypical recruitment of the frontoparietal network during the preparatory period of a forthcoming manual response evidenced by a lack of lateralised activity compared to the control group. This in turn may reflect atypical prioritisation of task-relevant locations. These findings fit with neuroimaging studies performed in DCD child populations and highlight atypical activation of neurological areas in relation to sensorimotor

transformations in this group.   Returning to our example of reaching towards a glass on the tabletop: If the individual with DCD is unable to effectively employ preparatory control mechanisms, he/she would ultimately make inefficient use of the spatial information available. This in turn may lead to inadequate/less optimal motor output.. The reach may be erratic and variable, possibly resulting in a misguided movement spilling the contents of the glass. Through this example, it is easy to see how an inability to apprioriately adapt visualspatial and preparatory processing based on available spatial information could have a serious impact on coordinated activity throughout daily life. Importantly the results presented within this chapter support continued atypical processing during motor preparation of the adult DCD group, and reflect inappropriate use of frontoparietal control processes which in turn may influence the modulation of sensory processing at task-relevant locations.

Chapter 7

Motor response onset in adults with Developmental Coordination Disorder: Analyses of the Response Locked Lateralised Readiness Potential

Abstract

This chapter aims to investigate the manner in which adults with DCD employ neurological motor areas prior to the onset of a speeded unimanual movement. By utilizing encephalographic measures of cortical motor activation over time, it is possible to examine the characteristics of movement related response processes preceding a unimanual reach to goal. These methods afford a detailed examination of the manner in which adults with DCD employ and activate motor control regions in order to determine if this group demonstrates similar motor related response proficiency as their typically developing peers. Results from this investigation showed that the DCD group demonstrated significantly reduced levels of lateralised activation of motor areas compared to the control group prior to the onset of a cued effector movement to goal.

Introduction

Motor control processes occur in a hierarchical fashion. In summary these involve an initial abstract representation of the goal and task organising and controlling actions that are viable for future programming. This is followed by the incorporation of distinct spatial parameters of the motor plan including effector and endpoint coordinates that allow for the establishment of timing and trajectory of the movement. During the final phase, neuromuscular potentials are synchronized leading to the

effectors being activated. Throughout these stages sensory feedback mechanisms are employed to help guide the movement and account for any online corrections that are necessary. The appropriate incorporation of motor control parameters is imperative for accurate and efficient goal directed behaviour. Within the DCD literature consistent difficulties have been shown when participants with DCD are required to produce a range of processes involved in motor control which would ultimately impact efficient motor output.

A heterogeneous collection of difficulties has been identified within those with DCD and it is still unclear how the atypical integration of sensorimotor and preparatory facilities directly influences movement planning and execution in those with DCD. Indeed, little is known about the processes that lead up to the activation of effectors for a forthcoming movement.   Consistent difficulties with movement preparation and execution have been evidenced in those with DCD through various behavioural outcomes including increased reaction time, movement time to goal, and performance error rates (Henderson, Rose, & Henderson, 1992; Smyth, 1991). It is well documented that children with DCD exhibit less optimal performance with tasks comprised of complex movements, suggesting that increasing the complexity and thus task constraints significantly compromises the manner in which they formulate and execute movement programmes (Wilson & McKenzie, 1998; Wilmut et al., 2006). Considering the literature as a whole, a delay between stimulus and response is present in most studies used to assess the performance of children with DCD. During the time between stimulus presentation and response activation a multitude of perceptual and processing sequences must occur. It is possible that the observed delayed behavioural deficits in those with DCD could stem from atypical cortical

activation underpinning activity of the response hand. This has not been investigated in a specific manner in and it remains to be seen if this process is atypical in those with DCD.

A collection of studies suggest that those with DCD experience difficulty interpreting task parameters and are slow to incorporate task requirements into functional movement plans. The performance benefit of precue information has been investigated with studies demonstrating that children with DCD are often unable to utilize this information to effectively produce efficient motor responses and modify forthcoming movements (Pettit et al., 2008; Smyth & Glencross, 1986; Van Dellen & Geuze, 1998). Other researchers have postulated that the underlying deficits are feedback related and that those with DCD are unable to utilize anticipatory programming mechanisms, forcing a greater reliance upon sensory monitoring which, in turn, restricts the initiation of anticipatory control mechanisms and incorporation of task parameters into appropriate motor programmes (Smits-Engelsman et al. 2003; van der Meulen et al., 1991). Thus, it can be suggested that atypical programming mechanisms upstream from the resulting motor activation may greatly impact the response stage of the intended movement. Processing abilities of individuals with DCD have been studied in detail focusing on kinaesthetic and spatial parameters. The findings of these studies are indicative of slow rates of processing across different modalities (Smyth & Glencross, 1986; Henderson et al., 1994). Although isolated modality difficulties and multisensory processing ability have been shown to be atypical in those with DCD, the significance of these deficits has not been considered with regards to the knock-on effect of effector activation and selection. It is suggested that atypical incorporation of basic sensory and task parameters into a

movement plan would impinge on appropriate effector activation, thereby resulting in the observed prolonged reaction time and movement times commonly reported in those with DCD.

Recent studies of online modulation of motor activity have further elucidated the difficulties faced by those with DCD. Studies involving the online correction of a movement have demonstrated that children with DCD performed poorly when reaching sequentially from one target to another (Wilmut et al., 2006). Recently Hyde and Wilson (2011) performed a double step reaching task with children with DCD. During this task the cued goal location stayed the same for a majority of the trials whilst for some trials this goal location was altered upon movement onset and the child must move to a novel peripheral goal location. These altered trials were termed jump trials. Children with DCD performed the task with greater movement time and error rates during jump trials when required to modulate an online movement in progress compared to the control group. Hyde and Wilson suggest that this atypical performance may reflect an inability to incorporate forward models to update concurrent movement plans. As mentioned in Chapter 1, earlier studies by Wilson and colleagues (2001, 2004) suggested atypical movement modelling in those with DCD based on results from studies of motor imagery and mental rotation tasks. It must be mentioned that other studies of mental rotation tasks have not supported deficits with this task in those with DCD (Snow et al., 1991; Lust et al., 2006), thus it is difficult to comment on the direct influence of feedforward modelling on performance capacity in those with DCD However in another study examining online movement corrections in DCD children, Plumb and colleagues (2008) did not identify a deficit in online correction within a DCD group as compared to typically developing children.

Plumb and colleagues suggest that a general difficulty in formulating movements may underlie the documented correction difficulties recorded in DCD.

However, a collection of additional literature suggests that those with DCD experience difficulties with predictive movement modelling. An earlier study of movement adaptation by Hoare and Larkin (1991) identified difficulties such as predicting flight trajectory, poor postural adjustment, and deficits of hand control across a number of children with DCD during ball catching tasks. These deficits are suggestive of a less organised motor control method and imply that those with DCD employ a compensatory method of muscular activation/adaptation. Studies of timing and force control have also identified difficulties within children with DCD, leading to further suggestions of a feedforward model corruption (Hill & Wing, 1998; 1999). Recent studies investigating more refined grasping activity have also shown that those with DCD have difficulty modulating reaching and grasping activity during dynamic grasping tasks (Leung, 2010, Mak, 2010). These authors suggest a carryover deficit between response cue and action onset relating to the incorporation of movement parameters involved in the feedforward model. Difficulties incorporating effector parameters during forward models of movement would ultimately impede accurate movement, potentially leading to delayed response onset. Imperative to the investigation presented within this chapter is the ability of individuals with DCD to correctly activate a cued effector with efficient time course parameters and commence a reaching task to target.

Motor control physiology has identified several cortical and subcortical structures which are responsible for response selection. The medial loop is often assumed to represent a feedforward system and is involved in the selection of responses that stem from cerebral cortex via the basal ganglia and thalamus back to the supplementary motor cortex (Cruthcer & Alexander, 2000; Strick, Dum & Picard, 1995). A more contextual sensory lateral loop encompassing somatosensory posterior areas appears to be feedback dependent and constitutes contextual adjustments based on current set parameters to improve the accuracy of impending movements (Goldberg, 1985). During simple movements the primary phase of the movement is suggested to reflect feedforward control whereas later stages of the movement fall under feedback control and constitute alterations in response to task requirements. It is still unclear as to the distinct motor control loop that may influence those with DCD however, as mentioned above, a collection of studies suggest atypical feedforward and feedback models may be involved in the observed patterns of atypical movement output in children with DCD (Hill & Wing, 1998; 1999, Hoare & Larkin, 1991; Hyde & Wilson, 2011; Plumb et al., 2008; Wilmut et al., 2006; Wilson et al., 2001; 2004).

One manner of utilizing electroencephalography (EEG) to investigate neurological effects of motor preparation is to study a measurement of movement preparation and activation termed the Lateralised Readiness Potential (LRP). As mentioned in Chapter 2, the LRP is utilized as a measure of motor preparation and is typically found whenever participants are required to execute a movement of the extremities. Previously the LRP has been used as a marker for information processing regarding perceptual abilities and response processes involving motor programming (Hackley & Miller, 1995). The LRP is derived from electrodes placed over the motor cortices

(Coles, 1989; Miller & Hackley, 1992). The LRP provides an excellent measure of the motor system priming for action as this component occurs prior to voluntary movements of the hand and demonstrates maximal enhancement at central sites contralateral to the cued hand (Coles, 1989). The neurologic generators of the LRP have been commonly isolated to the primary motor cortex (Kristeya, Cheyne, & Deecke, 1991; Saski, Gemaba, & Tsujimoto, 1990). The enhancement of this component has been shown to indicate relative central activation on the motor cortices when a response hand is activated and involves the processes that occur between response cue and onset of the response itself (Gratton et al., 1990, Miller & Hackley, 1992; Luethold et al., 1996). In addition, unique characteristics of the LRP have been identified that are suggested to represent conflict resolution prior to response onset during more complex tasks (See Chapter 2). Thus for the current investigation the LRP will be considered as an index of cortical activity underpinning the activation of motor cortices preceding an overt unimanual response.

Although it is evident that a reasonable collection of material is available proposing underlying neurological areas and associated motor control processes, the specific underlying neurological difficulty underpinning the difficulties in DCD is still unclear. In order to progress aetiologic understanding, it is important to combine the use of psychophysiological techniques with existing knowledge of cognitive behavioural performance in those with DCD in order to identify processes that are implicated in the difficulties experienced by those with DCD. All of the studies mentioned above suggest that those with DCD show some difficulty with organising responses or adapting response to varying contextual requirements. In order to properly organise a motor program, force level, direction, and response hand

parameters must be incorporated before a movement plan can commence (Ulrich et al., 1998). The assembly of concrete motor commands requires the selection of the motor programme as well as the specification of all parameters (Rosenbaum, 1980). As it is quite evident that effector parameters must be integrated during preparation of a movement, the difficulties faced by DCD individuals could represent atypical selection and integration of effector parameters into a movement plan or more specifically the activation of the response hand required to initiate the desired movement.

The LRP provides an excellent temporal measure of relative effector selection and represents the time at which response activation occurs. By utilizing this measure it is possible to provide direct psychophysiological evidence of motor activity and more importantly the time taken to initiate this selection from response cue. As mentioned previously behavioural difficulties expressed by those with DCD demonstrate some level of response preparation degradation is present through a variety of tasks. Vital to response preparation is the ability to determine the appropriate response hand and its interaction with other factors such as object location or skill demand of the task. A collection of underlying difficulties in the DCD group ultimately will have a great effect on the ability to incorporate basic requirements of a motor plan. To our knowledge this is the first study to utilize this encephalographic measurement to examine online movement preparation in a group of individuals with DCD. By examining the LRP prior to movement onset it is possible to a) determine if the adult DCD group employs effector activation strategies in a similar fashion to typically developing peers, b) examine the temporal characteristics of response onset following response cue in order to see if the activation of effector for action occurs with similar

timecourse characteristics as controls, c) compare the extent of motor cortex activation as an index of state preparedness, and d) examine the effect of movement complexity on effector activation characteristics.

<u>Hypotheses</u>

This study is the first of its kind to examine cortical activation underpinning effector activation in adults with DCD. Given the paucity of data available relating to the performance of this group, hypotheses are based on the limited experimental data from this population, and more directly on the performance profiles of children with DCD and previous studies examining LRP profiles in typically developing individuals. There are three hypotheses:

1. The DCD group will show delayed build-up and cortical activation following the response cue compared to the typically developing control group.

2. The control group will show delayed and larger LRP activity during the midline crossing condition as this movement involves more complex physical and spatial constraints that require conflict resolution before the response can be activated.

3. The DCD group will not display a differential pattern of lateralisation between the two movement conditions suggestive of a failure to incorporate and resolve complex movement patterns into effective preparatory strategies following a response cue.

Participants

Please refer to Chapter 4 for a review of participants. Data from five members of the control group and one member of the DCD group were removed from analyses as inspection revealed their data to contain a large amount of artefactual interference (movement/ occulomotor) during the time window analysed for the response locked LRP and yielded low numbers of acceptable trials for averaging procedures.

Experimental Procedure

Please refer to Chapter 3 for specific information regarding the experimental task. Figure 7.1 provides a general schematic of the experiment and segmentation time for the LRP examined within this chapter.
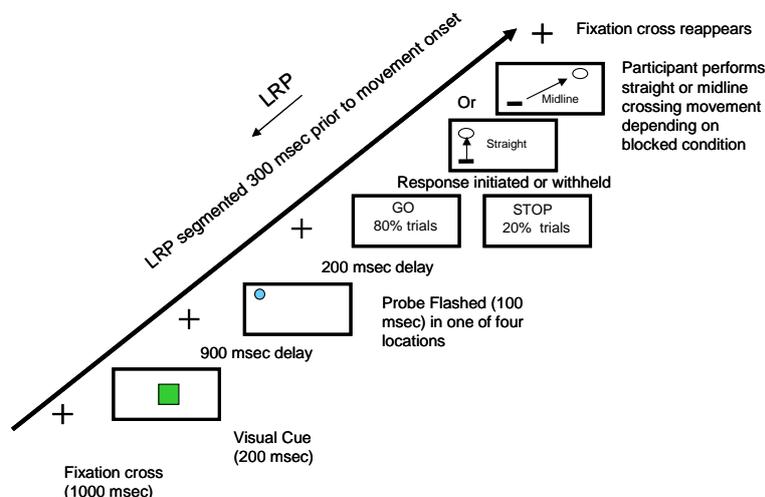
Figure 7.1. Outline schematic of trial. Participant fixates on a central cross, after 1000 msec a green or red square is seen for 200 msec, followed by a fixation cross for 900 msec. Then a probe is flashed in one of four locations (cued/uncued effector; cued/uncued goal) for 100 msec, followed after 200 msec by a stop or go signal replacing the central fixation cross at central screen location. In the 80% of go trials, the participant then initiated a response and moved to the target. Movement conditions were blocked and the participant knew whether the green or red square indicated right or left effector cue in advance of a block of trials. Note the response locked LRP segmentation is relation to response initiation.

EEG Data Recording and Acquisition

Please refer to Chapter 3 for specific information regarding EEG recording

procedures. Trials were initially segmented 500 msec pre response onset to 100 msec

post response onset for left and right handed responses for both movement conditions.

Mean waveform areas were obtained for one pairing of central electrodes (C3/4) for

50 msec time windows prior to movement onset beginning 300 msec baseline up to

movement onset. Anovas were performed on pooled mean area values for both

contralateral hemisphere electrodes and ipsilateral electrodes C3/C4 in relation to

cued effector. These factors were included in order to isolate hemisphere effects

which are present when lateralisation is elicited in relation to response cue and

forthcoming movement. Graphical LRP presentation will be shown in the format

following the double subtraction process (Figure 7.2: LRP= [Mean (C4 left hand-C4

right hand) − Mean (C3 left hand-C3 right hand)].

An initial repeated measures ANOVA was performed on mean area waveform values

prior to movement onset consisting of three within subject factors: Hemisphere

(contralateral, ipsilateral electrode to cued effector), Movement Condition (straight

movement, movement across midline), Time epoch prior to movement onset (0-

50msec, 50-100msec, 100-150msec, 200-250msec, and 250-300msec) and with

Group as the between subject factor. For all subsequent results any interactions where

the condition of sphericity has not been met (Mauchly's test statistic $p < .05$) are

reported using Greenhouse Geisser correction values.

Please refer to Figures 7.2 for LRP waveforms for both groups and movement

conditions and Figure 7.3 for topographic scalp maps reflecting the LRP. This initial

analysis did not identify a main effect of Group [$F(1,20)=.538$, $p=.472$]. A main effect of Movement Condition was identified [$F(1,20)= 11.62$, $p=.003$], however the Movement Condition x Group interaction was not significant [$F(1,20)= .463$, $p=.504$]. A main effect of Hemisphere was identified [$F(1,20)= 6.81$, $p=.017$] confirming greater activity in the contralateral hemispheres over the motor cortices prior to movement onset. As expected the main effect of Time [$F(5,100)= 4.83$, $p=.018$] confirmed differing levels of activity over the motor cortices prior to movement onset between time epochs leading up to the movement. However the Time x Group interaction was not significant [$F(5,100)= 1.88$, $p=.172$]. Movement condition appeared to have an effect on overall central activity prior to movement as evident by a significant interaction of Movement Condition x Time [$F(5,105)= 4.53$, $p=.014$] and Movement Condition x Time x Group [$F(5,100)= 7.96$, $p=.001$]. As expected the interaction of Hemisphere x Time [$F(5,100)= 21.94$, $p<.001$] confirmed that lateralised activity differed between epochs building up to movement onset. Furthermore, a significant interaction of Hemisphere x Time x Group [$F(5,100)= 16.17$, $p<.001$] identified that the groups showed a differing lateralised distribution of activity over the motor cortices prior to movement onset. In order to investigate the main effect of movement condition identified in the analysis above, a pairwise t- test comparing overall central activity for electrodes C3/4 was performed. This identified that pooled central activity was greater for the midline movement (M=-1.28, SD=1.79) compared to the straight movement condition (M=.027, SD=1.06); [$t(21)= 3.57$, $p=.002$].

Following this, the mean area waveform values prior to movement onset were considered for each movement condition separately, using a repeated measure ANOVA consisting of two within subject factors: Hemisphere (contralateral, ipsilateral electrode to cued effector) and Time epoch prior to movement onset (0-50msec, 50-100msec, 100-150msec, 200-250msec, and 250-300msec) with Group as the between subject factor.

For the straight movement condition there was no main effect of Group [$F(1,20)$= .097, p=.759]. As expected a main effect of Hemisphere [$F(1,20)$= 15.50, p=.001] confirmed lateralised distribution of activity over the motor cortices prior to a movement to goal during the straight movement condition. Lateralised activity was present over the motor cortices and differed between time epochs preceding the movement to goal as evident by a significant interaction of Hemisphere x Time [$F(5,100)$= 3.98, p=.017]. Furthermore, the significant interaction of Hemisphere x Time x Group [$F(5,100)$= 5.14, p=.002] confirmed differing patterns of lateralisation between the two groups between the time epochs examined prior to the straight movement to goal.
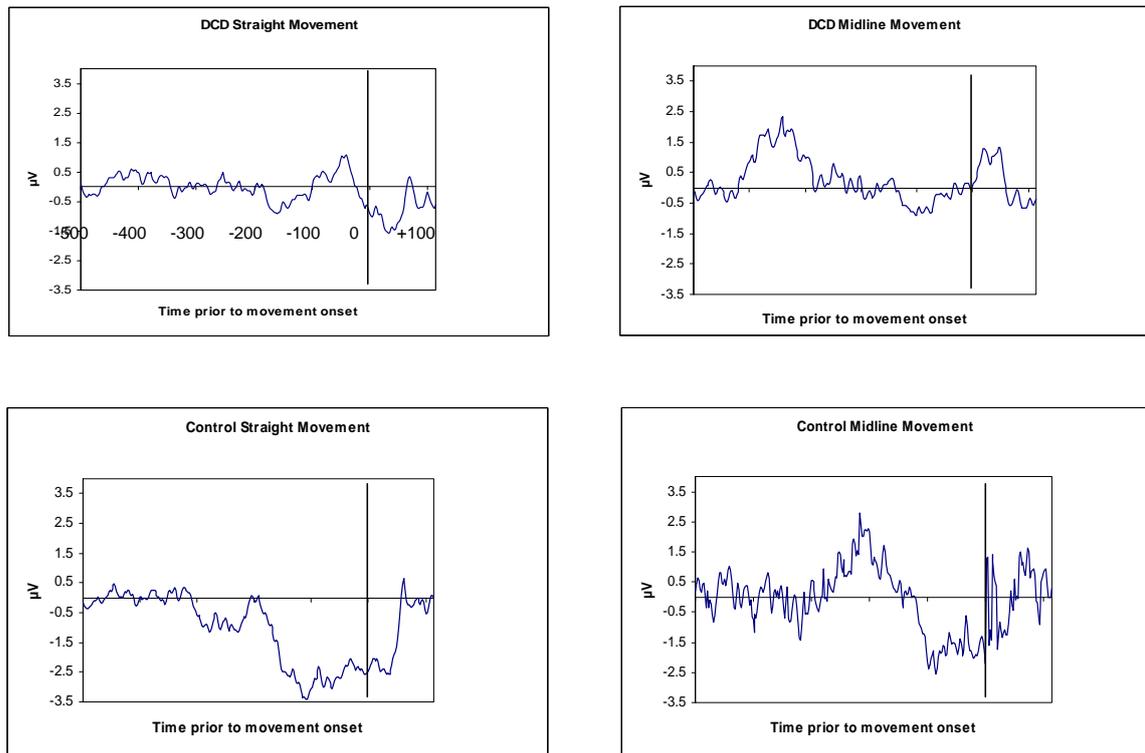
Figure 7.2. Response locked LRP waveforms for both groups and movement conditions. Note the robust negative lateralisation of the LRP for the control group in the bottom two panels prior to response onset (vertical line).

In order to identify the epochs where lateralised activity was present, LRP values were computed for each 50 msec time window prior to movement onset. These values were then t-tested against zero for each group separately in order to identify whether or not the lateralised activity was significant. The LRP was considered to be present if the t-test was significant (see Tables 7.1 and 7.2). The control group showed significant lateralised activity during the final four time epochs preceding movement. In contrast, the DCD group only showed significant lateralised activity over the motor cortex during the 150-200 msec time window preceding straight movement onset although the 0-50 msec time window was approaching significance (p=.053) (see Table 7.2).

225

For the midline crossing condition there was no main effect of Group [$F_{(1,20)}$= .667, p=.424], Hemisphere [$F_{(1,20)}$= .039, p=.846] or Hemisphere x Group interaction [$F_{(1,20)}$= .002, p=.963]. The predicted main effect of time [$F_{(1,20)}$= 7.33, p=.002] confirmed differing levels of central activity prior to movement onset. The significant interaction of Hemisphere x Time [$F_{(5,100)}$= 9.53, p<.001] indicated that lateralised activity over the motor cortices differed between time epochs preceding movement. Furthermore, the significant interaction of Hemisphere x Time x Group [$F_{(5,100)}$= 5.83, p=.004] identified differing hemisphere activity for the groups between the time epochs examined prior to movement onset during the midline crossing condition.

Midline LRP values were computed and t-tested against zero to confirm the presence/absence of lateralised activity for each time epoch prior to movement onset (see Tables 7.1 and 7.2). For the control group negative lateralised activity was observed during the final two epochs preceding movement and positive lateralised activity was present over the motor cortices during the 100-150 msec and 200-250 msec time windows. The DCD group did not show any significant lateralised values prior to the movement onset in the midline crossing condition.

Table 7.1

Results of Pairwise t-tests comparing LRP value to zero performed for 50 msec epochs prior to response onset for the control group during both straight and midline movement conditions.

	Straight	t(8)	Midline	t(8)
0-50 msec	-2.30(2.52)	-2.73, p=.026	-1.94(2.11)	2.77, p=.024
50-100 msec	-2.67(2.10)	-3.81, p=.005	-1.86(1.23)	4.52, p=.002
100-150 msec	-2.93(1.64)	-5.32, p=.001	2.93(1.64)	-5.33, p=.001
150-200 msec	-1.48(1.36)	-3.25, p=.012	.56(1.20)	-1.39, p=.202
200-250 msec	-.54(1.42)	-1.14, p=.286	1.82(1.77)	-3.07, p=.015
250-300 msec	.-88(1.85)	-1.43, p=.191	1.56(2.27)	-2.05, p=.074

Table 7.2

Results of Pairwise t-tests comparing LRP values to performed for 50 msec epochs prior to response onset for the DCD group during both straight and midline movement conditions.

