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ScienceDirect
Psychiatry Research 151 (2007) 189 – 199
PSYCHIATRY RESEARCH
www.elsevier.com/locate/psychres

Impaired secondary somatosensory gating in patients with schizophrenia

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Received 5 May 2006; received in revised form 30 June 2006; accepted 24 October 2006

Abstract

A large and growing literature has demonstrated a deficit in auditory gating in patients with schizophrenia. Although that deficit has been interpreted as a general gating problem, no deficit has been shown in other sensory modalities. Recent research in our laboratory has examined sensory gating effects in the somatosensory system showing no difference in gating of the primary somatosensory response between patients with schizophrenia and control subjects. This is consistent with recent structural studies showing no cortical structural abnormality in primary somatosensory area in schizophrenia. However, a significant decrease in cortical thickness and gray matter volume loss in secondary somatosensory cortex has recently been reported, suggesting this as a focus for impaired somatosensory gating. Thus, the current study was designed (1) to replicate previous work showing a lack of schizophrenia deficit in primary somatosensory cortex (SI) gating, and (2) to investigate a possible deficit in secondary somatosensory cortex (SII) gating. In a paired-pulse paradigm, dipolar sources were assessed in SI and SII contralateral to unilateral median nerve stimulation. Patients demonstrated no impairment in SI gating, but a robust gating deficit in SII, supporting the presence of cross modal gating deficits in schizophrenia.

Keywords: Schizophrenia; Sensory gating; Secondary somatosensory; Cortex; Magnetoencephalography; Electroencephalography

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doi:10.1016/j.psychres.2006.10.011

1. Introduction

Sensory gating is traditionally measured in the auditory system using electroencephalography (EEG) and is assessed at a central recording site, electrode Cz. When two binaural click stimuli, separated by less than 1000 ms, are presented to normal control subjects, the positive-going component 50 ms after stimulus presentation (P50) of the event-related brain potential (ERP) in response to the second click is substantially reduced compared with that of the first (Adler et al., 1982). This effect is thought to reflect the filtering out of redundant and/or distracting sensory information in order to protect processing of the first stimulus. In a standard P50 gating protocol, a gating ratio is calculated by dividing the amplitude of the ERP at Cz to the second click (Stimulus 2) by the amplitude of the response to the first (Stimulus 1). This computation typically results in a mean gating ratio that is approximately 0.33 for control subjects, although there is some variability across studies. For example, published ratios vary from 0.15 to 0.45 in control subjects (see Hetrick et al., 1996). In contrast, gating ratios in patients with schizophrenia typically range from 0.7 to 0.9 (Adler et al., 1982, 1998; Arnfred et al., 2001a), suggesting a failure of sensory inhibition that has been consistently associated with the disorder clinically (Adler et al., 1982; Freedman et al., 1983, 1987; Nagamoto et al., 1989; Boutros et al., 1991; Judd et al., 1992; Clementz et al., 1997a; Thoma et al., 2003). The P50 gating deficit has been described as the most robust physiological finding in schizophrenia research (Bramon et al., 2004; Heinrichs, 2004). While gating of various kinds has been demonstrated using many protocols in different sensory modalities, there has been relatively little research investigating the use of a paired-stimulus paradigm to investigate a possible somatosensory parallel to P50 auditory gating.

Research using magnetoencephalography (MEG) has attempted to tie the auditory sensory gating deficit to abnormal processing in areas of cortex. Clementz et al. (1997b; see also: Blumenfeld and Clementz, 1999) measured the regional field activity of left and right temporal MEG channels and averaged them to estimate bilateral gating of the 50 (M50) and 100 (M100) ms responses during a paired-click paradigm. Source strength for Stimulus 1 and Stimulus 2 were determined for each component, M50 and M100, resulting in the characteristic reduction in Stimulus 2 compared to Stimulus 1 in control populations and a gating "deficit" in patients with schizophrenia for M100 but not for M50. More recently, in collaboration with Adler (Huang et al., 2003; Edgar et al., 2003; Thoma et al., 2003; Hanlon et al., 2005), an auditory paired-click protocol was employed in conjunction with MEG recording in an attempt to further clarify the neural mechanisms associated with the auditory gating deficit in patients with schizophrenia. Equivalent current dipoles (ECDs) were modeled for M50 and M100 separately for each hemisphere, and each localized to superior temporal gyrus (STG). Gating ratios based on the source strength of each component ECD showed a sensory gating deficit in a group of patients with schizophrenia that was confined to the left hemisphere for M50 and bilateral for M100 (Thoma et al., 2003; Hanlon et al., 2005). These data concerning M50 were interpreted to suggest that circuitry involved in the EEG P50 auditory gating deficit is located in the left hemisphere, consistent with reports of reduced left STG volume in schizophrenia (McCarley et al., 1993, 2002; Pearlson, 1997; Kasai et al., 2003).

Three recent studies have examined somatosensory gating using EEG (Arnfred et al., 2001a,b) or MEG (Edgar et al., 2005), and each reported a significant gating effect using a paired-pulse paradigm similar to that used for auditory gating experiments. Arnfred et al. (2001a,b) demonstrated a significant gating effect in healthy subjects. Edgar et al. (2005), using MEG-computed dipoles modeling the 20 ms response (M20) that localized to primary somatosensory cortex, also showed a gating effect, but gating ratios did not differ between control subjects and patients with schizophrenia. It is possible that gating and/or gating deficits are better assessed via other, later components of the somatosensory response. For example, Arnfred and Chen (2004) documented abnormality in the amplitude of the 50 ms component of the somatosensory evoked potential in schizophrenia-spectrum patients, but no impairment of gating of this component.

Thoma et al. (2004) demonstrated that the extent of thinning in auditory cortex (STG auditory dipole location) was correlated with the extent of impairment in auditory gating ratio, suggesting that cortical structural abnormality was related in a consistent manner with regional cortical function. Cannon et al. (2002) measured cortical thickness of different brain areas in individuals with schizophrenia relative to their monozygotic co-twins. Tissue was relatively spared in occipital and almost all of parietal cortex, including area 3, the site of localization of primary somatosensory cortex activity. This finding is consistent with the lack of gating impairment in M20 localizing to primary somatosensory cortex (Edgar et al., 2005). Cannon et al. (2002) reported that, although superior and posterior parietal cortex appeared to be largely spared, the superior lip of the sylvian fissure, an area comprising inferior frontal and