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Principles of Magnetoencephalography

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Summary: Magnetoencephalography (MEG) is a new, noninvasive functional test equivalent to EEG. It has been used to localize the sources of evoked responses and interictal and ictal epileptiform discharges and to study patients with psychiatric illnesses, cerebrovascular accidents, and migraine. In epilepsy research, it is hoped that MEG will provide information similar to that yielded by depth or subdural electrode recording, or that the combination of these methods will provide more information than either one alone. The application of MEG appears to be widening, although it is not yet a routine clinical diagnostic tool. The utility of MEG is limited by technological problems, but new and more efficient systems are becoming available. Within several years, advances in the technology and understanding of MEG may modify the course of its application.
Key Words: Magnetoencephalography—Instrumentation—EEG—Evoked responses—Epilepsy.

Magnetoencephalography (MEG) is a new, noninvasive functional test equivalent to EEG. MEG has been used to localize the sources of evoked responses and interictal and ictal epileptiform discharges and to study patients with psychiatric illnesses, cerebrovascular accidents, and migraine. In epilepsy research, it is hoped that MEG will provide information similar to that yielded by depth or subdural electrode recording, or that the combination of these methods will provide more information than either one alone (Wood et al., 1985).

PHYSICS OF MEG

Generation of Biomagnetic Fields

The decrease in force with increasing distance of both the magnetic and electric forces suggests that electricity and magnetism are related. The relation between a magnetic field and its associated current was empirically defined by Jean Patiste Biot and Felix Savart. Biot-Savart's law states that the magnetic field due to a small current element varies as the inverse square of the distance of the current element, varies directly with the current, and varies with the sine of the angle between the directions of the current and of the vector leading to it. In modern notation,

$$d\mathbf{B} = \frac{\mu_0}{4\pi}\frac{i d\mathbf{l} \times \hat{r}}{r^2}$$

where $d\mathbf{B}$ is the differential magnetic field in tesla, μ_0 is the magnetic permeability of free space and is assigned the value of $4\pi \times 10^{-7}$ Tm/A, i is the current in amperes, $d\mathbf{l}$ the length of the current element in meters, $\hat{r}$ is the unit vector pointing from the location in space at which the magnetic field is evaluated to the location of the current element, and r is the distance between those two locations in meters. The cross-product can be interpreted by the right hand rule: $d\mathbf{B}$ is mutually perpendicular to both $d\mathbf{l}$ and $\hat{r}$. This relation is understood by placing the right hand in space at the location at which the magnetic field is

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to be evaluated. Point the hand parallel to the current element $id\mathbf{l}$. Excepting the thumb, point the fingers parallel to $\hat{r}$. Extend the thumb, and it will point along the direction of $d\mathbf{B}$. A bit of finger play shows that a magnetic field encircles a straight wire carrying current and forms a dipolar (donut-shaped) region around a loop of current. The superposition principle, which states that the field produced by a sum of sources is equal to the sum of the fields of the individual sources, allows the total magnetic field **B** to be calculated by summing up the contributions from the individual current elements. In this way, the magnetic field for a particular source model can be determined. Williamson and Kaufman (1990) have reviewed this subject in detail.

Instrumentation

The measurability of the neuromagnetic field produced by the flow of electric current in cerebral neurons is made more likely by the columnar arrangement of the cortical neurons, which leads to the summation and re-enforcement of the field of each of the firing neurons. Nonetheless, a typical neuromagnetic field is on the order of 10^{-12} T, several orders of magnitude less than the magnetic field of the earth. The measurability of the magnetic field is made successful by shielding the subject and the measuring instrument from extrinsic noise, and by the exquisite sensitivity of the measuring instruments.

Measuring Devices

If an electric current can give rise to a magnetic field, it is natural to ask if a magnetic field can give rise to an electric current. A magnetic field can give rise to an electric current as long as the magnetic field is changing. This effect is called induction and is the basis for the detection of magnetic fields. If a coil of wire is placed in a changing magnetic field, an electric current is generated in the coil. This current then becomes the signal of the field. Reorienting the coil and changing the number and distribution of wire turns in the coil change the signal.

