Mismatch negativity in dichotic listening: Evidence for interhemispheric differences and multiple generators

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Abstract

The characteristics of mismatch negativity (MMN) elicited by dichotic stimulation were examined using frequency-deviant stimuli presented to the right, to the left, or to both sides. The experiment was run twice, once using earphones and once using loudspeakers in free field. With both modes of stimulation, deviants presented in the left, right, or both ears, or tones that were switched between ears, elicited comparable MMNs, with a peak latency of about 180 ms. With earphones, the amplitude of the MMN was bigger at the frontal-lateral right hemisphere sites than at the homologous left-hemisphere sites for all deviance conditions. Scalp current density analysis revealed that deviance in the right side elicited bilaterally equivalent frontal current sinks and a trend towards stronger contralateral current sources at the mastoid sites. In contrast, left side deviance elicited frontal sinks and temporal current sources stronger over the right hemiscalp. These results are compatible with the multiple-generator model of MMN. The attention-related role of the MMN is discussed, suggesting comparable attention mechanisms for vision and audition.

Descriptors: Mismatch negativity, Dichotic listening, Scalp current densities, Auditory attention, Interhemispheric asymmetry, Event-related potential

The ability to detect deviations from a steady state in the sensory environment is an ecologically critical capacity of living organisms. Evidence for the existence of a low-level mechanism for the detection of such deviations has been provided by scalp recordings of event related potentials (ERPs). This evidence relates to a negative component labeled mismatch negativity (MMN) that is elicited by different types of infrequent changes in an otherwise repetitive stimulus sequence (Näätänen, Gaillard, & Mäntysalo, 1978). This phenomenon has been established predominantly in the auditory modality, whereas evidence for other modalities awaits further clarification (for a review, see Näätänen, 1990, 1992, pp. 136–200).

In a typical MMN paradigm, a deviant auditory stimulus is infrequently interspersed in a sequence of standard auditory stimuli. The MMN is evident in the difference waveform resulting from the subtraction of the ERP elicited by the standard stimulus from that elicited by the deviant stimulus. The difference waveform presents with a salient negativity, peaking between 120 and 250 ms, depending on the magnitude and the dimension of the deviance. MMN has been demonstrated by manipulating basic physical features of pure tones (pitch, intensity, duration, inter-stimulus interval, location) and more complicated dimensions of deviation, such as phonetic information and temporal order (e.g., Aaltonen, Niemi, Nyrke, & Tuhkanen, 1987; Näätänen, Paavilainen, Alho, Reimikainen, & Sams, 1987; Nordby, Roth, & Pfefferbaum, 1988; Paavilainen, Alho, Reimikainen, Sams, & Näätänen, 1991; Paavilainen, Karlsson, Reimikainen, & Näätänen, 1989; Sams, Paavilainen, Alho, & Näätänen, 1985). Most MMN studies to date have used monaural presentation of solitary sounds or binaural presentation of the same sound simultaneously to both ears. Whereas this method was useful at the stage of establishment of the phenomenon, it also needs to be extended to more ecologically valid situations in which the individual is confronted by more than one sound source at the same time. Therefore, one aim of the present study was to examine the characteristics of the MMN when two different tones were simultaneously presented in each trial (dichotic stimulation1). By giving precedence to processing of contralater-

1To avoid confusion we consistently use the term binaural to denote simultaneous presentation of identical stimuli to both ears and the term dichotic to denote simultaneous presentation of two different stimuli, one to each ear.
ally presented stimuli in each hemisphere while engaging both hemispheres simultaneously, dichotic stimulation may also emphasize any existing hemispheric asymmetry (Cohen & Martin, 1975; Milner, Taylor & Sperry, 1968; Sparks & Geschwind, 1968). Hence, dichotic stimulation may shed additional light on the cerebral source(s) of MMN.

There have been only two previous reports of MMN using dichotic stimulation (Praamstra & Stegeman, 1992; Winkler & Näätänen, 1993). Praamstra and Stegeman (1992) presented tones dichotically with spectral overlap in an attempt to enhance transmission from each ear to the contralateral hemisphere (Sidtis, 1984; Springer, Sidtis, Wilson, & Gazzamiga, 1978) and to restrict MMN to the hemisphere contralateral to the ear at which the deviance occurred. In standard trials, an identical stimulus was binaurally presented. Deviance was introduced by changing the stimulus in only one ear, thus forming a dichotic deviant trial. In an additional experiment in that study, the standard and the deviant trials consisted of dichotic stimuli and deviance was produced by reversing the assignment of the two different tones to the ears. In both experiments, MMN was elicited, but contrary to expectations it was not lateralized. Rather, its amplitude and latency were symmetrical across hemispheres, regardless of the ear at which the deviant stimulus was presented.

