Schizophrenia Research 191 (2018) 109–122

Contents lists available at ScienceDirect

Schizophrenia Research

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

Sensory prediction errors in the continuum of psychosis

R. Randeniya [a], L.K.L. Oestreich [a,b,d], M.I. Garrido [a,b,c,d,*]

[a] Queensland Brain Institute, The University of Queensland, Australia
[b] Centre for Advanced Imaging, The University of Queensland, Australia
[c] School of Mathematics and Physics, The University of Queensland, Australia
[d] ARC Centre for Integrative Brain Function, Australia

ARTICLE INFO

Article history:
Received 6 February 2017
Received in revised form 7 April 2017
Accepted 10 April 2017
Available online 28 April 2017

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.

© 2017 Elsevier B.V. All rights reserved.

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

* Corresponding author at: Queensland Brain Institute, The University of Queensland, Building 79, Brisbane, Australia.
E-mail address: m.garrido@uq.edu.au (M.I. Garrido).

http://dx.doi.org/10.1016/j.schres.2017.04.019
0920-9964/© 2017 Elsevier B.V. All rights reserved.

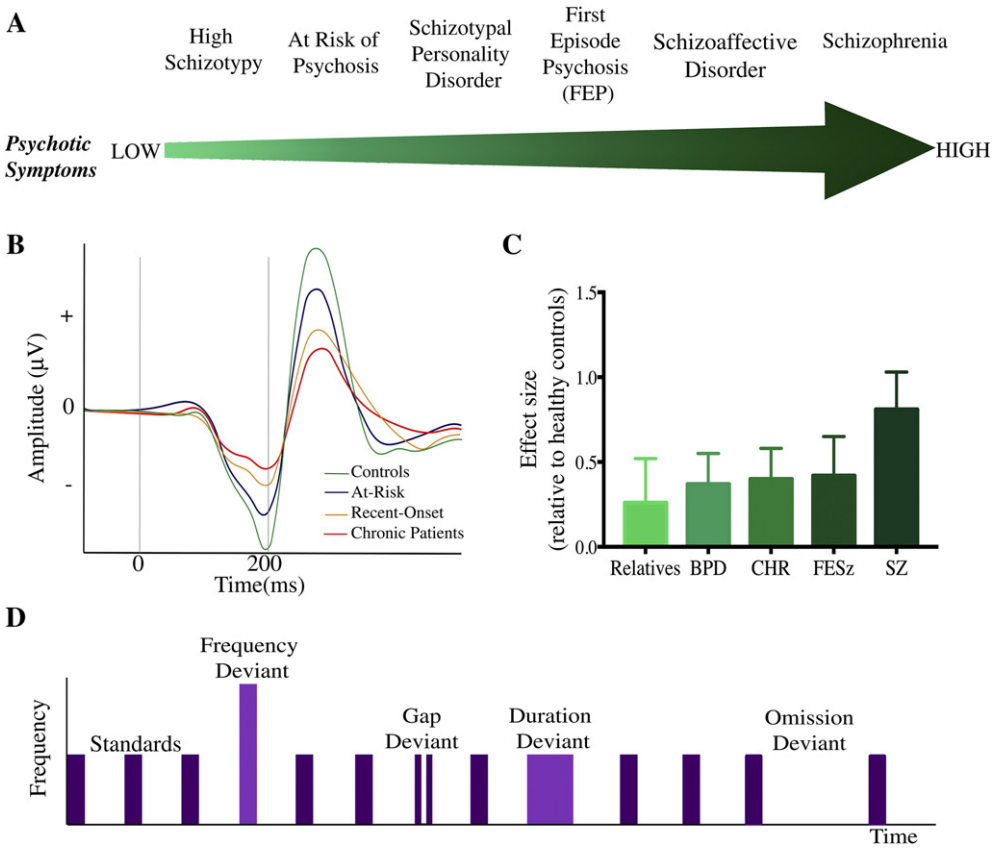

Fig. 1. MMN in the continuum of psychosis. (A) Psychotic symptoms ranging from low to high on a continuum of psychosis. (B) Duration MMN waveforms for healthy controls (green; $n = 28$), at-risk (blue; $n = 26$), recent-onset (yellow; $n = 31$) and chronic schizophrenia (red) patients ($n = 33$); adapted 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.

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 (Auksztulewicz 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).

2.2. Eliciting MMN: Oddball paradigms in schizophrenia

MMN attenuation in schizophrenia was first described using a simple two-tone duration deviant paradigm (Shelley et al., 1991). Since then, MMN amplitude, particularly in duration oddball paradigms, has been consistently shown to be attenuated in schizophrenia compared to healthy controls (Light et al., 2015; Nagai et al., 2013b; Todd et al., 2008). Subsequently, MMN studies in schizophrenia expanded to explore other physical properties of tones in the form of frequency and intensity deviants (Todd et al., 2008) as well as gap deviants (Fisher et al., 2008, 2012). While EEG is most commonly used in MMN studies, duration MMN attenuation in schizophrenia has also been shown using MEG (Shin et al., 2012; Suga et al., 2016; Thönnessen et al., 2008).

MMN paradigms have increased in complexity over time. *The Roving paradigm* (Cowan et al., 1993), presents a train of repeated sounds followed by a second set of sounds with different properties (e.g. new frequency or duration), the first tone in this second stimulus train serves as the deviant. Using this paradigm, Baldeweg and Hirsch (2015) suggested that frequency and duration MMN attenuation are specific to schizophrenia when compared to Alzheimer's patients and patients with BPD. However, this study may lack sufficient power to make such conclusion as the Alzheimer's disease group had a relatively small sample size ($n = 15$) compared to the BPD group ($n = 25$) and the group of schizophrenia patients ($n = 49$). *The 'optimal' multi-feature paradigm* by Näätänen et al. (2004), which includes multiple deviant types in the same stimulus train such as duration, frequency, intensity and gap, has provided important insights into MMN generation in individuals with schizophrenia. For example, Thönnessen et al. (2008) compared the 'traditional oddball' paradigm with the 'optimal' paradigm using both EEG and MEG, and concluded that using MEG in combination with the 'optimal' paradigm improved sensitivity in detecting MMN attenuation in schizophrenia. Using the 'optimal' paradigm, Fisher et al. (2012) found significant negative correlations between gap MMN amplitude and trait and state severity ratings of auditory hallucinations in patients with schizophrenia, indicating that the presence of auditory hallucinations may make a significant contribution to the widely reported MMN deficits in schizophrenia. This study is however limited by its relatively small sample size ($n = 12$ patients) and further research is needed to corroborate this finding. Another study by van Lutterveld et al. (2010) using an 'active' frequency oddball paradigm (where participants are asked to detect oddballs), found no significant differences in frequency MMN in non-psychotic individuals with auditory verbal hallucinations (AVH; $n = 18$), compared to individuals without AVH ($n = 18$). Simple variations of the basic oddball paradigm such as the inclusion of a third 'novelty' stimulus, for example a baby's cry (termed novelty MMN) have been shown to elicit smaller MMN amplitudes in schizophrenia patients compared to healthy controls. This novelty MMN has also been shown to be significantly positively correlated with auditory hallucinatory traits (Fisher et al., 2014), however this finding may also be limited by it's small sample size ($n = 10$ patients). In a systematic review of studies investigating AVH using oddball paradigms, Upthegrove et al. (2016) reported that MMN alone cannot explain AVH and further studies in non-clinical populations with AVH would be beneficial in verifying the underlying manifestations of AVH. Jarkiewicz and Wichniak (2015), provide a detailed review of oddball paradigms beyond frequency and duration deviants used in studying MMN in schizophrenia.

2.3. Do different deviant types represent trait or state of psychosis?

Evidence from a meta-analysis of 32 studies suggests that MMN attenuation in schizophrenia elicited by frequency deviants is significantly correlated with duration of illness (Umbricht and Krljes, 2005). Duration MMN attenuation on the other hand has been suggested to be more closely related to the genetic predisposition to develop schizophrenia (McGorry et al., 2014). This is supported by an attenuation in duration MMN in the early stages of disease, but attenuation of frequency MMN with increasing disease stage (Todd et al., 2008). Jahshan et al. (2012a) also found significant attenuation of duration MMN in at-risk, recent-onset, and chronic schizophrenia patient groups when compared with healthy controls. They also found that MMN amplitude reflected disease progression (Fig. 1B). Furthermore, positive symptoms in schizophrenia have been associated with reduced duration MMN amplitudes (Kärgel et al., 2014). Kim et al. (2014) found duration MMN attenuation in schizophrenia patients when compared to genetically high-risk relatives and healthy controls, and that reduced duration MMN amplitudes were associated with reduced state of functioning as measured by the Global Assessment of Functioning Scale (American Psychiatric Association, 2000). These findings suggest that duration MMN is a marker of state of functioning rather than a genetic marker of disease. However, based on a meta-analysis, which included relatives of patients with schizophrenia (Fig. 1C), Erickson et al. (2016) suggests that duration MMN may represent a genetic trait marker, but cautions on drawing this conclusion due to the small sample size in the relative group. Thus, it is not yet clear whether MMN impairment represents an index of an emerging illness or is better conceptualized as an endophenotype marker of genetic vulnerability (Erickson et al., 2016).

2.4. Theories of MMN generation

Two early theories have provided explanations on how MMN might be generated. *The model adjustment theory* suggests that the human brain forms a memory trace to standard events and constantly detects deviations to such sensory memory (Näätänen and Winkler, 1999). An alternative theory, *the adaptation hypothesis*, proposes that the neuronal populations tuned to the standards become less responsive to repeated stimuli, due to habituation, thus producing a suppression effect (Jääskeläinen et al., 2004; May et al., 1999). According to this account, when a deviant stimulus occurs, there is a release from adaptation, and a larger response is elicited in neuronal populations more tuned to deviant sounds. The adaptation model suggests that MMN is caused by the same mechanism and neuronal populations as those associated with the N1 component, which is limited to the primary auditory cortex; the model adjustment hypothesis argues against this model and states that MMN is caused by a neuronal population that is distinct from the neuronal population which causes the N1 component (Garrido et al., 2009).

A third and more recent perspective – predictive coding, can be viewed as a combination of the two hypotheses (Garrido et al., 2008; Garrido et al., 2009). *Predictive coding* theories suggest that the brain is constantly trying to minimize the discrepancy between actual sensory input and internal representations of the environment (Friston, 2005; Rauss and Pourtois, 2013). It views the brain as a hierarchical system in which each level is trying to achieve a compromise between the inputs from other levels (Friston, 2005), whereby sensory input is received at lower levels, and predictions are made at higher levels. According to this theory MMN is caused by prediction errors which arise during comparison between an incoming stimulus (and are conveyed through bottom-up connections) and a prediction based on a memory of previous standards (carried by top-down connections) ((Garrido et al., 2009); see Fig. 2A). The continuous interaction between top-down flow of predictions and bottom-up flow of prediction errors keeps our internal model of reality up-to-date (Stefanics et al., 2014a). Effective connectivity studies (Garrido et al., 2008) provide support for the predictive coding view of MMN, which gracefully marries the model adjustment and the adaptation hypotheses, in the sense that it predicts the generation of a model of current stimuli through plastic changes in synaptic connections akin to adaptation-like mechanisms.

