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Efficient neuromagnetic determination of landmarks in the somatosensory cortex

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Abstract

Objectives: An efficient procedure for the magnetoencephalographic determination of functional landmarks in the somatosensory cortex has been developed.

Methods: Digits 2–5 are stimulated in randomized order using balloon diaphragms. The interval between two stimuli is 500 ms. Source locations in area 3b are derived by interpreting the field component with a mean latency of 48 ms in terms of an equivalent current dipole.

Results: The signal-to-noise ratio achieved in a given time for each of the 4 stimulation sites turned out to be only slightly smaller than the one obtained by stimulating a single site with an optimal interstimulus interval (about 1 s).

Conclusions: Compared to a sequential investigation of the different sites, the proposed procedure allows the reduction of the overall measurement time by a factor of about 2.7.

Keywords: Somatosensory cortex; Evoked potentials; Somatosensory; Magnetoencephalography; Brain mapping; Somatosensory homunculus; Area 3b; Presurgical evaluation; Functional landmarks; Dipole source localization; Stimulation rate

1. Introduction

Since the risk of functional deficits after resection of intracranial lesions can be reduced by presurgical identification of eloquent cortex, precise non-invasive localization of the central sulcus is of great value in the case of lesions lying in or adjacent to the sensorimotor region. An identification of the central sulcus based on pure anatomical criteria (using magnetic resonance images, for example) may be difficult, however, especially in the case of large mass lesions. This problem can be overcome by using functional localization techniques like functional magnetic resonance imaging (fMRI) and dipole source localization based on measurements of somatosensory evoked potentials (SEP) or fields (SEF). The subject of the present article will be the latter technique.

Numerous studies have shown that the early SEF components arise from area 3b of the primary somatosensory cortex (SI) contralateral to the side of stimulation (see e.g. Hari and Forss, 1999 for a recent review). The underlying sources are generally arranged in an order known as the somatosensory 'homunculus' (Yang et al., 1993; Nakamura et al., 1998). A comparison between the sources derived from SEF measurements and the locations of phase reversal observed in intraoperative cortical SEP recordings yielded a good agreement (e.g. Kamada et al., 1993; Gallen et al., 1994; Rezai et al., 1996). Ganslandt et al. (1997), for example, reported a mean difference of only 5.9 mm.

The overall measurement time required for a complete SEF investigation of a patient generally corresponds to the product of mean interstimulus interval (ISI), number of epochs acquired per stimulation site, and number of stimulation sites. Since the ISI is typically of the order of 300–1000 ms and about 500–1000 epochs are required to achieve averaged SEF with a reasonable signal-to-noise ratio, the overall measurement time can be significant if several stimulation sites are to be investigated. Therefore, the question as to the most efficient measurement procedure arises. As a rule, an ISI reduction leads to a decrease of the response amplitude. On the other hand, a shorter ISI allows a faster acquisition of epochs. Since the noise level of the averaged epochs decreases with the number of epochs, there is an optimal ISI with the property that the signal-to-noise ratio achievable in a given period of time is maximized. One goal of the present study was to quantify this ISI. The other goal was to answer the question of whether the overall measurement time can be reduced by stimulating different

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sites in randomized order rather than investigating them one after the other.

2. Materials and methods

2.1. Subjects

Eight right-handed subjects (age 24–32 years) with no history of neurological or psychiatric disorders were investigated. Informed consent was obtained from all subjects after having explained the nature and the purpose of the investigation.

2.2. Stimulation

Tactile stimuli were presented using balloon diaphragms driven by bursts of compressed air. A plastic spring clipped these membranes onto the finger tips and ensured a stable and good contact to the skin. A scheme of this device is shown in Fig. 1.

The time course of membrane displacement is shown in Fig. 2. To derive this curve, the magnetic field disturbance caused by a tiny piece of ferromagnetic metal interposed between membrane and finger was measured (average of 100 epochs). The time axis was defined so that time zero corresponds to the steepest gradient of the displacement curve. Thus, not only was the delay between the electrical trigger and the arrival of the pressure pulse at the pneumatic stimulator compensated for (about 40 ms), but also the delay caused by the inertia of the stimulator attached to the finger (about 9 ms between the arrival of the pressure pulse and half-way displacement of the membrane).

Two main experiments were performed. In Experiment I, only the right index finger was stimulated. Five ISIs were tested in successive measurements: 0.5, 1, 2, 4 and 8 s ($\pm 10\%$ variation). The number of recorded epochs varied between 1024 and 64 so that for each ISI the total measurement time was about 512 s. Two independent measurements were performed for each condition.

In Experiment II, digits 2–5 of the right hand were stimulated in randomized order with an ISI of 0.5 and 1 s, respectively ($P = 0.25$ for each stimulus). At least one stimulation of a different digit was interspersed between two stimulations of the same digit. Thus, the minimal interval between two stimulations of the same digit was twice the ISI, whereas the respective mean interval was 4 times the ISI. The randomization procedure was controlled by a script running on a Unix workstation, which ensured that the total number of stimulus presentations was basically the same for all stimuli (list of stimuli calculated in advance). The number of recorded epochs per digit was 256 for the 0.5 s ISI and 128 for the 1 s ISI so that the total measurement time was again 512 s. The subjects were investigated in two independent sessions, and in each session two independent measurements were performed for each ISI. While the subjects always left the shielded room between two sessions, within a session they had to maintain their head position constant relative to the sensors.

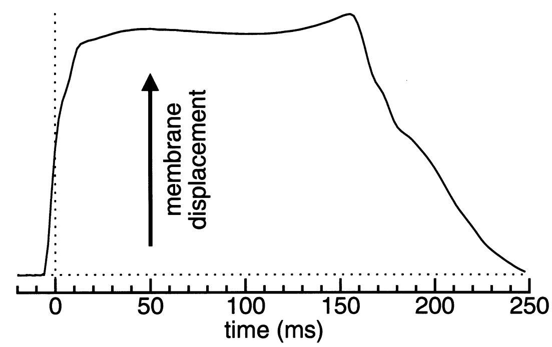

Fig. 2. Time course of membrane displacement.

