Magnetoencephalographic Correlates of Audiotactile Interaction

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To seek for correlates of an interaction between auditory and somatosensory processing, the brain’s magnetic field in response to simultaneously presented auditory (A) and tactile (T) stimuli was compared with the sum of the respective unimodal responses (A+T). The stimuli were binaural 1047-Hz tone bursts of 60 dB sensation level and tactile pressure pulses to the right thumb. The mean interval between two stimuli of the same modality was 1.95 s. The magnetic field was recorded using a 306-channel whole-scalp neuromagnetometer. A clear audiotactile interaction was revealed in the hemisphere contralateral to the side of tactile stimulation in six of eight subjects, whereas in the ipsilateral hemisphere an interaction was noticed in only three subjects. The time courses of these audiotactile interaction fields typically showed major deflections of opposite polarities around 140 and 220 ms. The first deflection appeared to arise in the region of the secondary somatosensory cortex (SII). The polarity of this interaction was consistent with the view that the auditory stimulus resulted in a partial inhibition in SII. In two subjects, strong indications of auditory contributions to the interaction were available, although in different hemispheres. The relatively high interindividual variability of the observed interaction, which represents potential neural substrates for multisensory integration, could indicate that the way subjects perceive the simultaneous presentation of auditory and tactile stimuli differs.

INTRODUCTION

We often perceive auditory and tactile stimuli simultaneously or as having a causal relationship. In many situations the tactile stimulus clearly dominates, and the related sound is merely a concomitant. This happens, for instance, when we scratch ourselves, rub our hands together (Jousmäki and Hari, 1998), stroke some surface texture, or turn over a page. Even though the auditory sensation may be faint under such circumstances, its complete absence would be readily noted. It also happens, of course, that the sound is perceived at least as strongly as the tactile stimulus. In other occasions the auditory sensation dominates. This is the case whenever the generation of sound determines our doing. Prototypical examples are knocking at a door or playing a musical instrument. A common feature of all these examples is that the brain manages quasi-instantaneously to relate auditory and somatosensory sensations to each other. This indicates the existence of an efficient integration of auditory and somatosensory processing. The inputs to both modalities can serve to modulate subsequent motor acts. For example, when knocking at a door in rapid succession, the sensory inputs in response to one knock can be used to adjust the force applied in the subsequent knock: Usually the force is increased if the auditory input is weaker than expected and decreased in the case of a painful sensation.

Audiotactile integration can be viewed in the wider context of multisensory integration, which is known to take place in the midbrain, thalamus, and cortex (see Stein and Meredith, 1993, for a review). One of the best studied structures with multisensory neurons is the superior colliculus (SC) in the midbrain. The multisensory neurons in the SC have receptive fields for visual, auditory, and somatosensory stimuli. Since these receptive fields are in spatial register with one another, a sensory cue, regardless of modality, activates neurons in the same SC location that corresponds to the position of the stimulus in the sensory space (Stein, 1998). This principle represents an efficient way to combine information from different sensory cues, often resulting in an enormous enhancement of the neural activity compared with the activity elicited by the respective unimodal stimuli (Meredith and Stein, 1983). SC has been proposed to play a major role in cross-modal attentive and orientation behaviors (Wallace et al., 1998). In cat, an intimate relationship seems to exist between SC and a specific region of the cortex, the anterior ectosylvian sulcus (AES). After a temporary deactivation of the AES, most multisensory SC neurons could no longer integrate the inputs to different modalities to produce an enhanced response (Wallace and Stein, 1994). Presumably, a functional homologue of AES will soon be found in other species (Stein, 1998).
Multisensory neurons have also been described in the posterior parietal cortex (Hyvärinen and Poranen, 1974) and in the superior temporal sulcus (Hikosaka et al., 1988).

Already decades ago, the relation between the electrical responses in the human brain and mental processes of integration and association was considered a challenging problem (Walter, 1964). The earliest indications of an interaction between auditory and somatosensory cortical processing were obtained for the slow vertex potential. According to Hay and Davis (1971), such an interaction can be noticed in the vertex potential even if the two modalities are stimulated with an onset asynchrony as long as 2.5 s, although statistically significant effects were observed in only a part of the experiments. More distinct results were presented in a subsequent study (Davis et al., 1972), in which the onset asynchrony was reduced to 500 ms. In the average across subjects, a tactile stimulus reduced the auditory response by nearly the same factor as an auditory stimulus reduced the response to the tactile stimulus (by about 35%). An onset asynchrony of 500 ms was also used by Huttunen et al. (1987), who studied both the slow vertex potential and the corresponding magnetic field in response to a tone burst preceded by a current pulse to the median nerve, and vice versa. None of the magnetic responses to the second stimulus differed in a statistically significant way from the control, i.e., the response to the respective stimulus presented alone. However, the somatosensory evoked potential showed an amplitude decrease of up to 23%. The deflection P200 of the auditory evoked potential was reduced by 36%, whereas no effect was found for deflection N100. At the same time, Greenwood and Goff (1987) investigated how the somatosensory evoked potential in response to electrical stimulation of the right median nerve was changed by clicks delivered to the right ear, either simultaneously or with onset asynchronies between 20 ms and 2.5 s. Basically no effect was found for the primary somatosensory response N20-P30, but suppressive cross-modal interaction was observed with increasing latency. The N55-P100 amplitude was reduced maximally at 20 ms and the effect decreased with increasing interstimulus intervals, whereas the N140-P190 amplitude showed a maximum interaction effect at intermediate interstimulus intervals.

