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Resting-state mu activity modulations are associated with aloofness

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ABSTRACT

Background: Autism-like symptoms in the non-clinical general population are referred to as the broad autism phenotype (BAP). To date there have been no studies investigating how BAP might correlate with measurements from the resting-state electroencephalogram (EEG).
Method: EEG resting-state data were collected in 20 young adults during both eyes-closed (EC) and eyes-open (EO) resting states. Permutation modelling was used to assess correlations of the Broad Autism Phenotype Questionnaire (BAPQ) with source localised resting alpha activity.
Results: Total scores on the BAPQ were strongly correlated with differences between oscillatory brain activity during EC and EO rest in a pattern that was classified as the mu rhythm. More mu activity during EC rest compared to EO rest was found to be associated with higher BAPQ scores (i.e. more prominent BAP symptoms).
Conclusions: Mu is a known correlate of activity in the mirror neuron system (MNS), which has been implicated in the social deficits associated with autism. It is therefore suggested that this BAPQ-correlated mu activity could reflect the readying of the MNS for social input by visual stimulation. These findings offer novel insights into how the BAP is reflected in resting-state recordings of brain activity.

1. Do resting-state mu activity modulations reflect the readying of systems that support social interaction?

Autism spectrum disorder (ASD) is typically defined by a triad of symptoms: impairments in social interaction, pragmatic language impairments, and repetitive or restricted behaviours and interests (Happé & Ronald, 2008). The observation of qualitatively similar traits at subclinical levels in the general population has been termed the broad autism phenotype (BAP) (Piven, Palmer, Jacobi, Childress, & Arndt, 1997). The present experiment aimed to investigate whether patterns of resting-state brain activity obtained using electroencephalography (EEG) are associated with the BAP, a possibility that might yield important insights into subclinical manifestations of autistic symptoms in the general population, and broader insights into social cognition.

Investigations of resting-state whole brain activity are becoming increasingly common, particularly in neurological populations (Cherkassky, Kana, Keller, & Just, 2006; Murias, Webb, Greenson, & Dawson, 2007). Aside from resting-state investigations being eminently repeatable as a paradigm, increasing evidence suggests that brain activity at rest is associated with specific task-related behaviours and cognitive functions (Hahn et al., 2012; Kunisato et al., 2011). In the context of autism, most studies have focused on clinically-significant ASD; few have examined correlations of resting activity with BAP symptoms in the general population.

The present study focused on eyes-open (EC) and eyes-closed (EC) resting-state oscillatory EEG activity in the alpha band (8–15 Hz). Alpha activity is one of the most prominent oscillatory patterns observed in resting EEG, and there is a long history of investigating alpha activity during rest (Barry, Clarke, Johnstone, Magee, & Rushby, 2007). With regard to autism, previous studies have found that individuals with ASD have a tendency to exhibit lower resting alpha power than controls, but elevated activity in other frequency bands (Wang et al., 2013). Mathewson et al. (2012) investigated alpha activity during EC and EO rest in a group of 15 adults with an ASD diagnosis and a matched group of 16 neurotypical controls. They found that global alpha power during EO rest compared to EC rest was lower in the ASD group compared to controls. Moreover, for individuals with ASD, EO resting alpha power in posterior regions was negatively correlated with scores on the subscale of the Autism-Spectrum Quotient (AQ) (Baron-Cohen, Wheelwright, Skinner, Martin, & Clubley, 2001) measuring repetitive or restricted behaviours and interests, but no other subscales. No relationship between measured symptoms and alpha activity was found in controls. Mathewson et al. (2012) concluded that abnormalities in the allocation of visual attention may be associated with some of the impairments seen in ASD.

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How the BAP is reflected in resting alpha activity has not been directly investigated. The present study investigated EC and EO resting-state alpha activity in individuals without an ASD diagnosis. Each participant was administered the Broad Autism Phenotype Questionnaire (BAPQ) (Hurley, Losh, Parlier, Reznick, & Piven, 2007), and the relationship between their scores and resting-state alpha was assessed. State of the art source localisation techniques were applied to thoroughly investigate the sources of spectral power, lending greater ability to draw conclusions about the spatial distribution of activity than previous studies. Based on the findings obtained in the non-clinical group of Mathewson et al. (2012), we tested the (null) hypothesis that scores on the BAPQ would not be correlated with alpha activity during EC rest, EO rest, nor with the difference in alpha between the two states.

2. Method

2.1. Participants

Twenty volunteers (13 female, 7 male) from the university community participated in the experiment. Participants were partially reimbursed for their time. There were 19 right-handed participants, and 1 left-handed. Participants ranged in age from 18 to 25 years (m = 21.25) and had normal or corrected-to-normal vision and hearing. They were screened for mental health disorders, and other conditions that might contraindicate EEG. Informed consent was obtained from all individual participants included in the study.

2.2. Materials

2.2.1. Instruments

The Wechsler Abbreviated Scale of Intelligence (WASI; Wechsler, 1999) was used to assess verbal and perceptual reasoning abilities. The WASI is an approximately 30-minute long experimenter-administered test used to estimate full-scale intelligence quotient (IQ) using two indices, verbal comprehension (VCI) and perceptual reasoning (PRI), on the basis of four tests: block design, vocabulary, similarities, and matrix reasoning.