2.5. Does auditory MMN represent prediction deficits in schizophrenia?

Despite the mounting evidence supporting the predictive coding view of MMN generation in healthy individuals, there are still some concerns as to whether MMN represents sensory adaptation deficits as opposed to

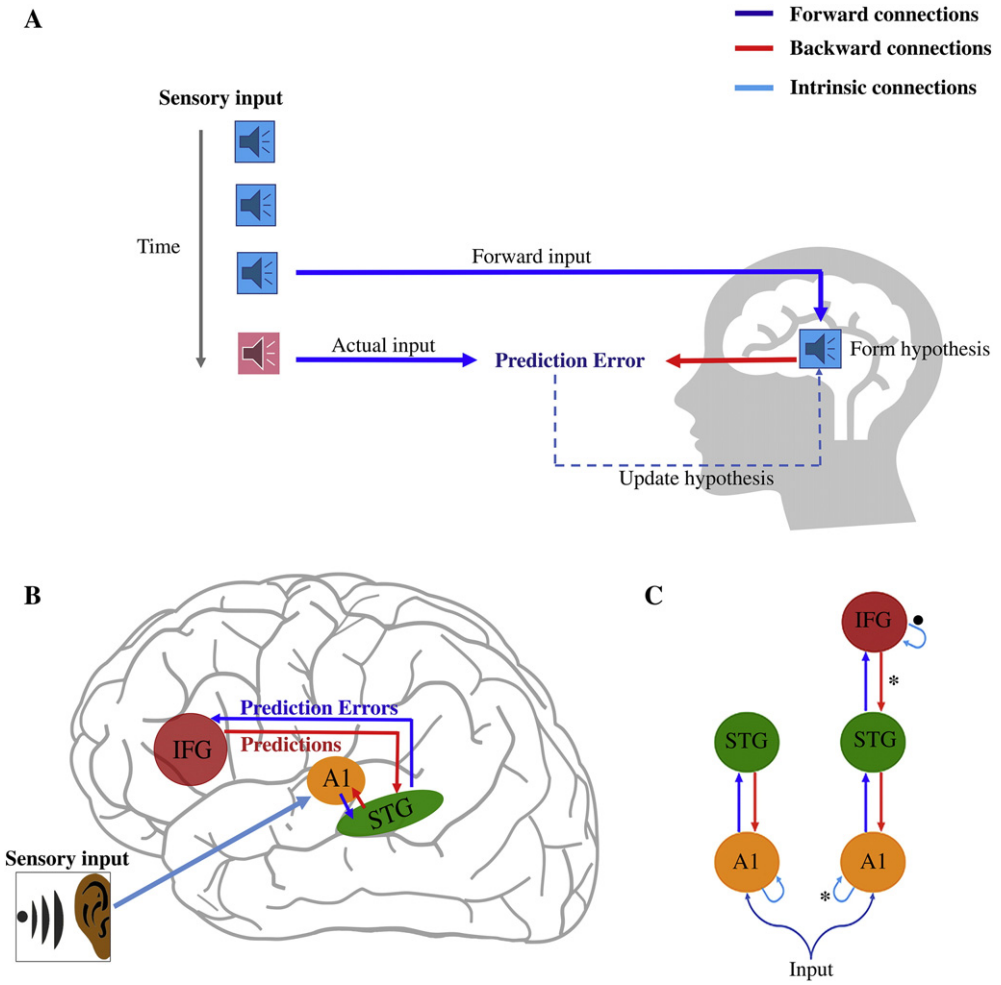

Fig. 2. Predictive Coding account of MMN generation. (A) The predictive coding account of MMN generation: as patterns, or rules, emerge with stimulus repetition, the brain forms an expectation of the next stimulus. Prediction errors arise when the actual stimulus does not match the predicted input (cf Garrido et al., 2009). (B) Brain regions active during the generation of MMN: sensory input enters the primary auditory (A1) cortex, superior temporal gyrus (STG) and inferior temporal gyrus (IFG), via which predictions flow top-down within this hierarchy and prediction errors flow bottom-up (C) effective connectivity underlying the generation of MMN in healthy people appears to be right lateralised (Garrido et al., 2008). (*) Indicates the connections found to be disrupted in Schizophrenia in Dima et al. (2012), which include intrinsic connections within right A1 (cyan), and the backward connection from right IFG to STG. (•) indicates disrupted intrinsic connectivity within the right IFG in patients with schizophrenia found in (Ranlund et al., 2016).

prediction deficits in schizophrenia (Michie et al., 2016). In other words, does attenuated MMN represent stimulus-specific adaptation effects in schizophrenia patients? To explore this further, more sophisticated paradigms that avoid stimulus-specific adaptation have been employed to elicit a 'complex MMN', which represents predictive deficits more specifically (Salisbury, 2012). These paradigms require sensory memory of standards that form a pattern (number of tones grouped temporally), while deviants are a variation in the structure, or violation of such patterns (such as a missing tone). If an individual remembers the grouping structure, or regularity, they learn to expect a particular tone and will be surprised if there is a discrepancy from that predicted tone. Importantly, studies of complex MMN have shown prediction deficits in chronic schizophrenia patients (Salisbury and McCathern, 2016) as well as early episode psychosis patients (Rudolph et al., 2015). Rentzsch et al. (2015) found a significant correlation between suppression measures and both frequency and duration MMN in healthy populations but not in patients with schizophrenia, suggesting a disruption in predictive coding mechanisms which can be distinguished from stimulus-specific adaptation.

2.6. Is MMN attenuation specific to schizophrenia?

MMN attenuation is present in both medicated and unmedicated patients with schizophrenia (Catts et al., 1995) and suggested to be specific to schizophrenia and not deficient in other psychiatric disorders such as major depression or obsessive-compulsive disorder (McGorry et al., 2014). It has since been demonstrated that patients with depression show context-specific attenuation of MMN elicited by oddball paradigms with sad speech syllables as stimuli (Pang et al., 2014). A review by Onitsuka et al. (2013), highlights several ERP abnormalities, including MMN deficits, in bipolar disorder with psychotic features. A recent meta-analysis found that while patients with bipolar disorder did show MMN attenuation compared to healthy controls, it was not as large as the effect size observed in schizophrenia, but more comparable to at-risk of psychosis states (Erickson et al., 2016); see Fig. 1C. This is supported through a study by Kaur et al. (2011), in which first-episode psychosis subgroups (see Table 1) show impairments in the fronto-central MMN consistent with findings in chronic schizophrenia patients, whereas,

Table 1
Recent findings in mismatch negativity (MMN) across the continuum of psychosis.

Paper	Sample	Paradigm	Findings
Schizophrenia			
(Suga et al., 2016)	Chronic SZ ($n = 42$) and HC ($n = 74$)	Passive oddball: frequency and duration; visual target detection task. (MEG Study)	↓ MMN to duration (but not frequency) for SZ in both hemispheres.
(Salisbury and McCathern, 2016)	SZ ($n = 14$) patients, HC ($n = 16$), groups matched for age, gender, handedness, and parental socioeconomic status	Double omission in a group standard	↓ MMN to omissions in patients
(Horacek et al., 2016)	SZ ($n = 31$) patients, HC ($n = 29$)	Duration decrement in predictable or unpredictable temporal order	↓ MMN for unpredictable (but intact for predictable) order in SZ
(Haigh et al., 2016)	SZ ($n = 22$), schizoaffective ($n = 5$) patients, HC ($n = 27$)	Simple MMN: Frequency and duration deviant blocks Complex MMN: 5 tones grouped together as standard, deviant: additional 6th tone in group	SZ showed ↓ frequency and duration MMN in simple MMN than HC. For complex MMN, the first negative deflection (~150 ms) was not significantly different between HC and SZ. The second negative deflection was significantly reduced in SZ.
(Chen et al., 2016)	Chronic SZ ($n = 30$) patients, HC ($n = 30$)	Oddball paradigm with threatening, happy and neutral voices.	Angry-derived MMN predicted positive symptoms of schizophrenia. Impairments of voice perception and acoustic discrimination seen in patients with chronic schizophrenia.
(Rentzsch et al., 2015)	SZ ($n = 25$) patients, HC ($n = 25$)	Frequency and duration deviant paradigm with repetition suppression (RS) paradigm with the same stimulus repeating	Correlation between MMN amplitudes and RS was significant in healthy controls but not in SZ.
(Fisher et al., 2014)	SZ ($n = 10$) patients, HC ($n = 13$), age and gender matched.	Passive oddball with frequency deviants and 'novel' environment sounds (e.g., baby cry)	SZ patients showed lengthened novelty MMN latencies and ↓ novelty MMN amplitudes compared to healthy controls Novelty MMN amplitudes were negatively correlated with measures of hallucinatory trait.
First Episode Psychosis (FEP)			
(Rudolph et al., 2015)	Early phase psychosis (within 5 years of onset) ($n = 13$), healthy controls ($n = 15$)	Complex MMN paradigm (Salisbury, 2012): two deviants: missing tone in 4th or 6th position	Patients showed ↓ MMN to missing 4th tone and 6th tone compared to healthy controls
(Hay et al., 2015)	Schizophrenia-spectrum ($n = 24$) patients early in the illness, healthy controls ($n = 21$).	Four auditory deviants: duration, frequency, intensity and duration + frequency ("double deviant")	↓ MMN in patients for all deviant types.
At-risk of psychosis			
(Pantlin and Davalos, 2016)	High-risk group ($n = 49$) scoring 6 or higher on PQ, controls ($n = 72$), scoring between 0 and 5 on PQ	Passive oddball duration decrement deviant while watching a silent movie.	High-risk group had ↓ MMN compared to controls
(Perez et al., 2014)	Clinical high-risk (CHR; $n = 38$), early SZ ($n = 19$), healthy controls ($n = 44$)	Three deviant blocks: duration, frequency, duration + frequency ("double deviant")	MMN ↓ in early SZ and CHR for all deviant types compared with HC, but was not different between SZ and CHR. Double deviant MMN was able to predict time to onset in 15 participants that converted to psychosis
Schizotypy			
(Broyd et al., 2016)	Healthy participants ($n = 35$, grouped based on SPQ scores and subscales)	Multi-feature MMN paradigm (long duration, frequency and intensity deviants	No differences in low and high schizotypy groups but, median-split on suspiciousness subscales showed ↑ MMN in high suspiciousness

SZ – schizophrenia, HC – healthy control, (↑) – increased, (↓) – reduced, PQ – 16 item prodromal questionnaire (Ising et al., 2012), SPQ – schizotypal personality questionnaire (Raine, 1991), CAARMS – comprehensive assessment of at-risk mental states (Yung et al., 2005).

the affective subgroup (patients with mood disorders) showed an 'intermediate' frontal response. In a study by Jahshan et al. (2012b), patients with bipolar disorder I and II have both shown attenuation in duration deviant MMN compared to healthy controls. These findings suggest that MMN reduction may be associated more generally with psychosis than schizophrenia specifically. However, findings show that duration MMN amplitude decreases as illness progresses and is nearly abolished in chronic schizophrenia (Baldeweg et al., 2004).

2.7. MMN in the continuum of psychosis

MMN has been studied across various populations in the continuum of psychosis. The studies in Table 1 were selected with the aim of providing an overview of the most recent MMN findings across the continuum of psychosis. For a review of MMN findings specific to schizophrenia and before 2014, see Näätänen et al. (2015) and Todd et al. (2014).

2.7.1. MMN in schizotypy

Schizotypy is a term that was first introduced in 1962 to refer to a vulnerability to schizophrenia spectrum disorders (Meehl, 1962). Schizotypy is a personality dimension, which refers to healthy individuals with psychotic-like experiences, such as delusions and/or hallucinations and is thought to be the sub-clinical manifestation of schizophrenia in the general population (Ettinger et al., 2015). It has also been suggested to be a specific predictor of schizophrenia spectrum disorders (Poulton et al., 2000). Schizotypy individuals differ from high-risk individuals in that the latter are by definition help-seeking and therefore considered at a higher risk for psychosis. Individuals who score highly on schizotypy and hallucinatory proneness, however, are difficult to differentiate from high-risk individuals and show similarities in distress and metacognitive abnormalities (Barkus et al., 2010).

One study investigating frequency MMN in schizotypy showed no differences in MMN between low and high schizotypal groups (Broyd et al., 2016). However, trend level differences of frequency MMN were reported when categorizing groups based on a suspiciousness subscale. Contrary to expectation, duration, frequency, and intensity MMN were enhanced (instead of reduced) in the high suspiciousness group compared to the low suspiciousness group. This suggests that attenuation of duration MMN may be an important tool in the differentiation of healthy individuals and individuals at actual risk of psychosis as opposed to individuals with personality traits of psychotic-like experiences as defined by schizotypy. Longitudinal studies of schizotypal individuals would provide a better understanding regarding the putative association of MMN and psychotic experiences, as well as an indication of whether MMN can be used as an early biomarker for conversion from schizotypy to florid psychosis.

2.7.2. MMN in people at risk for psychosis

Clinically high-risk (CHR) for psychosis, also known as "ultra-high risk (UHR)", "at-risk mental state (ARMS)", and "prodromal" (Fusar-Poli et al., 2013), is an important construct in studying the transition to psychosis. Several MMN studies have focused on ARMS populations, as defined by the comprehensive risk assessment of at-risk mental states (CAARMS) scale, and include individuals i) experiencing subthreshold psychotic symptoms ii) having experienced brief episodes of psychotic symptoms such as hallucinations or delusions iii) having a close biological relative with a psychotic disorder and having a significant loss of ability to carry out typical daily activities in a period of 12 months (Yung et al., 2005).