Okajima et al. (1995) studied the interaction during simultaneous presentation of a short tone burst and a painful electrical stimulus applied to the median nerve. To extract the interaction, the bimodal response was subtracted from the sum of the two unimodal responses. The resulting “interaction potential” showed, at all three electrodes (Cz, C3, and C4; linked earlobes as the reference), a clear deflection with a latency of about 120 ms. The polarity of this deflection was consistent with the assumption of a suppression of auditory and/or somatosensory activity. An analogous subtraction technique was used in a recent investigation by Foxe et al. (2000), who studied event-related potential (ERP) correlates of an interaction between auditory stimulation and electrical stimulation of the left median nerve. They provided, for the first time, topographical maps of the interaction potential. In another recent study, Lam et al. (1999) investigated the effect of continuous auditory stimulation (music) on the somatosensory evoked field (SEF) following electrical stimulation of the median nerve and described an auditory–somatosensory interaction in the ipsilateral secondary somatosensory cortex (SII).

This brief overview shows that, except for the observation of Lam et al. (1999), no clear magnetic correlate of an interaction between auditory and somatosensory systems is available so far. Consequently, the main objective of the present study was to prove the existence of a magnetic correlate of an audiotactile interaction and to provide a rough characterization of its temporal and spatial properties.

**MATERIALS AND METHODS**

**Subjects**

Eight normal-hearing subjects with no history of neurological or otological disorders participated in this study. The study had prior approval by the Ethical Committee of the Helsinki Uusimaa Hospital District, and an informed consent was obtained from each subject after explanation of the nature and purpose of the investigation.

**Stimuli**

Sounds to the ears and tactile pulses to the right thumb were presented separately as well as simultaneously. The auditory stimuli were 1047-Hz tone bursts of 60 dB sensation level, corresponding to note C7, with a duration of 100 ms (10 ms rise and fall time, 80 ms plateau). The stimuli were presented binaurally through plastic tubes to ear pieces tightly fitted into the ear canals. The right thumb was stimulated using a balloon diaphragm driven by bursts of compressed air (Mertens and Lütkenhöner, 2000).

The stimulus sequence was periodic with regard to the simultaneous presentation of the auditory and tactile stimuli (stimulus category AT) and pseudo-random with regard to auditory and tactile stimuli presented alone (stimulus categories A and T, respectively). The sequence, of a total length of 450 stimuli (150 for each stimulus category), was created by a script written in the computer language Perl. As the first step, a random binary sequence of length 75 was generated such that the digits 0 and 1 had about the same frequency. Then a mirror image of this sequence was generated by
exchanging digits 0 and 1 in that sequence. The two binary sequences were finally concatenated, and the digits 0 and 1 were interpreted as the sequences A–AT–T (auditory, simultaneous, tactile) and T–AT–A (tactile, simultaneous, auditory), respectively. This procedure ensures that the stimulus categories A, AT, and T have exactly the same frequency of occurrence.

The interval between the onsets of two successive stimulus presentations (irrespective of the stimulus category) was 1.3 s (stimulus onset asynchrony). Thus the onset asynchrony for simultaneous stimulations of both modalities was 3.9 s, and the mean onset asynchrony for each modality was 1.95 s.

**Magnetoencephalography**

Magnetoencephalography (MEG) was performed in a magnetically shielded room using a 306-channel whole-scalp neuromagnetometer (Vectorview, Neuromag Ltd.). This system is equipped with two orthogonal planar gradiometers and one magnetometer at each of the 102 measurement locations (arranged in a helmet-shaped array). The subjects were seated in a reclined chair with their head firmly resting on the posterior inner wall of the helmet. They were looking straight ahead, trying to fixate a point in front and to minimize blinking. They were asked to stay awake, to keep their eyes open, and not to move their head. No effort was taken to control the mental state of the subjects, who passively perceived the stimuli. Three independent runs of the experiment (each with 150 presentations of each stimulus category, as described above) were performed within a single session.

To allow a transformation between a device-based and a head-based coordinate system, the following procedure was used. Before the actual measurements, four head position indicator (HPI) coils were attached to the head, and their locations were determined relative to three well-defined anatomical landmarks (nasion and points just anterior to the two ear canals) using a 3D digitizer (Fastrak; Polhemus Navigation Sciences, Colchester, VT). When the subjects were in their final measurement positions, the magnetic fields generated by currents fed into the HPI coils were measured, and by means of a fit procedure the locations of the HPI coils were calculated in device-based coordinates.

