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Models of Brain Sources

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Summary: Two categories of models are available for the functional imaging of scalp recorded electric brain activity: single-time-point and spatio-temporal. Instantaneous models require strict assumptions that do not conform with the underlying physiology, because they rely on the few voltage differences measured at only one sampling point. Spatio-temporal models create a spatial image of discrete multiple sources and a temporal image of source current wave forms which reflect the time course of the local activity in circumscribed brain areas at a macroscopic level. The spatial image may be limited in accuracy because it depends both on model and data, but it can be validated by scanning the brain with regional dipole sources. In many cases of temporal lobe epilepsy, for example, interictal spikes can be described adequately by as few as two equivalent dipoles, which image the vertical source current arising from the medio-basal aspect of the temporal lobe and the horizontal source current from its lateral surface.

Key words: Brain source imaging; Regional source scanning; Spatio-temporal dipole model; Dipole localization; Epileptic spikes.

Introduction

As compared to MRI or PET, electroencephalographic (EEG) data are recorded at relatively few locations from the human scalp. However, the EEG has a much higher temporal resolution, and can form a data matrix with space and time providing independent information. Models are needed nevertheless, to solve the inverse problem, i.e., to compute equivalent brain sources from the voltage differences measured at the scalp. More sources can be estimated reliably on the basis of the spatio-temporal information than when the information at each time instance is considered separately. Accordingly, we can distinguish between instantaneous and spatio-temporal methods (figure 1). Instantaneous models are the basis for single moving dipole localization (Fender 1987) and minimum norm current density imaging (Hämäläinen and Ilmoniemi 1984). Spatio-temporal methods (Scherg and von Cramon 1985, 1986; Achim et al. 1988; Baumgartner et al. 1989; de Munck 1990; Scherg 1990; Scherg and Picton 1991) use a model with discrete sources to decompose the data matrix into a reduced number of source wave forms. These provide an image of brain function in terms of the magnitude and timing of the source currents in the activate brain areas.

Models can be further divided into a) infinitesimal models that estimate a current source density profile for the whole or a partial brain volume, and b) discrete models that estimate a finite number of equivalent sources. The inverse problem is ill-posed only if the number of estimated source parameters exceeds the number of independent variables in the data matrix. Hence, infinitesimal models, e.g., minimum norm methods, do not have a unique solution. In contrast, multiple or regional source models have a mathematically unique solution if the number of sources conforms with the degrees of freedom in the data matrix. In this case, the choice of the model depends mainly on how well the obtained source image can be related to the underlying morphology.

This paper discusses various single-time-point and spatio-temporal source models. Models were compared using averaged interictal spikes of patients with intractable complex partial seizures of the temporal lobe that exhibited type I and type II scalp voltage topography (Ebersole and Wade 1991).

Methods and Results

Scalp wave forms, mapping and minimum norm estimates

Results of the different models are presented for one patient (male, aged 46) who underwent presurgical EEG video-monitoring to evaluate his epilepsy (for details see Ebersole 1991). EEG was recorded from 27 scalp electrodes using the standard 10-20-system and lower