	Straight	t(12)	Midline	t(12)
0-50 msec	-.78(1.31)	-2.14, p=.053	.09(3.71)	.097, p=.924
50-100 msec	-.03(2.01)	-.068, p=.947	-.43(3.56)	-.431, p=.674
100-150 msec	-.76(1.86)	-1.48, p=.164	.765(1.86)	1.48, p=.164
150-200 msec	-1.03(1.52)	-2.46, p=.030	.01(3.21)	.011, p=.991
200-250 msec	-.54(2.04)	-.967, p=.353	.09(3.11)	.115, p=.910
250-300 msec	-.42(1.28)	-1.16, p=.267	.32(3.16)	.367, p=.720
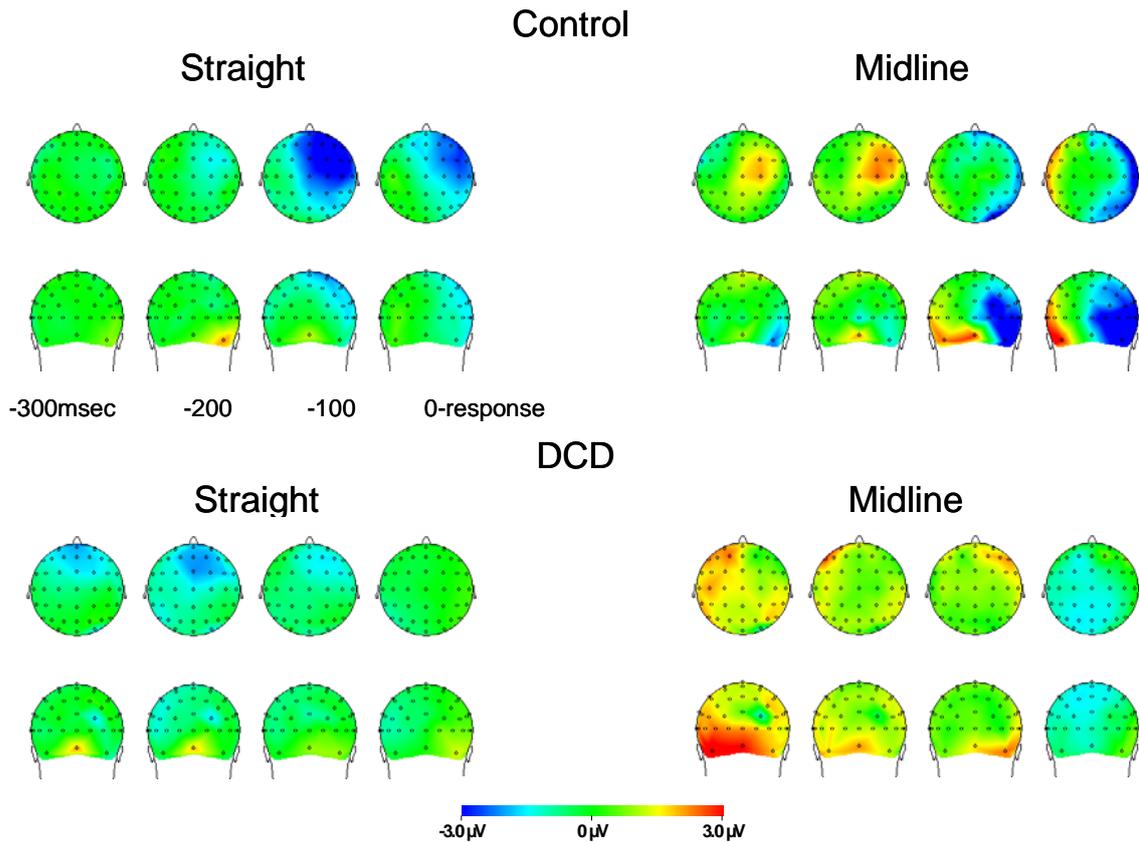
Figure 7.3. Topographic scalp maps of difference waves between electrodes C3/4 representing the lateralised distribution of activity prior to movement onset.

In order to investigate each group's performance a repeated measure ANOVA was performed on mean area waveform values prior to movement onset for each group separately. The ANOVA consisted of three within subject factors: Hemisphere (contralateral, ipsilateral electrode to cued effector), Movement Condition (straight movement, movement across midline) and Time epoch prior to movement onset (0-50msec, 50-100msec, 100-150msec, 200-250msec, and 250-300msec). The control group analysis will be presented first.

For the control group, there was significant main effects of Hemisphere [F(1,8)=8.54, p=.019] and Time [F(5,40)= 9.27, p=.004]. A significant main effect of Movement

Condition [F(1,8)= 13.68, p=.006] showed greater overall central activity for one of the movement conditions (for follow-up analysis of this effect, see below). As expected the Hemisphere x Time interaction was significant [F(5,40)= 9.46, p=.001] confirming the lateralised activity differed between time epochs prior to movement onset. However the Movement Condition x Hemisphere x Time interaction was not significant [F(5,40)= 1.69, p=.219] suggesting similar waveform distributions between the two movement conditions. A significant interaction between Hemisphere and Movement condition [F(1,8)= 12.93, p=.007] showed that contralateral and ipsilateral hemisphere activity differed between the two movement conditions. To explore the interaction of Hemisphere and Movement Condition, comparisons of pooled contralateral and ipsilateral hemisphere activity were compared between movement conditions. This analysis showed that greater activity was present only in the ipsilateral hemisphere during the midline crossing condition (M=-.87, SD= 1.01) compared to ipsilateral hemisphere activity when a movement to straight goal was about to occur (M=.51, SD= 1.22); [t(8)= 5.10, p=.001]. In order to explore the main effect of Movement Condition, analysis was performed on pooled central activity for each movement condition. This revealed that the control group showed greater overall activity over the motor cortices during preparation of the midline crossing vs. straight movements (M=-.91, SD=1.17 vs. M=.06, SD=1.01 respectively); [t(8)=2.92, p=.019].

For the DCD group, there was a significant main effect of Movement Condition [F(1,12)= 6.90, p=.022]. Mo further main effects or interactions were identified that would suggest the presence of lateralised activity over the motor cortices prior to movement onset for both movement conditions. In order to explore the main effect of

Movement Condition, analysis was performed on pooled central activity for each movement condition. This revealed that the DCD group showed greater overall activity over the motor cortices during preparation of the midline crossing vs. straight movements (M=-1.54, SD=2.12 vs.M=-.087, SD=1.13 respectively) [t(12)=2.62, p=.022].

In this chapter, the activation of the motor cortical regions underpinning adaptive and accurate limb activation required for a forthcoming movement to goal was examined using the Lateralised Readiness Potential. While preparing a limb movement, adults with DCD did not recruit similar patterns of motor cortical enhancement as their typically developing peers. This was evident by decreased lateralised distribution of activity over the motor regions prior to movement onset.

Discussion

This investigation examined the response related lateralised motor activity prior to the execution of an overt manual response to goal location. Two movement conditions were presented constituting movement to goal locations in the same hemifield as the cued effector or across midline to goals in the opposing hemifield from the cued effector. Based upon previous behavioural studies performed with DCD participants, as well as behavioural and electrophysiological findings using similar tasks in typical individuals, it was hypothesized that the LRPs of those with DCD would show significantly decreased and delayed activity over the motor cortices prior to movement onset. It was also hypothesized that the poor behavioural performance of the DCD group between the two movement conditions would manifest itself in LRP

characteristics that would not show a pattern associated with effective motor behaviour according to the task constraints. More specifically it was predicted that the control group would show an the LRP increased in amplitude and delayed during the midline movement condition compared to the straight movement suggesting a resolution of conflicting spatial codes prior to movement onset. It was further predicted that the DCD would not display a differential pattern of lateralisation between the two movement conditions suggesting a failure to incorporate complex movement patterns into effective preparatory strategies. Importantly, in line with the findings of the data reported in the two previous chapters, the analyses reported above were expected to identify further atypical sensorimotor abilities in an adult sample of individuals with DCD.

As expected, lateralised effects were identified over the motor cortices demonstrating cortical activity for the response hand preceding the onset of the response. It should be noted that these effects were only identified consistently in the control group. Comparison of waveform areas for 50 msec epochs prior to response onset revealed differing group enhancement of the lateralised effect and effects of movement complexity. Overall the control group showed more robust lateralisation prior to the onset of the overt movement to target than the DCD group for both movement conditions. Together with the better behavioural responses reported in Chapter 4 for the control group, this finding suggests that the group employed cortical motor areas in a more efficient and timely manner compared to the DCD group when required to reach to goal location. This was evident by the more robust onset and distribution of the LRP for the control group. It was predicted that the arguably more difficult midline crossing movement would induce lateralisations that were delayed and larger

in amplitude due to conflict resolution of the spatially incongruent movement for the control group. This was not the case as the lateralised activity over the motor cortices did not differ between movement conditions for the control group. However, the overall level of non- lateralised central activity was greater for movements to the goal during the midline crossing condition compared to the straight movement condition for both groups. This finding is inconsistent with previous studies that showed that complex movements evoke greater LRP values and greater activity of motor related areas (Hackley & Miller, 1995, Weinstein et al., 1997). The findings of movement complexity and enhanced LRPs in these studies were limited to multiple finger movements and not large limb movements such as those used in the present investigation. Furthermore, the results obtained here fail to support the hypothesis of movement complexity inducing larger LRP effects. It appears that when the typically developing participants as well as those with DCD reached to spatially incongruent locations during the arguably more complex task (i.e., across midline) both groups demonstrated increased central motor activation however this was not evident in the value of the lateralised activity.

Comparing the period of LRP onset for both straight and midline movement conditions, LRPs were minimal in the DCD group and only identified for a single time epoch prior to straight movement response. In addition the DCD group did not show any significant LRPs during the midline crossing condition. For both movement conditions, the control group showed significant LRPs during the time windows preceding the manual response. However the scope of the lateralisation did not differ between the two movement conditions. Given the consistent finding that the response locked LRP is found to be largest directly before movement onset (Kutas &

232

Donchin, 1980), it is interesting that the DCD group showed an LRP during the early time window preceding the straight movement although the lateralised activity appeared to degrade prior to movement onset. This was not the case for the control group in which the LRP was sustained for the time windows preceding the movements to goal. It is clear that an extended delay between peak LRP distribution and response onset was identified in the DCD group as the control group's lateralised activity was much closer to the actual onset of the movement and was sustained for the time windows preceding movement to goals. This may be suggestive of a delay between motor cortex activation and overt movement onset as the control group showed sustained activity over the motor cortices compared to the DCD group prior to response onset for both movement conditions. The inability of DCD individuals to execute response patterns with similar efficiency to their peers has been a consistent finding throughout the DCD literature. Previous studies have suggested that those with DCD posses an underlying difficulty generating internal representations of movements resulting in atypical projections of efference control signals to motor regions resulting in delayed response onset (Wilson et al., 1991). This finding has been taken to support the suggestion that a delay between effector related activation and manual response output is seen in DCD. The differing scope of activation and timecourse characteristics between the two groups may therefore reflect the different effort necessary for motor performance in both groups. Reduced ability to effectively engage motor areas would have serious consequences across a range of tasks and it is plausible that the reduced cortical activity underpinning movement reported in this chapter may account for the observed behavioural shortcomings seen in those with DCD. One possibility is that the timing of the activation is effected and that this impacts upon the adaptive action of the response in those with DCD. However, the

extent to which earlier sensorimotor transformations influence effector activation remains to be confirmed and it may be the case that for those with DCD atypical cortical activation upstream of the response selection process leads to the atypical behavioural responses observed. The findings of the current investigation are also supported by the behavioural data in which the DCD group showed delayed reaction times compared to the control group.

Another interesting finding occurred during the midline movement condition when investigating the direction of the lateralisation preceding response onset. Referring to Figure 7.2 note the positive deflection of the waveform prior to the negative deflection for the control group. Recent studies examining the LRP during tasks involving incompatible response stimuli have identified a positive going deflection prior to the negative shift of the LRP (Taylor et al., 2007; Valle-Inclan & Redondo, 1998). It is suggested that this negative shift represents partial programming of the incorrect response or a conflict monitoring procedure that must occur before the correct response is activated. This positive deflection was present during the 300 msec time window for the control group during the midline crossing condition. However the DCD group showed a much earlier positive deflection outside of the 300 msec time window considered for analysis. The control group showed a robust positive to negative shift representing the transition to response activation. Analysis of the DCD group data did not show any negative lateralisations that could be defined as a LRP following the positive deflection during the midline crossing condition. Thus, it appears that the DCD group employed this putative conflict monitoring procedure earlier than the control group although the DCD group did not appear to transfer to response onset processes as efficiently as the control group (evidenced by

the lack of lateralised response activity). Interestingly this positive deflection was not observed during the straight movement condition for either group and thus it appears that this conflict resolution procedure occurs only when a forthcoming movement contains spatially incongruent parameters. This fits with the aforementioned studies examining LRP characteristics during trials containing incompatible stimuli since this positive deflection was not identified during trials containing congruent response stimuli. It also appears that the DCD group may have difficulty shifting from response monitoring to response onset during more complex movement conditions. This would certainly account for the increase number of effector selection errors recorded for the DCD group throughout the experimental task particularly during the midline crossing condition (see Chapter 4).

  Since this is the first study to use electrophysiological recordings to investigate the likely differences between ERP signals in those with and without DCD, replication of the current findings is imperative. Further work could involve examining the prolonged period before response cue onset as this will provide an indication of executive processing/planning awareness prior to the execution cue.   The Contingent Negative Variation (CNV) is an ERP negative shift that is associated with an anticipated response to expected stimulus and indicates state readiness or expectancy representing sensori-motor processes (Walter, 1964). This would provide an excellent measure of readiness for a forthcoming movement and would provide additional investigation of motor readiness in individuals with DCD. This measurement may reveal interesting differences between the DCD and control groups regarding the planning stage of a movement. Finally it will be important to compare movements with varying degrees of complexity in order to identify specific tasks/conditions in which those with DCD fail to demonstrate effective response activation. These

comparisons would expand the information base surrounding task complexity and its influence on motor preparedness and may identify specific task constraints that influence the performance of those with DCD.

<u>Conclusions</u>

This investigation is the first to examine cortical motor activation using psychophysiological methods with a specific focus on the performance of an adult population with DCD. Overall the control group showed significantly greater levels of lateralisation over the motor cortices than the DCD group prior to movement onset. These findings suggest that the DCD group experiences control strategy difficulties and that these limit the control of efficient motor output and therefore response accuracy. Furthermore, this suggests that those with DCD experience difficulty recruiting the cortical areas required for response onset as well as transitioning to the response phase of the movement plan. Overall, then, it seems apparent that the DCD group failed to employ similar motor recruitment strategies as their typically developing peers.

Chapter 8

An ERP investigation of response inhibition in adults with Developmental Coordination Disorder

Abstract

This chapter aims to investigate the manner in which adults with DCD employ cognitive control processes related to manual response inhibition by examining the timecourse and distribution of ERPs correlated with response inhibition. Since children with DCD have demonstrated decreased inhibitory proficiency in a manual task and have presented difficulties that may suggest atypical inhibitory function with visual orientation, behavioural and biological responses on a Stop paradigm were investigated in an adult DCD vs. typical comparison sample. This allowed investigation of whether cognitive control difficulties are evidenced in both behavioural and biological measurements in adulthood. Results indicate that the adult DCD group demonstrated a decreased ability to recruit neurological inhibitory mechanisms as efficiently as their typically developing peers.

Introduction

Response inhibition is a key feature of executive control and refers to the efficient suppression of action that is deemed inappropriate following online contextual influences (Verbruggen & Logan, 2008). Examples of successful response inhibition include stopping oneself from leaving the pavement in response to an approaching vehicle or withholding a reach towards a hot pan that has just been removed from the oven. In addition, response inhibition has also been shown to be explicitly involved in response timing with overlapping neural areas and cognitive functions (Correa et al., 2010). The ability to effectively employ and modulate cognitive control

processes is of vital importance in order to maintain appropriate environmental and contextual performance (Garavan et al., 1997). Thus, inhibitory control supports flexible and goal-directed behaviour in ever changing environments.

Aspects of goal directed behaviour are atypical for children with DCD. As outlined in Chapter 1, response selection has been a key focus of research in this area with clear difficulties identified with adequate response preparation and modulation of response processes (Henderson et al., 1992; Mon-Williams et al., 2005; Petit et al., 2008; van Swieten et al., 2010). However, response selection is only one component of appropriate goal directed behaviour. A further component crucial for adequate goal directed behaviour to be achieved is response inhibition, and this has not been researched so widely in a DCD population. Possibly the first group of studies to propose evidence for inhibition difficulties in DCD were those of Wilson and colleagues who investigated visuospatial attention in children with DCD using a Posner-like covert orienting of visuospatial attention task (Wilson et al., 1997; Wilson & Maruff. 1999). Both studies reported that children with DCD took significantly longer to shift attention following invalid endogenous cueing compared to typically developing controls. Initially interpreted as a difficulty related to voluntary attention, an alternative explanation was later investigated by Mandich and colleagues. Mandich, Buckholz, and Polatajko (2003) proposed that this pattern of performance may reflect an atypical ability to disengage or inhibit voluntary attention from an invalid to a valid target. Mandich et al. evaluated performance on a similar attentional cueing paradigm in a group of children with DCD, although this time as an index of inhibitory control underlying the inhibitory urge to maintain attention at cued location, and replicated the findings of Wilson and colleagues. That is, children with DCD experienced

difficulty shifting their attention following invalid endogenous cueing yet showed similar performance as typically developing controls following exogenous cueing.

Other forms of inhibition have also been identified as atypical in DCD. Mandich, Buckholz, and Polatajko (2002) investigated manual response inhibition, indexed by an inability to suppress an inappropriate button pressing response during a Simon task compared to their typically developing counterparts. While this difficulty manifested itself via increased numbers of errors withholding a response, the DCD group did not take longer than the typical control group when required to complete the inhibition. In other work, Piek and colleagues (2007a) reported that children with DCD showed no response inhibition difficulties during Go/NoGo tasks compared to their typically developing peers, although the group were poorer on a range of other executive function tasks including working memory and set-shifting.. Thus, although the scant literature concerning the inhibitory abilities of those with DCD suggests inhibitory difficulties, the exact nature of these remains to be fully verified. With a clearer understanding of the nature and extent of inhibitory difficulties in DCD, it will be possible to understand the mechanisms underlying the disorder and thus target more appropriate interventions to these..

Over the past few decades theories proposing models of response inhibition have implied varying cognitive and neurological mechanisms from which response inhibition evolves. A pivotal model of response inhibition presented by Logan and Cowen (1984), termed 'the race model' proposes that inhibitory processes must be stronger than coexisting response processes in order to successfully withhold execution of a response. This requires the continuous assessment of ongoing actions and the endpoint goals of the action requirements coexisting with response

preparation.   If inhibitory response processes are terminated before the selective response

processes commence the response is withheld.   A typical paradigm used to investigate this

model is the Stop-signal-reaction-time task (SSRT) in which participants must stop a response in

accordance with a stop instruction following a go stimulus. For example the participant is

instructed to stop themselves from responding to a visual Go stimulus if it is followed by a

specific signal. Similar Stop-signal-reaction-time (SSRT) measurements across stop conditions

have led researchers to postulate that executive control mechanisms exist that oversee the online

modulation of outcome goals and this competing response model exerts an inhibitory function

over coexisting overt response preparation (De Jong et al., 1995). Consistently, neuroimaging

studies of response inhibition have suggested that the prefrontal cortex (PFC) exerts its effects on

subcortical and posterior-cortical regions including the anterior cingulated cortex (ACC) to

implement the executive control measures responsible for response inhibition (Aron et al., 2004).

It is this area that is suggested to detect conflict when the stimulus does not match the outcome

goal or, in other words, monitors situations that require a response to be inhibited in accordance

with variable environmental influences.

Although there is little research directly examining the inhibitory abilities of DCD individuals

across tasks, inhibitory dysfunction has been identified across a range of developmental and

neurological difficulties suggesting that this executive function is atypical in some of these cases.

While it is not the purpose of this thesis to consider other developmental disorders, it is worth

considering the case of ADHD since task methodologies and neurological correlates of

behavioural performance on these tasks are of relevance to the current study. ADHD is taken as

an example since it is a disorder in which response inhibition is often impaired and the disorder

has been considered by many to have behavioural inhibition at its core (Barkley, 1997). For example, children and adolescents with ADHD have performed poorly across a series of inhibitory measures including Go/Nogo and Simon tasks (Chamberlain et al., 2006; Mobbs et al., 2006; Oosterlaan et al., 1998; Nigg, 2001; Wodka et al., 2007). Neuroimaging data implicates frontal lobe structures including reduced activity in the ACC especially during failed inhibitions for those with ADHD (Pliszka et al., 2006; Rubia et al., 2006). To date, only one neuroimaging study of a DCD sample addresses a similar topic. During a Go/Nogo task, Querne and colleagues (2009) reported that children with DCD showed stronger ACC activation and weaker prefrontal activity compared to their typically developing age matched peers although the two groups did not differ with regards to total number of correct inhibitions, but responses were slower and more variable for the children with DCD compared to typically developing peers. This led Querne et al. to suggest that the abnormal activation patterns identified in children with DCD might suggest that those with DCD are less able than their typically developing peers to switch between Go and Nogo motor programs. While the difference in the activation patterns for the DCD and typical groups might reflect compensatory performance in those with DCD, it may indicate that those with DCD find the task more difficult than their typical peers since imaging studies of typically developing individuals has shown the ACC to be more active when response inhibition difficulty increases (Garavan et al., 2002). Further clues may come from neuroimaging studies that have identified a hemispheric effect in typically developing individuals, with increased right inferior frontal enhancement during response inhibition (Garavan et al., 1999; Rubia et al., 1999). These studies have yet to be investigated across development, thus it is difficult to comment on whether or not DCD children present with immature profiles of neuroanatomical activation related to response inhibition.

Although the exact processing stage of DCD difficulty is yet to be identified, results obtained

from the previously mentioned studies suggest that individuals with DCD may experience a lack

of efficiency in resolving appropriate response programming between the competing inhibition

and programmed response. As described by Buckolz and colleagues (2001), it appears those

with DCD show a response inhibition difficulty that can be compared to stopping a car whilst in

gear relying upon faulty brakes. Those with DCD may be attempting to prevent the movement

from commencing once the program and parameters are established, but may not be able to do so

effectively, ultimately resulting in undesirable movement outcomes. It is also plausible that those

with DCD are unable to effectively select the correct response program, or that they demonstrate

atypical compensatory neurological activation required to terminate an inappropriate response.

As mentioned previously, the data obtained from neuroimaging studies examining the

performance of individuals across a range of developmental and neurological disorders have

implied atypical frontal activation. Based on these findings and the limited number of studies

examining response inhibition in DCD, it is possible that those with DCD experience atypical

neuroanatomical activation patterns and that these may underlie the performance difficulties

observed in the DCD population. However, it remains to be confirmed whether response

inhibition is a general difficulty for which those with DCD and which they experience across

tasks and age groups.

As mentioned in Chapter 2, the most commonly reported ERP components of inhibitory activity

are the Nogo N200 and P300.   The exploration of these correlates typically results from using a

Go/NoGo task (e.g., Pferrerbaum et al., 1985) or a stop signal paradigm in which participants are

presented with a stop signal prior to response onset (e.g., Logan & Cowen, 1984). The Nogo

N200 has been shown to differ between tasks requiring a response and those when an overt response must be withheld, with increased enhancement during inhibition tasks (Bruin & Wijers, 2002). The Nogo N200 has been suggested to reflect the initial suppression of an incorrect response at the processing stage (Kaiser et al., 2003; Kim et al., 2007) or conflict resolution within the motor program (Donkers & van Boxtel, 2004).

The functional significance of the P300 remains a matter for debate although it appears as part of the inhibitory ERP continuum and in a similar fashion to the N200 demonstrates an increased amplitude in NoGo trials compared to trials requiring a response (Salisbury et al., 2003). Some researchers have hypothesized that this component reflects sensorimotor inhibition, with greater amplitude for successful inhibition as compared to failed attempts (Liotti et al., 2005; Roberts et al., 1994). Others have argued that the Nogo P300 may be elicited too late to reflect inhibition suggesting that this component may reflect the closure of a preceding inhibition process (Falkenstein, 1999; Nieuwenhuis et al., 2003). It is, however, the case that the P300 component shows a diminished amplitude in participants with ADHD (Liotti et al., 2005). This finding supports the view that a primary deficit lies in the ability to control and pursue the appropriate motor program in those with ADHD. Similar suggestions of a difficulty with motor program control have been made with respect to DCD .

In summary, enhanced N200 and P300 components are commonly elicited during Go-NoGo paradigms and have been linked to inhibitory function and control mechanisms. However, the exact performance processes that these two components discretely represent are yet to be determined. Candidates include conflict monitoring or other cognitive control strategies required for inhibition. These components have been suggested to be reduced in individuals with DCD.

The experimental analyses reported in the current thesis provide the first examination of the psychophysiological functioning of adults with DCD in relation to response inhibition.   The aim of this chapter was to examine if the reduced levels of response inhibition seen in the behavioural analysis (described in Chapter 4) are reflected in atypical ERP components in the DCD group as compared to the typically developing group.

Hypotheses

This study is the first of its kind to examine response inhibition in adults with DCD. Given the lack of data available relating to the performance of this group, hypotheses are based on the performance profiles of typical developing individuals, and reports of response inhibition in children with DCD. Note that the findings and hypotheses relating to the behavioural results of the paradigm have been reported in the Chapter 4 and will be discussed below.   Herein the focus is on predictions relating to the biological (ERP) data. There are two key hypotheses:

1. Atypical response inhibition profile will manifest itself as decreased and delayed inhibitory ERP components N200 and P300 in the DCD group relative to the control group.

2. The control group will show a greater Nogo N200 amplitude during the midline crossing vs. straight movement task confirming greater effort to inhibit more complex tasks. Regarding the DCD group, it is predicted that the DCD group will show a difficulty modulating inhibitory processes during the midline crossing condition as compared to the straight movement. This would be reflected by the DCD group showing decreased and delayed Nogo N200 and P300 during the midline crossing condition as compared to the straight movement condition.

Participants

Participant details are outlined in Chapter 3. The data from four members of the control group were removed from analysis due to their data containing a large number of trials containing physiological interference (occulomotor/facial muscular activity) during the segmentation of the ERPs. The DCD group consisted of 14 members. Please refer to Chapter 3 for group characteristics.