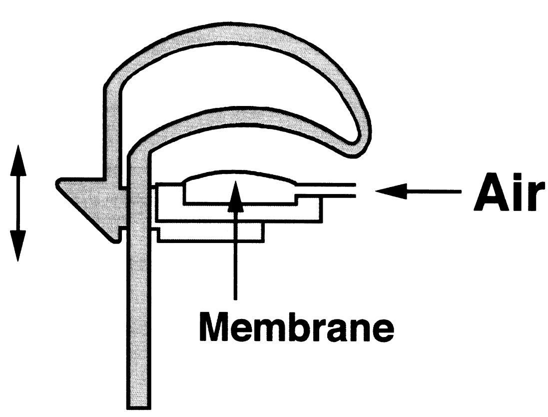

Fig. 1. Scheme of the pneumatic stimulation device.

The purpose of a supplementary third experiment was to provide a basis for a rough comparison between tactile and electrical stimulation. As such a comparison was not the actual objective of the present study, only a single subject (who did not participate in the other two experiments) was investigated. Tactile stimuli were applied to the index finger, as described above. Electrical stimuli (rectangular 0.5 ms constant-voltage pulses) were transcutaneously applied to the median nerve at the wrist. The pulse amplitude was adjusted so that the thumb showed a just noticeable movement. Two separate sets of data were recorded for both tactile and electrical stimulation, each set comprising 256 stimulus-related epochs. The interstimulus interval was 3 s. All measurements were done in a single session, taking care that the subject maintained his/her head position constant relative to the sensors.

2.3. Neuromagnetic measurements

Neuromagnetic measurements were done with a 37-channel first-order gradiometer system (Biomagnetic Technologies Inc., San Diego, CA) in a magnetically shielded room. During the measurements the subjects were lying comfortably on their right side, while the magnetic field was measured on the left side with the sensor array centered between positions C3 and T3 of the 10–20 system for electrode placement. The whole body was supported by a specially fabricated vacuum cushion. The right arm and hand were additionally supported with cushions so that the fingers could be kept relaxed. Prior to the actual measurement, the location of the sensor array relative to the head was checked in a short test measurement. Depending on the field pattern recorded in that run, the measurement system was occasionally repositioned to ensure that the essential portions of the field component with a latency around 50 ms were covered by the sensor array. Specifically, care was taken that the zero isocontour line between the two field extrema was located near the center of the sensor array. In many cases both field extrema were covered by the sensor array. The spatial locations of the sensors relative to the head were determined by means of a 3-dimensional digitizer unit (Polhemus 3space tracker), as described in Lütkenhöner (1998b). The coordinates given below refer to a coordinate system roughly defined as follows: origin located in the middle between left and right ear canal; x, y, and z axes pointing to nasion, left ear canal, and top of the head, respectively. The subjects were asked to maintain their position throughout the runs and to pay no attention to the stimuli. To facilitate the observance of the latter point, they were watching a video (without sound).

2.4. Data processing

After band-pass filtering (0.1–100.0 Hz) the data were sampled at a rate of 520.8 Hz (1041.7 Hz in the case of Experiment III) using a 16 bit analog-to-digital converter. Before further off-line processing, the data stored on a computer disk were baseline corrected (subtraction of the mean value in the 100 ms interval immediately preceding the stimulus) and low-pass filtered with a cut-off frequency of 30 Hz. Then they were averaged, rejecting all those epochs where the difference between the maximal and minimal field value exceeded 2.5 pT.

Source parameters were estimated independently for each time slice using the model of an equivalent current dipole (ECD) in a homogeneous sphere ('moving dipole model') and a least-squares fit procedure (Lütkenhöner, 1998a). The different measurement conditions were compared by inspecting the root-mean-square (RMS) values of the measured fields as well as the moments estimated for the ECD. The latter measure has the advantage that it does not depend on the distance between the measurement surface and the surface of the head. However, there is the risk that an inaccurate estimate of the dipole depth results in a systematic error (Hari et al., 1988; Lütkenhöner, 1998a). For this reason, a representative dipole location and direction was derived for each subject by calculating median coordinates on the basis of all measurements available (using the parameter values obtained for the RMS maximum in the interval 30–60 ms). In a subsequent least-squares fit, the amplitude of this dipole was calculated for all time slices available.

3. Results

3.1. Detailed results from one exemplary subject

SEF waveforms obtained by tactile stimulation of digit 2 are shown in Fig. 3. The results presented in the upper 5 panels were obtained by stimulating a single site with different ISIs (Experiment I), whereas in the bottom two panels multiple sites were stimulated in randomized order (Experiment II). It is evident that the early wave (latency 30–60 ms) and the later wave (maximum 70–130 ms) have a completely different ISI dependence. The results from Experiment II suggest, furthermore, that in the case of the early SEF wave the amplitude is determined by the mean interval between two stimulations of the same site (effective ISI), whereas the later wave appears to be dependent on the interval between two stimulations, irrespective of the site of stimulation (nominal ISI).

Fig. 4 reveals that at least two sources are required to explain the later wave. On the right, a representative data set is presented in a sensor-layout display (Experiment I, 4.0 s ISI). In the panels on the left, showing response wave-

