Running Head: TDCS of Right TPJ

Enhancing Social Ability by Stimulating Right Temporoparietal Junction

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Highlights

- Transcranial direct current stimulation (tDCS) of temporoparietal junction (TPJ).
- Excitatory stimulation improved the on-line control of self-other representations.
- Stimulation did not affect the attribution of mental states to the self or another.

Summary

The temporoparietal junction (TPJ) is a key node within the 'social brain' [1]. **Several studiessuggest that the TPJ controlsrepresentations of the self or another individual acrossa variety of low-level (agency discrimination [2], visual perspective taking[3], control of imitation [4]), and high-level (mentalizing, empathy [4***-***6]) socio-cognitive processes. We explored whether socio-cognitive abilitiesrelying on on-line control of self and other representationscould be** modulated using transcranial direct current stimulation (tDCS) of TPJ. **Participants received either excitatory (anodal), inhibitory (cathodal) or sham stimulation before completingthree socio-cognitive tasks. Anodal stimulation improved the on-line control of self-other representationselicited by theimitation** and perspective-taking tasks, while not affecting attribution of mental states **during a self-referential task devoid of such a requirement. Our findings demonstrate the efficacy of tDCS to improve social cognition and highlight the potential for tDCS to be used as a tool to aid self-other processing in clinical populations.**

Results

The majority of our knowledge concerning TPJ function has been provided by functional Magnetic Resonance Imaging (fMRI) studies. Brain stimulation methods such as tDCS are an important addition to fMRI, as they allow cortical excitability to be directly manipulated. TDCS is a non-invasive technique that stimulates the cerebral cortex with a weak constant electric current passed between two electrodes (anodal and cathodal) on the scalp. Current flows from an active to a reference electrode causing either decreased (cathodal) or enhanced (anodal) cortical excitability. In non-social domains, anodal stimulation has been shown to enhance perceptual [7] and motor [8] learning, while the effects of cathodal stimulation are less reliable [9]. In the social domain, studies employing tDCS remain limited and to the best of our knowledge, this is the first study to stimulate TPJ using tDCS.

Consistent TPJ activation across many socio-cognitive tasks suggests a basic function shared by both low-level and higher-order socio-cognitive processes. One potential candidate function is the on-line *control* of self-other representations i.e. the biasing of processing towards either the self or the other when task demands cause both the self and the other to be represented [4,10,11]. We tested the hypothesis that anodal stimulation of TPJ should lead to enhanced socio-cognitive abilities: specifically, by enhancing the ability to control, on-line, co-activated representations of the self and the other. Participants received either anodal (*N*=17), cathodal $(N=17)$ or sham $(N=15)$ stimulation – which produces the same sensation as active stimulation but has no effect on neuronal populations $[12]$ – of right TPJ for 20 minutes prior to completing three socio-cognitive tasks. Two of these tasks required self and other representations to be controlled (the perspective-taking task required the self to be inhibited and the other enhanced while the control of imitation task required the other to be inhibited and the self enhanced), whereas the third task (the self-referential task) did not require on-line self-other control.

During the control of imitation task participants were asked to perform either the same (congruent trials) or a different (incongruent trials) finger movement as that observed on a computer screen. Incongruent trials require participants to inhibit an imitative response and therefore distinguish and control motor representations evoked by the self and the other. *Self* representations must be enhanced, and *other* representations inhibited. Thus, improved imitative control is indexed by a reduced tendency to imitate (Imitation Effect: Incongruent $RT -$ Congruent RT) driven by faster performance on incongruent trials. This pattern was observed when the anodal group was compared to the cathodal group: The anodal group showed a significantly reduced Imitation Effect (anodal: $M = 16.15$ ms, $SE.M = 5.73$, cathodal: $M = 52.50$, *S.E.M*= 10.88, $p = 0.04$; **Figure 1a**). The comparison between the anodal and sham ($M=52.30$; $SEM = 13.21$ groups approached significance at $p = 0.051$. The decreased imitation effect found in the anodal (vs. cathodal) group was driven by faster responses on incongruent trials $(modal: M = 446.45, SE.M = 17.80; cathodal: M = 537.06, SE.M = 17.80; p = 0.002)$.