Experimental Procedure

A detailed outline of the experimental paradigm is given in Chapter 3. Please refer to Figure 8.1 below for a summary schematic of experimental trial outline. The number of unsuccessful inhibitions defined as movement after appearance of the Stop instruction were recorded and converted to an error percentage for each participant for preferred and non- preferred hands separately. Results from the behavioural analyses of these data can be reviewed in Chapter 4.
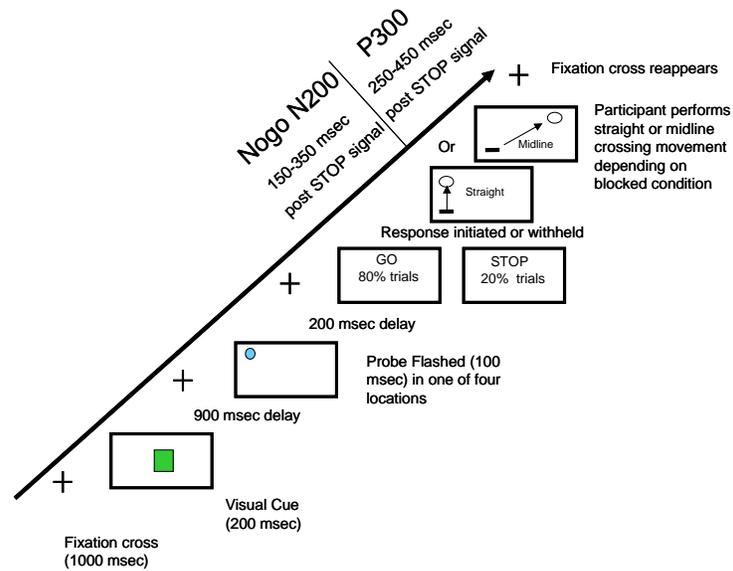
Figure 8.1: Outline schematic of trial. Participant fixates on a central cross, after 1000 msec a green or red square is seen for 200 msec, followed by a fixation cross for 900 msec. Then a probe is flashed in one of four locations (cued/uncued effector; cued/uncued goal) for 100 msec, followed after 200 msec by a stop or go signal replacing central fixation cross. In the 80% of go trials, the participant then initiated a response and moved to the target. Movement conditions were blocked and the participant knew whether the green or red square indicated right or left effector cue in advance of a block of trials. Note the Nogo N200 (150-350 msec) and Nogo P300 (300-600 msec) segmentation post Stop signal in relation to trial outline. Stop signals were presented in 20% of trials.

EEG Data Recording and Acquisition

Please refer to the Chapter 3 (Methods) for specific information regarding EEG recording

procedures. Trials containing Stop signals were collapsed across hands for both conditions.

Initial segmentation of 150-350 msec post STOP signal for both conditions was performed in

order to isolate negative going Nogo N200 ERP waveforms. The Nogo P300 ERP was isolated

for epochs occurring 300-600 msec post Stop signal and was defined as the positive going

deflection during this time frame. Mean waveform peak amplitudes and latencies were extracted

for the epochs mentioned above for both movement conditions for electrodes within each

hemisphere and region of interest, as follows: Frontal (left hemisphere F1/F3/F5 - right hemisphere F2/F4/F6), Central (left hemisphere C1/C3/C5 - right hemisphere C2/C4/C6), and Posterior (left hemisphere P1/P3/P5-right hemisphere P2/P4/P6). Prior to analysis electrodes were pooled within each regional hemisphere.

Results

Behavioural Results

Behavioural responses relating to the stop signal (present on 20% of trials) are outlined in Chapter 4. The key finding of interest to the ERP data reported here is the significant Group x Condition (straight; midline movement) interaction (see Chapter 4). Follow-up t-tests revealed that this interaction occurred because adults with DCD made significantly more inhibitory errors in the midline vs. straight movement condition, while the controls made similar numbers of errors across the two movement conditions. In the current chapter the focus is on analysis of the Nogo N200 and P300 waveforms in order to examine the electrophysiological correlates of behavioural inhibition. The analysis of the two waveforms was performed separately for each of the two ERP components. The first results section reports Nogo N200 findings including the peak amplitude component latency following the stop signal. The later portion of the results section examines the Nogo P300 for similar amplitude and latency measures.

NOGO N200

Initial repeated measures ANOVAs were performed using mean peak amplitudes obtained during predetermined time windows reflecting the appearance of the Nogo N200 (150-350 msecs post Stop cue). Within subject factors were Movement Condition (straight, midline movement),

Hemisphere (right, left), Region (frontal, central, posterior), Electrodes within region (frontal F1,F2,F3,F4,F5,F6-central C1,C2,C3,C4,C5,C6-posterior P1,P2,P3,P4,P5,P6) with Group as the between subjects factor. Interactions that violated Mauchly's Test of Sphericity (sig.<.05) are reported using Greenhouse-Geisser correctional adjustment. Figure 8.2 shows the topographic scalp distribution of the Nogo N200 component and Figure 8.3 contains the grand average Nogo N200 waveforms following Stop instruction for both groups and movement conditions. There was no main effect of Group [(1,22)= .078, p=.783] or Movement Condition [F(1,22)= 2.11, p=.160]. A main effect of Region [F(2,44)= 66.8, p<.001] showed that the Nogo N200 was greatest over the frontal region (See Figure 8.3 for grand average Nogo N200 waveforms). In addition a significant interaction of Region x Group [F(2,44)= 15.89, p<.001] revealed that regional enhancement of the Nogo N200 differed between the groups. Overall this initial analysis suggests that regional enhancement of the Nogo N200 ERP differed between regions and that the groups displayed differing levels of Nogo N200 amplitudes. In order to confirm the regional effect, pairwise t- tests were performed on pooled regional activity. This confirmed that the largest enhancement of the Nogo N200 was present over the frontal region compared to the central [t(23)= -3.64, p=.001] and the posterior region [t(23)=-8.14, p<.001] (See Figure 8.2 for topographic scalp distribution maps of the Nogo N200 and Figure 8.3 for grand average Nogo N200 and P300 ERP waveforms over the three regions following stop instruction). Based on the distribution of the Nogo N200 effect, as reflected by the main effect of region, and in line with the analytic approach reported in previous studies of inhibition investigating the performance of typically developing adults (e.g. Eimer, 1993; Jodo & Kayama, 1992), follow-up analysis will focus on effects observed in the frontal region, which is where the greatest Nogo N200 effects were identified.

In order to investigate frontal effects of the Nogo N200 component, a repeated measures ANOVA with three within subject factors was conducted. Movement Condition (straight,midline movement), Hemisphere (right,left) and Electrode (F1,F2,F3,F4,F5,F6) were included with Group as the between subject factor. Here, a significant main effect of Group was identified [$F(1,22)= 9.84$, $p=.005$], indicating an overall group difference of frontal Nogo N200 activity with the control group showing larger N200 amplitudes (see below for follow-up tests). There was no significant main effect of Movement Condition [$F(1,22)= 3.36$, $p=.080$] nor a significant interaction of Movement Condition x Group [$F(1,22)=1.70$, $p=.206$] showing that the Nogo N200 amplitudes over the frontal region were similar for the groups when withholding responses during the two movement conditions. Furthermore, a non significant interaction of Movement Condition x Hemisphere x Group [$F(1,22)= .924$, $p=.347$] confirmed similar distribution of the Nogo N200 over the two frontal hemispheres for both groups between movement conditions.

In order to investigate the frontal effects of the Nogo N200 for each movement condition, a repeated measures ANOVA with two within subject factors – Hemisphere (right,left) and Electrode (F1,F2,F3,F4,F5,F6) - was performed with Group as the between subject factor for each movement condition separately.

For the straight movement condition, analysis of the frontal Nogo N200 effects did not identify a main effect of Group [$F(1,22)= 3.03$, $p=.096$]. The interaction of Electrode x Group [$F(2,44)= 2.91$, $p=.065$] approached significance. In order to investigate the Electrode x Group interaction that was approaching significance, follow up t- tests were performed for individual

electrodes over the frontal region. This identified that the control group showed greater activity

for electrode F5 compared to the DCD group during the straight movement condition [t(23)= -

2.77, p=.011]. All other electrode comparisons were non significant. Please refer to Table 8.1

for frontal electrode activity for both movement conditions for the groups.

For the midline crossing movement condition, a significant main effect of Group was identified

[F(1,22)= 9.05, p=.006]. A non significant interaction of Hemisphere x Electrode x Group

[F(2,44)= .893, p=.417] revealed that all electrodes showed similar activity between the two

frontal hemispheres for the groups when the groups withheld a movement across midline.
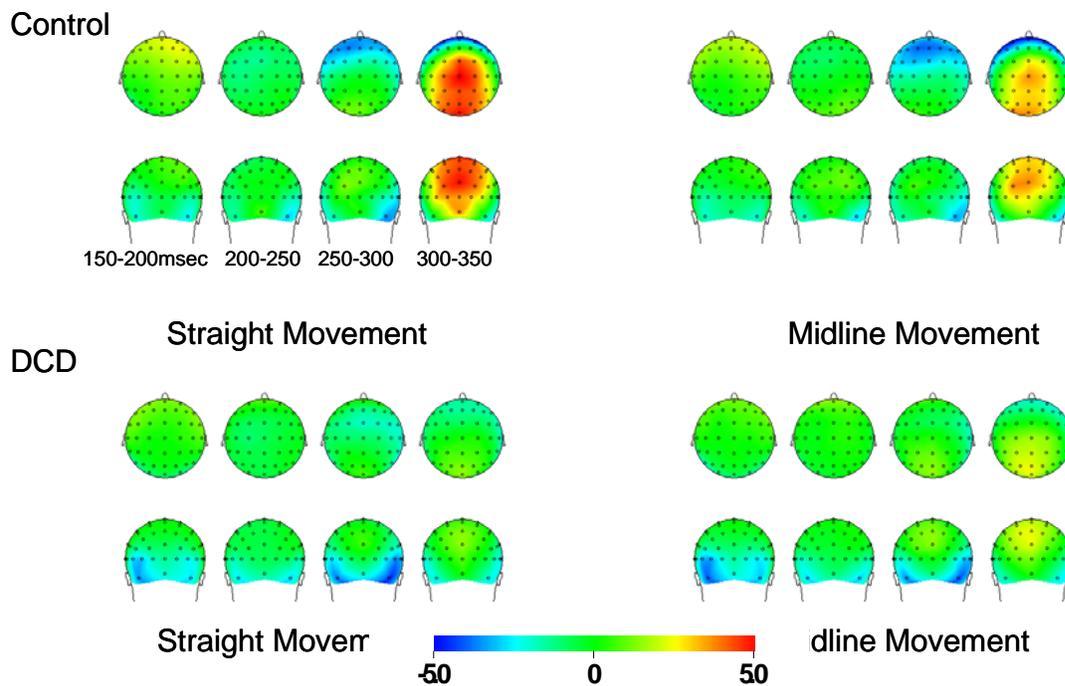
Figure 8.2. Topographic scalp distribution maps of the Nogo N200 150-350 msec post stop

instruction.
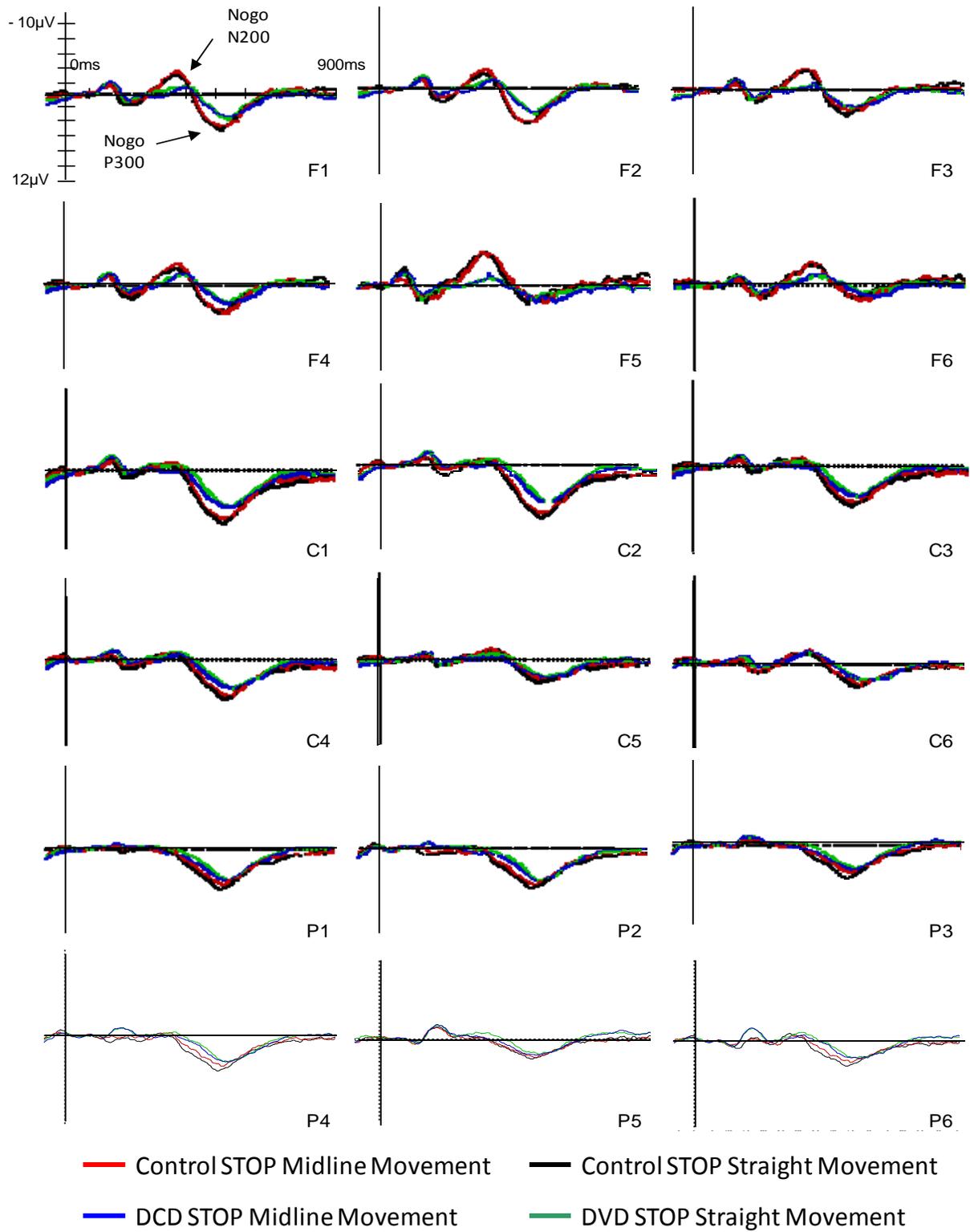
Figure 8.3. Grand average Nogo N200 and P300 waveforms following Stop instruction.

Table 8.1.

Mean values and standard deviations of the Nogo N200 amplitudes (µV) and latencies (msec) over frontal electrodes post STOP instruction for the DCD and control group.

	DCD		Control	
	Peak Amplitude	Peak Latency	Peak Amplitude	Peak Latency
Straight Movement				
F1	-3.57 (1.70)	304.40 (51.61)	-4.28 (1.63)	305.07 (15.8)
F2	-3.18 (.93)	312.63 (39.00)	-3.93 (1.65)	306.83 (13.03)
F3	-3.44 (1.76)	302.45 (52.9)	-4.35 (1.64)	314.64 (22.59)
F4	-3.53 (1.62)	313.89 (37.76)	-3.80 (1.43)	310.93 (17.94)
F5*	-2.81 (1.47)	306.22 (44.24)	-4.65 (1.77)	325.00 (12.96)
F6	-3.41 (1.45)	317.52 (37.67)	-4.63 (1.86)	315.03 (36.38)
Midline Movement				
F1	-3.6 (2.01)	314.31 (43.39)	-5.28 (1.38)	319.92 (17.06)
F2	-3.79 (1.87)	312.77 (40.96)	-4.99 (1.41)	313.08 (26.22)
F3	-3.17 (1.61)	298.54 (56.45)	-5.52 (1.70)	325.39 (16.62)
F4	-3.78 (1.79)	325.47 (32.38)	-5.27 (1.57)	314.84 (28.18)
F5	-3.01(1.54)	306.64 (52.04)	-5.94 (2.09)	332.42 (13.89)
F6	-3.78 (1.86)	325.61 (34.89)	-5.79 (1.87)	325.19 (17.74)

NOGO N200 Latency

As the Nogo N200 component was investigated over frontal regions, latency analyses will focus

on the frontal region within a 150-350 msec time window. Latencies were defined as the point at

which the Nogo N200 component reached its maximal amplitude within the predetermined time

window following the Stop instruction. An initial repeated measures ANOVA was performed

with three within subject factors Movement Condition (straight, midline movement), Hemisphere

(right, left), Electrode (F1,F2,F3,F4,F5,F6), and with Group as the between subject factor. No

main effect of Group was identified [$F(1,22)= .213$, $p=.649$]. A significant interaction of

Hemisphere x Group [$F(1,22)= 9.28$, $p=.006$] showed a group difference between hemisphere

latencies was identified. A non significant interaction of Movement Condition x Hemisphere x

Group [$F(1,22)= .666$, $p=.423$] showed that the frontal latency difference between the

hemispheres was not affected by the movement condition for the groups.   In order to investigate

the Hemisphere x Group interaction, follow-up pairwise t-tests comparing pooled hemispheric

latencies was performed. Results from this analysis identified that the control group showed

similar Nogo N200 peak latencies between the right (M=314.32, SD=16.07) and left (M=320.41,

SD=12.5) hemispheres [$t(9)= -2.01$, $p=.075$]. In contrast, the DCD group showed delayed Nogo

N200 peak latencies within the right hemisphere (317.98, SD=33.63) compared to the left

hemisphere (M=305.43, SD=41.5); [$t(13)= 2.69$, $p=.019$].

NOGO P300

Initial analysis of P300 (300-600 msecs post STOP cue) waveforms consisted of a repeated

measures ANOVA with Movement Condition (straight, midline), Hemisphere (right, left), and

Region (frontal, central, posterior), and Electrode within region (frontal-F1,F2,F3,F4,F5,F6-

central C1,C2,C3,C4,C5,C6- posterior P1,P2,P3,P4,P5,P6) as within subject factors, and Group

as the between subjects factor. Please refer to Figure 8.3 for grand average Nogo P300

waveforms following the Stop instruction and Figure 8.4 for topographic scalp distribution maps

of the Nogo P300 component). There was no significant main effect of Group identified

[F(1,22)= .462, p=.504], Movement Condition [F(1,22)= 1.24, p=.278] or Movement Condition

x Group interaction [F(1,22)= .689, p= .415] . As expected a main effect of Region was

identified [F(2,44)= 16.37, p<.001] showing that the Nogo P300 amplitude differed between the

regions (see Figure 8.2 for grand average ERPs post stop instruction).   No further significant

interactions were identified to suggest overall P300 enhancement differed for the groups between

movement conditions or hemispheres (See table 8.2 for mean peak amplitudes and latencies of

the Nogo P300 for the groups). In order to investigate the main effect of Region, pairwise t-tests

were performed for regional enhancement of the Nogo P300. The results from these confirmed

that the largest Nogo P300 ERPs were observed over the central region compared to the frontal

[t(23)= -5.95, p<.001] and posterior regions [t(23)= -2.50, p=.020].   This analysis shows that the

DCD and control group showed similar Nogo P300 enhancement between movement conditions,

regions, and hemispheres.
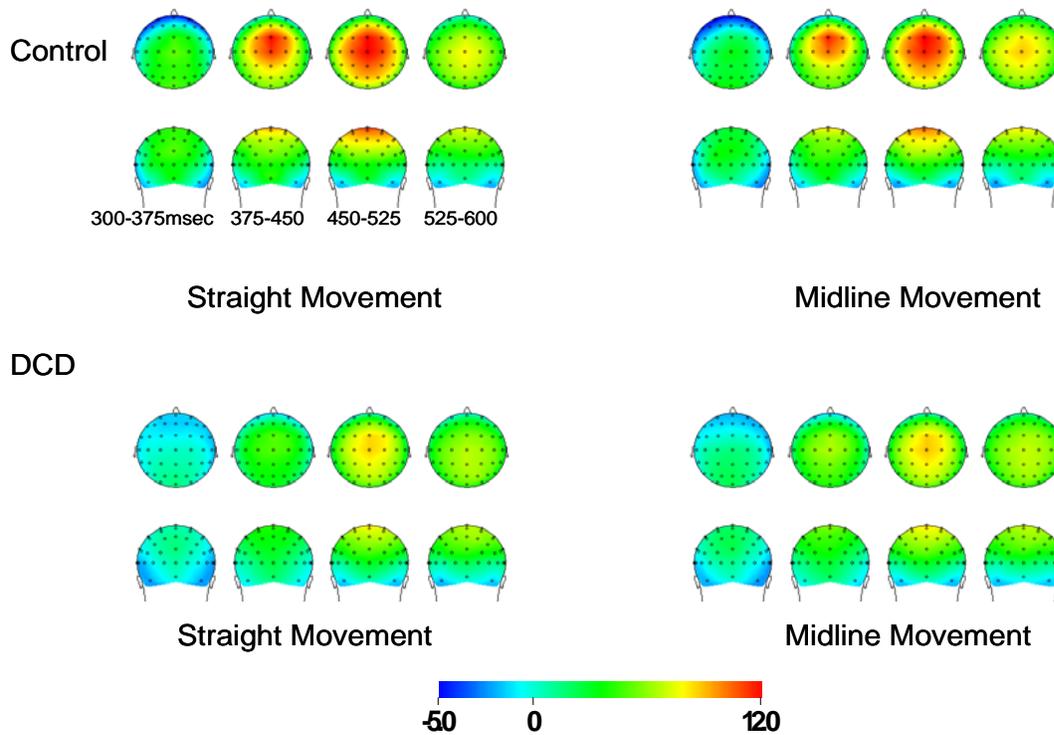
Figure 8.4: Topographic distribution maps of the Nogo P300 300-600 msec post stop instruction.

NOGO P300 Latency

Nogo P300 peak latencies were detected on central electrodes within a 300 msec to 600 msec time window over the central region. Thus for central electrodes, a repeated measures ANOVA was performed with three within subject factors: Movement Condition (straight, midline movement), Hemisphere (right, left), Electrode (C1,C2,C3,C4,C5,C6), and with Group as the between subject factor. No main effects of Group [$F(1,22)= 3.00$, $p=.097$] or Movement Condition [$F(1,22)=.008$, $p=.930$] were identified. A main effect of Hemisphere was seen [$F(1,22)= 7.07$, $p=.014$]. No further interactions were present confirming that the latencies of the Nogo P300 were similar between movement conditions for the two groups. These results indicate that the two groups showed similar Nogo P300 peak latencies post STOP instruction

over the central region. In order to investigate the main effect of Hemisphere a pairwise t-test was performed comparing the pooled latencies between the right and left hemisphere over the central region. This analysis identified that the Nogo P300 peak latencies were observed later over the right hemisphere (M=469.56, SD=33.17) than the left hemisphere (M=459.20, SD=29.64); [t(23)= 2.86, p=.009]. This analysis confirms that both groups showed similar peak latencies of the Nogo P300 over the central region.

Table 8.2

Mean values and standard deviations of the Nogo P300 amplitudes (µV) and latencies (msec) over central electrodes post STOP instruction for the DCD and control group.

	DCD		Control	
	Peak Amplitude	Peak Latency	Peak Amplitude	Peak Latency
Straight Movement				
C1	9.20 (4.16)	466.37 (47.04)	11.52 (5.15)	442.18 (23.65)
C2	9.16(3.76)	464.70 (44.81)	11.39 (5.19)	443.74 (26.20)
C3	7.49 (3.64)	469.44 (41.80)	9.11 (4.51)	440.23 (17.85)
C4	7.07 (2.83)	479.21 (52.34)	8.67 (4.54)	446.48 (27.74)
C5	4.83(2.54)	467.21 (25.51)	5.81 (3.01)	457.03 (35.13)
C6	4.83 (1.85)	507.95 (40.43)	5.59 (2.65)	470.11 (38.75)
Midline Movement				
C1	10.11 (4.96)	458.98 (42.74)	10.92 (4.97)	436.71 (22.72)
C2	10.09 (4.47)	463.86 (41.63)	11.76 (4.92)	440.82 (24.89)
C3	7.98 (3.76)	458.71 (39.02)	8.86 (3.52)	441.21 (23.89)
C4	8.07 (3.34)	470.28 (41.46)	9.01(4.25)	456.83 (20.18)
C5	5.10 (2.45)	478.23 (40.99)	5.36 (2.34)	476.56 (34.69)
C6	5.30 (2.29)	491.49 (43.41)	5.84 (2.87)	475.19 (43.61)

The focus of this chapter was ERP correlates of response inhibition. Since the Nogo N200 and P300 have been shown to be modulated by response selection during the onset or withholding of a manual response, these were the focus of the analyses reported. Analysis of the Nogo N200 component identified that adults with DCD demonstrated decreased frontal activation and a unique temporal distribution between the hemispheres when required to efficiently inhibit a forthcoming manual response. In contrast, no group difference was seen for the Nogo P300 component. The non significant group difference for the Nogo P300 component may indicate that the DCD group processes feedback in a similar way to their typically developing peers following modulation of a planned response.

Discussion

The focus of this chapter has been an examination of the neural correlates of manual response inhibition in adults with DCD. Inhibitory processes were studied in two conditions, one requiring participants to withhold a unimanual response to goal locations in the same hemifield as the cued effector (straight movement), and the other to a goal location in the hemifield opposite cued hand (midline crossing). By considering ERP measures it was possible to compare timecourse and amplitude characteristics of electrophysiological correlates of inhibitory processing, specifically Nogo N200 and P300. Overall, the DCD group showed decreased Nogo N200 activity over frontal regions as compared to the control group however this group difference was more evident when participants were required to withhold a movement during the midline crossing condition. Analysis of the Nogo N200 latency revealed that both groups showed similar peak latencies of the component. When comparing hemispheric distribution of the Nogo N200 latency, the DCD group showed an atypical delay of the N200 peak latency between the two frontal hemispheres. This was not the case for the control group as Nogo N200

latencies were similar between the two frontal hemispheres. Analysis of the Nogo P300 component did not identify any group differences for both peak amplitude or component latency.

