Combined mapping of human auditory EEG and MEG responses

Minna Huotilainen a,*, István Winkler a, b, Kimmo Alho a, c, Carles Escera c, Juha Virtanen a, d, Risto J. Ilmoniemi e, Iiro P. Jääskeläinen a, c, Eero Pekkonen a, c, f, Risto Näätänen a

a Cognitive Brain Research Unit, Department of Psychology, P.O. Box 13, FIN-00014 University of Helsinki, Helsinki, Finland
b Department of Psychophysiology, Institute for Psychology, Hungarian Academy of Sciences, Budapest, Hungary
Neurodynamics Laboratory, Department of Psychiatry and Clinical Psychology, University of Barcelona, Barcelona, Catalonia, Spain
d Department of Radiology, Helsinki University Central Hospital, FIN-00029 HYKS, Helsinki, Finland
e BioMag Laboratory, Medical Engineering Centre, Helsinki University Central Hospital, P.O. Box 508, FIN-00029 HYKS, Helsinki, Finland
f Department of Neurology, University of Helsinki, Helsinki, Finland

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Abstract

Auditory electric and magnetic P50(m), N1(m) and MMN(m) responses to standard, deviant and novel sounds were studied by recording brain electrical activity with 25 EEG electrodes simultaneously with the corresponding magnetic signals measured with 122 MEG gradiometer coils. The sources of these responses were located on the basis of the MEG responses; all were found to be in the supra-temporal plane. The goal of the present paper was to investigate to what degree the source locations and orientations determined from the magnetic data account for the measured EEG signals. It was found that the electric P50, N1 and MMN responses can to a considerable degree be explained by the sources of the corresponding magnetic responses. In addition, source-current components not detectable by MEG were shown to contribute to the measured EEG signals.

Keywords: Auditory evoked responses; Electroencephalography; Equivalent current dipole; Magnetoencephalography; P50; N1; Mismatch negativity; Source localisation; Event-related potentials

1. Introduction

Postsynaptic neuronal currents of a large number of synchronously-active pyramidal cells give rise to electric and magnetic field changes that can be measured on the scalp and outside the head. The measured electric potentials arise from both tangential and radial (with respect to the scalp) components of these postsynaptic currents (Regan, 1989). The corresponding magnetic field changes reflect the tangential component of these currents (Hämäläinen et al., 1993; Näätänen et al., 1994). The different conductivities of brain tissue, skull and scalp significantly influence the scalp-recorded electric signals. In contrast, as the magnetic permeabilities of these structures are practically equal, the influence on the signals recorded in magnetoencephalography (MEG) is slighter and easier to take into account.

Use of a spherical head model is more suitable for source localisation of magnetic than for electric responses (Yvert et al., 1996). However, magnetic fields produced by currents located close to the centre of the sphere are weak and hard to detect, requiring the use of a whole-head magnetometer and individual, realistic head models (Tesche, 1995; Tesche et al., 1996; Tesche and Karhu, 1997). In contrast, deep sources contribute significantly to the scalp-recorded electric signals (Hämäläinen et al., 1993). Measuring the MEG and the EEG simultaneously provides one with the opportunity to study activity from deep and radial sources as well as to locate accurately the tangential component of this brain activity.

The auditory electric P50 response and its magnetic counterpart, P50m, are assumed to originate from the primary
auditory cortex or from some adjacent brain area (Liegeois-Chauvel et al., 1994; Mäkelä et al., 1994), thus enabling one to locate the primary sensory area.

The auditory electric N1 response (Vaughan and Ritter, 1970), although composed of several components (Naätänen and Picton, 1987), has its major sources in the supratemporal area. The magnetic counterpart of N1, the N1m, reflects the tangential part of this supratemporal N1 component. Recent results from studies with variable inter-stimulus intervals (ISI) suggest multiple sources for the N1m (Lutkenhaus et al., 1992; Sams et al., 1993; Loveless et al., 1996), but in most cases, the N1m can be modelled by a single dipole, as these generators are very close to each other. Mäkelä et al. (1994) found that the N1m is located posterior to the P50m.