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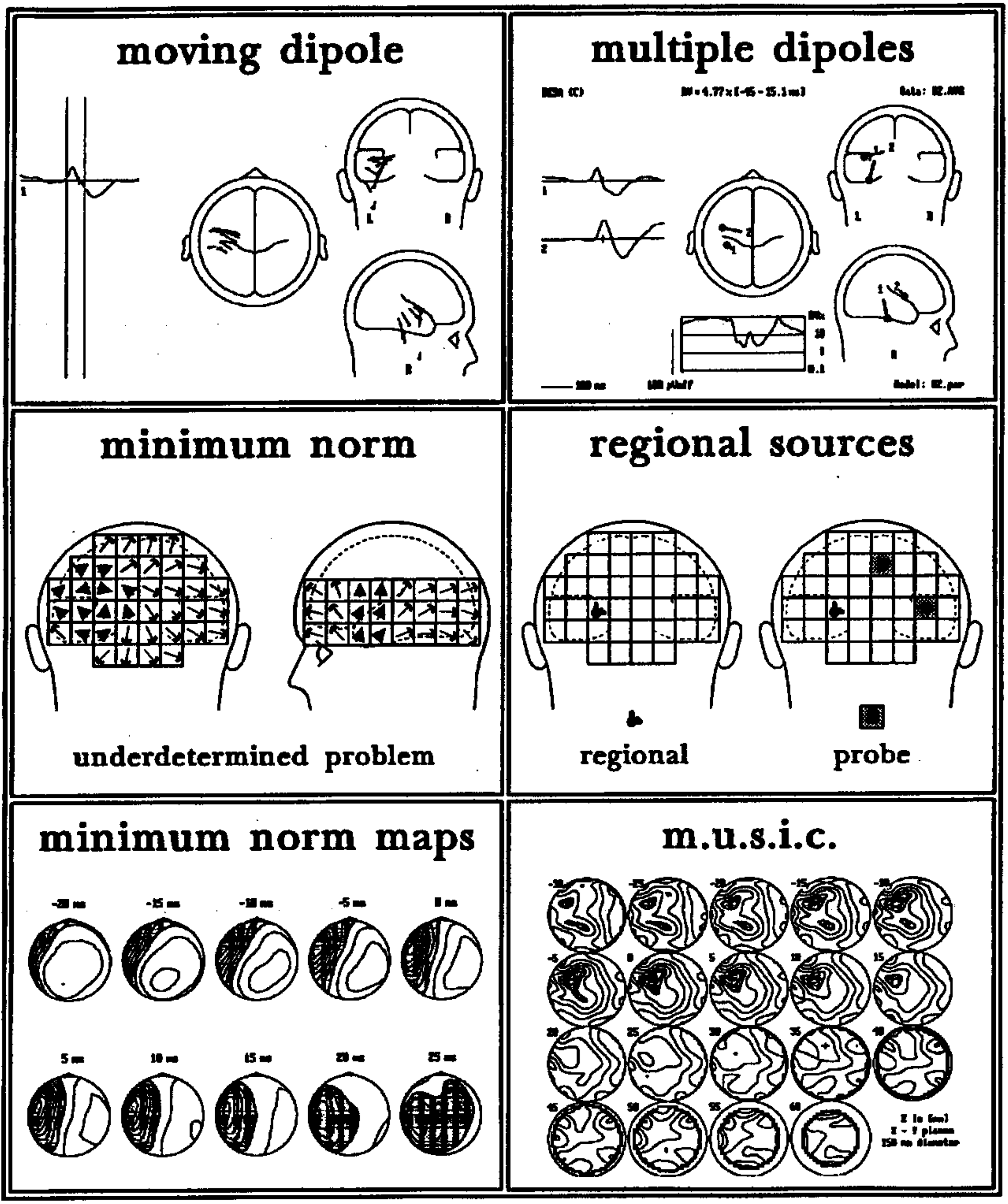

Figure 1. Brain Source Imaging by single-time-point (left) and spatio-temporal (right) models (for details see text). Moving dipole and multiple dipole solution (top) computed from -40 to +15 ms of spike peak. Principle of minimum norm current density estimate and regional/probe source scanning shown for a predefined volume and voxel size (middle). Scalp maps based on minimum norm interpolation (left) and horizontal brain slices of MUSIC probability maps (right) shown at bottom.