The limited research investigating response selection in DCD individuals clearly highlights atypical responses in children with DCD. However, the limited number of studies means that few, if any, conclusions can be drawn from these about inhibitory processing. The focus of the current chapter provides further detail of response inhibition in a manual task in those with DCD. Furthermore, not only is it the first to do so using an *electrophysiological* method, but it is also the first study of response inhibition in *adults* with DCD. The findings provide strong evidence of continued difficulties in terms of response inhibition in adulthood and could suggest an important focus for future investigations.

As noted above, previous studies of response processes in children with DCD have highlighted difficulty with accurate and fluid response execution in both manual response inhibition and visuospatial orientation tasks involving an inhibitory function (Wilson et al., 1999; Mandich et al., 2002). In addition to the few studies that explicitly examine manual response selection in children with DCD, response inhibition and other response based processes have been shown to be atypical in children with developmental disorders (e.g., Oosterlaan et al. 1998; Mobbs et al. 2006). However these findings have yet to be carried over to an adult DCD population

The results of the Nogo N200 analyses support the initial hypothesis that the DCD group would show a reduced frontal Nogo N200 amplitude in comparison to the typically developing group. This was particularly apparent during the midline crossing condition. Analysis of the straight

movement condition revealed reduced N200 enhancement for the DCD group compared to the control group, although this was limited a single electrode (F5). In contrast to the initial hypothesis that the DCD group would show reduced ERP enhancement between movement conditions, Nogo N200 amplitudes were equivalent across conditions for the DCD group. Similarly, the prediction that the control group would show increased Nogo N200 and P300 amplitudes during inhibition of the midline crossing condition was not supported..

Localisation studies have placed the suggested neural generators of the N200 component in the anterior cingulate cortex (ACC) and the supplementary motor area (SMA) (e.g. Huster et al., 2010). One key focus of the analyses was the involvement of the Nogo N200 which has been linked to the aforementioned frontal neuroanatomical structures.   The ACC in conjunction with other frontal structures is believed to evaluate the demand for cognitive control by monitoring for the occurrence of conflict in information processing with greater activity during more complex tasks being recorded during imaging studies of typically developing individuals (Carter et al., 1998; Garavan et al., 2002). The results obtained within the current study did not identify a movement condition effect for the Nogo N200, although the control group demonstrated greater frontal activity during inhibition of the midline movement compared to the DCD group. Interestingly, for the Nogo N200 enhancement, there was no difference between frontal hemispheres for either group and thus the results obtained here do not support the findings of increased right vs. left frontal hemisphere activity that have been reported in previous studies of response inhibition (e.g. Garavan et al., 1999; Rubia et al., 1999).

Comparison of the Nogo N200 latency effects revealed that the groups showed similar peak latencies of the Nogo N200 for both movement conditions. This suggests that the temporal characteristics of the Nogo N200 component are not affected by withholding preprogrammed responses when manual movements are made in different spatial planes under more complex movement conditions. In other words it appears that when required to withhold movements of varying complexity delayed Nogo N200 activity is not observed. Another interesting finding was the differing hemisphere latency effects identified for the DCD group who showed delayed peak latencies over the right compared to the left hemisphere. This finding may underlie an inability to efficiently recruit the right frontal mechanisms of the inferior frontal cortex and suggests atypical coherence between the frontal hemispheres. As mentioned previously, studies of typically developing individuals have identified a greater bias for enhancement observed over the right frontal hemisphere when withholding a response (Garavan et al., 1999; Garavan et al., 2002; Konishi et al., 1998). Interestingly, imaging studies of children and adolescents with ADHD have identified decreased right frontal activity during response inhibition tasks (Overtoom et al., 2002; Sowell et al., 2003). Although the activity between the hemispheres was similar for the DCD group, it appears that the onset of the Nogo N200 is delayed over the right frontal hemisphere in comparison to the left hemisphere in this group.   These findings of reduced inhibitory frontal control enhancement for the DCD group are also supported by the behavioural data which showed that the DCD group exhibited significant difficulty when required to properly withhold a response in comparison to their typical peers (i.e., go when they should stop, see Chapter 4). Thus the electrophysiological data presented here demonstrate an atypical prefrontal activation pattern both in terms of amplitude and timecourse for the DCD group when required to withhold a preprogrammed manual response.

While these findings may be unsurprising to many involved with individuals with DCD, there is a dearth of research in the area of executive functions within the DCD literature. A recent study conducted at Goldsmiths suggests subtle but persistent deficits in some (but not all aspects of) executive functions in a cohort of children with DCD in comparison to well-matched typically developing peers, and that these difficulties may show a different profile to the pattern of executive dysfunction seen in autism spectrum disorder (Pratt & Hill, in preparation; Hill, 2004). Thus the current study adds to a very limited set of data and extends this in terms of one aspect of executive functions – response inhibition – in an adult sample with both behavioural and electrophysiological data. Taken together, these two studies highlight the need to consider executive functions in children and adults with DCD, as well as the theoretical, educational and daily living implications of these.

As noted earlier, a widely accepted model of inhibitory processes termed "the race model" proposes competing processes between concurrent response sets (Logan, 1994: Osman et al., 1986). This model proposes that when two response sets exist in competition with one another, inhibition of the response is achieved only when the inhibitory process terminates before the overt response program. Based on the findings of the analysis of the Nogo N200 component and its suggested link with the initial stage of response inhibition it seems likely that adults with DCD demonstrate a difficulty with the recruitment of frontal structures required for the delineation between competing response patterns both in terms of temporal activity and in overall activity of frontal control structures. Interestingly the most striking group difference regarding Nogo N200 activation occurred during the midline movement condition. It may be that

when those with DCD are required to inhibit a more complex preprogrammed movement the group is unable to employ the initial response inhibition mechanisms as efficiently as when withholding a simple movement. The increased task complexity may delay the manner in which those with DCD select the schema for making a particular movement thus the competing response inhibition process is unable to terminate before the particular movement program is complete resulting in an error of inhibition. This would provide an explanation for the Nogo N200 differences identified between the groups during the midline crossing condition and the increased number of inhibitory errors for the DCD group during the midline crossing condition compared to the straight movement condition.

As mentioned earlier, the anterior cingulate (ACC) and prefrontal areas are responsible for error detection with increased activity within these areas during more complex inhibition tasks. It may be that adults with DCD are unable to effectively recruit these frontal structures in order to evaluate task requirements. The latency effects observed for the DCD group also provide support for an atypical coherence between frontal hemispheres. If those with DCD are unable to actively recruit these monitoring structures efficiently there may be a delay or inability to appropriately choose the correct response (i.e., inhibition) and terminate the programmed response. Although the current results suggest that the DCD group demonstrates decreased frontal activity particularly during a more complex manual response inhibition task, we are unable to attribute this specific finding to the ACC due to the limitations of EEG methodology and localising ERP effects to specific neural generators. Similarly, it is difficult to comment on how the findings of the current study fit with Querne and colleagues' (2009) finding of increased ACC activity in DCD children during a Go-Nogo task. However, it is certainly plausible that as

the ACC is considered a primary locus underpinning Nogo N200 activation, the results presented here can be taken as suggestive of decreased involvement of the ACC and other frontal structures during a response inhibition task for those with DCD. Certainly this proposition warrants future investigation.

In addition to the Nogo N200, the Nogo P300 was investigated as a neural correlate of response inhibition. In line with previous studies of typical adults during response inhibition tasks (e.g., Bruin & Wijers, 2001; Leuthold & Sommer, 1998; Polich, 1993), grand average waveforms and topographic distribution maps showed a maximum amplitude over central regions and these were the focus of further analysis. Overall the DCD group showed similar Nogo P300 amplitudes in comparison to the control group for both the straight and the midline crossing movement condition. Neither group produced differing levels of Nogo P300 amplitude or peak latencies between movement conditions, indicating that the Nogo P300 inhibitory complex was not affected by the experimental task parameters including increased movement complexity for either group.

Although the functional significance of the Nogo P300 is under some debate it seems apparent that this ERP represents a significant procedural aspect of the inhibitory continuum. Over time various interpretations have been put forward regarding the functional significance of the Nogo P300 component to the study of inhibitory processing. Dimoska and colleagues (2006) suggest that this component may reflect an outcome evaluation of the inhibitory process in the motor cortex. The specific cognitive correlate of the Nogo P300 may be obscured by its overlap with motor related activity and may reflect the pursuit of a motor response in comparison to not

pursing a motor program (Verleger, 2006). It seems apparent that the Nogo P300 demonstrates properties that relate to response inhibition, however the specific cognitive functionality it underlies is unclear. Previous work has shown that Nogo P300 enhancement is only present for Nogo trials compared to Go trials signaling that this component may be a better indicator of the execution of response inhibition than the Nogo N200 since it does not appear to be easily manipulated by stimuli and SOA variation (Donkers & Van Boxtel, 2004; Smith et al., 2007). The consistent elicitation and late onset of the Nogo P300 after responses have been initiated in Go trials has also been disregarded as reflecting the initial phase of the response inhibition process. Instead, it has been suggested that it may reflect closure of the process (Falkenstein et al., 1999). In other words, the Nogo N200 component may reflect the initial phase of response inhibition whereas the Nogo P300 may be responsible for closure of this process. Nevertheless the P300 waveform represents an important cognitive function regarding response selection. If this component does indeed reflect the closure of the response processing stage, then the similar amplitude patterns and latencies of the Nogo P300 between the DCD and control groups in the current study may suggest that those with DCD employ a similar feedback or closure mechanism following an inhibitory response as do their typically developing peers. Although feedback mechanisms have been shown to be atypical in DCD children, these findings have been limited to visuospatial and internal modelling paradigms at present (Zoia et al., 2005, Kagerer et al., 2006). Thus further research into this question is warranted.

Just as children with DCD experience difficulties with response selection, so too, it seems, do adults with DCD. Certainly the findings presented in this chapter demonstrate that adults with DCD display functional (behavioural) difficulties with regards to response selection, and suggest

that these are related to an electrophysiological index of atypical performance. Given the current findings, and those showing that children with DCD show atypical inhibition of voluntary attention from an invalid to valid target during visuospatial orientation tasks, as well as poor manual response inhibition, it seems likely that response inhibition difficulties transcend both age and task-type in those with DCD.

Future research should focus on the nature and range of response inhibition tasks that elicit the pattern of findings identified in the current study, as well as the practical difficulties associated with these. One such example can be seen in a recent study of driving abilities in adults with DCD which shoed that adults with DCD were more variable when responding to pedestrians and maintaining accurate driving paths in comparison to typically developing adults (de Oliveira & Wann, 2011). Relating the results reported in the current chapter to a driving task: Consider a situation where an adult with DCD is sitting at a traffic light waiting for the light to turn green. The individual prepares to put his/her foot on the accelerator to move the car forward when a pedestrian enters the area into which the car will travel. This would require the inhibition of the movement of the foot onto the accelerator to ensure that the car does not move forward. It is easy to see how difficulty with this task could be problematic for someone with DCD and thus the importance of understanding response inhibition in adaptive behaviour to ensure safe interactions with an ever changing environment are clear.

Conclusions

In summary, inhibitory mechanisms indexed by the frontal Nogo N200 component appear to be atypical in adults with DCD. Further studies incorporating cognitive behavioural and

neuroimaging methods are required to corroborate the findings presented here.   It will be crucial to study the neural correlates of impaired executive function (in this case, response inhibition) across several tasks, and within the same individuals, in order to evaluate how abnormalities of the Nogo N200 generalize across tasks, or are task-specific. By employing experimental methods that incorporate varying experimental factors such as differing stimulus onsets and double step inhibitory paradigms, more information could be obtained regarding the temporal and activation characteristics isolated within the current DCD group. Future work could also involve examining motor cortex activation and inhibitory processes in unison to examine if these effects demonstrate a symbiotic relationship.   Of course replication of the ERP effects found within this chapter is also needed to validate the findings presented, and comparison of the results with the performance of children on the same tasks would be important in order to demonstrate a profile of inhibitory difficulties that cover the lifespan of those with DCD.

Chapter 9

General Discussion and Implications for Future Research

<u>**Outline**</u>

This chapter will present an overall evaluation of the research conducted within this thesis. First, a brief review of the aims and objectives of the project will be provided. Second, brief summaries of the individual findings will be presented, and integrated with the existing DCD literature. In addition, a model will be presented that highlights the key areas of sensory and motor control dysfunction in those with DCD based on the data that emerged within this thesis. The implications of the current findings for developing understanding of the causes and consequences of DCD will be considered by providing directions for future research. Finally, the study limitations will be outlined.

<u>**Background and justification for current research**</u>

Sensory and motor control abilities are involved in a wide array of functional capacities that are crucial to goal directed and adaptive behaviour. As humans, sensory and cognitive processing mechanisms influence and shape our ability to interact with our environment. The literature reviewed in Chapters 1 and 2 provides evidence for specific processing and cognitive control procedures imperative for effective motor related behaviour. Indeed, the central concern of this thesis was the interface between sensory and motor control in adults with DCD. Previous research concerning DCD has focused primarily on cognitive-behavioural studies of the difficulties faced by children with DCD. Results from these studies have identified a unique range of performance difficulties (see Chapter 1). These difficulties might be

considered to be representative of atypical sensory integration and control mechanisms that are vital for adaptive behaviour. However, the manner in which these atypical processes influence the movement process has yet to be fully investigated in those with DCD. It was hoped that the investigations presented within this thesis would allow preliminary suggestions to be made concerning the possible interaction of sensory and motor control mechanisms in adults with DCD.

In order to investigate the nature of preparatory sensory and motor control difficulties experienced by adults with DCD, methodologies were adapted from a well-established body of research, in which electrophysiological correlates were examined to study sensory processing under different movement conditions. This approach affords the ability to examine cognitive and sensory driven processes over a finite time course during a range of behavioural tasks. In terms of the ERP measures, the collection of hypotheses within this thesis predicted that the adult DCD group would show atypical effects of the sensory and cognitive control mechanisms vital for coordinated behaviour. The work presented within this thesis is the first of its kind to direct these electrophysiological investigations of preparatory activity and motor control towards an adult DCD population. Importantly, the ERP correlates examined in this thesis have proven their usefulness in studying the interaction between sensory processing and cognitive mechanisms involved in motor control. Investigations examining these interactions are limited in previous research approaches within DCD.

The approaches adopted in the current thesis have proved to be beneficial, leaving many viable avenues for future research. What follows is a summary of the main findings of the research presented in the preceding chapters, along with the

implications of the work as a whole. In addition, beneficial approaches for future applications are described alongside the relevant findings.

<u>Motor preparation and sensory processing</u>

As reviewed in Chapter 1, a large collection of studies with DCD populations have emphasized the atypical relationship between sensory integrative abilities and response selection/modulation. This atypical relationship has primarily been identified through outcomes on behavioural measures in children with DCD. In line with studies overviewed in Chapter 1, the adults with DCD who participated in the current study showed clear movement difficulties in comparison to their peers.   These difficulties were evident not only in a motor assessment battery suitable for much younger individuals, but also in increased reaction and movement times as well as errors of response hand selection and inhibition when reaching to a target. These findings show that adults with DCD experience slow and variable motor output compared to their typically developing peers. Although these findings are interesting and support continued coordination difficulty they were not the key focus of this thesis and thus it is the EEG results that will be the focus of this chapter.

Research within the realm of cognitive psychology examining typically developing participants has identified various selective and sensory processing abilities that are explicitly linked to response preparation. As discussed in Chapters 1, 5 and 6, the information obtained from both behavioural and electrophysiological investigations has elucidated the link between movement preparation and underlying sensory activity exposing the sequential processes involved and their suggested contributions to movement preparation. This sequential organization contains a functional

foundation, which allows the system to accommodate parameters of the movement environment before building a motor plan for the forthcoming movement (Findley & Blythe, 2009).

The contribution of sensory processing to movement was investigated in Chapters 5 and 6. Early selective processes recruited during the preparation of unimanual movements are suggested to be vital for the selection of parameters on which a forthcoming movement is structured. Preparatory lateralised ERP effects (ADAN and LDAP) have been suggested to reflect frontoparietal cortical activity for an early selective attention network (Harter et al., 1989; Praamstra et al., 2005). This network is also suggested to establish profiles of the environment for which a forthcoming movement is being prepared, including trajectory and goal location parameters as a function of motor requirements (Churchland et al., 2006; Rizzolatti et al., 1994). Overall, the DCD group showed a delayed distribution of these preparatory ERP effects as compared to the control group suggesting an atypical reliance upon the frontoparietal structures required for early selective attentional processing following a movement cue. Structures involved in the production of the ADAN/LDAP complex are suggested to underpin control of visuospatial processing often described as having a primary role in the saliency of spatial locations and attention to these spatial locations for which the movement plan is assembled upon (Eimer et al., 2006). An investigation examining visuospatial processing at task relevant locations as a function of early sensory modulation stemming from preparatory motor activity was presented in Chapter 5. The visual N1 was examined as an index of visuospatial processing at locations in the movement environment constrained by the experiment. The data from Chapter 5 suggest that the DCD group showed a similar pattern of

enhanced visuospatial processing at both goal and effector locations as their typically developing peers during straight movements to goal. However, those with DCD demonstrated difficulty with the modulation of visuospatial processing during more complex midline movements. This was evident particularly with the processing at the goal locations of the desired reaching movement, as indexed by decreased enhancement of the N1 component for stimuli presented at the goal locations of the manual movements.

When required to reach to a target, an individual elaborates a motor plan, based on the initial movement conditions (i.e., the locations of the hand and target in action space) (Desmurgot & Grafton, 2000). The aforementioned early preparatory functions are suggested to underlie the ability of the motor system to modulate spatial representations in space for action in turn creating pragmatic spatial maps (Maringelli, McCarthy, Steed, Slater, & Umiltà, 2001; McCourt & Garlinghouse, 2000). These representations afford the existence of multiple accounts of space providing information for the placement of sensory and motor systems. The cue-induced preparatory ERP effects (ADAN/LDAP) are suggested to reflect movement of attentional focus across the visual scene (Harter et al, 1989). Theories of sensory processing have proposed that attentional control mechanisms could be serving as a navigator that helps to formulate primary computation for movement trajectories including action relevant locations (Castiello, 1999; Klein, 2004). Furthermore, it is suggested that the early selective functions indexed by the lateralised ERP complex (ADAN/LDAP) predispose the visuospatial processing (N1) of action related locations. These two processes appear to be symbiotic and act in unison for accurate goal directed movements (Klein, 2004). It is proposed that the early frontoparietal

(ADAN/LDAP) effects represent an initial selective process that guides processing faculties to locations of action as indexed by visuospatial N1 enhancement for stimuli presented at the action locations seen in Chapter 5 (Townsend, 1996).

The combination of results obtained from the analyses of the ADAN/LDAP and N1 data suggest that adults with DCD show atypical recruitment of these sensory processing mechanisms during the preparation of a manual response. Referring back to our experimental task, following the cue, these sensory functions serve to incorporate early reference inputs containing information about the environment within which a movement is required. These early reference inputs include hand and goal locations which aid the establishment of pragmatic spatial maps which are fed into a forward model. Below is a schematic incorporating the sequenced sensory aspects of the feedforward model proposed by Wolpert (1997) which has been adopted to highlight the incorporation of early sensory processing into the movement model and the suggested influence of these early preparatory functions (see Figure 9.1). As can be seen in Figure 9.1, this model receives early sensory information from the processes discussed above and generates an estimate of the movement end-point location as output. The spatial accuracy of the actual and predicted position of the body/movement endpoints may differ as a result of noise introduced into the system by either internal or external sources. It is suggested that adults with DCD are unable to use early sensory capacities reflecting ensuing control parameters resulting in inaccurate distribution of processing resources. The resulting atypical estimate of the movement environment may result in a knock-on effect with corrupt efferent sensory information – on which future motor commands are computed – being projected to the CNS.   It appears that the DCD group is unable to incorporate these early sensory

discrepancies into accurate action profiles and thus poor coordination may stem from

a dysfunction of early sensory inputs present during the preparation of a manual

response. According to the proposed model, if the actual and predicted body positions

differ the difference can be fed back as an input into the entire system so that an

adjusted set of motor commands can be formed to create a more accurate movement.

Although these feedback mechanisms were not examined directly within this thesis, it

is suggested that incorporation of early sensory into the motor planning stage may

also suggest an inability of those with DCD to use continual sensory information.

This would result in an ineffective monitoring strategy throughout the entire

movement process and lead to difficulty with modulating movements in response to

environmental task constraints.
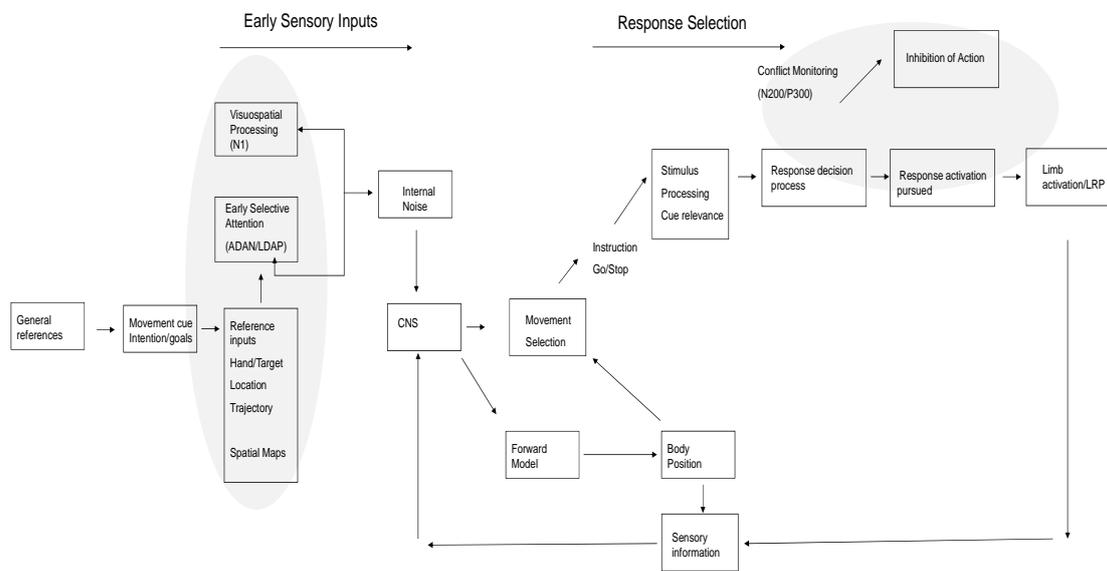
Figure 9.1. This schematic highlights the sequential order of sensory and motor control processes examined in this thesis. Earlier areas of the model are adapted from Wolpert's (1997) feedforward model. Later, response selection strategies are formulated on Riddernkhof et al.'s (2004) model of response selection. Please note the shaded areas are representative of key preparatory sensory and response selection stages of interest. This figure is essentially repeated in Figures 9.2 and 9.3 in which the two processes (sensory and motor

control; response selection) will be separated and the hypothesised difficulties faced by those with DCD highlighted.

The observed difficulties in the DCD group may be a result of inaccurate early reference inputs which establish movement related spatial maps (see Figure 9.2). If in fact the early selective processing stages predispose the visuospatial modulation of action relevant locations, it is possible that the coupling or relationship between these two stages is atypical in those with DCD. This would explain the atypical early processing seen in those with DCD and their difference in relation to their peers in goal location processing during the more complex midline crossing task. Thus, future movement models would be constructed upon inaccurate internal references for action space. This would ultimately have a severe knock on effect with future motor programmes being variable and relying on inaccurate movement related spatial profiles. However, the finding that atypical early processing was seen only during the more difficult movement (i.e., crossing midline) suggests that only complexity or conflicting spatial codes between initial hand location and intended goal have an effect on this relationship in adults with DCD.
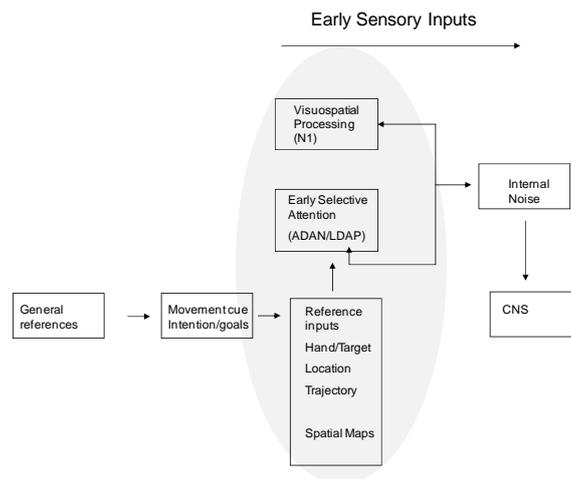
Figure 9.2. Schematic of early processing difficulties in those with DCD. Shaded areas represent levels of atypical movement related preparatory activity in those with DCD. An internal model formulated on abnormal spatial profiles would result in an inaccurate template for which the sensory consequences of the pursued movement are composed. Abnormal reference inputs may result in a distorted effect copy required for spatial representations of the desired motor act. Thus, the predictive representations that specify action coordinated spatial profiles would be atypical in those with DCD.