The mismatch negativity (MMN, Naätänen et al., 1978), and its magnetic counterpart, MMNm (Hari et al., 1984), is a response reflecting a pre-attentive auditory-change detection process based on sensory memory traces (for a review, see Näätänen, 1992). It is elicited by infrequent auditory stimuli (deviants) in repetitive sequences of a standard sound. The main MMN generators are located in the temporal lobes in the left and right auditory cortices (Scherg et al., 1989; Giard et al., 1990; Halgren et al., 1995; Kropotov et al., 1995; Levänen et al., 1996). An additional frontal generator of MMN has also been suggested (Giard et al., 1990; Ahlo et al., 1994; Molnár et al., 1995; Levänen et al., 1996). The MMNm (Hari et al., 1984) is generated a few millimetres anterior to the source of the N1m (Sams et al., 1991; Csépe et al., 1992; Huotilainen et al., 1993; Tiitinen et al., 1993).

The aim of the present study was to investigate the correspondence and differences between the electric and magnetic P50(m), N1(m), and MMNm(m) responses, by simultaneous EEG and MEG measurements. The degree to which sources located on the basis of the MEG recording alone could explain the EEG data was used to determine the extent of the contribution from sources not detected by MEG to the corresponding EEG responses.

2. Methods

2.1. Subjects, stimulation, and recording

Eight healthy right-handed adults (aged 22–38 years, 6 males) volunteered as subjects. None of them had a history of hearing disorders or neurological diseases.

Standard tones were presented with a probability of 85%, and randomly-embedded deviant tones and novel sounds had a probability of 7.5% each. The frequencies of the sinusoidal standard and the deviant tones were 600 and 660 Hz, respectively. The novel sounds were selected from a group of 60 complex ‘natural’ sounds having multiple spectral components within the frequency range of 300 Hz–5 kHz. Each deviant and novel sound was preceded by at least one standard. All stimuli were delivered at a sound pressure level of approximately 75 dB at the earpiece. The duration of the stimuli was 200 ms, including 10 ms rise and fall times, and the constant stimulus onset-to-onset time was 800 ms.

The subjects were instructed to ignore the tones during the experiment. They sat in a chair with the head inside the helmet-shaped Neuromag 122 channel MEG instrument and watched a silent video film. The stimuli were delivered binaurally through plastic tubes and earpieces, using a correction filter to compensate for the acoustical properties of the tubes (NeuroScan, USA). MEG with 122 channels (Ahonen et al., 1993) and EEG with 25 electrodes (see Fig. 1) were recorded in a magnetically-shielded room (Euroshield, Finland). Each two channel sensor unit measures two independent magnetic field (B) gradient components, $\frac{dB}{dx}$ and $\frac{dB}{dy}$, $B_z$ being normal to the local scalp surface. The gold-plated electrodes were placed on the scalp according to an extended international 10–20 system and were referred to an electrode at the nose. The exact 3D locations of the electrodes were measured using an Isotrak 3D digitiser. The recording passband was 0.03–100 Hz, the sampling rate was 397 Hz.

The position of the head with respect to the instrument was determined by measuring magnetic fields produced by 3 marker coils on the scalp (Ahlfors and Ilmoniemi, 1989), whose locations in relation to cardinal points of the head were determined before the experiment. The vertical and horizontal electro-oculogram (EOG) were also recorded bipolarly from electrodes placed above and below the left eye and from electrodes placed at the outer canthi of the right and the left eye. Epochs with an EOG change exceeding 150 μV, an EEG change exceeding 500 μV, and/or an MEG change exceeding 1.5 μT/cm were discarded, together with the responses to the first few stimuli of each sequence. In addition, responses to standard stimuli following a deviant or a novel sound were also discarded because these stimuli may elicit different components than the rest of the standards (Sams et al., 1984; Nousak et al., 1996; Winkler et al., 1996).

