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Confidence Interval of Single Dipole Locations Based on EEG Data

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Summary: Noise in EEG and MEG measurements leads to inaccurate localizations of the sources. A confidence volume is used to describe the amount of localization error. Previous methods to estimate the confidence volume proved insufficient. Thus a new procedure was introduced and compared with previous ones. As one procedure, Monte Carlo simulations (MCS) were performed. The confidence volume was also estimated using two methods with different assumptions about a linear transfer function between source location and the distribution of the potential. One method used variable (LVM) and the other fixed dipole orientations (LFM). Finally, the confidence volume was estimated through a procedure in which there was no linearization of the transfer function. This procedure scans the confidence volume by varying the dipole location in multiple directions. Confidence volumes were calculated for simulated distributions of the electrical potential and for experimental data including somatosensory evoked responses to stimulation of lower lip, thumb, and little finger. Results from simulated data indicated that confidence volumes calculated with the MCS method were largest, and those calculated with the LFM method were smallest. For dipole locations close to the brain surface, the confidence volume was smaller than for a central deeper source. An increase in electrode density resulted in smaller confidence volumes. When the noise was correlated, only the method using the MCS produced acceptable results. Since the noise in experimental data is highly correlated, only the MCS method would appear to be useful in estimating the size of the confidence volume of the dipole locations. Thus, using real data with the MCS method, we easily distinguished separate and distinct representations of the thumb, little finger, and lower lip in the somatosensory cortex (SI). It was concluded that adequate estimation of confidence volumes is useful for localizing neural activity. On a practical level, this information can be used prior to an experiment for determining the conditions necessary to distinguish between different dipole sources, including the required signal to noise ratio and the minimum electrode density.

Key words: Dipole localization; EEG; MEG; Monte Carlo; Confidence interval.

Introduction

Electroencephalography (EEG) and Magnetoencephalography (MEG) are used to localize the neural sources of human brain activity with high temporal resolution. It is important to obtain an estimate for the accuracy of source localization, particularly if a change in localization between experimental conditions is of interest or if two simultaneously active sources are to be differentiated. Knowledge of localization accuracy can be vital such as when the information of the localization assists in neurosurgical planning. In the present paper, we show that previous strategies used to estimate the confidence volume are insufficient and, in response, introduce a new procedure that avoids the simplifications of previous approaches without using too large computational needs.

To derive the source location from the measured scalp potentials or from the magnetic field around the head, physical models of the neural source and its activity propagation to the sensors are employed. In addition the electrical properties of the different head tissues and their geometry have to be taken into account. During the localization procedure the parameters (location in space, orientation and amplitude of current flow) of a source model are varied until its calculated field distribution fits best the measured activity. A simple and in many cases valid model of brain electrical activity assumes a focal source in a spherical shaped head. The single current dipole is then adequate to model the location in space, as well as the magnitude and orientation of current flow. The accuracy of localization depends on how well the head and source model is suited and on the precision with which this activity is measured. If the models applied are optimal, or if relative errors are the main concern, only the measurement errors need to be considered.

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Sources of noise which limit the measurement precision of brain activity can be placed in three categories (a) environmental noise, (b) instrumental noise and (c) biological noise.

The major source of environmental noise is the 50 or 60 Hz activity emitted from power lines and electrical devices. Disturbances in other frequency bands may originate from monitor screens, medical equipment, or from traffic outside the laboratory. Instrumental noise, such as amplifier or digitization noise, must also be taken into consideration. Because the spatial location of the electrodes in EEG and the pick up coils in MEG is required for the source localization procedure, measurement errors of the sensor positions lead to a deterioration of the localization accuracy (Cuffin 1986) and, consequently, to ghost sources, particularly when the current source density (CSD) is taken into consideration (Junghöfer et al. 1997). Biological noise refers to physiological activity generated from the subject that is not correlated with the brain activity being studied. In addition to electrical activity generated by external physiological functions such as the heart, muscular artifacts, eye-movements and electrical skin activity, background activity of the brain itself also contributes to biological noise. Regular rhythms in spontaneous brain activity, such as alpha waves, are not only large in amplitude but are also correlated between nearby sensors and thus distort the scalp topography systematically.