The overall findings of the N1/ADAN/LDAP analyses add support to theories of action and perception (Klein, 1980; Rizzolatti, 1994; Allport, 1989) which propose that processing of action environments is related to activation in specific movement related spatial maps. These maps are also considered relevant for attentional control, and thus our findings provide additional support for the relationship of sensory processing and response preparation. The data obtained from these analyses also highlight the anatomical and physiological considerations and the sequential organization of sensorimotor transformations that occurs during the preparation of a reaching movement in a group with a clear and overriding difficulty with these processes. In support of this sequenced processing, recent fMRI studies have identified activations of neurological areas in typically developing individuals that

suggest spatial profiles are established during the first phase of the sensorimotor

transformation process, with effector information being added to the movement

composition at a later point (Breuze et al., 2007; Churchland et al., 2006). In line with

the data presented here, these studies emphasize the activation and importance of

early preparatory sensory processes and their sequential influence on future kinematic

pursuits, thus providing additional support for the serial interaction of movement

preparation and early sensory control. Thus it appears that early sensory control

mechanisms upstream from the desired response influence effector selection.

Furthermore, it might be suggested that the unique sensory activity identified in the

DCD group may impact further on motor programming strategies such as the

establishment of accurate effector profiles in this group.

Although difficulty with early sensory capabilities has been documented to some

extent within cognitive-behavioural studies of children with DCD, the current study is

the first to investigate (and identify) difficulties with early preparatory ERP effects in

a sample of adults with DCD. These two measures of early sensory processing

discussed above are indicative of a motor system that is able to effectively incorporate

the early parameters required for adaptable goal-directed movement. Overall, the

ERP data collected here suggest a difficulty with initial sensory activity that reflects

an atypical profile of spatial processing resources for which a forthcoming movement

is structured. Further work is required to ascertain whether these atypical sensory

profiles, evidenced by sensory related ERPs, are present during differing movement

arrangements and tasks. This will be discussed below.

Cognitive control mechanisms of response selection and modulation

While Chapters 5 and 6 focused on early preparatory sensory activity associated with response preparation, another key aspect of adaptive behaviour was the focus of Chapters 7 and 8. This relates to the cognitive control mechanisms of response selection and modulation, specifically the ability to actively engage motor cortical regions underlying the activation of effectors for a pre-programmed response as well as to successfully inhibit a preplanned manual response following a stop instruction.

Overall, the DCD group showed significantly reduced amplitudes of both motor cortical related LRP and the inhibitory component N200 suggesting decreased efficiency with effector activation and response inhibition. These electrophysiological findings, coupled with the behavioural findings discussed above offer support for continued difficulties of motor programming in adults with DCD. These selective difficulties include both cortical activation of areas underlying effector response and the ability to inhibit a selected motor programme. Figure 9.3 proposes areas of difficulty during the response selection stage for those with DCD. This model is adapted from the response selection model proposed by Ridderinkhof and colleagues (2004) and considers the later stages of movement preparation presented in Figure 9.1.

As suggested earlier, all movements require the specification of effectors, movement direction, force and velocity in order to establish a motor program (Schmidt, 1975). The formation of these motor commands implies that specifications of the parameters take place in a hierarchical order and are achieved prior to effector movement onset in accordance with the early preparatory properties (Gnadt & Anderson, 1988;

Rosenbaum, 1980). It is commonly known that optimal motor performance is achieved by preparing the upcoming movements as much as possible in advance (Jentzsch et al., 2004). During the time prior to response onset, information regarding force, direction, and response hand is integrated before a movement plan can move forward (Larish, 1986). Thus, early sensory effects of response preparation are required to establish parameters for which subsequent effector activation is required.

Previous literature within the DCD child population has identified perceptual motor deficits as primary difficulties (Astill & Utley, 2006; Tsai et al., 2009). Research has suggested an overall difficulty with internal modelling or action representation during the internal feed forward model in those with DCD (Wilson, 2004). In summary, internal predictions are present which estimate the mapping of the individual to the parameters of the action environment and are required for successful planning and action execution (Caeyenberghs et al., 2009; Wolpert, 1997). The predictive ability can be used to formulate the potential outcome of a movement facilitating downstream motor areas for both timing and force control of the selected effector response. The interval of the response locked LRP reflects activity after response selection underlying preparatory control over pre-response selection processes and as such has been used as a measure of cortical motor activation upstream from the overt movement. By the time the LRP develops, as well as during the response selection stage, the individual organizes and initiates the appropriate response based on the motor programme. Thus, the LRP onset indicates the onset of the limb-specific motor system, movement direction, and the activation of the appropriate muscle groups. In the study presented here the participants had incorporated these premotoric processes prior to limb activation and were awaiting the response instruction of Go or Stop.
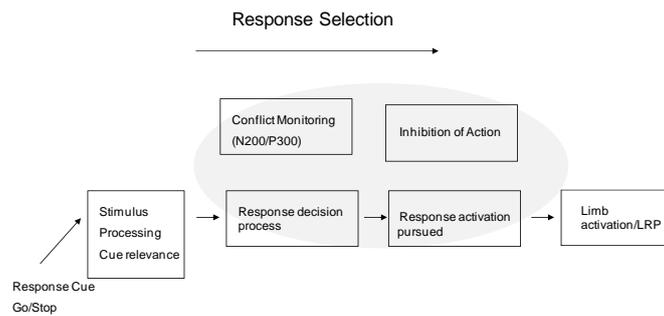
Figure 9.3. Schematic of response selection difficulites in those with DCD. Shaded areas represent levels of response difficulty in those with DCD. In this investigation the response selection strategies followed a response cue (Go/Stop) resulting in stimulus and associated decision processing. Vital to these processes is the ability to compare responses with incoming sensory information. In the case of those with DCD it appears that conflict monitoring via response decision selection and cognitive mechanisms monitoring for congruency between stimulus (Stop) and response is atypical. This results in poor response inhibition and an inability to withold a response. It also appears that movement selection and the neurological activity underlying limb activation appear to be decreased in those with DCD, suggesting that response selection underlying preparatory control over pre-response processes is atypical in those with DCD.

Based on the data obtained within this thesis it appears that the DCD group demonstrated difficulty with processes involved in response generation requiring more time needed to initiate a response. This may include prolonged response preparation particularly when conflicting spatial codes are present in the form of maladaptive reference inputs or during more complex movements (i.e., crossing midline). In other words the DCD group may be experiencing difficulty with establishing internal parameters on which the selection of effectors is constructed, thereby compromising predictive parameters of the movement plan mentioned above (see Figure 9.2). The results obtained here suggest that within the adult DCD group there was an overall difficulty with this procedure and the accompanying integration of movement parameters (see Chapters 5 and 6), particularly with activation of the cortical regions required during the late stage of movement preparation that is limb specific. As the preparatory stages prior to the overt movement involve early planning

and response selection initiated by sensory mechanisms, it may be that atypical incorporation of the early properties of movement has a knock on effect leading to delayed overt movement onset. This suggests that premotor planning, or more importantly feedforward models, may be corrupt in the DCD group providing support for atypical incorporation of movement parameters and a delay between stimulus and response as evident by chronometric markers of motoric processing such as reaction and movement time.

Another explanation of the reduced LRP effects for the DCD group may be its ability to interpret the Go stimulus. Previous literature has shown that children with DCD have a general difficulty in the interpretation of stimuli, and researchers have suggested that this difficulty may be an indicator of atypical planning and control of action (Henderson et al., 1992; O'Brien et al., 2008). Thus pre-motoric processes such as stimulus recognition and the selection of the appropriate response might be prolonged in those with DCD. In the model presented in Figures 9.1 and 9.3 it is suggested that the way preparation interacts with previous task interference involves overcoming difficulty in giving a response after that response has already been selected. This involves a transition stage from central to peripheral motor activity, as distinguished from a preceding motor programming stage (see Figure 9.3). In the proposed model it is suggested that upon appearance of the Go signal a participant must incorporate a decision process to enact the pre-potent response based on a current motor programme. The difficulty in performance identified in the DCD group could result from a feedback and working memory mechanism deficit, that would usually ensure that the response is appropriate for the current stimulus. This would result in a delay between the response decision process and the pursuit of response

activation as appears to be the case in those with DCD. An inability to actively interpret the Go stimulus would result in atypical LRP activation, as seen in the adult DCD group. This provides support for the view that decreased congruency between stimulus and response exists in this group. Certainly, an inability to actively recruit and activate an effector would ultimately lead to variable movement output, as is often observed in individuals with DCD.

Regarding the inhibitory function of the DCD group, behavioural and biological data suggest decreased proficiency of response inhibition in those with DCD. In the experimental paradigm utilized here the stop trials were infrequent (20%). It is suggested that the frequent response (Go) retained a stronger stimulus-response map, and thus the participant had a much higher level of readiness and was primed more efficiently for the required movement. When the participant was required to stop a response the competition between the two response pathways results in conflict monitoring which is a cognitive process undertaken by varying neurological structures (Braver et al., 2001). With reference to the adopted model, this process involves an adaptive approach between response stimulus and decision processing monitored by cognitive mechanisms to actively suppress a prepotent response (see Figure 9.3). In the model presented in Figure 9.3 it is suggested that when a Stop signal appears a response translation occurs in parallel to a response route. These two pathways come together at the response activation level where the two motor programs compete for a specific behavioural response. Response inhibition mechanisms monitor for conflict between the stimulus and response pathways. If the monitoring mechanisms are recruited in time they reduce the activation of the proponent response. In recent years, neural mechanisms of response inhibition have been identified in the supplementary

motor area/pre-supplementary motor area (SMA/ pre-SMA) and anterior cingulate cortex (ACC) since these are involved in the monitoring of response selection and error detection (Wang & Cai, 2010). Furthermore, there has been a close association between response inhibition and response selection, working memory, and attention, as the brain areas activated by these processes closely overlap (Carter et al., 1998). At this stage of investigation the decreased inhibitory activity demonstrated by the DCD group may be representative of a difficulty with response programme selection. It is suggested that the DCD group is unable to accurately integrate cognitive actions from the activation provided by the neurological structures essential for response programming and (more importantly) error monitoring that occurs after the Stop instruction. Similar to the response locked LRP, there may be a general difficulty with the efficiency of interpretation of the instruction signal (Stop in this case) and the modulation of a response after that response has already been selected. The DCD group may be unable to efficiently interpret the NoGo signal in time to employ the cognitive mechanisms required to interrupt the pre-programmed and competing go process before that process reaches activation threshold. Thus, those with DCD may not be able to employ conflict mechanisms to resolve the stronger stimulus-response map associated with the frequent Go trials.

Overall, the response inhibition ERP findings identified within the current thesis suggest that this adult DCD group has difficulty with cognitive control strategies regarding response selection and/or the ability to efficiently modulate a motor programme based on contextual influences, in this case conveyed by the Go or NoGo instruction. The decreased response inhibitory abilities of the DCD group is in line with other studies examining developmental disorders and response inhibition, and

suggest that this may be a common difficulty across disorders. An inability to appropriately modulate response programming would lead to atypical behavioural outputs which would compromise a vast array of daily interactions.

Although difficulty with the selective capabilities outlined above has been documented within cognitive-behavioural studies of children with DCD, this is the first study to investigate difficulties with these tasks both in a population of adults with DCD and through electrophysiological measures. Taken together, these two approaches suggest a less adaptable motor system that is less able to effectively incorporate motor control parameters and adjust output based on online contextual adjustments in DCD in comparison to peers. Overall, the behavioural and electrophysiological data obtained here suggest a difficulty with response selection in the DCD group in the form of overall motor program adaptation in response to contextual influences (inhibition) along with efficient incorporation of effectors into a programmed response. Further work is required to establish if these atypical profiles transcend tasks. This will be discussed below.

Singular or cumulative processing difficulty in DCD?

One question that arises from the data presented here is whether or not the atypical performance patterns identified in those with DCD are dependent upon a failure of a single processing stage or result from a collective difficulty regarding sensorimotor transformations across the continuum of movement preparation and execution. At this stage it is difficult to comment on the direct or specific level of corruption that may underpin the observed performance difficulties in those with DCD, however the discussion and models of dysfunction presented above highlight the key sensorimotor

difficulties that may contribute to the observed difficulties in those with DCD, based on the findings presented within this thesis. The investigation within this thesis poses a collection of unique difficulties in adults with DCD, posing more questions than answers regarding the organisation of functional difficulties observed in the DCD group. It is difficult at this stage to speculate on whether one of the two key areas focused upon here (early sensory processing vs. cognitive selection processes) would impact on coordination more than the other although the DCD group demonstrated clear difficulty with a range of sensorimotor functions. Importantly this thesis has identified discrete functional difficulties present in an adult sample with coordination difficulties and suggested ways in which these difficulties could have an effect on coordination. These findings highlight the importance of future research across the entire age range of individuals with DCD and emphasise the need to not only focus on children. The results obtained here also highlight the benefit of using psychophysiological measures to conduct research into the understanding of DCD since this affords the ability to examine activity between various sensory and performance based abilities. It is essential that follow-up studies are pursued in order to substantiate and extend the findings presented in this thesis.

An example of sequential difficulties during an everyday task for those with DCD

Although the findings within this thesis identify a spectrum of motor control and associated sensory difficulties within an adult DCD group, it is important that these findings can be discussed in terms of the overt behavioural performance of the DCD adult. To provide a simplified, but naturalistic example, the task of reaching for items placed in the environment requires processes examined throughout this thesis. In this

example we will consider an individual reaching towards a glass of water on the countertop placed across the body's midline. This individual – Joseph – has a diagnosis of DCD. Reaching to the glass (target) involves an initial cognitive representation of the goal directed behaviour. In our example Jospeh would first define an abstract representation of the motor strategies and the behaviours to be applied to reach and grasp the glass.   According to the model presented earlier, next, spatial and temporal conditions/characteristics would be evaluated as reference inputs. These characteristics include the distance between the hand (effector) and glass (goal) locations as well as consideration of the trajectory and velocity of the required movement. At this stage the reference inputs would be consolidated and introduced to the CNS to develop the motor command and forward model. The early contribution of early sensory processing activity would result in a spatial plan being made as a direct consequence of movement planning. The task space and goal direction movement parameters would be broken down into movements for the reaching limb and compared with the actual position of the body. Given that it is proposed that individuals with DCD may have difficulty establishing these early reference parameters, the prediction would be that Joseph would not have encoded adequate information regarding the direction and trajectory of his movement towards the glass based on the spatial configuration of the end state in relation to effector location. Thus at this stage Joseph would be lacking accurate information regarding these early parameters and the location of the glass would be converted into a set of inaccurate intrinsic coordinates applied to the effector being utilized. Moving to the final level in the hierarchy of action representation, action execution follows response selection. The motor commands for effectors coordinated by the central motor program become activated and lead to temporally coordinated neuromuscular activation and to

coordinated movements of the reaching limb. The response selection stage would have arranged the motor output process based on the organisation and initiation of the response. Joseph would commence reaching to the glass based on inaccurate spatial information and decreased cortical involvement, thus his reach may be variable and delayed. In addition, Joseph may also not be able to utilize incoming feedback information to modulate his reach in accordance with environmental influences. Imagine that before the reach he notices that the glass has been placed near the stove and it will therefore have become extremely hot. His ability to stop (inhibit) a prepared response would be delayed due to an atypical relationship between response monitoring mechanisms and preprogrammed response processes. Essentially, Joseph would be unable to stop a predominant response in accordance with environmental stimuli and he may not effectively withhold his reach, possibly burning himself as a result. Although the example provided may be simplistic, it provides an initial interpretation of how the atypical performance capabilities of those with DCD might impact even a relatively straightforward everyday activity.

Although the data obtained in the current study relates closely to a table-top reaching task, it also has relevance to other more dynamic activities, such as driving. Driving is another task for which adults with DCD report difficulty (de Oliviera & Wann, 2011; Kirby, Sugden, & Edwards, 2011). The act of driving is composed of a complex set of tasks requiring efficient sensory integration and control strategies for smooth control of the vehicle. This involves many sensory and cognitive processes with which an individual with DCD may have difficulty. Specifically, driving involves activities that require an action plan to be constructed on-line using moment-to-moment sensory feedback from the environment. For instance, during driving

individuals are required to monitor their environment via attention modulation. Although not isolated to singular goals per se, this act requires purposeful processing coupled with reflexive movement output. The data from the current study suggest that this coupling would be variable in those with DCD. An individual with DCD may not be able to form a congruency between incoming environmental stimuli and the appropriate motor response resulting in less than optimal vehicle control. Interpreting signals that influence movement output such as a traffic light or a pedestrian entering the road must be acted upon in an efficient manner. Maladaptive activity and reflexes must be monitored and overcome in order to successfully adjust control of the vehicle. For instance if the individual starts to depress the accelerator and notices an object in the path of the vehicle. This would require a quick modulation of the response to withhold the imperative foot movement (i.e., response inhibition). It is easy to see how the underlying sensorimotor and motor control difficulties proposed in the current thesis could translate to more dynamic age related tasks having an impact on successful activity engagement.

Developmental Influences

Another interesting question that arises from the data presented here is the contribution of sensorimotor functions to the *development* of motor control. The vast majority of studies of DCD are cross-sectional and thus provide a static view of performance. However, the process of development in a child with a developmental motor disorder is likely to be rather different from that seen in a child with no disorder, and the impact of the motor impairment is likely to have an impact on other developing systems (e.g., Hill, 2005; Karmiloff-Smith, 1998; 2009). Although it is difficult to comment on the likely implications of this at this stage (given the absence

of child data using the current methodology and the cross-sectional focus of research), it is certainly plausible that adults with DCD may present with an immature, or even atypical, profile. It is widely established that the development of motor behaviour requires orderly neural development and is dependent on the individual's interaction with the environment (Konczak & Dichgans, 1997). Humans require sensory stimulation to trigger processes of neural development that in turn influence the development of motor control. In addition, the flexibility of the nervous system as well as the development of efferent and afferent projections is dependent upon temporal influences. Young children undergo periods of development in which the nervous system requires certain sensory inputs. The absence, or reduction in input, of such stimuli during this period is thought to have adverse effects on certain aspects of sensorimotor development (McLennan & Hendry, 1981; Mei, 1994). As noted in Chapter 1, children with DCD often show delayed sensorimotor activity and developmental milestones. It is thus plausible that these children do not possess the required sensory prerequisites that form the foundation of motor control development, resulting in the observed performance difficulties. It is imperative that studies of young children with DCD incorporate measures such as ERPs to investigate the interaction of motor and sensory development from a young age. Again, at this stage it is difficult to comment on age related effects without direct comparison to a child sample on the experimental paradigm used. It is suggested that future work investigates the interaction of age with the processes that were the focus of the current study in order to investigate developmental contributions.

Directions for future research

The results obtained here provide an interesting glimpse into a collection of underlying functional difficulties that warrant further investigation into the sensorimotor capacities of individuals with DCD. Future research is required to support the initial findings within this thesis on all measures examined as well as the generality of these findings to other performance based contexts. Regarding the initial investigation of premotor visuospatial processing, the current study was limited to probing sensory processing at 200 msecs prior to movement onset. Further research should employ probe times of varying onset prior to response cue to examine the visual discrimination performance of individuals with DCD in response to varying task relevant and irrelevant locations.

Previous work has shown that typically developing individuals are able to isolate numerous task relevant locations during the planning stage (Land et al., 2003). By comparing the enhancement of the visually evoked potentials in response to the varying probe onsets one would obtain a more detailed timecourse representation of the distribution of visuospatial capacities within action space. Further investigations could involve altering the direction of movement in order to investigate whether there are specific directional attributes to visuospatial processing within the DCD group. A similar paradigm to the one used here containing alternative locations would afford an investigation into a) the manner in which spatially contrasted arrangements for effector and goal location influence spatial processing within a DCD group and b) whether there are specific movement characteristics that influence atypical spatial processing within the DCD group compared to typically developing individuals. For example, the movement targets could be arranged such as to require a perpendicular

reach across the midline or a reach back towards the body from one or more peripheral start locations.   This would present a more detailed picture of how those with DCD utilize spatial profiles through various movement directions in space and may identify specific movements that impact early sensory profiles in those with DCD. In addition, it would be beneficial to examine reaction time and error rates in relation to the perceptual benefit of visual probes delivered to intended goal locations. Studies have demonstrated a perceptual benefit with regards to reaction time when visual stimuli are presented adjacent to the target of the reach pursuit (van Donkelaar & Drew, 2002).   This benefit is suggested to arise from a maximization of attending to locations of interest resulting in more efficient prioritization of action (Barnes, 2008). By examining this process in those with DCD it would open another avenue for the investigation of sensory processing and its effects on movement production.

The atypical preparatory processes (ADAN/LDAP) identified in the DCD group may not be specific to a movement paradigm and it is suggested that attentional control processes are studied in the absence of a motor task. As the effects for ADAN/LDAP were sporadic during this initial investigation for both groups, it is suggested that the DCD group is tested using a modified Posner paradigm, as has been used in a majority of published ADAN/LDAP studies with typical individuals. This would allow an initial investigation of the early selective attention function before coupling unimanual movement with the task in order to obtain data that would provide further insights into the suggestion (in the current data) of atypical adaptation of the frontoparietal network in DCD. It is important that performance is contrasted during tasks requiring a manual response and one that does not in order to investigate

whether a basic difficulty with these early selective measures is present, or whether it is motor specific.

Future work investigating the LRP is required to support our initial claims of reduced cortical activation underlying the selection of the response hand. Future studies should examine varying the precueing effect or the application of cue direction and response hand in varying stages in order to see if those with DCD benefit from advanced information in effector selection. Within the current work the stimulus locked LRP was not detected. This was most likely due to the prolonged time interval between cue and response instruction. Differing levels of LRP enhancement have been observed for combinations of precue information, including isolated effector information and precue information containing both effector information and movement direction (Luethold et al., 1996). Leuthold and colleagues identified shorter stimulus locked LRP intervals for precue trials containing both movement direction and effector information in comparison to precue trials that contained only one of the movement parameters. This provided evidence that advanced information benefits premotor perceptual processes. It would be beneficial to compare cueing techniques in relation to the stimulus locked LRP in order to see if individuals with DCD show marked improvements in the activation of effectors dependent upon cueing information, thus demonstrating whether or not the group relies on more complete task information when processing effector availability. The LRP is also not restricted to movements of the upper limbs and is elicited during occulomotor and movements of the lower extremities (Jentzsch & Leuthold, 2002). Thus it would be interesting to compare LRP characteristics of the different effector scenarios as ocular and limb systems deal with unique movement parameters and operate in all tasks.

Examining various forms of response inhibition to distinguish if response inhibition translates across tasks is also necessary. This difficulty has been shown during manual inhibition, however other investigations of response inhibition are required including inhibitory activity that involves working memory and attention, since the brain areas activated by these processes closely overlap (Menan et al., 2001). As the function of inhibitory proficiency demonstrates a viable avenue for diagnostic measures it is important that a very clear understanding of the nature of response inhibition within a DCD group is obtained. This should include investigating response inhibition across a range of tasks and domains including the Stroop task (Stroop, 1935) and the Erikson task (Erikson & Erikson, 1974). Preliminary data suggest an interesting range of typical and atypical performance on these tasks (Pratt & Hill, in preparation).

Importantly the putative underlying deficits identified in the current thesis need to be examined in more contextually appropriate situations such as using similar measures during age appropriate activities of daily living (ADLs). As one of the primary diagnostic features of DCD is the impact that the coordination difficulties have on ADLs, it would be pertinent to apply the electrophysiological measures used in the current thesis to a set of daily tasks. With the advancement of virtual reality applications, previous studies outside the field of DCD have examined function during ADLs including activities such as meal preparation (e.g., Christiansen et al., 1998) and driving (Schulthesis, 2001). Such measures of evaluating task specific function would be an invaluable addition to the DCD literature as they would provide

additional evidence for the carryover of underlying sensorimotor difficulties to everyday task performance. By utilizing these measures it would be possible to identify the exact point(s) at which atypical brain activation leads to ADL difficulty, allowing for the development of more appropriate intervention and remediation strategies.

Overall, employing techniques that allow online investigation of neurological processes seems a viable avenue to pursue within the DCD research community. The advantages afforded by neuroimaging techniques provide an invaluable measure of examining performance on a multisensory level during a range of functional tasks. As a large collection of neuroimaging studies have involved theoretically driven paradigms examining the interaction of action and perception, the application of these procedures cannot be dismissed and should, indeed, be advocated in the study of the DCD population.

Concluding Remarks

This thesis aimed to explore the motor control abilities as well as the interaction of manual response preparation and early sensory activity in adults with DCD. The findings have important implications for those with DCD as they provide evidence for a difficulty with both sensorimotor preparation and the underlying programming capacities relating to response selection and inhibition. Furthermore, the investigation presented here provides direct evidence at both a psychophysiological and behavioural level for continued difficulty into adulthood for individuals diagnosed with DCD. The implications of the findings should have a wide impact on the manner

in which research is directed towards this group since they highlight continued and significant difficulties with evidence coming from both behavioural and biological levels of analysis. Added to the emerging literature on adults with DCD which highlights not only that, for the most part, DCD is not a disorder that is outgrown (e.g., Losse et al., 1991; Cantell et al., 2003), but also that there are significant continued motor (Cousins & Smyth, 2003; 2005; current data) as well as mental health (Hill & Brown, under review), quality of life satisfaction (Hill, Brown & Sorgardt, 2011) and functional difficulties (e.g., de Oliveria & Wann, 2011; Hill & Kirby, in preparation; Magill-Evans et al., 2008). The findings of the current thesis emphasise the importance of recognising DCD in adulthood. This focus on adults (as well as the developmental trajectory of DCD) should be emphasised not only for understanding the causes and consequences of the disorder for theoretical reasons, but importantly to aid the development of remediation and intervention techniques suitable at home, school and work for this group. It is hoped that the work presented in the current thesis provides the basis for conducting such research as well as highlighting useful directions from which to proceed.

