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P50 sensory gating deficits in schizotypy

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ABSTRACT

Sensory gating is the ability to filter out irrelevant stimuli from the environment. Individuals with schizophrenia consistently demonstrate deficits in this ability leading to sensory overload and cognitive fragmentation. This dysfunction has also been found in schizotypy, which is defined as a manifestation of nonclinical symptoms qualitatively similar to those found in schizophrenia. In the present study, auditory sensory gating was assessed in healthy individuals by testing the attenuation of the P50 event-related potential. The degree of suppression was then correlated with schizotypy by using the O-LIFE questionnaire. Relative to the low-scoring individuals, P50 suppression was significantly reduced in those with high levels of schizotypy. Furthermore, the degree of deficit in P50 gating correlated with both cognitive disorganisation and impulsive nonconformity dimensions of schizotypy. These results suggest that schizotypal individuals may have early sensory gating deficits similar to schizophrenia patients, especially if they display a disorganised or impulsive profile. As they do not exhibit overt psychotic symptoms, it is likely that such deficits represent an underlying core cognitive dysfunction within the schizophrenia spectrum.

1. Introduction

Sensory gating is defined as the pre-attentional habituation of responses to repeated sensory input, which is used to distinguish important stimuli from those that may be irrelevant and redundant (Hall, Taylor, Salisbury, & Levy, 2011). Research has shown that this ability to actively suppress and/or ignore unimportant information is greatly affected in schizophrenia patients, who often show reduced cognitive inhibition when performing tasks which require selective attention. This has led to the hypothesis that such deficits in sensory gating may be the cause of some of the behavioural symptoms observed in schizophrenia, such as psychotic hallucinations and sensory overload (Waters, Badcock, Maybery, & Michie, 2003).

A method to measure this dysfunction is the P50 paired-pulse paradigm, which has been well-used to examine sensory gating dysfunction in schizophrenia patients (Patterson et al., 2008) and their first degree relatives (Clementz, Geyer, & Braff, 1998), as well as those with schizotypal personality disorder (Cadenhead, Light, Geyer, & Braff, 2000). By using electroencephalography (EEG), the P50 can be measured as the largest positive deflection at vertex approximately 50 ms post-stimulus. The paradigm consists of two identical auditory clicks which are presented in close succession. In neurotypical subjects, the P50 wave elicited by the second stimulus (S_2) is reduced when compared to the wave elicited by the first stimulus (S_1). This relative decrease is taken to be evidence of an intact sensory gating mechanism. In contrast, those with schizophrenia show reduced P50 suppression, which suggests that such deficits in inhibiting excess and trivial information could lead to the development of disorder-related symptoms and cognitive behaviours (Bramon, Rabe-Hesketh, Sham, Murray, & Frangou, 2004).

As this evoked potential is thought to reflect early pre-attentive sensory information processing, it can be taken as a functional correlate of neuropathology rather than be a result of the disease process (Potter, Summerfelt, Gold, & Buchanan, 2006). Furthermore, because of the high heritability of schizophrenia, this method can be used to detect possible gating dysfunction in individuals with a genetic predisposition to the disorder, as well as those who display schizotypal traits (Cadenhead, Light, Geyer, McDowell, & Braff, 2002). Therefore, abnormalities of the P50 response may be an intermediate phenotype of the disease which could potentially be utilised as a biological marker for individuals who may be at risk of developing schizophrenia at a later date, such as those with high levels of schizotypy.

Schizotypy is a construct used to describe a cluster of subclinical symptoms and personality traits within a healthy population, which may lead to a predisposition to schizophrenia (Claridge, 1997). Individuals who score high in self-report measures of schizotypal characteristics exhibit specific psychological and biological abnormalities, which are qualitatively similar to those observed in schizophrenia patients but less severe (Mohanty et al., 2005). As

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there is substantial evidence of a genetic liability which links schizotypy and schizophrenia, symptoms of schizotypy may be especially effective in identifying those at risk of developing the disorder at a later date. However, although there is considerable evidence for impaired sensory gating in those with schizophrenia-spectrum disorders, there has been less focus on those who display high levels of schizotypy. Only a few studies have directly looked at the relationship between schizotypy and P50 sensory gating in nonclinical populations, which have all found a correlation between high levels of schizotypy and reduced P50 suppression (e.g., Evans, Gray, & Snowden, 2007; Wan, Crawfod, & Boutros, 2006).

There are two important covariates to consider when evaluating earlier research: smoking status of participants; and the dimensions of schizotypy. Smoking tobacco is thought to facilitate early sensory gating by stimulating nicotinic cholinergic receptors, which results in enhanced central nervous system functioning (Heishman, Taylor, & Henningfield, 1994). This normalisation is observed in individuals with schizophrenia where patients who smoke show temporary improvements in P50 sensory gating compared to non-smokers (Adler et al., 1998). Wan, Crawford, and Boutros (2006) found a similar result in schizotypy, where the high schizotypy group showed better P50 suppression than the low schizotypy group, but only among the smokers. Croft, Dimoska, Gonsalvez, and Clarke (2004) also found gating differences in schizotypy depending on the participants' smoking status, but this was only related to the 'unreality' dimension of schizotypy. These results indicate that smoking may be a major confound if not assessed and controlled for prior to testing.