Although interhemispheric symmetry of the MMN was reported also by at least one other group (Scherg, Vajsar, & Picton, 1989), in other studies the amplitude of the MMN was bigger over the right than over the left hemisphere regardless of the ear stimulated (Alain, Woods, & Ogawa, 1994; Giard, Perrin, Pernier, & Bouchet, 1990; Paavilainen et al., 1991). A possible explanation of this inconsistency is that, in fact, the MMN is not a unified phenomenon but reflects the concerted activity of several generators, each with its own pattern of interhemispheric distribution (Giard et al., 1990). Specifically, it was suggested that the temporal-lobe generators of the MMN may be bilateral with a predominance to the cortex contralateral to the side where the deviance occurred. These generators may mirror the stronger (but not exclusive) connections from the ear where the deviation occurred to the contralateral cortex (Rozenzweig, 1951). In addition, the MMN may have a frontal generator that is predominant in the right hemisphere, perhaps reflecting a higher level mechanism of attention (Giard et al., 1990; Näätänen et al., 1997). The interhemispheric distribution measured in a particular experiment may therefore depend on the specific experimental design, which may preferentially highlight a particular subset of generators. A thorough examination of this hypothesis would require manipulation of stimulation factors known to influence laterality (such as dichotic stimulation) combined with an improved spatial distribution analysis. Consequently, an additional aim of this study was to examine the spatial distribution of scalp current density and potentials related to MMN in general and the interhemispheric distribution of the MMN in particular using dichotic stimulation and a higher density array of electrodes.

Dichotic stimulation was previously used by Praamstra and Stegeman (1992), who examined the possibility of restricting the MMN to only one hemisphere. In one experiment in that study, the dichotic stimulus was used only in the deviant condition whereas the standard stimulus was binaural. As discussed by the authors, this procedure left open the possibility that the resulting MMN did not reflect the change in the nature of the stimulus presented to one ear but rather reflected the overall perceptual difference between a homogenous standard stimulus (binaural) and a compound deviant stimulus (dichotic). If this were the case, such a deviance would not have generated the expected asymmetrical activity across hemispheres. In an additional experiment (Exp. III), Praamstra and Stegeman attempted to avoid this problem using dichotic stimulation for both standard and deviant trials. However, the deviant condition in that experiment was produced by switching the stimuli between ears. Thus, whereas this procedure was adequate for reducing the overall perceptual difference between the deviant stimulus and the standard stimulus, it introduced deviance to both ears at the same time. Consequently, this procedure could not test the possibility of restricting the MMN to only one hemisphere. An additional problem is that the switch between the ears may be identified by the system not as a change in pitch (in each ear) but as a change in the relative locations of the two sound sources. A similar difficulty is evident in another study where dichotic or binaural stimuli were presented in standard trials, whereas the deviant was a monaural tone, produced by omitting the tone presented to one ear (Winkler & Näätänen, 1993).

In the current study, an array of 32 electrodes was used to examine the MMN elicited by infrequent changes in the pitch of pure tones presented dichotically in standard and deviant trials alike. In deviant trials, either one or both members of the dichotic pair was changed. A change in both ears was produced either by switching the assignments of tones to ears (as in the Praamstra & Stegeman, 1992, Exp. III) or by changing the pitch of the stimulus in each ear by 11% (one musical tone) toward the mean between them. In the latter condition, the change in pitch is not confounded by the apparent change in sound-source location, as it may be when the tone assignment is switched. Either way, when deviance was produced in both ears, the mean pitch of the two tones (“musical mean”) was the same as in the standard trials. This design was a way to rebut the possible (if unlikely) claim that the memory trace produced by the standard stimulus is related to some kind of an average between the pitch of the two stimuli (see Winkler, Paavilainen, & Näätänen, 1992). If this were the case, these deviants would elicit weaker or no MMN. However, if each member of the standard stimulus pair forms a separate memory trace, a change in both will yield an MMN that should be at least as strong as the MMN elicited when only one of the members of a pair is changed. Comparison between MMNs elicited by dichotic stimuli in conditions in which the deviance is limited to one ear, produced in both ears by switching the tone-to-ear assignment, or produced by simultaneously changing the tones presented to both ears should enable a well controlled examination of the interhemispheric asymmetry of MMN and address the question of multiple memory traces in dichotic stimulation.

The feasibility of eliciting solid MMN responses using dichotic stimulation may also be valuable in complementing studies of neuropsychological patients, particularly those with unilateral hemispheric lesions (e.g., De Renzi, Gentilini, & Barbieri, 1989; Soroker, Calamaro, Glickson, & Myoslobodsky, 1997). A free-field setup may be better suited for specific testing of these patients (e.g., Soroker, Calamaro, & Myoslobodsky, 1995a, 1995b). Consequently, in this study, we compared within subjects the MMN elicited in response to stimuli presented via earphones with that elicited when loudspeakers are used.