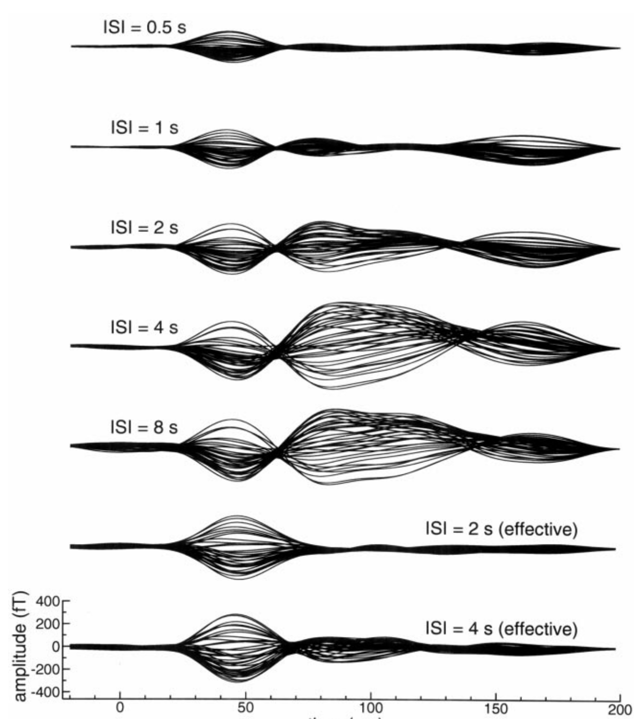

Fig. 3. Dependence of the SEF waveform on the stimulation paradigm (time functions recorded at the 37 measurement locations superimposed). (Upper 5 panels) Results obtained by stimulating a single site at mean interstimulus intervals of 0.5, 1, 2, 4, and 8 s. (Bottom two panels) Four different sites stimulated in randomized order (only the curves obtained for the index finger are displayed here). The mean interval between two stimulations of the same site (effective ISI) was 2 and 4 s, respectively.

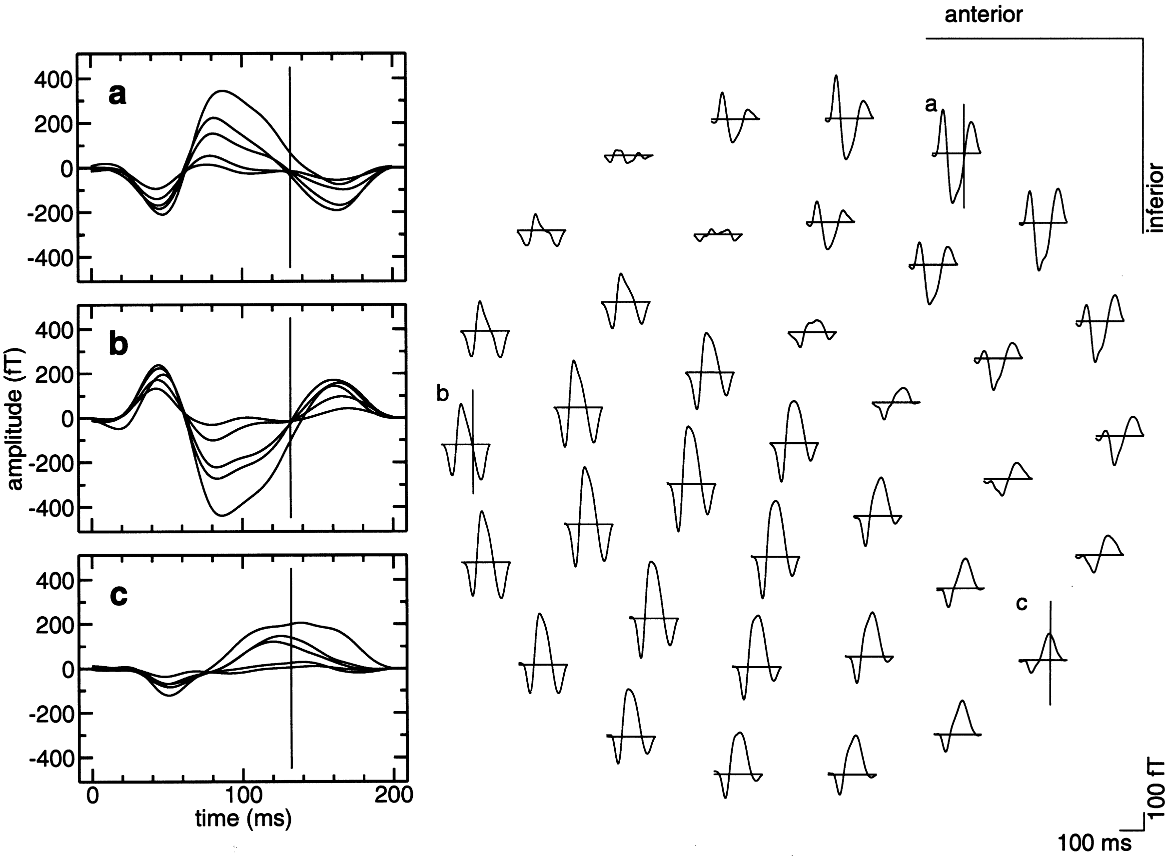

Fig. 4. Sensor-layout display of an SEF recording (4 s ISI) with magnified views of 3 channels displayed on the left. In the latter case, also the curves obtained at the other ISIs are presented.

forms for 5 different ISIs, 3 of the 37 channels are displayed in an enlarged scale. At a latency of approximately 132 ms the channels (a) and (b) are almost 'silent', whereas a significant peak appears in channel (c). The situation is reversed around 80 ms, where a pronounced peak arises in the first two channels, while the third one is almost 'silent'. Because our 37-channel measurement device covered only part of the relevant field pattern, a more detailed source analysis of the later wave turned out to be problematic so that only the results obtained for the early wave, having a latency of about 40–50 ms, will be considered below.

3.2. ISI dependence of dipole amplitudes

To quantify the amount of cortical activation in the 40–50 ms latency range, the dipole moment of the underlying source was estimated. The amplitudes obtained in this way are compiled in Fig. 5, where each panel represents one subject and each symbol represents one measurement. The ISI dependence of the dipole amplitudes derived from the data of Experiment I (' × ' symbols) can be described by the function

$$A(\mathrm{ISI}) = a \cdot f(\mathrm{ISI}) = a \cdot (1 - \exp(-\mathrm{ISI}/b)) \quad (1)$$

where a and b are constants estimated separately for each subject (see curves in Fig. 5). The figure shows also the dipole amplitudes derived from the data of Experiment II (circles). These amplitudes were plotted at abscissa values corresponding to the effective ISI (slightly shifted in addition to avoid overlap with the results of Experiment I).

A division by the asymptotic amplitude of the fitted curve (parameter a) resulted in the normalized amplitudes presented in Fig. 6a. The results from all 8 subjects are superposed in this figure. Fitting the function f(ISI) to the normalized data from Experiment I resulted in $b = 0.85$. The normalized amplitudes derived from Experiment II have median values of 0.80 (2 s effective ISI) and 1.07 (4 s effective ISI). These values roughly correspond to the respective values of function f(ISI), being 0.90 and 0.99, respectively. The figure corroborates the impression (suggested already by Fig. 3) that it is the effective ISI which determines the amplitude of the early SEF wave.

