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APPLICATION OF ERP MEASURES IN PSYCHOLOGICAL RESEARCH

Measurement and interpretation of the mismatch negativity

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The mismatch negativity (MMN) is a preattentive brain response elicited by changes in repetitive auditory stimulation. Usually, it is identified as the difference between the event-related potential elicited by a high-probability *standard* and that elicited by a low-probability *deviant* stimulus. Most likely, MMN is generated by the outcome of a comparison process that registers a difference between the neural representation of the actual input and the memory trace of the standard stimulation. Since its discovery by Näätänen and colleagues in 1978, MMN has become a useful tool for investigating the brain's auditory information processing in several hundred studies. The present paper describes problems related to the measurement and interpretation of MMN. First, it reviews important features of MMN. Second, it provides technical information about recording and parametrization of this brain wave. Third, it discusses various methodological aspects which may be taken into account in the designing of MMN experiments. Fourth, it addresses some conceptual problems that have to be considered in the proper interpretation of MMN.

The mismatch negativity (MMN) is a component of the event-related potential (ERP) that is elicited by an irregularity in discrete, repetitive auditory stimulation (for a review, see Näätänen, 1992). Such an irregularity can consist in a deviation from the standard sound in a first-order feature such as frequency, intensity, or location of a tone. However, it can also consist in a deviation from higher order features such as a deviant (irregular) feature conjunction or irregular order reversals of elements within tonal sequences. This preattentive brain response is believed to be generated by the outcome of a comparison process that registers a difference between the neural representation of the actual input and the memory trace of the invariances inherent in the recent standard stimulation. MMN was first described by Näätänen, Gaillard, and Mäntysalo (1978). Since then it has been employed as a tool in cognitive neuroscience in several hundred experiments to study various aspects of central auditory processing in normal and in clinical populations (for a recent review of different kinds of applications, see Näätänen & Kraus, 1995). In addition to general benefits of ERP recordings (providing knowledge on psychological and physiological levels, good time resolution, being noninvasive, directly reflecting electrophysiological brain activity), MMN is of special interest since it can be measured even when subjects are not attending to the auditory stimulation. That is, it is not contaminated by task-related processing, and it can be employed with subjects unable to behaviorally respond to the auditory input. Meanwhile, attempts have been made to utilize MMN in patients with auditory disorders and to assess cortical auditory function in different clinical groups (Picton, 1995). For example, MMN systems are currently being developed at the Burden Neurological Institute (England) and at INSERM (France) to monitor the state of coma patients (see, e.g., S. R. Butler, 1997; Morlet, 1997). The purpose of this paper is to deliver basic knowledge and to address some open issues regarding the measurement and interpretation of MMN. Before going into more technically, methodologically, and conceptually oriented considerations, I shall review some important characteristics of MMN.

MISMATCH NEGATIVITY

MMN is usually obtained in passive oddball paradigms in which a frequent *standard* sound and an infrequent *deviant* sound are randomly delivered to subjects not paying attention to the stimulation (Figure 1). It is defined as the difference between the ERPs elicited by the standard and those elicited by the deviant sounds (Figure 2). It can best be identified in deviant − standard difference waves, in

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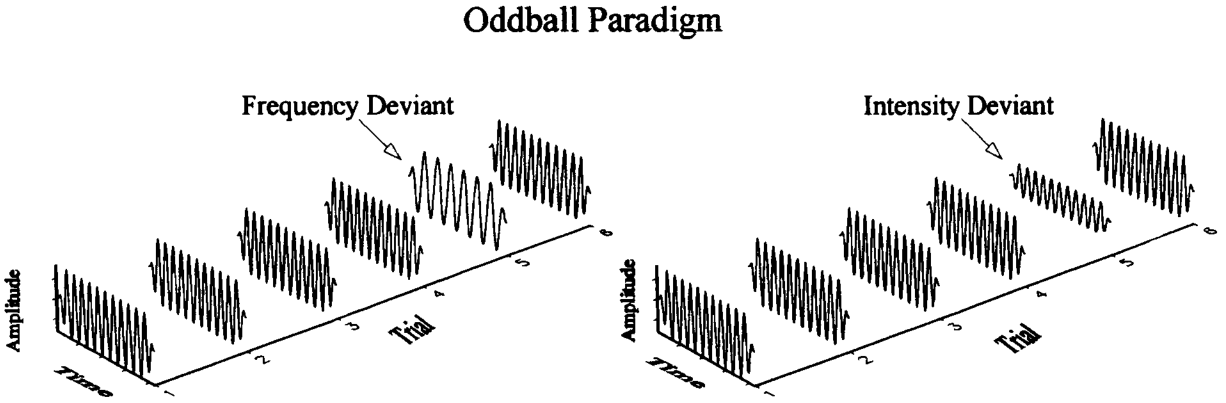

Figure 1. Illustration of the oddball paradigm with frequency change and with intensity change.

which the ERP to the standard is subtracted from the ERP to the deviant. MMN reveals a frontocentral, often right-hemispheric preponderant distribution and peaks between 100 and 250 msec from stimulus onset. When nose reference is used, it usually inverts polarity at leads positioned below the Sylvian fissure. MMN is characterized by a bundle of features that distinguish it from other exogeneous and endogeneous ERP components that are sensitive to irregularities in repetitive stimulation, such as the P1, N1, N2b, P3a, P3b, or N400. This special combination of features makes MMN an attractive tool for studying various aspects of central auditory information processing.

1. MMN is specific to the auditory modality. Since MMN is generated in the auditory cortex (see the next paragraph), and since an analog brain wave is not elicited by visual deviants, it may be regarded as a modality-specific brain wave. Nevertheless, it should be stated that negativities to deviant stimuli have also been reported in the visual modality (e.g., Alho, Woods, Algazi, & Näätänen, 1992; Czigler & Csibra, 1990; Nordby, Brønnick, & Hugdahl, 1996). However, the distributions of these negativities (and, therefore, their neural generators) are different from those of the auditory MMN.

2. MMN is elicited by a well-studied neural generator. Results from scalp-recorded electroencephalographic (e.g., Giard, Perrin, Pernier, & Bouchet, 1990; Scherg, Vajsar, & Picton, 1989) and magnetoencephalographic (e.g., Hari et al., 1984) recordings suggest that MMN is generated

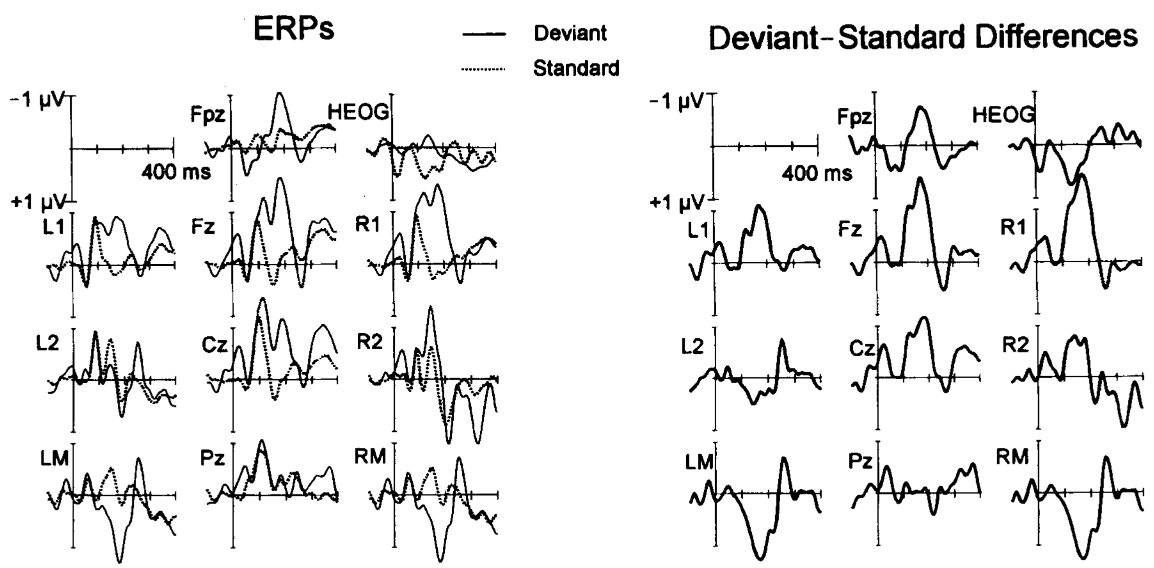

Figure 2. ERPs and difference waves resulting from a typical MMN experiment (Schröger & Wolff, 1997c). Left: ERPs elicited by a frequent standard tone (dotted lines) and an occasionally presented ($p = .10$) frequency deviant (continuous lines). Standard frequency was 600 Hz and deviant frequency was 660 Hz; constant offset-to-onset ISI was 650 msec; nose reference; subjects were reading in a book during stimulus presentation. Right: Difference waves, which were computed by subtracting the ERPs elicited by the standard from those elicited by the deviant. Distinct MMN can be observed. It reveals a fronto-central, right-preponderant distribution, and polarity reversal at the left and right mastoids (LM, RM), respectively.

within or in the vicinity of the primary auditory cortex. This is confirmed by the results of intracranial electrical recordings in animals (e.g., Csépe, Karmos, & Molnár, 1987; Javitt, Schroeder, Steinschneider, Arezzo, & Vaughan, 1992) and humans (Halgren et al., 1995; Kropotov et al., 1995). Neural generators in the auditory cortices also support the notion that MMN is modality specific. MMN generator location varies as a function of the stimulus dimension in which the deviance occurs, as is demonstrated by the finding that MMNs for changes in frequency, duration, and intensity are generated in different areas of the supratemporal cortex (Giard et al., 1995). Even within one stimulus dimension, the MMN generator differs slightly with the absolute value of the parameter being changed (Tiitinen et al., 1993).

Scalp current density analyses have suggested an additional MMN generator in frontal or prefrontal cortical areas (Giard et al., 1990). Because of small current amplitudes at short latencies, it has not been determined whether the temporal generator precedes the frontal one. Nevertheless, such a frontal generator is consistent with the presumed function of the brain processes underlying MMN—that is, the elicitation of attention switches toward deviations in the unattended acoustic input (Näätänen, 1992; Schröger, 1997b). Intracranial electrical recordings in humans suggest that the frontal cortex is involved in orienting (Baudena, Halgren, Heit, & Clarke, 1995).