Studies using long duration deviants have consistently shown an MMN attenuation in ARMS/UHR individuals (Atkinson et al., 2012; Nagai et al., 2013b; Perez et al., 2014; Shaikh et al., 2012; Solis-Vivanco et al., 2014). The findings are less robust with frequency MMN, with some studies showing attenuation (Perez et al., 2014) and others reporting no difference (Nagai et al., 2013b). Longitudinal studies in schizophrenia patients and ARMS have shown that individuals who converted to schizophrenia had baseline reductions in duration MMN compared to non-converters (Bodatsch et al., 2015; Higuchi et al., 2014). Perez et al. (2014) further showed that a paradigm with two deviants in the same block (frequency and duration) could significantly predict the time to psychosis onset in clinically high-risk participants, while two-tone paradigms with duration or frequency deviants could not. This is a remarkable finding as it demonstrates the potential for using duration MMN as a biomarker for detecting psychosis proneness (Bodatsch et al., 2015) as well as using double duration paradigms for predicting psychosis onset.

2.7.3. MMN in Schizotypal Personality Disorder (SPD)

Schizotypal Personality Disorder (SPD) is a personality disorder characterized by unusual perceptual experiences, odd or eccentric behaviour, magical and/or paranoid beliefs and few, if any, close relationships (Esterberg et al., 2010). SPD is more common in relatives of patients with schizophrenia, supporting the genetic diathesis for psychotic disorders (Kendler and Diehl, 1993) and the notion of a continuum of psychosis (Krabbendam et al., 2004).

A study by Niznikiewicz et al. (2009) reported that SPD individuals exhibited significantly reduced frequency MMN compared to healthy controls.

2.7.4. MMN in First Episode Psychosis (FEP)

FEP is a broad category which has traditionally been demarcated into three subgroups: (i) 'schizophrenia spectrum psychoses' (schizophrenia, schizoaffective disorder, and schizophreniform disorder); (ii) 'affective spectrum psychoses' (bipolar disorder with psychotic features and major depressive disorder with psychotic features); and (iii) 'other psychoses' (e.g. brief psychotic disorder and substance-induced psychotic disorder); (Kaur et al., 2011), usually including individuals no more than 5 years after onset of a psychotic episode (For a review on definitions of FEP see Breitborde et al., 2009).

MMN amplitude findings in FEP have been variable across studies, with some finding significant MMN attenuation compared to healthy controls (Atkinson et al., 2012; Hermens et al., 2010; Kaur et al., 2011; Solis-Vivanco et al., 2014) and others finding no differences (Kaur et al., 2013). Haigh et al. (2016) conducted a meta-analysis of frequency and duration MMN findings in 14 studies that included patients within 12 months of their first episode of psychosis. It was found that the overall effect size showed no MMN reduction in FEP patients to frequency deviants, and a small-to-medium reduction to duration deviants. The authors suggest that frequency MMN is not a candidate biomarker for schizophrenia prediction, while duration MMN may hold some promise. Salisbury et al. (2016) confirmed these findings in a meta-analysis of frequency and duration MMN in the first-episode schizophrenia-spectrum and FEP (mixed schizophrenia-spectrum and affective-spectrum).

2.8. Cognitive and pharmacologic modulators of MMN

An early meta-analysis by Umbricht and Krljes (2005) found that there were no significant effects of duration of illness, gender ratio, age of patients, and test paradigm on the effect sizes of MMN amplitudes in schizophrenia patients. However, in a meta-analysis of 9 studies (182 young and 165 elderly subjects), age has been shown to negatively correlate with both duration and frequency MMN amplitudes (Cheng et al., 2013) and more specifically found to alter significant findings of MMN attenuation in schizophrenia studies when included as a covariate (Kiang et al., 2009). Nicotine use is also an important consideration in MMN studies, as schizophrenia patients who smoke have been shown to have lower MMN amplitudes than non-smoking patients (Light et al., 2015).

MMN attenuation in schizophrenia has been correlated with impaired working memory (Kiang et al., 2007), and larger duration MMN amplitudes in patients have been found to be correlated with

better social cognition and with better work and independent living (Wynn et al., 2010). Moreover, MMN attenuation appears to index cognitive impairment in neuropsychiatric and neurological diseases in ageing (for a review see Näätänen et al. (2011)). However, Baldeweg and Hirsch (2015) found that working memory impairments correlated with MMN attenuation only in patients with schizophrenia but not in patients with Alzheimer's disease. Further studies have found MMN attenuation to be associated with impairment in psychosocial functioning in patients with schizophrenia (Kim et al., 2014; Light and Braff, 2005; Light et al., 2015). These findings suggest that MMN may represent a decline of social and cognitive functioning in schizophrenia.

Salisbury et al. (2016) found that MMN amplitude attenuation in frequency and duration paradigms were associated with lower estimates of premorbid intelligence in both healthy and first hospitalized schizophrenia patients and that MMN was associated with a higher quantity of positive symptoms in first hospitalized patients with schizophrenia. In another study, first-episode schizophrenia patients who had not attended college had smaller MMNs than healthy controls and FEP patients who attended college (Umbricht et al., 2006). Therefore, it was suggested that academic achievement and premorbid IQ might be important variables associated with duration-MMN findings.

Early work indicated that long duration MMN amplitude in patients who were taking antipsychotics was not significantly different from MMN recorded in patients free of antipsychotic medication in the prior 3–6 month period (Catts et al., 1995). Similarly, no differences were seen in frequency MMN amplitudes and latencies in patients medicated with Olanzapine (Korostenskaja et al., 2005). This finding is supported by subsequent studies that used other atypical antipsychotics such as Amisulpride (a dopamine receptor antagonist), which also reported no significant change in duration MMN amplitudes in first-episode schizophrenia patients between baseline and after 6 weeks of treatment (Düring et al., 2015). However, a study investigating the atypical antipsychotic Ariprizaole (a partial dopamine receptor antagonist), showed improvement in both frequency and duration MMN amplitudes of schizophrenia patients 8 weeks after treatment (Zhou et al., 2013). Clozapine doses were positively associated with frequency MMN amplitudes but negatively associated with the amplitude and latency of duration MMNs in patients with schizophrenia (Horton et al., 2011). These findings highlight the importance of differentiating between specific antipsychotics when studying effects of MMN in chronic patients (who are typically treated with antipsychotics).

2.9. The functional anatomy of MMN

Identifying the functional neuroanatomy of MMN generation is not trivial as the precise anatomical location of the MMN generation may depend on the physical characteristics of the stimuli used to elicit the MMN. In healthy populations, generation of auditory frequency MMN has been attributed to neural populations in the primary auditory cortex (A1), superior temporal gyrus (STG), and the inferior temporal gyrus (IFG) (Garrido et al., 2008; Opitz et al., 2002); (see Fig. 2C). Using fMRI, duration deviant mismatch responses have shown activation bilaterally in the STG, right IFG and middle frontal gyri in healthy individuals (Schall et al., 2003).

Dynamic causal modelling (DCM) of the frequency MMN response in patients with schizophrenia has shown that patients have reduced intrinsic connectivity within the right A1, as well as disrupted backward extrinsic connectivity between the right IFG and right STG (Dima et al., 2012). In another DCM study in which the gain (excitability) of superficial pyramidal cells was explicitly parameterised, both patients with psychosis (which included patients with schizophrenia ($n = 18$), schizoaffective disorder ($n = 3$), bipolar I disorder ($n = 2$), psychosis not-otherwise-specified ($n = 1$)) and unaffected relatives showed increased excitability in right IFG across task conditions, compared to controls as well as a reversal of the normal response to deviant stimuli. That is, a decrease in excitability during deviants in comparison to standard conditions in the right IFG (Ranlund et al., 2016); see Fig. 2C.

A study by Rasser et al. (2011) found reduced frequency MMN to be correlated with grey matter reduction in Heschl's gyrus, pre-and post-central gyri and frontal cortex, whereas reduced duration MMN was found to be correlated with reductions in the right Heschl's gyrus. This is in line with frequency MMN findings by Dima et al. (2012).

An fMRI study investigating frequency MMN found decreased activation of the STG in patients with schizophrenia compared to healthy controls in the deviant stimuli condition, whereas in the control condition (only standards presented) there were no differences between groups (Wible et al., 2001), further supporting that the MMN response is distinct from other auditory deficits in schizophrenia. Further, by using fMRI and an adapted 'optimal' paradigm (Thönnessen et al., 2008), Gaebler et al. (2015) found that patients with schizophrenia showed reduced activation compared to healthy controls in the right auditory cortex, the prefrontal cortex, the salience network (insula and anterior cingulate cortex), areas of the visual system, and the dorsal attention network.

Investigating the auditory system with fMRI poses some limitations due to the acoustic noise which is intrinsic to the technique (Ravicz et al., 2000) as well as poorer temporal resolution. Nevertheless, it is worth mentioning a number of elucidating findings. Mathiak et al. (2002) employed a frequency and duration MMN paradigm which mimicked the gradient switching noise as reflected in fMRI and investigated the elicited MMN using MEG. It was found that duration MMN was right lateralized in the secondary auditory cortex in healthy participants. Further imaging studies in patients with schizophrenia have shown contrasting activation patterns in intensity and duration deviant MMN. Kircher et al. (2004) employed a tone sequence constituting fMRI tones, which mimicked the gradient switching noise, as the auditory stimuli in both an experiment using both fMRI and MEG. The MEG experiment revealed an attenuation of MMN in patients, and the fMRI study showed a strong left lateralization for intensity deviants in patients. Such lateralization was not apparent for duration deviants in the patients, which is often seen over the right hemisphere in healthy individuals.

Using EEG source reconstruction methods, Fulham et al. (2014) found duration MMN generation within a temporal, parietal and frontal network, which was right hemisphere dominant only in healthy controls. Reduced frontal MMN amplitude was found in both recent-onset and chronic schizophrenia patient groups, which involved reduced hemispheric asymmetry, and was correlated with Global Assessment of Functioning (GAF) and negative symptom ratings. During the early phase of the MMN (110-160 ms), schizophrenia patients showed reduced bilateral temporal and parietal responses and no lateralization in frontal regions, whereas controls showed larger activity in the right hemisphere. For late MMN (160–210 ms), patients showed reduced bilateral parietal response but larger temporal activity in the right compared to the left hemisphere.

Overall, evidence from structural and functional neuroimaging suggest right lateralized structural deficits in both frequency and duration MMN in patients with schizophrenia. Further studies are needed to understand if such deficits exist in other populations along the continuum of psychosis.

2.10. Taking MMN forward

While the findings in MMN and sensory prediction errors in schizophrenia have expanded vastly with the development of complex paradigms, there is a lack of standardization and lack of sufficient normative data to move MMN to the clinic (Schall, 2016). Despite duration MMN paradigms showing reliability, there is still limited evidence for the best paradigm to be used in large multi-scale studies. However, a recent study from our group found that the left gap and duration MMN paradigm best predicts diagnosis with up to 80% accuracy (Taylor et al., 2017).

Promising attempts of taking MMN forward into the clinic include work by Light et al. (2015) who investigated duration MMN and P3a in multi-site studies of schizophrenia. The study recruited 966 schizophrenia patients and 824 healthy controls, across 5 tests sites in the USA as part of the Consortium on the Genetics of Schizophrenia (COGS). Critically, this study replicated typical duration MMN attenuation in patients, demonstrating the feasibility of conducting multi-site clinical studies for the advancement of findings in MMN.

The findings in MMN across the continuum do not show a clear linear trajectory and suggest that further longitudinal studies will be valuable for assessing whether MMN can be used in the early detection and treatment of psychosis. While there is evidence for a continuum of MMN deficits within the spectrum of clinically diagnosed psychosis, there is little evidence to confirm whether such continuity encompasses the healthy population. Deficiencies in self-generated sensory prediction errors, on the other hand have been found to be aligned on a continuum of psychosis within the schizophrenia spectrum that also extends to non-clinical individuals, such as individuals who score highly on schizotypy.

