Reduced P50 suppression is associated with the cognitive disorganisation dimension of schizotypy

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Abstract

Individuals with schizophrenia fail to demonstrate a reduction in the P50 event-related potential (ERP) to the second of two identical auditory stimuli presented in close succession. This deficit could lead to sensory overload, cognitive disintegration and perhaps some of the symptoms of schizophrenia. However, evidence linking poor P50 suppression to symptoms in patients with schizophrenia has been equivocal; possibly because of the effects of smoking status and antipsychotic medication on both of these variables. The aim of this study was to remove these potentially confounding factors by testing 74 healthy non-smoking participants and assessing the relationship between P50 suppression and dimensions of schizotypy. Multiple regression analyses revealed that individuals scoring highly on the cognitive disorganisation dimension of schizotypy had reduced P50 suppression and a smaller amplitude of response to the first stimulus. No robust associations were found between any P50 variables and the positive or negative dimensions of schizotypy. N100 suppression was also examined using the dual click paradigm but no relationships were found with any of the schizotypy dimensions. Thus individuals high in the cognitive disorganisation dimension of schizotypy have a deficit in inhibiting repetitive information at an early pre-attentive stage of processing, as measured by the P50 ERP, but this did not extend to a later early attentive stage, as reflected by the N100 wave. This research supports the view that there is a link between poor P50 suppression and certain symptom clusters in schizophrenia.

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1. Introduction

The ability of the brain to inhibit or suppress responses to repetitive or irrelevant information is a critical process. It ensures that higher cortical centres do not become overwhelmed with sensory information and are able to process stimuli effectively. Individuals within the schizophrenia spectrum have long been thought to have a faulty filtering mechanism, which results in them being “flooded” by external and perhaps even internal information (Braff and Geyer, 1990; Venables, 1964). One method that has been used to measure individual’s inhibitory ability is to examine the brain activity elicited by two identical clicks presented in close succession. The first stimulus activates or ‘conditions’ inhibitory circuits and the second stimulus ‘tests’ the strength of the inhibitory mechanism (Eccles, 1969). A number of event-related potentials (ERPs) are elicited using this...
paradigm; including P50, a positive-going vertex-
maximum modulation that peaks at 50 ms, and N100, a
negative deflection that is maximal at 100 ms after an
auditory stimulus. P50 has attracted a great deal of
interest in the schizophrenia domain because it appears
to be relatively resistant to participant’s mood states and
cognitive manipulations (Adler et al., 1982; Jerger et al.,
1992, although also see Gutierrez et al., 1992), whereas
N100 is affected by alertness and attention (Adler et al.,
1982; Jerger et al., 1992; White and Yee, 1997). It is
thought that the P50 wave reflects an early pre-attentive
stage of processing, whereas the N100 modulation taps
a latter early-attentive stage (see Näätänen, 1990 for a
review).

In healthy volunteers P50 is significantly attenuated
in response to the test stimulus compared to the con-
ditioning stimulus, termed P50 suppression, and indi-
cates an intact sensory gating mechanism. In contrast,
patients with schizophrenia generally fail to demonstrate
significant P50 suppression (Adler et al., 1982; Boutros
et al., 1999; Clement et al., 1998a; Freedman et al.,
1983; Judd et al., 1992; Nagamoto et al., 1989, 1991;
Ward et al., 1996); although there is some evidence that
their abnormal ‘gating’ ratios may be the result of
diminished responsivity to the conditioning stimulus
(Adler et al., 1982; Boutros et al., 1991; Judd et al., 1992;
Nagamoto et al., 1989). Further evidence of the utility of
this measure in schizophrenia research comes from the
findings that abnormal P50 suppression has also been
found in some of the relatives of individuals with
schizophrenia (Siegel et al., 1984; Wald et al., 1988)
and in individuals with Schizotypal Personality Disorder
(Cadenhead et al., 2000). Moreover, this deficit has been
linked to the alpha 7 nicotinic subunit receptor gene
located on chromosome 15q14 (Freedman et al., 1997).