2.2. Data analysis

The data were averaged on-line using a data-collection window starting at 150 ms before, and ending at 800 ms after, the beginning of the sound. Responses were filtered with a passband of 1–30 Hz. All data were baseline-corrected using a prestimulus period of 50 ms. The most prominent responses were the P50(m) and N1(m) to the standard tones. The deviant and novel difference curves were calculated by subtracting the response to the standard stimulus from those to the deviant and novel stimuli, to measure the MMNm(m) component elicited by these sounds. In the novel-minus-standard difference curve, a response resembling the MMNm(m) was observed. It will be termed the novel-MMNm(m) to distinguish it from the MMNm(m) elicited by the deviant stimuli (termed the deviant-MMNm(m)).
The latencies of these responses were determined at Cz for the P50 and N1, and Fz for the deviant-MMN and novel-MMN of the electric data and, for the magnetic data, at the temporal channel pair showing the highest-amplitude response (determined as the square root of the squared sum of the two field components). In all statistical compar-

![Image of brain responses and EEG data](image_url)
ions, analyses of variance (ANOVAs) for repeated measures were used, applying the Huynh–Feldt correction when appropriate.

2.3. Head model

Equivalent current dipole (ECD; see e.g. Hämäläinen et al., 1993) fitting of both MEG and EEG data was done in spherical head models using Neuromag and BESA software (Neuromag, Espoo, Finland). The ECD parameters were determined to explain the measured data optimally in the least-squares sense. The location and size of the sphere were determined individually for each subject by fitting a sphere to the individually-measured electrode locations. In EEG, a 4 shell model was used; the thicknesses of the scalp, skull and cerebrospinal fluid were taken to be 6, 7 and 1 mm, respectively, their conductivities were assumed to be 0.33, 0.0042 and 1 Ω/m, respectively, and a conductivity of 0.33 Ω/m was estimated for the innermost sphere, corresponding to the brain tissue. For the MEG modelling, spherical models were used with the same, individually-determined centres of symmetry as in EEG. The sphere origin locations and radii are presented in Table 1.

2.4. Model I: one tangential dipole in each hemisphere

The sources of the P50m, N1m and MMNm responses were modelled with ECDs of freely varying strength, location and (tangential) orientation. The location and orientation of the source of the magnetic field measured at a selection of 44 channels over each hemisphere was first determined with one dipole at a time. Fitting of the strengths of two simultaneously-active dipoles was done using periods of 10, 20 and 40 ms, centred around the peak of the magnetic response for the P50m, N1m and MMNm, respectively, and using both 122 magnetic channels in MEG and all 25 electrodes in EEG. The residual variance, which indicates the amount of MEG and EEG data left unexplained by these dipoles, was determined, and an average over the 10, 20 and 40 ms periods was calculated using all channels and all electrodes.

2.5. Model II: two tangential dipoles in each hemisphere

The orthogonal tangential pair was added to each dipole of Model I having an identical location with the original dipole, separately in each hemisphere, and the source strengths were determined for all channels/electrodes of the MEG and EEG data using these dipole pairs. Thus Model II corresponds to one dipole rotating in the tangential plane in each hemisphere.

2.6. Model III: EEG data analysis with 3 orthogonal dipoles in each hemisphere

For the EEG data, the third orthogonal dipole (the radial one) was set up at the same locations as the dipoles of Models I and II in each hemisphere and the source strengths were recalculated. Model III corresponds to one dipole rotating freely in each hemisphere, each dipole being a ‘regional source’ in Scherg’s terminology (Scherg, 1990).

3. Results

3.1. Peak latencies

The mean (±standard error) latencies of the electric P50 and N1 responses elicited by the standard tones were 62 ± 6 and 104 ± 4 ms, respectively, and the mean latencies of the magnetic P50m and N1m responses were 62 ± 6 and 99 ± 5 ms in the left and 56 ± 7 and 96 ± 4 ms in the right hemisphere, respectively. The mean latencies of the electric deviant- and novel-MMN responses were 153 ± 6 and 111 ± 6 ms, respectively. The corresponding magnetic responses peaked at 143 ± 6 and 120 ± 7 ms in the left and 147 ± 5 and 110 ± 8 ms in the right hemisphere. No significant differences were found between the MEG left and right hemisphere and EEG peak latencies for any of the components.

3.2. Source strengths

The source strengths were determined as averages of the Model I dipole moments over the 10, 20 and 40 ms latency ranges of the P50m, N1m and MMNm components, respectively, using data from all 122 MEG channels. Because of the small responses to the standard tones, the ECDs were not determinable in the left hemisphere for the P50m and N1m responses in subjects 1 and 2.