3. Prediction errors in self-generated stimuli

Sensory self-suppression refers to the phenomenon that sensations initiated by our own actions are typically less salient, and elicit an attenuated neural response, compared to sensations resulting from changes in the external world (Wolpert et al., 1995). The sensory consequence of a self-generated action is predicted and thereby attenuated in healthy individuals, allowing for salience enhancement of sensations that have external sources or are conflicting with the predicted sensation (Baess et al., 2011; Palmer et al., 2016; Wolpert et al., 1995). Schizophrenia patients however, show a deficiency in this process, manifest in an inability to attribute self-generated sensations to an internal source and an abnormal sense of agency (Fletcher and Frith, 2009; Ford, 2016; Franck et al., 2001; Martikainen et al., 2005; Martinelli et al., 2016).

3.1. Theories of sensory self-suppression

Sensory self-suppression has been explained in the context of *the Forward Model* (Fig. 3A): When we initiate a movement, a motor command of that movement is sent to the motor system. At the same time, an 'efference copy' of that action is sent to the sensory cortex, generating a 'corollary discharge' of the expected sensory consequence of the motor act (Wolpert et al., 1995). The expected sensation is then compared to the actual sensation, and the discrepancy between the two is the so-called prediction error. In the absence of a discrepancy, the sensation is experienced to be internally rather than externally generated.

Self-generated sensory prediction errors have been studied in the tactile, visual and auditory domains. In the tactile domain, suppression of self-generated sensations has been investigated mainly with force-matching paradigms in which participants receive an external pressure on their hand and are required to match the force received by pressing down on a button (Shergill et al., 2005). These studies show that self-generated tactile sensations are not attenuated in schizophrenia, suggesting a dysfunction in the ability to predict the sensory consequences of one's own actions (Martinelli et al., 2016; Shergill et al., 2005). Similarly, self-generated eye movements elicit an efference copy, which is sent to the visual cortex (Sperry, 1950), therefore, rather than perceiving the room to be moving, we recognize that the changes in visual field input are due to our eye movements. In the auditory domain, speech production areas in the frontal lobes send an efference copy of

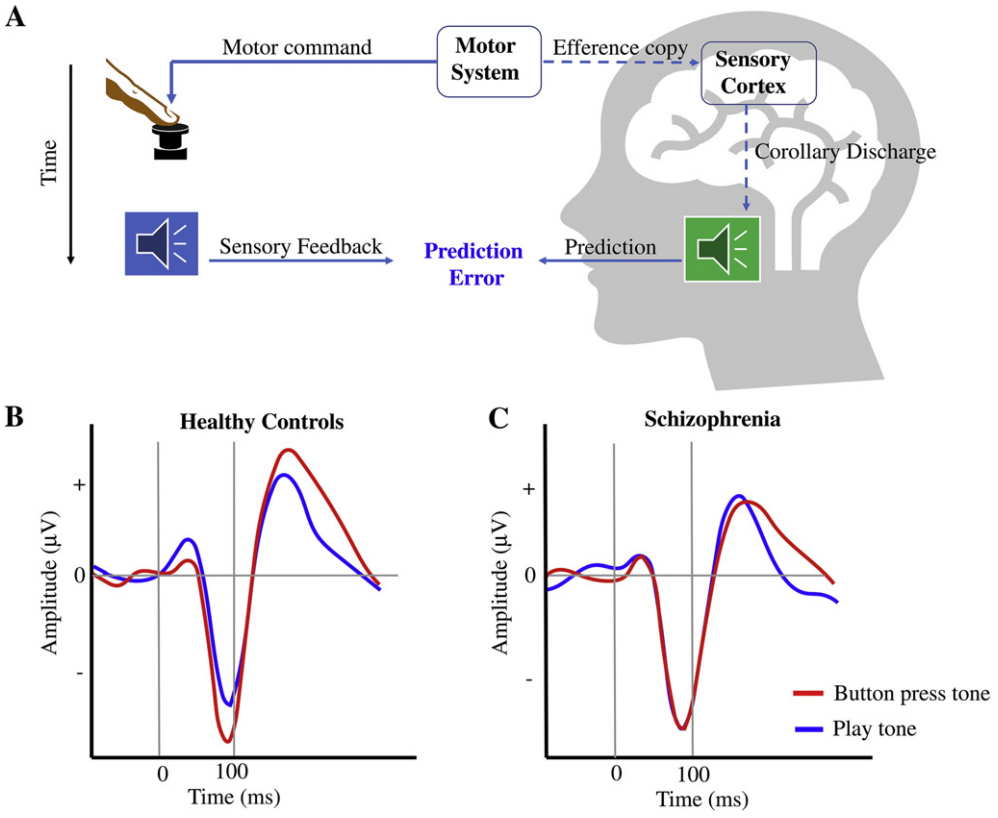

Fig. 3. The forward model for suppression of self-generated sensation in healthy individuals and its failure in schizophrenia. (A) The forward model: Before the initiation of any movement (button press) an efference copy of the motor command is sent to the sensory cortex, where a corollary discharge is generated which prepares the brain for incoming self-generated sensory input (tone). (B) Suppression of N1 responses in healthy individuals and (C) failure of suppression in patients with schizophrenia. Participants initiate a tone by pressing a button (blue) and passively listen to the same tone (red); adapted with permission from Ford et al. (2014).

self-generated speech sounds to the auditory cortex (Creutzfeldt et al., 1989). The corollary discharge then predicts the onset of our own speech (and arguably also thought) and thereby reduces the auditory cortical responsiveness. This enables the recognition of speech sounds (and thought) to be self-generated (Feinberg, 1978; Ford et al., 2007a). A failure of this system in producing a corollary discharge has been suggested as a possible cause for auditory verbal hallucinations (AVH), commonly experienced by schizophrenia patients (Blakemore et al., 2000; Ford and Mathalon, 2004; Frith, 1995).

Specifically, during speech production, patients with schizophrenia (particularly those experiencing AVH) show increased activity in temporal lobe structures, instead of suppression as observed in healthy individuals (Frith, 1991). Further speech production tasks have also suggested that reduced fronto-temporal functional connectivity may contribute to the misattribution of inner thoughts to external voices in schizophrenia (Ford et al., 2002). These findings are in line with forward models of sensory self-suppression, and suggest that the corollary discharge from speech areas in the frontal cortex fail to inform the temporal regions of the intention to speak (Ford and Mathalon, 2004).

While the forward model has strength in explaining passivity experiences, such as delusions of control, it has received criticism due to its limitations of studying AVH in schizophrenia directly. Specifically, Gallagher (2004) argues that there are no actual vs. predicted inner speech comparisons in AVH and that the 'comparator mechanism' fails to explain why all thoughts are not perceived as hallucinations. Brown et al. (2013) also draw attention to limitations of the forward model stating that it relates the intensity of the prediction error to the attenuation effects and that it overlooks the multidimensional nature of sensory attributes; they instead suggest a mechanism under *the predictive coding view*. Brown et al. (2013) suggest that sensory suppression is not a by-product of an initiating motor command, but a process based on active inference in which the precision of sensory evidence is attenuated during movement to allow proprioceptive predictions (that incite movement) to be fulfilled rather than being corrected by sensory prediction errors. This explanation is potentially important because a failure of sensory attenuation may result in false inference about the cause of self-generated events, which can explain known characteristics of the positive symptoms of schizophrenia such as delusions of self-control.

3.2. N1-suppression

The suppression of self-generated auditory sensations has been studied in healthy individuals and schizophrenia patients focusing on the N1 component of an ERP. N1-suppression is a measurable prediction error of self-generated auditory stimuli which is deficient (i.e., less suppressed) in patients with schizophrenia (Ford et al., 2007a; Ford and Mathalon, 2012; Ford et al., 2013). N1-suppression for self-generated tones also appears to occur independently of attention (like MMN) and indicates the operation of an internal predictive mechanism (Timm et al., 2013). In healthy individuals, it has been shown that the N1 amplitude can be reduced with training of temporal expectation, thus suggesting that training might potentially be used to alleviate subnormal sensory attenuation in patients with schizophrenia (Elijah et al., 2016).

N1-suppression is commonly studied using paradigms in which participants passively listen to a stimulus (control condition), compared with when they listen to a sound generated by their own actions. The most commonly employed tasks include Talk-Listen conditions in which participants self-generate speech and listen to a recording of their own voice played back to them (Ford et al., 2007a; Ford and Mathalon, 2004; Ford et al., 2001a), as well as conditions in which participants either passively listen to a tone or press a button to generate the same tone (Ford et al., 2010). N1-suppression has also been studied using pitch-shifted voices, to identify if participants could differentiate between their own voice and an altered voice. In healthy controls, N1 to unaltered self-voice feedback was dampened relative to N1 to altered self-voice or alien auditory feedback. This pattern was not seen in hallucinating patients, and showed a correlation between the severity of hallucinations and the percentage of misattribution errors (Heinks-Maldonado et al., 2007).

3.3. N1-suppression in the continuum of psychosis

Patients with schizophrenia and schizoaffective disorders have reduced N1-suppression compared to healthy controls (Ford et al., 2013; Ford et al., 2014); See Fig. 3B, 3C. While significant differences of N1-suppression deficits have also been shown in clinically high-risk (Perez et al., 2012) and in high schizotypal individuals compared to low schizotypal individuals (Oestreich et al., 2015, 2016), no significant differences were observed in first-degree relatives of patients when compared to patients and healthy controls, though an intermediate pattern between healthy controls and patients was observed (Ford et al., 2013). N1- suppression has also been found in bipolar disorder (Ford et al., 2013), implicating that corollary discharge dysfunction may be a common feature across psychotic disorders. Table 2 provides an overview of studies on N1-suppression arising from self-generated auditory stimuli in the continuum of psychosis.

Furthermore, similar to a study by Whitford et al. (2011), whereby a 50 ms delay between a button-press and a tone delivery was found to normalize N1-suppression in patients with schizophrenia, it has been shown that that a 25 ms time delay results in N1-suppression in highly schizotypal participants, which is similar to that of the undelayed condition in individuals with few schizotypal tendencies (Oestreich et al., 2016). This suggests that the predictive processes are still active but are affected by slow connectivity, possibly induced by conduction delays. These findings suggest the possibility of training patients to adjust to the time delay (Elijah et al., 2016).

4. Discussion

In this paper, we review MMN and N1-suppression to self-generated sounds, both of which are hallmarks of sensory prediction errors, which are impaired across the continuum of psychosis. Individuals with schizophrenia display aberrant sensory prediction errors, indexed by MMN attenuation as well as a failure to suppress N1 elicited by self-generated sounds, but current evidence suggests that these deficits may lie more broadly on a continuum, rather than being specific to schizophrenia. While studies using N1-suppression paradigms with self-generated stimuli report deficits in non-clinical individuals with high schizotypal characteristics (see Table 2 for a comprehensive list of references), MMN attenuation is seen more specifically in at risk groups rather than in healthy, high schizotypal individuals (Table 1, Fig. 1C). In other words, sensory prediction errors to internally and externally generated sensations can be observed across a broad spectrum in clinical and non-clinical individuals with psychotic symptoms. Moreover, these findings show that severe self-suppression deficits are characteristic to schizophrenia, possibly as a result of disease progression. However, current evidence does not point to a linear relationship between MMN attenuation and disease progression (Erickson et al., 2016). The current review supports that deficits in auditory prediction processes are an important aspect of studying the aetiology of schizophrenia, and show potential in being used as diagnostic tools and as predictors of disease prior to onset.

Elucidating the underlying mechanisms of sensory prediction error generation and what causes them to go awry in schizophrenia is essential for understanding disease progression, as well as determine their effectiveness as disease biomarkers. Theoretical conjectures inspired by predictive coding suggest that patients with schizophrenia form not only inaccurate but also imprecise predictions about incoming sensory information (via top-down connections), which then leads to the formation and propagation of inaccurate predictions upstream (via

Table 2
Summary of findings in N1-suppression across the continuum of psychosis.

