Optimized alpha band patterns correlated with trait anxiety

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***Abstract*—Anxiety is one of the most prevalent mental disorders, affecting approximately 5-10% of the adult population worldwide. It can severely impact quality of life, but also place a large burden on the health systems. Despite its omnipresence and impact on mental and physical health, most of the individuals suffering from anxiety do not receive appropriate treatment. Furthermore, while neuroimaging research consistently implicated subcortical structures such as amygdala, hippocampus and prefrontal cortex in anxiety, there is still a lack of consensus on the underlying neurophysiological processes contributing to this condition. Thus, the objective neurophysiological markers for anxiety remain elusive. Methods allowing non-invasive recording and assessment of cortical processing provide an opportunity to help identify anxiety signatures that could be used as interventional targets. In this paper, we tackle this problem by applying a regression spatial filter called Source-Power Comodulation (SPoC) to trait anxiety data of 43 individuals. By maximizing the correlation of alpha band power and the level of trait anxiety in resting state EEG we are able to obtain neurophysiologically meaningful patterns that should be helpful in the search of biomarkers for mental disorders.**

***Keywords*—Trait anxiety, EEG analysis, Alpha band, Correlation, Brain Patterns, Interpretability**

I. Introduction

Anxiety disorders affect 275 million individuals worldwide. On the subclinical level, heightened anxiety is becoming increasingly prevalent in light of growing uncertainty over the global health and economical situation in 2020-2021. In recent years, an enormous effort has been devoted to understanding the neurobiology of anxiety disorders, combining animal work with human neuroimaging studies in healthy and clinical populations.

Converging neuroimaging evidence in clinical and subclinical anxiety indicates that alterations in dorsal medial prefrontal (anterior cingulate) cortex and subcortical brain regions can explain an array of cognitive-affective alterations in these populations [1, 2, 3]. To date, however, our general understanding of the neurophysiological processes involved in anxiety is limited. Use of noninvasive techniques to record brain activity with high temporal resolution, such as EEG or MEG, provides an opportunity to assess changes in the dynamics of neural activity associated with anxiety. The analysis of neural oscillations, in particular, is ideally suited to identify markers of aberrant physiological processing in neuropsychiatric conditions. By linking alterations in neural oscillations to clinical and subclinical manifestations of anxiety, it would be possible to define novel neurophysiological targets for neuromodulatory and pharmacological interventions.

Previous EEG research pointed to cross-frequency correlations as a candidate marker for anxiety disorders ([3, 4, 5]). In particular, alterations in the amplitude-amplitude cross-frequency correlations (AAC) between delta ($<$ 4Hz) and beta (13-30 Hz) oscillations have been associated with social anxiety and with aberrant stress regulatory processes ([2, 3]). The direction of the effect remained, however, unclear, with some studies linking increased delta-beta AAC over frontal regions to pronounced social anxiety ([1]), while others associated this change with reduced trait anxiety ([6]). Analysis of phase-amplitude coupling (PAC), which is a different measure of information transfer between neuronal populations, may resolve these ambiguities, and can be reliably modulated on a within-subject level following a social anxiety manipulation ([4]). The functional significance of these effects remains elusive, however, despite suggestions that delta-beta AAC and PAC could reflect altered coupling between frontal and subcortical circuits implicated in anxiety disorders.

An alternative EEG marker of aberrant neural dynamics in anxiety conditions could be the oscillatory power over frontal regions, consistent with the vast fMRI evidence implicating the prefrontal cortex in clinical and subclinical anxiety. Measures of alpha power (8-12 Hz) have been used to obtain the index of frontal alpha asymmetry, which can be sensitive to a range of emotional changes including anxiety conditions [7, 8]. Yet the direction of this effect, as well as the sign of change in alpha power seem inconsistent [9, 10, 8]. A potential solution to these inconsistencies is to use methods that provide not