**Preprocessing of Data**

The signals were bandpass filtered between 0.03 and 200 Hz and digitized at 600 Hz. The recorded stimulus-related epochs lasted for 1200 ms, which included a 200-ms prestimulus period. Responses to different stimulus categories were averaged online. Epochs contaminated by muscle artifacts or by eye movements and blinks were omitted from the average on the basis of amplitude variations of more than 3 pT/cm in one of the MEG channels or at least 150 µV in the vertical electro-oculogram channel. The averaged responses were finally low-pass filtered with a cut-off frequency of 40 Hz. Magnetoencephalographic correlates of audiotactile interaction were obtained by subtracting the responses to simultaneous presentations of auditory and tactile stimuli from the sum of the responses to separate presentations of the two types of stimuli, i.e., by calculating responses $A + T - AT$. For the sake of simplicity, the result shall be denoted as the interaction.

**Source Analysis**

Cerebral sources of the signals were estimated in a head-frame coordinate system, which was defined using the nasion and points just anterior to the ear canals as landmarks. The x axis of this coordinate system runs from the left to the right preauricular point; the y axis runs toward the nasion perpendicular to the x axis in the posterior–anterior direction, and the z axis runs perpendicular to the xy plane in the inferior–superior direction. The estimations were based on the model of one or two current dipoles in a homogeneous sphere centered at the point (0,0,4) (coordinates in cm). The locations and orientations of the dipoles were assumed to be time invariant (fixed dipole), whereas their strengths were allowed to vary. The model parameters were optimized using a least-squares fit procedure described elsewhere (Lütkenhöner et al., 1991; Lütkenhöner, 1998; Lammertmann and Lütkenhöner, 2001). Briefly, the fit procedure exploited the fact that, given the time-invariant model parameters (three coordinates and one angle per dipole), the remaining optimization problem is linear so that inserting the solution of this linear problem into the original problem results, for N dipoles to be optimized, in a 4N-dimensional nonlinear minimization problem. Optimal values for the time-invariant parameters were obtained by solving this nonlinear minimization problem using the Fletcher–Powell algorithm. The subsets of channels used in the dipole fits typically consisted of about 30 pairs of gradiometers (magnetometers were not taken into account).

**RESULTS AND FIRST INTERPRETATIONS**

**Visual Inspection of AEF and SEF Data**

To provide a solid basis for the subsequent consideration of audiotactile interaction, we first consider the basic spatial features of responses to separate presentations of auditory and tactile stimuli. Figure 1 provides a compilation of isocountour maps for all eight subjects. The figure is organized as follows: Each row corresponds to one subject, and the five columns characterize the responses of left auditory cortices (L-ACx), left somatosensory cortices (two different patterns, de-
FIG. 1. Isocontour line maps characterizing the spatial pattern of the magnetic field in response to auditory and tactile stimuli. The latencies selected are indicated at the bottom of each map (in milliseconds). Each row represents one subject (initials given on the left). The five columns reflect the AEFs recorded over the left hemisphere (L-ACx), the SEFs recorded over the left hemisphere (columns L-SS1 and L-SS2) as well as the right hemisphere (R-SS2), and the AEFs recorded over the right hemisphere (R-ACx). The isocontour lines are spaced by 40 fT. Positive field values (magnetic flux out of the head) are indicated by red and negative field values by blue isocontour lines. The gradiometers which recorded the greatest field gradients are indicated by green squares.

FIG. 2. Time course of the interaction field in a sensor-layout representation (subject TT). Two curves, reflecting the activity measured by the two orthogonal planar gradiometers, are given for each measurement location. The time window ranges from 0 to 300 ms. Deflections clearly exceeding the noise can be found especially in the highlighted area.
noted L-SS1 and L-SS2), right somatosensory cortices (R-SS2), and right auditory cortices (R-ACx). The maps represent the latencies indicated at the bottom of each map (milliseconds after stimulus onset). To emphasize the considerable interindividual variability of the responses, the isocontour level increments are identical for all subjects and all conditions.

The two outermost columns in Fig. 1 show isocontour maps for the AEF deflection N100m, which occurs about 100 ms after the sound onset. The maps have a dipolar appearance, with two field extrema of opposite polarities and a polarity reversal zone (with near-zero field amplitudes) in between. For N100m, the magnetic field values in the left hemisphere are consistently negative (field into the head) at anterior-inferior locations (blue isocontour lines) and positive (field out of the head) at posterior-superior locations (red isocontour lines), whereas the reverse is true in the right hemisphere. The magnitude of the field, reflected in the total number of isocontour lines, exhibits a considerable interindividual variability.

The three middle columns of Fig. 1 characterize the basic spatial features of SEFs. The intention was to display activity arising from the left SI cortex in column L-SS1 and activities arising from the left and the right SII cortices in columns L-SS2 and R-SS2, respectively. This goal was clearly achieved in Subject LB, in whom the patterns closely agree with those described previously (e.g., Hari et al., 1984; Forss et al., 1994, 1995, 1996; Hari and Forss, 1999). In the other subjects, however, at least one of the three components was either weak or hard to identify or even missing. By focusing on early responses, SI activity was easily recognized at 50-70 ms in all subjects except TT, in whom SI-type pattern was observed around 90 ms. The latencies considered in column L-SS2 of Fig. 1 were chosen so that the associated spatial pattern differed maximally from the respective pattern in column L-SS1. This approach resulted in patterns that were roughly orthogonal to those shown in column L-SS2, except for Subject SC. Regarding the location of the steepest field gradient, only half of the subjects (AF, LB, NJ, and TT) showed distinct differences between the two columns. Dipolar field patterns clearly resembling SII activities were found in the right hemisphere, i.e., ipsilateral to the side of tactile stimulation, in only two subjects (LB and NJ), and only in Subject LB was the strength of this ipsilateral activity comparable to the strength of the contralateral activity.