The impact of measurement errors has been investigated both experimentally and theoretically and thus lend a foundation for the present discussion. Previous studies, for instance, have determined the dipole localization accuracy by simulating brain activity with implanted electrical current sources. Current delivered through electrodes, placed in either artificial head models or in patients with medically implanted electrodes, generated bipolar fields. The source locations were then calculated from the electrical or magnetic fields measured outside the head during the application. A comparison of the estimated dipole position with the position of the artificial current source derived from X-ray images provided information on the accuracy of the localization (Barth et al. 1986; Gharib et al. 1995; Cohen et al. 1990). In theoretical approaches, the characteristics of the measurement noise is evaluated to define a confidence region around the estimated source localization that contains the true, noise-free dipole location within a certain degree of probability. Normally, the confidence volume is calculated for probabilities up to 95% or 99%. Several methods have been proposed for determining such a confidence interval and are available in the literature (Sarvas 1987; Hari et al. 1988; Radich 1995; Kuriki et al. 1989; Mosher et al. 1993).

One straightforward but rather time consuming method is the Monte Carlo simulation (MCS). With this method the size of the confidence region of an estimated source is derived by localizing dipole sources of a number of noise distributions that are added to the measured field. The noise distributions are generated such that the signal to noise ratio and the noise correlation between the channels is equivalent to the noise of the measured data. The 95% or 99% percent of those sources which are next to the estimated source location are used to define the confidence volume.

A particular topography defines a point in signal space where each dimension corresponds to the activity measured at a single sensor. Noise does not allow a precise determination of the brain activity. Instead, for each sensor a confidence range that contains the exact activity with a certain probability has to be specified. Thus, considering all sensors a confidence volume in signal space is defined.

Whereas in Monte Carlo Simulations the confidence interval of the source localization is estimated by varying the noise distribution, other approaches vary the dipole location until the corresponding topography falls on the border of the confidence volume in signal space. Variation of the dipole location can be carried out either with a fixed dipole orientation or with a dipole moment that is fitted to the measured potential in order to achieve a minimum error. Because of the non-linearity of the relationship between changes of source location and changes in field topography resulting in a great amount of computations, linearization has been suggested (Sarvas 1987; Yamazaki et al. 1992). These authors used a fixed dipole moment for the estimation of the confidence volume. This method is therefore referred as 'linearization with fixed moment' (LFM) and is contrasted to a procedure with variable dipole strength and orientation (LVM). In both methods the variation of the source localization is performed in the three spatial dimensions. Other methods of parameter estimation based on Baysian statistics have also been suggested (Mosher et al. 1993; Radich 1995), but will not be discussed in this paper.

Based on this brief overview of various approaches to determine confidence volume, the primary aim of this study will be to compare the results of different strategies of confidence volume estimation including MCS, LVM and LFM. In addition, a confidence estimation procedure (ICE), which uses no linearization of the transfer function and which scans the confidence volume by varying the dipole location in multiple directions, allowing compensation by changing dipole orientation, is also introduced and compared to the above mentioned methods. Finally, it has been shown that the accuracy of a specific dipole localization depends not only on the noise level, but also on the degree of noise correlation between different electrodes, the number of sensors, the orientation and localization of the dipole source itself. Therefore, the comparison of the methods is performed under varying measurement and noise conditions.

Table 1. Parameter of the 4-shell spherical head model used in the computations of the confidence volumes.

Sphere	radius (mm)	conductivity 1/Ωm
1	78.02	0.3300
2	79.90	1.0000
3	87.42	0.0042
4	94.00	0.3300

Methods

Head model

To calculate the transfer function of dipole parameters and the potential at the electrodes the volume conducting properties of the head must be modeled. For the sake of easy computations the head is assumed to be spherical. Layers of different tissues are modeled by four concentric shells with specific conductivities. From inside to outside the spheres represent the brain, cerebrospinal fluid, skull and the scalp. Radii and conductivities of the spheres are given in table 1.