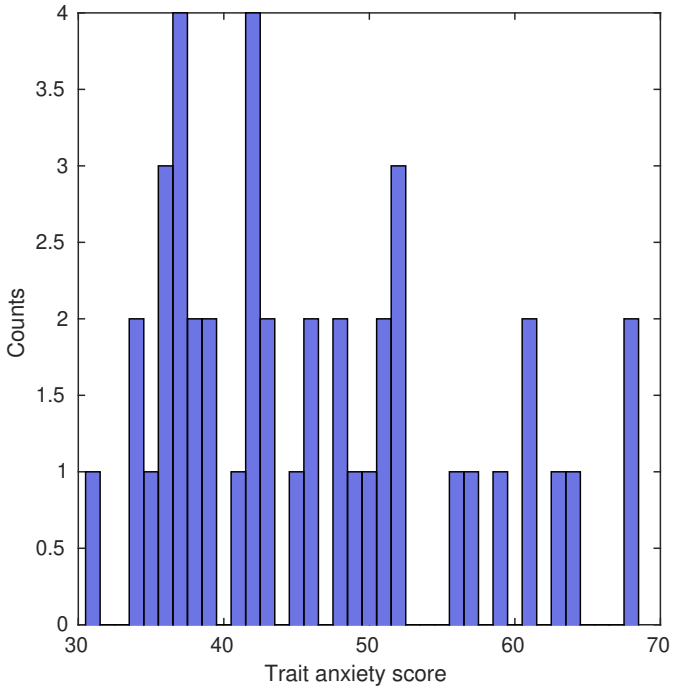

Fig. 1. Histogram of the Spielberger trait anxiety scores in our participant sample.

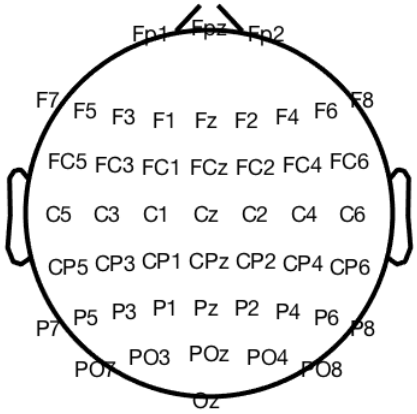

Fig. 2. Electrodes selected for the analyses.

only optimal solutions for the search of associations between neuronal measures and behavioral/psychological parameters, but also neurophysiologically interpretable results.

In this work we present results of applying a novel spatial filtering technique, called Source Power Comodulation (SPoC, [11]) to find brain patterns maximally correlated to a real valued variable. This variable is the trait anxiety level of 43 persons whose EEG resting state data was subsequently measured. We hypothesized that this method would find patterns more strongly correlated to anxiety than usual sensor-based correlations and that this pattern can then potentially be used in the future studies for guiding neuromodulation approaches (e.g. non-invasive brain stimulation, neurofeedback) to treat conditions associated with anxiety.

II. Methods

A. Data availability

The data used for the analyses in this paper were obtained from our previous study [12], which was approved by the local ethical review committee at Goldsmiths, University of London. EEG, ECG and EOG data was available from 43 participants during wakeful rest (5 minutes, eyes open). In addition, trait anxiety scores were available, which had been obtained with the Spielberger State-Trait scale (Trait sub-scale, 20 items, score in range 0-80). The trait values in our sample were distributed between 30 and 68 (Figure 1).

B. EEG acquisition and preprocessing

EEG, ECG and EOG signals were recorded using the BioSemi ActiveTwo system (64 electrodes, extended international 10–20, sampling rate 512 Hz). External electrodes were placed on the left and right earlobes to use as references upon importing the EEG data in the analysis software. ECG and EOG signals were recorded using bipolar configurations. For EOG, we used two external electrodes to acquire vertical and horizontal eye-movements, one on top of the zygomatic bone by the right eye, and one between both eyes, on the glabella. For ECG we used two external electrodes in a two-lead configuration.

EEG data had been preprocessed in the EEGLAB toolbox (Delorme and Makeig 2004) for Matlab®[12]. In that study, the continuous EEG data were filtered using a high-pass filter at 0.5 Hz (hamming window sinc finite impulse response filter with order 3380) and then notch-filtered at 48–52 Hz (filter order 846). Next, artefacts related to eye blinks, saccades and heartbeats were removed from the signals using independent component analysis (ICA, runICA implementation; 2.3 components were removed on average). See [12] for further details on pre-processing.