In contrast to the wealth of research which has been
conducted on P50 suppression very little research has
examined N100 suppression in schizophrenia using the
dual-click paradigm. One of the reasons for this might
be that early work into the N100 wave was discouraged
by the large within-participant variability found by Adler
et al. (1982). However a review by Smith et al. (1994)
found that on all ERP indexes (e.g. amplitude of conditioning and test response and suppression) N100 had equivalent, if not greater, reliability than P50. There
is now some evidence that N100 suppression is reduced
in patients with schizophrenia compared to healthy con-
trasts (Boutros et al., 1999, 2004), suggesting that a dif-
ficulty in inhibiting repetitive information may also be
evident at a later stage of processing in these individuals.

It has been hypothesised that a failure to gate out
repetitive or extraneous stimuli could result in sensory
overload and cognitive fragmentation, which could
ultimately lead to certain symptoms of schizophrenia,
such as thought disorder (Braff and Geyer, 1990). It
might therefore be expected that a deficit in P50 and/or
N100 suppression will be associated with some of the
symptoms of schizophrenia. Only one study could be
found which assessed the link between N100 suppres-
sion and clinical symptoms in individuals with schizo-
phrenia and this failed to find any association (Boutros
et al., 2004). There has been considerably more research
conducted on the link between P50 suppression and
symptomatology, but these results are equivocal. Jin
et al. (1998) paradoxically found that patients who
experienced severe perceptual anomalies had normal
P50 suppression, whereas those who reported no
perceptual difficulties had abnormal P50 ratios. Re-
search examining the negative symptoms of schizo-
phrenia has been equally confusing: one study has found
a negative relationship with P50 suppression (Louchart-
de la Chapelle et al., 2005), whereas another study found
no association (Adler et al., 1990). Boutros and col-
leagues (1991) have examined the disorganised/undi-
fferentiated subtype of schizophrenia and found that
these individuals exhibit less P50 suppression than
patients with paranoid schizophrenia or healthy con-
trols. Whereas Erwin et al. (1998) found that patients
with a marked impairment on P50 suppression had
higher scores on the attention subscale of the SANS
(Scale for the Assessment of Negative Symptoms; Andrasen, 1984). Finally, in other studies no relations-
ships have been found between symptoms and P50
performance (Boutros et al., 2004; Ward et al., 1996).

There are a number of potential explanations for
these diverse results. As pointed out by Light and Braff
(2000) patients with schizophrenia might be unable
to precisely report their symptoms, due to a lack of
awareness and insight into the experiences they might
be having. Moreover, there are also other factors which
might interfere with the ability of individuals with
schizophrenia to report their symptoms, such as atten-
tional problems, disorganised speech and lack of moti-
vation — all frequent features of schizophrenia. The
smoking status of the patients could also play a sig-
nificant role in whether relationships are found between
symptoms and P50 suppression. Adler et al. (1992,
1993) have demonstrated in patients with schizophrenia,
and their relatives who share the P50 suppression
deficit, that smoking can temporarily enhance P50
suppression to normal levels. There is also evidence to
suggest that nicotine can affect levels of symptomatol-
ogy (Goff et al., 1992; Ziedonis et al., 1994), and given
that a large number of individuals with schizophrenia
smoke (Dalack et al., 1998), nicotine could be an important mediator in the relationship between symptoms and P50 suppression.

Furthermore, many of the patients in these studies were taking antipsychotic medication which could adversely affect whether a relationship is found between symptoms and P50 suppression. Antipsychotic medication reduces the symptoms of schizophrenia (King, 1994; Gerlach and Peacock, 1995) and also affects levels of P50 suppression (Nagamoto et al., 1996). However, different classes of antipsychotic medications have different properties in reducing symptoms (Sharma, 1999) and typical antipsychotics do not normalise P50 suppression (Freedman et al., 1983), but some atypical antipsychotics may be effective (Adler et al., 2005; Becker et al., 2004; Light et al., 2000; Yee et al., 1998; but see also Arango et al., 2003 for a failure to find an enhancement with an atypical). It is possible that considering patients taking different types of antipsychotic medications in the same analysis may mask potential relationships between symptoms and P50 suppression. Also certain antipsychotic medications may introduce a decoupling of the link between symptoms of schizophrenia (or specific clusters) and level of suppression displayed, by working more effectively on one of these factors compared to the other. Finally, it is possible that taking certain antipsychotic medications might result in patients displaying a low level of symptoms and maybe not enough variability in them to demonstrate a relationship with P50 suppression.

