Mismatch Negativity (MMN) as an Index of Cognitive Dysfunction

Risto Näätänen · Elyse S. Sussman ·
Dean Salisbury · Valerie L. Shafer

Received: 24 July 2013 / Accepted: 29 April 2014
© Springer Science+Business Media New York 2014

Abstract Cognition is often affected in a variety of neuropsychiatric, neurological, and neurodevelopmental disorders. The neural discriminative response, reflected in mismatch negativity (MMN) and its magnetoencephalographic equivalent (MMNm), has been used as a tool to study a variety of disorders involving auditory cognition. MMN/MMNm is an involuntary brain response to auditory change or, more generally, to pattern regularity violation. For a number of disorders, MMN/MMNm amplitude to sound deviance has been shown to be attenuated or the peak-latency of the component

prolonged compared to controls. This general finding suggests that while not serving as a specific marker to any particular disorder, MMN may be useful for understanding factors of cognition in various disorders, and has potential to serve as an indicator of risk. This review presents a brief history of the MMN, followed by a description of how MMN has been used to index auditory processing capability in a range of neuropsychiatric, neurological, and neurodevelopmental disorders. Finally, we suggest future directions for research to further enhance our understanding of the neural substrate of deviance detection that could lead to improvements in the use of MMN as a clinical tool.

This is one of several papers published together in Brain Topography in the “Special Issue: Mismatch Negativity”.

R. Näätänen
Department of Psychology, University of Tartu, Tartu, Estonia

R. Näätänen
Center of Functionally Integrative Neuroscience (CFIN),
University of Aarhus, Aarhus, Denmark

R. Näätänen
Cognitive Brain Research Unit (CBRU), Institute of Behavioural
Sciences, University of Helsinki, Helsinki, Finland

E. S. Sussman (✉)
Departments of Neuroscience and Otorhinolaryngology, Albert
Einstein College of Medicine, 1300 Morris Park Avenue, Bronx,
NY 10461, USA
e-mail: elyse.sussman@einstein.yu.edu

D. Salisbury
Western Psychiatric Institute and Clinic, University of Pittsburgh
School of Medicine, Pittsburgh, PA, USA

V. L. Shafer
Ph.D. Program in Speech-Language-Hearing Sciences, The
Graduate Center of the City University of New York, New York,
NY, USA

Keywords Mismatch negativity (MMN) · Clinical
application · Neurodevelopmental · Neuropsychiatric ·
Neurological

Introduction

The mismatch negativity (MMN) component of event-related brain potentials (ERPs) has become a very popular tool to study auditory functions. The MMN measure enables one to gain insights into the neurobiological substrate of central auditory processing, particularly into auditory memory, as well as into various attention-related processes controlling the access of auditory input to conscious perception and higher forms of memory (Näätänen et al. 2011a, 2012; Sussman 2007; Sussman et al. 2013). MMN paradigms are being used to address a growing range of clinical questions, which is increasing our understanding of disease mechanisms of major neuropsychiatric, neurological, and neurodevelopmental disorders. The focus of this review is on providing an understanding of how MMN

amplitude and latency may be used in clinical applications to index cognitive dysfunction. We first provide a brief history of the MMN, followed by a review of studies that have used MMN to examine auditory processing in a range of neuropsychiatric, neurological, and neurodevelopmental disorders. The final section suggests directions that MMN research can take to address clinical questions related to adult and childhood disorders involving auditory cognition.

What is the MMN?

The auditory MMN is a memory-based change-detection brain response to any discriminable change in a stream of auditory stimulation, including abstract-type changes (automatically detected by the brain), such as detection of a violation of a multi-stimulus pattern regularity (Sussman et al. 1998, 1999; Tervaniemi et al. 1994; Schröger et al. 1994) or a rule (e.g., Saarinen et al. 1992; Paavilainen et al. 2007; Paavilainen 2013) derived from the recent auditory stimulation. The capability of MMN to index violations of abstractions from sequential patterns (e.g., rising vs. falling pitch or trajectory) indicates a link between automatic processes and higher-level cognitive functions at the level of auditory cortex. This gives rise to the concept of a primitive sensory intelligence, with substantial complex auditory analysis occurring outside the focus of perception (for reviews, see Näätänen et al. 2001, 2007, 2010; Näätänen 2001). Studies have shown that MMN is a vital tool that can be used for understanding more complex calculations of the auditory input. These investigations currently form an intense research focus in the field (Bakker et al. 2013; Bendixen et al. 2008, 2012, 2014; Besle et al. 2013; Bonte et al. 2005; Caclin et al. 2006; Chen and Sussman 2013; Colin et al. 2002; Cornella et al. 2012; Dyson et al. 2005; Grimm and Escera 2012; Herholz et al. 2009; Jacobsen et al. 2013; Koelsch 2009; Liu and Holt 2011; MacDonald and Campbell 2011; Müller et al. 2005; Nager et al. 2003; Paavilainen et al. 2007; Peter et al. 2012; Pulvermüller et al. 2008; Rahne and Sussman 2009; Salisbury 2012; Schechtman et al. 2012; Sculthorpe et al. 2009; Shtyrov et al. 2003; Sonnadara et al. 2006; Steinberg et al. 2010; Sussman et al. 1998, 1999, 2007; Sussman 2005; Todd and Robinson 2010; van Zuijen et al. 2005; Wacongne et al. 2012; Weise et al. 2012; Zion-Golumbic et al. 2007). Due to its ability to automatically index violations within complex auditory scenes, the MMN is now more often characterized in terms of a regularity-violation response rather than just as a sound-change response (Näätänen et al. 2001; Sussman 2007; Winkler 2007; Sussman et al. 2013).

To understand the place of the MMN in a wider context of the functioning of the organism, it is important to consider what the auditory sensory system must accomplish to

provide useful neural representations of the sound sources in the environment. First, the system must generate representations of the stimulus input, providing memory traces that represent the original sources, and the regularities derived from them. Secondly, the system must continuously up-date the representations to maintain the integrity of the ongoing sources (Rahne et al. 2007; Sussman and Steinschneider 2006; Sussman and Winkler 2001; Winkler et al. 1996). There has been a recent postulation that the processes indexed by MMN involve anticipation of the forthcoming representations of the immediate future (Näätänen et al. 2010; Bendixen et al. 2014; Lieder et al. 2013; Pieszek et al. 2013; Rohrmeier and Koelsch 2012; Winkler and Czigler 2012; Todd and Mullens 2011; Chennu et al. 2013; Garrido et al. 2008). Näätänen and colleagues have postulated that this sensory updating has a high-priority access to frontal mechanisms of attentional control, explaining the rapid involuntary attention-switch to stimulus change (for a review, see Näätänen et al. 2011a, b; Opitz et al. 2002; Rinne et al. 2006).

One might wonder why the MMN was reported as early as the end of the 1970s while cognitive neuroscience research using the MMN (and MMNm) measure has only recently intensified, as evidenced by more than 3,000 refereed English-language scientific articles using, or referring to, MMN. Furthermore, six major international congresses have already been dedicated to the MMN and its different applications, with the sixth, held in New York in May 2012 and culminating in the present Special Issue. This delay may be due to the strong cognitive *Zeitgeist* that prevailed in the field of cognitive neuroscience in the 1960s and 1970s, and may have had a biasing effect on cognitive brain research. Viewed against this background, an involuntary discrimination process between two very similar stimuli occurring in the absence of attention, and hence outside the conscious mind was received with skepticism. It was rather thought that such fine-grained discrimination processes could occur only when supported by attention and voluntary effort (Woldorff et al. 1991).

A second reason for the relatively late emergence of research using MMN is that in active oddball paradigms, there can be overlap with other ERP components, most notably the N1 component (May and Tiitinen 2010), and the N2 target detection component (Näätänen et al. 1978; Näätänen 1975). Methods developed to isolate the MMN from these two components included subtracting the standard ERP from the deviant ERP waveforms (Ford et al. 1976; Simson et al. 1976, 1977; Squires et al. 1975, 1976) and examining the topographical distribution (Alho 1995). The “N2” was divided into an earlier “automatic” MMN component (originally called the “N2a”) and a later attention-dependent “N2b” component (Näätänen et al. 1978, 1982; Näätänen and Michie

Fig. 1 Mismatch negativity (MMN) evoked during active detection of a deviant stimulus is elicited along with attention-related ERP components (N2b and P3b). Grand mean difference waveform (obtained by subtracting the ERP elicited by the deviant stimulus from the ERP elicited by the standard stimulus) is displayed. The MMN peak latency is denoted at the mastoid (*green trace*) because of overlap with N2b. The MMN is more frontally distributed and the peak of the MMN component is not well delineated at Fz (*black trace*) due to overlap with the N2b. The N2b component is seen clearest at the Cz electrode (*blue trace*). The P3b (*red trace*) is largest at the *midline* parietal electrode (Pz) (Color figure online)

1979). The N2b response has been noted to have a more central scalp distribution than the MMN (Alho 1995), and MMN shows a clear polarity inversion for simple tone feature deviants at sites inferior to auditory cortices when a nose reference is used. Figure 1 displays a schematic illustration of the different ERP components evoked in the auditory oddball paradigm during active detection of the oddball stimulus.

A third reason why research using the MMN measure has become more popular for cognitive neuroscience research is that it has become clear that MMN can be used to study listeners' processing of complex auditory scenes (e.g., Sussman et al. 1998, 1999, 2005, 2007; Colin et al. 2002; Sussman 2005), speech discrimination as it pertains to categorical perception (e.g., Aaltonen et al. 1997; Sharma et al. 1993; Maiste et al. 1995; Sandridge and Boothroyd 1996; Sharma and Dorman 1998; Bradlow et al. 1999) and to native-language experience (e.g., Näätänen et al. 1997; Winkler et al. 1999; Phillips et al. 1995; Dehaene-Lambertz 1997; Dehaene-Lambertz et al. 2000; Shafer et al. 2004). These advances in research demonstrated the utility of the MMN measure for use in a wide range of scientific and clinical applications. The clinical application of MMN flourished in particular because relative complex brain functions could be examined in the absence of complicated active behavior on the part of the participant. Because MMN can be elicited passively, it can be recorded from behaviorally and cognitively impaired subjects, providing an accurate functional measure of local and distributed cortical processing.

Several early studies showed that one could predict behavioral discrimination accuracy by the sensitivity of the MMN response to small stimulus changes. This was first shown by Lang et al. (1990), who found that the accuracy of the behavioral discrimination of a frequency difference between a pair of short tone pips presented in close succession strongly correlated with the MMN amplitude for frequency change recorded in a separate, passive session (Lang et al. 1990). Moreover, a large number of subsequent studies showed that with the MMN, one could monitor the improvement in sound discrimination as a function of practice, both for linguistic stimuli (Cheour et al. 2002; Kraus et al. 1995; Tremblay et al. 1997; Winkler et al. 1999) and non-linguistic stimuli (Näätänen et al. 1993; Tervaniemi et al. 2001). In addition, several studies showed that "musical" subjects tended to be more sensitive to changes along different musically-important dimensions, which were also indexed by MMN (Brattico et al. 2001, 2006, 2009; Garza Villarreal et al. 2011; Koelsch et al. 1999; Seppänen et al. 2007; Tervaniemi et al. 2006; van Zuijen et al. 2004, 2005). These various studies suggest that the MMN provides a level of assessment of auditory discrimination ability, as well as an index of improvement in discrimination ability with training or exposure to certain stimulation. Previously, in the absence of attention or a behavioral task, ERPs and other physiological responses appeared to provide only an objective index of whether the central auditory system of a person detected the presence of acoustic stimulus energy, but not whether sounds could also be discriminated (for objective ERP audiometry, see Rapin et al. 1966). Hence, a patient could have a "normal" ERP response to auditory input but nevertheless could have impaired speech-sound perception in the mother-tongue (Ilvonen et al. 2004). Consequently, finding a significant relationship between MMN and an individual's ability to perceptually discriminate a sound contrast without attending to the sounds or performing a task with them was notable. These studies demonstrating modulation of MMN amplitude and latency with learning provide an important link between perceptual processes and the sound detection mechanism indexed by MMN. This has been profitably utilized in the assessment of training programs, as described below for example, in individuals with specific language impairment (SLI).