In the perspective-taking task participants were required to adopt the viewpoint of a 'Director' who gave them instructions to move objects on a shelf (Figure S1). Experimental trials involved a conflict between the Director's and the participant's perspective, and therefore control of self and other representations was again necessary for accurate performance. However, in contrast to the control of imitation task, accurate performance on this task requires enhancement of the *other* and inhibition of the *self* perspective. Nevertheless, anodal stimulation to TPJ also improved performance on the perspective-taking task such that the anodal group (proportion correct $M = 0.86$, *S.E.M.* = 0.07) was better able to take the Director's perspective than the cathodal ($M = 0.60$, *S.E.M.* = 0.07; $p = 0.031$) and the sham ($M = 0.53$, *S.E.M.* = 0.07; $p = 0.006$) groups (**Figure1b**).

Finally, in the self-referential task, participants were asked to make mental ("think people should know they are appreciated") or physical ("have very smooth skin") judgements about themselves or another person, before later completing a surprise recognition memory test for the judgements. On each trial **either** the self **or** the other is represented, therefore in contrast to the previous tasks, there is no requirement for on-line control of co-activated self and other representations. As a consequence, despite the presence of the standard 'self-reference effect' [13] (indexed by faster RTs $[F_{(1,46)} = 16.33, p < 0.001,$ Figure 1c) and improved memory performance $[F_{(1,44)} = 24.19, p < 0.001]$ for self judgements in all three groups, rTPJ stimulation did not selectively affect processing of either physical or mental judgements concerning either the self or the other. The anodal group was faster on all judgements than the cathodal group ($p =$.003). However, none of the interactions between the type of stimulation, target of judgement [self vs other], and type of judgment [mental vs physical], factors were significant (all $ps \geq .24$). Performance on the surprise recognition memory test for self and other judgements also revealed no effect of stimulation (all $ps > 0.42$).

Discussion

Anodal stimulation of the right TPJ enhanced the ability to control imitation and take the visual perspective of another, but did not affect the ability to attribute mental states to the self or others. These findings suggest that within the realm of social cognition, the area of the right TPJ stimulated in this study is recruited in situations where on-line control of co-activated self and other representations is crucial for successful social interaction. The control of imitation task requires participants to distinguish between their own action intentions and those of the 'other' (represented by the stimulus hand on the screen), and carry out their own motor intention rather than the observed action. On-line control of self and other representations is also crucial in the visual perspective-taking task, except that in this task one must inhibit the self perspective and enhance that of the 'other'. In the self-referential task, faster responses of the anodal (compared

to the cathodal) group on all trial types suggest that anodal stimulation of TPJ improved participants' ability to make judgements about both the self and the other. This result therefore provides further support for the commonly reported role of TPJ in representation of the self and the other. We have suggested that successful performance on this task does not require the distinction or control of co-activated self and other representations. On each trial, before making a mental or physical judgement, participants are cued as to whether the judgement relates to the self or to the other and therefore it is likely that only the self, or the other, is represented, but not both. However, it could be argued that on every trial both the self and other is represented, despite the cue, and that therefore self-other control *is* required in this task. If so, then the main effect of stimulation further supports the role of the TPJ in the domain-general control of self and other representations. Regardless of which interpretation is correct, the absence of a significant interaction between type of stimulation and target (self vs. other) and judgement type (mental vs. physical) suggests that processes supporting the on-line control of self and other representations are independent of those required to attribute mental states [4].

Previous research using a combination of tDCS and fMRI [14] has shown that tDCS has a focal effect at the site of stimulation and on interconnected areas in a functional network, but does not affect neural responses of regions within the vicinity of the anodal electrode. Therefore, our results are unlikely to be due to a non-specific increase of cortical excitability in adjacent brain regions. Nevertheless, it is important to acknowledge that tDCS does not have the spatial specificity to allow us to distinguish functional subdivisions in the TPJ. Indeed, given that we did not include an active control site, the anatomical specificity of our results is difficult to determine. It will be interesting to examine the role that different subdivisions of the TPJ play in future studies, possibly using different brain stimulation methodologies like transcranial magnetic stimulation.