2These possibilities were put forward mainly because CV syllables, which were also used as stimuli in that experiment, hardly elicited any MMN in a control experiment (Praamstra & Stegema, 1992, Exp. 1) in which both the standard stimulus and the deviant stimulus were binaural, whereas a much bigger MMN was elicited in the main experiment, in which the deviant stimulus, but not the standard stimulus, was dichotic.
Methods

The experiment was run twice, once presenting the stimuli via headphones and once in a more natural situation using loudspeakers.

Subjects

Eighteen subjects participated in this study. Data from 2 subjects were discarded due to excessive eye movements. The remaining 16 subjects were 5 male and 11 female undergraduate and graduate students (20–27 years old) from the Hebrew University, who participated for course credit or payment. They were all right handed, with normal hearing, and without history of neurological disease or injury. Fifteen subjects (10 women, 5 men) participated in the earphones stimulation condition. Among those, 8 (6 women, 2 men) also participated in the loudspeakers stimulation condition along with a ninth woman who participated only in the loudspeakers condition. The time difference between the two recording sessions ranged for different subjects between 1 and 31 days. The subjects who participated in both sessions were designated to do so before the study started, so that there was no selection bias.

Stimuli

Each trial consisted of two dichotically presented pure tones differing in frequency. They were all of an equal duration of 100 ms (including 10-ms rise and fall) and intensity of 65 dB SPL. Across three blocks there were three types of standard pairs and six types of deviant pairs. In four of the deviant pairs, deviation was introduced on one side only, by upward or downward shifting the frequency of deviant pairs. In four of the deviant pairs, deviation was introduced either by changing both tones toward their mean by one musical tone or by switching the tone-to-ear assignment. The time difference between the two recording sessions ranged for different subjects between 1 and 31 days. The subjects who participated in both sessions were designated to do so before the study started, so that there was no selection bias.

Experimental Procedure

The subjects were seated in a reclining chair in a sound-attenuated and electrically shielded chamber with a reverberation time of less than 0.1 s at 1000 Hz (IAC, Model 403-A). While reading a book of their choice, the subjects were presented with the auditory stimuli. They were instructed to concentrate on their reading and to ignore the sounds. The three blocks of stimuli were presented in a counterbalanced order across subjects. A silent interval of variable length (as requested by the subject) was introduced between blocks. In each block, there were 2,400 stimuli of which 14% were equally divided between two types of deviant pairs. The remaining 86% were standard pairs. The standard and the deviant pairs were presented in a pseudo-random order (different for each subject) with the constraint that at least three consecutive standard pairs preceded each deviant pair. The interstimulus interval (ISI) was 400 ms, and a short break was introduced after 1,200 stimuli.

Electroencephalogram Recording and Averaging

The electroencephalogram (EEG) was recorded from 32 tin electrodes referenced to the tip of the nose. Scalp recording was from 30 electrodes mounted on a custom-made cap (ECI) and two additional electrodes placed over the left and right mastoid processes. The recording sites were based on the 10–20 system, with 10 additions (see Figure 1). The electrooculogram (EOG) was recorded by two electrodes, one located at the outer canthus of the right eye and the other located in the infraorbital region of the same eye.

The EEG was continuously sampled at 250 Hz, amplified 20,000 times with an analog band-pass filter of 0.1–100 Hz, and stored for off-line analysis. For ERP averaging, the EEG was parsed to 600-ms epochs starting 128 ms before the stimulus. Epochs with EEG or EOG exceeding ±100 μV or exceeding a level of variance (measured as root mean square of amplitudes) individually determined for each subject were excluded from averaging. The epochs were averaged separately for each stimulus pair and block, resulting in nine averaged ERPs per subject. The baseline was adjusted by subtracting the mean amplitude of the prestimulus period of each ERP from all the data points in the epoch. Frequencies <0.5 Hz and >33 Hz (−3 dB points) were digitally filtered out from the ERPs after averaging.

Data Analysis

MMN properties were measured on difference waveforms calculated by subtracting the ERPs elicited by standard pairs from those elicited by deviant pairs in the same block. The peak latency was determined in the grand averaged difference waveforms of each condition. Thereafter, the average amplitude within a latency window of ±12 ms from the peak latency was measured individually for each subject and channel. All statistical analyses were done within subjects. Differences among conditions were validated by analyses of variance (ANOVA) in which the dependent variables were calculated by averaging potential amplitudes recorded at clus-

Table 1. Frequency of Standard and Deviant Pairs and Their Probability Within Each Block