It is important to recognize that behavioral perception and MMN measures of discrimination are complementary, rather than redundant. Clearly there is a relationship between neural discrimination as indexed by the MMN and sound perception indexed by behavioral measures. However, there has been some discrepancy among studies, in that the relationship between behavior and the MMN measure is not always significantly correlated for tone features (e.g., cf. Chen and Sussman 2013; Horváth et al.

2008) and for speech sounds. In studies of speech processing, this is particularly enigmatic, with numerous studies providing evidence of behavioral discrimination for difficult speech contrasts (e.g., Hindi dental and retroflexed consonants) with no MMN elicitation to those contrasts, even for speakers for whom the contrast is native (e.g., Shafer et al. 2004). The disparate findings of these studies suggest that MMN may be indexing the earlier acoustic-phonetic components of the speech and not the effects of categorical perception (Dalebout and Stack 1999; Sussman et al. 2004; Sussman 2005). Overall, these findings do not detract from the utility of the MMN measure for studying cognitive aspects of auditory processing, but rather highlight the importance of understanding the benefits and limitations of MMN, which will allow for maximizing its utility in basic and clinical applications (see Sussman et al. 2013).

Neuropsychiatric and Neurological Disorders

There is considerable evidence for MMN differences in various neuropsychiatric and neurological disorders. We will briefly review these studies and consider potential mechanisms for the deficits in auditory processing revealed by MMN/MMNm.

Schizophrenia

Studies of schizophrenia have consistently reported attenuated MMN amplitudes to auditory contrasts compared to normal controls (Ford and Mathalon 2012; Shelley et al. 1991; Javitt 2010; Baldeweg et al. 2004; Baker et al. 2005; Umbricht and Krljes 2005; Kayser et al. 2014; Rissling et al. 2013; Salisbury et al. 2002, 2007). The ‘deficits’ in MMN have been associated with deficits in auditory discrimination at the behavioral level (Javitt et al. 1995), and with poor social/occupational and executive functioning (Kawakubo et al. 2007; Oades et al. 2006; for a recent review, see Kaur et al. 2011). Moreover, Light and Braff (2005a) found a strong association between the MMN measure of auditory discrimination and ratings on the global assessment of functioning (a rating of social, psychological, and occupational life functions), but no correlation with positive and negative symptoms. Some studies have suggested that the greater the MMN deficit, the weaker the cognitive or functional status of the patients (also Light and Braff 2005b; Baldeweg et al. 2004; Kawakubo et al. 2007; Kiang et al. 2007; Hermens et al. 2010; Kaur et al. 2013).

The first studies reporting an auditory deficit in patients with schizophrenia, at the level indexed by MMN, were those of Shelley et al. (1991) who found a deficit for tone-duration increment discrimination, and Javitt et al. (1993)

who observed a frequency-discrimination deficit in schizophrenia. Since these pioneering findings, the volume of research that has used the MMN/MMNm measure to elucidate auditory processing in schizophrenia has grown tremendously. For example, Thompson Reuters Science Citation Index currently includes more than 200 “Mismatch Negativity and Schizophrenia” Medline-referenced articles.

Although MMN is greatly reduced in schizophrenia within the first few years after first hospitalization for psychosis, it is not entirely clear whether MMN is reduced at or before first psychosis (Salisbury et al. 2002). Salisbury et al. reported that MMN to frequency deviants was not impaired at the first hospitalization for schizophrenia (also Magno et al. 2008; Devrim-Üçok et al. 2008). Similarly, Umbricht et al. (2006) demonstrated, on average, a relatively normal MMN in first-hospitalized patients to duration deviants compared to healthy controls. However, those first-episode schizophrenia patients with poor social functioning and low educational attainment had reduced MMNs compared to controls (Umbricht et al. 2006). In contrast, several papers have reported reduced MMN at first episode of psychosis in either mixed psychosis (schizophrenia and bipolar disorder, BD) or schizophrenia (Hermens et al. 2010; Kaur et al. 2011; Atkinson et al. 2012; Nagai et al. 2013). However, results from Umbricht et al. (2006) indicate that a difference in findings for first episode patients across studies may be, at least in part, due to whether or not patients were assessed according to premorbid IQs in psychosis groups. In studies in which experimental groups were matched for intellectual functioning, and followed longitudinally, MMN was not reduced at first episode, but became so during the early course of the disease (Kaur et al. 2013). There have also been differential findings for frequency and duration MMN at first episode, with some findings suggesting that duration MMN may reflect greater sensitivity to a first psychotic break than frequency MMN (Nagai et al. 2013). Kaur et al. also demonstrated that the greatest MMN deficits at follow-up testing were associated with the greatest impairments at first testing.

Although the findings of MMN reductions at first episode for psychosis are, at best, equivocal, several groups have examined whether reductions of MMN amplitude could serve as a biomarker for incipient psychosis in the schizophrenia prodrome, before florid psychosis has emerged. Brockhaus-Dumke et al. (2005) failed to detect any group mean MMN differences to frequency or duration deviants in prodromal subjects, but did not assess whether there was a subset of prodromal subjects with abnormal MMNs that later converted to schizophrenia. Bodatsch et al. (2011) found that those subjects who converted to psychosis during a follow-up period of 2 years had considerably smaller MMN amplitudes to tone-duration

increments at baseline, and this reduced MMN amplitude was comparable to that in first-episode patients. In contrast, subjects who did not convert to psychosis had MMN amplitudes comparable to that of healthy, age-matched controls. These results were subsequently corroborated (Atkinson et al. 2012; Higuchi et al. 2013; Kayser et al. 2014; Shaikh et al. 2012). Still, several reports have found no difference in frequency or duration MMN amplitudes between at-risk prodromal subjects and controls (Nagai et al. 2013 for review). Thus, although those who convert to psychosis may show reduced MMN amplitudes compared to those who do not convert, the effect size may be relatively small.

Recently, Perez et al. (2014b) compared amplitudes evoked by single and double deviant duration and frequency MMNs in high-risk individuals compared to early illness schizophrenia patients. They reported reduced MMN in those individuals who converted to psychosis compared to those that didn't convert, and additionally showed that the MMN amplitude evoked by double deviants amplitude (but not single duration or frequency MMNs) predicted the time lag to onset of psychosis in high-risk individuals (for reviews, Belger et al. 2012; Light and Näätänen 2013; Nagai et al. 2013; Perez et al. 2014a). These exciting findings indicate the potential for MMN to serve as an indicator of individuals at risk who are most likely to convert to psychosis. Recent research has also shown that adolescents recruited from the general population who show some psychotic symptoms tend to show attenuated MMN amplitudes to tone duration increments (Murphy et al. 2013), which suggests that the combination of some psychotic symptoms (but not sufficient for a clinical diagnosis) and a reduction in duration-MMN amplitude could serve as an indicator of risk-of-illness long before illness onset. Early interventions in individuals who are likely to experience psychosis in the near (or far) future may prevent, or at least delay the transition to psychosis. Thus the finding of improved prediction of psychosis by the inclusion of auditory function assessment via MMN is promising (Kaur et al. 2013; Umbricht et al. 2002).

Although the neural pathophysiology giving rise to schizophrenia remains unclear, recent theories suggest an imbalance in Glu and GABA. For example, lamotrigine (an anti-convulsant) reduces Glu and blocks ketamine-induced psychosis. One leading candidate mechanism for this imbalance in schizophrenia is dysfunction in synaptic plasticity via the *N*-methyl-D-aspartate (NMDA) receptor (Javitt et al. 2012; Javitt 2000, 2010, 2012; Krystal et al. 2003). The NMDA receptor and its glycine binding site play a crucial role in long term potentiation, long term depression, and synaptic plasticity. Importantly, it has been found that MMN elicitation is sensitive to activity at the NMDA receptor. In monkeys, administration of NMDA

antagonists led to a reduction in the MMN response, but no change to the initial sensory evoked responses (e.g., the N1 component, Javitt et al. 1996; Javitt 2000). In humans, administration of psychotomimetic drugs that act on the NMDA receptor led to a reduction of the MMN (Umbricht et al. 2000). Thus, MMN may serve as an index of function within a neural circuit that depends on a particular type of interneuronal communication and processing thought to be abnormal in schizophrenia, namely NMDA-mediated dendritic plasticity.

Thus, MMN may be a particularly good index of the underlying cortical pathophysiology in schizophrenia, and may be useful as an indicator for new pharmacological therapy (Lavoie et al. 2008). For example, *N*-acetyl-cysteine (NAC), is a glutathione precursor that not only acts as an antioxidant to counter the NMDA-mediated superoxide oxidative stress reaction, but is the essential building block of both Glu and GABA, and thus can potentiate the activity of the NMDA receptors. In a 6-week administration of NAC, patients showed increased MMN amplitude to a tone-frequency change (Lavoie et al. 2008). This suggests that a factor contributing to the attenuated MMN response in schizophrenic patients may be an NMDA deficit. However, the relationship could also be an indirect one, mediated by some other deficit in auditory function.

Bipolar Disorder (BD)

MMN results in patients with BD have been equivocal (Domján et al. 2012; Umbricht et al. 2003; Salisbury et al. 2007). However, compared to schizophrenia, MMN studies on BD are scarce in number (Andersson et al. 2008; Catts et al. 1995; Domján et al. 2012; Hall et al. 2009; Salisbury et al. 2007; Takei et al. 2010; Umbricht et al. 2003). MMNm peak latencies have been reportedly prolonged for tone-duration increments (Takei et al. 2010), tone duration decrements (Andersson et al. 2008), and for frequency changes (Takei et al. 2010) in these patients, as well as smaller in amplitude MMN compared to control subjects (Andersson et al. 2008). In contrast, shorter peak latency in individuals diagnosed with BD and longer peak latency only in individuals diagnosed with schizophrenia have also been reported (Domján et al. 2012). MMN findings in patients for first episode BD have been equivocal, as with first-episode schizophrenia. A few studies have shown reduced MMN in first episode bipolar psychosis (Hermens et al. 2010; Kaur et al. 2011, 2013), whereas others have found no reduction in MMN amplitude at first episode bipolar psychosis (Umbricht et al. 2006; Salisbury et al. 2007). Some discrepancy between findings for frequency and duration MMN has also been reported. Domján et al. (2012) found, a prolonged MMN peak latency to tone-frequency changes in bipolar patients with a history of

psychosis compared to controls, but with no significant group effect for MMN peak latency of tone-duration increments. Reite et al. (2009) observed structural and functional auditory-cortex abnormalities in patients with BD, which was suggested as possibly associated with the cognitive impairments found in these patients (Bruder et al. 1994). In summary, overall, these findings are somewhat inconclusive regarding whether patients with BDs exhibit deficits in auditory discrimination at the level measured by MMN.