Paper	Sample	Paradigm	Findings
Schizophrenia spectrum			
(Ford et al., 2014)	SZ ($n = 23$), schizoaffective ($n = 3$), HC ($n = 22$)	Button press sound generation	N1-suppression larger (↑) in HC than SZ.
(Whitford et al., 2011)	Chronic SZ ($n = 21$), HC ($n = 25$)	Button press initiation of participants pre-recorded voice, including un-delayed, 50 ms delayed and 100 ms delayed conditions	N1 suppression ↑ HC than in SZ for un-delayed condition. SZ showed ↑ N1 suppression than HC in 50 ms delayed condition, and no significant difference in the 100 ms delay condition.
(Ford et al., 2007a)	SZ ($n = 23$), schizoaffective ($n = 4$), HC ($n = 26$)	Talk-listen paradigm; agency condition: button-press to deliver speech sound, expectancy: speech sound preceded by visual warning	N1-suppression during talk-listen ↑ in HC than SZ; less N1-suppression during agency and expectancy only in HC, not SZ
(Ford et al., 2007b)	SZ and schizoaffective ($n = 24$), HC ($n = 25$)	Talk-listen paradigm	Pre-speech neural synchrony was related to subsequent N1-suppression in HC but not SZ
(Heinks-Maldonado et al., 2007)	SZ ($n = 20$), HC ($n = 17$), sex- and age-matched	Pitch-shifting voices "self", "other," or "unsure."	In HC, N1 to unaltered self-voice feedback was ↓ relative to N100 to altered self-voice or alien voices, but not in hallucinating patients.
(Ford et al., 2001a)	SZ ($n = 7$), HC ($n = 7$)	Talk-listen paradigm	N1-suppression larger (↑) in HC than SZ.
(Ford et al., 2001b)	SZ ($n = 12$), HC ($n = 10$)	Talk-listen paradigm; visual task	N1-suppression ↑ in HC than SZ; no N1-suppression in visual domain.
At-risk of psychosis			
(Perez et al., 2012)	CHR ($n = 40$) based on SIPS score, SZ patients ($n = 81$) including early illness SZ (ESZ) ($n = 41$) subgroup, healthy controls ($n = 89$)	Talk-listen paradigm	SZ showed ↓ speech-related N1 suppression relative to HC. This was also observed in ESZ. N1 suppression values in CHR were intermediate to HC and ESZ and not statistically distinguishable from either comparison group.
Psychotic patients and non-psychotic first-degree relatives			
(Ford et al., 2013)	SZ ($n = 30$), schizoaffective ($n = 19$), bipolar patients with a history of psychosis (BPP; $n = 39$), nonpsychotic relatives of SZ ($n = 30$), schizoaffective ($n = 23$), and BPD ($n = 50$) patients, and healthy controls ($n = 43$).	Talk-listen paradigm	N1- suppression was significantly ↓ in SZ and BPD patients, with a similar trend in the schizoaffective group. Patient groups did not differ, and unaffected relatives did not differ from controls or probands.
Schizotypy			
(Oestreich et al., 2016)	High Schizotypy ($n = 39$), Low Schizotypy ($n = 41$)	Button press sound generation. Time of tone onset after button press was temporally controlled	Low Schizotypy had ↑ levels of N1-suppression to un-delayed tones compared to High Schizotypy. N1-suppression was found to decrease linearly with increasing delays between the button press and the tone in the Low Schizotypy group, this was not the case in the High Schizotypy group.
(Oestreich et al., 2015)	High schizotypy ($n = 37$) and low schizotypy ($n = 37$)	Talk-Listen paradigm with an addition of cued listen condition in which participant listened to a recording of the vocalizations while simultaneously watching a video depicting the sound-wave of the forthcoming vocalizations, allowing them to be temporally predicted	Low schizotypy group showed significant N1-suppression in the Talk condition relative to the Listen and cued-listen conditions. The low schizotypy group also significant reduction in N1-amplitude in the cued listen condition compared to other conditions, but High schizotypy group did not.

All studies were conducted using EEG.
Schizophrenia (SZ), clinically high-risk for psychosis (CHR), healthy controls (HC); SIPS – structured interview for prodromal syndromes(Miller et al., 2002).

bottom-up connections), hence posing a difficulty in updating prior beliefs (Fletcher and Frith, 2009). Adams et al. (2016) suggest that if the accuracy of incoming sensory information is believed to be high, along with high uncertainty in the prior prediction, then the inference will be biased towards sensory information and away from the prior. This could explain why people with schizophrenia are less susceptible to optical illusions (Dima et al., 2009). In schizophrenia, this is represented as an imbalance or disruption of hierarchical information flow between top-down and bottom-up brain pathways (Adams et al., 2013), formalised in terms of the dysconnection hypothesis (Friston et al., 2016; Friston and Frith, 1995). This view is supported by resting state fMRI connectivity findings showing thalamic over-connectivity within bilateral sensory–motor cortices in patients with schizophrenia (compared to controls), and under-connectivity within prefrontal–striatal–cerebellar regions, which predicts positive symptoms (Anticevic et al., 2014). This is interpreted as possibly reflecting sensory gating and top-down control disturbances. Evidence from aberrant internal and external sensory prediction errors, indexed by reduced N1-suppresion and MMN amplitudes, fits well with the notion of imprecise belief formation in schizophrenia. Crucially, deficits in formation and encoding of valid predictions may increase as psychotic symptoms increase along the continuum of psychosis, as well as with disease progression. Indeed, false inference has been suggested to go hand-in-hand with positive symptoms, impaired learning, and cognitive difficulties (Friston et al., 2016). While there is strong evidence that psychotic symptoms and sensory prediction errors align on a continuum of psychosis, less is known about the neurobiological underpinnings. Future work is necessary to fill in the gaps of the disconnection hypothesis with regards to the continuum of psychosis as currently we only have very few data points (mostly on the extremes of the spectrum) for what happens in terms of brain (dis)connectivity in psychosis.

Current methods of diagnosing psychotic disorders show variability between clinicians and researchers (Wilson et al., 2014), demonstrating the qualitative nature of the diagnostic system. The combination of exposure to antipsychotics and the effects of the illness itself have profound impacts on cognitive performance (Frith et al., 1992) and lead to structural neuroatrophy (Ho et al., 2011). It is therefore of utmost importance to accurately identify the individuals who do need antipsychotic treatment, and predict which individuals will respond best to a particular treatment. Biomarkers are of extreme importance in providing objective diagnosis criteria and also in predicting who will convert to psychosis (Bodatsch et al., 2015). Validating which paradigms and parameters can be used to identify early predictors of schizophrenia is increasingly important to study the aetiology of this disorder and to develop prophylactic treatments (Kiehl et al., 2005). The recent studies of prediction errors in the continuum of psychosis and schizophrenia reviewed in this article provide a very promising basis for the development of better diagnostic tools for schizophrenia. Moreover, they suggest that prediction errors may be potential biomarkers for the identification of individuals at high-risk for psychosis who might benefit from prophylactic treatments.

Conflicts of interest

We declare no conflicts of interest and all authors have approved the submission of this manuscript.

Acknowledgments

We thank Patricia Michie and Ilvana Dzafic for comments on an earlier version of this manuscript. M.I.G. is supported by a University of Queensland Fellowship (2016000071). R.R. is supported through a University of Queensland International Research Scholarship.

References

Adams, R.A., Stephan, K.E., Brown, H.R., Frith, C.D., Friston, K.J., 2013. The computational anatomy of psychosis. Front. Psych. 4, 47.

Adams, R.A., Huys, Q.J., Roiser, J.P., 2016. Computational psychiatry: towards a mathematically informed understanding of mental illness. J. Neurol. Neurosurg. Psychiatry 87 (1), 53–63.

Aliu, S.O., Houde, J.F., Nagarajan, S.S., 2009. Motor-induced suppression of the auditory cortex. J. Cogn. Neurosci. 21 (4), 791–802.

American Psychiatric Association, 2000. Diagnostic and Statstical Manual of Mental Disorders. fourth ed. (Washington, DC).

American Psychiatric Association, 2013. Diagnostic and Statistical Manual of Mental Disorders. fifth ed. (Washington, DC).

Andreasen, N.C., Flaum, M., 1991. Schizophrenia: the characteristic symptoms. Schizophr. Bull. 17 (1), 27–49.

Anticevic, A., Cole, M.W., Repovs, G., Murray, J.D., Brumbaugh, M.S., Winkler, A.M., Savic, A., Krystal, J.H., Pearlson, G.D., Glahn, D.C., 2014. Characterizing thalamo-cortical disturbances in schizophrenia and bipolar illness. Cereb. Cortex 24 (12), 3116–3130 (New York, N.Y.: 1991).

Atkinson, R.J., Michie, P.T., Schall, U., 2012. Duration mismatch negativity and P3a in first-episode psychosis and individuals at ultra-high risk of psychosis. Biol. Psychiatry 71 (2), 98–104.

Auksztulewicz, R., Friston, K., 2015. Attentional enhancement of auditory mismatch responses: a DCM/MEG study. Cereb. Cortex 25 (11), 4273–4283.

Baess, P., Horvath, J., Jacobsen, T., Schroger, E., 2011. Selective suppression of self-initiated sounds in an auditory stream: an ERP study. Psychophysiology 48 (9), 1276–1283.

Baldeweg, T., Hirsch, S.R., 2015. Mismatch negativity indexes illness-specific impairments of cortical plasticity in schizophrenia: a comparison with bipolar disorder and Alzheimer's disease. J Psychophysiol]–>Int. J. Psychophysiol. 95 (2), 145–155.

Baldeweg, T., Klugman, A., Gruzelier, J., Hirsch, S.R., 2004. Mismatch negativity potentials and cognitive impairment in schizophrenia. Schizophr. Res. 69 (2–3), 203–217.

Barkus, E., Stirling, J., French, P., Morrison, A., Bentall, R., Lewis, S., 2010. Distress and metacognition in psychosis prone individuals: comparing high schizotypy to the at-risk mental state. J. Nerv. Ment. Dis. 198 (2), 99–104.

Blakemore, S.J., Smith, J., Steel, R., Johnstone, C.E., Frith, C.D., 2000. The perception of self-produced sensory stimuli in patients with auditory hallucinations and passivity experiences: evidence for a breakdown in self-monitoring. Psychol. Med. 30 (5), 1131–1139.

Bodatsch, M., Ruhrmann, S., Wagner, M., Muller, R., Schultze-Lutter, F., Frommann, I., Brinkmeyer, J., Gaebel, W., Maier, W., Klosterkotter, J., Brockhaus-Dumke, A., 2011. Prediction of psychosis by mismatch negativity. Biol. Psychiatry 69 (10), 959–966.

Bodatsch, M., Brockhaus-Dumke, A., Klosterkotter, J., Ruhrmann, S., 2015. Forecasting psychosis by event-related potentials-systematic review and specific meta-analysis. Biol. Psychiatry 77 (11), 951–958.

Breitborde, N.J., Srihari, V.H., Woods, S.W., 2009. Review of the operational definition for first-episode psychosis. Early Interv. Psychiatry 3 (4), 259–265.

Brown, H., Adams, R.A., Parees, I., Edwards, M., Friston, K., 2013. Active inference, sensory attenuation and illusions. Cogn. Process. 411–427.

Broyd, S.J., Michie, P.T., Bruggemann, J., van Hell, H.H., Greenwood, L.M., Croft, R.J., Todd, J., Lenroot, R., Solowij, N., 2016. Schizotypy and auditory mismatch negativity in a non-clinical sample of young adults. Psychiatry Res. 254, 83–91.

Catts, S.V., Shelley, A.M., Ward, P.B., Liebert, B., McConaghy, N., Andrews, S., Michie, P.T., 1995. Brain potential evidence for an auditory sensory memory deficit in schizophrenia. J Psychiatry]–>Am. J. Psychiatry 152 (2), 213–219.

Chen, C., Liu, C.C., Weng, P.Y., Cheng, Y., 2016. Mismatch negativity to threatening voices associated with positive symptoms in schizophrenia. Front. Hum. Neurosci. 10, 362.

Cheng, C.H., Hsu, W.Y., Lin, Y.Y., 2013. Effects of physiological aging on mismatch negativity: a meta-analysis. J Psychophysiol]–>Int. J. Psychophysiol. 90 (2), 165–171.

Cowan, N., Winkler, I., Teder, W., Naatanen, R., 1993. Memory prerequisites of mismatch negativity in the auditory event-related potential (ERP). J. Exp. Psychol. Learn. Mem. Cogn. 19 (4), 909–921.

