



Contents lists available at ScienceDirect

Schizophrenia Research

journal homepage: www.elsevier.com/locate/schres

Sensory prediction errors in the continuum of psychosis

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ARTICLE INFO

Article history:

Received 6 February 2017

Received in revised form 7 April 2017

Accepted 10 April 2017

Available online xxxx

Keywords:

Schizophrenia

MMN

Predictive coding

N1-suppression

Auditory oddball

Prodromal

ABSTRACT

Sensory prediction errors are fundamental brain responses that signal a violation of expectation in either the internal or external sensory environment, and are therefore crucial for survival and adaptive behaviour. Patients with schizophrenia show deficits in these internal and external sensory prediction errors, which can be measured using electroencephalography (EEG) components such as N1 and mismatch negativity (MMN), respectively. New evidence suggests that these deficits in sensory prediction errors are more widely distributed on a continuum of psychosis, whereas psychotic experiences exist to varying degrees throughout the general population. In this paper, we review recent findings in sensory prediction errors in the auditory domain across the continuum of psychosis, and discuss these in light of the predictive coding hypothesis.

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1. Introduction

The brain, once viewed as a passive recipient of sensory information is now thought to actively predict sensations (Picard and Friston, 2014). It manages an onslaught of incoming stimuli by amplifying relevant information and suppressing irrelevant or predictable information (Lakatos et al., 2013). An inability to accurately predict forthcoming sensations which are internal, self-generated or sensations that are externally-generated in the environment results in *sensory prediction errors*, which is a failure to suppress neuronal activity.

Sensory prediction errors have been studied extensively in the context of externally-generated stimuli, with mismatch negativity (MMN) being a key component of auditory or visual change detection in the environment (Fisher et al., 2012; Stefanics et al., 2014a; Todd et al., 2013). Self-generated sensory prediction errors have been studied in the tactile (Martinelli et al., 2016; Shergill et al., 2005; Wolpert et al., 1995), auditory (Aliu et al., 2009; Baess et al., 2011; Martikainen et al., 2005; Timm et al., 2013) and visual domains (Mifsud et al., 2016). Patients with schizophrenia demonstrate deficits in prediction of both external stimuli (Erickson et al., 2016; Fisher et al., 2012; Todd et al., 2008) and self-generated stimuli (Ford et al., 2007a; Ford and Mathalon, 2012; Ford et al., 2014). These deficits can also be seen in individuals at high-risk

for psychosis (Erickson et al., 2016; Ford and Mathalon, 2012; Umbricht et al., 2006).

Schizophrenia is a psychiatric disorder characterized by negative symptoms, such as blunted affect, poverty of speech, apathy and anhedonia as well as positive, psychotic symptoms, such as delusions and hallucinations (Andreasen and Flaum, 1991; Meehl, 1962). The current method of diagnosing schizophrenia is based on the categorical symptom specification according to standardised classification systems such as the Diagnostic and Statistical Manual (DSM-V; American Psychiatric Association (2013)) or the International Classification of Diseases (ICD-10; World Health Organization (1993)). This traditional categorical approach of diagnosing mental disorders views the general population as being composed of two simple categories of individuals i.e. healthy or unhealthy (Linscott and van Os, 2010). In psychotic disorders, such a binary categorisation has been challenged due to mounting evidence that psychotic experiences can also be present, to certain degrees, in otherwise healthy individuals (Kaymaz and van Os, 2010). This more recent perspective proposes that psychotic experiences in the general population vary across a continuum (van Os et al., 2009); (see Fig. 1A). A 'continuum of psychosis' implies that the same psychotic experiences seen in clinical populations with psychotic disorders can be seen in non-clinical populations, albeit to a lesser degree (van Os et al., 2009). Criticisms of this perspective centre around concerns that viewing psychosis on a continuum may pose a difficulty for clinicians to distinguish between clinical psychoses and healthy populations (Lawrie et al., 2010). A categorical approach is, nevertheless, more valuable for treatment in clinical practice when distinguishing amongst related