The analyses performed in this work were based on a subset of electrodes covering the whole scalp (Figure 2).

C. Sensor-based correlation

The usual way for to investigate association of power of neuronal oscillations and their relation to behavioral/clinical variables is to use data directly from channels. Specifically, sensor-based correlations are computed with respect to a variable of interest (the trait anxiety score in the current study). To that aim, the sensor signals of resting-state data were filtered in the alpha band (8-12 Hz) and then the data was cropped into 2 second windows. For each of those windows, the variance of each sensor was computed and averaged across windows, obtaining one power value per sensor. Finally, the correlation of each sensor to the external value (trait anxiety score) was computed. We employed the Spearman correlation

coefficient, that is robust against deviations from the normality assumption.

However, we want to remark that although correlation values between a variable of interest from individual channels and some neuroscientific related measure is a common way to establish relationships in neuroscience, these results cannot be interpreted to draw conclusions about relationships between variables of interest and brain sources. In fact, when the computation of the neuroscientific measures involves non-linear operations, linking the results with their cerebral origin is not possible anymore in sensor space. This is the case for example for power, where squaring data is necessary which in turn leads to the removal of phase information. However, phase information is important for the adequate reconstruction of neuronal sources, and thus such results cannot be related to the neuronal origin of the observed effects. In any case, and to reflect the difference between sensor based results and SPoC, we report both in this manuscript.

D. Source Power Comodulation, SPoC

Source Power Comodulation or SPoC is a method designed to decompose multivariate neuroimaging data (EEG/MEG) into source components by using the information contained in a external target variable to direct the decomposition [11]. As a result, a set of spatial filters is found that optimizes the covariation or correlation (depending on the selected objective function) between the external target z and the power time course of the corresponding SPoC source. That is, SPoC maximizes the correlation between neural signals and a variable of interest, thereby identifying the filters/patterns maximally related to the variable of interest. Furthermore, although SPoC was developed to find subject-specific patterns (intra-subject results), it is also possible to perform inter-subject calculations by defining each of the epochs as the data of one subject. Finally, unlike in section III-A, the obtained patterns can be neurophysiologically interpreted.

Although two different SPoC algorithms exist, for this paper we have selected the one providing an analytical solution. As described in [11], by maximizing the covariation between a brain source and an external variable, one can arrive at the following optimization problem:

$$\arg\max \boldsymbol{w}^T \boldsymbol{C}_z \boldsymbol{w} \tag{1}$$

with respect to the following norm constraint:

$$\boldsymbol{w}^T \boldsymbol{C} \boldsymbol{w} = 1 \tag{2}$$

with $\boldsymbol{C}_z$ being the covariance between the power (in form of a covariance matrix) of the band-pass filtered EEG signal at each epoch and the standardized external value z (with zero mean and unit variance); and $\boldsymbol{C}$ the averaged value of the epoch covariance matrices of the band-pass filtered EEG signal.

The aforementioned constrained optimization problem can be solved using the method of Lagrange multipliers. Setting the first derivative of the corresponding Lagrangian to zero leads to the following generalized eigenvalue equation:

$$\boldsymbol{C}_z \boldsymbol{w} = \boldsymbol{\lambda} \boldsymbol{C} \boldsymbol{w} \tag{3}$$

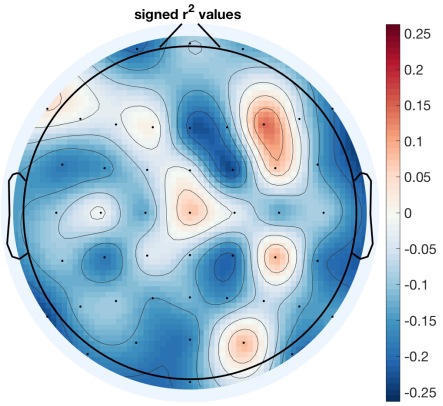

Fig. 3. Distribution over the scalp of signed correlation values at alpha frequency.