<table>
<thead>
<tr>
<th>Pair</th>
<th>p</th>
<th>Block 1</th>
<th>Block 2</th>
<th>Block 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Standard</td>
<td>.86</td>
<td>660, 932</td>
<td>932, 660</td>
<td>740, 932</td>
</tr>
<tr>
<td>Deviant 1</td>
<td>.07</td>
<td>740, 932 [LtUp]</td>
<td>932, 740 [RtUp]</td>
<td>660, 932 [LtDown]</td>
</tr>
<tr>
<td>Deviant 2</td>
<td>.07</td>
<td>660, 830 [RtDown]</td>
<td>830, 740 [Both]</td>
<td>932, 740 [Switched]</td>
</tr>
</tbody>
</table>

Note: In each pair the left and right numbers are the frequencies of tones presented simultaneously to the left and the right side of the subject, respectively.
ters of electrodes according to predetermined criteria as follows: overall differences were assessed averaging the MMN amplitude at the frontocentral sites ~FP1, FP2, F3, F4, FC5, FC6, F7, F8, FT7, FT8, C3, C4, Fz, Cz! . Interhemispheric differences were assessed separating the left and right sites and excluding the midline sites (Figure 1).

The MMN elicited in the earphone and free field conditions were compared within subjects using a series of ANOVAs with the origin of deviance ~left ear, right ear, switched, both! , direction ~upwards, downwards! , hemisphere ~right, left! , and mode of presentation ~earphones, loudspeakers! as variables.

Scalp Potentials and Current Density Mapping
Scalp potential maps were generated using a two-dimensional spherical spline interpolation ~Perrin, Pernier, Bertrand, & Echallier, 1989! and a radial projection from Cz, which respects the length of the meridian arcs. The scalp current density ~SCD! distributions were obtained by computing the second spatial derivatives of the spline functions used for potential mapping. SCDs are reference free and have sharper peaks and troughs than potential distributions, thus facilitating the interpretation in case of multiple overlapping sources ~Perrin, Perrin, & Bertrand, 1988! . For statistical analysis, the SCDs waveforms were computed at all electrodes, and the sinks and sources were detected on the grand average maps. The current values, averaged over the electrodes and time windows of interest, were used as the dependent variable in ANOVAs.

Results
Earphones Stimulation Condition
MMN was elicited by deviance on the right, left, or both sides. Apparently, the amplitude of the MMN was larger when the deviance was in both ears than when it was limited to only one ear and was larger when the deviance was on the left than when it was on the right side (Figure 2). These apparent differences, however, were not statistically significant, as revealed by a one-way ANOVA of the MMN for the origin of deviance ~left ear, right ear, switched, both! , $F(3,42) = 1.1, p = 0.37$.

Topographic Analysis of Scalp Potentials
For all experimental conditions, the MMN distributions were characterized by negative potentials over the frontocentral areas, with polarity inversion around the mastoid sites (Figure 3a). Whether the deviance was on the right, left, or both sides, the MMN recorded at right hemisphere sites was larger than that recorded at left hemisphere sites (Figures 3a and 4). The interhemispheric difference was confirmed by a significant main effect of hemisphere in an Origin of Deviance ~left ear, right ear, both! × Hemisphere ~left, right! ANOVA, $F(1,14) = 21.5, p < .001$. Neither the main effect of origin of deviance nor the interaction between the two variables were significan, $F(3,42) = 1.1, p = .37$ and $F(3,42) = 1.6, p = .21$, respectively.

The scalp distribution of the interhemispheric effect was not uniform, however. As evident in Figure 5, the interhemispheric difference was of similar amplitude at the central sites ~C3, FC5, FT7 vs. C4, FC6, FT8! and at the more anterior sites ~FP1, F7, F3

Figure 1. The layout of the 32-electrode array used in the present experiment. The dashed lines encircle the clusters of electrodes used to compare right and left hemisphere MMN amplitudes.

Figure 2. MMN elicited by changing the tone pitch in the right ear, in the left ear, or simultaneously in both ears or by switching the tones between ears. Both standards and deviants were dichotic. Left: Response to the standards and to each type of deviance. Right: The difference waves computed by subtracting the ERP elicited by the standard from that elicited by the deviant ~within the same block!. 
but was larger at more lateral sites than at the sites closer to the midsagittal line.

The significance of the above pattern was confirmed by a two-way ANOVA with the variables proximity to midline and anteroposterior dispersion. The interhemispheric difference was significantly larger at lateral than at more medial sites, $F(1,14) = 14.5$, $p < .005$, whereas the difference between the frontal and the central sites was not significant, $F(1,14) < 1.0$.

