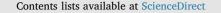
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Magnetoencephalography reveals an increased non-target P3a, but not target P3b, that is associated with high non-clinical psychosocial deficits



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ABSTRACT

Auditory processing deficits are frequently identified in autism and schizophrenia, and the two disorders have been shown to share psychosocial difficulties. This study used magnetoencephalography to investigate auditory processing differences for those with a high degree of a non-clinical autistic and schizotypal trait phenotype, Social Disorganisation (SD). Participants were 18 low (9 female) and 19 high (9 female) SD scorers (18–40 years) who completed a three-stimulus auditory oddball paradigm of speech sounds (standard: 100 ms 'o', deviant: 150 ms 'o', novel: 150 ms 'e'). Spatio-temporal cluster analysis revealed increased amplitude for the high SD group in a left (p = 0.006) and a right (p = 0.020) hemisphere cluster in response to the novel non-target. No cluster differences were found in response to the target deviant. These findings suggest that those with a high degree of the SD phenotype recruit more cortical resources when processing unattended, novel speech stimuli, which may lead to psychosocial deficits.

1. Introduction

The auditory P300 (P3) is one of the most widely studied electrophysiological potentials in human neuroscience. The P3 is a positive going electrical potential occurring between 250 and 500 ms in response to the onset of an auditory change or 'deviant'. There are two subcomponents of the P3: the P3b is elicited when the stimuli are attended to, and the deviant requires a behavioural response, and is typically reported in P3 studies. The P3a, on the other hand, is observed when attention is directed elsewhere, or in the case that it is an unexpected novel stimulus that should be ignored (Naatanen, 1992; Polich, 2007). The P3a response to an unattended, novel, auditory change originates in the frontal and anterior cingulate regions from 250 ms. The P3a indexes attention and working memory through the maintenance and monitoring of incoming information, although can be elicited in the absence of conscious awareness (Polich, 2007). The P3b, generated from temporal and parietal regions at around 300 ms, indexes an attention-driven comparison between the mental representation of the auditory environment in working memory and the incoming deviant (Friedman et al., 2001; Polich, 2007). The peak for the P3 response has been associated with the increasing cognitive demand, while P3 peak latency is thought to index the speed of stimulus detection and comparison (Polich, 2007).

In neuroscientific research, the three-stimulus auditory oddball

paradigm effectively elicits both P3a and P3b responses. In this paradigm, a repeated 'standard' stimulus is randomly interrupted by a target deviant and a non-target novel stimulus. Deviants and novels can differ in any or all tone properties, such as in duration, pitch and intensity. A P3b is elicited by the target, and a P3a by the non-target.

P3 abnormalities have been identified in several neuropsychological disorders, particularly schizophrenia spectrum disorders (Atkinson et al., 2012; Bridwell et al., 2014; de Wilde et al., 2008; Hermens et al., 2010; Jahshan et al., 2012; Javitt et al., 1995; Mathalon et al., 2000; Michie et al., 2000; Nuchpongsai et al., 1999; Schreiber et al., 1992). Several studies have identified a reduced or absent P3a in response to non-target duration-change stimuli for those with schizophrenia (Jahshan et al., 2012; Michie et al., 2000) and first-episode psychosis (Atkinson et al., 2012; Hermens et al., 2010; Jahshan et al., 2012; Jahshan et al., 2012; Nuchpongsai et al., 1999) and those with schizotypal personality disorder (Mannan et al., 2001).

Deficits in the P3a to duration-change non-targets have been suggested as a vulnerability marker for schizophrenia, with evidence for the deficit worsening with illness progression (Atkinson et al., 2012; Jahshan et al., 2012). The P3a has also been related to poor quality of life, social and occupational functioning, mental control, and auditory verbal learning in first-episode schizophrenia (Hermens et al., 2010) and with negative symptoms in those at-risk of psychosis (Jahshan

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et al., 2012). However, the P3a response to a duration-change nontarget has not been related to global functioning and symptom severity for those at-risk of psychosis, those with recent onset psychosis or those with chronic schizophrenia (Jahshan et al., 2012). This P3a deficit has been attributed to abnormalities in detecting and/or processing auditory change, which may subsequently lead to inappropriate responses to the auditory environment, resulting in cognitive and behavioural symptoms, such as inattentiveness and disorganisation (Braff and Light, 2004; Jahshan et al., 2012).

The specificity of the P3a and P3b as markers of schizophrenia symptom risk and progression is not yet clear (del Re et al., 2015; Devrim-Üçok et al., 2006). However, together, the P3 components have been suggested as a viable state marker of symptom severity, with fluctuations in symptom severity coinciding with the P3 deficit. This fluctuation is thought to represent an information-processing deficit that interrupts functional reorienting to salient novel and attended target auditory events in schizophrenia (Mathalon et al., 2000). Although the P3a and P3b have been associated with behavioural outcomes and symptom severity in clinical studies, to date, no studies investigate differences in the P3a or P3b across the non-clinical schizotypal trait spectrum.

Early work by Courchesne et al. (1984) found reduced P3a response to a novel non-target stimulus, and reduced P3b response to a target deviant whole-word change in adolescents with autism, suggesting a word processing deficit. A subsequent study also reported reduced P3a to non-target speech sounds, while there was no difference in the P3b to the target speech sound, although both stimuli were presented at equally frequency (Kemner et al., 1995).