Stroke and Aphasia

Lesions to cortical regions involving speech and language skills often result in significant deficits in communication ability, as well as deficits in related functions such as verbal working memory (Martin et al. 2012). Investigations of auditory discrimination using the MMN in patients with acquired aphasia due to cerebral infarct have generally found reduced amplitude or absent MMNs to speech stimuli (Aaltonen et al. 1993; Csépe et al. 2001). In addition, studies have shown that MMN amplitude significantly correlated with changes in cognitive ability post-stroke (Becker and Reinvang 2007; Ilvonen et al. 2003; Särkämö et al. 2010). For example, Ilvonen et al. (2003) found that patients had attenuated MMN amplitudes for tone duration and tone frequency changes to harmonically-rich tones presented to the right ear at 4 and 10 days following onset of left-hemisphere stroke. Recovery was indicated by an increase in MMN amplitudes to the approximate size of unimpaired age-matched controls 3 months following. Speech comprehension test scores also improved during this period. Moreover, these results demonstrated a close relationship between the increase in the duration-MMN amplitude and improvement on the speech-comprehension test from the Boston Diagnostic Aphasia Examination. Another study demonstrating recovery of functions in the 6 months following stroke onset found an increase in MMN amplitude that correlated with behavioral improvements on tasks of verbal memory (Särkämö et al. 2010). Although the precise mechanism of recovery is not known, some recent literature has suggested that listening to music or enriched auditory environments may facilitate recovery of auditory functions (Särkämö et al. 2008, 2010).

MMN has also indexed speech discrimination ability in patients with temporal lobe lesions. Auther et al. (2000) found that the presence of an MMN to speech-sound changes was an indicator of better speech comprehension compared to patients with an absent MMN to the same speech sounds. Pettigrew et al. (2005) also reported a strong correlation between auditory comprehension in patients with aphasia and MMN amplitudes to complex-tone duration decrement and to syllable changes. Wertz

et al. (1998) observed that a clear MMN to a speech-sound change was present in only 54 % of aphasic subjects. They also observed that for patients showing an MMN, its duration was related to severity (as measured by The Western Aphasia Battery, The Porch Index of Communicative Ability, and The Token Test), with shorter duration MMNs being found for more severe cases of aphasia.

These findings indicate potential clinical utility of the MMN as an objective tool for monitoring post stroke recovery and treatment efficacy. This is particularly important in patients with poor cognitive function, in particular poor communicative function, because it can be difficult to obtain reliable behavioral measures that indicate the source of breakdown in function or that can be used to monitor recovery, particularly in more severe cases. More specifically, poor language comprehension and production can interfere with obtaining an accurate measure of auditory discrimination and perception. In addition, MMN can provide a means for understanding the relationship between auditory processing deficits and sensory and cognitive deficits in cases of disorders caused by stroke.

Epilepsy

The few studies of auditory discrimination indexed by MMN in persons with epilepsy have indicated poorer function compared to age-matched controls (Miyajima et al. 2011; Korostenskaja et al. 2010; Liasis et al. 2000). Korostenskaja et al. (2010) employed the five-features MMN paradigm (Näätänen et al. 2004) to 13-year-old patients with epilepsy and found that the MMNm amplitude was attenuated for all five of the auditory deviant feature types. However, there has been some discrepancy as to the nature of the poorer auditory function, in particular regarding whether deficits are specific to speech input (Boatman et al. 2008; Rosburg et al. 2005). MMN has also been used to assess specific post-treatment recovery of function (Borghetti et al. 2007), as well as to assess the nature of the deficits (Korostenskaja et al. 2010). Consistent with this, Lin et al. (2007) reported that MMNm was temporally overlapped by a phase-locking response of alpha and theta rhythms, which was especially pronounced in the five patients who subsequently became seizure-free after the successful surgical removal of right temporal epileptic focus.

These findings indicate that the MMN measure can provide information regarding auditory function in patients with epilepsy and can possibly serve as a measure of the status of auditory cognitive function at different phases of recovery and treatment. Additional studies are needed to fully understand how discrimination indexed by MMN in these patients relates to important cognitive functions, such as speech and language and verbal working memory.

Fig. 2 Grand mean event-related potentials (ERPs) evoked by a standard vowel sound (*solid thin line*) and deviant vowel sound (*dashed line*) in a group of infants ages 3–47 months of age (adapted from Shafer et al. 2011). The difference waveform (deviant-minus-standard, *thick solid line*) delineates the mismatch response (MMR) which has a positive polarity (labeled pMMR) in this age group. The P1 component of the ERPs is also labeled. The displayed waveforms are recorded from a Geodesic net site (Geodesic 3), which is approximately 1 cm in front of and to the right of Fz

Other Neurological Disorders

The MMN has been used as a measure of auditory function in several studies of other neurological disorders. Smaller amplitude MMNs have been observed in patients with multiple sclerosis (Jung et al. 2006; Santos et al. 2006) Parkinson's disease (Pekkonen et al. 1995; Brønnick et al. 2010), and in elderly participants with dementia compared to healthy normal elderly controls (Schroeder et al. 1995; Mowszowski et al. 2012). Somewhat smaller MMNs have been found in normal, healthy, elderly participants compared to younger controls (Kisley et al. 2005; Foster et al. 2013) but not to the extent found for clinical disorders such as those individuals with dementia. Conversely, there is indication that in patients with Alzheimer's disease, intact auditory processing is indexed by MMN relative to attention-dependent processing (Gaeta et al. 1999; Vecchio and Määttä 2011).

Neurodevelopmental Disorders

The MMN measure has been increasingly used to explore the relationship between auditory processing and developmental disorders that show language-learning delays or deficits (e.g., Kemner et al. 1995; Ferri et al. 2003; Lalo et al. 2005; Jing et al. 2006; Dunn et al. 2008; Datta et al. 2010; Gomot et al. 2011). In addition, a number of recent studies have examined whether the MMN and the mismatch response (MMR) can serve as markers for risk of disorders (Kuhl et al. 2008; Leppänen et al. 1999, 2002; van Leeuwen et al. 2006; van Zuijlen et al. 2013). In infants,

the electrophysiological response to deviant stimuli has often been called the MMR (Fig. 2).

SLI and Developmental Dyslexia (Dyslexia)

SLI and dyslexia are two developmental disorders that have been closely linked to poor auditory processing (Tallal et al. 1993; Bishop 2006, 2007; Nitttrouer 2012). These studies have generally revealed poor MMN amplitudes to speech contrasts (Ahmmed et al. 2008; Baker et al. 2005; Bradlow et al. 1999; Datta et al. 2010; Davids et al. 2011; Koelsch et al. 2012; Holopainen et al. 1997; Korpilahti and Lang 1994; Noordenbos et al. 2012; Rinker et al. 2007; Shafer et al. 2005; Stoodley et al. 2006; Uwer et al. 2002). Reduced amplitude MMN is generally thought to reflect poorer representations of the phonetic categories within the speaker's native language, which may be the result of poor auditory resolution or poor language-specific learning of relevant phonetic cues (e.g., Shafer et al. 2005; Datta et al. 2010). One study of 6-year-old children at risk for dyslexia, in addition to reduced MMN to phonemic contrasts (e.g., /ba/ vs. /da/) observed larger MMN to a within-category difference (allophonic variants of /ba/) in the at-risk children compared to the matched controls (Noordenbos et al. 2012). This finding is consistent with an explanation of poor language-specific learning, since within-category differences should become irrelevant with language learning. Alternatively, it could represent the sensitivity of the MMN to acoustic variation in the speech signal (Sussman et al. 2004). The MMN measure can be used to address questions about the relationship between general auditory processing and language deficits in children with dyslexia and SLI (Baldeweg et al. 1999; Benasich et al. 2006; Bishop et al. 2010).

Autism Spectrum Disorder (ASD)

MMN amplitude and latency differences have also provided insights into auditory processing skills in children with ASD. For example, studies in children with ASD have shown robust, and even enhanced, MMN amplitudes to non-speech stimuli, but attenuated MMN responses to speech stimuli (Oram Cardy et al. 2005; Stoodley et al. 2006; Gomot et al. 2002; Ferri et al. 2003; Ceroni et al. 2003; Kuhl et al. 2005; Lepistö et al. 2005, 2008; Näätänen and Kujala 2011; for a recent review, Kujala et al. 2013). Roberts et al. (2011) found that in 7–9-year-old children with ASD the MMN peak latency for tone-duration and vowel changes was delayed compared to normally developing age-matched children. Importantly, this delay was considerably increased in duration if the child also suffered from a delay in linguistic development.

Cleft Palate

The MMN measure has also been used to examine children with cleft palates and/or with Catch-22 syndrome, who are known to have learning difficulties. Children with Catch-22 and cleft palates showed shorter auditory sensory memory compared to typically-developing controls, as indexed by the rapid disappearance of the MMN with the gradual prolongation of the stimulus-onset asynchrony (Cheour et al. 1998). In another study, children with cleft palates exhibited smaller amplitude MMN than controls (Yang et al. 2012).

Acquired Development Disorders

The MMN measure has also been used to evaluate possible damage to central auditory processing associated with acquired developmental deficits. Jansson-Verkasalo et al. (2003, 2004) found that the MMN amplitude elicited by a consonant change at 4 years of age (from conception), obtained in premature infants who had a low birth weight, was considerably smaller than that in age-matched control children. Further, they found that the absence of an MMN at 4–5 years of age significantly predicted naming difficulties when children were 6 years of age. In addition, children with epilepsy also showed attenuated MMN (Boatman et al. 2008; Liasis et al. 2001). For example, Boatman et al. (2008) tested a group of 7–11-year-old children with benign rolandic epilepsy, and found that the MMN was absent (or prolonged in latency) to speech-sound changes but not to tone changes. Importantly, no group differences in the amplitude or latency of the obligatory N1 component was found for either speech or tones. Moreover, those with no MMN to speech sounds also had the most severe cognitive impairments on behavioral testing.

These studies highlight the potential utility of MMN in serving as a clinical biomarker of language risk in developmentally-disordered populations, which is of particular interest in children who are difficult to test using behavioral measures (e.g., non-compliant children with ASD, and at-risk infants and toddlers). MMN shows promise as a clinical measure of auditory and speech processing in children. However, to date, fairly simple auditory stimuli and patterns have been used. Future studies using more complex stimuli and patterns (e.g., similar to Kujala et al. 2005; Lepistö et al. 2008; Bonte et al. 2007) could be undertaken to determine whether the sensitivity and specificity of the MMN response can be improved sufficiently for clinical use.

Infants and Early Identification of Risk

One challenge in infant studies is that the negative displacement of the deviant ERP waveform typically identified in the child and adult responses to oddball stimuli as MMN, is observed as a positive displacement in infants (Dehaene-Lambertz and Dehaene 1994; Trainor et al. 2003; Kushnerenko et al. 2007; Morr et al. 2002; Weber et al. 2004). This response in infants has been called the positive MMR (Fig. 2). However, several studies have reported both a positive MMR and a negative MMR. This may be a developmental issue. The negative MMR may be equivalent to the adult MMN (He et al. 2007, 2009; Shafer et al. 2010, 2011). With increasing age, the negative MMR becomes larger in amplitude and earlier in latency (Shafer et al. 2000, 2010; Morr et al. 2002). Concurrently, the positive MMR becomes earlier in latency and decreased in amplitude. By 7 years of age, the positive MMR is no longer present (Shafer et al. 2010). However, the developmental trajectory may differ in individuals with neurodevelopmental disorders (Ahmed et al. 2008; Kuhl et al. 2008; Friedrich et al. 2009). Kuhl et al. (2008) observed that infants with more negative MMRs to native-language speech sounds showed better language scores as preschoolers (also Friedrich et al. 2009). This finding is consistent with the suggestion that increased experience with native language speech sounds results in a stronger neural representation at a pre-attentive level, supporting automaticity of speech perception. Alternatively, it may be that infants who become better language users are more attentive to speech earlier on. In this latter case, the increased attention to the speech would allow for formation of more robust representations (Shafer et al. 2012).

Several recent studies suggest that the MMR elicited in infants is predictive of later language outcomes (Leppänen et al. 1999, 2002; van Leeuwen et al. 2006; van Zuijen et al. 2013). In contrast, other studies have been less sanguine about the potential utility of the MMR as a clinical tool (e.g., Benasich et al. 2006; Choudhury and Benasich 2011), perhaps due to the current lack of clarity in what the MMR reflects in the infant brain. Further studies are needed that examine both stimulus and task factors to elucidate factors contributing to the response, and improve its potential clinical application in infant populations. Nonetheless, these studies clearly establish the utility of using the MMN and MMR measures as research tools for better understanding the nature of developmental disorders involving speech and language impairments (Bishop et al. 2007; Bishop 2007).