In the non-social domain, right TPJ activation has been found in attention reorienting [15,16]. Although recent research suggests that attention reorienting and attribution of mental states recruit partially distinct regions of right TPJ [17], some researchers propose that the overlapping activation could reflect shared cognitive processes between these two mental abilities (for an overview see Corbetta, Patel & Shulman, 2008) [18]. The control of self and other representations as described here results in the biasing of processing towards self or other when both representations are active. It is plausible that the same TPJ-mediated processes that allocate attention to regions of space are also used to allocate attention to either self or other representations.

Appropriate control of self and other representations has been shown to be important for positive social interactions such as prosocial behaviour [19], and is impaired in those with autism spectrum conditions [20]. These findings therefore indicate the potential for tDCS to be used as a tool to enhance self-other processing, which may have therapeutic benefits in individuals in whom this process has broken down.

Experimental Procedures

Participants

Forty-nine right-handed adults (24 females, age range 18-45 years, $M = 26.5$, $S/D = 6.7$) participated in this study for a small monetary reward. Participants were randomly assigned to the anodal ($N=17$), cathodal ($N=17$), or control 'sham' ($N=15$) groups. Groups did not differ in terms of age ($F_{(2,48)} = 0.35$, $p = 0.7$) or gender ($\chi^2 = 0.16$, $p = 0.9$). All participants were healthy volunteers, without any known developmental or neurological disorders and no contraindications to tDCS. They were all naïve with respect to experimental hypotheses and remained unaware of what type of stimulation they received until the end of the experiment.

Procedure

Prior to the testing session, all participants were provided with written information about the study and a description of the tDCS procedure. The associated safety / risk warnings were explained and participants were asked to sign an informed consent form. This study received full ethical approval by the local Ethics Committee.

The stimulation was induced using 2 saline-soaked surface sponge electrodes 35 cm^2 in size and delivered by a battery-driven, constant current stimulator. For the stimulation of the rTPJ, the anodal or cathodal (depending on the group assignment) electrode was placed over CP6 (electroencephalography 10/20 system) [21]. The reference electrode was placed over the vertex, individually measured on each participant. A relatively weak electrical current (1mA) was delivered for 20 minutes. For the sham group, the set-up was identical to the anodal group, but the stimulator was only turned on for 15 seconds; participants felt the initial itching sensation associated with tDCS but received no active current for the rest of the stimulation period. Offline stimulation (i.e. stimulation preceding task performance) was used as previous work suggests that effects are more robust than on-line stimulation, at least for anodal stimulation [22].

Participants were not tested before and after stimulation due to the considerable likelihood of ceiling effects as a result of practice on the control of imitation and perspective-taking tasks. In addition, the self-referential task is not amenable to two testing sessions, as it requires a surprise memory test. It is unlikely that pre-existing differences in social ability (despite random allocation to groups) could explain the pattern of results, given the levels of statistical significance observed (likelihood of obtaining these data if the null hypothesis is true). However, given the considerable inter-individual variability in social ability, these results stand in need of

replication both in other samples and in those populations who are theorised to have atypical self-other control (e.g. Autism Spectrum Conditions).

In order to standardise the memory delay between the self-referential task and the surprise memory test, the tasks were administered to all participants in the following order: control of imitation, self-referential, perspective-taking and memory test for self-referential task. A description of each of the tasks is provided below. Significant effects of stimulation on the control of imitation and perspective-taking tasks suggest that, at minimum, stimulation effects lasted until the start of the self-referential memory task. However, stimulation is likely to have been effective over a longer time period. Previous studies have shown that, for humans, 13 minutes of off-line anodal tDCS at 1mA results in a sustained increase in cortical excitability for up to 90 minutes following stimulation, after which there is a linear decrease to baseline levels [23]. Increased duration of stimulation is known to prolong the effects of tDCS stimulation [24]. Therefore, the 20 minutes of off-line anodal tDCS at 1mA used here is expected to induce sustained increases in cortical excitability for at least 2 hours. This is significantly in excess of the 60 minute testing time

Control of imitation task [25]: the stimuli consisted of short videos showing either an index or middle finger performing a lifting movement. The stimulus hand was rotated around the sagittal and transverse planes with respect to the participant's hand, which rested on the computer keyboard. This set up allowed imitative effects to be separated from those due to spatial compatibility. Participants were asked to respond with an index or middle finger lifting action to a number cue that appeared between the fingers of the stimulus hand. They were asked to lift their index finger upon appearance of a 1, and their middle finger upon appearance of a 2. At the same time as the appearance of the number cue, there was a lifting movement of the index or middle finger of the stimulus hand. Although the observed movements were formally task-