The majority of the literature regarding the P3a in autism spectrum disorder (ASD) originates from mismatch negativity (MMN) studies, whereby repeated stimuli are interrupted by rare deviants while attention is directed elsewhere; the MMN is elicited in response to the deviant, which is followed by the P3a. Reduced P3a response to phoneme change, but not phoneme duration or pitch, has been reported in ASD (Lepistö et al., 2005, 2007, 2006), while no P3a was detected in response to a phoneme change for high functioning children with ASD, despite a visible P3a to novel simple pitch and complex tones (Ceponiene et al., 2003). For adults with high autistic traits, the P3 to social reward stimuli was reduced (Cox et al., 2015). These findings suggest greater compromised orientation to speech, but not pure tones, across the autism spectrum (Ceponiene et al., 2003; Lepistö et al., 2007, 2006). Orienting attention to speech is fundamental for the development of effective speech processing and comprehension, as well as the development of spoken language and communication (Haesen et al., 2011), compromised language and social development may have a downstream effect on social cognitive functioning. Altogether, the P3 components have been associated with auditory processing deficits across the autism and schizophrenia spectra, which have been related to psychosocial outcomes within the disorders.

Although clinically distinct, autism and schizophrenia spectrum disorders share similar psychosocial deficits, which extend to the subclinical population (Ford et al., 2017a; Ford and Crewther, 2014; Kanai et al., 2011; Spek and Wouters, 2010; Wakabayashi et al., 2012). Although, some characteristics, such as mentalising, are argued to be diametric (Abu-Akel and Bailey, 2000). Nevertheless, a shared nonclinical phenotype, termed Social Disorganisation, has been revealed through robust dimension reduction of responses to the autism spectrum quotient (AQ: Baron-Cohen et al., 2001) and schizotypal personality questionnaire (SPQ: Raine, 1991) subscales (Ford and Crewther, 2014). The Social Disorganisation factor comprises the AQ subscales of Social Skills, Communication and Attention Switching, and SPQ subscales of No Close Friends, Constricted Affect, Social Anxiety and Odd Behaviour, with weaker contributions from Suspiciousness, Ideas of Reference and Imagination. The presence of this shared phenotype was further supported through dimension reduction of AQ and SPQ items (Ford et al., 2017a).

As P3a and P3b deficits have been associated with the psychosocial dimension of the schizophrenia spectrum (Atkinson et al., 2012; Jahshan et al., 2012; Mathalon et al., 2000), and the psychosocial dimension of the SPQ is a major component of Social Disorganisation, it is possible that P3 components are related to this shared autism and schizophrenia spectra phenotype. In fact, a recent pure-tone MMN study using magnetoencephalography (MEG) study demonstrated reduced auditory P3am (magnetic P3a) field amplitude in a non-clinical population with a higher degree of the Social Disorganisation phenotype (Ford et al., 2017b). Specifically, spatio-temporal cluster analysis demonstrated disruption in the feed-forward and feed-backward connections between temporal and frontal regions for those with high Social Disorganisation (Ford et al., 2017c).

In the current study, a three-stimulus (standard, target and nontarget), phoneme-change, oddball paradigm was used to investigate differences in P3am and P3bm spatio-temporal cluster profiles between those with a high compared to a low degree of the Social Disorganisation phenotype. It was hypothesised that those with high Social Disorganisation would elicit reduced cortical activity in response to the target and non-target stimuli, in the P3bm and P3am time windows, respectively.

2. Methods

The Swinburne University Human Research Ethics Committee approved this study in accordance with the 1964 Declaration of Helsinki. All participants provided written informed consent to participate in the study. The oddball data were acquired within a larger experimental battery, which is reported elsewhere (Ford et al., 2017b, 2017c); only the oddball-related methodology and results are reported below.

2.1. Participants

Participants consisted of 18 low Social Disorganisation (9 female, mean age = 23.5[5.69]) and 19 high Social Disorganisation scorers (9 female, mean age = 22.11[4.64]). Participants were recruited based on the scores generated by factor analysis of the Autism Spectrum Quotient (AQ) and Schizotypal Personality Questionnaire (SPQ) subscales. High and low scoring groups were defined as those with Social Disorganisation *z*-scores in the top (z > 0.85) and bottom (z < -0.85) quintile, respectively. No participants reported hearing difficulties. Five participants in the high Social Disorganisation group reported a past history of psychiatric illness (3 depression, 1 bipolar, 1 anorexia), however, none of the participants were suffering from previous psychiatric conditions or taking psychiatric medications at the time of the study. No participants reported a clinical diagnosis of autism or schizophrenia.

2.2. Procedure

The AQ and SPQ items were combined and pseudo-randomised with items from the Coolidge Axis II Inventory (CATI+) Schizotypy and Schizoid scales, and Short Eysenck Personality Questionnaire-Revised Lie scale (EPQ-RL). Items were presented on a 4-point Likert scale from 1(*strongly disagree*) to 4(*strongly agree*). The questionnaire was completed by 428 males and 1250 females, aged 18–40 years. Participant AQ and SPQ subscale scores were then entered into a principal axis factor analysis with promax rotation in order to identify the shared autism and schizotypal trait factor, Social Disorganisation (for the full factor structure, see Ford and Crewther, 2014; Ford et al., 2017b).

For each participant, the standardised regression score (*z*-score) for Social Disorganisation was calculated, and those in the top (high group, z > 0.85) and bottom (low group, z < -0.85) quintile of *z*-scores were contacted via email. The first 20 respondents (10 male, 10 female) that met the inclusion criteria participated in the oddball study. Participants were asked to abstain from illicit drugs for one week and cigarettes for Download English Version:

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