**Scalp Current Densities**

The SCD maps revealed a more complex pattern of electrical activity with stable current distributions in the MMN time window.
Temporal sources. The left-side deviance generated right temporal current sources (at T6--RM averaged) that were stronger than those at the mirror sites over the left hemisphere, \( t(14) = 1.9, p < \ldots \)

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3SCD computation using Laplacian transformations amounts to applying a high-pass spatial filter on the potential distributions. SCDs are therefore much more sensitive to residual noise in the data and to small errors in electrode positioning than are potential maps. These effects are particularly pronounced when the distance between adjacent electrodes is small. SCDs were therefore estimated excluding electrodes FT7/FT8 and TP7/TP8, which are especially noisy because of muscle activity and are very close to F7/F8, T3/T4, and T5/T6 (see Figure 1).
spicuous when the deviance occurred in the left (−2.02 μV vs. −0.97 μV) than in the right (−1.18 μV vs. −0.98 μV) side. This pattern was tested by a two-way ANOVA that showed that the main effect of direction of deviance (upward, downward) was significant, $F(1,14) = 8.5, p < .02$, whereas neither the main effect of origin of deviance (left, right) nor the interaction between direction and origin of deviance were significant, $F(1,14) = 1.2, p = .29$, and $F(1,14) = 2.4, p = .14$, respectively.

The reliability of the direction of deviance effect was reinforced by subtracting the response to a stimulus pair serving as standard in one block from the response to the identical pair serving as deviant in another block (Figure 7). The design of the experiment enabled these comparisons for two pairs: 740–932 Hz which was standard in Block 3 and LtUp deviant in Block 1 and 660–932 Hz which was standard in Block 1 and LtDown deviant in Block 3.

The MMN resulting from such subtractions was almost identical to the MMN resulting from subtracting the response to standard from the response to deviant pairs within the same block (where the two pairs were different).

**Loudspeakers Stimulation Condition**

Data collection and analysis in this condition were similar to that used with earphones stimulation, except that only 9 subjects participated in this part of the study. The overall pattern of the MMN using loudspeakers was very similar to that observed using earphones (Figure 8).

As before, because the direction of deviance could not be fully nested into the origin of deviance variable (it could not be manipulated when the deviance was induced by changing the pitch of the tones presented in both loudspeakers), we have analyzed the effect of origin of deviance on the MMN in a one-way ANOVA averaging the upward and the downward deviations together. This analysis revealed that, as with earphones stimulation, the MMN was similar regardless of where the deviance occurred, $F(3,24) < 1.0$. A second analysis was run to examine the direction of deviance effect and the possible interaction between this effect and the origin of deviance (excluding both and switched conditions, where direction was not relevant). This Origin × Direction of Deviance ANOVA revealed that, although with loudspeakers, as with earphones, downward deviation in pitch elicited larger MMN, this effect only approached significance, $F(1,8) = 4.6, p = .065$. This effect did not interact with the origin of deviance, $F(1,8) < 1.0$. In contrast to the earphone condition, no statistically significant interhemispheric effect was found in a two-way Origin × Hemisphere ANOVA, $F(1,8) = 1.8, p = .22$.

The MMN in the two stimulation conditions was compared by a series of within-subject ANOVAs (for the 8 subjects that participated in both) including the mode of presentation (earphones/loudspeakers) as a variable. The interesting aspect of the results was that the MMN elicited by presenting the stimuli via earphones or loudspeakers was similar across experiments. In particular, across

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**Figure 6.** MMN (difference waves) elicited at Fz electrode by upwards and downwards pitch deviation of one tone, with stimuli presented through earphones. Downwards deviation elicited a larger MMN response than did upwards deviation, regardless of the ear at which deviation occurred.

**Figure 7.** Difference waves computed in two ways: (a) Subtracting the response to a standard pair presented within the same block of the deviant pair and (b) subtracting the response to a pair that is physically identical to the deviant pair (e.g., both are 740 + 932 Hz) but that served as a standard pair in another block (i.e., across blocks).

**Figure 8.** Difference waves in the four conditions in response to loudspeaker presentation.
experiments, the MMN recorded over the right hemisphere was significantly larger than that recorded over the left, $F(1,7) = 12.7$, $p < .01$, and the downward deviance elicited a larger MMN than did the upward deviance, $F(1,7) = 9.0$, $p < .03$.

Discussion

In the present study, we explored the nature of MMN elicited while both standard and deviant tone stimuli were dichotically presented. In different conditions, the frequency of the tone presented to either one or both ears was changed. We compared the effect of unilateral and bilateral sources of deviance on the MMN and the relationship between the side of deviance (right, left, both) and the scalp distribution of the MMN, emphasizing interhemispheric differences. In addition, we compared the MMN elicited using earphones with that elicited using loudspeakers.

The results revealed that whether the deviance is presented in only one ear or in both or whether stimuli are administered via earphones or loudspeakers, dichotic stimulation can be used for investigating the nature of interhemispheric asymmetries in MMN. The analysis of the SCDs showed that the MMN could be fractionated into at least two components, each with a different pattern of interhemispheric distribution. Taken together, the scalp voltage and current distribution suggest that, at least when dichotic stimulation is used, the MMN reflects a complex pattern of generators ipsilateral and contralateral to the side of deviation.