Creutzfeldt, O., Ojemann, G., Lettich, E., 1989. Neuronal activity in the human lateral temporal lobe. I. Responses to speech. Exp. Brain Res. 77 (3), 451–475.

Czigler, I., Weisz, J., Winkler, I., 2006. ERPs and deviance detection: visual mismatch negativity to repeated visual stimuli. Neurosci. Lett. 401 (1–2), 178–182.

DeRosse, P., Karlsgodt, K.H., 2015. Examining the psychosis continuum. Curr. Behav. Neurosci. Rep. 2 (2), 80–89.

Dima, D., Roiser, J.P., Dietrich, D.E., Bonnemann, C., Lanfermann, H., Emrich, H.M., Dillo, W., 2009. Understanding why patients with schizophrenia do not perceive the hollow-mask illusion using dynamic causal modelling. NeuroImage 46 (4), 1180–1186.

Dima, D., Frangou, S., Burge, L., Braeutigam, S., James, A.C., 2012. Abnormal intrinsic and extrinsic connectivity within the magnetic mismatch negativity brain network in schizophrenia: a preliminary study. Schizophr. Res. 135 (1–3), 23–27.

Düring, S., Glenthoj, B.Y., Oranje, B., 2015. Effects of blocking D2/D3 receptors on mismatch negativity and P3a amplitude of initially antipsychotic naive, first episode schizophrenia patients. Int. J. Neuropsychopharmacol. 19 (3), pyv109.

Elijah, R.B., Le Pelley, M.E., Whitford, T.J., 2016. Modifying temporal expectations: changing cortical responsivity to delayed self-initiated sensations with training. Biol. Psychol. 120, 88–95.

Erickson, M.A., Ruffle, A., Gold, J.M., 2016. A meta-analysis of mismatch negativity in schizophrenia: from clinical risk to disease specificity and progression. Biol. Psychiatry 79 (12), 980–987.

Esterberg, M.L., Goulding, S.M., Walker, E.F., 2010. A personality disorders: schizotypal, schizoid and paranoid personality disorders in childhood and adolescence. J. Psychopathol. Behav. Assess. 32 (4), 515–528.

Ettinger, U., Mohr, C., Gooding, D.C., Cohen, A.S., Rapp, A., Haenschel, C., Park, S., 2015. Cognition and brain function in schizotypy: a selective review. Schizophr. Bull. 41 (Suppl. 2), S417–S426.

Feinberg, I., 1978. Efference copy and corollary discharge: implications for thinking and its disorders. Schizophr. Bull. 4 (4), 636–640.

Fisher, D.J., Labelle, A., Knott, V.J., 2008. The right profile: mismatch negativity in schizophrenia with and without auditory hallucinations as measured by a multi-feature paradigm. Clin. Neurophysiol. 119 (4), 909–921.

Fisher, D.J., Labelle, A., Knott, V.J., 2012. Alterations of mismatch negativity (MMN) in schizophrenia patients with auditory hallucinations experiencing acute exacerbation of illness. Schizophr. Res. 139 (1–3), 237–245.

Fisher, D.J., Smith, D.M., Labelle, A., Knott, V.J., 2014. Attenuation of mismatch negativity (MMN) and novelty P300 in schizophrenia patients with auditory hallucinations experiencing acute exacerbation of illness. Biol. Psychol. 100, 43–49.

Fletcher, P.C., Frith, C.D., 2009. Perceiving is believing: a Bayesian approach to explaining the positive symptoms of schizophrenia. Nat. Rev. Neurosci. 10 (1), 48–58.

Ford, J.M., 2016. Studying auditory verbal hallucinations using the RDoC framework. Psychophysiology 53 (3), 298–304.

Ford, J.M., Mathalon, D.H., 2004. Electrophysiological evidence of corollary discharge dysfunction in schizophrenia during talking and thinking. J. Psychiatr. Res. 38 (1), 37–46.

Ford, J.M., Mathalon, D.H., 2012. Anticipating the future: automatic prediction failures in schizophrenia. J Psychophysiol]–>Int. J. Psychophysiol. 83 (2), 232–239.

Ford, J.M., Mathalon, D.H., Heinks, T., Kalba, S., Faustman, W.O., Roth, W.T., 2001a. Neurophysiological evidence of corollary discharge dysfunction in schizophrenia. J Psychiatry]–>Am. J. Psychiatry 158 (12), 2069–2071.

Ford, J.M., Mathalon, D.H., Kalba, S., Whitfield, S., Faustman, W.O., Roth, W.T., 2001b. Cortical responsiveness during inner speech in schizophrenia: an event-related potential study. J Psychiatry]–>Am. J. Psychiatry 158 (11), 1914–1916.

Ford, J.M., Mathalon, D.H., Whitfield, S., Faustman, W.O., Roth, W.T., 2002. Reduced communication between frontal and temporal lobes during talking in schizophrenia. Biol. Psychiatry 51 (6), 485–492.

Ford, J.M., Gray, M., Faustman, W.O., Roach, B.J., Mathalon, D.H., 2007a. Dissecting corollary discharge dysfunction in schizophrenia. Psychophysiology 44 (4), 522–529.

Ford, J.M., Roach, B.J., Faustman, W.O., Mathalon, D.H., 2007b. Synch before you speak: auditory hallucinations in schizophrenia. J Psychiatry]–>Am. J. Psychiatry 164 (3), 458–466.

Ford, J.M., Roach, B.J., Mathalon, D.H., 2010. Assessing corollary discharge in humans using noninvasive neurophysiological methods. Nat. Protoc. 5 (6), 1160–1168.

Ford, J.M., Mathalon, D.H., Roach, B.J., Keedy, S.K., Reilly, J.L., Gershon, E.S., Sweeney, J.A., 2013. Neurophysiological evidence of corollary discharge function during vocalization in psychotic patients and their nonpsychotic first-degree relatives. Schizophr. Bull. 39 (6), 1272–1280.

Ford, J.M., Palzes, V.A., Roach, B.J., Mathalon, D.H., 2014. Did I do that? Abnormal predictive processes in schizophrenia when button pressing to deliver a tone. Schizophr. Bull. 40 (4), 804–812.

Franck, N., Farrer, C., Georgieff, N., Marie-Cardine, M., Dalery, J., d'Amato, T., Jeannerod, M., 2001. Defective recognition of one's own actions in patients with schizophrenia. J Psychiatry]–>Am. J. Psychiatry 158 (3), 454–459.

Friston, K., 2005. A theory of cortical responses. Philos. Trans. R. Soc. Lond. Ser. B Biol. Sci. 815–836.

Friston, K.J., Frith, C.D., 1995. Schizophrenia: a disconnection syndrome? Clin. Neurosci. 3 (2), 89–97.

Friston, K., Brown, H.R., Siemerkus, J., Stephan, K.E., 2016. The dysconnection hypothesis (2016). Schizophr. Res. 176 (2–3), 83–94.

Frith, C., 1991. Positron emission tomography studies of frontal lobe function: relevance to psychiatric disease. CIBA Found. Symp. 163, 181–191 (discussion 191-187).

Frith, C., 1995. Functional imaging and cognitive abnormalities. Lancet 346 (8975), 615–620.

Frith, C.D., Friston, K.J., Liddle, P.F., Frackowiak, R.S., 1992. PET imaging and cognition in schizophrenia. R Soc Med]–>J. R. Soc. Med. 85 (4), 222–224.

Fulham, W.R., Michie, P.T., Ward, P.B., Rasser, P.E., Todd, J., Johnston, P.J., Thompson, P.M., Schall, U., 2014. Mismatch negativity in recent-onset and chronic schizophrenia: a current source density analysis. PLoS One 9 (6), e100221.

Fusar-Poli, P., Borgwardt, S., Bechdolf, A., Addington, J., Riecher-Rössler, A., Schultze-Lutter, F., Keshavan, M., Wood, S., Ruhrmann, S., Seidman, L.J., Valmaggia, L., Cannon, T., Velthorst, E., De Haan, L., Cornblatt, B., Bonoldi, I., Birchwood, M., McGlashan, T., Carpenter, W., McGorry, P., Klosterkötter, J., McGuire, P., Yung, A., 2013. The psychosis high-risk state: a comprehensive state-of-the-art review. JAMA Psychiat. 70 (1), 107–120.

Gaebler, A.J., Mathiak, K., Koten Jr., J.W., Konig, A.A., Koush, Y., Weyer, D., Depner, C., Matentzoglu, S., Edgar, J.C., Willmes, K., Zvyagintsev, M., 2015. Auditory mismatch impairments are characterized by core neural dysfunctions in schizophrenia. Brain 138 (Pt 5), 1410–1423.

Gallagher, S., 2004. Neurocognitive models of schizophrenia: a neurophenomenological critique. Psychopathology 37 (1), 8–19.

Garrido, M.I., Friston, K.J., Kiebel, S.J., Stephan, K.E., Baldeweg, T., Kilner, J.M., 2008. The functional anatomy of the MMN: a DCM study of the roving paradigm. NeuroImage 42 (2), 936–944.

Garrido, M.I., Kilner, J.M., Stephan, K.E., Friston, K.J., 2009. The mismatch negativity: a review of underlying mechanisms. Clin. Neurophysiol. 120 (3), 453–463.

Haigh, S.M., Coffman, B.A., Salisbury, D.F., 2016. Mismatch negativity in first-episode schizophrenia: a meta-analysis. Clin. EEG Neurosci.

Hay, R.A., Roach, B.J., Srihari, V.H., Woods, S.W., Ford, J.M., Mathalon, D.H., 2015. Equivalent mismatch negativity deficits across deviant types in early illness schizophrenia-spectrum patients. Biol. Psychol. 105, 130–137.

Heinks-Maldonado, T.H., Mathalon, D.H., Houde, J.F., Gray, M., Faustman, W.O., Ford, J.M., 2007. Relationship of imprecise corollary discharge in schizophrenia to auditory hallucinations. Arch. Gen. Psychiatry 64 (3), 286–296.

Hermens, D.F., Ward, P.B., Hodge, M.A., Kaur, M., Naismith, S.L., Hickie, I.B., 2010. Impaired MMN/P3a complex in first-episode psychosis: cognitive and psychosocial associations. Prog. Neuro-Psychopharmacol. Biol. Psychiatry 34 (6), 822–829.

Higuchi, Y., Seo, T., Miyanishi, T., Kawasaki, Y., Suzuki, M., Sumiyoshi, T., 2014. Mismatch negativity and p3a/reorienting complex in subjects with schizophrenia or at-risk mental state. Front. Behav. Neurosci. 8, 172.

Ho, B.C., Andreasen, N.C., Ziebell, S., Pierson, R., Magnotta, V., 2011. Long-term antipsychotic treatment and brain volumes: a longitudinal study of first-episode schizophrenia. Arch. Gen. Psychiatry 68 (2), 128–137.

Horacek, M., Kärgel, C., Scherbaum, N., Müller, B.W., 2016. The effect of deviance predictability on mismatch negativity in schizophrenia patients. Neurosci. Lett. 617, 76–81.

Horton, J., Millar, A., Labelle, A., Knott, V.J., 2011. MMN responsivity to manipulations of frequency and duration deviants in chronic, clozapine-treated schizophrenia patients. Schizophr. Res. 126 (1–3), 202–211.

Ising, H.K., Veling, W., Loewy, R.L., Rietveld, M.W., Rietdijk, J., Dragt, S., Klaassen, R.M.C., Nieman, D.H., Wunderink, L., Linszen, D.H., van der Gaag, M., 2012. The validity of the 16-item version of the prodromal questionnaire (PQ-16) to screen for ultra high risk of developing psychosis in the general help-seeking population. Schizophr. Bull. 38 (6), 1288–1296.

Jääskeläinen, I.P., Ahveninen, J., Bonmassar, G., Dale, A.M., Ilmoniemi, R.J., Levanen, S., Lin, F.H., May, P., Melcher, J., Stufflebeam, S., Tiitinen, H., Belliveau, J.W., 2004. Human posterior auditory cortex gates novel sounds to consciousness. U S A]–>Proc. Natl. Acad. Sci. U. S. A. 101 (17), 6809–6814.

Jahshan, C., Cadenhead, K.S., Rissling, A.J., Kirihara, K., Braff, D.L., Light, G.A., 2012a. Automatic sensory information processing abnormalities across the illness course of schizophrenia. Psychol. Med. 42 (1), 85–97.