Deviations in higher order features activate partly different neural generators than do deviations in first-order features (Alho, Huotilainen, & Näätänen, 1995). Alho and colleagues (Alho et al., 1996) have shown that frequency deviations in simple and in complex sounds are processed in different areas of the supratemporal cortex. Moreover, Paavilainen and colleagues as well as Tervaniemi and colleagues (Paavilainen, Saarinen, Tervaniemi, & Näätänen, 1995; Tervaniemi, Maury, & Näätänen, 1994) have found no consistent polarity inversion at leads below the level of the Sylvian fissure with MMN elicited by deviations from an abstract feature. In addition, Gomes and colleagues (Gomes, Bernstein, Ritter, Vaughan, & Miller, 1997) found no polarity reversal at the mastoids in the MMN elicited by irregular feature conjunctions. These findings indicate that although MMN generator structure is quite different from the structure of other ERP components, MMN is not a completely unitary phenomenon generated by a unique neural generator but may be regarded as a family of deviant-related negativities that are mainly generated in auditory areas.

3. MMN is an automatic brain response. MMN may be regarded as automatic or preattentive in the sense that it does not rely on the explicit intention of a person to detect deviants and may be elicited even in the absence of attention. Several studies have shown that the MMN elicited by a frequency change not only is present in the absence of attention but is not modulated by attention even with highly demanding primary tasks such as dichotic listening or visual tracking (Alho, Woods, & Algazi, 1994; Näätänen, Paavilainen, Tiitinen, Jiang, & Alho, 1993; Paavilainen, Tiitinen, Alho, & Näätänen, 1993; for an exception, see Trejo, Ryan-Jones, & Kramer, 1995). The automaticity hypothesis is strengthened by the finding that MMN is elicited in sleeping infants (e.g., Cheour-Luhtanen et al., 1996) and even in coma patients (Kane et al., 1996). However (as will be discussed in a later section), strong automaticity (Hackley, 1993) is not necessarily provided in all circumstances.

4. MMN is sensitive to rather small deviations. In principle, it is assumed that deviants that are close to the perceptual threshold (determined in attend condition, in which subjects discriminate deviants from standards) elicit MMN in ignore condition (in which subjects do not attend to the auditory stimulation). However, MMNs to such tiny deviants are rather small in amplitude and may (because of EEG background activity) hardly be visible in typical MMN experiments in which about 150–200 deviant responses are collected. Lang and colleagues estimated that about 10,000 deviant responses need to be averaged in order to resolve an MMN of about 0.3 μV (Lang et al., 1995). Nevertheless, pitch changes of only 2% for sinusoidal tones (Tiitinen, May, Reinikainen, & Näätänen, 1994) and only 1% for harmonic complex tones (Tervaniemi, Schröger, & Näätänen, 1997) have been found to elicit reliable MMN (measured in reading subjects) at a group level.

5. MMN is related to auditory sensory memory. The memory traces for the repetitive stimulus features underlying the elicitation of MMN reveal properties typical for the so-called long (Cowan, 1984) or synthesized (Massaro, 1975) auditory sensory store. That is, the memory traces underlying MMN last about 10 sec (Sams, Hari, Rif, & Knuutila, 1993), they may contain more than one item (Winkler, Paavilainen, & Näätänen, 1992), they represent the temporal structure of a sound pattern (Winkler & Schröger, 1995), and they are sensitive to backward masking (Winkler, Reinikainen, & Näätänen, 1993). As demonstrated by Winkler and Näätänen (1995), MMN may also tap into the functioning of the short auditory store, which lasts about 100–300 msec. In this experiment, MMN was impaired when the deviant stimulus was masked by a closely succeeding stimulus, although a memory trace for the standard stimulus has been established.

6. MMN is highly correlated with behavioral discrimination performance. A number of studies have revealed that the latency and amplitude of MMN measured in ignore condition are correlated with behavioral discrimination performance measured in attend condition (e.g., Lang, Nyrke, Ek, Aaltonen, Raimo, & Näätänen, 1990; Näätänen, Schröger, Karakas, Tervaniemi, & Paavilainen, 1993; Novak, Ritter, Vaughan, & Wiznitzer, 1990; Paavilainen, Jiang, Lavikainen, & Näätänen, 1993; Tiitinen et al., 1994; Winkler et al., 1993). More specifically, with an increasing physical difference between the deviant and the standard, MMN latency and reaction time are decreased, and MMN amplitude as well as hit rate is increased. This suggests that the neural traces underlying MMN create the informational basis for conscious deviant detection. More-

over, it has been found that both the behavioral distraction caused by task-irrelevant deviants and MMN amplitude increase with increasing difference between the standard and deviant (Schröger, 1996c).

TECHNICAL ISSUES

One can easily look for "paradigmatic" MMN studies published in the literature, in which the basic information regarding stimulus presentation, EEG recording, data analysis, and parametrization can be found for various purposes. There exist also a few papers containing general considerations of these practical issues of MMN measurement (e.g., Kraus, McGee, Carrell, & Sharma, 1995; Kurtzberg, Vaughan, Kreuzer, & Fliegler, 1995; Lang et al., 1995). This section provides additional remarks on the measurement of MMN which may be helpful for recording and analyzing MMN.

Recording

Electrodes. There is no general solution for the question of how many electrodes to use. This depends, for example, on whether or not one wishes to analyze MMN with topographic tools, and (in case one plans to use such tools) on which particular tool and which special algorithm are chosen. Nevertheless, for measuring and identifying MMN, at least electrodes at Fz, Cz, Pz, and mastoids, and two lateralized electrodes placed over the left and right frontal hemispheres (e.g., F3 and F4, or two electrodes placed at ⅓ of the arc connecting Fz to the left and right mastoids, respectively) are recommended. It is suggested that the reference electrode be placed at the nose (see, e.g., Näätänen, 1992). With this electrode montage, the frontocentral, often (but not always) right-preponderant, distribution and mastoid polarity inversion of MMN can be checked. In this case, MMN (which usually inverts polarity at the mastoids) can be distinguished from N2b (which does not invert polarity at the mastoids). N2b is a component that is elicited in active oddball paradigms, in which the subject is asked to detect occasionally presented target stimuli among a series of standard stimuli. However, although polarity reversal at the mastoids may be helpful for identifying MMN, it should be stated that this mastoid reversal is mainly obtained with changes in first-order features (such as frequency or location) and may be absent with deviations in higher order features (Gomes, Bernstein, et al., 1997; Paavilainen et al., 1995; Tervaniemi et al., 1994). These findings indicate that polarity reversal of the MMN is not necessarily a criterion for identifying MMN. However, in the absence of polarity reversal, the presence of genuine MMN should be carefuly discussed. To avoid contamination from eye movements, EOG must also be measured.

Filter settings. Since the duration of MMN quickly reaches a plateau with increasing physical separation between the standard and the deviant which does not exceed 150 msec (Tiitinen et al., 1994), a low-pass filter of about 25 Hz can be applied to the averaged data to get rid of high-frequency activity without affecting the MMN.

Delineating MMN. Usually, MMN is measured from the difference wave in which the ERP elicited by the standard is subtracted from the ERP elicited by the deviant. In most studies, all responses to the deviant and to the standard are averaged into the corresponding ERPs. However, Csépe and colleagues (Csépe, Pantev, Hoke, Hampson, & Ross, 1992) have shown that the magnetoencephalographically measured MMN is not affected if it is delineated by (instead of averaging all responses to the standard) taking only the standards preceding a deviant into the standard ERP. The finding according to which a reduced MMN may be elicited by the standard immediately following the deviant suggests that one exclude those standards from the analysis which follow a deviant (Nousak, Deacon, Ritter, & Vaughan, 1996; Sams, Alho, & Näätänen, 1984). Moreover, Sams et al. (1984) found that the MMN elicited by the second of two successive deviants is about half the amplitude of MMN to the first deviant. This suggests that one must construct stimulus sequences in such a way that a deviant cannot be preceded by a deviant. However, MMN to the second of two successive deviants is not reduced when the two deviants differ from the standard in different stimulus dimensions (Nousak et al., 1996). When MMN is close to noise level, it can be helpful to rereference frontocentrally measured MMN (e.g., Fz or R1) against MMN recorded from the mastoids. This increases the amplitude of MMN and, therefore, increases the signal-to-noise ratio. A very interesting idea for delineating MMN with short interstimulus intervals has recently been proposed by Buch Lund and co-workers (Buch Lund, Ilmoniemi, & Sinkkonen, 1997). They suggested that one first subtract each preceding standard response (epoch) from the corresponding deviant response (epoch) and then average these subtractions. This approach reveals the advantage that no explicit baseline correction is needed. However, it requires a large number of deviant (and, therefore, standard) trials for a sufficient signal-to-noise ratio to be provided.

It should be mentioned that the deviant − standard ERP subtraction procedure assumes that the other ERP components do not depend on the difference between deviant and standard stimuli. This is not always the case, however. If deviants and standards are, for example, different in frequency or in location, feature-specific or location-specific exogeneous ERP components such as the frequency-specific and the location-specific N1 may be affected. Accordingly, employing decrements in stimulus duration or reduction in stimulus intensity as deviations may result in smaller exogeneous components. These effects may artificially increase or decrease the MMN response. Moreover, the interpretation of MMN as an indicator of a memory comparison process may be questioned in such cases. In a later section, a technique will be provided that is suited for ascertaining memory-related enhancements in deviance-related negativites.

Parametrization

MMN amplitude. In most studies, the MMN amplitude is defined as the average of the mean amplitude of the individual difference waves in a particular time window. This time window is either fixed a priori according to specific knowledge about the latency of MMN that has to be expected in a particular experimental setting, or chosen a posteriori around the peak latency of the grand average. The duration of this measurement window varies between 25 and 100 msec. Sometimes, the peak amplitude of the individual differences waves is taken as a measure for the MMN amplitude. This approach carries with it two disadvantages. First, peak amplitudes are more sensitive to noise than are mean amplitudes. Second, the determination of the peak amplitude for individual difference waves may be difficult in the case of noisy data and in the case of multipeaked difference waves (both of which cases are very common).

MMN latency. The MMN latency is usually determined as the mean of the individual peak latencies. To determine the peak latency in individual difference waves may be difficult in the case of noisy data or multipeaked difference waves. The measurement of MMN peak and MMN latency may be improved by visual scoring since distributional information (e.g., polarity reversal or right-hemispheric preponderance) can easily be taken into account by visual inspection. However, although this approach may be reasonable in some instances, it (1) requires experience and (2) is not objective. An alternative method for determining the latency has been introduced by Pekkonen and co-workers (Pekkonen, Jousmäki, Partanen, & Karhu, 1993). They employed area measurements for MMN amplitude and defined MMN latency as the value that divides the MMN area in two equal parts in the time window from 100 to 200 msec. Rather sophisticated methods for optimizing the measurement of the amplitude and latency of MMN are currently being developed by Buch Lund et al. (1997).

