Analysis of Functional Connectivity during an Auditory Oddball Task in Schizophrenia

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***Abstract*—The aim of this study was to evaluate neural coupling patterns in schizophrenia (SCH) patients and healthy controls during an auditory oddball task. Two measures of functional connectivity were applied to 28 SCH patients and 51 healthy controls to characterize electroencephalographic (EEG) activity. Specifically, magnitude squared coherence (*MSC*) and the imaginary part of coherency (*ICOH*) were computed for five frequency bands: theta, alpha, beta-1, beta-2 and gamma. The results showed a statistically significant modulation increase in *MSC* and *ICOH* for controls with respect to SCH in the theta band, and a decrease in *ICOH* for the beta-2 band. Furthermore, controls showed more significant changes from the baseline and active task windows than SCH patients. Our findings suggest that SCH patients show coupling abnormalities during an auditory oddball task compared to healthy controls.**

I. INTRODUCTION

SCHIZOPHRENIA (SCH) is a psychiatric disorder characterized by a cluster of symptoms and signs, such as hallucinations, delusions and reduced motivation, among others, that vary among subjects [1]. These symptoms are frequently accompanied by impairment in cognitive processing. It has been suggested that SCH patients have an abnormal pattern of functional connectivity between different parts of the brain [2].

In this study, two measures of functional connectivity were computed to characterize neural coupling in SCH. Magnitude squared coherence (*MSC*) and the imaginary part of coherency (*ICOH*) are two non-directed measures that seek to capture independence and evaluate phase synchrony between signals [3]. *MSC* is a classical method that has been widely used in the literature. In contrast, *ICOH* is a novel measure that has gained some momentum over the past years in electroencephalographic (EEG) connectivity studies [3]. The aim of this study was to compute these two measures for SCH patients and healthy controls, in order to analyze abnormal coupling patterns in SCH.

II. MATERIALS AND METHODS

A. Subjects

Seventy-eight subjects were recruited for the study: 28 SCH patients (age 31.19±10.43 years, mean ± standard deviation, SD) and 51 healthy controls (age 29.30±9.74 years, mean ± SD). Patients were diagnosed according to the Diagnostic and Statistical Manual of Mental Disorders 5th edition (DSM-V).

B. Electroencephalographic Recordings

EEG recordings were acquired with a BrainVision® (Brain Products GmbH; Munich, Germany) system, consisting of 32 sensors mounted in an electrode cap (Electro-Cap International, Inc.; Eaton, Ohio, USA) and placed according to the International 10/20 System. Thirteen minute-length recordings were acquired at a sampling rate of 500 Hz. Channels TP9 and TP10 were discarded due to abundant muscle artifacts throughout. Participants underwent a three-stimulus auditory oddball task. The tones were presented in random 600 tone series consisting of target (500 Hz), distractor (1000 Hz), and standard (2000 Hz), with probabilities of 0.20, 0.20, and 0.60 respectively. The post-processing applied to the EEG signals after recording is described in [4].

C. Continuous Wavelet Transform

Time-frequency analysis can provide additional information that is not apparent in the ongoing EEG. It is often assumed that changes in EEG power reflect underlying changes in neuronal synchrony, as EEG rhythms are the product of synchronized activity among neuronal assemblies [5]. In this study, time-frequency maps were computed using the Continuous Wavelet Transform in the same way as [4].

D. Magnitude squared coherence

There are different measures that analyze the consistency between the EEG from different pairs of electrodes in order to characterize the regional connectivity and interregional interactions of the brain [5]. Coherency (*COH*) is defined as the standardized cross-spectrum of complex signals *X* and *Y* across trials, divided by the product of the power spectrum of *X* and *Y*. *COH* is defined as [5]:

$$COH_{xy}(f,t)=\frac{S_{XY}(f,t)}{\sqrt{P_X(f,t)P_Y(f,t)}} \qquad (1)$$

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where S_{XY} is the cross-spectrum of X and Y, and P_X and P_Y are the power spectra of X and Y respectively.