Mechanisms of Auditory Change Detection

This review has focused primarily on literature that has used the MMN measure to understand disorders of cognition and language. However, to fully explain the nature of an auditory processing deficit it is also important to understand the mechanisms of sound encoding, representation, and change detection that underlie behavioral perception. A more complete understanding of the neural processes that lead to the MMN, thus, is a necessary link in the chain. It is beyond the scope of this review to provide a full discussion of the debate surrounding the neural mechanisms underlying MMN (e.g., May and Tiitinen 2010; Bendixen et al. 2012; Fishman 2013). However, we note a number of important questions that need to be addressed in future studies.

Issues related to the underlying mechanisms contributing to the MMN response, such as whether MMN indexes neural adaptation (e.g., May and Tiitinen 2010), or stimulus predictions (Friston 2005; Schröger et al. 2013) have not been completely resolved. Almost all of the clinical studies reviewed above have focused on processing simple sensory stimulation. Although the simplest approach is often desirable, especially when assessing states of disorder, the use of more complex stimulation may reveal information not otherwise obtained, such as when trying to understand what breaks down for those who have difficulty hearing speech in noise. It is possible that the use of MMN with more complex auditory patterns will be enlightening in populations with language-related deficits (e.g., SLI, dyslexia, and central auditory processing disorders). For example, Bonte et al. (2007) found that children with dyslexia, unlike typical-reading children, did not show modulation of MMN amplitude in relation to the phonotactic probability of speech sounds in nonsense words. Examining change-detection in the context of more complex stimulus patterns is likely to enhance our understanding of auditory learning. For example, processing of tone features may be spared, or even enhanced in a particular disorder (e.g., ASD), where the process of learning sound patterns (e.g., phonotactic, syntactic patterns) is disordered.

It will also be important to further explore the role of NMDA receptor functioning in the deviance-detection process indexed by MMN. At least, studies of patients with Schizophrenia (e.g., Olney and Farber 1995; Coyle 2006), stroke (e.g., Dhawan et al. 2010), and normal aging (e.g., Magnusson et al. 2010) have linked impaired NMDA receptors to reduced amplitude MMN. This may be indicative of a wider distributed network in cortex (Kohlmetz et al. 2001) affecting learning and memory more generally. Specifically, an NMDA-receptor dysfunction may affect cognition in several different ways (Herrero et al. 2013), playing a critical role in the initiation of long-

term and working memory (Javitt et al. 1996; Newcomer et al. 1998), and in plastic changes in the brain (Gu 2002; Heekeren et al. 2008; Stephan et al. 2006). Clearly, deficient NMDA receptor functioning would have wide-ranging effects on cognitive function that go well beyond the auditory system. In this sense, poor MMN responses would simply be a reflection of this extensive breakdown. This possibility does not diminish findings that MMN can serve as a marker of risk for disorder (as has been found for psychosis, Perez et al. 2014a, b). A clearer understanding of the processes underlying deviance-detection will allow a better understanding of the causal relationships among the various factors associated with a clinical disorder.

Conclusion

This review provided a brief overview of clinical research that has used the MMN measure to help elucidate the nature of auditory processing in these various disorders, as well as demonstrating the use of MMN as a measure to assess treatment protocols, as a marker for risk of symptoms (e.g., psychosis in schizophrenia), or disorder (e.g., language delay or dyslexia). Future research should consider the use of more complex stimulus paradigms to allow a more detailed understanding of auditory and speech deficits. The recent increase in studies aimed at understanding neural mechanisms underlying MMN elicitation, and the role of NMDA receptor functioning in these processes is an exciting and potentially fruitful area of inquiry, which has tremendous potential for improving the use of MMN as tool for clinical investigation.

Acknowledgments A version of this paper was presented at the 6th International Conference on Mismatch Negativity and its Scientific and Clinical implications. We would like to thank Jean DeMarco and Emily Zane for assistance with the reference list. Support was provided by the National Institute on Deafness and Other Communications Disorders of the National Institutes of Health (R13DC012029 and R01DC004263, E.S.), the National Science Foundation (#1156635), and an Institutional Research Grant (IUT 02-13) from the Estonian Ministry of Education and Research (R.N.). The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health or the National Science Foundation.

References

- Aaltonen O, Tuomainen J, Laine M, Niemi P (1993) Cortical differences in tonal versus vowel processing as revealed by an ERP component called mismatch negativity (MMN). *Brain Lang* 44(2):139–152
- Aaltonen O, Eerola O, Hellstrom A, Uusipaikka E, Lang AH (1997) Perceptual magnet effect in the light of behavioral and psychophysiological data. *J Acoust Soc Am* 101(2):1090–1105

- Ahmed AU, Clarke EM, Adams C (2008) Mismatch negativity and frequency representational width in children with specific language impairment. *Dev Med Child Neurol* 50(12):938–944
- Alho K (1995) Cerebral generators of mismatch negativity (MMN) and its magnetic counterpart (MMNm) elicited by sound changes. *Ear Hear* 16(1):38–51
- Andersson S, Barder HE, Hellvin T, Løvdaal H, Malt UF (2008) Neuropsychological and electrophysiological indices of neurocognitive dysfunction in bipolar II disorder. *Bipolar Disord* 10(8):888–899
- Atkinson RJ, Michie PT, 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
- Auther LL, Wertz RT, Miller TA, Kirshner HS (2000) Relationships among the mismatch negativity (MMN) response, auditory comprehension, and site of lesion in aphasic adults. *Aphasiology* 14(5–6):461–470
- Baker K, Baldeweg T, Sivagnanasundaram S, Scambler P, Skuse D (2005) COMT Val108/158 Met modifies mismatch negativity and cognitive function in 22q11 deletion syndrome. *Biol Psychiatry* 58(1):23–31
- Bakker I, Macgregor LJ, Pulvermüller F, Shtyrov Y (2013) Past tense in the brain's time: neurophysiological evidence for dual-route processing of past-tense verbs. *Neuroimage* 71:187–195
- Baldeweg T, Richardson A, Watkins S, Foale C, Gruzeliér J (1999) Impaired auditory frequency discrimination in dyslexia detected with mismatch evoked potentials. *Ann Neurol* 45(4):495–503
- Baldeweg T, Klugman A, Gruzeliér J, Hirsch SR (2004) Mismatch negativity potentials and cognitive impairment in schizophrenia. *Schizophr Res* 69(2–3):203–217
- Becker F, Reinvang I (2007) Mismatch negativity elicited by tones and speech sounds: changed topographical distribution in aphasia. *Brain Lang* 100(1):69–78
- Belger A, Yucel GH, Donkers FC (2012) In search of psychosis biomarkers in high-risk populations: is the mismatch negativity the one we've been waiting for? *Biol Psychiatry* 71(2):94–95
- Benasich AA, Choudhury N, Friedman JT, Realpe-Bonilla T, Chojnowska C, Gou Z (2006) The infant as a prelinguistic model for language learning impairments: predicting from event-related potentials to behavior. *Neuropsychologia* 44(3):396–411
- Bendixen A, Prinz W, Horváth J, Trujillo-Barreto NJ, Schröger E (2008) Rapid extraction of auditory feature contingencies. *Neuroimage* 41(3):1111–1119
- Bendixen A, Schröger E, Ritter W, Winkler I (2012) Regularity extraction from non-adjacent sounds. *Front Psychol* 3:143
- Bendixen A, Scharinger M, Strauß A, Obleser J (2014) Prediction in the service of comprehension: modulated early brain responses to omitted speech segments. *Cortex* 53C:9–26
- Besle J, Hussain Z, Giard MH, Bertrand O (2013) The representation of audiovisual regularities in the human brain. *J Cogn Neurosci* 25(3):365–373
- Bishop DVM (2006) What causes specific language impairment in children? *Curr Dir Psychol Sci* 15(5):217–221
- Bishop DV (2007) Using mismatch negativity to study central auditory processing in developmental language and literacy impairments: where are we, and where should we be going? *Psychol Bull* 133(4):651–672
- Bishop DVM, Hardiman M, Uwer R, von Suchodoletz W (2007) Atypical long-latency auditory event-related potentials in a subset of children with specific language impairment. *Dev Sci* 10:565–575
- Bishop DVM, Hardiman MJ, Barry JG (2010) Lower-frequency event-related desynchronization: a signature of late mismatch responses to sounds, which is reduced or absent in children with specific language impairment. *J Neurosci* 30(46):15578–15584
- Boatman BF, Trescher W, Smith C, Ewen J, Los J, Wied HM, Gordon B, Kossoff EH, Gao Q, Vining EP (2008) Cortical auditory dysfunction in benign rolandic epilepsy. *Epilepsia* 49(6):1018–1026
- Bodatsch M, Ruhrmann S, Wagner M, Müller R, Schultze-Lutter F, Frommann I, Brinkmeyer J, Gaebel W, Maier W, Klosterkötter J, Brockhaus-Dumke A (2011) Prediction of psychosis by mismatch negativity. *Biol Psychiatry* 69(10):959–966
- Bonte ML, Mitterer H, Zelligui N, Poelmans H, Blomert L (2005) Auditory cortical tuning to statistical regularities in phonology. *Clin Neurophysiol* 116(12):2765–2774
- Bonte ML, Poelmans H, Blomert L (2007) Deviant neurophysiological responses to phonological regularities in speech in dyslexic children. *Neuropsychologia* 45(7):1427–1437
- Borghetti D, Pizzanelli C, Maritato P, Fabbrini M, Jensen S, Iudice A, Murri L, Sartucci F (2007) Mismatch negativity analysis in drug-resistant epileptic patients implanted with vagus nerve stimulator. *Brain Res Bull* 73(1–3):81–85
- Bradlow AR, Kraus N, Nicol TG, McGee TJ, Cunningham J, Zecker SG, Carrell TD (1999) Effects of lengthened formant transition duration on discrimination and neural representation of synthetic CV syllables by normal and learning-disabled children. *J Acoust Soc Am* 106(4 Pt 1):2086–2096
- Brattico E, Näätänen R, Tervaniemi M (2001) Context effects on pitch perception in musicians and nonmusicians: evidence from event-related-potential recordings. *Music Percept* 19(2):199–222
- Brattico E, Tervaniemi M, Näätänen R (2006) Musical scale properties are automatically processed in the human auditory cortex. *Brain Res* 1117(1):162–174
- Brattico E, Pallesen KJ, Varyagina O, Bailey C, Anourova I, Järvenpää MM, Eerola T, Tervaniemi M (2009) Neural discrimination of nonprototypical chords in music experts and laymen: an MEG study. *J Cogn Neurosci* 21(11):2230–2244
- Brockhaus-Dumke A, Tendokar I, Pukrop R, Schultze-Lutter F, Klosterkötter J, Ruhrmann S (2005) Impaired mismatch negativity in prodromal subjects and patients with schizophrenia. *Schizophr Res* 73:297–310
- Brønneck KS, Nordby H, Larsen JP, Aarsland D (2010) Disturbance of automatic auditory change detection in dementia associated with Parkinson's disease: a mismatch negativity study. *Neurobiol Aging* 31(1):104–113
- Bruder GE, Schnur DB, Fergeson P, Mukherjee S, Leite P, Sackeim HA (1994) Dichotic-listening measures of brain laterality in mania. *J Abnorm Psychol* 103(4):758–766
- Caclin A, Brattico E, Tervaniemi M, Näätänen R, Morlet D, Giard MH, McAdams S (2006) Separate neural processing of timbre dimensions in auditory sensory memory. *J Cogn Neurosci* 18(12):1959–1972
- Catts SV, Shelley AM, Ward PB, Liebert B, McConaghy N, Andrews S, Michie PT (1995) Brain potential evidence for an auditory sensory memory deficit in schizophrenia. *Am J Psychiatry* 152(2):213–219
- Ceponiene R, Lepistö T, Shestakova A, Vanhala R, Alku P, Näätänen R, Yaguchi K (2003) Speech-sound-selective auditory impairment in children with autism: they can perceive but do not attend. *Proc Natl Acad Sci USA* 100(9):5567–5572
- Chen S, Sussman ES (2013) Context effects on auditory distraction. *Biol Psychol* 94(2):297–309
- Chennu S, Noreika V, Gueorguiev D, Blenkmann A, Kochen S, Ibáñez A, Owen AM, Bekinshtein TA (2013) Expectation and attention in hierarchical auditory prediction. *J Neurosci* 33(27):11194–11205
- Cheour M, Haapanen ML, Ceponiene R, Hukki J, Ranta R, Näätänen R (1998) Mismatch negativity (MMN) as an index of auditory sensory memory deficit in cleft-palate and CATCH syndrome children. *Neuroreport* 9(12):2709–2712

