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Abnormal visuomotor processing in schizophrenia

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ABSTRACT

Subtle disturbances of visual and motor function are known features of schizophrenia and can greatly impact quality of life; however, few studies investigate these abnormalities using simple visuomotor stimuli. In healthy people, electrophysiological data show that beta band oscillations in sensorimotor cortex decrease during movement execution (event-related beta desynchronisation (ERBD)), then increase above baseline for a short time after the movement (post-movement beta rebound (PMBR)); whilst in visual cortex, gamma oscillations are increased throughout stimulus presentation. In this study, we used a self-paced visuomotor paradigm and magnetoencephalography (MEG) to contrast these responses in patients with schizophrenia and control volunteers. We found significant reductions in the peak-to-peak change in amplitude from ERBD to PMBR in schizophrenia compared with controls. This effect was strongest in patients who made fewer movements, whereas beta was not modulated by movement in controls. There was no significant difference in the amplitude of visual gamma between patients and controls. These data demonstrate that clear abnormalities in basic sensorimotor processing in schizophrenia can be observed using a very simple MEG paradigm.

1. Introduction

Schizophrenia is a psychiatric disorder characterised by a range of symptoms including hallucinations, delusions, disorganised thought and behaviour, and reduced cognitive and emotional capacity. Research tends to focus on these core symptoms; however, patients also experience impairments in more basic sensorimotor processes (Bombin et al., 2005; Butler et al., 2001; Vrtunski et al., 1986). Abnormalities in motor function have been noted since the earliest descriptions of the disorder (Kraepelin, 1921) and are a well-accepted feature of schizophrenia, with the vast majority of patients exhibiting at least one type of motor symptom (Peralta et al., 2010; Walther et al., 2012). These symptoms include involuntary movements, catatonia, Parkinsonism and deficits in the production of both simple and complex movements such as coordination, reflexes and motor sequencing (Bombin et al., 2005; Kraepelin, 1921; Vrtunski et al., 1989). Similarly, patients with schizophrenia exhibit deficits in low-level visual function, particularly in processing stimuli of low spatial frequencies, as evidenced by reduced contrast sensitivity, centre-surround interference and abnormal motion perception (Butler et al., 2001; Cadenhead et al., 2013; Keri et al., 2002; Slaghuis, 1998).

There is significant evidence that these subtle abnormalities in basic sensorimotor processing are present in childhood, at the onset of core symptoms and in relatives of individuals with schizophrenia (Chen et al., 2000; Walther et al., 2012; Whitty et al., 2009), indicating that they are likely to be inherent to the disorder rather than being a consequence of long-term exposure to medication. Importantly, visual and motor deficits, as well as other neurological abnormalities, correlate with the primary symptoms of schizophrenia such as affective flattening, apathy and disorganisation (Bombin et al., 2005; Jahn et al., 2006; Liddle, 1987; Peralta et al., 2010), and with illness severity (Jahn et al., 2006), social functioning (Dickerson et al., 1996; Jahn et al., 2006; Lehoux, 2003) and functional outcome (Boden et al., 2014; Javitt, 2009), suggesting that they could be used as a biomarker for the disorder.

Understanding the neuronal basis of these symptoms could therefore ultimately contribute to development of treatments permitting improved quality of life; however, at present the neuronal mechanisms underlying sensorimotor processing deficits in schizophrenia are not known. It is likely that different types of symptoms have different aetiologies (Chen et al., 2000). Visual deficits have been reported to be

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due to abnormalities in lower-level visual pathways, particularly in magnocellular neurons (Butler et al., 2001). These neurons rely on N-methyl-D-aspartate (NMDA)-type glutamate receptors, which may show dysfunctional transmission in schizophrenia (Javitt, 2009). A review of motor symptoms and their potential aetiology by Walther and Strik (2012) describes reductions in volume of the anterior cingulate cortex and midbrain structures (putamen, caudate and thalamus), and disturbed gamma-aminobutyric acid (GABA)-ergic neurotransmission in these areas and the primary motor cortex. Neuroimaging techniques are of great use in measuring the structural and physiological abnormalities that may contribute to sensorimotor abnormalities in schizophrenia.

Magnetoencephalography (MEG) allows non-invasive inference of current flow in neuronal cell assemblies through measurement of extracranial magnetic fields. MEG signals are dominated by oscillations, which result from rhythmic activity in large populations of neurons. Neuronal oscillatory responses to visual and motor stimulation have been well characterised in healthy volunteers: in motor cortex, the amplitude of beta (13–30 Hz) oscillations decreases during movement (event-related beta desynchronisation (ERBD)) and increases above baseline on movement cessation (post-movement beta rebound (PMBR)), returning to baseline ~4 s after movement offset (Pfurtscheller et al., 1999). In the visual cortex, a decrease in alpha (8–12 Hz) oscillatory amplitude occurs alongside a concomitant increase in gamma (30–70 Hz) oscillations (Siegel et al., 2010). Notably, individual differences in the amplitude of motor beta oscillations correlate with electromyogram measures of muscle control (Jain et al., 2013; Mima et al., 2000), whilst visual gamma oscillations correlate with orientation discrimination performance (Edden et al., 2009). Measurement of these electrophysiological features is therefore likely to offer insight into the neuronal basis of motor and visual deficits in schizophrenia.

