Letter to the Editors

Visual sensory processing deficits in first-episode patients with Schizophrenia

Dear Editors,

It is now well-established that patients with schizophrenia exhibit early visual sensory processing deficits as indexed by substantial amplitude decrements in the P1 component of the visual evoked potential (VEP). This P1 deficit has been consistently reported across a large number of studies, almost all of which were conducted in chronic patients (see Table 1 Yeap et al., in press). More recently, however, a similar decrement was found in the P1 of unaffected first-degree relatives of patients with schizophrenia (Yeap et al., 2006), suggesting that this deficit may well be endophenotypic for the disorder and that it is not simply a function of the disease state itself. Only one study that we are aware of has assessed VEPs in first-episode patients and in contrast to the extensive literature showing P1 deficits in chronic patients, they reported no amplitude or latency differences between first-episode patients and healthy controls (Katsanis et al., 1996). However, these investigators used a very limited recording montage in their study, and their P1 measure was obtained at just 3 central scalp sites (C3, CZ, C4), sites where the extrastriate-generated P1 signal is highly attenuated, if indeed it is seen at all. In contrast, a recent study by Haenschel et al. (2007) designed primarily to assess working memory function in schizophrenia patients, did show an incidental but robust P1 deficit in adolescents with schizophrenia. Here, we revisited this issue in a cohort of first-episode patients with schizophrenia during their first presentation to the psychiatric services to expressly measure whether the P1 deficit is already evident at this early stage of the disorder. Given our previous finding of a P1 deficit in healthy first-degree relatives, we fully expected to see a similar deficit in first-episode patients, in contrast to the findings of Katsanis et al. (1996).

Our patient sample comprised 21 (4 female) first-episode psychosis patients, aged 17 to 47 years (mean±SD=27.9±9.0 years), from the St. Vincent’s Psychiatric Hospital in Fairview, Dublin, Ireland. All 21 patients met DSM-IV criteria for schizophrenia and were within a mean±SD of 20.7±14.1 days of presentation to the psychiatric services at the time of testing. All patients were unmedicated and drug-naïve at the time of first presentation. 18 of the 21 were medicated subsequent to admission at a mean±SD chlorpromazine dose of 378.5±376.7 mg/day. The mean±SD scores in the Brief Psychiatric Rating Scale (BPRS) and the Scale of Assessment of Negative Symptoms (SANS) were 51.7±19.5 and 46.4±27.7 respectively. Control subjects who were recruited from the local and hospital staff community, comprised 26 (12 female) paid volunteers aged 21 to 48 years, (mean±SD=30.2±8.3 years). The mean age of patients and controls did not differ significantly [t(47) = 1.38, p=0.33]. Eighteen of the 21 patients and 23 of the 25 controls were right-handed as assessed by the Edinburgh Handedness Inventory. All subjects reported normal or corrected-to-normal vision. Controls were medication-free and free of any psychiatric illness or symptoms by self-report using criteria from the SCID-NP and reported no history of alcohol or substance abuse.

The stimuli used here were exactly as used in our previous studies (see Yeap et al., 2006) where a fully detailed description can be found). Briefly, in each experimental block, we presented subjects with 100 isolated check images, grey on a white background (4°×4° visual angle) at 64% contrast, and 40 line
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(a) Graphs showing waveforms for different scalp locations (F3, F4, C3, C4, PO3, PO4) comparing controls and patients with respect to amplitude (μV) over time in milliseconds

(b) Three-dimensional visualizations depicting the distribution of waveforms for Controls, 1st Episodes, and their difference

(c) Heatmap with scalp regions (FP, AF, F, FC, C, CP, P, PO, O) and time in milliseconds (0-500 ms). The color scale indicates a significant difference (P < 0.05) for specific regions.
drawings of 2 kinds of animal (2.4° wide × 1.8° high) on a white background. Subjects were required to maintain central fixation and respond to one of the animal stimuli with a button push while withholding responses to the second animal stimulus. The target animal was indicated at the beginning of each block. Participants completed between 10–15 blocks each. The timing of the presentations was such that each image appeared for 60 ms with a variable inter-stimulus interval (ISI) between 740 and 1540 ms (randomly in steps of 200 ms) during which there was a blank white screen. Continuous electroencephalogram (EEG) was acquired through the ActiveTwo Biosemi electrode system (BioSemi, the Netherlands) from 72 scalp electrodes, digitised at 512 Hz with an open pass-band from DC to 150 Hz. Data were analysed using BESA Version 5.1.8.10 (Brain Electric Source Analysis, Gräfelfing, Germany) and re-referenced to the nasion. The data were subsequently filtered with a 45 Hz low-pass filter (24 dB/octave; zero phase shift). Epochs were calculated for a time-window from 200 ms pre-stimulus to 500 ms post-stimulus, and baseline-corrected relative to the interval −80 to 20 ms. All electrode channels were subjected to an artifact criterion of ±120 µV from −200 to 500 ms to reject trials with excessive EMG or other noise transients. The vertical and horizontal electro-oculograms were also visually inspected for blinks and large eye movements. Accepted trials were then averaged for the isolated-check stimuli only.

Inspection of the grand-average data showed the average P1 peak amplitude occurring at a latency of approximately 90 ms with a bilateral occipital distribution, as is entirely typical for stimulation of this nature (see Fig. 1). Since our previous studies have consistently identified electrode sites over the right parieto-occipital scalp as those sites showing the strongest between-groups P1 effects (e.g. Foxe et al., 2001, 2005; Yeap et al., 2006; Butler et al., 2007), peak P1 amplitude measures were derived for each subject and each condition within an 80 ms to 100 ms time interval at right parieto-occipital scalp site PO4. A simple student’s t-test was then conducted to test for the P1 effect. A significant difference between the first-episode group and the controls for P1 amplitude was observed \[t(44) = 2.84, p < 0.01\], which constitutes a large effect size of \[d = 0.86\] according to Cohen’s criteria. One unexpected finding that will merit replication can be seen in Fig. 1b, where it appears that the P1 deficit is larger over left lateral occipital scalp than over right which is at odds with our previous studies. Finally, a statistical cluster plot illustrates the prominent group differences in the posterior electrode sites within the time range of the P1 (see Fig. 1c). Although detection rates for the target stimuli were high for both control subjects and patients, there was a significant difference in performance between groups. The mean ± SD target hit rate (the percentage of correct responses) for the patients was 84.0 ± 19.6% and 96.3 ± 9.0% for the controls \[t(45) = 2.86, p < 0.006\].

In summary, our finding here in first-episode patients strengthens the hypothesis that there are impairments in early visual sensory function before the onset of the illness in schizophrenia. Taken together with our previous finding of P1 deficits in healthy first-degree relatives, these data point to the P1 as a trait rather than a state marker for the disease. As a potentially stable trait marker, this opens up the possibility for use of simple visual P1 measures as a tool for identification and treatment assessment in patients during earlier stages of this debilitating illness. However, it is unlikely that measures of the visual P1 alone will achieve the necessary levels of sensitivity to be used in isolation and efforts to combine multiple endophenotypic markers across sensory modalities may represent the best strategy for future development (see e.g. Price et al., 2006).

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