Within subjects, when earphones were used and regardless of whether the deviance was unilateral or bilateral, the spatial distribution of voltage over the scalp showed larger amplitudes of MMN at right frontolateral than at homologous left hemisphere sites, a finding consistent with several previous reports (e.g., Alain et al., 1994; Giard et al., 1990; Paavilainen et al., 1991). Our results extended the previous findings, however, by showing that in addition to the fact that the asymmetry holds regardless of the side of the deviance, asymmetry also persists when the deviance is bilateral and similar at both sides. The significant interaction between the interhemispheric asymmetry and the laterality of the compared areas (i.e., the distance from the midline) may help explain the discrepancy in results between previous studies in which voltage asymmetry was found and studies in which the MMN was symmetrical across hemispheres (Praamstra & Stegeman, 1992; Scherg et al., 1989). In the symmetry studies, interhemispheric differences were measured between C3 and C4. As our results suggest, the asymmetry is significantly larger more laterally.

Voltage maps may reflect the summed activity of several loci of neural activity with different interhemispheric distributions. Various techniques for localizing electric-field generators in the brain have indicated several generators. As indicated by converging evidence from EEG, magnetoencephalography (MEG), intracranial recordings in epileptic patients, and cerebral blood flow studies, one set of generators for MMN is probably located bilaterally in the supratemporal planes, somewhat anterior to the generators of N1 in the tonotopic auditory cortices (Giard et al., 1990; Giard, Perrin, & Pernier, 1991; Hari et al., 1984; Halgren et al., 1995; Huotilainen et al., 1993; Kropotov et al., 1995; Levänen, Hari, McEvoy, & Sams, 1993; Sams, Kaukoranta, Hämläinen, & Näätänen, 1991; Scherg et al., 1989; Tiitinen et al., 1993; for a comprehensive review, see also Alho, 1995). Dipole modeling techniques based on ERP and on MEG revealed that the exact location of these generators in the supratemporal plane may depend on the dimension of deviance (Giard et al., 1995; Levänen et al., 1993; Levänen, Ahonen, Hari, McEvoy, & Sams, 1996). The relationship between the side at which the deviance occurs and the interhemispheric distribution of these temporal generators is not sufficiently clear. Previous SCD analyses (Giard et al., 1990) and the results of the present study suggested that, at least when the tone’s frequency is manipulated, this temporal generator is more active at the hemisphere opposite the ear in which the deviance occurred. Similarly, modeling the ERP sources, Scherg et al. (1989) found that the MMN generators peaked earlier and were slightly larger in the temporal lobe contralateral to the side of deviance. However, in modeling the sources of magnetic fields elicited by mismatch (MMF), Levänen et al. (1996) found larger activity in the right than in the left supratemporal planes regardless of side of deviance. This pattern was observed in 5 of 7 subjects. This discrepancy cannot be easily explained because crucial differences between methods prohibit a straightforward comparison between ERP and MEG data. In particular, SCDs are relatively insensitive to deep generators, and MEG is insensitive to radial dipoles. Therefore, the MEG and SCD manifestations of the same generator may be sensitive to different aspects of the activity. For example, a right hemisphere dominance could be always observed by MEG if the right hemisphere dipole is more tangential than the left hemisphere dipole. Neither the SCD nor the ERP dipole modeling should be affected by this difference.

The temporal generator of the MMN has been interpreted as reflecting a mechanism of change detection, one relying on an auditory sensory memory trace, or echoic memory (e.g., Alho, 1995; Cowan, Winkler, Teder & Näätänen, 1993; Näätänen, 1990, 1992; Ritter, Deacon, Gomes, Javitt, & Vaughan, 1995). The contralateral predominance of this MMN component observed in the current study suggests that the manipulation of frequency at one ear during dichotic stimulation was indeed identified by the system as a unilateral change rather than a global change in a compound stimulus. More importantly, this interhemispheric distribution lends support to the possibility that during dichotic stimulation each of the two tones established its own auditory memory trace, a trace that was probably bilateral but stronger in the contralateral hemisphere. Hence, the deviant in one ear elicited a stronger mismatch response when compared with the stronger contralateral trace, and switching the location of the tones between ears resulted in an MMN because the input to each ear deviated from both the stronger contralateral and the weaker ipsilateral traces formed by the previous tone presented to that ear.

A similar hypothesis has been previously examined and partly rejected by Praamstra and Stegeman (1992). However, as they discussed, the failure to elicit asymmetrical MMN in their study, which was the basis of their rejection, may be interpreted in more than one way. In their Experiment II, the standard trials consisted of binaural stimulation, and MMN was elicited by infrequently changing the tone in one of the ears, thus creating a dichotic deviant stimulus. Consequently, the frequency change in one ear may have been confounded with a change from a homogenous binaural stimulus to a compound dichotic one, a global change that could partly explain their observed interhemispheric symmetry of the MMN. In contrast, the frequency change in our unilateral deviance conditions was not confounded by a perceptual difference between a homogenous and a compound stimulus. Therefore, the MMN elicited in those conditions could be ascribed with a greater confidence to the frequency change on one side rather than to a global change.