COH is a complex number. *MSC* summarizes the contribution of its magnitude. Therefore, it is defined as:

$$MSC_{xy}(f,t) = \left|COH_{xy}(f,t)\right|^2 = \frac{\left|S_{XY}(f,t)\right|^2}{P_X(f,t)P_y(f,t)} \quad (2)$$

E. Imaginary part of coherency

When *COH* is plotted onto the imaginary axis, the *ICOH* is obtained. The main advantage of *ICOH* is that it is able to remove instantaneous interactions, which may be spurious due to volume conduction, as it discards interactions at a phase difference of 0° or 180° [3]. It is, however, generally a small measure, which increases the risk of missing meaningful interactions [6].

F. Statistical Analysis

One second-length target trials were decomposed into the baseline, defined as the [-300 0] ms window and the response [150 450] ms window. *MSC* and *ICOH* were computed separately for each of these windows and averaged in five frequency bands: theta (θ, 4-8 Hz), alpha (α, 8-13), beta-1 (β1, 13-19 Hz), beta-2 (β2, 19-30 Hz) and gamma (γ, 30-70 Hz). A *z-score* baseline correction procedure was carried out in order to capture event-related changes in brain activity [5].

Initially, an exploratory analysis was performed to analyze data distribution. Normality was tested with a Kolmogorov-Smirnov test and homoscedasticity with a Levene test. These analyses revealed that the data did not meet parametric test assumptions. Wilcoxon signed rank tests were used to analyze the within-group statistical differences between *MSC* and *ICOH* in the baseline and response windows. Mann-Whitney *U*-tests were performed to assess coupling differences between SCH patients and controls. A false discovery rate (FDR) correction was applied in order to minimize type I error.

III. RESULTS AND DISCUSSION

Fig. 1 shows the results of the Mann-Whitney *U*-tests for θ and β2 bands, which were the only bands that showed statistically significant differences. Connections were only shown if they obtained statistically significant differences between the stimulus response and the baseline after FDR correction ($p<0.05$). Our analyses showed a statistically significant increase of *MSC* and *ICOH* in controls with respect to patients in θ band, and a decrease of *ICOH* in β2 band.

SCH patients did not show as many statistically significant changes ($p<0.05$) between the response and baseline windows as the control group. This is especially clear in β2 band, in which patients do not display any significant changes ($p<0.05$). Controls experimented an increase in *MSC* coupling in θ band and a decrease in β2 band, which is in agreement with previous studies [4].

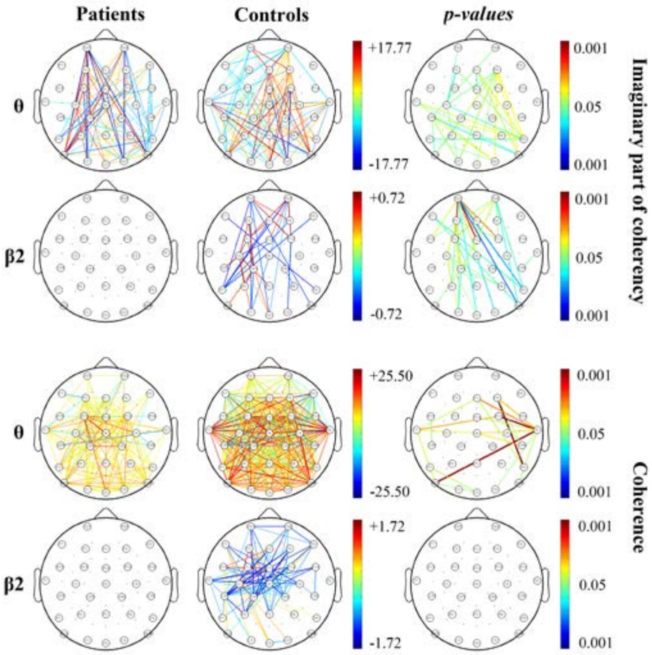

Fig. 1. Spatial analyses of coupling in θ and β2 bands for *MSC* and *ICOH*. The left and central columns show the *z*-values for SCH patients and controls. Hot colors represent a coupling increase during auditory response in comparison to baseline. The right column displays statistically significant *p*-values for the between-groups comparison. Hot colors represent higher *z*-values for controls than for SCH patients.

Our findings suggest that SCH patients are not able to reconfigure their brain coupling patterns as controls when attending to target stimuli during an auditory oddball task. These results point to an abnormal reorganization of neural coupling in SCH. Furthermore, *ICOH* exhibited a significant difference between groups in the β2 band, which suggests that *ICOH* could be sensitive to weak but relevant interactions that *MSC* is not able to detect.

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