3.3. Signal-to-noise ratio consideration

The number of epochs acquired in a fixed period of time T is $n = T/\mathrm{ISI}$, where ISI is the mean ISI. Thus, if σ characterizes the standard deviation of the noise in a single epoch and A(ISI) is the amplitude of the evoked signal, the signal-

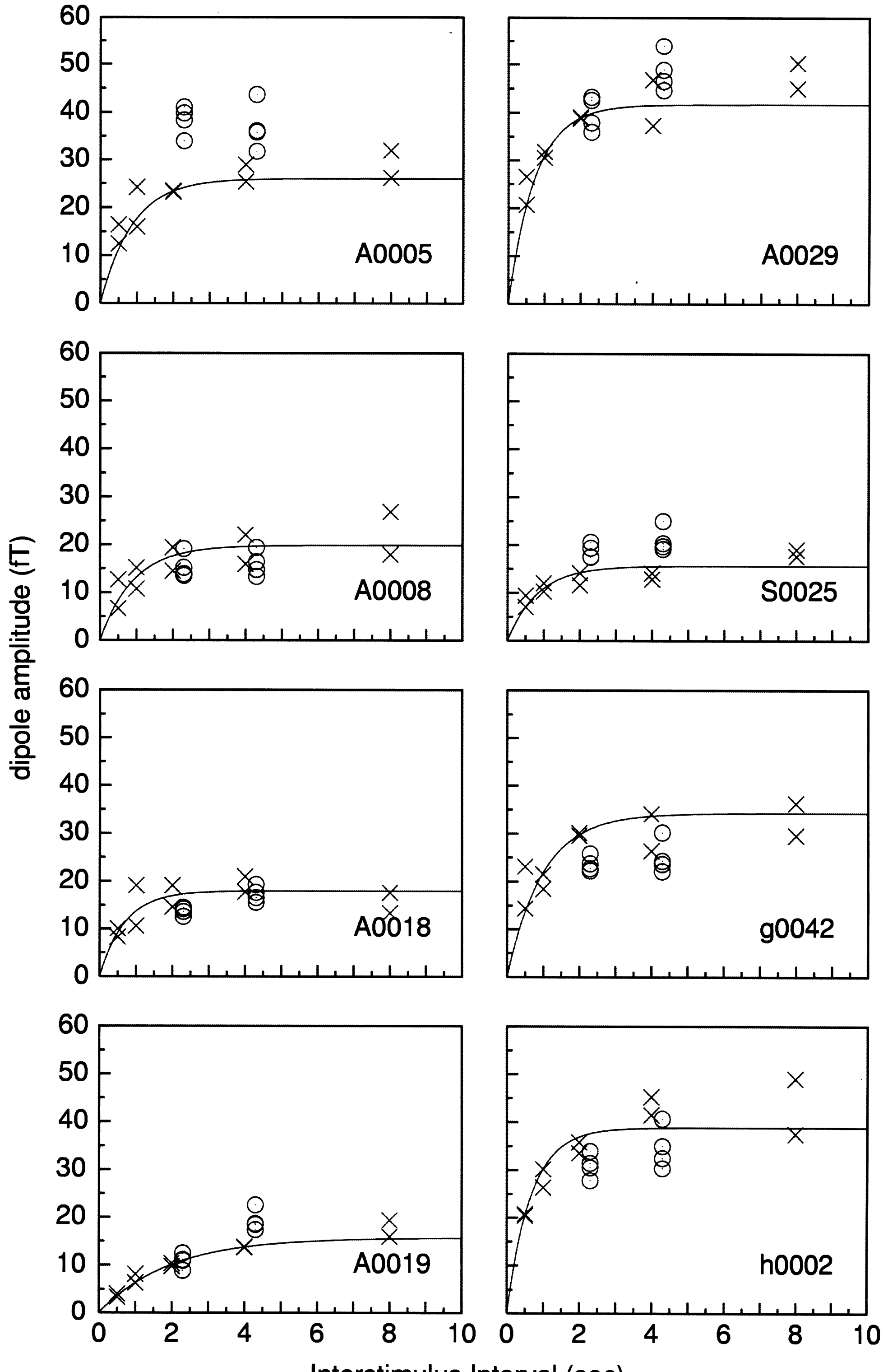

Fig. 5. Interstimulus interval (ISI) dependence of the dipole amplitude estimated for the early SEF component (mean latency of 48 ms) displayed separately for each subject. Amplitudes derived from Experiment I are represented by '×' symbols, and those derived from Experiment II are indicated by the circles.

to-noise ratio achieved by averaging the epochs recorded in the time period T is (Ahlfors et al., 1993)

$$\mathrm{SNR} = \frac{A(\mathrm{ISI})}{\sigma/\sqrt{n}} = \frac{a\sqrt{T}}{\sigma}\cdot\frac{f(\mathrm{ISI})}{\sqrt{\mathrm{ISI}}} \qquad (2)$$

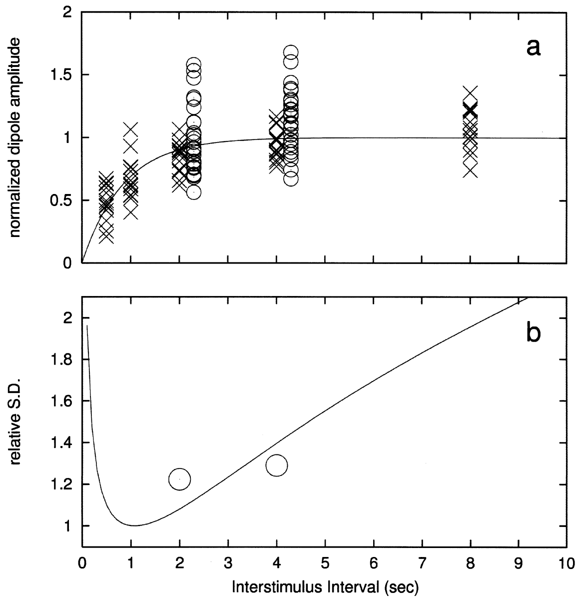

Fig. 6. (a) Normalized dipole amplitudes from all subjects. (b) Relative standard deviation of a parameter estimated from the data. The total measurement time is assumed to be the same for all conditions.