The scalp potential at m electrodes $\bar{u}^T = (\bar{u}_1 \cdots \bar{u}_m)$ of a single dipole source located at $\vec{r}$ with a dipole moment $\vec{q}$ is given by $\bar{u} = G(\vec{r})\vec{q}$ where G is the transfer matrix describing the projection from source to signal space (Cuffin and Cohen 1979; Mosher et al. 1993). G depends on dipole location and electrical and geometrical characteristics of the head model.

Noise Estimation

To estimate the error of the potential and its mutual dependencies between the electrodes, either the covariance matrix based on single trials or the covariance matrix derived from the prestimulus interval can be used. Using single trials the covariance matrix is $C = \frac{1}{n(n-1)} u_s u_s^T$ whereby $u_s = (u_{ijk} - \bar{u}_{ij}), i = 1,m;\ j=1,l;\ k=1, n$ is a $m \times nl$ matrix that describes the potential of m electrodes at l time samples for n trials. $\bar{u}_{ij}$ is the average potential of the n trials at electrode i and sample j.

The covariance matrix based on sample points of the prestimulus baseline is given by $C = \frac{1}{n} u_B u_B^T$ where $u_B=(u_{ij}), i=1, m; j=1,l$ represents the potential distribution of the l sample points of the prestimulus baseline. The average prestimulus baseline is assumed to be zero. A transformation from signal space to the corresponding eigensystem eliminates the noise correlation between electrodes. The transformation matrix T^T can be determined by a singular value decomposition (SVD): $C=T\lambda T^T$. The diagonal matrix λ contains the eigenvalues of C.

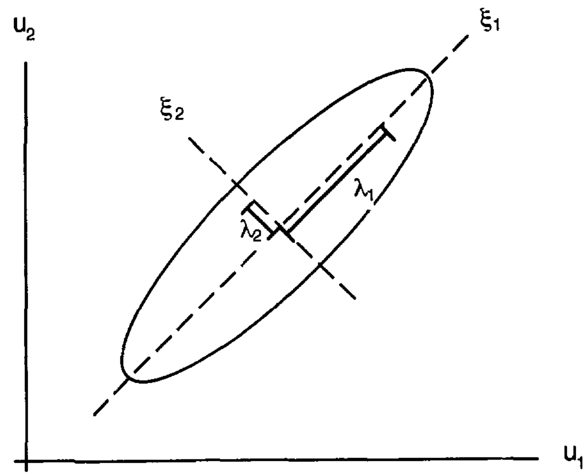

Figure 1. Confidence region in signal space is defined by the root of the eigenvalues of the covariance matrix I and the χ^2 for a given probability and for a specified number of degrees of freedom. Moving the dipole in source space in one direction will lead to a line L in signal space. Crossing the confidence interval in signal space defines the confidence limits in source space.

Monte Carlo Simulation (MCS)

In order to estimate the confidence volume of a single dipole location with Monte Carlo simulation, different noise distributions with covariance matrices identical to that of the measured data must be generated. The noise is added to the noise-free scalp potential that corresponds to the estimated dipole source and the dipole source location of each topographical distribution is calculated. The confidence limits can then be derived from the variability of the determined locations. The modeling is performed in the eigensystem of the given covariance matrix. As a result, the noise activity in this system is no longer correlated and its probability density for each dimension i is assumed to be gaussian, with a mean of zero and a standard deviation of λ_i (figure 1). The transformation from the eigensystem ξ to the signal space is described by the rotation matrix $T: u = T\xi + \bar{u}$.

N=5000 scalp potentials distributions with different noise distributions were simulated. For each distribution the corresponding single dipole location was calculated by a least square fit. Depending on the selected confidence criterion γ the volume that included the γN source locations next to the location $\vec{r}$ defined the size of the confidence volume of the dipole location. In this study γ was set to 95% in all computations. To calculate the confidence volume the three principle axes of an ellipsoid enclosing the cloud of dipole locations were determined. The maximum projections a_k, k=1..3 of the γN dipole locations to the principle axes were taken as half axes of the confidence ellipsoid having a volume of $V = \frac{4\pi}{3} a_1 a_2 a_3$.