Table 1

<table>
<thead>
<tr>
<th>Spherical head model</th>
<th>Subject</th>
<th>Radius of the outermost sphere (mm)</th>
<th>Sphere origin (mm)</th>
</tr>
</thead>
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<tr>
<td></td>
<td></td>
<td>x</td>
<td>y</td>
</tr>
<tr>
<td>S1</td>
<td>92</td>
<td>−0.8</td>
<td>19.4</td>
</tr>
<tr>
<td>S2</td>
<td>91</td>
<td>−1.5</td>
<td>12.0</td>
</tr>
<tr>
<td>S3</td>
<td>93</td>
<td>0.5</td>
<td>1.5</td>
</tr>
<tr>
<td>S4</td>
<td>93</td>
<td>0.3</td>
<td>8.4</td>
</tr>
<tr>
<td>S5</td>
<td>90</td>
<td>0.4</td>
<td>5.5</td>
</tr>
<tr>
<td>S6</td>
<td>95</td>
<td>4.2</td>
<td>7.3</td>
</tr>
<tr>
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<td>89</td>
<td>2.0</td>
<td>6.9</td>
</tr>
<tr>
<td>S8</td>
<td>89</td>
<td>−0.4</td>
<td>11.8</td>
</tr>
</tbody>
</table>

A 4 shell model for EEG data analysis was constructed on the basis of this outermost sphere. In MEG, a one shell spherical volume model was used, whose origin was the same as in EEG. The positive z-axis penetrates through the right preauricular point, the positive y-axis through the nasion and the positive x-axis approximately through vertex.
Significant inter-hemispheric differences were found in the response strengths. Single-factor ANOVAs indicated higher dipole moments in the left than in the right hemisphere for the N1m ($n = 7$, mean difference 1 nAm, $P < 0.01$) and deviant-MMNm ($n = 8$, mean difference 15 nAm, $P < 0.01$). A similar tendency was found for the P50m ($n = 6$, mean difference 4 nAm, $P < 0.07$).

3.3. Source locations

As seen from Figs. 2 and 3 and Table 2, the co-ordinates for the P50m, N1m, deviant-MMNm and novel-MMNm ECDs suggest that the generators of these responses are located in the auditory cortex in the superior temporal plane. The location of the N1m response was considered to be a landmark against which other source locations were compared.

In the right hemisphere, the ECD locations of the P50m, deviant-MMNm, and novel-MMNm were, on average, anterior to that of the N1m by 11, 18 and 5 mm, respectively, but these differences did not reach statistical significance. In the left hemisphere, the ECD location of the deviant-MMN was significantly medial and inferior to the N1m location ($n = 8$, mean differences 8 and 12 mm, $P < 0.05$ and $P < 0.01$, respectively).

Although the inter-hemispheric differences of the dipole locations in the anterior-posterior direction (see Table 2) did not reach statistical significance, the tendencies corroborate the findings of previous anatomical (Gershwind and Levitsky, 1968) and functional MEG studies (Mäkelä et al., 1994) demonstrating the more anterior location of right-hemisphere auditory cortex compared with that of the left hemisphere.

3.4. MEG residual variances

The mean residual variances of the MEG models are presented in Table 3. The magnetic P50m and N1m responses could be explained with reasonable confidence by only one (tangential) dipole in each hemisphere. The residual variances over a period of 10 and 20 ms around the peak of the P50m and N1m responses were both 15.3% when the data from all 122 magnetic channels was taken into account in Model I (one dipole in each hemisphere). Adding the orthogonal tangential component to the solution (switching from Model I to Model II) reduced the residual variances of the P50m and N1m responses, to 14.6 and 14.0%, respectively (by 5% and 9% of the Model I residual variance).

For the deviant- and novel-MMNm responses, the residual variances over a period of 40 ms around the peak of the response in Model I were 27.2% and 21.7%. When Model II was applied, the variances of the deviant- and novel-MMNm responses were reduced to 24.0% and 20.4%, respectively.
respectively (by 12% and 6% of the Model I residual variances).