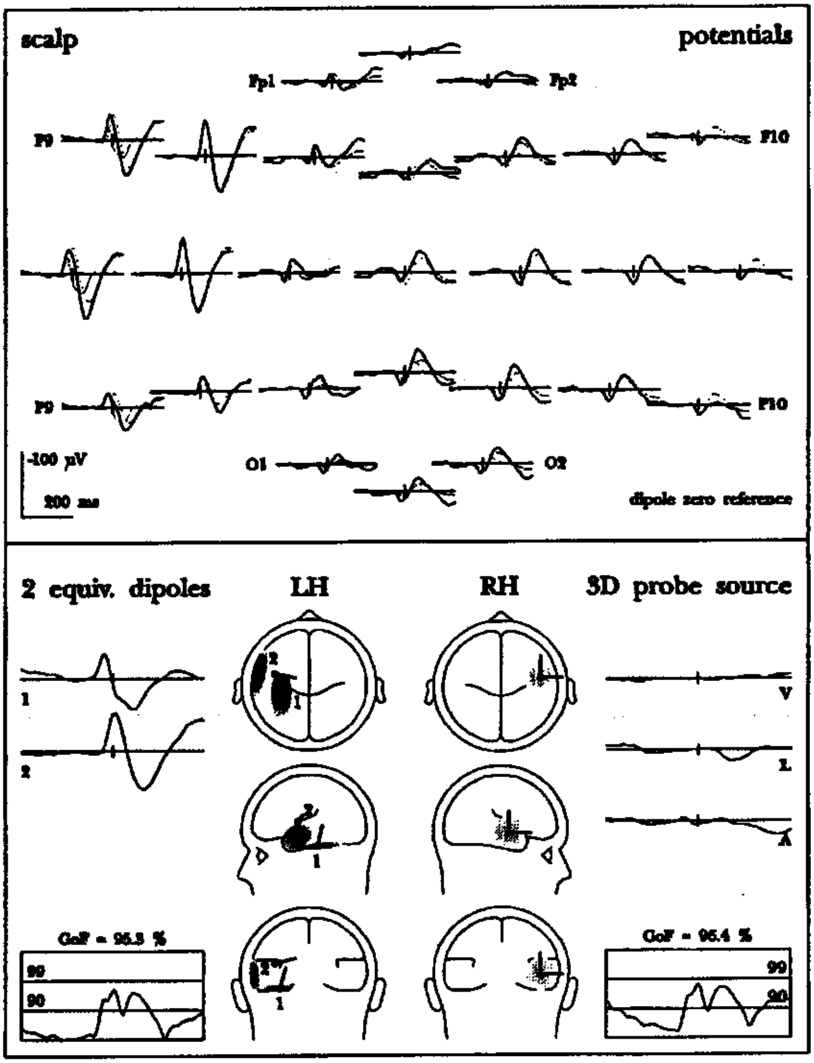

Figure 2. Brain Source Imaging by multiple dipoles: the scalp wave forms (top, thick solid lines) of averaged epileptic spikes are reduced to 2 (5) source potential wave forms (bottom). Dipoles 1 & 2 (left, LH) depict mesio-basal and lateral source activity in the left temporal lobe (cortical areas corresponding to these dipoles are hatched). Vertical (V), lateral (L) and anterior (A) source current wave forms of the regional probe source in the right hemisphere (right, RH) do not show significant activity early during the spike. Goodness of fit (semi-logarithmic scale) shown on bottom for the two (left) and five (right) dipole solutions. Contribution of source 1 (thin solid lines) and 2 (dotted lines) to the scalp wave forms shown on top. Note the latency difference of the spike between F9/T9 and F7/T7, and the prominence of the mesio-basal activity at F9/T9/P9 and Cz/Pz (inverted polarity).

lateral electrodes (F9/10, T9/10, P9/10). Ten interictal spikes with similar scalp topography were averaged after aligning peak latencies at F7. Data were digitally filtered (3-20 Hz) and analyzed using the Brain Electric Source Analysis program (BESA Version 1.9, NeuroScan, Inc., Herndon VA; this program incorporates all methods outlined here). The 27 scalp wave forms are displayed in top view in figure 2. Using the final source model of figure 2, the potential at the (average) reference was estimated and added to each wave form to obtain a "reference free" display. This differed little from the average reference data.

Minimum norm methods provide a statistical estimate of the source current density distribution at every point or over a very large number of voxels in the brain (figure 1). For mapping, we distributed 162 equivalent dipoles evenly over a spherical surface representing the cortex (eccentricity 0.65 in a homogeneous sphere of radius 1). The minimum norm magnitude of each of these dipoles was estimated using the singular value decomposition

(SVD) of the forward matrix (dipole to electrode). By projecting the minimum norm sources onto 225 new virtual electrodes, scalp potentials could be interpolated at the head surface over an elevation angle of +-110° in a top equidistant meridian projection around Cz (figure 1). Computation of maps was fast using this time independent transformation and nearest neighbor interpolation. Differences to simulated dipole and spherical spline maps were negligible.

Single-time-point models

Single dipoles were fitted independently at each sampling point from 40 ms before to 15 ms after the spike peak at F7. In figure 1 locations are depicted by dots and dipole moment by lines vectors pointing away from the dots. The single dipole seemed to move from far below the left temporal lobe to its crown, then laterally and back to lower locations. Fitting more than one dipole to these data at a single time point was impossible without additional constraints. Using minimum norm constraints, a distributed dipole density image can be estimated at a single time as illustrated schematically in figure 1. Image quality depends heavily on the correctness of a priori weights given to each brain voxel (zero outside assumed source region).

Spatio-temporal models

Three different spatio-temporal models are shown in figure 1: multiple dipole imaging, regional source imaging and multiple signal classification (MUSIC). Multiple and regional source models use dipoles that do not change location and orientation over time. Hence, the spatial image holds for the whole epoch of analysis. However, it is only schematic, because each dipole may reflect the activity of quite a large area of the brain, as illustrated in figure 2 by the shaded areas. They represent extended cortical surfaces of the left temporal lobe that provide the most realistic match in location and orientation with each equivalent dipole. Because there are only two (almost orthogonal) dipoles in the left hemisphere in our example, each summated all source currents in those regions of the temporal lobe surface which have either a vertical surface normal (medio-basal aspect, dipole 1) or a lateral surface normal (lateral aspect, dipole 2). Dipole localization presents a "center of gravity" for each activity. Dipole magnitude (and to some degree depth) partially reflects the extent of the active brain surface.