Linearization with (LVM) and without (LFM) variable dipole moment

The estimation of the confidence volume with a linear approximation of the relationship between changes of source space and corresponding changes in signal space is extensively described in Sarvas (1987) and, therefore, the basic concept will only be briefly outlined here. The confidence ellipsoid around a given source can be specified if the relationship between potential changes and location changes, expressed by the Jacobian matrix, $A = (a_{ik}) = \left(\frac{\partial u_i}{\partial x_k}\right)$ is known. The amount of variations of the source localization $\delta^T=(\delta_1, \delta_2, \delta_3)$ that leads to a deviation in signal space of $\varepsilon^T=(\varepsilon_1, ..., \varepsilon_m)$, where ε is assumed to be noise of zero mean and variance one, can be calculated by solving $\varepsilon=A\delta$. Because this is an overdetermined equation system its solution is given by $(A^TA)^{-1} A^T \varepsilon=\delta$. The three half axes ρ_k of the confidence ellipsoid in source space can be derived by a SVD decomposition of the $\delta\delta^T=(A^TA)^{-1}=V\omega V^T$ leading to $\rho_k=\chi^2(\gamma)\omega_k^{1/2}$. Instead of decomposing the inverse of $(A^TA)^{-1}$, the matrix $(A^TA)=V\omega^{-1}V^T$ can be used to calculate the eigenvalues ω_k. If noise with an arbitrary covariance matrix C is taken into consideration, a transformation $\lambda^{-1/2}T^T(u-\bar{u})=\varepsilon$ leads to correlated noise with a mean of zero and a variance of one. λ and T result from an SVD decomposition of $C=T\lambda T^T$. The determination of the Jacobian matrix was carried out experimentally by shifting the source location by one millimeter in all three directions in space, while maintaining the dipole orientation and strength as constant (LFM). The potential changes were then rotated with matrix T^T and weighted with $\lambda^{-1/2}$. In order to estimate the confidence volume for source locations allowing variations of the dipolemoment (LVM), the corresponding Jacobian matrix was used. Potential changes due to shifts of the source locations in the three spatial dimensions were selected after the dipole orientation and strength were recalculated so that a best fit of the potential was achieved.

Iterative confidence interval estimation (ICE)

Assuming that a dipole location $\vec{r}$ was estimated for the potential distribution $\bar{u}$, a confidence region in source space can be specified around $\bar{u}$ based on the estimated noise. This region contains with a probability of γ the potential distribution that would be measured if no noise were present. The length of the half axes of the confidence ellipsoid are given by $\chi_n^2(\gamma)\lambda_i$. Thereby, $\chi_n^2(\gamma)$ is the chi-square belonging to a probability of γ with n degrees of freedom and λ_i is the eigenvalue of the i^th^ axis. A topographical distribution is within the confidence region, if $\chi_n^2(\gamma) \geq \sum_m \frac{\xi_i^2}{\lambda_i}$ (see figure 1). To find the limits of the confidence interval in source space a test dipole is moved around the estimated location and its scalp potential is calculated. If the scalp potential calculated in this way reaches the limits of the confidence region in signal space then this location of the test dipole is chosen as the outer limit of the confidence volume in source space. With this method, the surrounding region of the estimated dipole location can be scanned resulting in a surface enclosing the confidence interval for the dipole location. The number of degrees of freedom n chosen is also crucial. The maximum number of degrees of freedom may not be higher than the total number of electrodes. Because small displacements of the test dipole lead to distributions of the potentials that are located in a subspace of the signal space, it is generally necessary to reduce the number of degrees of freedom.

If the test dipole is displaced by $\Delta\vec{r}$, the corresponding potential distribution is given as $u^* = G(\vec{r}+\Delta\vec{r})\vec{q}^*$. The dipole moment $\vec{q}^*$ is recalculated after each step in order to get a best fit $\|u^* - \bar{u}\| \stackrel{!}{=} \min$. Because the scanning is performed in an iterative procedure this method is termed 'iterative confidence estimation *(ICE)*'. In this study the scanning was repeated for a total of 266 directions. The test dipole was varied along one direction until the limits of the confidence volume were reached. The condition for reaching the confidence is given by

$$\left[T\left(G(\vec{r}+\Delta\vec{r})\vec{q}^* - \bar{u}\right)\right]^T \lambda^{-1}\left[T\left(G(\vec{r}+\Delta\vec{r})\vec{q}^* - \bar{u}\right)\right] = \chi_n^2(\gamma)$$

The number of degrees of freedom was set at 3, in correspondence with the 3 dipole location parameters that were varied independently.