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irrelevant, the relationship between the observed movement and the movement required by the number defined two trial types. On congruent trials, the required finger movement was the same as the observed movement; whereas on incongruent trials, the required finger movement was different from the observed movement. Thus, on incongruent trials participants were required to inhibit an imitative response and perform the pre-instructed movement. Twenty trials in each of the four combinations of observed and executed finger movements were presented in a random order.

Perspective-taking task [26]: This task required participants to take into account the point of view of a character, introduced as 'the director'. The visual stimuli consisted of a 4x4 grid $('shelves')$ containing 8 different objects. Five slots were occluded from the view of the director, who stood on the other side of the shelves (see Supplemental Materials Figure S1). Participants listened to auditory instructions from the director who asked them to move specified objects in a particular direction. On experimental trials, there was a conflict between the participant's and the director's perspective. For example, if the participant was presented with the array shown in Figure S1a, and was asked to "move the large candle up", they should ignore the largest candle they can see, the 'competitor object', (because the director cannot see it), and instead move the next largest candle, which is visible to the director. There were two control conditions: C1 and C2. In C1, the director instructed participants to move an object placed in one of the clear slots (e.g. the mug), and therefore there was no conflict between the perspectives of the participant and the director. In C2, an irrelevant object replaced the 'competitor' item from the experimental condition but the instruction remained the same (see Figure S1b). Accuracy of the selection and movement of the target object and reaction times were recorded.

Self-referential task: This task was adapted from a previous version used by Lombardo and colleagues [27]. Participants were asked to make either mental or physical judgements about

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themselves or a famous person (Lady Gaga). At the beginning of the task they read a brief bio of Lady Gaga and were told that they would be asked to rate how likely either Lady Gaga (other) or the participant themselves (self) were to have certain opinions, likes, and dislikes. For example, an 'other-mental' judgement would be: how likely is **she**to enjoy the adrenaline rush of taking risks? whereas, a 'self-physical' judgement could be: how likely are *you* to have large feet? Prior to each trial, the word 'YOU' or 'LADY GAGA' was presented on the screen for 2 seconds (font size 45pts). Therefore, participants knew before the start of data (RT) collection whether the following opinion judgement would relate to the self or the other. There were 20 items in each trial type (self-mental, self-physical, other-mental, other-physical). Participants made judgements on a scale of $1 - 4$ (1= not at all likely, 4= very likely). The self vs. other statements were counterbalanced within each group. To encourage participants to engage with the task and therefore elicit 'other' thoughts in the Lady Gaga condition, they were told that their answers would be compared to the answers given by her over a number of interviews and they would receive an 'accuracy score' at the end. This 'score' was randomly generated and presented on the screen at the end of the task. Reaction times for each trial type were recorded.

Surprise Memory test: This was administered after completion of the perspective-taking task, approximately 25 minutes after the self-referential task. Participants were presented with a judgement statement and asked to rate how confident they were that they had seen it before on a scale of 1-6 (1=definitely not seen it, 2=probably not seen it, 3 = possibly not seen it, 4= possibly seen it, 5 = probably seen it, 6 = definitely seen it). For items they thought they had seen before (those rated from 4-6) they were further asked to rate how confident they were that the statement was in reference to themselves or to Lady Gaga (1= definitely self, 6= definitely Lady Gaga). Twenty 'old' (previously presented) and twenty 'new' (matched for number of words) statements for each condition were presented.

Statistical Analyses: For a description of statistical analyses performed and a full description of control analyses see Supplementary Experimental Procedures.

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Competing Interests Statement

The authors declare no competing financial interests.

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Figure Legends

Figure 1. Anodal tDCS of rTPJ improves on-line control of self-other representations. (A) Control of imitation: This task examined the ability to distinguish and control motor representations evoked by the self and the other. Improved performance following anodal stimulation (in comparison to cathodal and sham stimulation) is indexed by a reduced tendency to imitate. **(B)** Perspective-taking: This task required participants to take another's perspective and inhibit their own (See Supplemental Figure S1). Anodal stimulation resulted in more accurate performance. (C) Self-referential: This task examined participants' ability to attribute mental states to the self or another individual. Unlike the tasks that required on-line control of self-other representations (control of imitation and perspective taking), no effect of rTPJ stimulation was found on mental state attribution (self-referential task). Error bars represent S.E.M.