- Cheour M, Shestakova A, Alku P, Ceponiene R, Näätänen R (2002) Mismatch negativity shows that 3–6-year-old children can learn to discriminate non-native speech sounds within two months. *Neurosci Lett* 325(3):187–190
- Choudhury N, Benasich AA (2011) Maturation of auditory evoked potentials from 6 to 48 months: prediction to 3 and 4 year language and cognitive abilities. *Clin Neurophysiol* 122(2):320–338
- Colin C, Radeau M, Soquet A, Dachy B, Deltenre P (2002) Electrophysiology of spatial scene analysis: the mismatch negativity (MMN) is sensitive to the ventriloquism illusion. *Clin Neurophysiol* 113(4):507–518
- Cornella M, Leung S, Grimm S, Escera C (2012) Detection of simple and pattern regularity violations occurs at different levels of the auditory hierarchy. *PLoS ONE* 7(8):e43604
- Coyle JT (2006) Glutamate and schizophrenia: beyond the dopamine hypothesis. *Cell Mol Neurobiol* 26(4–6):365–384
- Csépe V, Osman-Sági J, Molnár M, Gósy M (2001) Impaired speech perception in aphasic patients: event-related potential and neuropsychological assessment. *Neuropsychologia* 39(11):1194–1208
- Dalebout SD, Stack JW (1999) Mismatch negativity to acoustic differences not differentiated behaviorally. *J Am Acad Audiol* 10(7):388–399
- Datta H, Shafer VL, Morr ML, Kurtzberg D, Schwartz RG (2010) Electrophysiological indices of discrimination of long-duration, phonetically similar vowels in children with typical and atypical language development. *J Speech Lang Hear Res* 53(3):757–777
- Daids N, Segers E, van den Brink D, Mitterer H, van Balkom H, Hagoort P, Verhoeven L (2011) The nature of auditory discrimination problems in children with specific language impairment: an MMN study. *Neuropsychologia* 49(1):19–28
- Dehaene-Lambertz G (1997) Electrophysiological correlates of categorical phoneme perception in adults. *Neuroreport* 8(4):919–924
- Dehaene-Lambertz G, Dehaene S (1994) Speed and cerebral correlates of syllable discrimination in infants. *Nature* 370(6487):292–295
- Dehaene-Lambertz G, Dupoux E, Gout A (2000) Electrophysiological correlates of phonological processing: a cross-linguistic study. *J Cogn Neurosci* 12(4):635–647
- Devrim-Üçok M, Keskin-Ergen HY, Üçok A (2008) Mismatch negativity at acute and post-acute phases of first-episode schizophrenia. *Eur Arch Psychiatry Clin Neurosci* 258(3):179–185
- Dhawan J, Benveniste H, Nawrocky M, Smith SD, Biegón A (2010) Transient focal ischemia results in persistent and widespread neuroinflammation and loss of glutamate NMDA receptors. *Neuroimage* 51(2):599–605
- Domján N, Csifcsák G, Drótos G, Janka Z, Szendi I (2012) Different patterns of auditory information processing deficits in chronic schizophrenia and bipolar disorder with psychotic features. *Schizophr Res* 139(1–3):253–259
- Dunn MA, Gomes H, Gravel J (2008) Mismatch negativity in children with autism and typical development. *J Autism Dev Disord* 38(1):52–71
- Dyson BJ, Alain C, He Y (2005) Effects of visual attentional load on low-level auditory scene analysis. *Cogn Affect Behav Neurosci* 5(3):319–338
- Ferri R, Elia M, Agarwal N, Lanuzza B, Musumeci SA, Pennisi G (2003) The mismatch negativity and the P3a components of the auditory event-related potentials in autistic low-functioning subjects. *Clin Neurophysiol* 114(9):1671–1680
- Fishman YI (2013) The mechanisms and meaning of the mismatch negativity. *Brain Topogr*. doi:10.1007/s10548-013-0337-3
- Ford JM, Mathalon DH (2012) Anticipating the future: automatic prediction failures in schizophrenia. *Int J Psychophysiol* 83:232–239
- Ford JM, Roth WT, Kopell BS (1976) Attention effects on auditory evoked potentials to infrequent events. *Biol Psychol* 4:65–77
- Foster SM, Kisley MA, Davis HP, Diede NT, Campbell AM, Davalos DB (2013) Cognitive function predicts neural activity associated with pre-attentive temporal processing. *Neuropsychologia* 51(2):211–219
- Friedrich M, Herold B, Friederici AD (2009) ERP correlates of processing native and non-native language word stress in infants with different language outcomes. *Cortex* 45(5):662–676
- Friston K (2005) A theory of cortical responses. *Philos Trans R Soc Lond B* 360(1456):815–836
- Gaeta H, Friedman D, Ritter W, Cheng J (1999) Changes in sensitivity to stimulus deviance in Alzheimer's disease: an ERP perspective. *Neuroreport* 10(2):281–287
- Garrido MI, Friston KJ, Kiebel SJ, Stephan KE, Baldeweg T, Kilner JM (2008) The functional anatomy of the MMN: a DCM study of the roving paradigm. *Neuroimage* 42(2):936–944
- Garza Villarreal EA, Brattico E, Leino S, Ostergaard L, Vuust P (2011) Distinct neural responses to chord violations: a multiple source analysis study. *Brain Res* 1389:103–114
- Gomot M, Giard MH, Adrien JL, Barthelemy C, Bruneau N (2002) Hypersensitivity to acoustic change in children with autism: electrophysiological evidence of left frontal cortex dysfunctioning. *Psychophysiology* 39(5):577–584
- Gomot M, Blanc R, Clery H, Roux S, Barthelemy C, Bruneau N (2011) Candidate electrophysiological endophenotypes of hyper-reactivity to change in autism. *J Autism Dev Disord* 41(6):705–714
- Grimm S, Escera C (2012) Auditory deviance detection revisited: evidence for a hierarchical novelty system. *Int J Psychophysiol* 85(1):88–92
- Gu Q (2002) Neuromodulatory transmitter systems in the cortex and their role in cortical plasticity. *Neuroscience* 111(4):815–835
- Hall MH, Schulze K, Rijdsdijk F, Kalidindi S, McDonald C, Bramon E, Murray RM, Sham P (2009) Are auditory P300 and duration MMN heritable and putative endophenotypes of psychotic bipolar disorder? A Maudsley Bipolar Twin and Family Study. *Psychol Med* 39(8):1277–1287
- He C, Hotson L, Trainor LJ (2007) Mismatch responses to pitch changes in early infancy. *J Cogn Neurosci* 19(5):878–892
- He C, Hotson L, Trainor LJ (2009) Development of infant mismatch responses to auditory pattern changes between 2 and 4 months old. *Eur J Neurosci* 29(4):861–867
- Heekeren K, Daumann J, Neukirch A, Stock C, Kawohl W, Norra C, Waberski TD, Gouzoulis-Mayfrank E (2008) Mismatch negativity generation in the human 5HT_{2A} agonist and NMDA antagonist model of psychosis. *Psychopharmacology* 199(1):77–88
- Herholz SC, Lappe C, Pantev C (2009) Looking for a pattern: an MEG study on the abstract mismatch negativity in musicians and nonmusicians. *BMC Neurosci* 10:42
- Hermens DF, Ward PB, Hodge MA, Kaur M, Naismith SL, Hickie IB (2010) Impaired MMN/P3a complex in first-episode psychosis: cognitive and psychosocial associations. *Prog Neuropsychopharmacol Biol Psychiatry* 34(6):822–829
- Herrero JL, Gieselmann MA, Sanayei M, Thiele A (2013) Attention-induced variance and noise correlation reduction in macaque V1 is mediated by NMDA receptors. *Neuron* 78(4):729–739
- Higuchi Y, Sumiyoshi T, Seo T, Miyaniishi T, Kawasaki Y, Suzuki M (2013) Mismatch negativity and cognitive performance for the prediction of psychosis in subjects with at-risk mental state. *PLoS ONE* 8(1):e54080
- Holopainen IE, Korpilahti P, Juottonen K, Lang H, Sillanpää M (1997) Attenuated auditory event-related potential (mismatch negativity) in children with developmental dysphasia. *Neuropediatrics* 28(5):253–256
- Horváth J, Czigler I, Jacobsen T, Maess B, Schröger E, Winkler I (2008) MMN or no MMN: no magnitude of deviance effect on the MMN amplitude. *Psychophysiology* 45(1):60–69