Provided that the signal-to-noise ratio of the measured data is sufficiently high, the standard deviations of the estimated dipole parameters are roughly proportional to the noise-to-signal ratio 1/SNR (Lütkenhöner, 1996). The curve in Fig. 6b, representing a function $g(\mathrm{ISI}) \sim \sqrt{\mathrm{ISI}}/f(\mathrm{ISI})$, shows how the standard deviations derived in this way depend on the ISI. The curve was normalized so that its minimum has the value 1. The figure suggests that the most efficient ISI (i.e. the ISI resulting in an optimal signal-to-noise ratio, given a fixed period of time for data acquisition) is about 1 s. Fig. 6b also shows relative standard deviations for the case where multiple sites are stimulated in randomized order (circles). These estimates were derived from the median of the normalized amplitudes given in Fig. 6a, accounting for the effective rather than the nominal ISI.

3.4. Source locations

The field in the latency range corresponding to the early wave (RMS value peaking between 44 and 50 ms) could be explained quite well by a dipole located in the SI cortex, as verified by overlaying the estimated dipole locations with magnetic resonance images. The dipole moment pointed in the posterior direction. Neither the peak latencies nor the estimated dipole locations revealed any obvious dependence on the ISI or the stimulation mode (stimulation of a single site versus randomized stimulation of multiple sites).

A more careful analysis of the estimated dipole locations, inspired by a recent high-resolution study of auditory evoked fields (Lütkenhöner and Steinsträter, 1998), is presented in Fig. 7. The analysis itself was performed for all 3 coordinates, though only x and z are considered in the figure, which displays projections of the estimated dipole locations into the x–z plane. Each subject is represented by its own symbol. Fig. 7a shows the locations derived from the data of Experiment I. Except for one outlier in the bottom right corner (500 ms ISI in subject A0019), the locations derived for the individual subjects form distinct clusters. The extent of these clusters is generally only a few millimeters, which is about the order of magnitude expected in view of the noise contained in the measured data. In most subjects, at least 4 of the 5 locations show coordinate differences of the order of 2 mm, so that a possible ISI dependence of the dipole location is evidently beyond the resolution limits.[1]

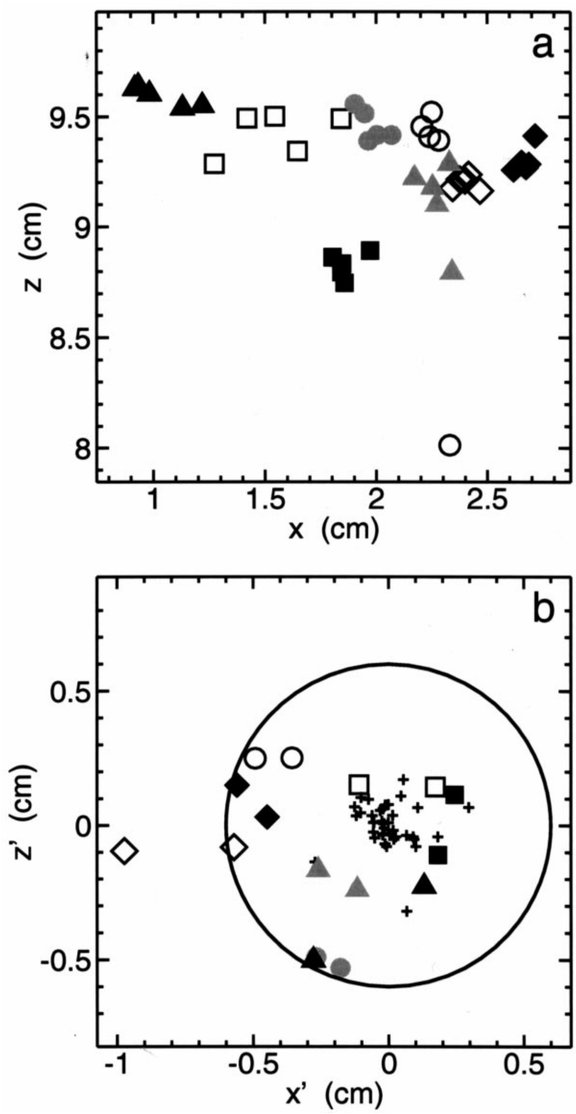

Fig. 7. Comparison between the coordinates derived from Experiments I and II.

[1] A comparable variability was found in a recent reproducibility study (see Fig. 4b of Lütkenhöner, 1998b). The outlier observed in the present study is caused by a relatively unfavorable signal-to-noise ratio.

By shifting each cluster in such a way that the respective mean location coincided with the origin of the coordinate system, the small crosses shown in Fig. 7b were obtained. Exactly the same coordinate transformation was applied to the locations derived from Experiment II, which are represented by the larger symbols in the figure. The two symbols displayed for each subject correspond to the two different ISIs (each symbol representing the median of 4 runs). Except for one obvious outlier (500 ms ISI in subject A0005), which was ignored in the further statistical evaluations, all symbols are lying within a circle around the origin with a radius of 6 mm (median values of the shifted coordinates x', y', z': 2.3, 0.1, and 0.6 mm, respectively). None of the coordinate differences proved to be significant (*t* test and one-sample sign test). Moreover, the estimated coordinates showed no significant ISI dependence.