Statistical test. The presence of MMN is usually determined via testing the mean amplitude against zero level by means of Student's *t* test. However, as in the case of any other ERP parameters, more sophisticated and more appropriate methods (such as standard nonparametric tests or randomization tests) are easily available (see, e.g., Blair & Karniski, 1993; Guthrie & Buchwald, 1991). Since many MMN studies have been published from which empirical estimates of the effect sizes can be taken, it is possible to perform a posteriori power calculations (for a proper application in the case of the P3 wave, see, e.g., Naumann, Bartussek, Diedrich, & Laufer, 1992). This information is important for interpreting nonsignificant results.

METHODOLOGICAL ISSUES

In this section, various factors determining MMN will be reviewed. Knowledge about the influence of particular experimental settings and stimulus parameters on MMN may be useful for designing appropriate MMN experiments. This section focuses mainly on aspects that have not yet been included in previous reviews (e.g., Kraus et al., 1995; Kurtzberg et al., 1995; Lang et al., 1995; Näätänen, 1992).

Stimulus Presentation

Paradigm. Usually, MMN is obtained in passive oddball paradigms employing a low-probability deviant and a high-probability standard sound presented in pseudorandom order (Figure 1). However, random presentation is not a prerequisite to eliciting MMN. Scherg et al. (1989) reported that MMN was not impaired when the occurrence of deviants could be predicted. In their experiment, MMN elicited in a situation in which every fifth stimulus was a deviant was not affected as compared with a situation in which the occurrence of a deviant was not predictable. In other experiments, stimuli were not presented in random order but there were trains of stimuli separated by long silent intertrain intervals (Cowan, Winkler, Teder, & Näätänen, 1993; Grau, Escera, Yago, & Polo, 1997; Schröger & Wolff, 1997b; Winkler, Schröger, & Cowan, 1997). The trains consisted of about 4–12 tones in which deviants could occur only at particular positions within the train (e.g., only at the last position). MMN was elicited in these paradigms too. It is also not necessary to have a repetitive, constant standard stimulus but only to keep a single stimulus feature (such as frequency) constant, while other features of the sound (such as intensity, duration, envelope, function, and harmonic structure) are varied from trial to trial. If the constant feature is changed, MMN is elicited (Gomes, Ritter, & Vaughan, 1995; Huotilainen et al., 1993). Finally, MMN is also elicited by changes in continuous stimulation; that is, a silent interval between successive stimuli is not required (Pihko, Leppäsaari, & Lyytinen, 1995; Schröger, Paavilainen, & Näätänen, 1994; Winkler & Schröger, 1995).

Type of deviation. As mentioned above, MMN can be elicited by almost any stimulus deviation, such as frequency (see, e.g., Sams, Paavilainen, Alho, & Näätänen, 1985), intensity (e.g., Näätänen, Paavilainen, Alho, Reinkainen, & Sams, 1987b), duration (e.g., Näätänen, Paavilainen, & Reinikainen, 1989), rise time (e.g., Lyytinen, Blomberg, & Näätänen, 1992), location in free-field condition (e.g., Paavilainen, Karlsson, Reinikainen, & Näätänen, 1989), location when manipulated via interaural time and level differences in ear-phone stimulation (e.g., Schröger, 1996b), and timing of stimulus presentation (e.g., Ford & Hillyard, 1981). With more complex tones such as sequences of alternating high- and low-pitch tones (Nordby, Roth, & Pfefferbaum, 1988), tonal patterns consisting of several, concatenated sinusoidal tones (e.g., Schröger, Näätänen, & Paavilainen, 1992), or harmonic complex tones (e.g., Alho et al., 1996), changes of single elements within the complex sounds elicit MMN. MMN is also elicited by changes in synthetically produced piano tones (see, e.g., Tervaniemi, Alho, Paavilainen, Sams, & Näätänen, 1993) or speech sounds (e.g., Aaltonen, Niemi, Nyrke, & Tuhkanen, 1987).

Usually, changes in first-order stimulus features elicit larger MMN than do changes in higher order features. Moreover, MMN elicited by a change affecting the whole stimulus is larger than MMN to a change of a single segment in a temporally extended stimulus consisting of several segments. When a deviant is different from the standard in more than one stimulus dimension, MMN is larger than when it differs in one feature only. In several studies, the MMN elicited by a two-dimensional change was almost equal to the sum of the MMNs elicited by the corresponding one-dimensional deviants. This has been found for MMN to a simultaneous change in frequency and interstimulus interval (ISI), frequency and duration, frequency and location, duration and intensity, interaural time and interaural level differences (Kurtzberg, Kreuzer, Fliegler, Ritter, & Vaughan, 1997; Levänen, Hari, McEvoy, & Sams, 1993; Schröger, 1995, 1996b; Schröger, Tervaniemi, Winkler, Wolff, & Näätänen, 1997; Wolff & Schröger, 1995). Unlike the amplitude, the latency of MMNs to two-dimensional deviants was not different from that of the MMNs to the one-dimensional deviants. This indicates that multidimensional deviants can be employed to increase amplitude of MMN. A related finding has been reported by Tervaniemi et al. (1993). In their study, identical frequency changes in harmonically complex tones (piano tones including harmonics) have been found to elicit larger MMN than do such changes in simple tones. Probably MMN to these more complex tones was composed of contributions from several mismatch processes being performed in parallel for all harmonics. Currently, the research unit around Risto Näätänen is optimizing the parameters that are suited to yield the most reliable MMN in individuals (Joutsiniemi et al., 1997).

Amount of deviation. An increase in the frequency difference between deviant and standard results in an increase in amplitude and in a decrease in latency of MMN, although MMN amplitude is saturated earlier than MMN latency (see, e.g., Sams et al., 1985; Tiitinen et al., 1994). Except for the difference in saturation of MMN amplitude and MMN latency, similar relationships between parameters of MMN and increase in the amount of deviation have been reported for the location MMN (Paavilainen et al., 1989). On the basis of these findings one may be tempted to conclude that large deviant − standard differences are optimal for obtaining maximal MMN. With large deviants, however, MMN may be confounded by differential refractoriness effects on the N1 component to standards and deviants (Näätänen & Picton, 1987; Scherg et al., 1989). Therefore, it is recommended that the difference be rather small if one wants to measure "pure" MMN. Deouell and Bentin (1997) suggested that one choose the amount of deviation relative to the subject's individual psychophysical discrimination threshold.

Stimulus Parameters

Stimulus duration. Duration can be rather short (i.e., 50 msec or even less) if one intends to elicit full-amplitude frequency MMN (e.g., Paavilainen et al., 1993). An exception to this is the MMN elicited by changes in the missing fundamental frequency, where longer stimulus duration is required (Winkler, Tervaniemi, & Näätänen, 1997). In this study, no clear MMN was elicited when stimulus duration was 150 msec, whereas clear MMN was visible with a stimulus duration of 500 msec. The MMN for an intensity change also increases as a function of stimulus duration for durations from 4 to 300 msec (Paavilainen et al., 1993). This decrease in MMN with decreasing stimulus duration is probably due to a deteriorated representation of the standard with shorter stimulus durations. Thus, in order to enable the elicitation of MMN, stimulus duration has to be sufficiently long so that an appropriate feature representation of the standard stimulus can be established.

Stimulus intensity. MMN can be elicited even with weak stimulus intensity. Provided that the deviant and the standard are clearly discernible, 30 dB SPL can be sufficient to obtain frequency MMN (Schröger, 1994). However, MMN for an intensity change is modulated by the absolute loudness of stimulation (Schröger, 1996a). Moreover, in contrast to MMN for changes in frequency and duration, MMN elicited by an intensity deviation depends on whether stimuli are presented monaurally or binaurally (Lavikainen, Tiitinen, May, & Näätänen, 1997). The influence of stimulus intensity on MMN elicited by other feature changes has not yet been determined.

Interstimulus interval (ISI). Frequency MMN is relatively stable with offset-to-onset ISIs ranging from about 0.3 to 10 sec (e.g., Böttcher-Gandor & Ullsperger, 1992; Czigler, Cibra, & Csontos, 1992; Imada, Hari, Loveless, McEvoy, & Sams, 1993). It can be elicited with ISIs as short as 26 msec (Näätänen, Paavilainen, Alho, Reinkainen, & Sams, 1987a). However, with the usual oddball paradigm, shortening the ISI results in a decrease of the interdeviant interval. If this is too short, MMN may be reduced in amplitude. MMN was not reduced with an ISI of 26 msec, when the effect of reducing the interdeviant interval by shortening the ISI was controlled. When this effect is not taken into account, full-amplitude frequency MMN is still elicited with ISIs of 350 msec (Schröger, 1996a). Since short ISIs result in short experimental sessions, the ISI should be as short as possible. It has to be considered that most of these findings were obtained with the mismatch response elicited by a frequency deviant. MMN for other feature changes may behave in a different way. For example, intensity MMN has been found to be more sensitive to variations in ISI (Schröger, 1996a; Schröger & Winkler, 1995), whereas location MMN is not reduced with an ISI as short as 10 msec (Schröger & Wolff, 1997b).

The maximal ISI where MMN is still elicited is about 10 sec (Sams et al., 1993), although this limit may be higher for single individuals. However, it has to be considered

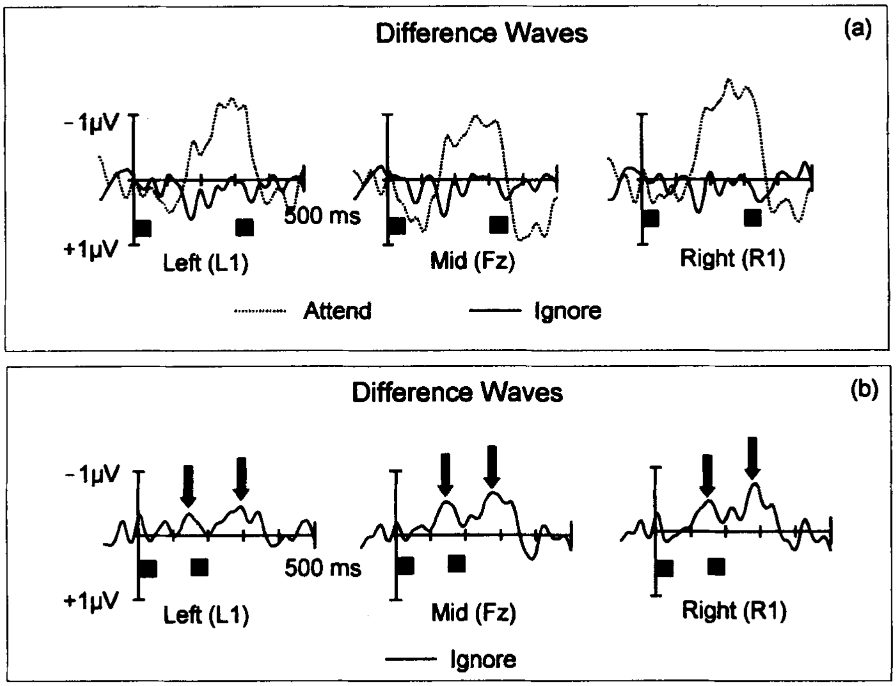

Figure 3. Deviant − standard difference waves from two experiments; in order to maximize MMN, data were rereferenced against the left mastoid. (a) Standard tone pairs consisted of a tone slightly lateralized to one side followed by a tone slightly lateralized to the opposite side. Intertone interval was 250 msec. The deviant consisted in an order reversal within a tone pair. Distinct MMN-like effects were obtained in the attend condition (dotted lines) but not in the ignore condition (continuous lines), in which subjects were reading in a book. The black squares indicate the first and the second tone within the pair (Schröger & Wolff, unpublished data). (b) Same as the ignore condition in panel a, except that the intertone interval was 100 msec. Distinct MMN was elicited by the order reversal in reading subjects. MMNs elicited by the first and second tone within a pair are indicated by black arrows (adapted from Schröger & Wolff, 1997a).