- Ilvonen TM, Kujala T, Kiesiläinen A, Salonen O, Kozou H, Pekkonen E, Roine RO, Kaste M, Näättänen R (2003) Auditory discrimination after left-hemisphere stroke: a mismatch negativity follow-up study. *Stroke* 34(7):1746–1751
- Ilvonen T, Kujala T, Kozou H, Kiesiläinen A, Salonen O, Alku P, Näättänen R (2004) The processing of speech and non-speech sounds in aphasic patients as reflected by the mismatch negativity (MMN). *Neurosci Lett* 366(3):235–240
- Jacobsen TK, Steinberg J, Truckenbrodt H, Jacobsen T (2013) Mismatch negativity (MMN) to successive deviants within one hierarchically structured auditory object. *Int J Psychophysiol* 87(1):1–7
- Jansson-Verkasalo E, Ceponiene R, Valkama M, Vainionpää L, Laitakari K, Alku P, Suominen K, Näättänen R (2003) Deficient speech-sound processing, as shown by the electrophysiologic brain mismatch negativity response, and naming ability in prematurely born children. *Neurosci Lett* 348(1):5–8
- Jansson-Verkasalo E, Korpilahti P, Jäntti V, Valkama M, Vainionpää L, Alku P, Suominen K, Näättänen R (2004) Neurophysiologic correlates of deficient phonological representations and object naming in prematurely born children. *Clin Neurophysiol* 115(1):179–187
- Javitt DC (2000) Intracortical mechanisms of mismatch negativity dysfunction in schizophrenia. *Audiol Neurotol* 5(3–4):207–215
- Javitt DC (2010) Glutamatergic theories of schizophrenia. *Isr J Psychiatry Relat Sci* 47(1):4–16
- Javitt DC (2012) Twenty-five years of glutamate in schizophrenia: are we there yet? *Schizophr Bull* 38(5):911–913
- Javitt DC, Doneshka P, Zylberman I, Ritter W, Vaughan HG Jr (1993) Impairment of early cortical processing in schizophrenia: an event-related potential confirmation study. *Biol Psychiatry* 33(7):513–519
- Javitt DC, Doneshka P, Grochowski S, Ritter W (1995) Impaired mismatch negativity generation reflects widespread dysfunction of working memory in schizophrenia. *Arch Gen Psychiatry* 52(7):550–558
- Javitt DC, Steinschneider M, Schroeder CE, Arezzo JC (1996) Role of cortical *N*-methyl-D-aspartate receptors in auditory sensory memory and mismatch negativity generation: implications for schizophrenia. *Proc Natl Acad Sci USA* 93(21):11962–11967
- Javitt DC, Zukin SR, Heresco-Levy U, Umbricht D (2012) Has an angel shown the way? Etiological and therapeutic implications of the PCP/NMDA model of schizophrenia. *Schizophr Bull* 38(5):958–966
- Jing H, Flax J, Roesler CP, Choudhury N, Benasich AA (2006) Auditory event-related responses in children with semi-lobar holoprosencephaly. *Brain Dev* 28(4):207–214
- Jung J, Morlet D, Mercier B, Confavreux C, Fischer C (2006) Mismatch negativity (MMN) in multiple sclerosis: an event-related potentials study in 46 patients. *Clin Neurophysiol* 117(1):85–93
- Kaur M, Battisti RA, Ward PB, Ahmed A, Hickie IB, Hermens DF (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 RS, Ward PB, Naismith SL, Hickie IB, Hermens DF (2013) Longitudinal associations between mismatch negativity and disability in early schizophrenia- and affective-spectrum disorders. *Prog Neuropsychopharmacol Biol Psychiatry* 46:161–169
- Kawakubo Y, Kamio S, Nose T, Iwanami A, Nakagome K, Fukuda M, Kato N, Rogers MA, Kasai K (2007) Phonetic mismatch negativity predicts social skills acquisition in schizophrenia. *Psychiatry Res* 152(2–3):261–265
- Kayser J, Tenke CE, Kroppmann CJ, Alschuler DM, Fekri S, Ben-David S, Corcoran CM, Bruder GE (2014) Auditory event-related potentials and alpha oscillations in the psychosis prodrome: neuronal generator patterns during a novelty oddball task. *Int J Psychophysiol* 91(2):104–120
- Kemner C, Verbaten MN, Cuperus JM, Camfferman G, van Engeland H (1995) Auditory event-related brain potentials in autistic children and three different control groups. *Biol Psychiatry* 38(3):150–165
- Kiang M, Light GA, Prugh J, Coulson S, Braff DL, Kutas M (2007) Cognitive, neurophysiological, and functional correlates of proverb interpretation abnormalities in schizophrenia. *J Int Neuropsychol Soc* 13(4):653–663
- Kisley MA, Davalos DB, Engleman LL, Guinther PM, Davis HP (2005) Age-related change in neural processing of time-dependent stimulus features. *Brain Res Cogn Brain Res* 25(3):913–925
- Koelsch S (2009) Music–syntactic processing and auditory memory: similarities and differences between ERAN and MMN. *Psychophysiology* 46(1):179–190
- Koelsch S, Schröger E, Tervaniemi M (1999) Superior pre-attentive auditory processing in musicians. *Neuroreport* 10(6):1309–1313
- Koelsch S, Schröger E, Tervaniemi M (2012) Neural evidence of allophonic perception in children at risk for dyslexia. *Neuroreport* 10(6):1309–1313
- Kohlmetz C, Altenmüller E, Schuppert M, Wieringa BM, Münte TF (2001) Deficit in automatic sound-change detection may underlie some music perception deficits after acute hemispheric stroke. *Neuropsychologia* 39(11):1121–1124
- Korostenskaja M, Pardos M, Fujiwara H, Kujala T, Horn P, Rose D, Byars A (2010) Neuromagnetic evidence of impaired cortical auditory processing in pediatric intractable epilepsy. *Epilepsy Res* 92(1):63–73
- Korpilahti P, Lang HA (1994) Auditory ERP components and mismatch negativity in dysphasic children. *Electroencephalogr Clin Neurophysiol* 91(4):256–264
- Kraus N, McGee T, Carrell TD, Sharma A (1995) Neurophysiologic bases of speech discrimination. *Ear Hear* 16(1):19–37
- Krystal J, D'Souza DC, Mathalon D, Perry E, Belger A, Hoffman R (2003) NMDA receptor antagonist effects, cortical glutamatergic function, and schizophrenia: toward a paradigm shift in medication development. *Psychopharmacology* 169:215–233
- Kuhl PK, Coffey-Corina S, Padden D, Dawson G (2005) Links between social and linguistic processing of speech in preschool children with autism: behavioral and electrophysiological measures. *Dev Sci* 8(1):F1–F12
- Kuhl PK, Conboy BT, Coffey-Corina S, Padden D, Rivera-Gaxiola M, Nelson T (2008) Phonetic learning as a pathway to language: new data and native language magnet theory expanded (NLM-e). *Philos Trans R Soc Lond B* 363(1493):979–1000
- Kujala T, Lepistö T, Nieminen-von Wendt T, Näättänen P, Näättänen R (2005) Neurophysiological evidence for cortical discrimination impairment of prosody in Asperger syndrome. *Neurosci Lett* 383(3):260–265
- Kujala T, Lepistö T, Näättänen R (2013) The neural basis of aberrant speech and audition in autism spectrum disorders. *Neurosci Biobehav Rev* 37:697–704
- Kushnerenko E, Winkler I, Horváth J, Näättänen R, Pavlov I, Fellman V, Huotilainen M (2007) Processing acoustic change and novelty in newborn infants. *Eur J Neurosci* 26(1):265–274
- Lalo E, Vercueil L, Bougerol T, Jouk PS, Debû B (2005) Late event-related potentials and movement complexity in young adults with Down syndrome. *Neurophysiol Clin* 35(2–3):81–91
- Lang HA, Nyrke T, Ek M, Aaltonen O, Raimo I, Näättänen R (1990) Pitch discrimination performance and auditory event-related potentials. In: Brunia CHM, Gaillard AWK, Kok A, Mulder G, Verbaten MN (eds) *Psychophysiological brain research 1990*, vol 1. Tilburg University Press, Tilburg, pp 294–298
- Lavoie S, Murray MM, Deppen P, Knyazeva MG, Berk M, Boulton O, Bovet P, Bush AI, Conus P, Copolov D, Fornari E, Meuli R,

- Solida A, Vianin P, Cuénod M, Buclin T, Do KQ (2008) Glutathione precursor, *N*-acetyl-cysteine, improves mismatch negativity in schizophrenia patients. *Neuropsychopharmacology* 33(9):2187–2199
- Lepistö T, Kujala T, Vanhala R, Alku P, Huottilainen M, Näätänen R (2005) The discrimination of and orienting to speech and non-speech sounds in children with autism. *Brain Res* 1066(1–2): 147–157
- Lepistö T, Kajander M, Vanhala R, Alku P, Huottilainen M, Näätänen R, Kujala T (2008) The perception of invariant speech features in children with autism. *Biol Psychol* 77(1):25–31
- Leppänen PH, Pihko E, Eklund KM, Lyytinen H (1999) Cortical responses of infants with and without a genetic risk for dyslexia: II. Group effects. *Neuroreport* 10(5):969–973
- Leppänen PH, Richardson U, Pihko E, Eklund KM, Guttorm TK, Aro M, Lyytinen H (2002) Brain responses to changes in speech sound durations differ between infants with and without familial risk for dyslexia. *Dev Neuropsychol* 22(1):407–422
- Liasis A, Towell A, Boyd S (2000) Intracranial evidence for differential encoding of frequency and duration discrimination responses. *Ear Hear* 21(3):252–256
- Liasis A, Towell A, Alho K, Boyd S (2001) Intracranial identification of an electric frontal-cortex response to auditory stimulus change: a case study. *Brain Res Cogn Brain Res* 11(2):227–233
- Lieder F, Stephan KE, Daunizeau J, Garrido MI, Friston KJ (2013) A neurocomputational model of the mismatch negativity. *PLoS Comput Biol* 9(11):e1003288
- Light GA, Braff DL (2005a) Mismatch negativity deficits are associated with poor functioning in schizophrenia patients. *Arch Gen Psychiatry* 62(2):127–136
- Light GA, Braff DL (2005b) Stability of mismatch negativity deficits and their relationship to functional impairments in chronic schizophrenia. *Am J Psychiatry* 162(9):1741–1743
- Light G, Näätänen R (2013) Mismatch negativity is a breakthrough biomarker for understanding and treating psychotic disorders. *Proc Natl Acad Sci USA* 110(38):15175–15176
- Lin YY, Hsiao FJ, Shih YH, Yiu CH, Yen DJ, Kwan SY, Wong TT, Wu ZA, Ho LT (2007) Plastic phase-locking and magnetic mismatch response to auditory deviants in temporal lobe epilepsy. *Cereb Cortex* 17:2516–2525
- Liu R, Holt LL (2011) Neural changes associated with nonspeech auditory category learning parallel those of speech category acquisition. *J Cogn Neurosci* 23(3):683–698
- Macdonald M, Campbell K (2011) Effects of a violation of an expected increase or decrease in intensity on detection of change within an auditory pattern. *Brain Cogn* 77(3):438–445
- Magno E, Yeap S, Thakore JH, Garavan H, De Sanctis P, Foxe JJ (2008) Are auditory-evoked frequency and duration mismatch negativity deficits endophenotypic for schizophrenia? High-density electrical mapping in clinically unaffected first-degree relatives and first-episode and chronic schizophrenia. *Biol Psychiatry* 64(5):385–391
- Magnusson KR, Brim BL, Das SR (2010) Selective vulnerabilities of *N*-methyl-D-aspartate (NMDA) receptors during brain aging. *Front Aging Neurosci* 2:11
- Maiste AC, Wiens AS, Hunt MJ, Scherg M, Picton TW (1995) Event-related potentials and the categorical perception of speech sounds. *Ear Hear* 16(1):68–90
- Martin N, Kohen F, Kalinyak-Fliszar M, Soveri A, Laine M (2012) Effects of working memory load on processing of sounds and meanings of words in aphasia. *Aphasiology* 26(3–4):462–493
- May PJ, Tiitinen H (2010) Mismatch negativity (MMN), the deviance-elicited auditory deflection, explained. *Psychophysiology* 47(1):66–122
- Miyajima M, Ohta K, Hara K, Iino H, Maehara T, Hara M, Matsuura M, Matsushima E (2011) Abnormal mismatch negativity for pure-tone sounds in temporal lobe epilepsy. *Epilepsy Res* 94(3):149–157
- Morr ML, Shafer VL, Kreuzer JA, Kurtzberg D (2002) Maturation of mismatch negativity in typically developing infants and pre-school children. *Ear Hear* 23(2):118–136
- Mowszowski L, Hermens DF, Diamond K, Norrie L, Hickie IB, Lewis SJ, Naismith SL (2012) Reduced mismatch negativity in mild cognitive impairment: associations with neuropsychological performance. *J Alzheimers Dis* 30(1):209–219
- Müller D, Widmann A, Schröger E (2005) Auditory streaming affects the processing of successive deviant and standard sounds. *Psychophysiology* 42(6):668–676
- Murphy JR, Rawdon C, Kelleher I, Twomey D, Markey PS, Cannon M, Roche RA (2013) Reduced duration mismatch negativity in adolescents with psychotic symptoms: further evidence for mismatch negativity as a possible biomarker for vulnerability to psychosis. *BMC Psychiatry* 13:45
- Näätänen R (1975) Selective attention and evoked potentials in humans—a critical review. *Biol Psychol* 2(4):237–307
- Näätänen R (2001) The perception of speech sounds by the human brain as reflected by the mismatch negativity (MMN) and its magnetic equivalent (MMNm). *Psychophysiology* 38:1–21
- Näätänen R, Kujala T (2011) The mismatch negativity and its magnetic equivalent: an index of language impairment or more general cognitive decline in autism? *Biol Psychiatry* 70(3):212–213
- Näätänen R, Michie PT (1979) Early selective-attention effects on the evoked potential: a critical review and reinterpretation. *Biol Psychol* 8(2):81–136
- Näätänen R, Gaillard AW, Mäntysalo S (1978) Early selective-attention effect on evoked potential reinterpreted. *Acta Psychol (Amst)* 42(4):313–329
- Näätänen R, Simpson M, Loveless NE (1982) Stimulus deviance and evoked potentials. *Biol Psychol* 14(1–2):53–98
- Näätänen R, Paavilainen P, Tiitinen H, Jiang D, Alho K (1993) Attention and mismatch negativity. *Psychophysiology* 30(5): 436–450
- Näätänen R, Lehtokoski A, Lennes M, Cheour M, Huottilainen M, Iivonen A, Vainio M, Alku P, Ilmoniemi RJ, Luuk A, Allik J, Sinkkonen J, Alho K (1997) Language-specific phoneme representations revealed by electric and magnetic brain responses. *Nature* 385(6615):432–444
- Näätänen R, Tervaniemi M, Sussman E, Paavilainen P, Winkler I (2001) “Primitive intelligence” in the auditory cortex. *Trends Neurosci* 24(5):283–288
- 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, Paavilainen P, Rinne T, Alho K (2007) The mismatch negativity (MMN) in basic research of central auditory processing: a review. *Clin Neurophysiol* 118(12):2544–2590
- Näätänen R, Astikainen P, Ruusuvirta T, Huottilainen M (2010) Automatic auditory intelligence: an expression of the sensory-cognitive core of cognitive processes. *Brain Res Rev* 64(1):123–136
- Näätänen R, Kujala T, Kreegipuu K, Carlson S, Escera C, Baldeweg T, Ponton C (2011a) The mismatch negativity: an index of cognitive decline in neuropsychiatric and neurological diseases and in ageing. *Brain* 134(Pt 12):3435–3453
- Näätänen R, Kujala T, Winkler I (2011b) Auditory processing that leads to conscious perception: a unique window to central auditory processing opened by the mismatch negativity and related responses. *Psychophysiology* 48(1):4–22
- Näätänen R, Kujala T, Escera C, Baldeweg T, Kreegipuu K, Carlson S, Ponton C (2012) The mismatch negativity (MMN)—a unique window to disturbed central auditory processing in ageing and different clinical conditions. *Clin Neurophysiol* 123(3):424–458