3.5. Comparison between electrical and tactile stimulation

To provide some additional material for the discussion below, SEFs to tactile and electrical stimuli were compared in one subject. The results are presented in Fig. 8. As the two independent data sets recorded for each condition were visualized separately, the high reproducibility of the measurements can be assessed as well from the figure. In the upper panel, the initial 100 ms time range of the response to tactile stimuli (solid curves) and electrical stimuli (dashed curves) is visualized for one representative gradiometer channel. The response to the electrical stimuli shows clear peaks at about 23 ms (N20m) and 42 ms, whereas the response to the tactile stimuli shows its first significant peak at about 48 ms. The channel visualized here was selected in a way that the peak latencies corresponded to those of the root-mean-square (RMS) value, calculated on the basis of all 37 channels available. The latter curves are presented in the second panel of Fig. 8. Low-pass filtering of the response to the electrical stimuli would evidently result in a time course quite similar to the response to the tactile stimuli, at least within the first 50 ms. Thus, it appears reasonable to assume that the 42 ms peak in the response to the electrical stimuli and the 48 ms peak in the response to the tactile stimuli are closely related.[2]

A dipole source analysis corroborated this view. The bottom 3 panels of Fig. 8 show the estimated dipole locations as functions of time. The locations derived from the

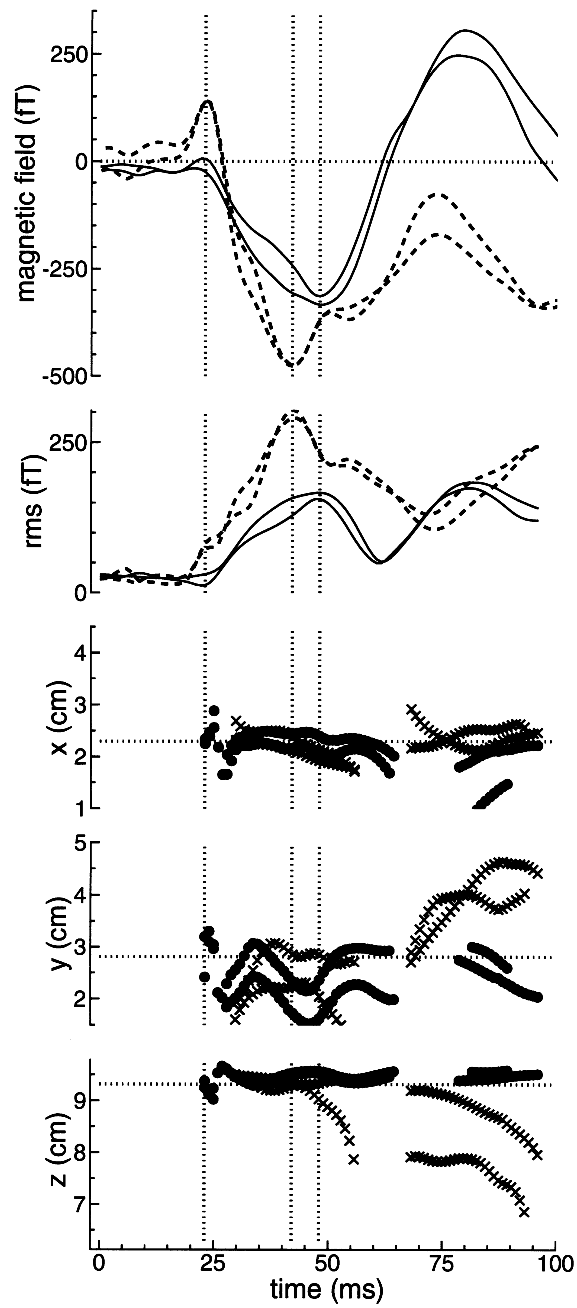

Fig. 8. Comparison between tactile and electrical stimulation. (Upper two panels) Time courses of the magnetic field of a representative channel and of the root-mean-square (RMS) value derived from all 37 channels. Solid curves represent responses to the tactile stimuli. Dashed curves represent responses to the electrical stimuli. (Bottom three panels) Time courses of the estimated dipole coordinates. Filled circles represent responses to the tactile stimuli. '×' symbols represent responses to the electrical stimuli.

responses to the electrical stimuli are represented by '×' symbols, whereas those derived from the responses to the tactile stimuli are represented by filled circles (generally overlapping so that they appear as a thick line). The dipole coordinates are more or less constant within the 30–50 ms

[2] A closer look at the responses to the electrical data shows a high complexity. In fact, the peak latencies turned out to be channel-dependent, which means that a single source is not able to explain the data sufficiently. An obvious consequence is that the gradiometer configuration (axial versus planar) can have a considerably influence on the SEF time course. This may explain why the most significant peak in the RMS curves occurs slightly later than expected in view of a related study of Forss et al. (1994). A clear peak occurring about 15 ms after peak N20m was observed indeed in a subset of channels (P35m), but the RMS curves are obviously dominated by a slower wave. For the same reason, peak N20m causes only a small deflection in the RMS curves, though this peak is clearly visible in the channel presented in the upper panel of Fig. 8.

time range, and systematic differences between the two types of stimulation are not discernible.[3]

4. Discussion

4.1. ISI dependence and signal-to-noise ratio considerations

The ISI dependence of the SEF and its electrical correlate, the somatosensory evoked potential (SEP), has been considered in several previous studies (see e.g. the overview given by Wikström et al., 1996). In most SEF studies, electrical stimuli were applied to the median nerve. While peak N20m seems to be basically unaffected by the stimulus rate, peak P35m gradually decreases with decreasing ISI, generally being completely abolished at an ISI of 0.15 s (Wikström et al., 1996). The data published in Fig. 4 of Wikström et al. (1996) suggest that the dipole strengths obtained at ISIs of 0.3 and 1 s are roughly 1/3 and 2/3, respectively, of the asymptotic value for long ISIs. These estimates are in good agreement with the curve shown in our Fig. 6a.

To the best of our knowledge, the effect of stimulating multiple sites in randomized order has not been investigated so far. The finding that the amplitude of our early SEF wave is only little effected by interspersed stimuli applied to different sites gives not only some insight into the functional properties of the underlying generator, but is also of great practical value. As suggested by Fig. 6b, randomized stimulation of 4 digits with a rate of 2/s (corresponding to an effective ISI of 2 s) results, for each of the 4 conditions, in a standard deviation being only 1.22 times greater than the standard deviation obtained by stimulating a single site with the optimal ISI of about 1 s. To obtain exactly the same relative standard deviations, the total measurement time for the randomized stimulation of 4 sites would have to be increased by a factor of $1.22^2 \simeq 1.5$. On the other hand, a successive investigation of 4 sites would increase the total measurement time by a factor of 4. Thus, the net advantage of the randomized stimulation paradigm is about $4/1.5 \simeq 2.7$.