that the critical lower limit of the maximal ISI still eliciting full-amplitude MMN can be shorter for particular groups of subjects, such as children (Gomes, Sussman, et al., 1997), elderly people (Pekkonen et al., 1993; see, however, Czigler et al., 1992), Alzheimer's patients (Pekkonen, Jousmäki, Könönen, Reinikainen, & Partanen, 1994), and schizophrenics (Javitt, Doneshka, Grochowski, & Ritter, 1995; Shutara et al., 1996).

Probability of a deviant. The probability of the deviant stimulus is inversely related to the amplitude of MMN (Näätänen, 1992). When one is using the oddball paradigm with random presentation of the deviant, the probability of a deviant should not exceed .15 in order to elicit a reliable MMN. In most studies, .10 is taken as the probability of a deviant. However, not only a deviant that is preceded by several standards but also a standard that is preceded by several deviants elicits MMN (see, e.g., Winkler, Karmos, & Näätänen, 1996). That is, not the global but the local probability of a stimulus change determines the elicitation of MMN. Because at least 100–200 responses to the deviant have to be averaged for each subject for measuring MMN (see above), the recording time becomes rather long when MMNs to several types of deviants have to be determined. A technique for increasing the probability of a deviant to .30 and still eliciting an MMN as large as that obtained with a deviant probability of .10 has been provided by Deacon and colleagues (Deacon, Nousak, Pilotti, Ritter, & Yang, in press; Deacon, Pilotti, & Tinsley, 1995). They have shown that when three different deviants were presented within a block, each having a probability of .10 (resulting in an overall probability for a deviant of .30), the MMN was the same as it was when three blocks were run (one block for each deviant) in which the probability for a deviant was .10. This reduces recording time to one third of that what would have been required if for each deviant a separate block with deviant probability of .10 would have been run.

CONCEPTUAL ISSUES

The following section focuses on selected problems encountered when one wants to interpret MMN in a particular way. Moreover, it offers solutions which may be helpful in the resolution of some of these problems. The three issues to be discussed relate to the automaticity assumption, the memory comparison assumption, and the assumption that MMN is a stable measure in the sense that MMN measurements in an individual in repeated sessions will yield comparable results. Of course, it has already been established that these assumptions are valid in many circumstances. However, there is no guarantee that they hold in any particular experimental setting. One should thus be sensitive to these problems and should learn to develop ways to make sure that the assumptions hold.

MMN Is an Automatic Brain Response

As mentioned above, it has been shown in numerous studies that MMN is automatic in the sense that it is elicited even in the absence of attention. In the case of the frequency MMN, there is even evidence that it is not prone to attentional modulations. This notion is also supported by the finding that MMN has been observed in sleeping infants (see, e.g., Cheour-Luhtanen et al., 1996), during stage 2 sleep preceding a K-complex in adults (e.g., Loewy, Campbell, & Bastien, 1996; Sallinen, Kaartinen, & Lyytinen, 1994), in coma patients (Kane et al., 1996), and in sleeping and anesthetized cats (e.g., Csépe et al., 1987). All of these studies were done with spectral changes in tonal or speech stimuli. MMN to changes in the duration of a sound also seems to be highly insensitive to the nature of the primary task (Lißmann, Klugman, Gruzelier, & Baldeweg, 1997).

However, this strong form of automaticity is not necessarily fulfilled for MMN elicited by changes in other features (cf. Hackley, 1993). For example, although MMN to an intensity change is also elicited when subjects are reading during stimulus presentation, it has been found that it can be largely reduced when attention is strongly focused to a demanding primary task (Näätänen, Paavilainen, et al., 1993; Woldorff, Hackley, & Hillyard, 1991). Similarly, Alain and Woods (1997) found a distinct attenuation of MMN to deviations in spectro-temporal patterns in dichotic listening tasks—that is, when the subjects' attention was strongly focused on the contralateral ear. Corroborating evidence was obtained in an experiment done by Schröger and Wolff (1997c). In this experiment, subjects received tone pairs consisting of a tone located slightly to one side followed by a tone being located slightly to the opposite side. The tones within a pair were separated by a silent interval of 250 msec. An occasional order reversal elicited MMN (indicating the existence of a memory trace for the spatiotemporal information within the tone pairs) only when subjects attended to the stimulation but not when they were reading (Figure 3a). It should be mentioned that distinct MMN to these order reversals was elicited in the reading condition when the intertone interval was shortened to 100 msec (Figure 3b). This finding indicates that minor changes in the experimental setting (such as the increase in intertone interval from 100 to 250 msec) can deteriorate MMN.

In sum, these results suggest (1) that the automaticity of MMN is dependent on the feature being changed and (2) that it may be regarded as attention independent only with regard to a specific primary task that has been employed, and (3) that presumably negligible changes in the stimulus parameters may modulate MMN. Thus, if one wants to ascertain that MMN elicited by a particular change represents a completely automatic brain response, the use of a highly demanding primary task has to be recommended. Nevertheless, a reading condition will be adequate for most purposes, especially when it is sufficient to demonstrate that the MMN is weakly automatic in the sense that it represents an obligatory response which may be elicited without or even despite the subject's attention (Hackley, 1993). A post hoc method for assessing whether subjects have attended to the stimulation or not is to determine whether N2b and P3 components are elicited in addition to MMN. Except with very large deviants, they are usually only observed when subjects attend to the stimuli.

MMN Is the Result of a Memory Comparison Process

There is a large body of evidence demonstrating that MMN is generated by a preattentive process detecting a difference between the neural representation of the actual stimulus and the memory trace of the standard stimulus (see above). That is, the occurrence of MMN implicates the existence of a memory trace for the standard and a memory comparison between representations of the standard and the deviant. However, the elicitation of MMN can, in principle, also be explained by the "refractoriness hypothesis." According to this hypothesis, deviance-related ERP effects are due to the fact that neural populations specifically responding to the feature of the standard are more refractory than those being specific to the deviant. Therefore, more neural activity can be expected when a deviant is presented than when a standard is presented. This explanation can usually not be applied to MMN for changes in higher order features such as order reversal of segments within a tonal pattern tones (see, e.g., Winkler & Schröger, 1995), unless one believes that there exist specialized neurons for any kind of higher order feature that are able to elicit MMN. However, for particular first-order features, the refractoriness hypothesis seems to be valid. This is indicated, for example, by the finding that the exogoneous N1 reveals frequency and location specifity (e.g., R. A. Butler, 1968, 1972; McEvoy, Hari, Imada, & Sams, 1993; Näätänen et al., 1988). Usually, it is believed that the influence of this differential state of refratoriness is crucial for the memory-comparison interpretation of MMN only when large deviations are employed (Scherg et al., 1989; Tiitinen et al., 1994). Nevertheless, to make sure that MMN elicited by a deviation from a first-order feature obtained in a particular experimental setting cannot be sufficiently explained by the refractoriness hypothesis, a proper control condition may be required.

An easy technique for implementing such a control condition has recently been proposed by Schröger and

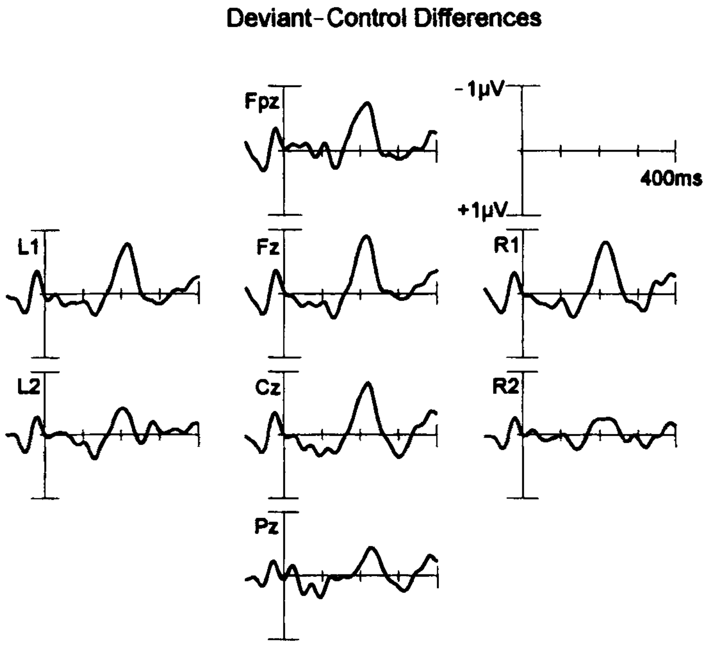

Figure 4. Deviant − control difference waves. The ERPs to the deviant stimulus were obtained in oddball blocks. In half of the oddball blocks, the deviant sound (p = .14) was lateralized by an interaural time difference (ITD) of .7 msec, whereas the standard revealed an ITD of .4 msec only. In the other half of the oddball blocks, deviants had an ITD of −.7 msec and standards of −.4 msec. The ERPs to the control stimulus were obtained in a condition in which tones revealed ITDs of −.7, −.4, −.2, .0, .2, .4, and .7 msec with equal probability. Only ERPs to stimuli revealing an ITD of −.7 or .7 msec were averaged into the control ERPs. In order to maximize MMN, data were rereferenced against the left mastoid. The subjects were reading in a book during stimulus presentation (adapted from Schröger & Wolff, 1996).