- Nagai T, Tada M, Kirihaara K, Araki T, Jinde S, Kasai K (2013) Mismatch negativity as a “translatable” brain marker toward early intervention for psychosis: a review. *Front Psychiatry* 4:115
- Nager W, Teder-Sälejärvi W, Kunze S, Münte TF (2003) Preattentive evaluation of multiple perceptual streams in human audition. *Neuroreport* 14(6):871–874
- Newcomer JW, Selke G, Melson AK, Gross J, Vogler GP, Dagogo-Jack S (1998) Dose-dependent cortisol-induced increases in plasma leptin concentration in humans. *Arch Gen Psychiatry* 55:995–1000
- Nittrouer S (2012) A new perspective on developmental language problems: perceptual organization deficits. *Perspect Lang Learn Educ* 19(3):87–97
- Noordenbos MW, Segers E, Serniclaes W, Mitterer H, Verhoeven L (2012) Neural evidence of allophonic perception in children at risk for dyslexia. *Neuropsychologia* 50(8):2010–2017
- Oades RD, Wild-Wall N, Juran SA, Sachsse J, Oknina LB, Röpcke B (2006) Auditory change detection in schizophrenia: sources of activity, related neuropsychological function and symptoms in patients with a first episode in adolescence, and patients 14 years after an adolescent illness-onset. *BMC Psychiatry* 6:7
- Olney JW, Farber N (1995) NMDA antagonists as neurotherapeutic drugs, psychotogens, neurotoxins, and research tools for studying schizophrenia. *Neuropsychopharmacology* 13(4):335–345
- Opitz B, Rinne T, Mecklinger A, von Cramon DY, Schröger E (2002) Differential contribution of frontal and temporal cortices to auditory change detection: fMRI and ERP results. *Neuroimage* 15(1):167–174
- Oram Cardy JE, Flagge EJ, Roberts W, Roberts TP (2005) Delayed mismatch field for speech and non-speech sounds in children with autism. *Neuroreport* 16(5):521–525
- Paavilainen P (2013) The mismatch-negativity (MMN) component of the auditory event-related potential to violations of abstract regularities: a review. *Int J Psychophysiol* 88(2):109–123
- Paavilainen P, Arajärvi P, Takegata R (2007) Preattentive detection of nonsalient contingencies between auditory features. *Neuroreport* 18(2):159–163
- Pekkonen E, Rinne T, Näätänen R (1995) Variability and replicability of the mismatch negativity. *Electroencephalogr Clin Neurophysiol* 96(6):546–554
- Perez VB, Swerdlow NR, Braff DL, Näätänen R, Light GA (2014a) Using biomarkers to inform diagnosis, guide treatments and track response to interventions in psychotic illnesses. *Biomark Med* 8:9–14
- Perez VB, Woods SW, Roach BJ, Ford JM, McGlashan TH, Srihari VH, Mathalon DH (2014b) Automatic auditory processing deficits in schizophrenia and clinical high-risk patients: forecasting psychosis risk with mismatch negativity. *Biol Psychiatry* 75(6):459–469
- Peter V, McArthur G, Thompson WF (2012) Discrimination of stress in speech and music: a mismatch negativity (MMN) study. *Psychophysiology* 49(12):1590–1600
- Pettigrew C, Murdoch B, Kei J, Ponton C, Alku P, Chenery H (2005) The mismatch negativity (MMN) response to complex tones and spoken words in individuals with aphasia. *Aphasiology* 19(2):131–163
- Phillips C, Marantz A, McGinnis M, Pesetsky D, Wexler K, Yellin E (1995) Brain mechanisms of speech perception: a preliminary report. In: Schutze CT, Ganger JB, Broihier K (eds) *MIT Working Papers in Linguistics*, vol 26. MIT Press, Cambridge, pp 125–163
- Pieszek M, Widmann A, Gruber T, Schröger E (2013) The human brain maintains contradictory and redundant auditory sensory predictions. *PLoS ONE* 8(1):e53634
- Pulvermüller F, Shtyrov Y, Hasting AS, Carlyon RP (2008) Syntax as a reflex: neurophysiological evidence for early automaticity of grammatical processing. *Brain Lang* 104(3):244–253
- Rahne T, Sussman E (2009) Neural representations of auditory input accommodate to the context in a dynamically changing acoustic environment. *Eur J Neurosci* 29(1):205–211
- Rahne T, Böckmann M, von Specht H, Sussman ES (2007) Visual cues can modulate integration and segregation of objects in auditory scene analysis. *Brain Res* 1144:127–135
- Rapin I, Schimmel H, Tourk LM, Krasnegor NA, Pollak C (1966) Evoked responses to clicks and tones of varying intensity in waking adults. *Electroencephalogr Clin Neurophysiol* 21(4):335–344
- Reite M, Teale P, Rojas DC, Reite E, Asherin R, Hernandez O (2009) MEG auditory evoked fields suggest altered structural/functional asymmetry in primary but not secondary auditory cortex in bipolar disorder. *Bipolar Disord* 11(4):371–381
- Rinker T, Kohls G, Richter C, Maas V, Schulz E, Schecker M (2007) Abnormal frequency discrimination in children with SLI as indexed by mismatch negativity (MMN). *Neurosci Lett* 413(2):99–104
- Rinne T, Särkkä A, Degerman A, Schröger E, Alho K (2006) Two separate mechanisms underlie auditory change detection and involuntary control of attention. *Brain Res* 1077(1):135–143
- Rissling AJ, Park SH, Young JW, Rissling MB, Sugar CA, Sprock J, Mathias DJ, Pela M, Sharp RF, Braff DL, Light GA (2013) Demand and modality of directed attention modulate “pre-attentive” sensory processes in schizophrenia patients and nonpsychiatric controls. *Schizophr Res* 146(1–3):326–335
- Roberts TP, Cannon KM, Tavabi K, Blaskey L, Khan SY, Monroe JF, Qasmieh S, Levy SE, Edgar JC (2011) Auditory magnetic mismatch field latency: a biomarker for language impairment in autism. *Biol Psychiatry* 70(3):263–269
- Rohrmeier MA, Koelsch S (2012) Predictive information processing in music cognition. A critical review. *Int J Psychophysiol* 83(2):164–175
- Rosburg T, Trautner P, Dietl T, Korzyukov OA, Boutros NN, Schaller C, Elger CE, Kurthen M (2005) Subdural recordings of the mismatch negativity (MMN) in patients with focal epilepsy. *Brain* 128(Pt 4):819–828
- Saarienen J, Paavilainen P, Schöger E, Tervaniemi M, Näätänen R (1992) Representation of abstract attributes of auditory stimuli in the human brain. *Neuroreport* 3(12):1149–1151
- Salisbury DF (2012) Finding the missing stimulus mismatch negativity (MMN): emitted MMN to violations of an auditory gestalt. *Psychophysiology* 49(4):544–548
- Salisbury DF, Shenton ME, Griggs CB, Bonner-Jackson A, McCarley RW (2002) Mismatch negativity in chronic schizophrenia and first-episode schizophrenia. *Arch Gen Psychiatry* 59(8):686–694
- Salisbury DF, Kuroki N, Kasai K, Shenton ME, McCarley RW (2007) Progressive and interrelated functional and structural evidence of post-onset brain reduction in schizophrenia. *Arch Gen Psychiatry* 64(5):521–529
- Sandridge SA, Boothroyd AJ (1996) Using naturally produced speech to elicit the mismatch negativity. *J Am Acad Audiol* 7(2):105–112
- Santos MA, Munhoz MS, Peixoto MA, Haase VG, Rodrigues JL, Resende LM (2006) Mismatch negativity contribution in multiple sclerosis patients. *Braz J Otorhinolaryngol* 72(6):800–807
- Särkkä T, Tervaniemi M, Laitinen S, Forsblom A, Soinila S, Mikkonen M, Autti T, Silvennoinen HM, Erkkilä J, Laine M, Peretz I, Hietanen M (2008) Music listening enhances cognitive recovery and mood after middle cerebral artery stroke. *Brain* 131(Pt 3):866–876
- Särkkä T, Pihko E, Laitinen S, Forsblom A, Soinila S, Mikkonen M, Autti T, Silvennoinen HM, Erkkilä J, Laine M, Peretz I, Hietanen M, Tervaniemi M (2010) Music and speech listening enhance the recovery of early sensory processing after stroke. *J Cogn Neurosci* 22(12):2716–2727