Given these problems in testing patients with schizophrenia an alternative strategy has been to adopt a dimensional approach to schizophrenia and measure schizotypy (Claridge, 1997). According to this approach healthy individuals display analogues of the behaviour and personality characteristics present in patients with schizophrenia, albeit perhaps fewer in quantity and/or in an attenuated form. This concept has been well supported in the literature. The dimensions of schizotypy are similar to those found in schizophrenia (Vollema and van den Bosch, 1995) and these individuals also exhibit parallel cognitive (Evans et al., 2007; Poreh et al., 1995) and psychophysiological (Evans et al., 2005; O’Driscoll et al., 1998) deficits as those found in schizophrenia. By examining schizotypy in healthy volunteers the potential confounds highlighted above are avoided, as these individuals should be able to report their feelings and experiences more accurately, non-smokers can be easily found, and they are not taking antipsychotic medication. This construct can be measured using a psychometric approach, where individuals are given questionnaires to fill in, and thus is not to be confused with Schizotypal Personality Disorder which is a clinical disorder.

A number of studies have taken the psychometric approach to try to delineate the relationship between schizotypy and P50 suppression. Croft et al. (2004) and Wan et al. (2006) examined this issue and also sought to determine if there was an interaction between smoking status and schizotypy levels; as a consequence their sample sizes were relatively small for non-smokers (20 participants in each study). Nonetheless both studies found that high levels of schizotypy (the dimension of unreality in the Croft et al. study) were associated with poor P50 suppression. In the other two studies which have been completed on this issue these either contained smokers (Wang et al., 2004) or the smoking status of participants was not reported (Croft et al., 2001). Both found that high levels of schizotypy were associated with a deficit in P50 suppression. However, Croft et al. (2001) found that it was the unreality dimension of schizotypy, whereas Wang et al. (2004) found that it was the withdrawn dimension. One problem with the Wang et al. (2004) study is that they used a 250 ms interstimulus interval (ISI), in contrast to the usual ISI of 500 ms. It is difficult to know if the symptom correlates at this interval are the same as at the more standard interval. This is especially pertinent given that Wang et al. found a relationship with the negative dimension of schizotypy (withdrawn), whereas both of the Croft et al. studies (2001, 2004) found a relationship with the positive dimension of schizotypy (unreality). It is worth noting that in the Croft et al. studies (2001, 2004) the schizotypy questionnaire used — the PSQ (Personality Syndrome Questionnaire, developed by Gruzelier) has not had its psychometric properties published, despite work on this questionnaire beginning in 1995 (Gruzelier et al., 1995). Finally, the Wan et al. (2006) study does not allow any conclusions to be made regarding which dimension of schizotypy is associated with a deficit in P50 suppression as a global schizotypy questionnaire was used.

The aim of the present study was to assess the relationship between dimensions of schizotypy and P50 and N100 suppression in a large sample of healthy non-smoking volunteers. Participants were administered the Oxford–Liverpool Inventory of Feelings and Experiences (O-LIFE; Mason et al., 1995) to measure schizotypy. It was hypothesised that the healthy volunteers would demonstrate significant P50 suppression but this effect would be moderated by schizotypy, so that individuals high in schizotypy would exhibit significantly less P50 suppression than those low. As the O-LIFE measures four dimensions of schizotypy this
will also allow us to determine which dimension is associated with a deficit in P50 suppression. It was also predicted that our healthy volunteers would exhibit significant N100 suppression; however no hypotheses could be made as to whether any dimensions of schizotypy would modulate this effect.

2. Methods and materials

2.1. Participants

Eighty-one undergraduate students (49 females) took part in this study for course credit. These individuals were aged between 18 and 31 (mean = 20.79). Participants reported no neurologic or psychiatric history, were not taking psychotropic medication, had intact hearing abilities, were non-smokers and had not taken recreational drugs in the month prior to the experiment. All participants were asked to refrain from alcohol for at least 24 h before the study and no caffeine was permitted for at least an hour before recording. All participants gave written informed consent and were free to withdraw from the study at any time without penalty. The study was approved by the Ethics Committee at Cardiff University.