Wolff (1996). They suggested that one collect data not only in the oddball condition in which frequent standard and infrequent deviant stimuli are presented. There should be also a condition in which stimuli vary with respect to the dimension on which the standard and deviant differ in such a way that the state or refractoriness of neural populations being specific to the control stimulus (which has to be physically identical to the deviant stimulus) is comparable to that of neural populations being responsive to the deviant stimulus presented in oddball blocks (cf. Näätänen & Alho, 1997; Schröger 1997a). In the experiment reported by Schröger and Wolff (1996), the state of refractoriness of neural populations being specific to location was controlled for in the following way. In oddball blocks, deviants (p = .14) had an interaural time difference (ITD) of −0.7 msec; the input to the left ear was presented slightly earlier than the input to the right ear, resulting in a subjective lateralization in the azimuth plane of about −80°. Standards had an ITD of −0.4 msec, resulting in a lateralization of about −50°. In control blocks, seven different stimuli were presented with equal probability (p = .14 each). The ITDs were −0.7, −0.4, −0.2, 0.0, +0.2, +0.4, and +0.7 msec (causing subjective lateralizations from about −80° to +80°). That is, the sound revealing an ITD of −0.7 msec (i.e., the control stimulus) had the same probability as in oddball blocks. Moreover, all the other sounds revealed equal or larger azimuth distances to the control stimulus than did standards to the deviant. Therefore, the state of refractoriness cannot be higher for the control stimulus than for the deviant. If there were still deviant-related negativities in the deviant − control comparison, they can only be explained with the memory comparison hypothesis. Indeed, these difference waves revealed distinct MMN (Figure 4).

It should be mentioned that the "true" MMN is even underestimated in the deviant − control comparison, since it is likely that less location-specific refractoriness occurred with control stimuli than with deviant stimuli (because of larger azimuth distances between control and "noncontrol" stimuli in control blocks in comparison with the azimuth distances between deviants and standards in oddball blocks). Moreover, it has been shown by Winkler and

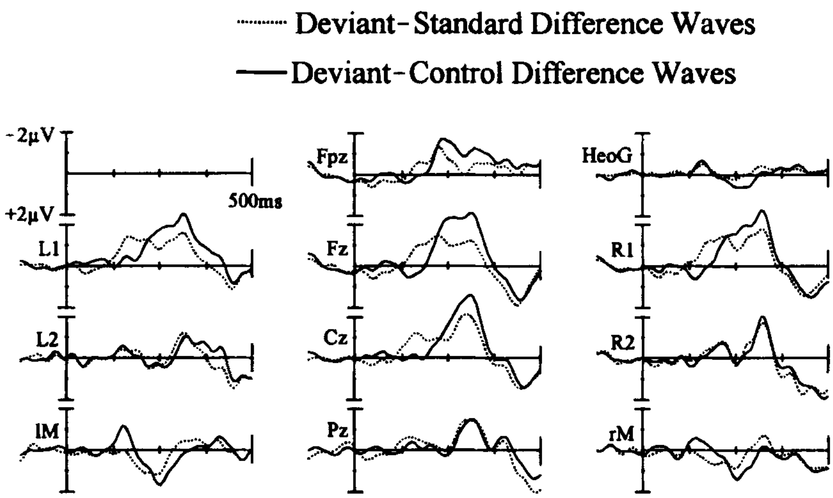

Figure 5. Deviant − standard (dotted) and deviant − control (continuous) difference waves. Deviants presented in oddball blocks had a frequency of 700 Hz ($p = .10$) and standards had a frequency of 750 Hz; in half of the blocks, the roles of deviants and standards were reversed. In control blocks, frequencies could be 700, 750, 800, 900, 950, 1000, 1050, 1100, or 1200 Hz ($p = .10$ each). Distinct MMN can be seen with each subtraction method (data from an experiment described in Schröger, 1996d).

co-workers that extreme substandards may elicit an MMN of their own (Winkler et al., 1990). Indeed, stimuli presented in control blocks with ITDs of ± 700 µsec representing extreme substandards (they caused the largest lateralizations) elicited small MMN.

In a recent experiment (Schröger, 1996d), the technique of controlling for refractoriness effects has been adopted for the frequency MMN. In separate oddball blocks, the frequency of the standard and deviant ($p = .10$), respectively, were 700 and 750 Hz (the role of standard and deviant being exchanged between blocks). In control blocks, the frequency was 700, 750, 800, 900, 950, 1000, 1050, 1100, or 1200 Hz ($p = .10$ each). Again, the deviant − control comparison revealed distinct MMN which cannot be due to differential states of refractoriness (Figure 5).

MMN Is a Stable Measure

For many clinical applications, it has to be assumed that MMN is a stable measure which can track the state of the central auditory system during repeated measures. Such repeated measurements may be useful for monitoring the restoration in hearing in cochlear implant users (see, e.g., Ponton & Don, 1995) or for predicting the return of consciousness in coma patients (e.g., Kane et al., 1996). In several studies, the stability or replicability of MMN at a group level has been studied by performing *t* tests or analyses of variance (ANOVAs) between the MMN amplitudes measured in a test and in a retest session, whereas stability of replicability at an individual level has been investigated by calculating Pearson's product-moment correlation coefficient between the MMNs obtained in the two sessions (Escera & Grau, 1996; Pekkonen, Rinne, & Näätänen, 1995; Uwer, Minow, & Suchodoletz, 1996). In these studies, *t* tests and ANOVAs did not yield significant results. The absence of significant differences in the MMNs from the two sessions was interpreted as demonstrating that MMN has good replicability at group level. However, without information about the β error probability (i.e., the probability of falsely accepting the null hypothesis) the validity of this conclusion is not warranted. Furthermore, depending on electrode position and experimental setting, these studies yielded either moderate correlation coefficients of about 0.5 reaching a significance level of .05 or rather small, nonsignificant correlations of about 0.1. As suggested by Escera and Grau (1996), it seems likely that the correlation could be improved by increasing the number of summations.

Although these studies yielded partly promising results regarding the stability of MMN at an individual level, Pearson's product-moment correlation coefficient is not optimal for assessing all aspects of test–retest stability or replicability. As can be seen easily, the computation of correlation coefficient $r_{Y^{(1)},\,Y^{(2)}}$ between two vectors $Y^{(1)}$ and $Y^{(2)}$ containing the individual MMNs of Sessions 1 and 2 gets rid of differences in means and variances:

$$r = \sqrt{\sum_{i=1}^{n} \frac{\left(Y_i^{(1)} - \overline{Y^{(1)}}\right)\left(Y_i^{(2)} - \overline{Y^{(2)}}\right)}{\sum_{i=1}^{n}\left(Y_i^{(1)} - \overline{Y^{(1)}}\right)^2\left(Y_i^{(2)} - \overline{Y^{(2)}}\right)^2}},$$

where n is the number of subjects, $Y_i^{(1)}$ and $Y_i^{(2)}$ are the MMNs of subject i measured in the two sessions, an $\overline{Y^{(1)}}$ and $\overline{Y^{(2)}}$ are their respective means. That is, if the profiles

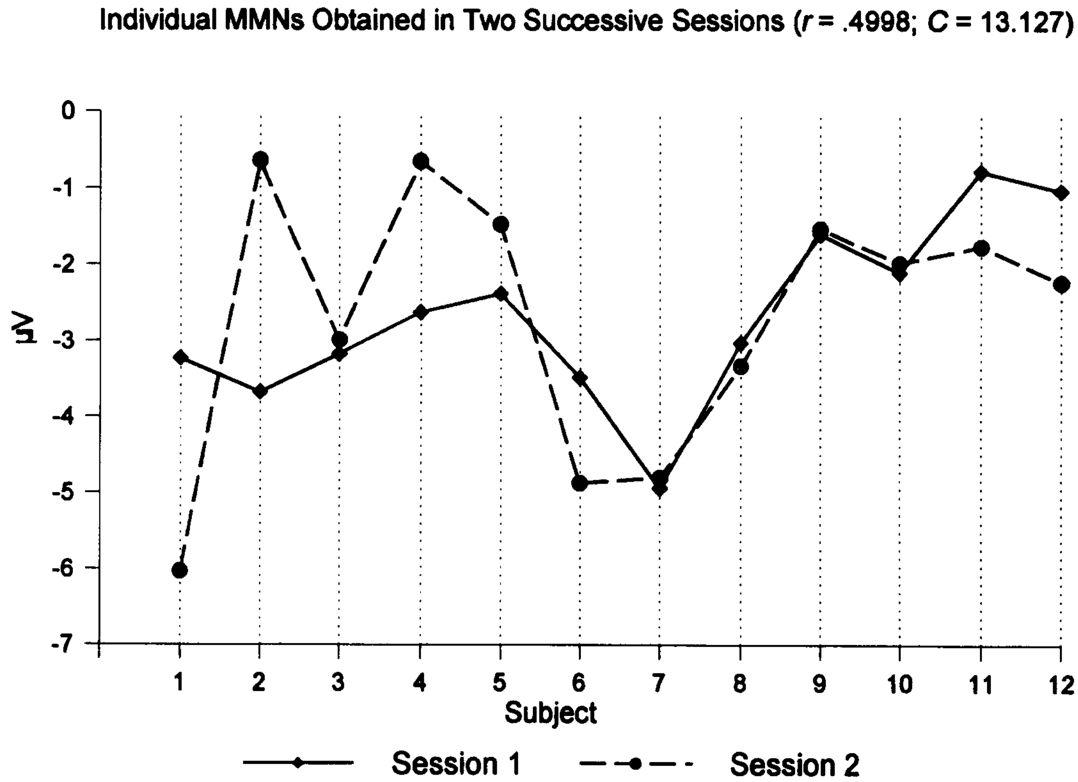

Figure 6. Individual mean MMNs from 12 subjects obtained before (Session 1, circles) and after (Session 2, diamonds) a coffee break. The product-moment correlation coefficient r is .4998. The city-block distance C is 13.127. Data were rereferenced against the left mastoid. The subjects were reading during stimulus presentation (Schröger & Wolff, 1997c).

of the MMNs are highly similar but the means largely differ between sessions (MMN may, e.g., increase because of learning or decrease because of habituation), the correlation coefficient will indicate a high individual replicability. On the other hand, if all the individuals show high similarity of MMN within and between sessions, the correlation coefficient will indicate low individual replicability. One may, for example, think about a sample of "perfect" subjects each eliciting very high MMN in each session, which can result in very small variances of $Y^{(1)}$ and $Y^{(2)}$ and which might, in turn, prevent a high correlation. For these reasons, additional coefficents are needed that deliver information about aspects of replicability or stability that are not covered by the correlation coefficient.