Jahshan, C., Wynn, J.K., Mathis, K.I., Altshuler, L., Glahn, D.C., Green, M.F., 2012b. Cross-diagnostic comparison of duration mismatch negativity and P3a in bipolar disorder and schizophrenia. Bipolar Disord. 14 (3), 239–248.

Jarkiewicz, M., Wichniak, A., 2015. Can new paradigms bring new perspectives for mismatch negativity studies in schizophrenia? Neuropsychiatr. Electrophysiol. 1 (1), 12.

Javitt, D.C., Sweet, R.A., 2015. Auditory dysfunction in schizophrenia: integrating clinical and basic features. Nat. Rev. Neurosci. 16 (9), 535–550.

Kärgel, C., Sartory, G., Kariofillis, D., Wiltfang, J., Müller, B.W., 2014. Mismatch negativity latency and cognitive function in schizophrenia. PLoS One 9 (4).

Kaur, M., Battisti, R.A., Ward, P.B., Ahmed, A., Hickie, I.B., Hermens, D.F., 2011. MMN/P3a deficits in first episode psychosis: comparing schizophrenia-spectrum and affective-spectrum subgroups. Schizophr. Res. 130 (1–3), 203–209.

Kaur, M., Lagopoulos, J., Lee, R.S.C., Ward, P.B., Naismith, S.L., Hickie, I.B., Hermens, D.F., 2013. Longitudinal associations between mismatch negativity and disability in early schizophrenia- and affective-spectrum disorders. Prog. Neuropsychopharmacol. 46, 161–169.

Kaymaz, N., van Os, J., 2010. Extended psychosis phenotype—yes: single continuum—unlikely. Psychol. Med. 40 (12), 1963–1966.

Kendler, K.S., Diehl, S.R., 1993. The genetics of schizophrenia: a current, genetic-epidemiologic perspective. Schizophr. Bull. 19 (2), 261–285.

Kiang, M., Light, G.A., Prugh, J., Coulson, S., Braff, D.L., Kutas, M., 2007. Cognitive, neurophysiological, and functional correlates of proverb interpretation abnormalities in schizophrenia. J. Int. Neuropsychol. Soc. 13 (4), 653–663.

Kiang, M., Braff, D.L., Sprock, J., Light, G.A., 2009. The relationship between preattentive sensory processing deficits and age in schizophrenia patients. Clin. Neurophysiol. 120 (11), 1949–1957.

Kiehl, K.A., Stevens, M.C., Celone, K., Kurtz, M., Krystal, J.H., 2005. Abnormal hemodynamics in schizophrenia during an auditory oddball task. Biol. Psychiatry 57 (9), 1029–1040.

Kim, M., Kim, S.N., Lee, S., Byun, M.S., Shin, K.S., Park, H.Y., Jang, J.H., Kwon, J.S., 2014. Impaired mismatch negativity is associated with current functional status rather than genetic vulnerability to schizophrenia. Psychiatry Res. Neuroimaging 222 (1–2), 100–106.

Kimura, M., Katayama, J., Ohira, H., Schroger, E., 2009. Visual mismatch negativity: new evidence from the equiprobable paradigm. Psychophysiology 46 (2), 402–409.

Kircher, T.T., Rapp, A., Grodd, W., Buchkremer, G., Weiskopf, N., Lutzenberger, W., Ackermann, H., Mathiak, K., 2004. Mismatch negativity responses in schizophrenia: a combined fMRI and whole-head MEG study. J Psychiatry]–>Am. J. Psychiatry 161 (2), 294–304.

Korostenskaja, M., Dapsys, K., Siurkute, A., Maciulis, V., Ruksenas, O., Kahkonen, S., 2005. Effects of olanzapine on auditory P300 and mismatch negativity (MMN) in schizophrenia spectrum disorders. Prog. Neuro-Psychopharmacol. Biol. Psychiatry 29 (4), 543–548.

Krabbendam, L., Myin-Germeys, I., van Os, J., 2004. The expanding psychosis phenotype. Int. J. Psychol. Psychol. Ther. 4 (2), 411–421.

Kremlacek, J., Kreegipuu, K., Tales, A., Astikainen, P., Poldver, N., Näätänen, R., Stefanics, G., 2016. Visual mismatch negativity (vMMN): a review and meta-analysis of studies in psychiatric and neurological disorders. Cortex 80, 76–112.

Lakatos, P., Schroeder, C.E., Leitman, D.I., Javitt, D.C., 2013. Predictive suppression of cortical excitability and its deficit in schizophrenia. J. Neurosci. 33 (28), 11692–11702.

Lawrie, S.M., Hall, J., McIntosh, A.M., Owens, D.G., Johnstone, E.C., 2010. The 'continuum of psychosis': scientifically unproven and clinically impractical. Br. J. Psychiatry 197 (6), 423–425.

Light, G.A., Braff, D.L., 2005. Mismatch negativity deficits are associated with poor functioning in schizophrenia patients. Arch. Gen. Psychiatry 62 (2), 127–136.

Light, G.A., Swerdlowa, N.R., Thomas, M.L., Calkins, M.E., Green, M.F., Greenwood, T.A., Gur, R.E., Gur, R.C., Lazzeroni, L.C., Nuechterlein, K.H., Pela, M., Radant, A.D., Seidman, L.J., Sharp, R.F., Siever, L.J., Silverman, J.M., Sprock, J., Stone, W.S., Sugar, C.A., Tsuang, D.W., Tsuang, M.T., Braff, D.L., Turetsky, B.I., 2015. Validation of mismatch negativity and P3a for use inmulti-site studies of schizophrenia: characterization of demographic, clinical, cognitive, and functional correlates in COGS-2. Schizophr. Res. 163 (1–3), 63–72.

Linscott, R.J., van Os, J., 2010. Systematic reviews of categorical versus continuum models in psychosis: evidence for discontinuous subpopulations underlying a psychometric continuum. Implications for DSM-V, DSM-VI, and DSM-VII. Annu. Rev. Clin. Psychol. 6, 391–419.

van Lutterveld, R., Oranje, B., Kemner, C., Abramovic, L., Willems, A.E., Boks, M.P., Glenthoj, B.Y., Kahn, R.S., Sommer, I.E., 2010. Increased psychophysiological parameters of attention in non-psychotic individuals with auditory verbal hallucinations. Schizophr. Res. 121 (1–3), 153–159.

Martikainen, M.H., Kaneko, K., Hari, R., 2005. Suppressed responses to self-triggered sounds in the human auditory cortex. Cereb. Cortex 15 (3), 299–302 (New York, N.Y.: 1991).

Martinelli, C., Rigoli, F., Shergill, S.S., 2016. Aberrant force processing in schizophrenia. Schizophr. Bull.

Mathiak, K., Rapp, A., Kircher, T.T., Grodd, W., Hertrich, I., Weiskopf, N., Lutzenberger, W., Ackermann, H., 2002. Mismatch responses to randomized gradient switching noise as reflected by fMRI and whole-head magnetoencephalography. Hum. Brain Mapp. 16 (3), 190–195.

May, P., Tiitinen, H., Ilmoniemi, R.J., Nyman, G., Taylor, J.G., Näätänen, R., 1999. Frequency change detection in human auditory cortex. J. Comput. Neurosci. 6 (2), 99–120.