3.5. EEG residual variances

The mean residual variances of the EEG models are presented in Table 4. The mean residual variances of the P50 and N1 responses in Model I were 21.2% and 19.5%, respectively. When Model II was applied, the residual variances were reduced to 16.8% and 13.8%, respectively (by 21% and 29% of the Model I residual variances). Finally, when Model III was applied, the residual variances were further reduced to 6.6% and 7.9%, respectively (by 61% and 43% of the Model II variances).

The mean residual variances of the deviant-MMN and novel-MMN responses in Model I were 21.0 and 37.8%, respectively. When Model II was applied, the residual variances were reduced to 13.5% and 18.1% (by 36% and 52% of the Model I residual variances), and with Model III, a further reduction to 6.6% and 9.3% (51% and 49% of the Model II variances) was observed.

To assess the quality of the MEG-based models for describing the EEG responses (with respect to the quality of the original MEG model), the ratio between the residual variances in the EEG and MEG was calculated separately in Models I and II for each target component in each subject. The smaller this number, the better the MEG-based model accounts for the EEG data. A reduction of this number between Models I and II would mean that the additional tangential component improved (in
II, the corresponding ratios were 1.15, 0.99, 0.55 and 0.89. The angle $\alpha$ is determined counterclockwise (viewed from the right) with the positive y-axis. The ECD strengths are from MEG Model I.

The difference between the Model I and the Model II EEG/MEG residual variance ratios was tested by single-factor ANOVAs, separately for each component. All of these tests, except the one for the deviant-MMN(m), produced significant results ($P^50m$: $F(1,5) = 9.74$, $P < 0.05$; $N1m$: $F(1,6) = 8.69$, $P < 0.05$; deviant-MMN(m): $F(1,7) = 3.16$, not significant; novel-MMN(m): $F(1,6) = 28.55$, $P < 0.01$). This means that by adding the orthogonal tangential dipole, the MEG-based models of $P^50m$, $N1m$ and the novel-MMN(m) improved the description of the EEG data significantly more than that of the MEG responses. To assess the relative quality of the models across different components, a two-factor ANOVA (component: $N1m$, deviant-MMN(m), novel-MMN(m) times Model I, II) was calculated. All measures were available only for 6 subjects. The $P50m$ component was omitted from this analysis because the lack of acceptable ECDs in two subjects for this component (see above) would have further reduced the number of subjects included in the test to 4. The significant interaction between the two factors ($F(2,10) = 5.06$, $P < 0.05$, Huynh–Feldt $\epsilon = 0.99$) resulted from a much larger EEG/MEG residual variance ratio reduction for the novel-MMN(m) than for any other component ($F(1,10) = 17.37$, $P < 0.01$ for the novel-MMN(m) vs. $F(1,10) = 4.49$ and $F(1,10) = 1.78$, for the $N1m$ and deviant-MMN(m) components; respectively; post-hoc tests were conducted by Scheffe-type pairwise comparisons). The significant result of the Component factor ($F(1,10) = 5.13$, $P < 0.05$, Huynh–Feldt $\epsilon = 0.78$) was due to the large difference between the residual variance ratios of the novel- and the deviant-MMN(m) ($F(2,10) = 5.23$, $P < 0.05$). In accordance with the single-factor ANOVA results, the Model factor showed a significant reduction of the EEG/MEG residual variance ratios from Model I to Model II ($F(1,5) = 13.02$, $P < 0.05$).

4. Discussion

4.1. Source locations

The locations of the $P50m$, $N1m$, and MMNm responses are in line with the findings of previous studies indicating that supratemporal generators are the main sources of these responses (Hari, 1990; Pantev et al., 1990, 1995; Rogers et al., 1990; Mäkelä et al., 1994; Reite et al., 1994; Nakasato et al., 1994). That deviant-MMNm and $P50m$ source locations are anterior to $N1m$ is also in agreement with recent findings (Sams et al., 1991; Csépe et al., 1992; Huotilainen et al., 1993; Levänen et al., 1993; Tiitinen et al., 1993; Alho et al., 1996), although some of these differences did not reach significance in the present data.

4.2. Peak latencies

No significant differences were found for the peak latency of any of the responses when the latencies from Fz/Cz of the EEG and latencies from the left and right hemispheres in MEG were compared. Thus we can assume that the responses in MEG and EEG at least partly represent the same neuronal sources.

