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N100 and P300 amplitude to Go and No–Go variants of the auditory oddball in siblings discordant for schizophrenia

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Abstract

Background: P300 amplitude reduction is reliably seen in schizophrenia. Inconsistent reports of isolated frontal and/or parietal deficits in unaffected family members may be clarified using a task that places greater load on frontal function.
Method: Go and No–Go versions of the auditory oddball task were performed by eighteen schizophrenia patients, age-matched unaffected siblings and healthy controls matched closely to unaffected siblings on age, sex, education, socioeconomic-status, handedness and ethnicity. Groups were compared on P300 and N100 amplitude and latency. Spearman correlations were used to test the relationship between ERP amplitudes and neuropsychological measures of executive function and memory. The relationship between schizotypy – as measured using the structured interview – and ERPs was explored in a combined group of siblings and controls.
Results: Independent of task, patients had lower P300 than controls and reduced parietal amplitude compared to siblings. Siblings had enhanced frontocentral N100 compared to controls. No–Go P300 amplitude and N100 latency was associated with executive function measures. There were significant intraclass correlations between patients and siblings for No–Go P300 amplitude, particularly at the central midline electrode. Frontocentral N100 and P300 amplitude were positively correlated with anxiety-related aspects of schizotypy.
Conclusion: Enhanced N100 is present in unaffected siblings. Parietal P300 is intact in unaffected siblings, but reduced in patients. The No–Go-oddball is more sensitive than the Go-oddball to executive function deficits in patients and as an index of heritability.

Keywords: Schizophrenia; Siblings; Event-related potentials; N100; P300; Anxiety; Executive function

1. Introduction

Patients with schizophrenia demonstrate reduction in auditory P300 amplitude, an event-related-potential (ERP) measure of attention, memory and contextual

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updating (Coull, 1998; Gruzelier et al., 1999; Bharath et al., 2000; Gruzelier, 2003; Jeon and Polich, 2003; Bramon et al., 2005). Such deficits have been associated with impairments in executive function and verbal learning (Nieman et al., 2002; Kim et al., 2003), though not in all cases (Kim et al., 2003; Dichter et al., 2006). Findings of reduced P300 amplitude in unaffected siblings are inconsistent (Bharath et al., 2000). Some authors report no difference (Karoumi et al., 2000; Winterer et al., 2001; Bramon et al., 2005), whilst others find a decrease (Turetsky et al., 2000) or increase in frontal P300 amplitude (Winterer et al., 2003). A metaanalysis (Bramon et al., 2005) suggested central and posterior sites as most suitable for obtaining P300 endophenotypes, but did not account for age differences present in many family studies (e.g. Frangou et al., 1997).

Reduction in the earlier N100 component is also found in schizophrenia patients, reflecting initial sensory processing and/or early selective attention deficits (Frangou et al., 1997; Coull, 1998; Gallinat et al., 2002; Sumich et al., 2006). However, no difference was seen between unaffected relatives and healthy comparisons (Frangou et al., 1997). In contrast, enhanced N100 in a sensory gating task was seen in unaffected relatives and was interpreted as reflecting a compensatory mechanism (Waldo et al., 1988). Enhanced N100 is also seen in anxiety disorders and in response to ketamine administration which is thought to model schizophrenia (Oranje et al., 2000; Alcaini et al., 1994). Given previous poor control for confounding variables such as age and personality disorder, the presence of N100 and P300 abnormalities in "truly" unaffected relatives remains unclear.

A task that places greater load on frontal function may be more sensitive to P300 abnormalities in siblings. Enhanced anterior–central P300 amplitude is seen to rare stimuli in a *No–Go* variant of the oddball task during which participants respond to frequent rather than rare stimuli (Salisbury et al., 2004). The effect on N100 of the No–Go oddball task is unclear.

The current study investigated N100 and P300 amplitudes in probands, unaffected siblings and closely matched healthy controls in *Go* and *No–Go* oddball tasks. Higher P300 amplitudes were expected at frontal sites in the No–Go, compared to the Go task. Compared to controls, patients were expected to demonstrate a reduction in P300 and N100. Siblings were expected to demonstrate a specific frontal P300 reduction. However, whether N100 reduction or enhancement would be present in siblings was unclear. The relationship between ERP amplitudes and neuropsychological measures of executive function and memory recall were also investigated. It was expected that ERP responses to the No–Go Oddball would be more closely associated with frontal executive processes.

2. Method and materials

2.1. Subject recruitment

Study procedures were approved by the Institute of Psychiatry and South London and Maudsley Research ethics committee. Following a detailed description of the study procedures, all participants provided written informed consent to take part. Details on recruitment are published elsewhere along with clinical, neuropsychological, eye-movement and sensory gating data on this sample (Hughes et al., 2005; Ettinger et al., 2004). Table 1 shows clinical and demographic data. Briefly, siblings were recruited via probands from in- or outpatient services within and around South London. Of the 25 sibling pairs that participated in our previous studies (Hughes et al., 2005; Ettinger et al., 2004), 18 pairs consented to undergo event-related potential assessments. No more than two siblings (1 affected, 1 unaffected) came from the same family. The Structured Clinical interview for DSM-IV Axis 1 disorders (SCID 1; First et al., 1996a) was used to confirm diagnosis of schizophrenia in patients. Controls were recruited via advertisement placed in a South London newspaper and were matched to unaffected siblings on age (within 5 yrs), gender, ethnicity, years of education (within 4 yrs) and handedness (Oldfield, 1971). An additional 4 unaffected siblings and controls participated, but are not

Table 1
Demographic and clinical variables

	Patients	Siblings	Controls	Total
	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)
Age	30.67 (6.41)	28.61 (6.59)	28.39 (6.48)	29.22 (6.45)
Years of education	12.72 (1.78)	12.72 (2.05)	13.33 (2.95)	12.93 (2.29)
% female	44.4	72.2	72.2	63.0
% smoker	66.7	50	66.7	61.1
% right handed	77.8	94.4	94.4	88.9
% Caucasian	61.1	61.1	61.1	61.1
% Afro-Caribbean	33.3	33.3	33.3	33.3
% other	5.6	5.6	5.6	5.6
Antipsychotic use				
Atypical	$n=14$	na	na	na
Typical	$n=3$	na	na	na
Unmedicated	$n=1$	na	na	na
Illness duration	7.7 (5.65)	na	na	na