References

Adam, J. J., Paas, F. G. W. C., & Eyssen, I. C. J. M., Slingerland, H., Bekkering, H., & Drost, M. R. (1995). The control of two element, reciprocal aiming movements: Evidence for chunking, *Human Movement Sciences*, 14, 1–11.

Alloway, T.P., & Archibald, L. (2008). Working Memory and Learning in Children with Developmental Coordination Disorder and Specific Language Impairment. *Journal of Learning Disabilities*, 41(3), 251–262.

Allport, D. A. (1987). Selection for action: Some behavioural and neurophysiological considerations of attention and action. In H. Heuer & A. F. Sanders (Eds.), *Perspectives on perception and action* (pp. 395–419). Hillsdale, NJ: Lawrence Erlbaum Associates.

Allport D.A. (1989). Visual attention. In M. I. Posner (Ed.), *Foundations of cognitive science* (pp 631-682). Cambridge MA: MIT Press.

American Psychiatric Association. (1987). Diagnostic and statistical manual of mental disorders (3rd ed., revised). Washington, DC: Author.

American Psychiatric Association. (1994). Diagnostic and statistical manual of mental disorders (4th ed). Washington, DC: Author.

American Psychiatric Association. (2000). Diagnostic and statistical manual of mental disorders (4th ed., text revision). Washington, DC: Author.

Anllo-Vento, L. & Hillyard, S.A. (1996). Selective attention to the color and direction of moving stimuli: Electrophysiological correlates of hierarchical feature selection. *Perception & Psychophysics*, 58, 191-206.

Andersen, R. A., & Bueno, C. A. (2002). Intentional maps in posterior parietal cortex. *Annual Review Neuroscience*, 25, 189–220.

Ansuini C., Pierno A.C., Lusher D., & Castiello U. (2006). Virtual reality applications for the remapping of space in neglect patients. *Restorative Neurology and Neuroscience*, 24, 431-441.

Aron A.R., Robbins T.W., & Poldrack R.A. (2004). Inhibition and the right inferior frontal cortex, *Trends in Cognitive Neuroscience*, 4, 170 –177.

Astafiev, S.V., Shulman, G.L., Stanley, C.M., Snyder, A.Z., Van Essen, D.C. & Corbetta, M. (2003) Functional organization of human intraparietal and frontal cortex for attending, looking, and pointing, *Journal of Neuroscience*, 23, 4689–4699.

Astill, S., & Utley, A. (2006). Ball catching in children with developmental coordination disorder, *Motor Control*, 10, 109-124.

Ayres, J.A. (1972b). Sensory integration and learning disabilities. Los Angeles: Western Psychological Services.

Baldauf, D., Wolf, M., & Deubel, H. (2006). Deployment of visual attention before sequences of goal-directed hand movements, *Vision Research*, 46, 4355–4374.

Baldauf, D., & Deubel, H. (2008a). Properties of attentional selection during preparation of sequential saccades, *Experimental Brain Research*, 184(3), 411–425.

Baldauf, D., & Deubel, H. (2008b). Visual attention during the preparation of bimanual movements, *Vision Research*, 48, 549–563.

Baldauf, D., & Deubel, H. (2009). Attentional selection of multiple goal positions before rapid hand movement sequences: An ERP study. *Journal of Cognitive Neuroscience*, 21(1), 18–29.

Baldauf, D. & Deubel, H. (2010). Attentional landscapes in reaching and grasping. Minireview, *Vision Research*, 50, 999-1013.

Banaschewski, T., Brandeis, D., Heinrich, H., Albrecht, B., Brunner, E., & Rothenberger A. (2004). Questioning inhibitory control as the specific deficit of ADHD – Evidence from brain electrical activity, *Journal of Neural Transmission,* 111, 841–864.

Barlow, J.S. (2002). The cerebellum and adaptive control, Cambridge University Press, Cambridge, UK.

Barkley, R. A., & Biederman, J. (1997). Towards a broader definition of the age of onset criterion for attention deficit hyperactivity disorder. *Journal of the American Academy of Child and Adolescent Psychiatry*, 36, 1204–1210.

BattagliaMayer A., Ferraina S., Mitsuda T., Marconi B., Genovesio A., Onorati P., Lacquaniti F., & Caminiti R. (2000). Early coding of reaching in the parietooccipital cortex. *Journal of* Neurophysiology, 83, 2374–2391.

Baylis, G.C., & Baylis, L.L. (2001). Visually misguided reaching in Balint's syndrome, *Neuropsychologia,* 39, 865–875.

Beurze S.M., de Lange F.P., Toni I., & Medendorp W.P. (2007). Integration of target and effector information in the human brain during reach planning, *Journal of Neurophysiology*, 97, 188–199.

Beurze S.M., de Lange F.P., Toni I., & Medendorp W.P. (2009). Spatial and effector processing in the human parietofrontal network for reaches and saccades. *Journal of Neurophysiology*, 101, 3053–3062.

Biancotto M, Skabar A, Bulgheroni M, Carrozzi M, & Zoia S. (2011). Neuromotor deficits in developmental coordination disorder: evidence from a reach-to-grasp task. *Research in Developmental Disabilities*, 32(4), 1293-1300.

Blakemore, S. & Sirigu, A. (2003). Action prediction in the cerebellum and in the parietal lobe, *Experimental Brain Research,* 153, 239-245.

Booth, J. R., Burman, D. D., Meyer, J. R., Lei, Z., Trommer, B. L., Davenport, N. D., Li, W., Parrish, T. B., Gitelman, D. R., & Mesulam, M. M. (2003). Neural development of selective attention and response inhibition, *Neuroimage*, 20, 737-751.

Bonifacci, P. (2004). Children with low motor ability have lower visual-motor integration ability but unaffected perceptual skills. *Human Movement Science*, 23, 157–168.

Braver, T.S., Barch, D.M., Gray, J.R., Molfese, D.L., & Snyder, A. (2001). Anterior cingulate cortex and response conflict: Effects of frequency, inhibition, and errors, *Cerebral Cortex,* 11, 825-836.

Bruin, K.J., & Wijers, A.A. (2002). Inhibition, response mode, and stimulus probability: a comparative event-related potential study, *Clinical Neurophysiology*, 113, 1172–1182.

Bruininks, R. H. (1978). Bruininks-Oseretsky Test of Motor Proficiency- Owner's Manual. Circle Pines, MN: American Guidance Service.

Bruininks, R., & Bruininks, B. (2005). Bruininks-Oseretsky Test of Motor Proficiency-2nd edition manual. Minneapolis, MN: NCS Pearson.

Bunge, S. A., Dudukovic, N. M., Thomason, M. E., Vaidya, C. J., & Gabrieli, J. D. E. (2002). Immature frontal lobe contributions to cognitive control in children: evidence from fMRI, *Neuron*, 33, 301-311.

Burke D, Hagbarth K.E, Lofstedt L, & Wallin BG. (1976). The responses of human muscle spindle endings to vibration during isometric contraction, *The Journal of* Physiology, 261, 695–671.

Buckolz, E., Mandich, A., Buckolz, K., & Polatajko, H. (2000). Inhibitory function in children with developmental co-ordination disorder (DCD): Disengaging an ongoing manual response, manuscript in preparation.

Callaway, E., & Halliday, R. (1982). The effect of attentional effort on visual evoked potential N1 latency, *Psychiatry Research*, 7, 299-308.

Cantell, M., Smyth, M. M., & Ahonen, T. P. (1994). Clumsiness in adolescence: Educational, motor and social outcomes of motor delay detected at five years. *Adapted Physical Activity Quarterly*, 11, 159-129.

Cantell, M.H, Smyth, M.M, & Ahonen, T.P. (2003). Two distinct pathways for developmental coordination disorder: persistence and resolution. *Human Movement Science,* 22(4-5), 413-31.

Cantin, N., Polatajko, H.J., Thach, W.T., & Jaglal, S. (2007). Developmental coordination disorder: exploration of a cerebellar hypothesis. *Human Movement Science*, 26, 491-509.

Casey, B. J., Trainor, R. J., Orendi, J. L., Schubert, A. B., Nystrom, L. E., Giedd, J. N., Castellanos, F. X., Haxby, J. V., Noll, D. C., & Cohen, J. D. (1997). A developmental functional MRI study of prefrontal activation during performance of a Go-No-Go task, *Journal of Cognitive Neuroscience*, 9, 835-847.

Caeyenberghs, K. Tsoupas, J., Wilson, P.H., & Smits-Engelsman, B.C.M. (2009). Motor imagery in primary school children, *Developmental Neuropsychology,* 34, 103-121.

Carter, C.S., Braver, T.S., Barch, D.M., Botvinick, M.M., Noll, D.C., & Cohen, J.D. (1998). Anterior cingulate cortex, error detection, and the online monitoring of performance, *Science*, 280, 747–749.

Castiello, U. (1996). Grasping a fruit: Selection for action, *Journal of Experimental Psychology: Human Perception and Performance*, 22(3), 582–603.

Cermak, S.A., Trimble, H., Coryell, J. & Drake, C. (1990). Bilateral motor coordination in adolescents with and without learning disabilities, *Physical and Occupational Therapy in Pediatrics*, 10, 5-18.

Cermak, S A, & Ayres, A J. (1984). Crossing the body midline in learning-disabled and normal children. *American journal of Occupational Therapy*, 38, 35-39.

Chamberlain S.R., Fineberg N.A., Blackwell A.D., Robbins T.W., & Sahakian B.J. (2006). Motor inhibition and cognitive flexibility in obsessive-compulsive disorder and trichotillomania, *American Journal of Psychiatry*, 163, 1282–1284.

Christiansen, C., Abreu, B., Ottenbacher, K., Huffman, K., Massel, B. & Culpepper, R. (1998). Task performance in virtual environments used for cognitive rehabilitation after traumatic brain injury, *Archives of Physical Medicine and Rehabilitation,* 79, 888-892.

Churchland, M.M., Yu, B.M., Ryu, S.I., Santhanam, G., & Shenoy, K. (2006). Neural variability in the premotor cortex provides a signature of motor preparation. *The Journal of Neuroscience,* 26(14), 3697-3712.

Clark, V.P., Fan, S., & Hillyard, S.A. (1995). Identification of Early Visual Evoked Potential Generators by Retinotopic and Topographic Analyses. *Human Brain Mapping*, 2, 170-187.

Clements-Stephens, A.M., Rimrodt, S.L., & Cutting, L.E. (2009). Developmental sex differences in basic visuospatial processing: differences in strategy use? *Neuroscience Letters*, 16, 155–160.

Colby, C.L., & Duhamel, J.R. (1991). Heterogeneity of extrastriate visual areas and multiple parietal areas in the macaque monkey. *Neuropsychologia*, 29(6), 517-537Connolly, K. J. (1970). Skill development: problems and plans. In: Mechanisms of Motor Skill Development (ed. K. J. Connolly), pp.3–17. Academic Press, London, UK.

Coles, M.G. (1989). Modern mind-brain reading: psychophysiology, physiology, and cognition. *Psychophysiology*, 26(3), 251-269.

Connolly, J.D., Andersen, R.A., & Goodale, M.A. (2003). FMRI evidence for a 'parietal reach region' in the human brain. *Experimental Brain Research*, 153(2), 140-145.

Corbetta, M., Akbudak, E., Conturo, T.E., Snyder, A.Z., Olinger, J.M., Drury, H.A., Linenweber, M.R., Peterson, S.E., Raichle, M.E., Van Essen, D.C., & Shulman, G.L. (1998). A common network of functional areas for attention and eye movements. *Neuron*, 21, 761-773.

Corbetta, M., Kincade, J.M., Ollinger, J.M., McAvoy, M.P. & Shulman, G.L. (2000) Voluntary orienting is dissociated from target detection in human posterior parietal cortex. *Nature Neuroscience,* 3, 292–297

Corbetta, M., & Shulman, G. L. (2002). Control of goal-directed and stimulus-driven attention in the brain. *Nature Reviews Neuroscience,* 3, 201–215.

Correa, A., Trivino, M., Perez-Duenas, C., Acosta, A., & Lupiáñez, J. (2010). Temporal preparation, response inhibition and impulsivity. *Brain and Cognition*, 73, 222-228.

Cousins, M. & Smyth, M.M. (2003). Developmental coordination impairments in adulthood. *Human Movement Science*, 22, 433-459.

Craighero, L., Fadiga, L., Rizzolatti, G., & Umilta, C.A. (1999). Movement for perception: a motor-visual attentional effect. *Journal of Experimenal Psychology: Human Perception and Performance*, 25(6), 1673-1692.

Crutcher, M.D. & Alexander, G.E. (1990). Movement-related neuronal activity selectively coding either direction or muscle pattern in three motor areas of the monkey. *Journal of Neurophysiology*, 64, 151–163.

Curtis C.E., & D'Esposito M. (2007). Selection and maintenance of saccade goals in the human frontal eye fields. *Journal of Neurophysiology,* 95, 3923–3927.

D'Esposito M., Postle B.R., & Rypma B. (2000). Prefrontal cortical contributions to working memory: evidence from event-related fMRI studies. *Experimental Brain Research*, 133, 3-11.

Darling S., Della Sala S., Logie R.H., & Cantagallo A. (2006). Neuropsychological evidence for separating components of visuo–spatial working memory. *Journal of Neurology*, 253,176–180.

de Castelnau, P., Albaret J.M., Chaix, Y. & . Zanone, P.G. (2007). Developmental coordination disorder pertains to a deficit in perceptuo-motor synchronization independent of attentional capacities. *Human Movement Science*, 26, 477–490.

de Castelnau, P., Albaret, J., Chaix, Y. & Zanone, P.G. (2008). A study of EEG coherence in DCD children during motor synchronization task. *Human Movement Science, 27,* 230–241.

de Oliveira, R.F., Wann, J.P. (2011). Driving skills of young adults with Developmental Coordination Disorder: Regulating speed and coping with distraction. *Research in Developmental Disabilities*, 32(4), 1302-1308.

De Jong, R., Wierda, M., Mulder, G., & Mulder, L.J.M. (1988). Use of partial stimulus information in response processing. *Journal of Experimental Psychology: Human Perception and Performance*, 14,682-692.

De Jong, R., Coles, M.G., & Logan, G.D. (1995). Strategies and mechanisms in nonselective and selective inhibitory motor control. Journal of Experimental Psychology: *Human Perception and Performance,* 21(3), 498-511.

Deiber, M.P., Passingham, R.E., Colebatch, J.G., Friston, K.J., Nixon, P.D., & Frackowiak, R.S. (1991). Cortical areas and the selection of movement: a study with positron emission tomography. *Experimental Brain Research*, 84, 393–402.

Denckla, M. B. (1973). Development of speed in repetitive and successive finger movements in normal children. *Developmental Medicine and Child Neurology*, 12, 635-645.

Denckla, M.B. (1984). Developmental dyspraxia: The clumsy child. In M.D. Levine & P. Satz (Eds.), *Middle childhood: Development and dysfunction* (pp. 245-260). Baltimore, MD: University Park Press.

Dempster, F.N. (1992). The rise and fall of the inhibitory mechanism: Toward a unified theory of cognitive development and aging. *Developmental Review,* 12, 45-75.

Desmurget M. & Grafton S. (2000). Forward modelling allows feedback control for fast reaching movements. *Trends in* Cognitive *Sciences,* 4, 423–431.

Desmurget, M., Pelisson, D., Rosseti, Y., & Prablanc, C. (1998). From eye to hand: Planning goal-directed movements. *Neuroscience and Biobehavioural Reviews*, 22(6), 761-788.

Deubel, H., & Schneider, W. X. (1996). Saccade target selection and object recognition-evidence for a common attentional mechanism. *Vision Research*, 36, 1827–1837.

Deubel, H., Schneider, W. X., & Paprotta, I. (1998). Selective dorsal and ventral processing: Evidence for a common attentional mechanism in reaching and perception. *Visual Cognition,* 5, 81–107.

Deubel, H., & Schneider, W. X. (2003). Delayed saccades, but not delayed manual aiming movements, require attention. *Annals of the New York Academy of Sciences*, 1004, 289–296.

Dewey, D., Wilson, B., Crawford, S. G., & Kaplan, B. J. (2000). Comorbidity of developmental coordination disorder with ADHD and reading disability. *Journal of the International Neuropsychological Society*, 6, 152.

Diamond, A. (2000). Close interrelation of Motor Development and Cognitive Development and of the Cerrebellum and Prefrontal Cortex. *Child Development,* 71(1) 44-56.

Dimoska, A., Johnstone, S.J., & Barry, R.J. (2006). The auditory evoked N2 and P3 components in the stop stignal task/ indices of inhibition, response-conflict or error detection? *Brain and Cognition*, 62(2), 98-112.

Di Russo, F., Martinez, A., Sereno, M.I., Pitzalis, S., & Hillyard, S.A. (2002). Cortical sources of the early components of the visual evoked potential. *Human Brain Mapping*, 15(2), 95-111.

Donkers, F.C., & van Boxtel, G.J. (2004). The N2 in go/no-go tasks reflects conflict monitoring not response inhibition. *Brain and Cognition*, 56 (2), 165-176.

Dunford, C., Street, E., O'Connell, H., Kelly, J. & Sibert, J. R. (2004). Are referrals to occupational therapy for developmental coordination disorder appropriate? *Archives of Disease in Childhood*. 89, 143-147.

Dupré, E. (1925). Pathologie de L'Imagination et de L'Emotivite. Paris, Pavot

Eimer, M. (1993). Effects of attention and stimulus probability on ERPs in a Go-Nogo task. *Biological Psychology*, 35 (2), 123-138.

Eimer, M., & Van Velzen, J. (2002). Crossmodal links in spatial attention are mediated by supramodal control processes: Evidence from event-related brain potentials. *Psychophysiology*, 39, 437-449.

Eimer, M., Van Velzen, J., Forster, B., & Driver, J. (2003). Shifts of attention in light and in darkness: An ERP study of supramodal attentional control and crossmodal links in spatial attention. *Cognitive Brain Research*, 15, 308-323.

Eimer, M., Forster, B., Van Velzen, J., & Prabhu, G. (2005). Covert manual response preparation triggers attentional shifts: ERP evidence for the premotor theory of attention. *Neuropsychologia*, 43, 957-966.

Eimer, M., & Van Velzen, J. (2006). Covert manual response preparation triggers attentional modulations of visual, but not auditory processing.Clinical *Neurophysiology*, 117, 1063-1074.

Eimer., M., van Velzen, J., & Driver, J. (2002). Cross-modal interactions between audition, touch, and vision in endogenous spatial attention: ERP evidence on preparatory states and sensory modulations. *Journal of Cognitive Neuroscience*, 14(2), 254-271.

Eimer, M., Van Velzen, J., Gherri, E., & Press, C. (2006). Manual response preparation and saccade programming are linked to attention shifts: ERP evidence for covert attentional orienting and spatially specific modulations of visual processing, *Brain Research*, 1105, 7–19.

Eriksen, B.A., & Eriksen, C.W. (1974). Effects of noise letters upon the identification of target letters in a non-search task, *Perception & Psychophysics,* 16, 143-149.

Falkenstein, M., Hoorman, J., & Hohnsbein, J. (1999). ERP componenets in Go/Nogo tasks and their relation to inhibition. *Acta Psychologia*, 101 (2-3), 267-291.

Farne, A., Roy, A.C., Paulignan, Y., Rode, G., Rossetti, Y., Boisson, D., & Jeannerod, M. (2003). Visuo-motor control of the ipsilateral hand: Evidence from right braindamaged patients. *Neuropsychologia*, 41(6), 739-75.

Findlay, J. M., & Blythe, H. I. (2009). Saccade target selection: Do distractors affect saccade accuracy? *Vision Research*, 49, 1267–1274.

Fisk, J.D., & Goodale, M.A. (1985). The organization of eye and limb movements during unrestricted reaching to targets in contralateral and ipsilateral visual space. *Experimental Brain Research,* 60, 159-178.

Fisk, J.D., & Goodale, M.A. (1989). The effects of instructions to subjects on the programming of visually directed reaching movements. *Jorunal of Motor Behvaiour,* 21, 5-19.

Fitts, P.M. & Posner, M.I. (1967). Human performance. Oxford, England: Brooks and Cole.

Filimon F., Nelson J.D., Hagler D.J., & Sereno M.I. (2007). Human cortical representations for reaching: mirror neurons for execution, observation, and imagery. *Neuroimage*, 37,1315–1328.

Fliers, E., Rommelse, N., Vermeulen, S.H., Altink, M., Buschgens, C.J., Faraone, S.V., Sergeant, J.A., Franke, B., & Buitelaar, J.K. (2008). Motor coordination problems in children and adolescents with ADHD rated by parents and teachers: Effects of age and gender. *Journal of Neural Transmission*, 115, 211–220.

Folio, M. R., & Fewell, R. R. (1983). Peabody Developmental Motor Scales and activity cards. Texas: DLM Teaching Resource

Forster, B., & Eimer, M. (2007). Covert unimanual response preparation triggers attention shifts to effectors rather than goal locations. *Neuroscience Letters*, 419, 142-146.

Fort, A., Besle, J., Giard, M., & Pernier, J. (2005). Task-dependent activation latency in human visual extrastriate cortex. *Neuroscience Letters*, 379(2), 144-148.

Gabbard C., Rabb C, & Gentry V. (1998). Attentional stimuli and programming hand selection: a developmental perspective. *Journal of* Neurophysiology, 96, 205–221.

Gabbard & Helbig (2004). What drives children's limb selection for reaching in hemispace? *Experimental Brain Research,* 156, 325-332.

Gallese, V. (2000b). The inner sense of action: Agency and motor representations. *Journal of Consciousness Studies*, 7 (10), 23–40.

Gamba, H., & Sasaki, K. (1990). Potential related to nogo-reaction in go/nogo hand movement with discrimination between tone stimuli of different frequencies in the monkey. *Brain Research,* 537, 340–344.

Garavan, H., Ross, T. J., & Stein, E. A. (1999). Right hemispheric dominance of inhibitory control: An event-related functional MRI study. *Proceedings of the National Academy of Sciences of the United States of America*, 96, 8301–8306.

Garavan, H., Ross, T. J. Murphy, K., Roche, R. A. P., & Stein, E. A. (2002). Dissociable executive functions in the dynamic control of behavior: Inhibition, error detection, and correction. *Neuroimage*, 17, 1820-1829.

Gentilini, M., Barbieri, C., De Renzi, E., & Faglioni, P. (1989). Space exploration with and without the aid of vision in hemisphere-damaged patients. *Cortex*, 25(4), 643-651.

Geuze, R.H. & Kalverboer, A.F. (1987). Inconsistency and adaptation in timing of clumsy children. *Journal of Human Movement Studies*, 13, 421-432.

Geuze, R.H. & Kalverboer, A.F. (1994). Tapping a rhythm: A problem of timing for children who are clumsy and dyslexic. *Adapted Physical Activity Quarterly*, 11, 203-213.

Geuze, R.H. (2003). Static balance and developmental coordination disorder. *Human Movement Science*. 22, 527-548.

Geuze, R. (2005). Postural Control in Children with Developmental Coordination Disorder. *Neural Plasticity,* 12, 2-3, 183-196.

Geuze, R.H., Jongmans, M.J., Schoemaker, M.M. & Smits-Engelsman, B.C.M. (2001). Clinical and research diagnostic criteria for Developmental Coordination Disorder. *Human Movement Science*, 20, 7-47.

Gibson, J. J. (1950). The perception of the visual world. Boston: Houghton Mifflin

Gillberg, C. (1986). Attention deficit disorder: diagnosis, prevalence, management and outcome. *Pediatrician*, 13 (2-3), 108–118.

Gherri, E., & Eimer, M. (2010). Manual response preparation disrupts spatial attention: an electrophysiological investigation of links between action and attention. *Neuropsychologia*, 48(4), 961-969.

Gherri, E., Van Velzen, J., & Eimer, M. (2007). Dissociating effector and movement direction selection during the preparation of manual reaching movements: Evidence from lateralized ERP components. *Clinical Neurophysiology*, 118, 2031-2049.

Ghez C., & Thach, W.T.(2000). The cerebellum, E. Kandel, Editor, Principles of neural science, McGraw-Hill Professional Publishing, New York pp. 832–851.

Gnadt, J.W., & Anderson, R.A. (1988). Memory related motor planning activity in parietal cortex of Macaque, *Experimental Brain Research*, 70, 216-220.

Goble, D.J., Coxon, J.P., Van Impe, A., De Vos, J., Weneroth, N., & Swinnen, S.P. (2010). The neural control of bimanual movements in the elderly: Brain regions exhibiting age-related increases in activity, frequency-induced neural modulation, and task-specific compensatory recruitment, *Human Brain Mapping,* 31(8), 1281-1295.

Goldberg, E. (1985). Akinesia, tardive dysmentia and frontal lobe disorder in schizophrenia. *Schizophrenia Bulletin*, 11, 255-263.

Goodale, M.A. & Milner,A.D. (1992). Separate visual pathways for perception and action. *Trends in Neurosciences*, 15, 20–25.

Gratton, G., Coles, M.G., Sirevaag, E.J., Erikson, C.W., & Donchin, E. (1988). Pre- and poststimulus activation of response channels: a psychophysiological analysis. Journal of Experimental Psychology: *Human Perception and Performance,* 14(3), 331-344.

Gratton, G., Bosco, C.M., Kramer, A.F., Coles, M.G., Wickens, C.D., & Donchin, E. (1990). Event-related brain potentials as indices of information extraction and response priming. *Electroencephalography and Clinical Neurophysiology*, 75(5), 419-432.

Green, D., Baird, G. Sugden, D.A. (2006). A pilot study of psychopathology in Developmental Coordination Disorder. *Child: Care, Health and development*, 32, 741-750.