The concept of dimensionality in schizotypy is another important consideration. Similar to those of schizophrenia, schizotypy symptoms can also be divided into positive, negative, and disorganisation factors, all of which seem to have different effects on cognitive function and performance (Fanous, Gardner, Walsh, & Kendler, 2001). Therefore, it is necessary to assess not only global schizotypy, but also each of the separate contributing dimensions as some may be better predictors of attenuated P50 suppression than others. In this regard the data are inconsistent. Some studies found a relationship between a positive dimension with atypical gating (Croft, Lee, Bertolot, & Gruzelier, 2001), whereas others found this deficit to be related to either the negative dimension (Wang, Miyazato, Hokama, Hiramatsu, & Kondo, 2004), or the disorganisation dimension of schizotypy (Evans et al., 2007). Furthermore, these studies used different schizotypy scales, which could add to the variability of the results. These include the Schizotypal Personality Questionnaire (SPQ; Raine, 1991), the Personality Syndrome Questionnaire (PSQ) and the Oxford-Liverpool Inventory of Feelings (O-LIFE; Mason, Claridge, & Jackson, 1995).

Overall, the converging evidence suggests a link between reduced P50 suppression and schizotypy in nonclinical populations, but the exact nature of this relationship is not yet clear. In the present study, we investigated the role of schizotypy on P50 suppression in healthy non-smoking individuals. We expected that individuals with high global schizotypy scores would display reduced P50 sensory gating compared to control participants. We also examined the relations between the different dimensions of schizotypy and P50 gating to investigate the link between schizotypy subgroups and sensory gating deficits.

2. Methods

2.1. Participants

A total of 48 participants (mean age = 23.42 years; SD = 4.50; 17 males) were recruited from a tertiary institution. Exclusion criteria were: (1) being outside the 18–40 years age bracket; (2) being a regular smoker; (3) currently taking antidepressant or antipsychotic medications; and (4) having hearing deficits (hearing was assessed using an Otovation Amplitude T3 series audiometer; Otovation LLC, King of Prussia, PA). Participants gave their written informed consent to participate in the study. All experimental procedures were approved by the university's ethics committee.

2.2. Schizotypy assessment

The Oxford-Liverpool Inventory of Feelings and Experiences (O-LIFE; Mason et al., 1995) was used to assess the level of schizotypy in all participants. The O-LIFE consists of 104 self-reported 'yes/no' items that load onto four factors of schizotypy. These include: unusual experiences, which refer to items that describe perceptual and hallucinatory experiments including magical thinking; cognitive disorganisation, which measures the level of social anxiety as well as poor attention, concentration, and decision making; introvertive anhedonia which describes a lack of enjoyment from both physical and social sources; and lastly, impulsive nonconformity, which consists of items that refer to impulse-driven, anti-social, and disinhibited behaviour (Mason et al., 1995).

The O-LIFE was chosen to assess the level of schizotypy in the current study as it is based on a 'fully dimensional' model where it takes a more personality-based approach, and considers schizotypal traits as part of normal personality differences (Claridge, 1997). This is in contrast to the SPQ (Raine, 1991; another well-used and validated measure in the literature) which is a questionnaire based on the DSM-III-R criteria for schizotypal personality disorder (a clinically diagnosed disorder). Therefore, the SPQ treats schizotypy as a possible precursor to schizophrenia, and follows the three-factor structure of the disorder (positive, negative, and disorganised), compared to the O-LIFE which includes a fourth impulsive behaviour factor. This difference may be due to the design of the O-LIFE, which was derived using factor-analytic studies of nonclinical personality measures, and therefore the broader nature of this questionnaire is particularly suited to testing nonclinical populations, who may provide a more stable investigative opportunity (Mason et al., 1995).

Furthermore, it also has good psychometric properties, including good test–retest reliability, good validity, high internal consistency, and acceptable levels of skewness and kurtosis (Burch, Steel, & Hemsley, 1998). Therefore, it was also chosen instead of the PSQ, which, to date, has no published psychometric properties (Gooding, Gjini, Burroughs, & Boutros, 2013).

2.3. EEG procedure and analyses

EEG was conducted with Electrical Geodesics Inc. amplifiers (300 mV input impedance) using 128-channel Ag/AgCl electrode nets. Participants were seated comfortably in a reclining chair in an electromagnetic shielded and sound-attenuating room. They were asked to focus on a black fixation cross, which was presented on a grey background on a 24 inch computer monitor at a distance of 57 cm. This was done to ensure that they did not fall asleep. EEG was recorded continuously at a 1000 Hz sampling rate with a 0.1–400 Hz analogue bandpass, and was acquired using a common vertex (Cz) reference, which was later re-referenced to the average reference offline. All electrode resistances were less than 40 kΩ. The participants wore ER2 insert earphones (Etymotic Research Inc., Elk Grove Village, IL) for auditory stimulus presentation and were instructed to listen to the clicks through the earphones. Audio clicks were 4 ms in duration with a frequency of 1000 Hz (stereo recording at 44100 Hz sampling rate) and were presented to both ears at 77 dB. Forty identical pairs of these clicks were presented binaurally through the earphones, with a 500 ms interstimulus interval and a randomised 9–12 s intertrial interval. This block was repeated twice.