**Visual Inspection of Interaction Data**

Figure 2 illustrates the interaction field of an exemplary subject (TT) in a sensor-layout style. The arrangement of the curves roughly reflects the spatial arrangement of the sensors (the colors blue and red distinguish the two orthogonal gradiometers per measurement location). The time window corresponds to the first 300 ms after stimulus onset. Even though the interaction field displayed here is relatively noisy, the curves in the highlighted area show deflections clearly exceeding the noise floor. By carefully inspecting such sensor-layout displays, clear indications of an interaction in the left hemisphere were obtained in six of eight subjects. In the right hemisphere such evidence was available in only three subjects, one of which (the case shown in Fig. 2) was excluded from further considerations because of an insufficient signal-to-noise ratio and a peculiar spatial structure (briefly indicated below).

Figure 3 provides a compilation of the observed time courses. The upper six graphs show interaction in the left hemisphere, whereas the next two graphs show interaction in the right hemisphere (indicated by the “r” appended to the initials of the subjects). The three curves in each graph represent the channel with the highest interaction amplitude and two neighboring channels. The grand average of all left-hemisphere curves is represented by the thick curve at the bottom; exclusion of the subjects with the weakest interaction field (LC and SR) resulted in the thin curve.
highest interaction amplitude and two neighboring channels. If more than two reasonable alternatives were available for the selection of the latter two channels, preference was given to the curve best matching the other two curves. The sign was adjusted so that the dominant deflection in the latency range between 100 ms (subject LB) and 150 ms (subject AF) was negative. Owing to the relatively low signal-to-noise ratio, part of the observed latency variability is certainly due to noise. All in all, the curves are in good qualitative agreement so that it appears justified to calculate a grand average. The thick curve at the bottom of Fig. 3 is based on all curves from the left hemisphere, whereas the thin curve was obtained after excluding the two subjects with the weakest interaction (LC and SR). To prevent the results being dominated by the subjects with the highest interaction amplitudes, the curves were weighted with a subject-dependent factor, which was inversely proportional to the highest interaction amplitude observed in the respective subject (this is basically the same kind of scaling as underlying the upper plots, i.e., the plots for the individual subjects). The grand average curves show peaks of opposite polarities with latencies of about 140 and 220 ms. An early positive deflection at about 70 ms, visible only in the thick curve, has to be considered with more reservation, because it results mainly from the responses of subjects LC and SR, though weak deflections in this time range can be found in a few other subjects as well.

Figure 4 shows isocontour maps of the interaction field. The latency considered in the left half of the figure, specified in milliseconds at the bottom of each interaction map, corresponds to the dominating negative deflection in Fig. 3, whereas the latency considered in the right half corresponds to the subsequent positive deflection. In addition, isocontour maps of AEFs and SEFs are shown, for the same latency as the corresponding map of the interaction field. The green squares in the maps, situated close to the steepest gradients of the interaction fields, indicate the measurement locations examined in the respective panels of Fig. 3.

First, the interaction fields recorded over the left hemisphere shall be studied. It is a consistent feature of the earlier interaction patterns (left half of Fig. 4) that the value of the magnetic field tends to be positive (red contour lines) at anterior locations and negative (blue contour lines) at posterior locations. This finding could indicate that the essential mechanism underlying the interaction is basically the same for all subjects. Further clues as to the origin of the interaction are provided by the three subjects with the strongest interaction fields (LB, NJ, TT). The maps obtained for the interaction field and the SEF are similar in these subjects. A comparison with the maps presented in Fig. 1 suggests that the main source of the interaction field is the SII region. In the other three subjects, the signal-to-noise ratio achieved for the interaction field is too low to give conclusive evidence for alternative hypotheses. It should not be overlooked, however, that, in subject SR, an argument analogous to that presented above would lead to the conclusion that mainly activity of the auditory areas might be responsible for the interaction field. In this context it seems important that, for the latency considered here, activity originating in the SII cortex is negligible in Subject SR, as suggested by a comparison between the SEF pattern in the left half of Fig. 4 and the respective patterns shown in Fig. 1. Thus, a good working hypothesis could be as follows. In subjects exhibiting strong SII activity, the interaction field basically reflects activation changes in the SII region. Potential contributions from auditory areas are masked by this strong activity, except for those subjects in whom the SII activity is relatively weak (e.g., subject SR).

In all subjects except LB and TT, the later interaction patterns (right half of Fig. 4) qualitatively resemble the earlier ones (left half of Fig. 4), except that the polarity is reversed. In subject NJ, the later interaction map is similar to the corresponding SEF map, but it is not too different from the AEF map either. In subject SR, the interaction resembles again more the AEF than the SEF. Subject TT is special insofar as the left-hemisphere pattern is basically monopolar. Because this pattern is presumably associated with a similar monopolar pattern over the right hemisphere, the map displayed in the figure represents a view from the top rather than from the left, since such a representation was considered to be more informative.