In an attempt to address the same confounding problem, Praamstra and Stegeman (1992) used a condition similar to the switched condition in the present study. As they argued, however, this solution was incomplete because switching the sides of the two tones may have been perceived as sound-source location shift rather than
an independent pitch change in each side. The earlier onset and the longer duration of the MMN elicited in the switched condition, as compared with the other conditions in the present study, suggest that the MMN elicited in the Switched condition may indeed reflect the combined effect of the response to the infrequent change in the frequency and the location of the tone (see also Levänen et al., 1993; Schröger, 1995). By this account, the earlier part of this MMN is probably a consequence of the location shift that occurs relatively early (Schröger, 1995; Schröger & Wolff, 1997) especially considering the extreme shift in sound-source location (180°), whereas the later part of the MMN may have reflected the response to the frequency deviance in both ears. The mixture of deviance in sound-source location and in the sound frequency in each ear, which characterized the switched condition in both Praamstra and Stegeman’s (1992) study and our study, was partly addressed in the present study by the inclusion of the Both condition. The MMN elicited in the both condition can be attributed more securely to the change in the frequency of the tones because changing the frequency simultaneously by one tone in each ear does not change the perception of the source-location. Taken together, the results of the present study and of that of Praamstra and Stegeman support a bihemispheric representation of echoic memory traces, which are probably asymmetrical and more robust in the hemisphere contralateral to the ear where the stimulus occurs.

A model suggesting a bilateral representation of the sound in the brain may be considered inconsistent with the ability to elicit MMN to changes in location, such as suggested for the Switched condition. This possible inconsistency is suggested by the view that because the determination of source location relies on information from both ears, the brain must have a single localized representation where binaural information converges. According to this view, the MMN elicited by shifts in the location of the sound source should reflect the unified representation. Such a unitary model is appealing from a Cartesian point of view, where there must be a convergence of information onto some central point that a higher order system can monitor. However, a connectionist approach would allow for the sound to be represented by a distributed network or assembly of neurons, which may even be spread across hemispheres. According to such an approach, the location of the sound source may be encoded in the specific balance of activity in different parts of the network (see Dennett & Kinsbourne, 1992, for a theoretical discussion of this issue). There may be some truth in both views. Binaural convergence does occur already in brain stem nuclei, which include neural computation mechanisms that may contribute to location coding (e.g., Carr & Konishi, 1989). However, even these nuclei, probably at the level of the superior olivary complex, are bilateral and project to the two hemispheres. Thus, the information about the source location may be encoded with the memory traces of the sound that are established bilaterally in the cortex. Therefore, the possibility that the memory trace is bilateral, albeit stronger in the hemisphere contralateral to the deviant stimulus, is not implausible.

The results of the present study suggest that the MMN may reflect this asymmetry of memory traces if, a priori, the dichotic stimuli install different echoic traces in each hemisphere in the standard trials. The difference in the nature of the standard trials may account for the difference in the interhemispheric distribution of the MMN between the present study (in which two traces with opposite interhemispheric asymmetries were putatively established) and that of Praamstra and Stegeman’s (1992) Experiment II (in which only one trace was established, symmetrically across hemispheres). The possibility of storing traces of more than one frequency simultaneously is supported by the finding that dipoles of the magnetic equivalent of MMN vary in their orientation (i.e., do not overlap) according to the frequency of the stimuli (Tiitinen et al., 1993) and by the findings of studies using two different standards intermixed in the same block (e.g., Winkler, Karmos & Näätänen, 1996; Winkler et al., 1992). MMN generators outside the supratemporal cortex have also been suggested (Alho, Woods, Algazi, Knight & Näätänen, 1994; Giard et al., 1990, 1996). The present SCD distribution replicated previous findings (Giard et al., 1990) showing frontally distributed MMN-related currents in addition to those observed over the temporal sites. The interhemispheric distribution of this activity was clearly different from that ascribed to the temporal generator, suggesting that these two activities have separate origins. Indeed, the presently observed frontal scalp activity does not necessarily imply a frontal cortex generator. However, the possibility that such a generator exists is corroborated by a recent positron emission tomography study in which an increased right frontal cerebral blood flow was found in a MMN-like paradigm (Näätänen et al., 1997). Less consistent evidence for the frontal generator was reported by Levänen et al. (1996). In an MEG study, these authors found that the right hemisphere MMFs could be best explained by an inferior parietal dipole (in addition to the supratemporal one). In 2 of their 7 subjects, however, a fourth dipole was implicated, and this more anterior-superior dipole may correspond to a frontal generator, consistent with Giard et al.’s (1991) dipole modeling results. As suggested by Alho (1995), the absence of this dipole in the other subjects could have resulted from more radial frontal dipoles, to which the MEG was insensitive. Although the present results match those of Giard et al. (1990) in finding a frontal scalp activity, there are also interesting differences. Whereas Giard et al. reported an overall right hemisphere dominant frontal component that was less asymmetrical for left side deviance, the present data show a more complex pattern. In both left and right deviant conditions contralateral currents were evident at frontal electrodes. In addition, in both deviance conditions ipsilateral currents were also observed at frontal scalp sites. However, whereas the ipsilateral currents were barely seen following left side deviance, they were highly conspicuous following right side deviance, to an extent that the interhemispheric difference disappeared during the early phase of the MMN. In other words, the frontal scalp activity was significantly lateralized to the right in response to left side deviants but was quite symmetrical in response to right side deviants. This pattern may be related to the hypothesis that MMN is associated with an involuntary attention-
shift mechanism (Escera, Alho, Winkler, & Näätänen, in press; Giard et al., 1990; Lyytinen, Blomberg, & Näätänen, 1992; Näätänen, 1990, 1992; Novak, Ritter & Vaughan, 1992; Schröger, 1996), particularly to the suggestion that this mechanism is reflected by a frontal (Giard et al., 1990, 1991; Näätänen & Michie, 1979; Näätänen et al., 1997) or a parietal (Levänen et al., 1996) component of the MMN, and may fit into a broader conceptualization that evolved in cognitive neuropsychology of brain mechanisms that mediate attention.