In order to apply SPoC we proceeded as follows: the data was pre-processed as in section II-C, i.e. it was filtered in the alpha band (8-12 Hz) and cropped into 2-second long windows. Then, instead of the variance of each electrode, the corresponding covariance matrix was computed for each window and averaged over epochs. Thus we obtained one covariance matrix per subject, which was used to feed the selected SPoC algorithm together with the standardized trait score results of each participant.

III. Results

This section is divided into two parts. In the first one, we present results on sensor-based correlations. The second part presents SPoC-related outcomes.

A. Sensor based correlations

As seen in Figure 3, sensor-based correlations for alpha power are mostly negative (blue color in Figure 3, that correspond to the 48 sensors depicted in Figure 2), although positive values are also present (6 sensors). The absolute correlation values were small, ranging between -0.23 (*p-value* $= 0.054$) and 0.14 (*p-value*$= 0.125$). None of the sensor-based correlation results were significant.

The largest correlation values – albeit non-significant – spread over the medial-frontal regions, yet the sign shifted from negative to positive values in neighboring electrodes.

B. SPoC on resting state EEG data

In this section we present the results of applying SPoC to band-passed filtered $(8 - 12$ Hz) resting state EEG.

We observed that the largest signed-correlation value was -0.67, with a *p-value* of $3.57 * 10^{-7}$. This result corresponds to the pattern presented in Figure 4. This pattern has a fronto-central distribution with central and right lateralized maxima, corresponding to neuronal sources in the frontal cortex.

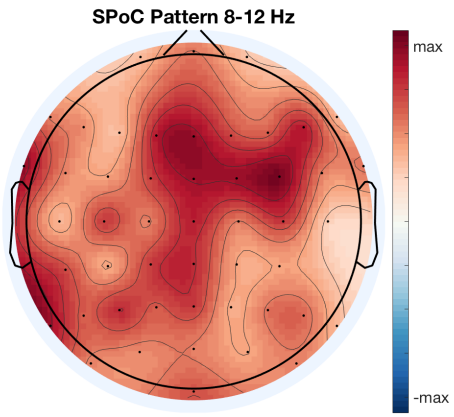

Fig. 4. Maximally correlated SPoC pattern. Note that this Figure does not represent a distribution of signed-correlation values over the scalp, but a pattern related to a maximally correlated source to trait anxiety levels.

IV. Discussion

This paper aimed to assess the usefulness of SPoC to identify topographic patterns in EEG oscillatory activity reflecting maximum correlation with trait anxiety scores. Using EEG recordings in healthy participants with different trait anxiety scores, our SPoC analysis demonstrated a consistent pattern of alpha power associated with maximal negative and significant correlations with the trait scores. In contrast to the results on standard correlation analysis, which revealed different signs of correlations in neighbouring electrodes, and low non-significant correlation values, SPoC demonstrated a coherent pattern with frontocentral maxima. These results suggest that SPoC presents a unique opportunity to mitigate inconsistencies in the previous EEG-anxiety correlation findings.

Unlike classic correlation analyses, SPoC patterns can be neurophysiologically interpreted [11]. The frontocentral distribution of negative correlations between alpha power and trait scores is aligned with the spatial distribution of effects in previous work on anxiety. In particular, existing empirical evidence linked frontal alpha asymmetry to resting state, but also to approach and avoidance behaviour, in social anxiety [9, 10, 8]. Some of this work proposed that greater left frontal power asymmetry could be a valid marker of anxiety and depression [10]. However, there is still a lack of consensus on how (social) anxiety modulates frontal alpha power and power asymmetry, as some attempts to validate these markers did not found significant effects [9]. Using SPoC to detect patterns of maximum correlations between EEG power and experimental variables (trait scores, behavioral indexes) could mitigate confounds from standard correlation analyses and provide an optimised topographical pattern that could be used to localise anatomical sources.

Follow-up work will aim to localise in the source space the SPoC patterns reported here, and will clarify whether the negative association between frontocentral alpha power and trait anxiety scores is mediated by activity in the prefrontal cortex, which is one of the key cortical regions implicated in anxiety disorders [13].

Acknowledgment

The work of CV was supported by MINECO-RyC-2014-15671. Furthermore, the research leading to these results has received partial funding from the Basic Research Program at the National Research University Higher School of Economics (MHR, VN).

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