The Broad Autism Phenotype Questionnaire (BAPQ; Hurley et al., 2007) was used to measure subclinical autistic traits. Unlike some other instruments, the BAPQ was specifically designed to measure the BAP, as opposed to ASD. The BAPQ is a self-administered 36-item instrument. Participants are asked to indicate on a scale of 1–6 how often short statements apply to them (e.g. "People have to talk me into trying something new"). The BAPQ has three subscales assessed by 12 items each. The subscales are: aloof personality, pragmatic language impairments, and rigid personality, analogous to the triad of autistic symptoms. A total score is generated by finding the mean score across all items (with a similar strategy used to find subscale scores). The maximum score is 6, and higher scores indicate more expression of the BAP. The original cutoff for indication of the BAP was 3.15 (Hurley et al., 2007), although a more recent empirical study has suggested a higher cutoff may be more appropriate for males (Sasson et al., 2013). The BAPQ in this experiment was presented using a web browser. Question order was randomised for each participant. As the BAP can be difficult to discriminate from schizotypal personality, items from the cognitive-perceptual scale of the Schizotypal Personality Questionnaire–Brief (SPQ-B-CP; Raine & Benishay, 1995) were randomly intermingled amongst the BAPQ items. Responses to the SPQ-B-CP items were gathered on the same Likert scale as the BAPQ items, as opposed to the prescribed yes/no scale, to ensure that they did not stand out from the BAPQ.

The Edinburgh Handedness Inventory–Short Form (EHI-SF; Veale, 2014) was used to evaluate handedness. The EHI-SF is a version of the original EHI (Oldfield, 1971) with some of the less relevant items removed. It is a self-report instrument in which the participant indicates which hand they generally use to perform four tasks on a five-point scale.

2.2.2. Hardware

Neuropsychological tests were administered using two Windows XP computers. One computer presented the stimuli and recorded responses (the *stimulus computer*), and the other recorded the participant's electroencephalogram (the *EEG computer*). Triggers were sent from the stimulus computer to the EEG computer via a parallel port connection. EEG was recorded using a 32-channel Ag/AgCl sintered Advanced Neuro Technology (ANT) WaveGuard cap in the standard 10–20 configuration, connected to an ANT Refa8 32-channel amplifier. Conductive gel was used to couple the electrodes to the scalp, and impedance was maintained below 5 kΩ at all electrodes. A linked mastoid reference was used, and the ground electrode was located halfway between Fpz and Fz. EEG data were continuously recorded at 1024 Hz using ANT Advanced Source Analysis (ASA) software version 4.7.3.1.

2.2.3. Software

The experiment was presented using a program written in Matlab using Psychtoolbox (version 3.0.10; see Kleiner et al., 2007). The experimenter monitored the participant in the EEG room using a live video feed and secondary monitors in a conjoining room.

Most processing of EEG data was performed using EEGLAB (version 13.3.2; Delorme & Makeig, 2004). EEGLAB is an open-source Matlab toolbox for analysing and manipulating EEG data. Source analyses were undertaken using the eLORETA functionality of the LORETA-KEY analysis package (version 20150415), the latest development in the LORETA family of inverse solutions. This software was developed by the KEY Institute at the University of Zurich and is freely available online. Using eLORETA, the scalp EEG is assembled into a $29 \times 34 \times 24$ matrix of cortical generators containing $6239 \cdot 5\ mm^3$ voxels. Localisation by eLORETA is theoretically exact, albeit with low spatial resolution. Technical details can be found in Pascual-Marqui (2007). Although eLORETA generates images visually similar to those of metabolic techniques, the basis of the value at each voxel differs. The eLORETA source localisation images presented in this paper represent where differences in the generation of spectral activity occurred.

Correlations between localised spectral source density and covariates were undertaken using an implementation of Statistical Non-Parametric Modelling (SnPM) programmed in Matlab. This implementation was created to combine some of the options in the eLORETA software and some of those from the SnPM13 toolbox for SPM12. The principles of SnPM are described in Nichols and Holmes (2002). Essentially, SnPM is a permutation-based approach that can be used to compare voxel images with minimal assumptions, while correcting for multiple comparisons.

2.3. Procedure

All procedures performed in this study were in accordance with the ethical standards of the authors' research institute, and with the 1964 Helsinki declaration and its later amendments. After administration of the WASI, BAPQ, and EHI-SF, participants were presented with instructions for the EEG task. In addition to the specific instructions about what was to take place, participants were instructed to let their minds wander without focusing on anything in particular (standard instructions for resting state protocols). Eight minutes of resting state EEG data were collected from each participant in a series of 2-minute trials alternating between eyes-closed (EC) and eyes-open (EO) rest. The first trial consisted of random selection between EC and EO conditions. Participants wore headphones, and were alerted to the end of the trial by a tone. After each trial participants were asked to respond on a Likert scale to four questions regarding what they were thinking about during the preceding trial. Data from these questions will not be analysed in this paper.