Simulated data

The confidence interval of a dipole source location depends on both the characteristics of the dipole itself and on measurement conditions. To study the influence of the dipole position on the localization accuracy a central position and locations with eccentricities of .375 and .750 were studied. In order to disentangle differences due to

Table 2. Confidence volume size for different dipole characteristics, noise levels and electrode densities calculated with the MCS-, ICE- and LFM-method.

eccentricity	orientation	noise [%] c: correlated u: uncorrelated	number of electrodes	confidence volume [mm³]		
				MCS	ICE	LFM
.750	mixed	10/u	60	405	143	58
.750	mixed	5/u	60	41	19	7
.750	mixed	20/u	60	2600	1165	462
.750	mixed	5/c	60	3	-	-
.750	mixed	10/c	60	22	-	-
.750	mixed	20/c	60	310	-	-
.750	mixed	10/u	15	6519	1559	542
.750	mixed	10/u	30	775	414	170
.750	radial	10/u	60	493	208	62
.750	tangential	10/u	60	193	104	55

the linearization and due to the missing or admitted interaction of location, orientation and strength parameters, these confidence volumes are calculated with MCS, ICE, LVM and LFM. The effects of dipole orientation on the size of the confidence interval were investigated with the MCS, ICE and LFM method, using a tangentially and a radially orientated dipole. The impact of different noise levels and noise characteristics were also studied. The confidence limits of three different noise ratios (5%, 10%, 20%), defined as the ratio of RMS (noise) to RMS (signal), were compared. For all noise levels it was distinguished between uncorrelated and correlated noise. The uncorrelated noise was simulated by adding random numbers with a mean of zero and a standard deviation corresponding to the selected error level to the potential at each electrode. The correlated noise was modeled by averaging the potential distribution of 1000 arbitrarily placed dipoles at an eccentricity of 70 mm. The noise amplitude was adjusted so that the root mean square of the correlated noise was identical to the uncorrelated noise. In order to check the influence of the electrode density on the size of the confidence volume, the original 60 electrodes array was reduced to 30 and 15 electrodes. The area covered by the electrodes was kept constant. The three methods MCS, ICE and LFM were applied to these conditions.

Experimental data

Somatosensory evoked potentials of a single subject, who was stimulated sequentially at the thumb and the little finger of the left hand and at the left and right lower lip, were used for dipole analysis. In order to determine whether the identified sources were due to the somatotopic organization of the corresponding brain area or whether they were purely random, confidence intervals were calculated and their overlap was estimated. To compute the confidence intervals LVM, ICE, and the Monte Carlo approach were applied. The subject was stimulated 1000 times at all four body sites. A pressure pulse was exerted through a pneumatic device over a circular area of skin with a diameter of 10 mm, serving as a tactile stimulator. The stimulus lasted for 75 ms. The interstimulus interval was 700 ms. Evoked potentials were measured at an electrode array of 6 x 10 electrodes covering the somatosensory cortices of both hemispheres and were referenced to linked ears. Data were amplified and collected with a Neuroscan amplifier using a digitization rate of 1000 Hz. The time constant was set to 1 s and the lowpass filter to 250 Hz. Data were collected continuously and partitioned in epochs of 500 s duration with a prestimulus baseline of 50 ms offline.

To obtain an estimate of the error of the potential and of the interaction between the channels, the covariance matrix of all 60 electrodes was calculated based on 50 samples of the prestimulus interval.