Imitation Effect Incongruent RT - Congruent RT (ms) 10 20 50 60 70 \circ 30 40 $\overline{1}$ Anodal **Group** Cathodal Sham

A

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B

Figure 1c

Inventory of Supplemental Information

Figure S1 (related to Figure 1b): Perspective-taking task

Stimuli for the perspective-taking task.

Supplemental Experimental Procedures

Full description of statistical analyses performed and details of control analyses.

Supplemental References

Supplemental Figures

Figure S1 (related to Figure 1b): Perspective-taking task

(A) Example of an experimental trial requiring participants to inhibit the 'self' perspective and adopt the perspective of the 'other' when instructed to "move the large candle." Participants must ignore the largest candle they can see and choose the medium-sized candle that the 'other' can see. (B) Example of the control trials where the self and other perspectives are not in conflict (same instruction as A).

Supplemental Experimental Procedures

Statistical Analyses

Where sphericity assumptions were not met, Greenhouse-Geisser corrected values are reported. Bonferroni corrections were used for post hoc multiple comparisons.

Control of imitation task

The RT and accuracy data were analysed using ANOVA with group as the between-subjects factor (anodal vs. cathodal vs. sham) and trial type as the within-subject factor (congruent vs. incongruent).

RT

Prior to the statistical analysis, extreme RT scores identified by the 1.5 x inter-quartile range rule¹ were removed from each participant's dataset. The analysis revealed a significant main effect of trial type, $F(1,46)$ = 46.89, $p < 0.001$, $\eta^2 \pi p = .51$; indicating that responses on congruent trials were executed faster than those on incongruent trials. The main effect of group was also significant, $F(2,46)$ = 6.14, *p* = .004, η^2 _, = .21. Pairwise comparisons showed that this effect was driven by the difference in performance between the anodal and the cathodal group (*p* = .003). Crucially, the group x trial type interaction was also significant, $F(2,46)$ = 4.31, p = 0.019, $\eta^2_{\text{ p}}$ = .16; indicating a smaller RT difference between congruent and incongruent trials in the anodal than in the cathodal and sham groups. This was confirmed with a one-way ANOVA - including all three groups - on the imitation effect (incongruent - congruent RT), $F(2,48) = 4.31$, $p = 0.019$, pairwise comparisons revealed a difference in performance between the anodal (*M* = 16.15ms, *S.E.M=* 5.73)*,* and the cathodal (*M* = 52.50ms, *S.E.M=* 10.88 *; p* = 0.040) groups; the comparison between anodal and sham (*M* = 52.30, *S.E.M=* 13.21) approached significance (*p* = 0.051). Raw RTs on Congruent trials mean (and SEM) in milliseconds were: Anodal 430 (13); Cathodal 485 (13); and Sham 454 (14). The same data on Incongruent trials were as follows: Anodal 446 (18); Cathodal 537 (18); Sham 506 (19).

Accuracy

The mean total number of errors was 6.08, *S.E.M. =* 0.95. The main effect of trial type was significant, *F*(1,46) = 19.07, *p* < 0.001, η^2_{p} = 0.29; overall, participants made more errors in the incongruent (*M* = 3.95, *S.E.M. =* 0.62) than in the congruent (*M* = 2.14, *S.E.M.* = 0.40) trials. The main effect of group and the group x trial type interaction were not significant, (*p* =0.84. and *p =*0*.*49, respectively*)*, indicating that the type of stimulation did not affect accuracy on this task.

Perspective-taking task

The accuracy and RT data were analysed using ANOVA with group as a between-subject factor and trial type (Exp vs. C1 vs. C2) as the within-subjects factor.

