Available online at www.sciencedirect.com

SCIENCE DIRECT®

Psychiatry Research 136 (2005) 17–25

PSYCHIATRY RESEARCH

www.elsevier.com/locate/psychres

Auditory recovery cycle dysfunction in schizophrenia: A study using event-related potentials

Nathan J. Clunas*, Philip B. Ward

Schizophrenia Research Unit, Level 1, Don Everett Building, Liverpool Hospital, South Western Sydney Area Health Service, Locked Bag 7103, Liverpool, BC, NSW 1871, Australia
School of Psychiatry, University of New South Wales, Sydney, Australia

Received 3 August 2004; received in revised form 17 April 2005; accepted 28 May 2005

Abstract

Previous event-related potential (ERP) studies reported evidence of impaired auditory information processing in patients with schizophrenia. The recovery cycle of the auditory N1 ERP component was measured in 17 patients with schizophrenia and 17 age- and sex-matched healthy volunteers. Subjects performed a visual distraction task while listening to 80-dB SPL, 1000-Hz tone pairs, presented with intra-pair intervals of 1, 3, 5 or 7 s, with inter-pair intervals of 9–13 s. Patients with schizophrenia had significantly reduced N1 amplitudes for S1 stimuli compared with healthy volunteers. For N1 amplitudes elicited by S2 stimuli, there was a significant group effect whilst the main effect of intra-pair interval was not significant. These results provide additional evidence of inhibitory auditory processing deficits in schizophrenia.

Keywords: Evoked potentials; N1; Inhibition; Attention

1. Introduction

It has been proposed that schizophrenia may be associated with a deficit in inhibition, evidenced behaviourally by a patient's inability to attend selectively to relevant information in the environment, including auditory stimuli. Auditory processing deficits in people with schizophrenia have been extensively investigated using a range of auditory event related potential (ERP) components, including sensory gating of P50 amplitude and reduced amplitude of the mismatch negativity component elicited by infrequent deviant auditory events (Adler et al., 1982; Shelley et al., 1991; Ward et al., 1996).

Adler et al. (1982) showed that the amplitude and latency of the P50 waveform was significantly reduced for patients with schizophrenia compared with healthy volunteers. Maximum suppression of the P50 test response was seen at the 0.5-s conditioning–testing interval for both schizophrenia and healthy

* Corresponding author. Schizophrenia Research Unit, Level 1, Don Everett Building, Liverpool Hospital, South Western Sydney Area Health Service, Locked Bag 7103, Liverpool, BC, NSW 1871, Australia. Tel.: +61 2 9828 6184; fax: +61 2 9828 6181.
E-mail address: nathanc@student.unsw.edu.au (N.J. Clunas).

0165-1781/$ - see front matter © 2005 Elsevier Ireland Ltd. All rights reserved.
doi:10.1016/j.psychres.2005.05.009

volunteer groups. Adler and colleagues suggested that these findings reflected a marked reduction of normally present inhibitory mechanisms in people with schizophrenia. Freedman et al. (1983) showed that the failure of these inhibitory mechanisms may be responsible for the defects in auditory sensory gating in schizophrenia (Freedman et al., 1983). As transient P50 gating deficits have also been observed in mania, cocaine abuse, and post-traumatic stress disorder, it has been proposed that such deficits may serve as a phenotypic marker rather than a diagnostic tool (Adler et al., 1999). Dissociation between self-reported perceptual anomalies and P50 gating deficits has also been reported (Jin et al., 1998). Other investigators have examined different aspects of mid latency sensory gating, and proposed a complex multi-stage process that gives rise to differential gating of P50 and later components (Boutros and Belger, 1999).

Mismatch negativity (MMN) is elicited when an infrequent deviant stimulus is embedded within a periodic sequence of high probability "standard" stimuli. The generation of MMN reflects context-dependent information processing in the sensory auditory cortex (Näätänen et al., 2001). Shelley et al. (1991) demonstrated an attenuation of the MMN component in patients with schizophrenia that they interpreted as evidence that attentional deficits in schizophrenia may be due to impairments in pre-attentive mechanisms and a specific dysfunction in sensory memory. The schizophrenia vs. healthy volunteer difference in MMN amplitude has been widely replicated (Baldeweg et al., 2002; Hirayasu et al., 1998; Javitt et al., 1995, 1998, 2000; Kreitschmann-Andermahr et al., 1999; Michie et al., 2000; Shelley et al., 1991). In a recent study (Kisley et al., 2004), response suppression of mid-latency auditory ERP components was compared with MMN amplitude in healthy adults. P50 sensory gating, but not N1 sensory gating, was significantly correlated with MMN amplitude. Subjects that showed stronger P50 suppression tended to show larger MMN waveforms. This study provided more evidence that P50 sensory gating and N1 sensory gating measured with the paired-click paradigm represent distinct phenomena, and it demonstrated a direct relationship between P50 gating and MMN amplitude for the first time.

The N1 component of the auditory ERP is a prominent fronto-centrally distributed negativity that peaks approximately 100 ms post-stimulus. Shorter latencies and reduced amplitudes of the auditory N1 waveform have frequently been observed in people with schizophrenia (Boutros et al., 1997; Kayser et al., 2001). Laurent et al. (1999) reported reduced N1 amplitudes but normal N1 latency for unmedicated patients with schizophrenia, suggesting that reduced N1 amplitude may be independent of the effects of antipsychotic medication. No previous study has specifically examined another index of inhibitory deficits in schizophrenia, namely the recovery cycle of N1 amplitude elicited by paired tones.

The recovery cycle is a term used to describe variation in ERP component amplitudes when a stimulus is preceded by an identical stimulus at varying inter-stimulus intervals (ISIs). Davis et al. (1966) described the relationship between N1 amplitude and the interval between pairs of stimuli in regular sequences. The resulting recovery curve showed that pairs of stimuli separated by longer intervals (4–6 s) elicited larger peak to peak N1–P2 amplitudes than pairs with shorter intervals (1–3 s) (Davis et al., 1966). Similar findings were reported by Nelson and Lassmann (1968) for ISIs ranging from 0.25 through 10 s, with N1–P2 amplitude increasing about 1.85 μV with each two-fold increase in ISI between 0.25 s to at least 6.0 s (Nelson and Lassman, 1968). Roth et al. (1976) presented tone pips to healthy subjects with intervals between tones of 0.75, 1.5 or 3.0 s. Tones following the 3.0-s interval evoked larger N1s than did tones following the 1.5-s interval at Cz. N1 amplitudes following tones presented at 1.5- and 0.75-s intervals were not significantly different. N1 amplitude and latency was unaffected by changes in tone intensity. This study also demonstrated that the recovery cycle for N1 differed from that observed for the subsequent positive peak, termed P2, indicating that baseline to peak amplitude measures were preferable to the N1–P2 peak-to-peak amplitudes employed by earlier researchers. Roth et al. (1976) also found that directing attention to the auditory stimuli had no significant effect on the N1 amplitude recovery cycle. Attention-related increases in N1 amplitude are usually found using more demanding selective attention tasks (Hillyard et al., 1973). ISI-