Seven participants (4 females) had to be excluded from the study due to problems with their ERP data (e.g. excessive baseline activity or a large number of trials excluded). Furthermore, five individuals’ (3 females) data from one test session had to be excluded (see Section 2.4 for details of the test session). Thus there were 74 participants (45 females) in the final sample (n = 72 in the first test session and n = 71 in the second test session). For the participants included in the study the mean number of trials rejected in the first test session was 5.49 (SD = 5.22) and in the second test session 6.35 (SD = 5.61).

2.2. The assessment of schizotypy

The O-LIFE (Mason et al., 1995) measures four orthogonal dimensions of schizotypy, which have parallels with those found in schizophrenia (Liddle, 1987). The unusual experiences dimension measures deviant perceptual experiences as well as magical thinking and is thought to be consistent with the positive symptoms of psychosis. Cognitive disorganisation describes deficits in attention and concentration together with social anxiety and is analogous to the disorganised dimension of psychosis. The introvertive anhedonia dimension taps a loss of feelings of pleasure and corresponds to the negative symptoms of psychosis. Finally, impulsive non-conformity measures recklessness and a liking for dangerous activities, this dimension does not have a similar psychotic parallel. This questionnaire has good psychometric properties; including high internal consistency and acceptable levels of skewness and kurtosis (Mason et al., 1995), as well as good test–retest reliability (Burch et al., 1998). In addition, the O-LIFE appears to have good validity. Individuals at ultra-high risk for psychosis score higher on all O-LIFE dimensions, except for impulsive non-conformity, compared to non-patients (Morrison et al., 2006) and schizophrenia patients score higher on all dimensions compared to individuals without psychopathology (Nettle, 2006). The mean scores (standard deviation in parentheses) obtained in this study for each of the schizotypy dimensions were as follows: unusual experiences 6.96 (5.59), cognitive disorganisation 12.01 (5.63), introvertive anhedonia 4.73 (4.37), and impulsive non-conformity 9.15 (4.27).

2.3. Apparatus and procedure

Stimuli were generated and data collected using a San Diego Instruments SR-LAB startle response unit (San Diego, CA). Electroencephalogram (EEG) was recorded from the vertex (Cz) using silver/silver chloride electrodes and the ground was placed in the middle of the forehead, both of these electrodes were housed in an elastic cap referenced to linked mastoid electrodes. The EEG activity was recorded using analogue 1 Hz high-pass and 300 Hz low-pass filters. The data were sampled at 1000 Hz, the data acquisition time was from 100 ms before to 400 ms after each click. All electrode resistances were kept below 5 kΩ.

The participant was seated in a comfortable chair in a sound attenuated laboratory, and wore Maico (TDH-39-P) headphones for auditory stimulus presentation. Participants were told to sit back, relax and keep their eyes closed; but not to fall asleep while their brain waves were recorded. They were also told that they would hear a number of pairs of clicks and their task was to count how many pairs of clicks were presented, this was done to try and keep participants alert. Prior to the testing session participants were given a short practice session (5 pairs of clicks) to familiarise themselves with the stimuli that they would hear. These trials were not included in the data set. Participants then heard the complete dual-click paradigm. After this session participants completed a different task for 10 min (see Evans et al., 2007), with the electrodes still attached, and then completed another dual-click session. This format was adopted to reduce participant’s boredom and to
reduce the risk of participant’s entering a slow wave state or falling asleep.

2.4. Stimulus presentation characteristics

The SR-LAB system was used to generate square wave clicks with near instantaneous rise times of 1 ms in duration. The average intensity of the clicks was 92 dB [A]. They were presented in pairs separated by 500 ms (conditioning and test stimuli, respectively). The intertrial-interval was randomly varied between 8 and 12 s, with an average of 10 s. Prior to the presentation of the clicks there was an acclimation period of 2 min, where just white noise was presented (60 dB [A]); this continued throughout the duration of the session. In each session there were 50 pairs of clicks and participants completed two of these sessions, which were identical.