A more direct way to express stability or replicability between two measurements would be to (1) compute for each subject the difference of the MMNs measured in two sessions, (2) take the absolute value of the difference, and (3) sum the values over the number of subjects. If the resulting number is small, similar MMN values have been obtained in the two sessions for each subject; this, in turn, may be interpreted as indicating that the MMN is a stable or replicable measure. If, on the other hand, this coefficient is large, rather different MMNs have been obtained in the two sessions; that is, MMN values have not been successfully replicated on an individual level. The proposed coefficient is known as the city-block distance (cf. Schröger, Rauh, & Schubö, 1993). A city-block distance C between two variables is calculated as

$$C = \sum_{i=1}^{n} X_i,$$

where $X_i = |Y_i^{(1)} - Y_i^{(2)}|$. That is, C represents the sum of absolute values of the differences of the MMNs measured in the two sessions over all subjects. It is highly intuitive for the purposes of expressing stability on an individual level and reveals a number of features not warranted by the correlation coefficient often employed as measure of stability. The city-block distance C is a special case of the "Minkowski distances" representing the distance between two vectors in an n-dimensional space spanned by n orthogonal axes:

$${}_nM_r = \left(\sum_{i=1}^{n} X_i^r\right)^{\left(\frac{1}{r}\right)},$$

where n is the number of elements of each vector, r is the exponent of the Minkowski metric, and $X_i = |Y_i^{(1)} - Y_i^{(2)}|$ with $Y_i^{(1)}$ and $Y_i^{(2)}$ representing the ith elements of the vectirs $Y^{(1)}$ and $Y^{(2)}$. If r is set to 1, M equals C.

A proper interpretation of a particular value of C requires information about what a "small" and "large" value is. The distribution function of C would deliver the information that is required in order to interpret a particular value of C or to test the statistical significance of such a value. To develop the probability distributions of C, the probability distributions of $Y^{(1)}$ and $Y^{(2)}$ (or of X) have to be known (cf. Schröger et al., 1993). However, in the case of small sample sizes or in the case of unknown distributions of $Y^{(1)}$ and $Y^{(2)}$, a randomization test can be used (e.g., Edgington, 1980). For this purpose, it is suggested that one (1) pool the MMNs from both measurement sessions, resulting in a sample size of $2n$; (2) draw a large number (e.g., 50,000) of random samples from this pool, dividing the data pool in two groups of size n; (3) compute C for each sample; (4) compute the cumulative distribution function of the values of C; and (5) determine the critical value for a given significance level α.

As an empirical example, we reanalyzed an existing data set of one of our Munich MMN experiments. In this experiment, the MMN for a location change was measured in 12 subjects. We computed the individual mean MMNs in the interval from 135 to 185 msec relative to stimulus onset, separately for the data collected before and after the coffee break, resulting in two MMNs for each subject. The individual mean amplitudes are illustrated in Figure 6. The product-moment correlation coefficient between the MMNs obtained in the two "sessions" is .4998 and the city-block distance is 13.127. According to Steps 1–5 described above, we computed the cumulative distribution function of the city-block distance and also that of Pearson's product-moment correlation coefficient. The probability for a correlation of .4998 or higher was .052 (which is very close to the value of .049 that is obtained when the appropriately transformed correlation is tested with Student's t distribution) and the probability for a city-block distance of 13.127 or smaller was .019. That is, the particular correlation and city-block distance of the MMNs are significant or close to significance with an α level of .05, indicating stability of MMN at an individual level in this study.

In contrast to the product-moment correlation coefficient, the city-block distance C does not assume equal expectancies of MMNs in the two sessions. Instead (similar to the t test), this test statistic is also sensitive to systematic differences in means between the two sessions. However, unlike the paired t test or its nonparametric analogues testing for differences in means or medians (such as the Wilcoxon matched pairs test or the randomization test for matched pairs proposed by Conover, 1980, pp. 330ff.), the present test can exhibit dissimilarities between the values obtained in two measurement sessions in situations in which t tests (and corresponding nonparametric tests) would indicate no difference. For example, a data set in which each subject who has a positive score in the first session (e.g., +3) has a corresponding negative score in the second session (e.g., −3) and vice versa has identical means and medians. A paired t test or its nonparametric analogues would "indicate" similar distributions (i.e., mean) between the two samples, whereas the proposed test employing C can detect that the measurements are not stable on an individual level (although their means are equal).

In addition (unlike the t test), the proposed test is constructed to test the similarity in the measurements between two sessions. Unless the β-risk is controlled, the t test is only able to indicate dissimilarity; in the case of a nonsignificant result, one may not infer that there is no difference in means. Moreover, C represents a very simple and intuitive measure of stability. For example, when C is divided by the number of subjects n, the average difference between two sessions is expressed in terms of microvolts. This information can be related to the minimum and maximum MMN obtained in the sample. Finally, the estimation of the probability distribution from the empirical MMNs bears the main advantage of randomization tests; that is, there is no underlying assumption about the distribution of the test statistic. It should be mentioned that the city-block distance may, of course, also be taken as a measure of stability in subsequent recording sessions for other ERP components.

CONCLUSION

So far, it has been shown that MMN may serve as a powerful tool for studying the brain's preattentive auditory functioning. We have considered various aspects of MMN which may be helpful for the design, analysis, and interpretation of future MMN experiments. It should be mentioned, of course, that only a small set of the range of important aspects could be covered in this paper. It is not possible to provide a recipe for how to appropriately measure and interpret MMN in all possible applications. This is mainly due to the fact that most of the problems that we have to deal with are dependent on the particular experimental or clinical questions that we ask. Nevertheless, some pitfalls may hopefully be avoided in the future if one takes into account some of the information provided in this paper.

REFERENCES

Aaltonen, O., Niemi, P., Nyrke, T., & Tuhkanen, M. (1987). Event-related brain potentials and the perception of a phonetic continuum. *Biological Psychology*, **24**, 197-207.

Alain, C., & Woods, D. L. (1997). Attentional modulation of auditory pattern memory as revealed by event-related brain potentials. *Psychophysiology*, **34**, 534-546.

Alho, K., Huotilainen, M., & Näätänen, R. (1995). Are memory traces for simple and complex sounds located in different regions of auditory cortex? Recent MEG studies. In G. Karmos, M. Molnár, V. Csépe, I. Czigler, & J. E. Desmedt (Eds.), *Perspectives of event-related potentials research* (pp. 197-203). Amsterdam: Elsevier.

Alho, K., Tervaniemi, M., Huotilainen, M., Lavikainen, J., Tiitinen, H., Ilmoniemi, R. J., Knuutila, J., & Näätänen, R. (1996). Processing of complex sounds in the human auditory cortex as revealed by magnetic brain responses. *Psychophysiology*, **33**, 369-375.

Alho, K., Woods, D. L., & Algazi, A. (1994). Processing of auditory stimuli during auditory and visual attention as revealed by event-related potentials. *Psychophysiology*, **31**, 469-479.

Alho, K., Woods, D. L., Algazi, A., & Näätänen, R. (1992). Intermodal selective attention: II. Effects of attentional load on processing of auditory and visual stimuli in central space. *Electroencephalography & Clinical Neurophysiology*, **82**, 356-368.

Baudena, P., Halgren, E., Heit, G., & Clarke, J. M. (1995). Intracerebral potentials to rare target and distractor auditory and visual stimuli: III. Frontal cortex. *Electroencephalography & Clinical Neurophysiology*, **94**, 251-264.

Blair, R. C., & Karniski, W. (1993). An alternative method for significance testing of waveform difference potentials. *Psychophysiology*, **30**, 518-524.

Böttcher-Gandor, C., & Ullsperger, P. (1992). Mismatch negativity in event-related potentials to auditory stimuli as a function of varying interstimulus interval. *Psychophysiology*, **29**, 546-550.

Buch Lund, K., Ilmoniemi, R. J., & Sinkkonen, J. (1997, January). *Techniques for optimizing the MMN paradigm and signal analysis techniques*. Paper presented at the 2nd Project Meeting of European COBRAIN Collaboration, Lyon, France.

Butler, R. A. (1968). Effects of changes in stimulus frequency and intensity on habituation of the human vertex potential. *Journal of the Acoustical Society of America*, **44**, 945-950.

Butler, R. A. (1972). The influence of spatial separation of sound sources on the auditory evoked response. *Neuropsychologia*, **10**, 219-225.

Butler, S. R. (1997, January). *MMN and coma*. Paper presented at the 2nd Project Meeting of European COBRAIN Collaboration, Lyon, France.

Cheour-Luhtanen, M., Alho, K., Sainio, K., Rinne, T., Reinikainen, K., Pohjavuori, M., Renlund, M., Aaltonen, O., Eerola, O., & Näätänen, R. (1996). The ontogenetically earliest discriminative response of the human brain. *Psychophysiology*, **33**, 478-481.

Conover, W. C. (1980). *Practical nonparametric statistics*. New York: Wiley.

Cowan, N. (1984). On short and long auditory stores. *Psychological Bulletin*, **96**, 341-370.

Cowan, N., Winkler, I., Teder, W., & Näätänen, R. (1993). Memory prerequisites of mismatch negativity in the auditory event-related potentials (ERP). *Journal of Experimental Psychology: Learning, Memory, & Cognition*, **19**, 909-921.

Csépe, V., Karmos, G., & Molnár, M. (1987). Evoked potential correlates of stimulus deviance during wakefulness and sleep in cat—animal model of mismatch negativity. *Electroencephalography & Clinical Neurophysiology*, **66**, 571-578.

Csépe, V., Pantev, C., Hoke, M., Hampson, S., & Ross, B. (1992). Evoked magnetic responses of the human auditory cortex to minor pitch changes: Localization of the mismatch field. *Electroencephalography & Clinical Neurophysiology*, **84**, 538-548.

Czigler, I., & Csibra, G. (1990). Event-related potentials in a visual discrimination task: Negative brain waves related to attention and detection. *Psychophysiology*, **27**, 669-676.

Czigler, I., Csibra, G., & Csontos, A. (1992). Age and inter-stimulus interval effects on event-related potentials to frequent and infrequent auditory stimuli. *Biological Psychology*, **33**, 195-206.

Deacon, D., Nousak, J. M., Pilotti, M., Ritter, W., & Yang, C. M. (in press). Automatic change detection: Does the auditory system use representations of individual stimulus features or gestalts? *Psychophysiology*.

Deacon, D., Pilotti, M., & Tinsley, C. (1995). Is the preattentive comparison of auditory stimuli affected on the basis of featural or gestalt representations? In G. Karmos, M. Molnár, V. Csépe, I. Czigler, & J. E. Desmedt (Eds.), *Perspectives of event-related potentials research* (pp. 190-196). Amsterdam: Elsevier.

Deouell, L., & Bentin, S. (1997). *The variability of mismatch negativity elicited by equally distinct deviance in different auditory dimensions: A within subject and within block comparison*. Manuscript submitted for publication.

Edgington, E. S. (1980). *Randomization tests*. New York: Dekker.