Fig. 6b suggests that in the case of the randomized stimulation paradigm, a further reduction of the nominal ISI might result in a slight additional improvement of the relative standard deviation. However, as pointed out already by Ahlfors et al. (1993), short ISIs involve the risk that the responses to successive stimuli overlap, which may impair the accuracy of the estimated source locations. For this reason we abstained from working with ISIs smaller than 0.5 s. A further question is whether the randomization scheme used in this study is really optimal. It cannot be excluded that repetition of deterministic sequences (like digit 2, digit 3, digit 4, digit 5, digit 2, digit 3, and so on) would result in an even better signal-to-noise ratio.

In principle there are numerous other possibilities to further enhance the signal-to-noise ratio. One important possibility is spectral filtering, either using predefined filter characteristics or time-varying filtering techniques as developed by de Weerd (1981). Improvements are promised also by maximum likelihood estimation techniques making use of the noise covariance matrix (Sekihara et al., 1992; Lütkenhöner, 1998a,b), or by source models with appropriate spatial constraints (Lütkenhöner et al., 1995; Kincses et al., 1999). However, regarding the relative merits of the stimulation paradigm suggested here, such questions are obviously unimportant.

4.2. Some physiological issues

The SEF component considered in the present study was investigated in numerous previous studies (see e.g. Yang et al., 1993; Elbert et al., 1995; Flor et al., 1995; Knecht et al., 1996; Nakamura et al., 1998), and it is beyond all doubts that it arises from sources located in the primary somatosensory cortex SI. However, the question remains as to how this component is related to the SEF to electrical stimuli, since a detailed comparison between the latter responses and the responses to the tactile stimuli used here is hitherto missing. While it is evidently beyond the scope of the present study to fill this gap, suggestive first hints are given by the results presented in Fig. 8. It seems that the initial part of the response to tactile stimuli roughly corresponds to a low-pass filtered version of the response to electrical stimuli. A striking argument in favor of this interpretation is provided by the fact that the estimated source locations are basically identical.

A plausible explanation for the lack of faster components in the responses elicited by the tactile stimuli follows from the indistinct onset of the stimulus. After the arrival of the pressure pulse it takes about 18 ms until the membrane displacement reaches a more or less constant plateau level.[4] As the threshold of the rapidly adapting mechanoreceptors, which transform the stimulus into neural responses, exhibits a certain statistical distribution, such a stimulus necessarily results in a temporally smeared input to the somatosensory cortex. Thus, the fact that a correlate of peak N20m is apparently missing in the responses to tactile stimuli could simply indicate an insufficient synchronization of the respective neural population.

Airpuff stimuli obviously result in a significantly higher neural synchronization than the tactile stimuli used in the present study. This was convincingly demonstrated by Forss et al. (1994), who compared responses to airpuff and electrical stimuli. While electrical stimuli applied to the median

[3] The variability of the y coordinate is evidently much higher than that of the x coordinate, which itself has a higher variability than the z coordinate. These differences can be explained by the spatial orientation of the source and the limited measurement area (Lütkenhöner, 1998a,b).

[4] Nakamura et al. (1998) reported a rise time of 20 ms for the same type of stimulation device.

nerve elicited SEF with peak latencies of about 21–22 ms (N20m) and 36 ms (P35m), airpuffs presented perpendicular to the hairy skin at the dorsum of the proximal phalanx of the middle finger resulted in peak latencies of 28 and 43–46 ms, respectively. Except for an evident latency shift, the responses were quite similar. The high synchronization power of the airpuff stimuli used by Forss et al. (1994) certainly results from the fact that the rise time of their stimulus was only 7 ms. Taking into account the different amount of synchronization, the responses to tactile stimuli as observed in the present study are consistent with the curves shown in Fig. 4 of Forss et al. (1994), the initial part of which can be crudely described as 'faster waves riding on a slower wave'. Owing to the lower synchronization, only the slower wave was observed in the present study. The two studies have in common, furthermore, that tactile and electrical stimulation resulted in basically identical source locations within the primary somatosensory cortex.

This study has shown that interspersed stimulation of other fingers has only a small effect on the early SEF component elicited by tactile stimulation of the index finger. Such a finding is somewhat surprising as there is ample evidence that the fingers have an overlapping representation in the SI cortex. For example, Biermann et al. (1998) found that simultaneous stimulation of two fingers results in an inhibitory interaction, being stronger for the adjacent digits II and I than for the non-adjacent digits II and V. Inhibitory interaction occurs also between responses to non-simultaneous stimuli. For example, Huttunen et al. (1992) noticed that the N20m amplitude in response to electrical median nerve stimulation was considerably reduced by a preceding electrical stimulus applied to the ulnar nerve, provided that the interval between the two stimuli was 80 ms or shorter. This observation clearly indicates some type of interaction between the afferent volleys from the two nerves, either in the ascending pathways, or at the cortical level, or both. However, this type of interaction is obviously not very relevant for the interpretation of the results of the present study, because the interstimulus interval used here was 500 ms or greater, whereas Huttunen et al. (1992) noticed almost complete recovery at an interstimulus interval of 120 ms. In this context a study of Forss et al. (1995) shall also be mentioned, in which the P35m amplitude in response to 'deviants' (electrical stimulation of the little finger) interspersed among 'standards' (electrical stimulation of the thumb) turned out to be not much smaller than the amplitude in response to deviants alone (i.e. without the interspersed standards). Since the interstimulus interval was 0.6 s for standards and on average 4 s for deviants, the situation considered in that paper is comparable to the 4 s effective ISI condition as considered in the present study, despite various methodological differences. The finding that the interspersed standards resulted in only a relatively small amplitude reduction of the responses to the deviants is evidently consistent with the present study.