2.5. Signal processing and ERP scoring

Analyses were conducted blind to participant’s schizotypy scores. The algorithms for signal processing and scoring closely parallel those suggested by Clementz et al. (1997). Each individual trial was digitally filtered with a 7-point low-pass smoothing routine and a recursive high-pass filter (\( A = 0.95 \); Coppola, 1979). Each filter was applied twice, in both the forward and reverse direction, to increase rolloff and to preserve waveform latency. Individual trials were rejected if they showed electrical activity greater than 50 \( \mu \)V in the 100 ms before or after a click was presented. Trials were also rejected if they contained excessive movement artifacts.

The grand average waveforms for the conditioning and test responses were then compiled, separately for each ERP session. The P50 wave was identified as the most positive peak between 40 and 80 ms after the click and the N100 wave was the greatest negative peak 70 to 140 ms after the click. Amplitudes of these waves were determined relative to the mean amplitude of the 100 ms period of activity prior to the presentation of the stimuli (given the difficulties found in detecting a pre-peak trough for many participants), as suggested by Clementz and Blumenfeld (2001). If a P50 or N100 wave was not present to the test stimulus this was scored as 0.01 \( \mu \)V to facilitate data analysis. P50 and N100 suppression were calculated using the ratio formula \( [1 - (\text{test amplitude/conditioning amplitude})] \times 100 \). To minimise skewed distributions ratios greater then \( \pm 100\% \) were assigned the value 100\%. P50 and N100 suppression were also calculated using a difference formula (conditioning amplitude—test amplitude). Using these measures positive P50 and N100 scores indicate gating whereas negative scores reflect enhancement.

2.6. Statistical analyses

Multiple regression was used to assess the relationship between the four schizotypy dimensions (unusual experiences, cognitive disorganisation, introverted anhedonia, and impulsive non-conformity) and the P50 and N100 suppression variables, and amplitude and latency to the conditioning and test stimuli. Furthermore, gender was also added as a predictor variable due to some studies finding differences between males and females on P50 and N100 variables (Hetrick et al., 1996). Gender was coded as male = 0 and female = 1. The advantage of using multiple regression is that as some of the schizotypy dimensions are significantly correlated with each other (see Mason et al., 1995 for more details) this technique can assess the unique contribution of each of the schizotypy dimensions in the prediction of the dependent variable.

3. Results

3.1. P50 and N100 suppression

The grand average waveform for the conditioning and test stimuli can be seen in Fig. 1. As can be seen from this figure and Table 1 participants exhibited
suppression of their P50 and N100 responses from the conditioning to the test stimulus, in both the first and second test session. Paired *t*-tests confirmed that there was a statistically significant difference in responses to the conditioning and test stimuli in the first session for P50 and N100 \([t(71) = 10.00\) and 8.50 respectively, both \(p < .001\)] and in the second session for P50 and N100 \([t(70) = 9.80\) and 7.65 respectively, both \(p < .001\)]. In order to determine the reliability of the P50 and N100 indices intraclass correlation coefficients were calculated between the first and second session. These are summarised in Table 2 and are broadly consistent with previous work in the area (Smith et al., 1994).

### 3.2. P50 suppression and schizotypy

In order to achieve the best signal to noise ratio in the following analyses an average measure of P50 suppression has been utilised. Initially a multiple regression was run with a ratio measure of P50 suppression as the dependent variable and the four schizotypy dimensions and gender as the predictor variables. There was a significant negative relationship between the percentage of P50 suppression and cognitive disorganisation \((p = .005)\) and a trend for a negative relationship with gender \((p = .089)\). This indicates that those participants with high cognitive disorganisation scores exhibit attenuated P50 gating. In addition, there was a trend for females to demonstrate less P50 suppression compared to males. To ensure the results were not affected by the particular measure of P50 suppression used (ratio), the analyses were also conducted with a difference measure. The relationship between P50 suppression and cognitive disorganisation was replicated \((p = .008)\), but no association was found with gender \((p > .1)\). Importantly, the association between cognitive disorganisation and reduced P50 suppression remains even if a Bonferroni correction \((0.05/4 = 0.0125)\) is made for the number of schizotypy dimensions entered into the model; due to there being no a priori hypothesis regarding which dimension of schizotypy would be related to a deficit in P50 suppression. Full details of these regression models can be seen in Table 3.