The latency of the novel-MMN(m) response was clearly earlier than that of the deviant-MMN(m). This may be due...
to the fact that the novel-MMN(m) response was only partly caused by a true MMN-type response. A simultaneous enhanced N1(m) was probably overlapping this response (Scherg et al., 1989). The N1(m) to novel sounds was presumably enhanced, due to their wider frequency-spectra activating such frequency-specific neurons as had not become refractory by the repetition of the 600 Hz standard tone.

4.3. MEG residual variances

Model I dipoles account well for the P50m and N1m responses. The larger deviant-MMNm and novel-MMN residual variances can be explained partly by the fact that these components are obtained by subtraction (which increases noise level), and partly by the fact that the deviant and novel responses had originally fewer summations in the average than the standard responses.

The transition from Model I to Model II reduced the residual variations by only 5–12% of the original residual variance. This reduction is so small that one can conclude that Model I (one dipole in each hemisphere) is sufficient for describing the magnetic P50m, N1m, deviant-MMNm and novel-MMNm responses. In general, no consistent peak latency differences were found across subjects between the two source potential curves of Model II within the modelled intervals. This suggests that the orthogonal tangential dipole accounted for temporal changes in the source direction rather than describing additional sources. Model II of the deviant-MMNm(m) in the right hemisphere (Fig. 2) is an exception. The small early (approx. 80–120 ms) wave of the orthogonal tangential source potential might reflect the contribution from an increased N1(m) component (cf. Scherg et al., 1989).

4.4. EEG residual variances

The lower EEG/MEG residual variance ratios in Model II than in Model I suggest that addition of the second dipole reduces the residual variance significantly more in EEG than in MEG. This indicates that the MEG-based dipole locations are not optimal to explain even the tangential part of the EEG responses. This may be due to contributions from deep sources in the EEG data.

The MEG-based models are not equally good in describing the different EEG components. Results of the statistical analysis (specifically the interaction between the Component and Model factors) suggest that the source location calculated for the novel-MMN component from the MEG data was less optimal than that for the other components. This might be due to the novel-MMN reflecting two separate processes (and, therefore, probably deriving from multiple sources). As was mentioned above, the response to rare, widely-deviating sounds activates both the N1 and MMN generators (Scherg et al., 1989). It is possible that in addition to the supratemporal N1, other subcomponents of the N1 (Naäätänen and Picton, 1987) were also differentially affected by the standard and the novel sounds. Attempting to describe the overlapping effects of several generators by a single ECD results in relatively large amounts of residual variance, which is then significantly reduced by including additional dipoles in the model.

The radial component placed in the MEG-based location (replacing Model II with Model III) had a marked effect: the residual variance was reduced by 43–61%. A more optimal solution for EEG modelling would be to separately search a location for the radial dipole, since the MEG-based location may not be optimal for the EEG data. This would enable the radial dipole to better account for the deep and radial sources not visible in MEG.

5. Conclusions

When tangential current sources are located close to the surface of the brain, MEG-based dipole modelling is a fine tool for locating the sources. The relatively high residual variances when EEG was explained by the MEG-based models show that it would be beneficial to use MEG and EEG simultaneously to aid modelling of electromagnetic data. MEG-based modelling is a good starting point from which the model can be refined by adding further dipoles to account for the activity not detected by MEG.

The aim of the present investigation was to assess how well MEG-based dipole models of the target components account for the corresponding electrical activity observed in EEG. In order to make MEG and EEG source modelling comparable, only single-dipole models restricted to specific components were considered. This was necessary because the magnetic activity measured by MEG and the electrical signals recorded in parallel by EEG do not fully correspond to each other and, therefore, comparisons between multidipole models describing several components in MEG and EEG would have yielded highly complex results. In the search for optimal solutions, the present ECD models can be further refined. For example, whereas the addition of an orthogonal tangential dipole at the same location (Model II) did not significantly decrease the residual variance in the MEG model, the addition of a second dipole at a different location could have. Therefore, the modelling strategy applied in the present study reflected the goals of this investigation, not limitations of MEG or EEG modelling in general.

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