Gubbay, S. S. (1975a). Clumsy children in normal schools. *Medical Journal of Australia*, 1975(1), 233–236.

Gubbay, S.S. (1975b). The clumsy child - A study of developmental apraxia and agnostic ataxia. In Major problems in neurology, Vol. 5. Philadelphia: W.B. Saunders.

Hackley, S. A., & Miller, J. O. (1995). Response complexity and precue interval effects on the lateralized readiness potential. *Psychophysiology,* 32, 230-241.

Harter, M.R., Miller, S.L., Price, N.J., LaLonde, M.E., & Keyes, A.L. (1989). Neural processes involved in directing attention. *Journal of Cognitive Neuroscience*, 1, 223-237.

Hayhoe, M., Shrivastava, A., Mruczek, R., & Pelz, J. B. (2003). Visual memory and motor planning in natural tasks. *Journal of Vision*, 3, 49–63.

Heilman, K., Watson, R., & Valenstein, E. (1985). Neglect and related disorders. In K. Heilman, & E. Valenstein (Eds.), *Clinical neuropsychology* (pp. 243-294). New York: Oxford University Press.

Heinze, H.J., Luck, S.J., Munte, T.F., Gos, A., Mangun, G.R., & Hillyard, S.A., (1994). Attention to adjacent and separate positions in space: an electrophysiological analysis. *Perception & Psychophysics*, 56, 42–52.

Hellgren, L., Gillberg, I.C., Bagenholm, A. & Gillberg, C. (1994b). Children with deficits in attention, motor control and perception (DAMP) almost grown up: Psychiatric and personality disorders at age 16 years. *Journal of Child Psychology and Psychiatry*, 35, 1255-1271.

Henderson, S.E. & Henderson, L. (2002). Toward an understanding of developmental coordination disorder. *Adapted Physical Activity Quarterly*. 19, 11-31.

Henderson, S.E., Barnett, A. & Henderson, L. (1994). Visuospatial difficulties and clumsiness: On the interpretation of conjoined deficits. *Journal of Child Psychology and Psychiatry*, 35, 961-969.

Henderson, L., Rose, P., & Henderson, S. E. (1992). Reaction time and movement time in children with a developmental coordination disorder. *Journal of Child Psychology and Psychiatry*, 33(5), 895-905.

Henderson S. & Sugden D. (1992). The Movement Assessment Battery for Children. Psychological Corporation.

Henderson S.E., Sugden, D.A., & A.L. Barnett, A.L. (2007) Movement assessment battery for children (2nd ed.), Pearson Assessment, London.

Heuninckx, S., Wenderoth, N., & Swinnen, S.P. (2008). Systems Neuroplasticity in the Aging Brain: Recruiting Additional Resources for Succesful Motor Performance in Elderly Persons, *The Journal of Neuroscience*, 28(2), 91-99.

Hill, E. (2001). Non-specific nature of specific language impairment: a review of the literature with regard to concomitant motor impairments. *International Journal of Language & Communication Disorders*, 36 (2), 149-171.

Hill, E. L. (2004). Evaluating the theory of EF deficits in autism. *Developmental Review*, 24, 189–233.

Hill, E. L. & Bishop, D. V. M. (1998). A reaching test reveals weak hand preference in specific language impairment and developmental coordination disorder, *Laterality*, 3, 295-310.

Hill, E. L. & Wing, A. M. (1998). Developmental disorders and the use of grip force to compensate for inertial forces during voluntary movement. In: K. J. Connolly (Ed.), The Psychobiology of the Hand (pp. 199-212). London: Mac Keith Press.

Hill, E.L. & Wing, A.M. (1999). Coordination of grip force and load force in developmental coordination disorder: A case study. *Neurocase*, 5 (6), 537-544.

Hillyard, S.A., Mangun, G.R. Jr., 1987. Sensory gating as a physiological mechanism for visual selective attention. In: Johnson, R. Jr., Parasuraman, R., Rohrbaugh, J.W. (Eds.), Current Trends in Event-Related Potential Research. Elsevier, New York, pp. 61–67.

Hoare, D. & Larkin, D. (1991a). Kinaesthetic abilities of clumsy children. *Developmental Medicine and Child Neurology*, 33, 671-678.

Hoare, D. (1994). Subtypes of developmental coordination disorder. *Adapted Physical Activity Quarterly*, 11, 158-169.

Hofman, J.E., & Subramaniam, B. (1995). The role of visual attention in saccadic eye movements. *Perception and Psychophysics,* 57, 787-795.

Hopf, J. M., & Mangun, G. R. (2000). Shifting visual attention in space: An electrophysiological analysis using high spatial resolution mapping. *Clinical Neurophysiology*, 111, 1241–125.

Hulme, C., Smart, A. & Moran, G. (1982). Visual perceptual deficits in clumsy children. *Neuropsychologia,* 20, 475-481.

Hyde, C. & Wilson, P. (2011). Online motor control in children with developmental coordination disorder: chronometric analysis of double-step reaching performance. *Child: Care, Health and Development*, 37(1), 111-122.

Irwin, D. E., & Gordon, R. D. (1998). Eye movements, attention, and transsaccadic memory. *Visual Cognition*, 5, 127-155.

Jakobson LS, Servos P, Goodale MA, Lassonde M (1994). Control of proximal and distal components of prehension in callosal agenesis. *Brain,* 117, 1107–1113.

Jeannerod, M. (1994). The representing brain: Neural correlates of motor intention and imagery. *Behavioral and Brain Sciences*, 17, 187-245.

Jeannerod, M (1997). The cognitive neuroscience of action. Oxford, Blackwell

Jeannerod M., & Frak V. (1999). Mental imaging of motor activity in humans. *Current Opinion* in *Neurobiology*, 9, 735–739.

Jentzsch, I., Leuthold, H., & Ridderinkhof, R. (2004). Beneficial effects of ambiguous precues: Paralle; motor preparation or reduced premotoric processing time? *Psychophysiology*, 41, 231-244.

Jodo, E. & Kayama, Y. (1992). Relation of a negative ERP component to response inhibition in a Go/No-go task. *Electroencephalography and Clinical Neurophysiology,* 82(6), 477-482.

Johnston, L.M., Burns, Y.R., Brauer, S.G. & Richardson, C.A. (2002). Differences in postural control and movement performance during goal directed reaching in children with developmental coordination disorder. *Human Movement Science*, 21, 583-601.

Jonkman, L.M, van Melis, J.J., Kemner C., & Markus, C. (2007). Methylphenidate improves deficient error evaluation in children with ADHD: an event-related brain potential study. *Biological* Psychology, 76, 217–229.

Jordan M.I., Flash T., & Arnon Y. (1994). A model of the learning of arm trajectories from spatial deviations. *Journal of Cognitive Neuroscience*, 6, 359 –376.

Kadesjö, B. & Gillberg, C. (1999). Developmental Co-ordination disorder in Swedish 7 year-olds. *Journal of the American Academy of Child and Adolescent Psychiatry,* 38, 820-828.

Kagerer F.A., Bo J., Contreras-Vidal J.L., & Clark J. (2004). Visuomotor adaptation in children with Developmental Coordination Disorder. *Motor Control,* 8(4), 450-460.

Kagerer, F.A., Contreras-Vidal, J.L., Bo, J., Clark, J.E., 2006. Abrupt, but not gradual visuomotor distortion facilitates adaptation in children with developmental coordination disorder. *Human Movement Science*, 25, 622–633.

Kaiser, S., Unger, J., Kiefer, M., Markela, J., Mundt, C., & Weisbrod, M. (2003). Executive control deficit in depression: Event-related potentials in a Go/Nogo task. Psychiatry Research: *Neuroimaging*, 122, 169–184.

Karmiloff-Smith, A. (1998). Development itself is the key to understanding developmental disorders. *Trends in Cognitive Sciences*, *2*(10), 389–398.

Karmiloff-Smith, A. (2009). Nativism versus neuroconstructivism: Rethinking the study of developmental disorders. *Developmental Psychology*, *45*(1), 56–63.

Karnath, H.O., Dick, H., & Konczak, J. (1997). Kinematics of goal-directed arm movements in neglect: Control of hand in space. Neuropsychologia, 35(4), 435-444.

Kashiwagi, M., Iwaki, S., Narumi, Y., Tamai, H., & Suzuki, S. (2009). Parietal dysfunction in developmental coordination disorder: a functional MRI study. *Neuroreport*, 20, 1319–1324.

Katschmarsky, S., Cairney, S., Maruff, P., Wilson, P., & Currie, J. (2001). The ability to execute saccades on the basis of efference copy: impairments in double-step saccade performance in children with developmental coordination disorder. *Experimental Brain Research,* 136, 73-78.

Kaufman, L.B. & Schilling, D.L. (2007). Implementation of a strength training program for a 5-year old child with poor body awareness and developmental coordination disorder. *Journal of the American Physical Therapy Association,* 87(4), 455-467.

Kawato, M. (1999). Internal models for motor control and trajectory planning. *Current Opinion in Neurobiology,* 9, 718-727.

Kelso, J.A.S. (1986). Pattern formation in multi-degree of freedom speech and limb movements. *Experimental Brain Research*, 15, 105-128.

Kessler, R.C., Adler, L., Ames, M., Demler, O., Faraone, S., Hiripi, E., Howes, M.J., Jin, R., Secnik, K., Spencer, T., Ustun, T.B., Walters, E.E. (2005). The World Health Organization Adult ADHD Self-Report Scale (ASRS). *Psychological Medicine,* 35(2), 245-256.

Kessler R.C., Adler L.A., Gruber M.J., Sarawate C.A., Spencer T., & Van Brunt DL. (2007). Validity of the World Health Organization Adult ADHD Self-Report Scale (ASRS) Screener in a representative sample of health plan members. *International Journal of Methods* in *Psychiatric Research*, 16(2), 52-65.

Kim, M. S., Kim, Y. Y., Yoo, S. Y., & Kwon, J. S. (2007). Electrophysiological correlates of behavioral response inhibition in patients with obsessive-compulsive disorder. *Depression and Anxiety*, 24(1), 22–31.

Kirby, A., Edwards, L., & Sugden, D. (2011). Emerging adulthood in developmental co-ordination disorder: parent and young adult perspectives. *Research in Developmental Disabilities*, 32(4), 1351-1360.

Klein, R. (1980). Does oculomotor readiness mediate cognitive control of visual attention? In R. Nickerson (Ed.), *Attention and performance III* (pp. 259-276). Hillsdale, NJ: Erlbaum.

Knuckey, N. W., & Gubbay, S. S. (1983). Clumsy children: A prognostic study. *Australian Paediatric Journal*, 19, 9–13.

Kochanska, G., Murrary, K., Jacques, T.Y., Koenig, A.L., & Vandegeest, K.A. (1996). Inhibitory control in young children and its role in emerging internalization. *Child Development*, 67, 490-507.

Kornhuber, S., & Deecke, L. (1965). Changes in the Brain Potential in Voluntary Movements and Passive Movements in Man: Readiness Potential and Reafferent Potentials. *Pflügers Archiv: European Journal of Physiology*, 284, 1-17.

Konczak, J., & Dichgans, J. (1997). The development toward stereotypic arm kinematics during reaching in the first 3 years of life, *Experimental Brain Research,* 117, 346-354.

Kusunoki, M. & Godberg, M. (2002). The time course of perisaccadic receptive field shifts in the lateral intraparietal area of the monkey. *Journal of Neurophysiology,* 89, 1519-1527.

Kutas, M., & Donchin, E. (1980). Preparation to respond as manifested by movement-related brain potentials. *Brain Research*, 24 (1), 95-115.

Land, M.F. (1998). The visual control of steering. In: Harris LR, Jenkin H (eds) Vision and action.Cambridge University Press, Cambridge UK, pp 172-191.

Land, M. F., Mennie, N., & Rusted, J. (1999). The roles of vision and eye movements in the control of activities in daily living. *Perception*, 28, 1311–1328.

Lansbergen, M.M., Böcker, K.B.E., Bekker, E.M., & Kenemans, J.L. (2007). Neural correlates of stopping and self-reported impulsivity. *Clinical Neurophysiology*, 118 (9), 2089-2103.

Larkin, D. & Parker, H.E. (1998). Teaching landing to children with and without developmental coordination disorder. *Pediatric Exercise Science*, 10, 12-136.

Laszlo, J.I. & Bairstow, P.J. (1983). Kinaesthesis: Its measurement, training and relationship to motor control. *Quarterly Journal of Experimental Psychology*, 35a, 411-421.

Laszlo, J. I., & Bairstow, P. J. (1985). Perceptual-motor behaviour: Developmental assessment and therapy. London: Holt, Rinehart & Winston.

Laszlo, J.I. & Sainsbury, K.M. (1993). Perceptual-motor development and the prevention of clumsiness. Special issue: Motor control and sensory-motor integration. *Psychological Research/Psychologische Forschung,* 55, 167-174.

Leconte P, & Fagard J. (2004). Influence of object spatial location and task complexity on children's use of their preferred hand depending on their handedness consistency. *Developmental Psychobiology*, 45(2), 51-8.

Lee, K.M., Chang, K.H., & Roh, J.K. (1999). Subregions within the supplementary motor area activated at different stages of movement preparation and execution. *NeuroImage*, 9, 117–123.

Lestou V., Pollick F.E., & Kourtzi Z. (2008) Neural substrates for action understanding at different description levels in the human brain. *Journal of Cognitive Neuroscience,* 20, 324–341.

Leuthold, H., & Sommer, W. (1998). Postperceptual effects and P300 latency. *Psychophysiology,* 35, 34–46.

Leuthold, H., Sommer,W., & Ulrich, R. (1996). Partial advance information and response preparation: Inferences from the lateralized readiness potential. *Journal of Experimental Psychology*: *General,* 125, 307-323.

Lingam, R., Hunt, L., Golding, J., Jongmans, M. & Emond, A. (2009). Prevalence of Developmental Coordination Disorder Using the DSM-IV at 7 Years of Age: A UK Population–Based Study. *Pediatrics*, 123(4), 693-700.

Liotti, M., Pliszka, S., Perez R., Kothmann, D. & Woldorff, M.G. (2005). Abnormal brain activity related to performance monitoring and error detection in children with ADHD. *Cortex*, 41 (3), 377–388.

Logan, G. D., & Cowan, W. B. (1984). On the ability to inhibit though and action: a theory of an act of control. *Psychological Review*, 91, 295-327.

Logan, G. D. (1994). On the ability to inhibit thought and action: A users' guide to the stop signal paradigm. In D. Dagenbach & T. H Carr (Eds.), *Inhibitory processes in action, memory, and language* (pp. 189–239). San Diego, CA: Academic Press

Losse, A., Henderson, S. E., Elliman, D., Hall, D., Knight, E., & Jongmans, M. (1991). Clumsiness in children - do they grow out of it? A 10-year follow-up study. *Developmental Medicine and Child Neurology*, 33, 55-68.

Lord, R. & Hulme, C. (1987a). Perceptual judgments of normal and clumsy children. *Developmental Medicine and Child Neurology*, 29, 250-257.

Lord, R. & Hulme, C. (1987b). Kinaesthetic sensitivity of normal and clumsy children. *Developmental Medicine and Child Neurology*, 29, 720-725.

Lord, R. & Hulme, C. (1988a). Visual perception and drawing ability in normal and clumsy children. *British Journal of Developmental Psychology*, 6, 1-9.

Lord, R. & Hulme, C. (1988b). Patterns of rotary pursuit performance in clumsy and normal children. *Journal of Child Psychology and Psychiatry*, 29, 691-701.

Luck, S.J. (2005). An introduction to the Event-Related Potential Technique. Cambridge, MA: MIT Press.

Lundy-Ekman, L., Ivry, R., Keele, S. & Woollacott, M. (1991). Timing and force control deficits in clumsy children. *Journal of Cognitive Neuroscience*, 3, 367-376.

Luria, A.R. (1966). Higher Cortical Functions in Man. Basic Books, Inc.: New York.

Lust, J., Geuze, R., Wijers, A., & Wilson, P. (2006). An EEG study of mental rotation-related negativity in children with developmental coordination disorder. *Child: care, health and development*, 32, 649-663.

Macnab, J.J., Miller, L.T. & Polatajko, H.J. (2001). The search for subtypes of DCD: Is cluster analysis the answer? Human Movement Science, 20, 49-72.

Magalhães L.C., Cardoso A.A., & Missiuna C. (2011). Activities and participation in children with developmental coordination disorder: a systematic review. *Research in Developmental Disabilities*, 32(4), 130-1316.

Magill-Evans, J., Galambos, N., Darrah, J. & Nickerson, C. (2008). Predictors of employment for young adults with developmental motor disabilities. Work, 31, 433–442.

Mak, M.K (2010). Reaching and grasping a moving target is impaired in children with developmental coordination disorder. *Pediatric Physical Therapy*, 22(4), 384-391.

Malloy-Miller T., Polatajko H. & Anstett, B. (1995). Handwriting error patterns of children with mild motor difficulties. *Canadian Journal of Occupational Therapy,* 62, 258-267.

Mandich, A.D., Polatajko, H.J. & Rodger, S. (2003). Rites of passage: Understanding participation of children with developmental coordination disorder. *Human Movement Science.* 22, 583-595.

Mandich, A., Buckolz, E. & Polatajko, H. (2002). On the ability of children with developmental coordination disorder (DCD) to inhibit response initiation: The simon effect. *Brain & Cognition*, 50, 150-162.

Mandich, A.D., Buckolz, E. & Polatajko, H.J. (2003). Children with developmental coordination disorder (DCD) and their ability to disengage ongoing attentional focus: more on inhibitory function. *Brain and Cognition*, 51 (2), 346-356.

Mangun, G.R. & Hillyard, S.A. (1991). Modulations of sensory-evoked brain potentials indicate changes in perceptual processing during visual–spatial priming. *Journal of Experimental Psychology: Human Perception and Performance*, 17,1057–1074.

Mari, M., Castell, U., Marks, D., Marraffa, C. & Prior, M. (2003). The reach-to-grasp movement in children with autism spectrum disorder. *Philosophical Transactions of the Royal Society of London*, 358, 393-403.

Maringelli, F., McCarthy, J., Steed, A., Slater, M. & Umilta, C. (2001). Shifting visuo-spatial attention in a virtual three-dimensional space. *Cognitive Brain Research*, 10, 317-322.

Mark LS, Nemeth K, Gardner D, Dainoff MJ, Paasche J, Duffy M, Grandt K (1997). Postural dynamics and the preferred critical boundary for visually guided reaching. *Journal of Experimental Psychology of Human Performance*, 23, 1365–137.

Maruff, P., Wilson, P.H., Trebilcock, M. & Currie, J. (1999). Abnormalities of imagined motor sequences in children with developmental coordination disorder. *Neuropsychologia*, 37, 1317-1324.

Matelli, M., Luppino, G. & Rizzolatti, G. (1985). Patterns of cytochrome oxidase activity in the frontal agranular cortex of macaque monkey. Behavioural *Brain Research*, 18, 125–137.

McCourt, M.E & Garlinghouse, M. (2000). Stimulus modulation of pseudoneglect; Influence of line geometry, *Neuropsychologia*, 38, 520-524.

McLennan, I.S., & Hendry, I.A. (1981). Effect of peripheral deprivation on mammalian mototneurone development, *Brain Research,* 227 (3), 440-443.

Mei, J. (1994). The northern Chinese custom of rearing babies in sandbags: implications for motor and intellectual development. J.H.A Van Rossum & J.L. Laszlo (Eds.), *Motor development: aspects of normal and delayed development*. Amsterdam: VU University Press, 41-48.

Menon, V., Adelman, N.E., White, C.D., Glover, G.H, & Reiss, A.L. (2000). Error-related brain activiation during a Go/NoGO response inhibition task, *Human Brain Mapping,* 12, 131-143.

Mesulam, M.M. (1981). A cortical network for directed attention and unilateral neglect. *Annals of Neurology*, 10, 309-325.

Miller, E.K. & Cohen, J.D. (2001). An integrative theory of prefrontal cortex function. *The Annual Review of* Neuroscience*, 24 (1), 167–202.

Miller, J. & Hackley, S.A. (1992). Electrophysiological evidence for temporal overlap among contingent mental processes. *Journal of Experimental Psychology: General* 121, 195-209.

Milner, A.D. & Goodale, M.A. (1995). *The Visual Brain in Action*. Oxford: Oxford University Press.

Missiuna, C. (1994). Motor skill acquisition in children with Developmental Coordination Disorder. *Adapted Physical Activity Quarterly*, 11, 214-235.

Missiuna C., Moll S., King S., King G., & Law M., (2007). A trajectory of troubles: parents' impressions of the impact of developmental coordination disorder. *Physical & Occupational Therapy in Pediatrics*, 27(1), 81-101.

Missiuna, C., Rivard,L. & Bartlett, D. (2003). Early identification and risk management of children with development coordination disorder. *Pediatric Physical Therapy,* 15, 32-38.

Mobbs, D., Eckert, M.A., Mills, D., Korenberg, J., Bellugi, U., Galaburda, M., & Reiss, A.L. (2007). *Biological Psychiatry,* 62(3), 256-261.

Mon-Williams, M.A., Pascal, E. & Wann, J.P. (1994). Ophthalmic factors in Developmental Coordination Disorder. *Adapted Physical Activity Quarterly,* 11, 170-178.

Mon-Williams, M., Tresilian, J.R. & Wann, J.P. (1999). Perceiving limb position in normal and abnormal control: An equilibrium point perspective. *Human-Movement-Science,* 18, 397-419.

Mon-Williams M, Tresilian JR, Coppard V, Bell V, & Carson RC (2005). The preparation of reach-to-grasp movements in adults, children and children with developmental coordination disorder. *The Quarterly Journal of Experimental Psychology (A),* 58, 1153-1344.

Munzert, J., Lorey, B. & Zentgraf, K. (2009). Cognitive motor processes: the role of motor imagery in the study of motor representations. *Brain Research Reviews,* 60, 306–332.

Neumann, O. (1987). Beyond capacity: a functional view of attention. In H. Heuer & A. F. Sanders (Eds.), *Perspectives on perception and action* (pp. 361–394). Hillsdale, NJ: Lawrence Erlbaum Associates.

Nieuwenhuis, S., Yeung, N., van der Wildenburg, W., & Ridderinkhof, K.R. (2003). Electrophysiological correlates of anterior cingulated function in a go/no-go task: effects of response conflict and trail type frequency. *Cognitive, Affective, and Behavioural Neuroscience,* 3(1), 17-26.

Nigg, J.T. (2001). Is ADHD a disinhibitory disorder? *Psychological Bulletin*, 127, 571–598.

Nobre, A.C., Sebestyen, G.N., & Miniussi, C. (2000). The dynamics of shifting visuospatial attention revealed by event-related potentials. *Neuropsychologia,* 38, 964-974.

Nunez, P.L., & Srinivasan, R. (2006). Electric Fields of the Brain: *The Neuropsychologia*, 38(7), 964-974.

O'Brien, J.C., Williams, H.G, Bundy, A., Lyons, J., & Mittal, A. (2008). Mechanisms that underlie coordination in children with Developmental Coordination Disorder, *Journal of Motor Behaviour,* 40(1), 43-61.

Okada, Y.C., Williamson, S.J., & Kaufman L. (1982). Magnetic field of the human sensorimotor cortex. *International Journal of Neuroscience*,17, 33–38.

Oosterlaan J., Logan G.D., & Sergeant J.A.. (1998). Response inhibition in AD/HD, CD, comorbid AD/HD+CD, anxious, and control children: A meta-analysis of studies with the stop task. *Journal of Child Psychology and Psychiatry*, 39,411–425.

Orton, S. T. (1937) Reading, Writing and Speech Problems In Children. New York, W. W. Norton

Osman, A., Kornblum, S., & Meyer, D. E. (1986). The point of no return in choice reaction time:Controlled and ballistic stages of response preparation. Journal of Experimental Psychology: *Human Perception and Performance*, 12, 243–258.

Osman, A., Moore, C. M., & Ulrich, R. (1995). Bisecting RT with lateralized readiness potentials: precue effects after LRP onset. *Acta Psychologica*, 90, 111-122.

Otten, L.J., & Rugg, M.D. (2004). Interpreting Event-Related Brain Potentials. In T.C. Handy (Ed.), *Event-Related Potentials: A methods Handbook* (pp. 3-16). Cambridge, MA: MIT Press.

Parsons, L. M., Fox, P. T., Downs, J. H., Glass, T., Hirsch, T. B., Martin, C. C., Jerabek, P. A., & Lancaster, J. L. (1995). Use of implicit motor imagery for visual shape discrimination as revealed by PET. *Nature*, 375, 54–58.

Peters, J. M., Henderson, S. E., & Dookun, D. (2004). Provision for children with developmental co-ordination disorder (DCD): Audit of the service provider. *Child: Care, Health and Development*, 30(5), 463-479.

Pettit L, Charles J, Wilson AD, Plumb MS, Brockman A, Williams JHG, Mon-Williams M (2008) Constrained action selection in children with developmental co-ordination disorder.*Human Movement Science*, 27 (2), 286-295.

Pfefferbaum, A., Ford, J.M., Weller, B.J., & Kopell, B.S. (1985). ERPs to response production and inhibition. *Electroencephalography and Clinical Neurophysiology*, 60 (5), 423-434.

Picton, T.W. (1992). The P300 wave of the human event-related potential. *Journal of Clinical Neurophysiology*, 9, 456-579.

Picton, T.W., Bentin, S., Berg, P., Donchin, E., Hillyard, S.A., Johnsons, R., Jr., Miller, G.A., Ritter, W., Ruchkin, D.S., Rugg, M.D., & Taylor, M.J. (2000). Guidelines for using human event-related potentials to study cognition: Recording standards and publication criteria. *Psychophysiology*, 37, 127-152.