Escera, C., & Grau, C. (1996). Short-term replicability of the mismatch negativity. *Electroencephalography & Clinical Neurophysiology*, **100**, 549-554.

Ford, J. M., & Hillyard, S. A. (1981). Event-related potentials (ERPs) to interruptions of a steady rhythm. *Psychophysiology*, **18**, 322-330.

Giard, M. H., Lavikainen, J., Reinikainen, K., Perrin, F., Bertrand, O., Pernier, J., & Näätänen, R. (1995). Separate representations of stimulus frequency, intensity, and duration in auditory sensory memory. *Journal of Cognitive Neuroscience*, **7**, 133-143.

Giard, M.-H., Perrin, F., Pernier, J., & Bouchet, P. (1990). Brain generators implicated in the processing of auditory stimulus deviants: A topograhic event-related potential study. *Psychophysiology*, **27**, 627-640.

Gomes, H., Bernstein, R., Ritter, W., Vaughan, H. G., Jr., & Miller, J. (1997). Storage of feature conjunctions in transient auditory memory. *Psychophysiology*, **34**, 712-716.

Gomes, H., Ritter, W., & Vaughan, H. G., Jr. (1995). The nature of pre-attentive storage in the auditory system. *Journal of Cognitive Neuroscience*, **7**, 81-94.

Gomes, H., Sussman, E., Ritter, W., Kurtzberg, D., Cowan, N., & Vaughan, H. G., Jr. (1997). *Electrophysiological evidence of developmental changes in the duration of auditory sensory memory*. Manuscript submitted for publication.

Grau, C., Escera, C., Yago, E., & Polo, M. D. (1997). *Mismatch negativity and the clinical evaluation of auditory sensory memory*. Manuscript in preparation.

Guthrie, D., & Buchwald, J. S. (1991). Significance testing of difference potentials. *Psychophysiology*, **28**, 240-244.

Hackley, S. A. (1993). An evaluation of the automaticity of sensory processing using event-related potentials and brain-stem reflexes. *Psychophysiology*, **5**, 415-428.

Halgren, E., Baudena, P., Clarke, J. M., Heit, G., Liegeois, C., Chauvel, P., & Musolino, A. (1995). Intracerebral potentials to rare target and distractor auditory and visual stimuli: I. Superior temporal plane and parietal lobe. *Electroencephalography & Clinical Neurophysiology*, **94**, 191-220.

Hari, R., Hämäläinen, M., Ilmoniemi, R., Kaukoranta, E., Reinikainen, K., Salminen, J., Alho, K., Näätänen, R., & Sams, M. (1984). Responses of the primary auditory cortex to pitch changes: Neuromagnetic recordings in man. *Neuroscience Letters*, **50**, 127-132.

Huotilainen, M., Ilmoniemi, R. J., Lavikainen, J., Tiitinen, H., Alho, K., Sinkkonen, J., Knuutila, J., & Näätänen, R. (1993). Interaction between representations of different features of auditory sensory memory. *NeuroReport*, **4**, 1279-1281.

Imada, T., Hari, R., Loveless, N., McEvoy, L., & Sams, M. (1993). Determinants of the auditory mismatch response. *Electroencephalography & Clinical Neurophysiology*, **87**, 144-153.

Javitt, D. C., Doneshka, P., Grochowski, S., & Ritter, W. (1995). Impaired mismatch negativity generation reflects widespread dysfunction of working memory in schizophrenia. *Archives of General Psychiatry*, **52**, 550-558.

Javitt, D. C., Schroeder, C. E., Steinschneider, M., Arezzo, J. C., & Vaughan, H. G., Jr. (1992). Demonstration of mismatch negativity in the monkey. *Electroencephalography & Clinical Neurophysiology*, **83**, 87-90.

Joutsiniemi, S. L., Ilvonen, T., Huotilainen, M., Tervaniemi, M., Lehtokoski, A., Rinne, T., & Näätänen, R. (1997, January). *The MMN for duration deviants in healthy subjects—incidence, replicability, and age-dependence*. Paper presented at the 2nd Project Meeting of European COBRAIN Collaboration, Lyon, France.

Kane, N. M., Curry, S. H., Rowlands, C. A., Manara, A. R., Lewis, T., Moss, T., Cummins, B. H., & Butler, S. R. (1996). Event related potentials—neurophysiological tools for predicting emergence and early outcome from traumatic coma. *Intensive Care Medicine*, **22**, 39-46.

Kraus, N., McGee, T., Carrell, T., & Sharma, A. (1995). Neurophysiological bases of speech discrimination. *Ear & Hearing*, **16**, 19-37.

Kropotov, J. D., Näätänen, R., Sevostianov, A. V., Alho, K., Reinikainen, K., & Kropotova, O. V. (1995). Mismatch negativity to auditory stimulus change recorded directly from the human temporal cortex. *Psychophysiology*, **32**, 418-422.

Kurtzberg, D., Kreuzer, J. A., Fliegler, K. Z., Ritter, W., & Vaughan, H. G., Jr. (1997). *The additivity of mismatch negativity to multiple stimulus features*. Manuscript in preparation.

Kurtzberg, D., Vaughan, H. G., Jr., Kreuzer, J. A., & Fliegler, K. Z. (1995). Developmental studies and clinical application of mismatch negativity: Problems and prospects. *Ear & Hearing*, **16**, 105-117.

Lang, A. H., Eerola, O., Korpilahti, P., Holopainen, I., Salo, S., & Aaltonen, O. (1995). Practical issues in the clinical application of mismatch negativity. *Ear & Hearing*, **16**, 118-130.

Lang, A. H., Nyrke, T., Ek, M., Aaltonen, O., Raimo, I., & Näätänen, R. (1990). Pitch discrimination performance and auditory event-related potentials. In C. H. M. Brunia, A. W. K. Gaillard, A. Kok, G. Mulder, & M. N. Verbaten (Eds.), *Psychophysiological brain research* (Vol. 1, pp. 294-298). Tilburg: Tilburg University Press.

Lavikainen, J., Tiitinen, H., May, P., & Näätänen, R. (1997). Binaural interaction in the human brain can be non-invasively accessed with long-latency event-related potentials. *Neuroscience Letters*, **222**, 37-40.

Levänen, S., Hari, R., McEvoy, L., & Sams, M. (1993). Responses of the human auditory cortex to changes in one vs. two stimulus features. *Experimental Brain Research*, **97**, 177-183.

Lißmann, I., Klugman, A., Gruzelier, J., & Baldeweg, T. (1997, May). *Auditory mismatch evoked potentials are not affected by the visual distractor task.* Poster presented at the 3rd European Congress of Psychophysiology, Konstanz.

Loewy, D. H., Campbell, K. B., & Bastien, C. (1996). The mismatch negativity to frequency deviant stimuli during natural sleep. *Electroencephalography & Clinical Neurophysiology*, **98**, 493-501.

Lyytinen, H., Blomberg, A. P., & Näätänen, R. (1992). Event-related potentials and autonomic responses to a change in unattended auditory stimuli. *Psychophysiology*, **29**, 523-534.

Massaro, D. W. (1975). *Experimental psychology and information processing.* Chicago: Rand McNally.

McEvoy, L., Hari, R., Imada, T., & Sams, M. (1993). Human auditory cortical mechanisms of sound lateralization: II. Interaural time differences at sound onset. *Hearing Research*, **67**, 98-109.

Morlet, D. (1997, May). *Coma monitoring system.* Paper presented at the 3rd Project Meeting of European COBRAIN Collaboration, Konstanz.

Näätänen, R. (1992). *Attention and brain function.* Hillsdale, NJ: Erlbaum.

Näätänen, R., & Alho, K. (1997). Higher-order processes in auditory change detection. *Trends in Cognitive Sciences*, **2**, 44-45.

Näätänen, R., Gaillard, A. W. K., & Mäntysalo, S. (1978). Early selective attention effect on evoked potential reinterpreted. *Acta Psychologica*, **42**, 313-329.

Näätänen, R., & Kraus, N. (Eds.) (1995). Mismatch negativity as an index of central auditory processing [Special issue]. *Ear & Hearing*, **16** (1).

Näätänen, R., Paavilainen, P., Alho, K., Reinikainen, K., & Sams, M. (1987a). Inter-stimulus interval and the mismatch negativity. In C. Barber & T. Blum (Eds.), *Evoked potentials III* (pp. 392-397). London: Butterworths.

Näätänen, R., Paavilainen, P., Alho, K., Reinikainen, K., & Sams, M. (1987b). The mismatch negativity to intensity changes in an auditory stimulus sequence. In R. Johnson, Jr., J. W. Rohrbaugh, & R. Parasuraman (Eds.), *Current trends in event-related brain potentials research* (pp. 125-131). Amsterdam: Elsevier.

Näätänen, R., Paavilainen, P., & Reinikainen, K. (1989). Do event-related potentials to infrequent decrements in duration of auditory stimuli demonstrate a memory trace in man? *Neuroscience Letters*, **107**, 347-352.

Näätänen, R., Paavilainen, P., Tiitinen, H., Jiang, D., & Alho, K. (1993). Attention and mismatch negativity. *Psychophysiology*, **30**, 436-450.

Näätänen, R., & Picton, T. (1987). The N1 wave of the human electric and magnetic response to sound: A review and an analysis of the component structure. *Psychophysiology*, **24**, 375-425.

Näätänen, R., Sams, M., Alho, K., Paavilainen, P., Reinikainen, K., & Sokolov, E. N. (1988). Frequency and location specificity of the human vertex N1 wave. *Electroencephalography & Clinical Neurophysiology*, **69**, 523-531.

Näätänen, R., Schröger, E., Karakas, S., Tervaniemi, M., & Paavilainen, M. (1993). Development of a memory trace for a complex sound in the human brain. *NeuroReport*, **4**, 503-506.

Naumann, E., Bartussek, D., Diedrich, O., & Laufer, M. E. (1992). Assessing cognitive and affective information processing functions of the brain by means of the late positive complex of the event-related potential. *Journal of Psychophysiology*, **6**, 285-298.

Nordby, H., Brønnick, K. S., & Hugdahl, K. (1996). Processing of deviant visual events reflected by event-related potentials. In C. Ogura, Y. Koga, & M. Shimokochi (Eds.), *Recent advances in event-related brain potential research: Proceedings of the XIth International Conference on Event-Related Potentials* (pp. 99-104). Amsterdam: Elsevier.

Nordby, H., Roth, W. T., & Pfefferbaum, A. (1988). Event-related potentials to breaks in sequences of alternating pitches or interstimulus intervals. *Psychophysiology*, **25**, 262-268.

Nousak, J. M. K., Deacon, D., Ritter, W., & Vaughan, H. G., Jr. (1996). Storage of information in transient auditory memory. *Cognitive Brain Research*, **4**, 305-317.