Previous studies have identified electrophysiological visuomotor abnormalities in schizophrenia and related disorders: Wilson et al. (2011) showed that adolescents with early-onset psychosis exhibit enhanced ERBD and reduced PMBR whilst conducting a motor task. Since beta oscillations are thought to reflect inhibition (Cassim et al., 2001; Gaetz et al., 2011), reduced amplitude may reflect a greater degree of processing required to plan and execute movements in patients. In visual cortex, either no change (Uhlhaas et al., 2006) or a reduction in amplitude (Grutzner et al., 2013) and frequency (Spencer et al., 2004) of gamma oscillations have been reported in schizophrenia. However, available data are sparse and typically relate to complex stimuli (e.g. faces or Gestalt stimuli) that require integration of visual features. The question of whether patients with schizophrenia show abnormalities in oscillations reflecting low-level visual and motor processing therefore remains. In this study, we measure ERBD and PMBR in sensorimotor cortex and gamma oscillations in the visual cortex during a simple visuomotor task, to test the hypothesis that these well characterised phenomena are perturbed in schizophrenia.

2. Methods

2.1. Participants

The study received ethical approval from the National Research Ethics Service and all participants gave written informed consent. The patient group was recruited from community-based mental health teams in Nottinghamshire, Derbyshire and Lincolnshire, United Kingdom. Diagnoses were made in clinical consensus meetings through a review of case files and a standardised clinical interview (Signs and Symptoms of Psychotic Illness or SSPI; Liddle, 2002) in accordance with the procedure of Leckman et al. (1982). All patients were in a stable phase of illness with no change in antipsychotic, antidepressant, or mood- stabilising medications, nor a change of more than 10 points in occupational and social function scored according to the Social and Occupational Function Assessment Scale (SOFAS) (APA, 1994), in the 6 weeks prior to the study. Patients were taking a range of psychotropic medication, with a mean defined daily dose (DDD) of 1.8 (SD 1.3). Controls were selected to match the patient group in terms of demographic variables. There were seventeen male and six female patients with schizophrenia and the same number of male and female controls. There was no significant difference between the ages of the two groups (patients and controls' mean ages 26.8 (SD 7.0) and 26.7 (SD 7.2), respectively; $U = 264.5$, $p = 1.0$). Groups were also matched for socio-economic background using the National Statistics Socio-economic Classification (NS-SEC) self-coded method. NS-SEC scores are given in Table 1 and did not differ significantly between groups ($\chi^2(4, N = 46) = 2.3$, $p = .69$). All participants had normal or corrected to normal vision.

2.2. Symptom severity measurement

In order to derive a score for overall severity of psychotic illness in the patient group, we followed the procedure employed by Palaniyappan et al. (2013a). We computed the first principal component of: the scores for the three characteristic syndromes of schizophrenia (reality distortion, psychomotor poverty and disorganisation) assessed using the SSPI; speed of cognitive processing assessed using a variant of the Digit Symbol Substitution Test (Wechsler, 1940); and scores from the Social and Occupational Function Scale (SOFAS; APA, 1994). Unlike Palaniyappan et al. (2013b), who focussed on chronic symptom burden, we did not include duration of illness in our measure of current illness severity.

2.3. Paradigm

The task comprised visual stimulation with a centrally-presented maximum contrast vertical square wave grating (3 cycles per degree), which subtended an 8° visual angle and was displayed behind a red fixation cross on a mean luminance background. The grating was presented for 2 s followed by a 7 s fixation only baseline period. Participants were instructed to press a button with their right index finger regularly but as many times as they chose during the 2 s presentation of the grating, though ensuring that they did not press so vigorously as to cause their arm to move. There were 45 trials, giving a total task length of 7 min. A short practice of the task was given outside the scanner. Stimuli were generated on a PC using MATLAB (The Mathworks, Inc., Natick, MA) and were back-projected via a mirror system onto a screen inside a magnetically shielded room at a viewing distance of 46 cm. All participants were scanned in a supine position. Right index finger button presses were recorded via a response pad (Lumitouch Photon Control Response System).

2.4. Data acquisition and analysis

MEG data were obtained using a 275 channel whole head CTF system (MISL, Coquitlam, Canada), with four channels switched off due to excessive sensor noise. Twenty-nine reference channels were also recorded for noise cancellation purposes and the primary sensors were analysed as synthetic third order gradiometer measurements (Vrba et al., 2001). Data were acquired at a csampling frequeny of 600 Hz with a 150 Hz low-pass anti-aliasing hardware filter. The position of the head within the MEG helmet was measured continuously during the recording by energising three electromagnetic head position indicator coils located at the nasion and left and right pre-auricular points,

Table 1
National Statistics Socio-economic Classification (NS-SEC) scores.

	NSSEC score	1	2	3	4	5	Mean	SD
Number of participants	Schizophrenia	13	1	4	1	4	2.2	1.6
	Controls	11	2	5	3	2	2.3	1.4

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