In order to try and assess the source of this deficit in sensory gating multiple regressions were also completed with mean amplitude to the conditioning and test P50 responses as the dependent variables. For the conditioning response it was found that there was a significant negative association with cognitive disorganisation and gender. For the conditioning response it was found that there was a significant negative association with cognitive disorganisation.

### Table 1

<table>
<thead>
<tr>
<th>P50 ERP</th>
<th>N100 ERP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amplitude (μV)</td>
<td>Latency (ms)</td>
</tr>
<tr>
<td>Mean</td>
<td>SD</td>
</tr>
<tr>
<td>Conditioning stimulus (1st)</td>
<td>5.74</td>
</tr>
<tr>
<td>Test stimulus (1st)</td>
<td>2.62</td>
</tr>
<tr>
<td>Conditioning stimulus (2nd)</td>
<td>5.70</td>
</tr>
<tr>
<td>Test stimulus (2nd)</td>
<td>2.49</td>
</tr>
<tr>
<td>Ratio suppression, % (1st)</td>
<td>46.99</td>
</tr>
<tr>
<td>Ratio suppression, % (2nd)</td>
<td>48.35</td>
</tr>
<tr>
<td>Difference suppression (1st)</td>
<td>3.13</td>
</tr>
<tr>
<td>Difference suppression (2nd)</td>
<td>3.20</td>
</tr>
</tbody>
</table>

Note: 1st and 2nd refer to the session number and SD = standard deviation.

### Table 2

<table>
<thead>
<tr>
<th>P50 ERP</th>
<th>N100 ERP</th>
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<tbody>
<tr>
<td>The reliability of P50 and N100 indices</td>
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</table>

| Conditioning stimulus | .67 | .72 |
| Test stimulus | .40 | .45 |
| Ratio suppression | .30 | .16 |
| Difference suppression | .56 | .59 |

### Table 3

<table>
<thead>
<tr>
<th>Suppression</th>
<th>Amplitude</th>
</tr>
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<tbody>
<tr>
<td>Ratio</td>
<td>Difference</td>
</tr>
<tr>
<td>Conditioning</td>
<td>Test</td>
</tr>
<tr>
<td>UE</td>
<td>.20</td>
</tr>
<tr>
<td>CD</td>
<td>-.41**</td>
</tr>
<tr>
<td>IA</td>
<td>.09</td>
</tr>
<tr>
<td>IN</td>
<td>-.12</td>
</tr>
<tr>
<td>Gender</td>
<td>-.22*</td>
</tr>
</tbody>
</table>

\(R^2\) = .17 | .11 | .12 | .18

Note: UE = unusual experiences, CD = cognitive disorganisation, IA = introverted anhedonia and IN = impulsive non-conformity.

* \(p < .1\), ** \(p < .05\), *** \(p < .01\).
In contrast, there were no significant relationships between the schizotypy dimensions and amplitude to the test stimulus \((p > .1)\). There was, however, a robust relationship between gender and amplitude of the test response \((p = .008)\). Those participants scoring highly on the cognitive disorganisation dimension had a smaller P50 response to the conditioning stimulus, but there was no difference in their response to the test stimulus. Also females had a larger response to the test stimulus compared to males, but they did not differ in their response to the conditioning stimulus. More details of all these regression models can be seen in Table 3.

### 3.3. P50 latency characteristics and schizotypy

Two multiple regressions were also completed examining whether any of the schizotypy dimensions were associated with the mean latency of the P50 wave to the conditioning and test stimuli. None of these relationships were significant \((p > .1)\).

### 3.4. Gender

As highlighted in Section 3.1 there was a significant difference in P50 test responses and a trend for a difference in P50 suppression between males and females. These results can be seen in Fig. 2. It was therefore assessed whether there was a gender difference in cognitive disorganisation scores on the O-LIFE as this might suggest that the results found with P50 suppression are related to gender rather than cognitive disorganisation. An independent \(t\)-test revealed that there was no significant difference in the scores of males and females on cognitive disorganisation [\(t(72) = 0.79, p > .1\)]. Thus gender is not confounding the relationship found between cognitive disorganisation and P50 suppression.