- Schechtman E, Shrem T, Deouell LY (2012) Spatial localization of auditory stimuli in human auditory cortex is based on both head-independent and head-centered coordinate systems. *J Neurosci* 32(39):13501–13509
- Schroeder MM, Ritter W, Vaughan HG Jr (1995) The mismatch negativity to novel stimuli reflects cognitive decline. *Ann NY Acad Sci* 769:399–401
- Schröger E, Paavilainen P, Näätänen R (1994) Mismatch negativity to changes in a continuous tone with regularly varying frequencies. *Electroencephalogr Clin Neurophysiol* 92(2):140–147
- Schröger E, Bendixen A, Denham SL, Mill RW, Böhm TM, Winkler I (2013) Predictive regularity representations in violation detection and auditory stream segregation: from conceptual to computational models. *Brain Topogr*. doi:10.1007/s10548-013-0334-6
- Sculthorpe LD, Ouellet DR, Campbell KB (2009) MMN elicitation during natural sleep to violations of an auditory pattern. *Brain Res* 1290:52–62
- Seppänen M, Brattico E, Tervaniemi M (2007) Practice strategies of musicians modulate neural processing and the learning of sound-patterns. *Neurobiol Learn Mem* 87(2):236–247
- Shafer VL, Morr ML, Kreuzer JA, Kurtzberg D (2000) Maturation of mismatch negativity in school-age children. *Ear Hear* 21(3):242–251
- Shafer VL, Schwartz RG, Kurtzberg D (2004) Language-specific memory traces of consonants in the brain. *Brain Res Cogn Brain Res* 18(3):242–254
- Shafer VL, Morr ML, Datta H, Kurtzberg D, Schwartz RG (2005) Neurophysiological indexes of speech processing deficits in children with specific language impairment. *J Cogn Neurosci* 17(7):1168–1180
- Shafer VL, Yu YH, Datta H (2010) Maturation of speech discrimination in four to seven-year old children as indexed by event-related potential mismatch responses. *Ear Hear* 31(6):735–745
- Shafer VL, Yu Y, Datta H (2011) The development of English vowel perception in monolingual and bilingual infants: neurophysiological correlates. *J Phon* 39:527–541
- Shafer VL, Yu Y, Datta H (2012) Electrophysiological indices of vowel discrimination in monolingually and bilingually exposed infants. *Neurosci Lett* 526(1):10–14
- Shaikh M, Valmaggia L, Broome MR, Dutt A, Lappin J, Day F, Woolley J, Tabraham P, Walshe M, Johns L, Fusar-Poli P, Howes O, Murray RM, McGuire P, Bramon E (2012) Reduced mismatch negativity predates the onset of psychosis. *Schizophr Res* 134(1):42–48
- Sharma A, Dorman MF (1998) Exploration of the perceptual magnet effect using the mismatch negativity auditory evoked potential. *J Acoust Soc Am* 104(1):511–517
- Sharma A, Kraus N, McGee T, Carrell T, Nicol T (1993) Acoustic versus phonetic representation of speech as reflected by the mismatch negativity event-related potential. *Electroencephalogr Clin Neurophysiol* 88(1):64–71
- Shelley AM, Ward PB, Catts SV, Michie PT, Andrews S, McConaghy N (1991) Mismatch negativity: an index of a preattentive processing deficit in schizophrenia. *Biol Psychiatry* 30(10):1059–1062
- Shtyrov Y, Pulvermüller F, Näätänen R, Ilmoniemi RJ (2003) Grammar processing outside the focus of attention: an MEG study. *J Cogn Neurosci* 15(8):1195–1206
- Simson R, Vaughan HG, Ritter W (1976) The scalp topography of potentials associated with missing visual or auditory stimuli. *Electroencephalogr Clin Neurophysiol* 40(1):33–42
- Simson R, Vaughn HG Jr, Ritter W (1977) The scalp topography of potentials in auditory and visual discrimination tasks. *Electroencephalogr Clin Neurophysiol* 42(4):528–535
- Sonnadara RR, Alain C, Trainor LJ (2006) Effects of spatial separation and stimulus probability on the event-related potentials elicited by occasional changes in sound location. *Brain Res* 1071(1):175–185
- Squires NK, Squires KC, Hillyard SA (1975) Two varieties of long-latency positive waves evoked by unpredictable auditory stimuli in man. *Electroencephalogr Clin Neurophysiol* 38:387–401
- Squires KC, Wickens C, Squires NK, Donchin E (1976) The effect of stimulus sequence on the waveform of the cortical event-related potential. *Science* 193(4258):1142–1146
- Steinberg J, Truckenbrodt H, Jacobsen T (2010) Preattentive phonotactic processing as indexed by the mismatch negativity. *J Cogn Neurosci* 22(10):2174–2185
- Stephan KE, Baldeweg T, Friston KJ (2006) Synaptic plasticity and disconnection in schizophrenia. *Biol Psychiatry* 59(10):929–939
- Stoodley CJ, Hill PR, Stein JF, Bishop DV (2006) Auditory event-related potentials differ in dyslexics even when auditory psychophysical performance is normal. *Brain Res* 1121(1):190–199
- Sussman ES (2005) Integration and segregation in auditory scene analysis. *J Acoust Soc Am* 117(3 Pt 1):1285–1298
- Sussman E (2007) A new view on the MMN and attention debate: auditory context effects. *J Psychophysiol* 21(3–4):164–175
- Sussman E, Steinschneider M (2006) Neurophysiological evidence for context-dependent encoding of sensory input in human auditory cortex. *Brain Res* 1075(1):165–174
- Sussman E, Winkler I (2001) Dynamic sensory updating in the auditory system. *Cogn Brain Res* 12:431–439
- Sussman E, Ritter W, Vaughan HG Jr (1998) Attention affects the organization of auditory input associated with the mismatch negativity system. *Brain Res* 789(1):130–138
- Sussman E, Ritter W, Vaughan HG Jr (1999) An investigation of the auditory streaming effect using event-related brain potentials. *Psychophysiology* 36(1):22–34
- Sussman E, Kujala T, Halmetoja J, Lyytinen H, Alku P, Näätänen R (2004) Automatic and controlled processing of acoustic and phonetic contrasts. *Hear Res* 190(1–2):128–140
- Sussman E, Bregman AS, Wang WJ, Khan FJ (2005) Attentional modulation of electrophysiological activity in auditory cortex for unattended sounds in multistream auditory environments. *Cogn Affect Behav Neurosci* 5(1):93–110
- Sussman E, Horváth J, Winkler I, Orr M (2007) The role of attention in the formation of auditory streams. *Percept Psychophys* 69(1):136–152
- Sussman ES, Chen S, Sussman-Fort J, Dinces E (2013) The five myths of MMN: redefining how to use MMN in basic and clinical research. *Brain Topogr*. doi:10.1007/s10548-013-0326-6
- Takei Y, Kumano S, Maki Y, Hattori S, Kawakubo Y, Kasai K, Fukuda M, Mikuni M (2010) Preattentive dysfunction in bipolar disorder: a MEG study using mismatch negativity. *Prog Neuro-psychophysiol* 34:903–912
- Tallal P, Miller S, Fitch RH (1993) Neurobiological basis of speech: a case for the preeminence of temporal processing. *Ann NY Acad Sci* 682:27–47
- Tervaniemi M, Maury S, Näätänen R (1994) Neural representations of abstract stimulus features in the human brain as reflected by the mismatch negativity. *Neuroreport* 5(7):844–846
- Tervaniemi M, Rytkönen M, Schröger E, Ilmoniemi RJ, Näätänen R (2001) Superior formation of cortical memory traces for melodic patterns in musicians. *Learn Mem* 8(5):295–300
- Tervaniemi M, Castaneda A, Knoll M, Uther M (2006) Sound processing in amateur musicians and nonmusicians: event-related potential and behavioural indices. *Neuroreport* 17:1225–1228
- Todd J, Mullens D (2011) Implementing conditional inference in the auditory system: what matters? *Psychophysiology* 48(10):1434–1443
- Todd J, Robinson J (2010) The use of conditional inference to reduce prediction error—a mismatch negativity (MMN) study. *Neuropsychologia* 48(10):3009–3018

- Trainor L, McFadden M, Hodgson L, Darragh L, Barlow J, Matsos L, Sonnadara R (2003) Changes in auditory cortex and the development of mismatch negativity between 2 and 6 months of age. *Int J Psychophysiol* 51(1):5–15
- Tremblay K, Kraus N, Carrell TD, McGee T (1997) Central auditory system plasticity: generalization to novel stimuli following listening training. *J Acoust Soc Am* 102(6):3762–3773
- Umbricht D, Krljes S (2005) Mismatch negativity in schizophrenia: a meta-analysis. *Schizophr Res* 76(1):1–23
- Umbricht D, Schmid L, Koller R, Vollenweider FX, Hell D, Javitt D (2000) Ketamine-induced deficits in auditory and visual context-dependent processing in healthy volunteers. *Arch Gen Psychiatry* 57:1139–1147
- Umbricht D, Koller R, Vollenweider FX, Schmid L (2002) Mismatch negativity predicts psychotic experiences induced by NMDA receptor antagonist in healthy volunteers. *Biol Psychiatry* 53:400–406
- Umbricht D, Koller R, Schmid L, Skrabo A, Grübel C, Huber T, Stassen H (2003) How specific are deficits in mismatch negativity generation to schizophrenia? *Biol Psychiatry* 53(12):1120–1131
- Umbricht D, Bates JA, Lieberman JA, Kane JM, Javitt DC (2006) Electrophysiological indices of automatic and controlled auditory information processing in first-episode, recent-onset and chronic schizophrenia. *Biol Psychiatry* 59:762–772
- Uwer R, Albrecht R, von Suchodoletz W (2002) Automatic processing of tones and speech stimuli in children with specific language impairment. *Dev Med Child Neurol* 44(8):527–532
- van Leeuwen T, Been P, Kuijpers C, Zwarts F, Maassen B, van der Leij A (2006) Mismatch response is absent in 2-month-old infants at risk for dyslexia. *Neuroreport* 17(4):351–355
- van Zuijen T, Sussman E, Winkler I, Näätänen R, Tervaniemi M (2004) Grouping of sequential sounds—an event-related potential study *comparing* musicians and non-musicians. *J Cogn Neurosci* 16(2):331–338
- van Zuijen T, Sussman E, Winkler I, Näätänen R, Tervaniemi M (2005) Auditory organization of sound sequences by a temporal or numerical regularity—a mismatch negativity study comparing musicians and nonmusicians. *Cogn Brain Res* 23:270–276
- van Zuijen TL, Plakas A, Maassen BA, Maurits NM, van der Leij A (2013) Infant ERPs separate children at risk of dyslexia who become good readers from those who become poor readers. *Dev Sci* 16(4):554–563
- Vecchio F, Määttä S (2011) The use of auditory event-related potentials in Alzheimer’s disease diagnosis. *Int J Alzheimers Dis* 2011:1–7
- Wacongne C, Changeux JP, Dehaene S (2012) A neuronal model of predictive coding accounting for the mismatch negativity. *J Neurosci* 32(11):3665–3678
- Weber C, Hahne A, Friedrich M, Friederici AD (2004) Discrimination of word stress in early infant perception: electrophysiological evidence. *Brain Res Cogn Brain Res* 18(2):149–161
- Weise A, Bendixen A, Müller D, Schröger E (2012) Which kind of transition is important for sound representation? An event-related potential study. *Brain Res* 1464:30–42
- Wertz RT, Auther LL, Burch-Sims GP, Abou-Khalik RA, Kirshner HS, Duncan GW (1998) A comparison of the mismatch negativity (MMN) event-related potential to tone and speech stimuli in normal and aphasic adults. *Aphasiology* 12:499–507
- Winkler I (2007) Interpreting the mismatch negativity. *J Psychophysiol* 21:147–163
- Winkler I, Czigler I (2012) Evidence from auditory and visual event-related potential (ERP) studies of deviance detection (MMN and vMMN) linking predictive coding theories and perceptual object representations. *Int J Psychophysiol* 83(2):132–143
- Winkler I, Karmos G, Näätänen R (1996) Adaptive modeling of the unattended acoustic environment reflected in the mismatch negativity event-related. *Brain Res* 742(2):239–252
- Winkler I, Kujala T, Tiitinen H, Sivonen P, Alku P, Lehtokoski A, Czigler I, Csépe V, Ilmoniemi RJ, Näätänen R (1999) Brain responses reveal the learning of foreign language phonemes. *Psychophysiology* 36(5):638–642
- Woldorff MG, Hackley SA, Hillyard SA (1991) The effects of channel-selective attention on the mismatch negativity wave elicited by deviant tones. *Psychophysiology* 28(1):30–42
- Yang FF, McPherson B, Shu H, Xiao Y (2012) Central auditory nervous system dysfunction in infants with non-syndromic cleft lip and/or palate. *Int J Pediatr Otorhinolaryngol* 76(1):82–89
- Zion-Golumbic E, Deouell LY, Whalen DH, Bentin S (2007) Representation of harmonic frequencies in auditory memory: a mismatch negativity study. *Psychophysiology* 44(5):671–679