In spatio-temporal models, the term "activity" stands for the macroscopic source current in a circumscribed brain region that contributes significantly to the surface signals. An estimate of this temporal "activity" is the source potential of the stationary dipole over time (figure 2, bottom). Multiple source wave forms image the temporal pattern of activity in different brain regions, provided that at least one equivalent dipole is included in the model for each active region. For example, in our spike model the vertical dipole exhibited earlier source activity than the laterally oriented dipole. This is commonly observed in patients with type I spikes and seems to correspond to mesio-basal onset. Model quality is shown by the residual variance (RV) in figure 1 and by goodness of fit (1-RV) in figure 2.

A special case of multiple source models is the regional source model that defines a volume source by three collocated orthogonal dipoles. Such a source model can image the current flow of a localized brain volume in any direction. During regional source imaging (Scherg 1992) the sources reside at the centers of discrete brain voxels (figure 1), and thereby, maintain a minimal distance from each other. Scanning of the brain involves the testing of a discrete number of source locations to select those voxels for which the regional source explains a maximal amount of variance while having the least amount of covariance with the other regional sources. If the number of regional sources exceeds the number of underlying macroscopic areas of activity, one or more regional sources begin to show low amplitude source waves (figure 2, bottom). When they become inactive, regional sources can act like probes and exclude the presence of source currents in a surrounding brain region. For example, the regional probe source shown in the right temporal lobe in figure 2 was positioned at a location which was mirror symmetric to that found in the left hemisphere during the brain scan with one regional source. The source wave forms of the probe source documented that there were no significant macroscopic currents in the right temporal lobe during the initial phase of the spike-wave complex. Furthermore, the source wave forms imaged by the mesio-basal and lateral dipoles in the left temporal lobe were practically unchanged, when the probe source was added or moved to left frontal, parietal and occipital areas. Stability of the 2-dipole model was proven by this.

When using a probe source to scan the brain along horizontal slices, a probability function for localized currents can be defined by MUSIC. This method, first applied to MEG by Mosher et al. (1992) and to EEG by Scherg (1992), is limited by the implicit assumption that source activities are not correlated over time. Probability maps of the interictal spike are shown in figure 1 for horizontal slices ranging from a level around A1-A2 (-30 mm) to about C1-C2 (60 mm). Because the medio-basal and lateral source activities were only moderately correlated over time, two separate foci of probability were visible in the left temporal lobe in our example, while there was no obvious focal activity in the right hemisphere.

Discussion

To be valid and clinical useful, any model of brain sources must provide an approximate image of the anatomical configuration and of the physiological processes underlying the scalp EEG. A good model should characterize a pathological process over time and identify the brain region from which it originates. It should also provide ease of interpretation and data reduction. In this sense, discussion of localization accuracy is secondary, because the first question is that of an adequate choice of model.

From the present data and evoked potential analyses (e.g., Scherg 1992) it is obvious that instantaneous models rarely yield results which are compatible with the underlying anatomy. Interpretation, e.g., of the moving dipole in figure 1, is difficult because it is not obvious when a location is significant or when the equivalent dipole stands for a single source region. The dipole movement (figure 1, left) gives the appearance of sequential activation of discrete and momentary sources located between mesio-basal and lateral areas of the temporal lobe. This impression is incorrect and may lead to misinterpretations. Such "saltatory" propagation of a single dipole source with large dipole moment through the white matter and over the cortex is not consistent with physiology. To the contrary, the spatio-temporal dipole model showed activities from adjacent cortical regions that overlapped in time. This model could not be invalidated by placing an additional probe dipole at locations of the moving dipole solution. These instantaneous sources where thus only equivalent centers of a multiple source configuration.

The spatio-temporal dipole model required only two dipoles to arrive at a physiologically plausible solution. Each of these dipoles demonstrated a similar pattern of source activity, but that from the mesio-basal region began earlier. Only by constraining location and orientation parameters over time can such temporal imaging of different source processes be achieved. Point-sized dipoles poorly portray an accurate spatial image of the underlying cortical sources, however. It seems more appropriate to consider the source, which a dipole depicts, as a small area of cortex with indeterminate boundaries (figure 2). This imprecision in location does not adversely affect the temporal image. Dipoles could be mislocated by as much as 25 mm, yet still image the same temporal wave shapes due to the dominance of the orientation in the inverse computation. Hence, the local propagation of epileptic activity may not become obvious in the source analysis of scalp data before it spreads to a cortical region of different orientation. In this sense the 2-dipole model is simplistic, because it summates the local propagations along the mesio-basal and lateral aspects of the temporal lobe, respectively. Data with a very high signal-to-noise ratio would be needed to image this local propagation.

The regional source imaging technique and the MUSIC method were found useful to scan the brain for important source regions. Furthermore, they were helpful in excluding the presence of source currents in the contralateral hemisphere and in areas intermediate between the two dipoles. The improvement and combination of the various methods outlined here holds promise to lead to a true "Brain Source Imaging".

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