RT

A significant main effect of trial type was found, $F(1.75, 77.14)$ =80.87, $p < 0.001$, $\eta^2_{p} = 0.65$. Overall, participants responded faster to the C1 (*M* = 2.62s, *S.E.M*. = 48.53) trials than to the experimental (*M* = 3.03s, *S.E.M*. = 74.64, *p* <.001) or the C2 trials (*M* = 2.96s, *S.E.M*. = 65.58, *p* <.001). Neither the main effect of group nor the group x trial type interaction were significant, (all *p*s > .40).

Accuracy

There was a main effect of trial type, $F(1.02, 44.96)$ = 54.52, p < 0.001, η^2_{p} = 0.55. Overall, performance (proportion of correct responses) was worse on experimental trials (*M* = 0.66, *S.E.M*. = 0.04) than on control trials: C1 (*M* = 0.96, *S.E.M*. = 0.01), C2 (*M* = 0.93, *S.E.M* = 0.01); confirming the previously reported difficulty in taking the director's perspective observed using this task². The main effect of group was also significant *F*(2,44) = 4.35, *p*< 0.02, $\eta^2_{\;\:p}$ = 0.17. Post-hoc pairwise comparisons showed that performance of the anodal group (*M* = .93, *S.E.M*. = .03) was significantly better than the sham group (*M* = .81, *S.E.M*. = .03, *p* = 0.03) while the comparison with the cathodal group failed to reach significance (*M* = .83, *S.E.M*. = .03, *p* = 0.06). The predicted group x trial type interaction was significant, F(1.02, 44.96) = 6.37; $p = 0.003$; η^2 _, = 0.23. Post-hoc analysis showed that while all groups performed similarly on control trials, on experimental trials, the anodal group (*M* = .86, *S.E.M*. = .03) performed significantly better than both the cathodal (*M* = .60, *S.E.M*. = .083, *p* =0.031) and the sham (*M* = .54, *S.E.M*. = .09, *p*= 0.006) groups. Thus, anodal stimulation enhanced performance by making participants better at separating their own perspective from that of the director's when the perspectives were in conflict.

Self-referential task

RT data were analysed using ANOVA with group as a between-subject factor and target (self vs. other) and trial type (mental vs. physical) as the within-subjects factors. There was a main effect of target, $F(1,46) = 16.33$; $p < 0.001$; $\eta^2_{p} = 0.26$. Overall, participants responded faster in 'self' (M = 3.31 s, *S.E.M.* = 0.16) than in 'other' trials (*M* = 3.56 s, *S.E.M.* = 0.17; *p* <0.001). The main effect of group was also significant *F* (2,46)= 6.17, *p* = 0.004, η^2_{p} = 0.21). Pairwise comparison showed that overall, the anodal group (*M* = 2.72 s, *S.E.M.* = 0.28) was faster than the cathodal group (*M* = 4.13 s, *S.E.M*. = 0.28; *p* = 0.003). No other main effects or interactions were significant (all *p*s>0.24). In order to ensure that the significant main effect of group did not represent an effect of stimulation on self-other control *between* trials, trials were subdivided into 'switch' trials (where a 'self' trial is preceded by an 'other' trial or vice versa) and 'noswitch' trials (where the target of the judgement is the same on trial n and n-1). If there was an effect of stimulation on self-other switching between trials on this task, one would expect this effect to be greater on switch trials than on noswitch trials, resulting in a type of stimulation x trial type (switch / noswitch) interaction. However, the stimulation x trial type interaction was not significant ($p = 0.33$).

Surprise memory test

The RT data and accuracy data were analysed using repeated measure ANOVAs with group as a between subject factor and target (self vs. other) and trial type (mental vs. physical) as within subject factors. Accuracy was assessed using Signal Detection Theory (d' values)³.

Accuracy

Again, a main effect of target was found *F* (1,44) =24.19, *p* < 0.001, η_{p}^{2} = 0.36. Across all groups, participants were better able to remember items that were self-related (*M* = 0.81, *S.E.M.* = 0.23) than other-related (*M =* 0.74, *S.E.M.* = 0.25). No other main effects or interactions were significant (all *p*s > 0. 42). The lack of a 3-way and a group x target interaction in both the self-referential task and the memory test suggests that stimulation to the rTPJ did not have an effect on attribution of either physical or mental characteristics to another.

Supplemental References

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- 3. Green, D. M., and Swets, J. A., (1966). Signal detection theory and psychophysics. (New York: Wiley).