### 3.5. N100 suppression and schizotypy

Two multiple regressions were computed using overall ratio N100 suppression and difference N100 suppression as the dependent variables and the four schizotypy dimensions and gender as the predictor variables. There were no significant relationships \((p > .1)\).

### 3.6. N100 latency characteristics and schizotypy

Two multiple regressions were also completed examining whether any of the schizotypy dimensions were associated with the mean latency of the N100 wave to the conditioning and test stimuli. There were no significant relationships \((p > .08)\).

### 4. Discussion

Consistent with previous research, participants in the present study exhibited robust P50 and N100 suppression; their amplitude responses to the test stimulus were significantly smaller than their responses to the conditioning stimulus. However, the degree of P50 suppression was found to be moderated by the schizotypy dimension of cognitive disorganisation. Individuals

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Fig. 2. The amplitudes of the conditioning and test stimuli and the percentage of P50 suppression in females \((n = 45)\) and males \((n = 29)\). The error bars represent ±1 standard error of the mean.
scoring highly on this dimension exhibited poorer gating compared to the low scorers, which was evident using the ratio and difference measures of P50 suppression. Moreover, when participants’ P50 responses to the conditioning and test stimuli were examined a significant negative relationship was found between the amplitude of the conditioning stimulus and cognitive disorganisation. Those participants with high scores on this symptom cluster of schizotypy exhibited a smaller amplitude of P50 response to the conditioning stimulus than the low individuals. No relationships were found between any dimensions of schizotypy and P50 amplitude to the test stimulus or latency of response to the conditioning or test stimuli. Interestingly, the deficit in P50 suppression that individuals high in cognitive disorganisation exhibited did not extend to N100 suppression. Indeed, there were no significant associations between this suppression measure and any dimensions of schizotypy. This suggests that healthy individuals high in the cognitive disorganisation dimension of schizotypy have problems in inhibiting information at an early pre-attentive stage of processing but not at a later early attentive stage.

The finding that it is the cognitive disorganisation dimension of schizotypy that moderates P50 suppression is in contrast to the studies of Croft et al. (2001, 2004) who found that it was a positive dimension (unreality). It is possible that this disparity between studies can be reconciled by examining the schizotypy scale used by Croft et al. (2001, 2004), the PSQ. Although a paper on this questionnaire has not yet been published, looking at other papers which have used this questionnaire it is possible to glean more details on it. According to Kaiser and Gruzelier (1999) the unreality dimension has four subscales: cognitive unreality, perceptual unreality, suspiciousness and ideas of reference; whereas the active dimension has five subscales: active speech, odd speech, cognitive failures, odd behaviour and activity. It appears that the questions relating to the disorganised aspect of schizotypy have been included in the unreality dimension (the cognitive unreality subscale seems a good candidate) and the active dimension (possibly under the cognitive failures category). It is interesting to note that Croft et al. (2001) also found a trend for a relationship between P50 suppression and the active dimension, but no association with withdrawn. Hence it is possible that the results found in this study were being driven by an association between the disorganised dimension of schizotypy, rather than any of the other symptom dimensions.

The particular dimension of schizotypy that was found to be associated with a deficit in P50 suppression is analogous to that found by Boutros et al. (1991, 1993) who tested individuals with schizophrenia. Importantly, however, the present study ruled out the possible confounding effects of antipsychotic medication and treatment history by testing healthy volunteers. Boutros et al. (1991, 1993) found that those patients with a disorganised/undifferentiated profile displayed poorer P50 suppression and had a smaller amplitude of response to the conditioning stimulus compared to both paranoid schizophrenia patients and healthy controls. Furthermore, Ringel et al. (2004) found that patients with a hebephrenic/disorganised schizophrenia subtype did not show significant P50 suppression and had significantly smaller amplitudes of response to the conditioning stimulus compared to healthy controls. Hence, it appears that a disorganised profile is associated with impaired sensory gating ability and this can co-occur with a diminished response to the conditioning stimulus.