Results

Simulated data

The different conditions simulated in this study were compared to a standard condition given by a dipole at an eccentricity of .75 with radial and tangential components $\vartheta_{orientation} = 60°$, $\varphi_{orientation} = 10°$. The noise of this condition was uncorrelated and its noise level was 10 %. The potential of the standard dipole was measured at sixty electrode positions. The confidence volumes estimated with MCS, ICE and LFM for different correlated and uncorrelated noise levels (5%, 10% and 20%), electrode numbers (15, 30 and 60), dipole eccentricities (0.000, .375, 0.750) and dipole orientations (radial, tangential and

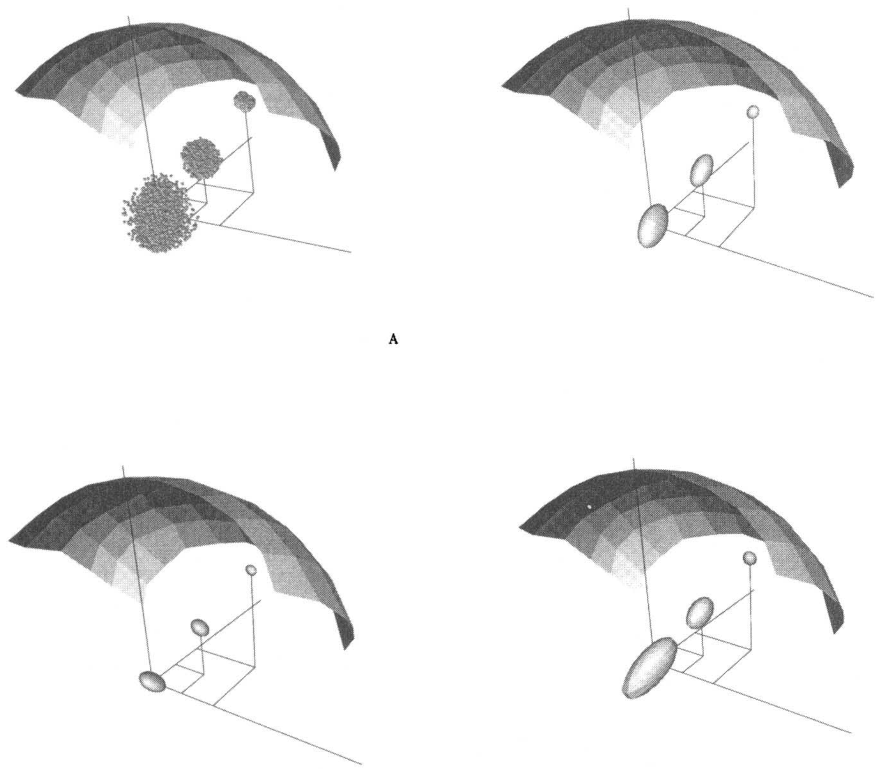

Figure 2. Three dimensional display of the confidence volumes of three dipoles located in the center of the sphere, at an eccentricity of .375 and .75 estimated with four different methods. The grid of 60 electrodes is displayed as a sheet. A) Monte Carlo simulation (MCS): the dipole locations of N=5000 potential distributions were calculated. 95% of the N potential distribution being closest to the potential of the given were selected to define the size of the confidence volume. B) Iterative confidence volume estimation (ICE): the space around the given dipole location was scanned in 266 directions. The confidence limits in each direction are the support points for the surface of the confidence volume. Linearization of the transfer function with variable (LVM) C) and fixed moment vector (LFM) D).

mixed) are concluded in table 2. In all conditions where uncorellated noise was used the same pattern of volume size could be found. Monte Carlo Simulations yielded the largest ICE medium and LFM smallest values. Increasing the electrode density led to a decrease of confidence volume size. In the case of uncorrelated noise, the size of the confidence volume showed the expected dependency from the signal to noise ratio with a resulting large confidence volume for 20% noise, and a smaller confidence volume for 5% noise. Using only correlated noise, the MCS method showed reasonable values and the ICE and LFM calculated sizes of less than 1 mm^3. The different orientations of the dipole showed only small effects on the confidence volume.

The comparison of different eccentricities yielded the largest confidence volume for a central source (table 3). Depending on the method used, the size of the longest half axis was 19.3 mm (MCS), 20 mm (ICE),10.8 mm (LVM) and 5.8 mm (LFM). The shape of the confidence regions differed remarkably between the 4 methods (figure 2). The

Table 3. Confidence volume size for different dipole locations relative to the scalp calculated with the MCS-, ICE-, LFM-and LVM-method.

eccentricity	confidence volume [mm^3]			
	MCS	ICE	LFM	LVM
.750	405	143	58	86
.375	3792	1097	295	700
.000	25576	4820	729	1838