McGorry, P., Keshavan, M., Goldstone, S., Amminger, P., Allott, K., Berk, M., Lavoie, S., Pantelis, C., Yung, A., Wood, S., Hickie, I., 2014. Biomarkers and clinical staging in psychiatry. World Psychiatry 13 (3), 211–223.
Meehl, P.E., 1962. Schizotaxia, schizotypy, schizophrenia. American Psychologist]–>Am. Psychol. 17 (12), 827.
Michie, P.T., 2001. What has MMN revealed about the auditory system in schizophrenia? J Psychophysiol]–>Int. J. Psychophysiol. 42 (2), 177–194.
Michie, P.T., Malmierca, M.S., Harms, L., Todd, J., 2016. The neurobiology of MMN and implications for schizophrenia. Biol. Psychol. 116, 90–97.
Mifsud, N.G., Oestreich, L.K., Jack, B.N., Ford, J.M., Roach, B.J., Mathalon, D.H., Whitford, T.J., 2016. Self-initiated actions result in suppressed auditory but amplified visual evoked components in healthy participants. Psychophysiology 53 (5), 723–732.
Miller, T.J., McGlashan, T.H., Rosen, J.L., Somjee, L., Markovich, P.J., Stein, K., Woods, S.W., 2002. Prospective diagnosis of the initial prodrome for schizophrenia based on the structured interview for prodromal syndromes: preliminary evidence of interrater reliability and predictive validity. J Psychiatry]–>Am. J. Psychiatry 159 (5), 863–865.
Näätänen, R., Winkler, I., 1999. The concept of auditory stimulus representation in cognitive neuroscience. Psychol. Bull. 125 (6), 826–859.
Näätänen, R., Pakarinen, S., Rinne, T., Takegata, R., 2004. The mismatch negativity (MMN): towards the optimal paradigm. Clin. Neurophysiol. 115 (1), 140–144.
Näätänen, R., Kujala, T., Kreegipuu, K., Carlson, S., Escera, C., Baldeweg, T., Ponton, C., 2011. The mismatch negativity: an index of cognitive decline in neuropsychiatric and neurological diseases and in ageing. Brain 134 (Pt 12), 3435–3453.
Näätänen, R., Shiga, T., Asano, S., Yabe, H., 2015. Mismatch negativity (MMN) deficiency: a break-through biomarker in predicting psychosis onset. J Psychophysiol]–>Int. J. Psychophysiol. 95 (3), 338–344.
Näätänen, R., Todd, J., Schall, U., 2016. Mismatch negativity (MMN) as biomarker predicting psychosis in clinically at-risk individuals. Biol. Psychol. 116, 36–40.
Nagai, T., Tada, M., Kirihara, K., Araki, T., Jinde, S., Kasai, K., 2013a. Mismatch negativity as a "translatable" brain marker toward early intervention for psychosis: a review. Front. Psychol. 4, 115.
Nagai, T., Tada, M., Kirihara, K., Yahata, N., Hashimoto, R., Araki, T., Kasai, K., 2013b. Auditory mismatch negativity and P3a in response to duration and frequency changes in the early stages of psychosis. Schizophr. Res. 150 (2–3), 547–554.
Niznikiewicz, M.A., Spencer, K.M., Dickey, C., Voglmaier, M., Seidman, L.J., Shenton, M.E., McCarley, R.W., 2009. Abnormal pitch mismatch negativity in individuals with schizotypal personality disorder. Schizophr. Res. 110 (1–3), 188–193.
Oades, R.D., Dittmann-Balcar, A., 1995. Mismatch negativity (MMN) is altered by directing attention. Neuroreport 6 (8), 1187–1190.
O'Donnell, B.F., Salisbury, D.F., Niznikiewicz, M.A., Brenner, C.A., Vohs, J.L., 2017. Abnormalities of event-related potential components in schizophrenia. In: Kappenman, E.S., Luck, S.J. (Eds.), The Oxford Handbook of Event-Related Potential Components.
Oestreich, L.K., Mifsud, N.G., Ford, J.M., Roach, B.J., Mathalon, D.H., Whitford, T.J., 2015. Subnormal sensory attenuation to self-generated speech in schizotypy: electrophysiological evidence for a 'continuum of psychosis'. J Psychophysiol]–>Int. J. Psychophysiol. 97 (2), 131–138.
Oestreich, L.K., Mifsud, N.G., Ford, J.M., Roach, B.J., Mathalon, D.H., Whitford, T.J., 2016. Cortical suppression to delayed self-initiated auditory stimuli in schizotypy: neurophysiological evidence for a continuum of psychosis. Clin. EEG Neurosci. 47 (1), 3–10.
Onitsuka, T., Oribe, N., Kanba, S., 2013. Neurophysiological findings in patients with bipolar disorder. Suppl. Clin. Neurophysiol. 62, 197–206.
Opitz, B., Rinne, T., Mecklinger, A., von Cramon, D.Y., Schroger, E., 2002. Differential contribution of frontal and temporal cortices to auditory change detection: fMRI and ERP results. NeuroImage 15 (1), 167–174.
van Os, J., Linscott, R.J., Myin-Germeys, I., Delespaul, P., Krabbendam, L., 2009. A systematic review and meta-analysis of the psychosis continuum: evidence for a psychosis proneness-persistence-impairment model of psychotic disorder. Psychol. Med. 39 (2), 179–195.
Palmer, C.E., Davare, M., Kilner, J.M., 2016. Physiological and perceptual sensory attenuation have different underlying neurophysiological correlates. J. Neurosci. 36 (42), 10803–10812.
Pang, X., Xu, J., Chang, Y., Tang, D., Zheng, Y., Liu, Y., Sun, Y., 2014. Mismatch negativity of sad syllables is absent in patients with major depressive disorder. PLoS One 9 (3), e91995.
Pantlin, L.N., Davalos, D., 2016. Neurophysiology for detection of high risk for psychosis. Schizophr. Res. Treat. 2016.
Perez, V.B., Ford, J.M., Roach, B.J., Loewy, R.L., Stuart, B.K., Vinogradov, S., Mathalon, D.H., 2012. Auditory cortex responsiveness during talking and listening: early illness schizophrenia and patients at clinical high-risk for psychosis. Schizophr. Bull. 38 (6), 1216–1224.
Perez, V.B., Woods, S.W., Roach, B.J., Ford, J.M., McGlashan, T.H., Srihari, V.H., Mathalon, D.H., 2014. Automatic auditory processing deficits in schizophrenia and clinical high-risk patients: forecasting psychosis risk with mismatch negativity. Biol. Psychiatry 75 (6), 459–469.
Picard, F., Friston, K., 2014. Predictions, perception, and a sense of self. Neurology 83 (12), 1112–1118.
Poulton, R., Caspi, A., Moffitt, T.E., Cannon, M., Murray, R., Harrington, H., 2000. Children's self-reported psychotic symptoms and adult schizophreniform disorder: a 15-year longitudinal study. Arch. Gen. Psychiatry 57 (11), 1053–1058.
Raine, A., 1991. The SPQ: a scale for the assessment of schizotypal personality based on DSM-III-R criteria. Schizophr. Bull. 17 (4), 555–564.
Ranlund, S., Adams, R.A., Diez, A., Constante, M., Dutt, A., Hall, M.H., Maestro Carbayo, A., McDonald, C., Petrella, S., Schulze, K., Shaikh, M., Walshe, M., Friston, K., Pinotsis, D., Bramon, E., 2016. Impaired prefrontal synaptic gain in people with psychosis and their relatives during the mismatch negativity. Hum. Brain Mapp. 37 (1), 351–365.
Rasser, P.E., Schall, U., Todd, J., Michie, P.T., Ward, P.B., Johnston, P., Helmbold, K., Case, V., Soyland, A., Tooney, P.A., Thompson, P.M., 2011. Gray matter deficits, mismatch negativity, and outcomes in schizophrenia. Schizophr. Bull. 37 (1), 131–140.
Rauss, K., Pourtois, G., 2013. What is bottom-up and what is top-down in predictive coding? Front. Psychol. 4.
Ravicz, M.E., Melcher, J.R., Kiang, N.Y.S., 2000. Acoustic noise during functional magnetic resonance imaginga. J. Acoust. Soc. Am. 108 (4), 1683–1696.
Rentzsch, J., Shen, C., Jockers-Scherubl, M.C., Gallinat, J., Neuhaus, A.H., 2015. Auditory mismatch negativity and repetition suppression deficits in schizophrenia explained by irregular computation of prediction error. PLoS One 10 (5), e0126775.
Rudolph, E.D., Ells, E.M.L., Campbell, D.J., Abriel, S.C., Tibbo, P.G., Salisbury, D.F., Fisher, D.J., 2015. Finding the missing-stimulus mismatch negativity (MMN) in early psychosis: altered MMN to violations of an auditory gestalt. Schizophr. Res. 166 (1–3), 158–163.
Salisbury, D.F., 2012. Finding the missing stimulus mismatch negativity (MMN): emitted MMN to violations of an auditory gestalt. Psychophysiology 49 (4), 544–548.
Salisbury, D.F., McCathern, A.G., 2016. Abnormal complex auditory pattern analysis in schizophrenia reflected in an absent missing stimulus mismatch negativity. Brain Topogr. 29 (6), 867–874.
Salisbury, D.F., Polizzotto, N.R., Nestor, P.G., Haigh, S.M., Koehler, J., McCarley, R.W., 2016. Pitch and duration mismatch negativity and premorbid intellect in the first hospitalized schizophrenia spectrum. Schizophr. Bull.
Sams, M., Paavilainen, P., Alho, K., Näätänen, R., 1985. Auditory frequency discrimination and event-related potentials. Electroencephalogr. Clin. Neurophysiol. 62 (6), 437–448.
Schall, U., 2016. Is it time to move mismatch negativity into the clinic? Biol. Psychol. 116, 41–46.
Schall, U., Johnston, P., Todd, J., Ward, P.B., Michie, P.T., 2003. Functional neuroanatomy of auditory mismatch processing: an event-related fMRI study of duration-deviant oddballs. NeuroImage 20 (2), 729–736.
Shaikh, M., Valmaggia, L., Broome, M.R., Dutt, A., Lappin, J., Day, F., Woolley, J., Tabraham, P., Walshe, M., Johns, L., Fusar-Poli, P., Howes, O., Murray, R.M., McGuire, P., Bramon, E., 2012. Reduced mismatch negativity predates the onset of psychosis. Schizophr. Res. 134 (1), 42–48.
Shelley, A.M., Ward, P.B., Catts, S.V., Michie, P.T., Andrews, S., McConaghy, N., 1991. Mismatch negativity: an index of a preattentive processing deficit in schizophrenia. Biol. Psychiatry 30 (10), 1059–1062.
Shergill, S.S., Samson, G., Bays, P.M., Frith, C.D., Wolpert, D.M., 2005. Evidence for sensory prediction deficits in schizophrenia. J Psychiatry]–>Am. J. Psychiatry 162 (12), 2384–2386.
Shin, K.S., Kim, J.S., Kim, S.N., Koh, Y., Jang, J.H., An, S.K., O'Donnell, B.F., Chung, C.K., Kwon, J.S., 2012. Aberrant auditory processing in schizophrenia and in subjects at ultra-high-risk for psychosis. Schizophr. Bull. 38 (6), 1258–1267.
Solis-Vivanco, R., Mondragon-Maya, A., Leon-Ortiz, P., Rodriguez-Agudelo, Y., Cadenhead, K.S., de la Fuente-Sandoval, C., 2014. Mismatch negativity reduction in the left cortical regions in first-episode psychosis and in individuals at ultra high-risk for psychosis. Schizophr. Res. 158 (1–3), 58–63.
Sperry, R.W., 1950. Neural basis of the spontaneous optokinetic response produced by visual inversion. J. Comp. Physiol. Psychol. 43 (6), 482–489.
Stefanics, G., Kimura, M., Czigler, I., 2011. Visual mismatch negativity reveals automatic detection of sequential regularity violation. Front. Hum. Neurosci. 5, 46.
Stefanics, G., Astikainen, P., Czigler, I., 2014a. Visual mismatch negativity (vMMN): a prediction error signal in the visual modality. Front. Hum. Neurosci. 8, 1074.
Stefanics, G., Kremlacek, J., Czigler, I., 2014b. Visual mismatch negativity: a predictive coding view. Front. Hum. Neurosci. 8, 666.
Suga, M., Nishimura, Y., Kawakubo, Y., Yumoto, M., Kasai, K., 2016. Magnetoencephalographic recording of auditory mismatch negativity in response to duration and frequency deviants in a single session in patients with schizophrenia. Psychiatry Clin. Neurosci. 70 (7), 295–302.
Sur, S., Sinha, V.K., 2009. Event-related potential: an overview. Ind. Psychiat. J 70–73.
Taylor, J.A., Matthews, N., Michie, P.T., Rosa, M.J., Garrido, M.I., 2017. Auditory prediction errors as individual biomarkers of schizophrenia (under review).
Thönnessen, H., Zvyagintsev, M., Harke, K.C., Boers, F., Dammers, J., Norra, C., Mathiak, K., 2008. Optimized mismatch negativity paradigm reflects deficits in schizophrenia patients. A combined EEG and MEG study. Biol. Psychol. 77 (2), 205–216.
Timm, J., SanMiguel, I., Saupe, K., Schroger, E., 2013. The N1-suppression effect for self-initiated sounds is independent of attention. BMC Neurosci. 14, 2.
Todd, J., Michie, P.T., Schall, U., Karayanidis, F., Yabe, H., Näätänen, R., 2008. Deviant matters: duration, frequency, and intensity deviants reveal different patterns of mismatch negativity reduction in early and late schizophrenia. Biol. Psychiatry 63 (1), 58–64.
Todd, J., Harms, L., Schall, U., Michie, P.T., 2013. Mismatch negativity: translating the potential. Front. Psychiat. 4, 171.
Todd, J., Whitson, L., Smith, E., Michie, P.T., Schall, U., Ward, P.B., 2014. What's intact and what's not within the mismatch negativity system in schizophrenia. Psychophysiology 51 (4), 337–347.
Umbricht, D., Krljes, S., 2005. Mismatch negativity in schizophrenia: a meta-analysis. Schizophr. Res. 76 (1), 1–23.
Umbricht, D.S., Bates, J.A., Lieberman, J.A., Kane, J.M., Javitt, D.C., 2006. Electrophysiological indices of automatic and controlled auditory information processing in first-episode, recent-onset and chronic schizophrenia. Biol. Psychiatry 59 (8), 762–772.
Upthegrove, R., Broome, M.R., Caldwell, K., Ives, J., Oyebode, F., Wood, S.J., 2016. Understanding auditory verbal hallucinations: a systematic review of current evidence. Acta Psychiatr. Scand. 133 (5), 352–367.
Whitford, T.J., Mathalon, D.H., Shenton, M.E., Roach, B.J., Bammer, R., Adcock, R.A., Bouix, S., Kubicki, M., De Siebenthal, J., Rausch, A.C., Schneiderman, J.S., Ford, J.M., 2011. Electrophysiological and diffusion tensor imaging evidence of delayed corollary discharges in patients with schizophrenia. Psychol. Med. 41 (5), 959–969.
Wible, C.G., Kubicki, M., Yoo, S.S., Kacher, D.F., Salisbury, D.F., Anderson, M.C., Shenton, M.E., Hirayasu, Y., Kikinis, R., Jolesz, F.A., McCarley, R.W., 2001. A functional magnetic resonance imaging study of auditory mismatch in schizophrenia. J Psychiatry]–>Am. J. Psychiatry 158 (6), 938–943.
Wilson, J.E., Nian, H., Heckers, S., 2014. The schizoaffective disorder diagnosis: a conundrum in the clinical setting. Eur. Arch. Psychiatry Clin. Neurosci. 264 (1), 29–34.
Woldorff, M.G., Hackley, S.A., Hillyard, S.A., 1991. The effects of channel-selective attention on the mismatch negativity wave elicited by deviant tones. Psychophysiology 28 (1), 30–42.
Wolpert, D.M., Ghahramani, Z., Jordan, M.I., 1995. An internal model for sensorimotor integration. Science 269 (5232), 1880–1882.

World Health Organization, 1993. ICD-10, the Classification of Mental and Behavioural Disorders: Diagnostic Criteria for Research. World Health Organization, Geneva.

Wynn, J.K., Sugar, C., Horan, W.P., Kern, R., Green, M.F., 2010. Mismatch negativity, social cognition, and functioning in schizophrenia patients. Biol. Psychiatry 67 (10), 940–947.

Yung, A.R., Yuen, H.P., McGorry, P.D., Phillips, L.J., Kelly, D., Dell'Olio, M., Francey, S.M., Cosgrave, E.M., Killackey, E., Stanford, C., Godfrey, K., Buckby, J., 2005. Mapping the onset of psychosis: the comprehensive assessment of at-risk mental states. Aust. N. Z. J. Psychiatry 39 (11 – 12), 964–971.

Zhou, Z.H., Zhu, H.M., Chen, L., 2013. Effect of aripiprazole on mismatch negativity (MMN) in schizophrenia. PLoS One 8 (1).