Piek, J.P. & Coleman-Carman, R. (1995). Kinaesthetic sensitivity and motor performance of children with developmental co-ordination disorder. *Developmental Medicine and Child Neurology*, 37, 976-984.

Piek, J., Dyck, M., Francis, M., & Conwell, A. (2007a). Working memory, processing speed, and set-shifting in children with developmental coordination disorder. *Developmental Medicine and Child Neurology*, 49, 678-683.

Piek, J.P., Pitcher, T.M. & Hay, D.A. (1999). Motor coordination and kinaesthesis in boys with attention deficit-hyperactivity disorder. *Developmental Medicine and Child Neurology*, 41, 159-165.

Piek, J.P. & Skinner, R.A. (1999). Timing and force control during a sequential tapping task in children with and without motor coordination problems. *Journal of the International Neuropsychology Society*, 5, 320-329.

Pitcher, T.M., Piek, J.P. &Barrett, N.C. (2002). Timing and force control in boys with attention deficit hyperactivity disorder: Subtype differences and the effect of comorbid developmental coordination disorder. *Human Movement Science*, 21, 919-945.

Pliszka, S.R., Liotti, M., Bailey, B.Y., Perez, R., Glahn, D. & Semrud-Clikeman, M. (2007). Electrophysiological effects of stimulant treatment on inhibitory control in children with attention-deficit/hyperactivity disorder. *Journal of Child Adolescent Psychopharmacology*, 17 (3), 356–366.

Plumb., M., Wilson, A., Mulroue, A., Brockman, A., Williams, J., & Mon-Williams, M. (2008). Online movement in children with and without DCD. *Human Movement Science,* 27, 695-704.

Polatajko H.J,, A.M. Fox, A.M., & Missiuna, C. (1995). An international consensus on children with developmental disorder. *Canadian Journal of Occupational Therapy*, 62, 3–6.

Posner, M.I., & Peterson, S.E. (1990). The attention system of the human brain. *Annual Review of Neuroscience*, 13, 25-42.

Posner, M. I., & Dehaene, S. (1994). Attentional networks. *Trends in Neuroscience,* 17(2), 75–79.

Praamstra, P., Boutsen, L., & Humphreys, G.W. (2005). Frontoparietal control of spatial attention and motor intention in human EEG. *Journal of Neurophysiology,* 94, 764-774.

Prado J, Clavagnier S, Otzenberger H, Scheiber C, Kennedy H, Perenin MT

(2005) Two cortical systems for reaching in central and peripheral vision.

Neuron, 48, 849– 858.

Pratt, M.L. & Hill, E.L. (2011). Anxiety profiles in children with and without developmental coordination disorder. *Research in Developmental Disabilities*, 32(4), 1253-1259.

Pryde, K.M., Bryden, P.J.,&. Roy, E.A. (2000). A developmental analysis of the relationship between hand preference and performance: I. Preferential reaching into hemispace. *Brain and Cognition,* 43, 370–374.

Querne, L., Berquin, P., Vernier-Hauvette, M.P., Fall, S., Deltour, L., Meyer, M.E. (2008). Dysfunction of the attentional brain network in children with developmental coordination disorder: an fMRI study. *Brain Research,* 1244, 89–102.

Rasmussen, P. & Gillber C. (2000). Natural outcome of ADHD with Developmental Coordination Disorder at Age 22 Years: A Controlled, Longitudinal, Community-Based Study. *Journal of the American Academy of Child and Adolescent Psychiatry,* 39 (11), 1424-1431.

Raynor, A.J. (2001). Strength, power, and coactivation in children with developmental coordination disorder. *Developmental Medicine and Child Neurology*, 43, 676-684.

Ribot-Ciscar E, Rossi-Durand C, & Roll J.P (1998). Muscle spindle activity following muscle tendon vibration in man. *Neuroscience Letters*, 258, 147–150.

Riek, S., Tresilian, J. R., Mon-Williams, M., Coppard, V. L., & Carson, R. G. (2003). Bimanual aiming and overt attention: One law for two hands. *Experimental Brain Research,* 153(1), 59–71.

Robbins, T. W., James, M., Owen, A. M., Sahakian, B. J., Lawrence, A. D., McInnes, L. & Rabbitt, P. M. A. (1998). A study of performance on tests from the CANTAB battery sensitive to frontal lobe dysfunction in a large sample of normal volunteers: implications for theories of executive functioning and cognitive aging. *Journal of the International Neuropsychological Society*, 4, 474–490.

Roberts, L.E., Rau, H., Lutzenberger, W., & Birbaumer, N. (1994). Mapping P300 waves onto inhibition: Go/No-Go discrimination. *Electroencephalography and Clinical Neurophysiology*, 92, 44–55.

Rodger S., Ziviani J., Watter P., Ozanne, A., Woodyattm, G. and Springfield, E. (2003): Motor and functional skills of children with Developmental Coordination Disorder (DCD): A pilot investigation of measurement issues. *Human Movement Science*, 22, 461-478.

Ricker, K. L., Elliot, D., Lyons, J., Gauldie, D., Chua, R., & Byblow, W. (1999). The utilization of visual information in the control of rapid sequential aiming movements. *Acta Psychologica,* 103, 103–112.

Ridderinkhof, R.K., van den Wildenburg, W.P.M., Segalowitz, S.J., & Carter, C.S. (2004). Neruocognitive mechanisms of cognitive control: The role of prefrontal cortex in action selection, response inhibition, performance monitoring, and reward-based learning, *Brain and Cognition,* 56, 129-140.

Rizzolatti, G., Riggio, L. & Sheliga, B. (1994). Space and selective attention. In C. Umilta & M. Moscovitch, (Eds.). *Attention and Performance XV* (pp. 231-265). Cambridge, MA: MIT Press.

Rosenbaum, D.A., Vaughn, J., Barnes, H.J., & Jorgenson, M.J. (1992). Time course of movement planning: Selection of handgrips for object manipulation. *Learning, Memory, and Cognition,*18(5), 1058-1073.

Rosenbaum, D. A. (1980). Human movement initiation: Specification of arm, direction, and extent. *Journal of Experimental Psychology: General*, 109, 444– 474.

Rubia, K., Overmeyer, S., Taylor, E., Brammer, M., Williams, S., Simmons, A. et al. (1999). Hypofrontality in attention deficit hyperactivity disorder during higher-order motor control: A study with functional MRI. *American Journal of Psychiatry,* 156, 891–896.

Rubia, K., Smith, A. B., Wooley, J., Nosarti, C., Heyman, I., Taylor, E., & Brammer, M. (2006). Progressive increase in frontostriatal activation from childhood to adulthood during event-related tasks of cognitive control. *Human Brain Mapping*, 27, 973-993.

Rubia, K., Smith, A., Brammer, M., Toone, B. & Taylor, E. (2005). Abnormal brain activation during inhibition and error detection in medication-naive adolescents with ADHD. *American Journal of Psychiatry,* 162 (6),1067–1075.

Ryding E, Decety J, Sjoholm H, Stenberg G, Ingvar DH (1993) Motor imagery activates the cerebellum regionally. A SPECT rCBF study with 99mTc-HMPAO. *Cognitive Brain Research,* 1, 94–99.

Sainsbury, D.F, Griggs, C.B, Shenton, M.E, McCarley, R.W. (2004). The Nogo P300 anteriorization Effect and Response Inhibition. *Clinical Neruophysiology,* 115(7), 1550-1558.

Saltzman, E. L. & Munhall, K. G. (1989). A dynamical approach to gestural patterning in speech production. *Ecological Psychology*, 1(4), 333-382.

Sanders, A.F. (1980). Some effects of instructed muscle tension on choice reaction time and movement time. In R. Nickerson (Ed.), *Attention and Performance VIII* (pp. 59-74). Hillsdale, NJ: Lawrence Erlbaum.

Sasaki, K., Gemba, H., & Tsujimoto, T. (1990). Cortical field potential associated with hand movement on warning-imperative stimulus and cerebellum in the monkey. *Brain Research*, 519 (1) 343-346.

Sahyoun, C.P., Belliveau, J.W., Soulieres, I., Schwartz, S., & Mody, M. (2010). Functional and structural networks of pictorial reasoning in high functioning autism. *Neuropsychologia*, 48, 86-95.

Schiegg, A., Deubel, H., & Schneider, W. X. (2003). Attentional selection during preparation of prehension movements. *Visual Cognition,* 10(4), 409-431.

Schmidt, R.A. (1975). A schema theory of discrete motor skill learning. *Psychological Review,* 82, 225-260.

Schoemaker, M.M., Wees M. van der, Flapper B., Verheij-Janssen N., Scholten-Jaegers S. & Geuze R.H. (2001). Perceptual skills of children with Developmental Coordination Disorder. *Human Movement Science,* 20, 111-133.

Schweinsburg, A.D. Nagel, B.J. & Tapert, S.F. (2005). fMRI reveals alteration of spatial working memory networks across adolescent development. *Journal of the International Neuropsychological Society*, 11 (5), 631-644.

Screws, D.P., Eason, B.L., & Surburg, P.R. (1998). Crossing the midline: A study of four year-old children. *Perceptual Motor Skills,* 86(1), 201-203.

Sigmundsson, H. (2003). Perceptual deficits in clumsy children: inter and intramodal matching approach-a window into clumsy behavior. *Neural plasticity,* 10, 27-38.

Sigmundsson, H., Ingvaldsen, R.P. & Whiting, H.T.A. (1999). Proximal versus distal control in proprioceptively guided movements of motor-impaired children. *Brain Behaviour Research*, 106, 47-54.

Sergeant, J.A., Geurts, H.M., & Oosterlaan, J. (2002). How specific is a deficit of executive functioning for Attention-Deficit/Hyperactivity Disorder? *Behavioural Brain Research,* 130, 3–28.

Shallice, T. (1988). From neuropsychology to mental structure. Cambridge: Cambridge University Press.

Shibasaki, H., & Hallet, M. (2006). What is the Bereitschaftspotential? *Clinical Neurophysiology*, 117 (11), 2341-2356.

Sims, K., Henderson, S.E., Hulme, C. & Morton, J. (1996a). The remediation of clumsiness. I: an evaluation of Laszlo's kinaesthetic approach. *Developmental Medicine and Child Neurology*, 38, 967-987.

Sims, K., Henderson, S.E., Morton, J. & Hulme, C. (1996b). The remediation of clumsiness. II: Is kinaesthesis the answer? *Developmental Medicine and Child Neurology*, 38, 988-997.

Sirigu, A., Duhamel, J.R., Cohen, L., Pillon, B., Dubois, B., & Agid, Y. (1996) The mental representation of hand movements after parietal cortex damage. *Science,* 273, 1564–1568.

Skinner, R.A. & Piek, J.P. (2001). Psychosocial implications of poor motor coordination in children and adolescents. *Human Movement Science,* 20, 73-94.

Smith, J. L., Johnstone, S. J. & Barry, R. J. (2007). Response priming in the Go/Nogo task: The N2 reflects neither inhibition nor conflict. *Clinical Neurophysiology*, 118, 343-355.

Smits-Engelsman, B.C.M., Wilson, P.H., Westenberg, Y. & Duysens, J. (2003). Fine motor deficiencies in children with developmental coordination disorder and learning disabilities: An underlying open-loop control deficit. *Human Movement Science*. 22, 495-513.

Smyth, T. R. (1992). Impaired motor skill (clumsiness) in otherwise normal children: a review. *Child: Care, Health and Development,* 18, 283-300.

Smyth, M.M. & Mason, U.C. (1997). Planning and execution of action in children with and without Developmental Coordination Disorder. *Journal of Child Psychology and Psychiatry*, 38, 1023-1037.

Smyth, M.M. & Mason, U.C. (1998a). Direction of response in aiming to visual and proprioceptive targets in children with and without Developmental Coordination Disorder. *Human Movement Science*, 17, 515-540.

Smyth, M.M. & Mason, U.C. (1998b). Use of proprioception in normal and clumsy children. *Developmental Medicine & Child Neurology*, 40, 672-681.

Smyth, T.R. (1991). Abnormal clumsiness in children: a defect of motor programming? *Child: Care, Health and Development,* 18, 283-300.

Smyth, T.R. & Glencross, D.J. (1986). Information processing deficits in clumsy children. *Australian Journal of Psychology,* 38, 13-22.

Snow, J.H., Blondis, T.A. & English R.A. (1991). Neuropsychological skills with motor dysfunctional and motor normal children. *Archives of Clinical Neuropsychology*, 6, 271-278.

Snyder, L. H., Batista, A. P., & Andersen, R. A. (1997). Coding of intention on the posterior parietal cortex. *Nature*, 386, 167–170.

Sober SJ, Sabes PN (2003). Multisensory integration during motor planning. *Journal of Neuroscience*, 23, 6982–6993.

Sober SJ, Sabes PN (2005) Flexible strategies for sensory integration during motor planning. *Nature Neuroscience*, 8, 490–498.

Steele, C. (1994). Latency measurements of anticipatory postural reactions in clumsy and non-clumsy children. Unpublished Masters Thesis, University of Queensland, Brisbane.

Stief, V., Leuthold, H., Miller, J., Sommer, W., & Ulrich, R. (1998). The effect of response complexity on the lateralized readiness potential. *Zeitschrift für Psychologie*, 206, 305-319.

Strick, P.L., Dum, R.P., & Picard, N. (1995). Macro-organization of the circuits connecting the basal ganglia with the cortical motor areas. In J.C. Houk, J.L Davis, & D.G. Beiser (Eds.), *Models of information processing in the basal ganglia* (pp.117-130). Cambridge, MS: MIT Press.

Stroop, J.R. (1935). Studies of interference in serial verbal reactions, *Journal of Experimental Psychology,* 18 (6), 643-662.

Stott, D. H., Moyes, E. A. and Henderson, S. E. (1984) The Henderson Revision of the Test of Motor Impairment, London: The Psychological Corporation.

Sugden, D.A. and Chambers, M.E. (1998). Intervention approaches and children with developmental coordination disorder. *Pediatric Rehabilitation,* 2, 139-147.

Sugden, D.A. & Chambers, M.E. (2001) Management and intervention in children with developmental coordination disorder: the role of teachers and parents. *Research Report submitted to Action Research*, 124.

Sugden, D.A., Chambers, M., & Utley, A. (2006). Leeds Consensus Statement. Developmental Coordination Disorder as a Specific Learning Difficulty. Leeds: University of Leeds.

Sugden, D.A. and Chambers, M.E. (2005). *Children with Developmental Coordination Disorder.* London: Whurr Publishers Ltd.

Summers, J., Larkin, D., & Dewey, D. (2008). Activities of daily living in children with developmental coordination disorder: Dressing, personal hygiene, and eating skills. *Human Movement Science*, 27(2), 215-229.

Sutton, S., Braren, M., & Zubin, J. (1965). Evoked-potential correlates of stimulus uncertainty. *Science*, 150, 1187-1188.

Tamm, L., Menon, V., & Reiss, A. L. (2002). Maturation of brain function associated with response inhibition. *Journal of the American Academy of Child and Adolescent Psychiatry*, 41 (10), 1231-1238.

Taylor, P.C.J, Nobre, A.C., & Rushworth, M.F.S. (2007). Subsecond chances in top-down control exerted by human medial frontal cortex during conflict and action selection: A combined transcranial magnetic stimulation-electro encephalography study, *The Journal of Neuroscience,* 27(42), 11343 -11353.

Tereo, Y., Andersson, N. E. M., Flanagan, J. R., & Johansson, R. S. (2002). Engagement of gaze in capturing targets for future sequential manual actions. *Journal of Neurophysiology*, 88, 1716–172.

Townsend J., Harris, N.S., & Courchesne, E. (1996). Visual attention abnormalities in autism: delayed orienting to location. *Journal* of the *International Neuropsychological Society*, 2, 541–550.

Tsai, C.L., Pan, C.Y., Cherng, R.J., Hsu, Y.W. & Chiu, H.H. (2009). Mechanisms of deficit of visuospatial attention shift in children with developmental coordination disorder: a neurophysiological measure of the endogenous Posner paradigm. *Brain and Cognition*, 71(3), 246-258.

Tsiotra, G.D., Nevill, A.M., Lane, A.M. & Koutedakis, Y. (2009). Physical fitness and developmental coordination disorder in Greek children. *Pediatric Exercise Science*, 21(2), 186-195.

Turano, K.A., Broman, A.T., Bandeen-Roche, K., Munoz, B., Rubin, G.S., & West, S.K. (2004). Association of Visual Field Loss and mobility Performance in Older Adults: Salisbury Eye Evaluation Study. *Optometry and Vision Science*, 120, 298-307.

Ulrich, R., Leuthold, H., & Sommer, W. (1998). Motor programming of response force and movement direction. *Psychophysiology*, 35, 721-728.

Utley, A., Steenbergen, B. & Astill, S.L. (2007). Ball catching in children with developmental coordination disorder: control of degrees of freedom. *Developmental Medicine and Child Neurology*, 49 (1), 34-38.

Valle-Inclan, F. & Redondo, M. (1998). On the automaticity of ipsilateral response activation in the Simon effect. *Psychophysiology*, 35(4), 366-371.

Van Dellen, T. & Geuze, R.H. (1988). Motor response processing in clumsy children. *Journal of Child Psychology and Psychiatry*, 29, 489-500.

Van Dellen, T. & Geuze, R.H. (1990). Experimental studies on motor control in clumsy children. In A.F. Kalverboer (Ed.), *Developmental biopsychology: Experimental and observational studies in children at risk* (pp.187-206). Ann Arbor: University of Michigan Press

Van der Meulen, J.H.P., Denier van de Gon, J.J., Gielen, C.C.A.M., Gooskens, R.H.J. & Willemse, J. (1991a). Visuomotor performance of normal and clumsy children I: Fast goal directed arm movements with and without visual feedback. *Developmental Medicine and Child Neurology*, 33, 40-54.

Van der Meulen, J.H.P., Denier van de Gon, J.J., Gielen, C.C.A.M., Gooskens, R.H.J. & Willemse, J. (1991b). Visuomotor performance of normal and clumsy children II: Arm-tracking movements with and without visual feedback. *Developmental Medicine and Child Neurology,* 33, 118-129.

Van Donkelaar, P., Lee, J.H., & Drew, A.S. (2002). Eye-Hand interactions difer in the human premotor cortices, *Human Movement Science*, 21 (3), 65-74.

Van Hof, P., van der Kamp., J. & Savelsbergh, G.J.P. (2002). The relation of unimanal and bimanual reaching to crossing the midline. *Child Development*, 73 (5), 1353-1362.

van Swieten, L.M., van Bergen, E., Williams, J.H.G., Wilson, A.D., Plumb, M.S., Kent, S.W. and Mon-Williams, M.A. (2009). A test of motor (not executive) planning in developmental coordination disorder and autism. *Journal of Experimental Psychology Human Perception and Performance*, 36(2):493-499.

van Velzen, J., Gherri, E., & Eimer, M. (2006). ERP effects of movement preparation on visual processing: Attention shifts to the hand, not the goal. *Cognitive Processing*, 100, 101.

Van Voorhis,S. & Hillyard, S.A. (1977). Visual evoked potentials and selective attention to points in space. *Perception and Psychophysics*, 22(1), 54-62.

Van Waelvelde H, De Weerdt W, De Cock P, Smits-Engelsman BCM, et al. (2004). Ball catching performance in children with Developmental Coordination Disorder. *Adapted Physical Activity Quarterly,* 21(4), 348-363.

Verbruggen F. & Logan G.D. (2008). Automatic and controlled response inhibition: Associative learning in the go/no-go and stop-signal paradigms. *Journal of Experimental Psychology*, 137(4):649-72.

Verleger, R., Vollmer, C., Wauschkuhn, B., van der Lubbe, R.H., & Wascher, E. (2000). Dimensional overlap between arrows as cueing stimuli and responses? Evidence from contra-ipsilateral differences in EEG potentials. *Cognitive Brain Research*, 10, 99-109.

Verleger, R., Jaskowski, P., & Wascher, E. (2005). Evidence for an integrative role of P3b in linking reaction to perception. *Journal of Psychophysiology*, 19(3), 165-181.

Verleger, R., Kuniecki, M., Moller, F., Fritzmannova, M., and Siebner, H. R. (2009). On how the motor cortices resolve an inter-hemispheric response conflict: an event-related EEG potential-guided TMS study of the flankers task. *European Journal of Neuroscience,* 30, 318-326.

Verleger, R., Paehge, T., Kolev., Yordanova, J., & Jaskowski, P. (2006). On the relation of movement related potentials to the go.no-go effect on P3. *Biological Psychology*, 73(3), 298-313

Visser, J. (2003). Developmental coordination disorder: a review of research on subtypes and comorbidities. *Human Movement Science,* 22, 479-193.

Von Hofsten C, Rösblad B. (1988) The integration of sensory information in the development of precise manual pointing. *Neuropsychologia*, 26, 805–821.

Walter, W.G, Cooper, R., Aldridge, V.J., McCallum, W.C. & Winter, A.L. (1964). Contingent Negative Variation: an electric sign of sensorimotor association and expectancy in the human brain. *Nature,* 203, 380–384.

Wann JP. (1991) The integrity of visual–proprioceptive mapping in cerebral palsy. *Neuropsychologia*, 29, 1095–106.

Wann, J.P., Mon-Williams, M. & Rushton, K. (1998). Postural control and co-ordination disorders: The swinging room revisited. *Human Movement Science*, 17, 491-514.

Wang, Y. & Cai, H.D. (2010). Mental processing models and neural mechanisms for response inhibition, *Advances in Psychological Science,* 18(2), 220-229.

Wang, L., Kuroiwa, Y., Li, M., Wang, J., & Kamitani, T. (2001). Do P1 and N1 evoked by the ERP task reflect primary visual processing in Parkinson's disease? *Documenta Opthalmologica,* 102, 83-92.

Ward, J. (2006). *The Student's Guide to Cognitive Neuroscience.* New York: Psychology Press.

Ward, N.S. & Frackowiak, R.S. (2003). Age-related changes in the neural correlates of motor performance, *Brain*, 18, 670-674.

Weinstein, J.M., Balaban, C.D., VerHoeve, J.N. (1991). Directional tuning of the human presaccadic spike potential. *Brain Research*, 543(2), 243–250.

Wilmut, K., Brown, J.H. and Wann, J. P (2007) Attention Disengagement in children with Developmental Coordination Disorder. *Disability and rehabilitation* (1), 47-55.

Wilmut, K., Wann, J. P., & Brown, J. H. (2006). Problems in the coupling of eye and hand in the sequential movements of children with developmental coordination disorder. *Child: Care, Health and Development*, 32, 665–678.

Williams, H.G., Woollacott, M.H. & Ivry, R. (1992). Timing and motor control in clumsy children. *Journal of Motor Behavior,* 2, 165-172.

Williams, J., Thomas, P., Maruff, P., Butson, M., & Wilson, P. (2006). Motor, visual and egocentric transformations in children with developmental coordination disorder. *Child: care, health, and development,* 32, 633-647.

Wilson, B.N., Kaplan, B.J., Crawford, S.G., Campbell, A. & Dewey, D. (2000). Reliability and validity of a parent questionnaire on childhood motor skills. *American Journal of Occupational Therapy*, 54(5), 484-493.

Wilson, P.H., Maruff, P. & McKenzie, B. E. (1997). Covert orienting of visuospatial attention in children with developmental coordination disorder. *Developmental Medicine and Child Neurology*, 39, 736-745.

Wilson, P.H. & McKenzie, B. E. (1998). Information processing deficits associated with Developmental Coordination Disorder: A meta-analysis of research findings. *Journal of Child Psychology and Psychiatry*, 39, 829-840.

Wilson, P.H. & Maruff, P. (1999). Deficits in the endogenous control of covert visuospatial attention in children with developmental coordination disorder. *Human Movement Science,* 18, 421-442.

Wilson, P., Maruff, P., Butson, M., Lum, L., & Thomas, P. (2004). Internal representation of movement in children with developmental coordination disorder: a mental rotation task. *Developmental Medicine and Child Neurology*, 46, 754-759.

Wilson, P.H., Maruff, P., Ives, S. & Currie, J. (2001). Abnormalities of motor and praxis imagery in children with DCD. *Human Movement Science*, 20, 135-160.

Woodard, R., & Surburg, P. (1999). Midline crossing behaviour in children with learning disabilities. *Adopted Physical Activity Quarterly*, 16, 155-166.

Wodka, E. (2007). Evidence that response inhibition is a primary deficit in ADHD. Journal of Clinical Experimental. *Neuropsychology.* 29,345-356.

Wolpert D.M., Ghahramani Z., & Jordan M.I. (1995). An internal model for sensorimotor integration. *Science,* 269,1880 –188.

Wolpert, D. M. (1997). Computational approaches to motor control. *Trends in Cognitive Sciences*, 1(6), 209–219.

World Health Organisation. (1992). ICD-10 Classifications of Mental and Behavioural Disorder: Clinical Descriptions and Diagnostic Guidelines. Geneva. World Health Organisation.

Yamaguchi, S., Tsuchiya, H., & Kobayashi, S. (1994). Electroencephalographic activity associated with shifts of visuospatial attention. *Brain*, 117, 553–562.

Zoia, S., Castiello, U., Blason, L. & Scabar, A. (2005). Reaching in Children with and without Developmental Motor Coordination Disorder and under normal and perturbed vision. *Developmental Neuropsychology*, 25, 257-273.

Zwicker, J.G., Missiuna, C., Harris, S.R., & Boyd, L.A. (2011). Brain activation associated with motor skill practice in children with developmental coordination disorder: an fMRI study. *International Journal of Developmental Neuroscience,* 29(2),145-152.

.

.

.

.

.