Finally, the interaction in the right hemispheres of Subjects LB and NJ shall be considered (bottom two rows in Fig. 4). The earlier interaction pattern in Subject LB (left half of the figure) is similar to the corresponding SEF pattern, and the situation is analogous to that in the left hemisphere. However, the later interaction pattern in subject LB (right half of the figure) as well as both interaction patterns in subject NJ differ from the corresponding patterns of both AEF and SEF. It is quite remarkable that both interaction patterns in subject NJ are similar to the corresponding AEF pattern in Fig. 1. Thus, the interaction observed over the right hemisphere of subject NJ could be of auditory origin. However a simple amplitude reduction of the auditory activity (reflecting, e.g., inhibition of neurons in the auditory cortex) can be excluded, because the AEF observed at the latency of the interaction has a quite different spatial pattern.

**Dipole Source Analysis**

Motivated by the results of the visual inspection of the data, the first dipole source analyses were based on the hypothesis that the interaction field can be ex-
plained by two dipoles in the somatosensory cortex, each having a time-invariant location and direction ("fixed dipole"). All time-invariant parameters were derived from the SEF data. The isocontour maps in the first two columns of Fig. 5 show, for each subject, the magnetic field patterns associated with the two estimated dipoles. For the estimation of the first source, only the time range 40–60 ms was considered (except for subject SC, in whom the time range was 60–100 ms). For the estimation of the second source, the time range was extended to 40–140 ms, and a two-dipole model was fitted to the data, retaining the location and the direction of the first dipole, but recalculating its strength. In five subjects this procedure resulted in a location clearly different from that of the first one. However, in the other three subjects, indicated by a "+", the two dipoles resulted in a serious interaction, characterized by nearly identical locations and huge moments of opposite polarities. This phenomenon generally indicates that a reliable source separation is not possible (Lütkenhöner et al., 1992; Lütkenhöner and Pantev, 1993). In such cases, the dipole orthogonal to the first one was used as the second source, resulting in the model of a "rotating dipole." A comparison with the respective maps in Fig. 1 generally shows a good agreement (differences in the absolute field amplitudes are irrelevant in this context). Greater discrepancies occur only in Subject LC, in whom the second dipole was not very well defined (a rotating dipole would have been a good alternative also in this case). While the first dipole presumably reflects a source in the SI cortex, the physiological basis of the second dipole is more equivocal. This uncertainty is reflected, for instance, in the fact that in half of the subjects (LC, SC, SR, and TT) it was problematic or even impossible to separate the second source reliably from the first one. Nevertheless, it appears reasonable to assume that in all subjects except LC the SII cortex contributes predominantly to the second dipole.

The plots in the third column of Fig. 5 provide some insight into the dipole fit procedure itself. The root-mean-square (RMS) values of the magnetic field data are visualized as hatched areas, whereas the RMS values of the residuals (difference between measured data and model prediction) are represented by black curves. The ratio of these two measures allows for an assessment of the quality of the dipole fit (for instance, a ratio of 5, which was exceeded at least in some occasions, indicates that the percentage of variance accounted for by the model, generally called the "goodness of fit," corresponds to 96%). The RMS values associated with each of the two sources are represented by the magenta and green curves, respectively. These two curves allow us to assess the relative impacts of the two sources, i.e., they indicate to which extent the respective source really contributes to the explanation of the measured data (high amplitudes of the estimated dipole moments can be misleading in the case of a deep source). The time courses of the estimated dipole moments are shown in the fourth column.

Finally, the interaction field was analyzed, retaining the locations and directions of the two dipoles derived from the SEF data. The time courses of the estimated dipole moments are displayed in the rightmost column of Fig. 5. Deflections clearly exceeding the noise level can be recognized only in Subjects AF, LB, NJ, and TT. It is remarkable that all significant indications of an interaction refer to the second source, represented by the green curves. This finding provides further support for the hypothesis that the interaction field observed in this study mainly results from sources in the SII region. It shall be finally mentioned that plots as provided in the third column turned out to be more or less uninformative in the case of the interaction field, owing to its poor signal-to-noise ratio. However, for subject LB such plots yielded at least some indications of a second source in the time range 180–280 ms. Moreover, in subject NJ, the RMS of the residuals deviated systematically from the prestimulus baseline, suggesting that the two dipoles did not optimally explain the measured data, either because of suboptimal locations and orientations of the dipoles or because of an additional source not accounted for.

The ultimate challenge of a dipole source analysis is, of course, an unconstrained optimization of all parameters. In three subjects (LB, NJ, and TT) the signal-to-noise ratio of the interaction field was indeed sufficient for such an analysis, and in subject LB even both hemispheres could be successfully analyzed. The results are presented in the right half of Fig. 6. For comparison, field patterns derived for the auditory cortex and SII are displayed in the left half of Fig. 6.