Table 4. Locations, orientations and confidence volumes of dipole source based on experimental data. Confidence volumes were calculated using the MCS-method. a and b are the largest and smallest half axes of the confidence ellipsoid.

site	localization			orientation		noise signal	confidence region		
	x [mm]	y [mm]	z [mm]	ϑ [°]	φ [°]	[%]	volume [mm^3]	a [mm]	b [mm]
thumb	-45	11	39	54	-66	20.3	223	4.7	2.5
little finger	-52	17	42	66	-72	27.0	744	6.4	4.7
left lip	-53	-34	35	46	-86	22.4	1204	7.0	6.0
right lip	53	11	49	47	-104	42.8	1518	10.8	4.3

MCS revealed a rather spherical volume, whereas the other methods showed ellipsoids with half axes of different lengths. The spatial orientation of the volume calculated by the method using a linearization and a fixed dipole moment differed totally from that estimated by ICE and LVM procedure. For LFM the longest half axes of the ellipsoid was in the direction of the dipole orientation. For LVM and ICE the longest half axes are perpendicular to the dipole vector and point to the direction sparsely covered by the electrode grid.

Experimental data

For all four stimulation conditions (thumb and little finger of the left hand, right and left lower lip) the dipole localization of the maximum activity in a time window ranging from 35 to 55 ms after stimulus onset was calculated. The noise level of the prestimulus interval was similar in all four conditions. The corresponding confidence volumes were calculated, but only the Monte Carlo simulation yielded meaningful values. See results in table 4 and figure 3. LFM and LVM computed volumes smaller than 1 mm^3.

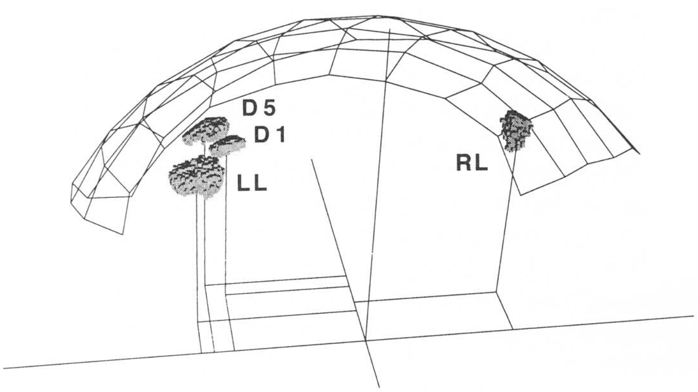

Figure 3. Three dimensional display of the confidence volumes of dipole locations calculated from somatosensory evoked potentials following stimulation of the left thumb (D1) and little finger (D5) and left (LL) and right lower lip (RL). The covariance of noise between electrodes was estimated from the prestimulus baseline. N=5000 potential distributions were used for the Monte Carlo simulation. The 95% of the N the topographical distributions were chosen which showed minimum distance to the potential distribution of the estimated dipole. Electrodes are located in the corners of the displayed mesh.

Discussion

The simulations performed in this study revealed that the size of the confidence volume of a single dipole location depends on both, measurement conditions and dipole parameters. The measurement conditions considered in this investigation were different types and different levels of noise as well as high versus low electrode density. Confidence volumes were smallest of course for low noise amplitudes and large numbers of electrodes. Careful electrode montage, noise reduction by using a large number of trial replications and adequate filtering are means to achieve this goal. Increasing the electrode density improves the localization accuracy. As there is usually a tradeoff between number of electrodes and data quality the calculation of confidence volumes can provide information on the number of electrodes that lead to optimal localization results. In order to economize the number of electrodes it is reasonable to use high electrode densities close to the cortical brain areas where the source is expected and to use a reduced number of electrodes for the rest of the head (Ogura and Sekihara 1993). In this case simulations of the confidence volume may be helpful to check whether the chosen electrode configuration leads indeed to an accurate dipole location.