Forss et al. (1995, 1996) have shown that electrical stimuli presented at random ISIs activate sources in the contralateral SI cortex as well as in both SII cortices and the posterior parietal cortex (PPC). Additionally, they detected a novel response in the latency range 120–160 ms which was generated in the mesial cortex close to the central sulcus. Indications of a complex nature of the later components can also be found in our data, though the limited area covered by our 37-channel measurement system prevented a detailed source analysis. Our data allow us to conclude at least that randomized stimulation of multiple sites affects early and later components in a completely different way. While the amplitudes of the former seem to be dependent mainly on the effective ISI, in the case of the latter there is a strong interaction with interspersed stimuli applied to other digits.

5. Conclusion

The tactile stimuli delivered by the balloon diaphragms used in this study elicit a highly reproducible SEF wave with a mean latency of 48 ms. The dipole locations derived from this wave represent excellent functional landmarks. Since the amplitude of this wave is basically dependent on the mean interval between two identical stimuli, the total measurement time for multiple SEF measurements can be considerably reduced by stimulating multiple sites in randomized order. Later waves, however, are seriously affected by interspersed stimuli applied to other digits.

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References

Ahlfors S, Ilmoniemi R, Portin K. The effect of stimulation rate on the signal-to-noise ratio of evoked responses. Electroenceph clin Neurophysiol 1993;88:339–342.

Biermann K, Schmitz F, Witte O, Konczak J, Freund H, Schnitzler A. Interaction of finger representation in the human first somatosensory cortex: a neuromagnetic study. Neurosci Lett 1998;251:13–16.

de Weerd J. A posteriori time-varying filtering of averaged evoked potentials. I. Introduction and conceptual basis. Biol Cybern 1981;41:211–222.

Elbert T, Pantev C, Wienbruch C, Rockstroh B, Taub E. Increased cortical representation of the fingers of the left hand in string players. Science 1995;270:305–307.

Flor H, Elbert T, Knecht S, Wienbruch C, Pantev C, Birbaumer N, Larbig W, Taub E. Phantom limb pain as a perceptual correlate of massive cortical reorganization in upper extremity amputees. Nature 1995;375:482–484.

Forss N, Salmelin R, Hari R. Comparison of somatosensory evoked fields to airpuff and electric stimuli. Electroenceph clin Neurophysiol 1994;92:510–517.

Forss N, Jousmäki V, Hari R. Interaction between afferent input from fingers in human somatosensory cortex. Brain Res 1995;685:68–76.

Forss N, Merlet I, Vanni S, Hämäläinen M, Maguiere F, Hari R. Activation of human mesial cortex during somatosensory target detection task. Brain Res 1996;734:229–235.

Gallen C, Bucholz R, Sobel D. Intracranial neurosurgery guided by functional imaging. Surg Neurol 1994;42:523–530.

Ganslandt O, Steinmeier R, Kober H, Vieth J, Kassubek J, Romstöck J, Strauss C, Fahlbusch R. Magnetic source imaging combined with image-guided frameless stereotaxy: a new method in surgery around the motor strip. Neurosurgery 1997;41:621–627.

Hari R, Forss N. Magnetoencephalography in the study of human somatosensory cortical processing. Phil Trans R Soc Lond, Ser B 1999;354:1145–1154.

Hari R, Joutsiniemi S, Sarvas J. Spatial resolution of neuromagnetic records: theoretical calculations in a spherical model. Electroenceph clin Neurophysiol 1988;71:64–72.

Huttunen J, Ahlfors S, Hari R. Interaction of afferent impulses in the human primary sensorimotor cortex. Electroenceph clin Neurophysiol 1992;82:176–181.

Kamada K, Takeuchi F, Kuriki S, Oshiro O, Houkin K, Abe H. Functional neurosurgical simulation with brain surface magnetic resonance images and magnetoencephalography. Neurosurgery 1993;33:269–273.

Kincses W, Braun C, Kaiser S, Elbert T. Modeling extended sources of event-related potentials using anatomical and physiological constraints. Hum Brain Mapping 1999;8:182–193.

Knecht S, Henningsen H, Elbert T, Flor H, Höhling C, Pantev C, Taub E. Reorganization and perceptual changes after amputation. Brain 1996;119:1213–1219.

Lütkenhöner B. Current dipole localization with an ideal magnetometer system. IEEE Trans Biomed Eng 1996;43:1049–1061.

Lütkenhöner B. Dipole source localization by means of maximum likelihood estimation: I. Theory and simulations. Electroenceph clin Neurophysiol 1998a;106:314–321.

Lütkenhöner B. Dipole source localization by means of maximum likelihood estimation: II. Experimental evaluation. Electroenceph clin Neurophysiol 1998b;106:322–329.

Lütkenhöner B, Steinsträter O. High-precision neuromagnetic study of the functional organization of the human auditory cortex. Audiol Neuro-Otol 1998;3:191–213.

Lütkenhöner B, Menninghaus E, Steinsträter O, Wienbruch C, Gißler H, Elbert T. Neuromagnetic source analysis using magnetic resonance images for the construction of source and volume conductor model. Brain Topogr 1995;7:291–299.

Nakamura A, Yamada T, Goto A, Kato T, Ito K, Abe Y, Kachi T, Kakigi R. Somatosensory homunculus as drawn by MEG. Neuroimage 1998;7:377–386.

Rezai A, Hund M, Kronberg E, Zonenshayn M, Cappell J, Ribary U, Kall B, Llinás R, Kelly P. The interactive use of magnetoencephalography in stereotactic image-guided neurosurgery. Neurosurgery 1996;39:92–102.

Sekihara K, Ogura Y, Hotta M. Maximum-likelihood estimation of current-dipole parameters for data obtained using multichannel magnetometer. IEEE Trans Biomed Eng 1992;39:558–562.

Wikström H, Huttunen J, Korvenoja A, Virtanen J, Salonen O, Aronen H, Ilmoniemi R. Effects of interstimulus interval on somatosensory evoked magnetic fields (SEFs): a hypothesis concerning SEF generation at the primary sensorimotor cortex. Electroenceph clin Neurophysiol 1996;100:479–487.

Yang T, Gallen C, Schwartz B, Bloom F. Noninvasive somatosensory homunculus mapping in humans by using a large-array biomagnetometer. Proc Natl Acad Sci USA 1993;90:3098–3102.