In the left hemisphere of subject LB, two sources could be clearly separated. As a first step, dipoles with time-invariant location and direction were fitted separately to the time ranges 80–120 and 180–250 ms. Retaining all time-invariant parameters, a simultaneous two-dipole fit was used to estimate the time courses of the dipole moments. The latter exhibited peaks at about 100 and 230 ms, respectively. A comparison of the associated spatial patterns with those derived from AEF and SEF strongly suggests that the first source represents activity in the SII region. The fact that the second source does not match very well the auditory pattern shown on the left is not necessarily contradictory to the assumption of an auditory origin of this activity, as the auditory pattern shown here is certainly not representative of all sources in the hemisphere of subject NJ.
auditory areas. A consideration of auditory field patterns at different latencies shows indeed a substantial variability, and the pattern displayed here has to be considered a compromise which may not represent very well the auditory source(s) affected by the somatosensory input.

In the other cases considered in Fig. 6, the limited signal-to-noise ratio thwarted all attempts to fit more than one source to the interaction data. The field pattern of the dipole derived for the right hemisphere of subject LB clearly suggests a source in the SII region. The analysis window for the time-invariant parameters was 80–120 ms in this case. In subjects NJ and TT (analysis windows of 120–250 and 100–200 ms, respectively), the origin of the interaction field is not so clear at the first glance, since the rough orientation of the pattern obtained for the interaction appears to represent a compromise between the patterns shown for the AEF and the SEF. A comparison of the estimated dipole locations, however, suggests that also in these subjects the interaction field is mainly arising from the SII region. Figure 7 illustrates this for the yz plane, i.e., for coordinates representing the posterior–anterior (y) and the inferior–superior (z) direction. To compensate for interindividual differences in the cortical anatomy, the coordinates of the auditory dipole were subtracted from those of the other dipoles. Thus, the origin of the coordinate system in Fig. 7 roughly corresponds to the

FIG. 4. Isocontour maps for AEFs, SEFs, and interaction fields in all subjects. The latencies, indicated at the bottom of each interaction map (in milliseconds), roughly correspond to the major deflections of the curves in Fig. 3. The green squares indicate the locations of the gradiometer channels considered in Fig. 3 (representing the channel with the highest interaction amplitude and two neighboring channels). The isocontour line spacing is 20 fT in all cases.
FIG. 5. Two-dipole source analysis of the interaction fields of all eight subjects. The dipole locations and orientations were assumed to be identical with those derived from the SEF data. Isocontour maps of the field patterns associated with the two dipoles (sources 1 and 2) are presented in the first two columns (the simulated dipoles had a moment of 25 nAm; the isocontour line spacing was 40 fT). The symbol “+” attached to the initials of a subject indicates that two orthogonal dipoles with the same location were selected (“rotating dipole”), because a sufficiently stable and reliable separation of two independent dipoles turned out to be impossible. The third column shows the RMS values of the data (shaded area) and the differences between data and model predictions (black curve). The RMS values corresponding to the individual sources are represented by the magenta curve (first source) and the green curve (second source). The time courses estimated for the dipole moments are shown in the fourth column (for the SEF) and the fifth column (for the interaction field).
location of the auditory cortex. The filled symbols represent the dipoles derived for SII (from responses to stimuli T), whereas the open symbols represent the dipoles derived for the interaction field (in Subject LB, the second interaction source is the one next to the origin). The mean xyz coordinates (in cm) of the SII sources were $x = 0.34$, $y = -0.03$, and $z = 2.59$, whereas the mean coordinates of the source derived from the interaction data were $x = -0.01$, $y = 0.19$, and $z = 1.88$ (second source in Subject LB not used for these calculations). Thus, also the mean dipole coordinates support the hypothesis that the SII region is the dominant source of the interaction field. A possible explanation for the systematic $z$ coordinate differences between the presumed SII source and the interaction source is that the first source is pulled in a superior direction by small contributions of the SI cortex, whereas the latter source is pulled into the opposite direction by auditory contributions to the interaction field.

Subjective Experience of the Subjects

All subjects perceived the auditory and tactile stimuli basically as two independent streams. Moreover, the auditory stimuli were perceived as more intense than the tactile stimuli. This means that the dominant impression was that of an auditory sequence with irregular omissions. Whereas subject FN noticed an attenuation of the tactile perception during the simultaneous auditory stimulation, the other subjects either reported no change or were not sure about a change.

DISCUSSION

Contralateral Interaction Field

Despite the considerable interindividual variability observed in this study, some basic features appear to be common to all subjects (excluding two subjects who showed no interaction at all). It seems, for example, that, in the hemisphere contralateral to the side of somatosensory stimulation, the time course of the dominating component of the interaction field roughly corresponds to the grand average shown at the bottom of Fig. 3, exhibiting pronounced maxima at about 140 and 220 ms in both hemispheres. Moreover, Fig. 4 suggests that the spatial patterns associated with the 140 ms deflection are also roughly consistent: Calculation of a grand average would evidently result in a pattern with outgoing magnetic flux at anterior scalp locations and magnetic flux into the head at posterior locations. Such a pattern would be oriented roughly orthogonal to the scalp current density maps of Foxe et al. (2000), who noticed, at a latency of 65 ms, extrema of opposite polarities over the vertex and the right central/post-central scalp and, at a latency of 80 ms, a slightly different pattern with a polarity reversal in the region of the superior surface of the temporal lobe. Although a comparison of that study with ours is problematic, owing to the considerable methodological differences, the observed spatial patterns are roughly consistent, because the electrical potential and the magnetic field arising from a current dipole are oriented orthogonal to each other. Thus the underlying sources seem basically the same.