The impact of dipole eccentricity and dipole orientation on the localization accuracy were studied, too. Dipoles deep in the brain have larger confidence regions than more superficially located ones. The size of ±20 mm confidence regions for a dipole in the center of the head and ±15 mm for a dipole location with an eccentricity of .375 prove that it is difficult or even impossible to distinguish between different deep sources with EEG dipole localization procedures. Comparable results for EEG were reported from Ogura and Sekihara (1993), Mosher et al. (1993) and for MEG from Hari et. al (1988). Different orientations of the dipole seem to have only minor effects on the size of the confidence interval. At least under the simulated conditions of radially and tangentially orientated dipole sources at an eccentricity of .75 the volume of the tangential dipole was slightly smaller than that of the radial source.

The four methods used for confidence volume estimation in this study differed in various aspects from each other. In all simulations where uncorrelated noise was used the Monte Carlo simulation revealed the largest and LFM the smallest confidence volumes. This is in accordance with Stok (1987) who reported the same findings. In the LFM method the dipole orientation and strength is kept constant while varying the dipole location in the three spatial dimensions. In contrast, dipole orientation and strength are updated for each spatial displacement in order to minimize this field deviation in the LVM and ICE method. As the confidence volume is given by a certain amount of field change its limits are reached already at smaller location shifts with LFM than with LVM and ICE. In addition, the shape of the confidence volume is also different. In MEG (using spherical but not realistic head models) this problem is not as severe as in EEG because there is one fewer parameter that can compensate for localization shifts, because radial orientations do not contribute to the magnetic field.

The smaller size of the LVM method, in comparison to the ICE procedure, can be attributed to the linearization of the relationship between source localization and potential distribution in the surrounding of the dipole source. Confidence volume sizes estimated with MCS were 2.5 times the size of volumes calculated with ICE. For ICE, the topographical noise distributions only fill a very small part of the entire error ellipsoid in signal space. This is a consequence of calculating the potential as forward solution of the test dipole that scans the source space. In contrast, Monte Carlo simulations consider arbitrary potential topographies from inside this ellipsoid. The localization of these potential distributions that resulted in most cases in residual variances greater than zero may be responsible for the larger confidence volume of MCS.

The volumes calculated with MCS were smaller for correlated noise than for uncorrelated noise. This is in accordance with results described by Huizenga and Molenaar (1995). The confidence volumes for correlated noise calculated with ICE, LVM and LFM failed to give any reasonable results as the volumes were below 1 mm^3. All methods that use the inverse of the covariance matrix in order to derive the confidence volume of the dipole location encounter difficulties with highly correlated noise, because the covariance matrix tends to be singular. Regularization techniques like the addition of uncorrelated noise requires a rule of how much noise should be added. Truncation of the covariance matrix by eliminating eigenvalues of zero assume an appropriate cutoff criterion. As there are no conclusive strategies available to handle singular covariance matrices, Monte Carlo simulation is therefore the method of choice to estimate confidence volumes of source localization. The Cramer Rao lower bound method proposed by Radich (1995) and Mosher et al. 1993) considers only uncorrelated noise and is therefore not an alternative. The problem of correlated noise is more important in EEG than MEG, because the reference electrode in EEG introduces identical noise to all other channels, leading to a correlation between the electrodes (Huizenga and Molenaar 1995). This correlation can be reduced using an average reference where the absolute noise amplitude is smaller than in the case of a single reference electrode.

For the experimental data dipole locations were estimated for the stimulation of left D1 (thumb) and D5 and left and right lower lip in central brain regions of the hemisphere contralateral to the stimulation. Estimation of the confidence interval with MCS proved that these locations can be differentiated from each other and that the different locations cannot be explained by random. The investigation of the confidence volume with the other three methods (ICE, LFM and LVM) yielded, due to the high noise correlation, a confidence volume size of less than 1 mm^3. It may be possible that the high noise correlation in this data is the consequence of a very short time epoch of 50 samples that was used to determine the noise covariance matrix (Yamazaki et al. 1992). An estimation of the covariance matrix based on single trials would probably have produced better results for ICE, LVM and LFM. Besides testing the accuracy of a dipole solution, the simulation of confidence volumes allows an estimation of the preconditions necessary to distinguish between different dipole sources. Based on the desired resolution of source localization the required signal to noise ratio and, hence, the number of trials in an EEG-study can be deduced (Hari et al. 1988). In addition, information about the minimum electrode density that is necessary for a certain localization resolution can be gained.

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