Reduced P50 suppression in participants high in cognitive disorganisation is consistent with the symptom correlates of other measures of gating, such as Prepulse Inhibition (PPI). This phenomenon refers to the reduction of the startle response if a startling stimulus is preceded by a weaker stimulus (Graham, 1975). It has been found that poor PPI is associated with high levels of distractibility (Karper et al., 1996) and thought disorder (Perry and Braff, 1994; Perry et al., 1999). Moreover, high scores on the schizotypy dimension of cognitive disorganisation, the same dimension as was found in this study, have been found to be associated with reduced PPI (Evans et al., 2005). Thus it appears that impairments in the ability to inhibit extraneous stimuli are associated with symptoms or experiences of disorganisation.

The format of the inhibitory testing adopted in this study, two sessions separated by 10 min, allowed for an assessment of the reliability of P50 and N100 parameters. This is an important issue to examine as there is now a burgeoning literature examining P50 suppression and schizophrenia and its potential utility as an endophenotype for this disorder. In a review on this issue Smith et al. (1994) found that generally for both P50 and N100 the amplitude of the conditioning and test stimuli can be measured reliably, but the ratio suppression measure is not reliable. As an alternative they suggest the arithmetic difference suppression score, which was found to have higher reliability than the ratio measure. The results from this study are consistent with these findings: the difference suppression score was more reliable than the ratio for both P50 and N100. Furthermore, in this study both of the P50 suppression measures were more reliable than those reported by
Smith et al. (1994). This might have been one of the reasons why this study was able to demonstrate a strong relationship between a schizotypy dimension and P50 suppression. In contrast, both of the N100 suppression measures were less reliable than those reported by Smith et al. (1994), which might have adversely affected finding relationships with schizotypy dimensions. It is interesting to note that when Kathmann and Engel (1990) examined the reliability of P50 parameters in healthy volunteers and patients with schizophrenia none of the P50 indices were found to be reliable in the patients. The unreliability of P50 measures in schizophrenia patients might be yet another reason why some researchers have failed to find significant relationships between symptoms (or clusters of them) and P50 suppression. It is clear that more research needs to be conducted to find ways of enhancing the reliability of P50 and N100 suppression indices so that electrophysiological measures of inhibition can become even more powerful tools in schizophrenia research.

One limitation of this study is that P50 was only measured and calculated at the vertex. This site was chosen as previous work had found that P50 is maximal at the vertex and this site is also the best for discriminating between schizophrenia patients and healthy controls (Clementz et al., 1998a). More recent evidence using integrated electroencephalography (EEG) and magnetoencephalography (MEG) has found that the P50 signal typically found at the vertex is largely a function of the activity of two neural sources which localise to the bilateral superior temporal gyrus (Huang et al., 2003). Hence by using the vertex site to measure P50 this could be masking possible hemispheric differences in the relationship between sensory gating and symptoms of schizophrenia. Thoma et al. (2005) have assessed the relationship between M50, the MEG analogue of P50, and symptoms in patients with schizophrenia. It was found that poor right, but not left, hemisphere M50 suppression was associated with more severe negative symptoms. In contrast, no relationships were found when P50 was examined. This study indicates that using techniques which are better able to identify the individual generators of sensory gating might permit a greater understanding of the dysfunction found in schizophrenia and the relationship between inhibition and symptoms. It remains to be seen whether the same or different schizotypy dimensions, as found in this study with P50, would be associated with M50 and whether there would be hemispheric differences.

In conclusion, these results replicate other studies that have found that individuals high in schizotypy have reduced P50 suppression. However, by testing a large number of individuals and administering a psychometrically sound multi-dimensional measure of schizotypy we have been able to delineate this relationship further. Our findings suggest that the cognitive disorganisation dimension of schizotypy is associated with reduced P50 suppression. Future studies, in schizophrenia patients and healthy controls, now need to extend this work by assessing sensory gating at a variety of electrode sites to determine if there are hemispheric differences in the relationship between certain symptoms or experiences and sensory gating and the significance of this.

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Contributors
L.H. Evans designed and set-up the study, ran all the participants, analysed the data and completed the writing of the manuscript. N.S. Gray and R.J. Snowden contributed to the design of the study and drafting of the paper.

Conflict of interest
None of the authors have any conflict of interest.

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