The first major deflection of the interaction field in the contralateral hemisphere, occurring at a latency of about 140 ms, appears to arise mainly from the SII region. Several findings support this conclusion. The strongest evidence was provided by the subjects with the best signal-to-noise ratios (LB, NJ, and TT), in whom the observed interaction field was strong enough for an unconstrained dipole source analysis. The dipoles derived for the interaction field deviated by less than 1 cm from the presumed location of SII, whereas they deviated by about 2 cm from the location derived for the auditory cortex. But also the two subjects in whom absolutely no interaction field was noticed (FN and SC) support this SII hypothesis, as they were those with the weakest SII activity. Since the spatial pattern associated with the second major deflection of the interaction field, occurring at about 220 ms, resembled that associated with the first one (except for subjects LB and TT), it seems likely that SII significantly contributed also to that later deflection. This conclusion is corroborated by the finding that the dipole derived for the later deflection in subject LB was situated between the locations estimated for auditory cortex and SII (cf. Fig. 7), suggesting that both structures contribute to this signal. The polarity of the observed SII-related interaction fields was consistent with the view that the auditory stimulus results in a partial inhibition of neurons in SII. However, latency differences between the major deflections of the SEF and the interaction field indicate that the idea of a pure amplitude reduction of the activity evoked by the tactile stimuli is definitely too simple. Either the auditory input affects only a subpopulation of neurons in SII or the simultaneous presentation of an auditory stimulus not only reduces the amplitude of the somatosensory response, but also changes its timing.

An attempt to reveal, by means of dipole modeling, contributions of the SI region to the contralateral interaction field failed (cf. Fig. 5). Although this does not completely rule out the possibility that such contributions exist, it can at least be concluded that SI has a significantly smaller impact on the interaction field than SII. Clear indications of auditory contributions to the contralateral interaction field were obtained only in Subject LB and only for the later stage of the interaction (latency of about 220 ms). The location of the estimated dipole almost in the middle between the dipoles derived from AEF and SEF (cf. Fig. 7) suggests,
However, that the SII region is also active at that latency. The auditory cortex might have been involved also in the generation of the weak interaction field in Subject SR, though this finding has to be considered with more reservation, owing to the relatively poor signal-to-noise ratio in that subject.

Ipsilateral Interaction Field

Findings concerning the interaction field in the ipsilateral hemisphere are of an anecdotal nature, because in only two subjects the signal-to-noise ratio sufficed for a more detailed analysis. In one subject (LB) the early stage of the interaction field corresponded well to the contralateral hemisphere so that an origin in SII is likely. Additional sources, becoming relevant in later stages, could not be resolved. In the second subject (NJ) already the early stage of the interaction field appeared to be dominated by activity arising from the auditory cortex. However, the interaction did not correspond to a simple amplitude modulation of the AEF, as auditory stimulation alone resulted in a completely different spatial pattern at the time of maximal interaction. The results obtained for the ipsilateral hemisphere provide, by the way, further support for the hypothesis that, in subjects with strong SII activity to tactile stimuli presented alone, the SII region plays an important role in the generation of the interaction field: As suggested by Fig. 1, only subject LB displayed really strong somatosensory activity in the ipsilateral hemisphere, and it is probably not pure coincidence that this subject showed also an exceptionally strong SII-like interaction field in that hemisphere. The data of Subject NJ are not necessarily contradictory to the above hypothesis, because the strong ipsilateral interaction seen in this subject was presumably of auditory rather than somatosensory origin. At this point, a brief comment appears appropriate, on the study of Lam et al. (1999) on the effect of continuous music stimulation on SEFs elicited by electrical stimulation of the median nerve. The only auditory–somatosensory interaction effect was found in the ipsilateral SII. This finding is in strong contrast to the present study, but the experimental designs were also clearly different. Foxe et al. (2000) already pointed out that neural integration processes between sensory modalities depend highly on the temporal concordance of the stimuli and that subjects perceiving continuous auditory stimulation, as in the study of Lam et al. (1999), are unlikely to relate this stimulation strongly to the somatosensory pulses.

Methodological Considerations

When devising this study it was unclear whether the experiments would be sensitive enough to provide incontrovertible evidence of an interaction between auditory and tactile processing. In retrospect such concern was not completely unfounded, as in two of the eight subjects indeed no indication of interaction was detected, and in two other subjects the interaction just exceeded the noise level. Thus, it was probably a wise decision to choose a relatively simple experimental paradigm, which avoided a distribution of the available measurement time among different conditions (this would have inevitably worsened the signal-to-noise ratio of the data). But a price had to be paid: It was not possible to control how the subjects behaved during the measurements so that it cannot be completely excluded that some subjects ignored all stimuli, whereas others selectively attended to the auditory, the tactile, or the audiotactile stimuli. It is well-known that selective spatial attention can have considerable intermodal as well as cross-modal effects (regarding the latter topic, see recent reviews by Driver and Spence, 1998a,b, 2000). However, we think that such effects were not a real problem here. The clear dominance of the auditory perception made it difficult for the subjects to focus their attention for a longer period selectively to the T or the AT stimuli, especially since the stimuli followed each other in relatively rapid succession (1.3 s). Thus, there was little time to reflect a percept of any stimulus within the stimulus sequence. For the same reasons, it appears unlikely that subjects tried (and managed) to follow the structure of the stimulus sequence for a longer time. This view is corroborated by the fact that all subjects perceived the auditory and tactile stimulation as independent: The perception of two stimulus streams strongly suggests that the subjects paid little attention to the three stimulus categories (A, T, AT) determining the short-term structure of the stimulus sequence. It is well conceivable, however, that the situation would be quite different if the stimuli of the two different modalities would fuse better to a percept of a single audiotactile object.