Novak, G. P., Ritter, W., Vaughan, H. G., Jr., & Wiznitzer, M. L. (1990). Differentiation of negative event-related potentials in an auditory discrimination task. *Electroencephalography & Clinical Neurophysiology*, **75**, 255-275.

Paavilainen, P., Jiang, D., Lavikainen, J., & Näätänen, R. (1993). Stimulus duration and the sensory memory trace: An event-related potential study. *Biological Psychology*, **35**, 139-152.

Paavilainen, P., Karlsson, M.-L., Reinikainen, K., & Näätänen, R. (1989). Mismatch negativity to change in spatial location of an auditory stimulus. *Electroencephalography & Clinical Neurophysiology*, **73**, 129-141.

Paavilainen, P., Saarinen, J., Tervaniemi, M., & Näätänen, R. (1995). Mismatch negativity to changes in abstract sound features during dichotic listening. *Journal of Psychophysiology*, **9**, 243-249.

Paavilainen, P., Tiitinen, H., Alho, K., & Näätänen, R. (1993). Mismatch negativity to slight pitch changes outside strong attentional focus. *Biological Psychology*, **37**, 32-41.

Pekkonen, E., Jousmäki, V., Könönen, M., Reinikainen, K., & Partanen, J. (1994). Auditory sensory memory impairment in Alzheimer's disease: An event-related potential study. *NeuroReport*, **5**, 2537-2540.

Pekkonen, E., Jousmäki, V., Partanen, J., & Karhu, J. (1993). Mismatch negativity area and age-related auditory memory. *Electroencephalography & Clinical Neurophysiology*, **87**, 321-325.

Pekkonen, E., Rinne, T., & Näätänen, R. (1995). Variability and replicability of the mismatch negativity. *Electroencephalography & Clinical Neurophysiology*, **96**, 546-554.

Picton, T. W. (1995). The neurophysiological evaluation of auditory discrimination. *Ear & Hearing*, **16**, 1-5.

Pihko, E., Leppäsaari, T., & Lyytinen, H. (1995). Brain reacts to occasional changes in duration of elements in a continuous sound. *NeuroReport*, **6**, 1215-1218.

Ponton, C. W., & Don, W. (1995). The mismatch negativity in cochlear implant users. *Ear & Hearing*, **16**, 131-146.

Sallinen, M., Kaartinen, J., & Lyytinen, H. (1994). Is the appearance of mismatch negativity during stage 2 sleep related to the elicitation of K-complex? *Electroencephalography & Clinical Neurophysiology*, **91**, 140-148.

Sams, M., Alho, K., & Näätänen, R. (1984). Short-term habituation and dishabituation of the mismatch negativity of the ERP. *Psychophysiology*, **21**, 434-441.

Sams, M., Hari, R., Rif, J., & Knuutila, J. (1993). The human auditory sensory memory trace persists about 10 sec: Neuromagnetic evidence. *Journal of Cognitive Neuroscience*, **5**, 363-370.

Sams, M., Paavilainen, P., Alho, K., & Näätänen, R. (1985). Auditory frequency discrimination and event-related potentials. *Electroencephalography & Clinical Neurophysiology*, **62**, 437-448.

Scherg, M., Vajsar, J., & Picton, T. W. (1989). A source analysis of the late human auditory evoked potentials. *Journal of Cognitive Neuroscience*, **1**, 336-355.

Schröger, E. (1994). Automatic detection of frequency change is invariant over a large intensity range. *NeuroReport*, **5**, 825-828.

Schröger, E. (1995). Processing of auditory deviants with changes in one vs. two stimulus dimensions. *Psychophysiology*, **32**, 55-65.

Schröger, E. (1996a). The influence of stimulus intensity and inter-stimulus interval on the detection of pitch and loudness changes. *Electroencephalography & Clinical Neurophysiology*, **100**, 517-526.

Schröger, E. (1996b). Interaural time and level differences: Integrated or separated processing? *Hearing Research*, **96**, 191-198.

Schröger, E. (1996c). A neural mechanism for involuntary attention shifts to changes in auditory stimulation. *Journal of Cognitive Neuroscience*, **8**, 527-539.

Schröger, E. (1996d). A new auditory distraction task: Electrophysiological and behavioral effects of task-irrelevant sound change. *Psychophysiology*, **33** (Suppl. 1), S75.

SCHRÖGER, E. (1997a). Higher-order processes in auditory-change detection: Response from Schröger. *Trends in Cognitive Sciences*, **2**, 45-46.

SCHRÖGER, E. (1997b). On the detection of auditory deviants: A preattentive activation model. *Psychophysiology*, **34**, 245-257.

SCHRÖGER, E., NÄÄTÄNEN, R., & PAAVILAINEN, P. (1992). Event-related brain potentials reveal how non-attended complex sound patterns are represented by the human brain. *Neuroscience Letters*, **146**, 183-186.

SCHRÖGER, E., PAAVILAINEN, P., & NÄÄTÄNEN, R. (1994). Mismatch negativity to changes in a continuous tone with regularly varying frequencies. *Electroencephalography & Clinical Neurophysiology*, **92**, 140-147.

SCHRÖGER, E., RAUH, R., & SCHUBÖ, W. (1993). Probability functions of Minkowski distances between discrete random variables. *Educational & Psychological Measurement*, **53**, 379-398.

SCHRÖGER, E., TERVANIEMI, M., WINKLER, I., WOLFF, C., & NÄÄTÄNEN, R. (1997). Separated and integrated processing of interaural cues for directional hearing as revealed by event-related potentials. In A. Schick & M. Klatte (Eds.), *Contributions to psychological acoustics: Results of the 7th Oldenburg Symposium on Psychological Acoustics* (pp. 49-56). Oldenburg: Universität Oldenburg, Bibliotheks- und Informationssystem der Carl von Ossietzky.

SCHRÖGER, E., & WINKLER, I. (1995). Presentation rate and magnitude of stimulus deviance effects on human pre-attentive change detection. *Neuroscience Letters*, **193**, 185-188.

SCHRÖGER, E., & WOLFF, C. (1996). Mismatch response of the human brain to changes in sound location. *NeuroReport*, **7**, 3005-3008.

SCHRÖGER, E., & WOLFF, C. (1997a). Fast preattentive processing of location: A functional basis for selective listening. *Neuroscience Letters*, **232**, 5-8.

SCHRÖGER, E., & WOLFF, C. (1997b). *Time necessary for establishing a memory trace for a standard sound.* Manuscript in preparation.

SCHRÖGER, E., & WOLFF, C. (1997c). Unpublished raw data.

SHUTARA, Y., KOGA, Y., FUJITA, K., TAKEUCHI, H., MOCHIDA, M., & TAKEMASA, K. (1996). An event-related potential study on the impairment of automatic processing of auditory input in schizophrenia. *Brain Topography*, **8**, 285-289.

TERVANIEMI, M., ALHO, K., PAAVILAINEN, P., SAMS, M., & NÄÄTÄNEN, R. (1993). Absolute pitch and event-related brain potentials. *Music Perception*, **10**, 305-316.

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**, 844-846.

TERVANIEMI, M., SCHRÖGER, E., & NÄÄTÄNEN, R. (1997). Pre-attentive processing of spectrally complex sounds with asynchronous onsets: An ERP study. *Neuroscience Letters*, **227**, 197-200.

TIITINEN, H., ALHO, K., HUOTILAINEN, M., ILMONIEMI, R. J., SIMOLA, J., & NÄÄTÄNEN, R. (1993). Tonotopic auditory cortex and the magnetoencephalographic (MEG) equivalent of the mismatch negativity. *Psychophysiology*, **30**, 537-540.

TIITINEN, H., MAY, P., REINIKAINEN, K., & NÄÄTÄNEN, R. (1994). Attentive novelty detection in humans is governed by pre-attentive sensory memory. *Nature*, **372**, 90-92.

TREJO, L. J., RYAN-JONES, D. L., & KRAMER, A. F. (1995). Attentional modulation of the mismatch negativity elicited by frequency differences between binaurally presented tones. *Psychophysiology*, **32**, 319-328.

UWER, R., MINOW, F., & SUCHODOLETZ, W. VON (1996). Zur Reliabilität der Mismatch Negativity (MMN). In A. Schorr (Ed.), *Experimentelle Psychologie: 38. Tagung experimentell arbeitender Psychologen, Katholische Universität Eichstätt* (pp. 334-335). Lengerich: Pabst Science Publishers.

WINKLER, I., KARMOS, G., & NÄÄTÄNEN, R. (1996). Adaptive modeling of the unattended acoustic environment reflected in the mismatch negativity event-related potential. *Brain Research*, **742**, 239-252.

WINKLER, I., & NÄÄTÄNEN, R. (1995). The effects of auditory backward masking on event-related brain potentials. In G. Karmos, M. Molnár, V. Csépe, I. Czigler, & J. E. Desmedt (Eds.), *Perspectives of event-related potentials research* (pp. 185-189). Amsterdam: Elsevier.

WINKLER, I., PAAVILAINEN, P., ALHO, K., REINIKAINEN, K., SAMS, M., & NÄÄTÄNEN, R. (1990). The effect of small variation of the frequent auditory stimulus on the event-related brain potential to the infrequent stimulus. *Psychophysiology*, **27**, 228-235.

WINKLER, I., PAAVILAINEN, P., & NÄÄTÄNEN, R. (1992). Can echoic memory store two traces simultaneously? A study of event-related brain potentials. *Psychophysiology*, **29**, 337-349.

WINKLER, I., REINIKAINEN, K., & NÄÄTÄNEN, R. (1993). Event-related brain potentials reflect traces of echoic memory in humans. *Perception & Psychophysics*, **53**, 443-449.

WINKLER, I., & SCHRÖGER, E. (1995). Storing temporal features of complex sound patterns in auditory sensory memory. *NeuroReport*, **6**, 690-694.

WINKLER, I., SCHRÖGER, E., & COWAN, N. (1997). The effect of the predeviant interval on the MMN event-related potential. *Journal of the Acoustical Society of America*, **102**, 1072-1082.

WINKLER, I., TERVANIEMI, M., & NÄÄTÄNEN, R. (1997). Two separate codes for missing-fundamental pitch in the human auditory cortex. *Journal of the Acoustical Society of America*, **102**, 1072-1082.

WOLDORFF, M. G., HACKLEY, S. A., & HILLYARD, S. A. (1991). The effects of channel-selective attention on the mismatch negativity wave elicited by deviant tones. *Psychophysiology*, **28**, 30-42.

WOLFF, C., & SCHRÖGER, E. (1995). MMN elicited by one-, two-, and three-dimensional deviants. *Journal of Psychophysiology*, **9**, 374.