Evidence from neuropsychological as well as neurophysiological research has suggested that the right hemisphere is capable of allocating attention to both sides of the sensory space, whereas the left hemisphere is dedicated to controlling attention in the right hemisphere (e.g., Anzola, Bertoloni, Buchtel, & Rizzolatti, 1977; Corbetta, Miezin, Shulman, & Petersen 1993; Desmedt, 1977; Heilman & Van Den Abell, 1980; Howes & Boller, 1975; Mangun et al., 1994). This model was based primarily on studies of visual selective attention and unilateral visual neglect. However, accumulating reports of left-side auditory neglect (De Renzi et al., 1989; De Renzi, Gentilini, & Pattacini, 1984; Heilman & Valenstein, 1972; Soroker et al., 1997) suggest that a similar interhemispheric distribution of attention mechanisms may exist in the auditory modality. Our results may be tentatively interpreted as consistent with this analogy. Whereas both hemispheres were as active following potentially attention-attracting auditory events occurring on the right side, similar events on the left side elicited activity that was more intense over the right than over the left hemisphere. The same interpretation may explain the difference between these results and those of Giard et al. (1990). Unlike the present pattern of asymmetry, Giard et al. reported a more symmetrical pattern when the deviants were on the left side. However, whereas the subjects in the present study were reading a book, in Giard et al.’s non-attended condition, subjects were attending to the ear contralateral to the side of deviance. Therefore, it is possible that although our deviants attracted attention to the side where they occurred, the attention of Giard et al.’s subjects was directed voluntarily to the other side. In Giard et al.’s attended condition, when the subjects’ attention was directed to the same ear where the deviance occurred, the right frontal component was significant regardless of the side of deviance, whereas the left frontal component was not.

An unexpected result in the current study was the larger MMN for downward than for upward deviation in frequency. Consequently, any account for this phenomenon is necessarily post hoc. The larger MMN for downward than for upward deviation may reflect a contribution of a larger N1 for lower tones then for higher tones (Jacobson, Lombardi, Gibbens, Ahmad, & Newman, 1992; for a comparable argument, see Gomes, Ritter, & Vaughan, 1995). However, this explanation is challenged by two facts: (a) the peak latency of the MMN in the present study was remote in time from the N1 latency, and (b) larger MMN for LiDown condition than for LiUp condition was found even when the standard and deviant tones were physically identical (subtracted across blocks), although under these circumstances N1 differences related to the absolute frequency of the tones should have been minimized (Figure 7). Additional research is necessary to clarify the origin of this effect.

Although overall similar MMNs were obtained using earphones and loudspeakers, the interhemispheric difference was less consistent when loudspeakers were used. A possible explanation of this difference between the earphones and the loudspeakers conditions is that with the loudspeakers the differential stimulation of each ear was less distinct. The feasibility of eliciting solid MMN responses using dichotic stimulation via loudspeakers as well as earphones may be particularly valuable in complementing studies of neuropsychological patients suffering from unilateral hemispheric lesions. Particularly because the elicitation of MMN does not require any specific cooperation from the subject, this paradigm may be useful for studying the way the damaged brain processes information, without the need to resort to patients’ accounts.

REFERENCES


Multiple generators of the MMN in dichotic listening


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