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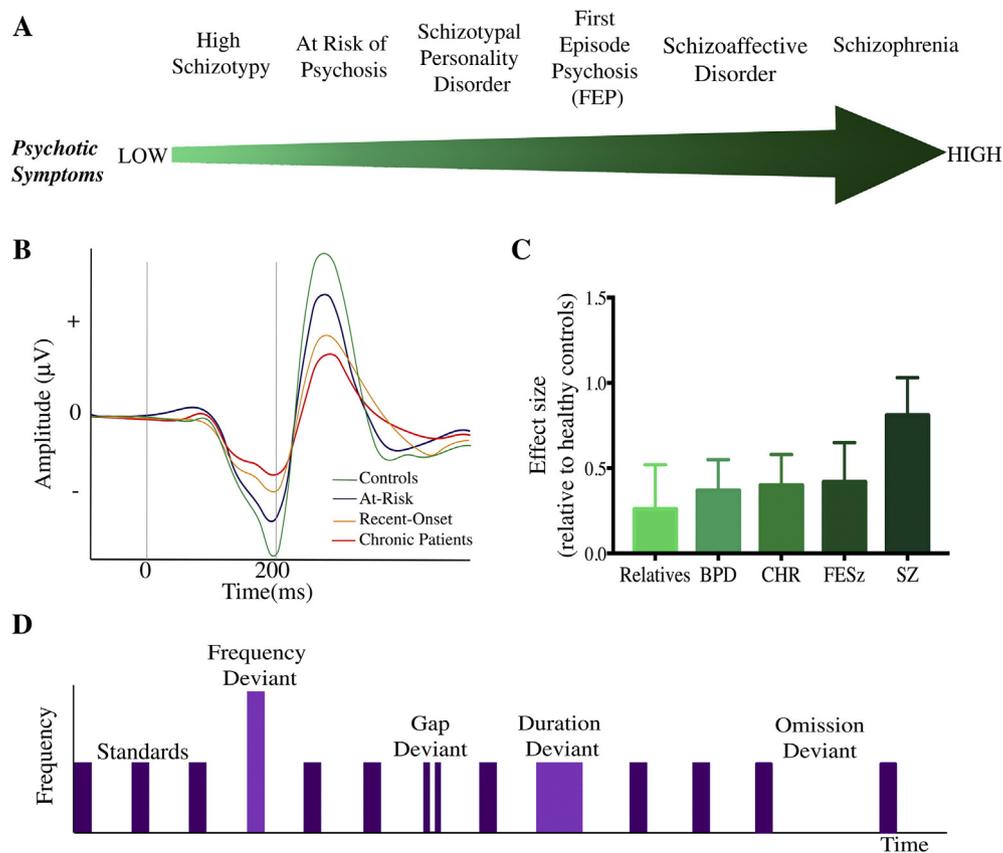


Fig. 1. MMN in the continuum of psychosis. (A) Psychotic symptoms ranging from low to high on a continuum of psychosis. (B) Duration MMN waveforms for healthy controls (green; $n = 28$), at-risk (blue; $n = 26$), recent-onset (yellow; $n = 31$) and chronic schizophrenia (red) patients ($n = 33$); adapted with permission from Jahshan et al. (2012a). (C) Effect sizes of MMN amplitudes, relative to healthy controls ($n = 3960$ (105 samples)), in first-degree relatives ($n = 3797$ (13 samples)), bipolar disorder (BPD; $n = 240$ (9 samples)), clinically high risk (CHR; $n = 505$ (16 samples)), first episode schizophrenia (FESz; $n = 300$ (13 samples)), chronic schizophrenia (SZ; $n = 268$ (13 samples)) patients (error bars indicate 95% confidence intervals; adapted with permission from meta-analysis by Erickson et al. (2016)). (D) Auditory oddball paradigm showing different deviant types. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

psychotic disorders such as schizophrenia and bipolar disorder (BPD) which show considerable differences in risk factors, pathology and treatment response (Lawrie et al., 2010). Nevertheless, the perspective of a continuum is useful for developing measures of psychosis proneness and for studying the aetiology of schizophrenia (DeRosse and Karlsgodt, 2015).

2. Prediction errors in external sensory stimuli

Responses to externally-generated auditory stimuli have been studied in detail using event-related potentials (ERPs) with the use of electroencephalography (EEG) and magnetoencephalography (MEG). Patients with schizophrenia show significant reductions in N1, P1, N2, P50, P300 and P3a components compared to healthy controls (for an overview of ERP components see (O'Donnell et al., 2017; Sur and Sinha, 2009)). The mismatch negativity (MMN) component is a hallmark of sensory prediction errors (Garrido et al., 2009), arguably a highly robust neurophysiological signature of schizophrenia (Michie, 2001; Nagai et al., 2013a), and a potential biomarker for prediction of conversion to psychosis in high-risk individuals (Bodatsch et al., 2011; Näätänen et al., 2016).

2.1. Mismatch negativity (MMN)

MMN is elicited by a violation to a regularity or pattern of auditory or visual stimuli (see Fig. 1D for examples of auditory regularity

violations). In order to elicit an MMN response, the sensory system must recognize a stimulus as being different (deviant) to, or unexpected, given a learnt pattern of stimuli (standards). MMN is the negative component obtained by subtracting an ERP to a standard from the ERP to a deviant, typically peaking at about 100–250 ms from change onset. It exhibits the highest intensity at fronto-temporal scalp regions. While attending to auditory stimuli has been shown to result in larger MMN amplitudes (Aukstulewicz and Friston, 2015; Oades and Dittmann-Balcar, 1995; Woldorff et al., 1991), MMN can be captured even when the participant's attention is deployed to an unrelated task (Garrido et al., 2008; Sams et al., 1985). The elicitation of MMN appears to reorient attention towards salient events and the deficiency in this process may lead to a disconnection of individuals with schizophrenia with the external environment and/or their own sensations (Javitt and Sweet, 2015).

MMN is most commonly evoked using auditory stimuli, however MMN has also been investigated in the visual domain (vMMN) and is described as the electrophysiological response to the automatic detection of unpredicted changes in the visual environment (Stefanics et al., 2014b). vMMN has been studied in relation to a number of features including colour (Czigler et al., 2006; Stefanics et al., 2011), and orientation (Kimura et al., 2009), often using gabors and also more complex visual objects such as faces arranged within oddball paradigms. For the purposes of this review we focus on auditory prediction errors (but see Kremlacek et al. (2016), for a review of vMMN in psychiatric and neurological disorders and Stefanics et al. (2014b), for a predictive coding account of vMMN).

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