Also the data themselves support our firm conviction that the results of this study were not seriously affected by uncontrolled attentional effects. The strongest argument is provided by the findings that, in the contralateral hemisphere of the subjects showing an audiotactile interaction, earlier interactions (with latencies shorter than about 160 ms) were reasonably consistent. Thus, provided that the subjects were attending to certain features of the stimulus sequence, they were apparently using basically the same strategies, which appears unlikely regarding the fact that the subjects had no opportunity to harmonize their strategies. Furthermore, in most subjects, activity was found already well before 100 ms, which appears quite early in view of the intermodal and cross-modal attention effects observed, e.g., in ERP studies of visuotactile interactions (Eimer and Schröger, 1998; Eimer and Driver, 2000). More plausible appears the hypothesis (already discussed above) that the early activity observed in this study is closely related to the observations of Foxe et al. (2000). Since no slow shifts were

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seen before stimulus onsets, anticipation of a stimulus (especially of the periodically presented AT stimulus) did not seem to be a problem here.

A fundamental aspect not accounted for in this study is spatial concordance. The auditory stimuli had to be delivered through plastic tubes because both ears were located in the helmet-shaped neuromagnetometer system. The stimuli were delivered binaurally at least. It is likely that the relatively simple models used (consisting of one or two dipoles) did account merely for the major components of the recorded interaction fields. Especially when the signal-to-noise ratio did not permit a full optimization of all parameters (including the dipole coordinates), it was not possible to exclude deviation of the true source constellation from the model. Thus nonsomatosensory areas may play a more important role than suggested by the analyses presented here.

**General Discussion**

The brain has to discriminate multisensory objects and events from those cases in which stimuli of the different modalities are entirely unrelated (Driver and Spence, 2000). Temporal and spatial concordance of the different sensory inputs favor multisensory integration. In our study, the auditory and tactile stimuli occurred simultaneously and thus the AT stimuli probably triggered at least part of the processes involved in multisensory integration. The subjects’ percepts of the auditory and tactile stimulation as independent are not necessarily contradictory to this supposition, as the percepts refer to stimulus sequences, not to the individual events.

We have already mentioned that the spatial patterns observed in this study are roughly consistent with those described by Foxe et al. (2000). There are, however, some discrepancies in the interpretation.
FIG. 7. Dipole locations estimated for the source of the interaction field (open symbols) and the SII source (filled symbols) for three subjects (both hemispheres for subject LB). The AEF source (same as in Fig. 6) served as the origin of the coordinate system. The yz plane shown represents the directions posterior–anterior as well as inferior–superior.

Whereas Foxe et al. attributed the activity at 65 ms to somatosensory cortical areas in the postcentral gyrus and interpreted the activity at 80 ms as an involvement of auditory cortical areas, we came to the conclusion that SII plays a major role in the generation of the interaction field. Two important methodological differences are presumably responsible for these differences. First, the 700- to 900-ms interstimulus intervals used by Foxe et al. might have been too short for eliciting significant contributions from SII, since SII responses are almost abolished at such a short interstimulus interval (Hari et al., 1993). Second, electrical stimulation of the median nerve as used by Foxe et al. most likely yields a much stronger percept than the tactile stimulus used here. Thus, the cross-modal effect on auditory cortical areas is probably stronger than that of our tactile stimulation. The more synchronous afferent volleys and cortical responses with electrical than with tactile stimulation could also explain the more consistent early interactions in the Foxe et al. study.

The audiotactile interaction we attributed to SII is possibly related to spatial localization, but further speculations would be premature. It seems important in this context that Schroeder et al. (2001) recently described a potential neural substrate for multisensory integration at an early stage of auditory cortical processing. In the macaque monkey they noticed a somatosensory responsiveness in regions including the caudomedial auditory association cortex (area CM), which represents a second level of cortical auditory processing (Kaas and Hacket, 1998). Spatially overlapping neuronal populations were clearly activated by each modality. An analogous areal convergence in SII could possibly contribute to the interaction field observed in the present study.

Whatever the functional significance of the interaction field observed in this study may be, it is clear that only relatively elementary mechanisms of cross-modal integration contributed to its generation. Under realistic conditions, multisensory integration comprises many additional aspects. For instance, during knocking at a door (an example given in the Introduction), the audiotactile stimuli accompany a motor act and could give rise to a highly complex spatiotemporal brain response, which is probably difficult to understand without having at least some basic comprehension of the simpler condition considered here.

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