One device has become standard in neuromagnetic measurements: the superconducting quantum interference device (SQUID), which allows very sensitive measurements of the magnetic field. The SQUID is made of a niobium ring with a weak link, an extremely thin gap, which has a "tunneling" effect in which the wave phase of the superconducting current responds to magnetic fields. There are two types of SQUID: rf-SQUID, which has a weak link and is biased with radiofrequency current, and DC-SQUID, which has two weak links and is biased by DC current. The latter is less noisy than the former and therefore has been used in most of the recent magnetometers. The SQUID itself can be used as a magnetometer, but its combination with detection coils of various configurations allows a flexible design of measuring devices. The superconducting state is typically obtained when niobium is cooled below 23K when immersed in a bath of liquid helium at 4.2K. Erne (1983) has reviewed SQUIDs as used in biomagnetism.

Detection coil configurations can be classified by the aspect of the magnetic field to which they are most responsive. In this system, a magnetometer is a zeroth-order gradiometer. A first-order gradiometer is sensitive to the first spatial derivative of the field, and so on. Coils aligned axially are sensitive to the derivatives along their axis, and coils aligned in a plane are sensitive to the derivatives in that plane. The most common design is a second-order axial gradiometer with its axis approximately perpendicular to the head. However, this configuration introduces the possibility of signal loss or reduction of sensitivity by virtue of layers of coils (the distance between adjacent coils is a baseline). The recent trend is to utilize the first-order gradiometer configuration. In fact, the first-order gradiometer is already used in the recent larger neuromagnetometers (Biomagnetic Technologies, 1989; Gudden et al. 1989).

In a typical arrangement, detection coils are inductively coupled to a SQUID. Associated circuitry provides an electrical potential that is proportional to the magnetic field near the detection coils. The detection coils and SQUID are cooled to superconducting temperatures by a liquid helium bath in a dewar. Although its primary purpose is the operation of the SQUID, the cold bath provides some benefits and inconveniences. The chief advantage of the cold bath is the great reduction in noise. Among the inconveniences are the need to maintain the liquid helium and the necessity for dewar insulation, which inhibits the mechanical positioning of the device. These problems hamper efforts to incorporate large numbers of sensors into the dewar. A cryocooler system with multiple stages of gaseous cooling was developed to try to overcome this inconvenience. The prototype was used at New York University, but the magnetic noise level was increased by the electric motors used to help circulate the gaseous coolants.

Increasing the number of sensors in the dewar provides the ability to take simultaneous recordings across large areas of the head, as in EEG. Early MEG systems used a single channel. As the arrays grew, a hexagonal arrangement became popular, and the next largest size was the 7-channel machine. Currently, two more rings of coils have been successfully added, producing 37-channel machines that cover an area of 14.4 or 20 cm in diameter for the Biomagnetic Technologies system and Siemens' system, respectively. Machines with as many as 100 channels for full head coverage are being designed.

The use of high-temperature superconducting material is well in line with technology advancement in biomagnetism, but preliminary experiments suggest that a SQUID made with such materials is too noisy to be of practical use (Clarke and Koch, 1988).

Shielding

Magnetic shielding is typically provided by building a smaller room inside a larger one. The smaller room houses the dewar with the SQUID, associated circuitry, a gantry for movement of the dewar, and a chair or bed for a human subject. The inner room is called the shielded room, and its walls are usually made of several layers of a conductor such as aluminum or copper, which provides eddy current shielding of higher frequency noise, and several layers of mu-metal or other highly magnetically permeable material, which provide shielding of lower frequency noise. Erne and Romani (1990) have reviewed magnetically shielded rooms.

In some measuring environments, gradiometer coil designs provide spatial filtering of magnetic fields, which might obviate the need for extensive and expensive shielding. In the hospital environment, however, with many medical machines and other sources of interference, a magnetically shielded room is mandatory.

COMPARISON OF MEG AND EEG

There are some important differences between EEG and MEG. The electrical potentials measured by EEG are field potentials, or so-called volume cur-

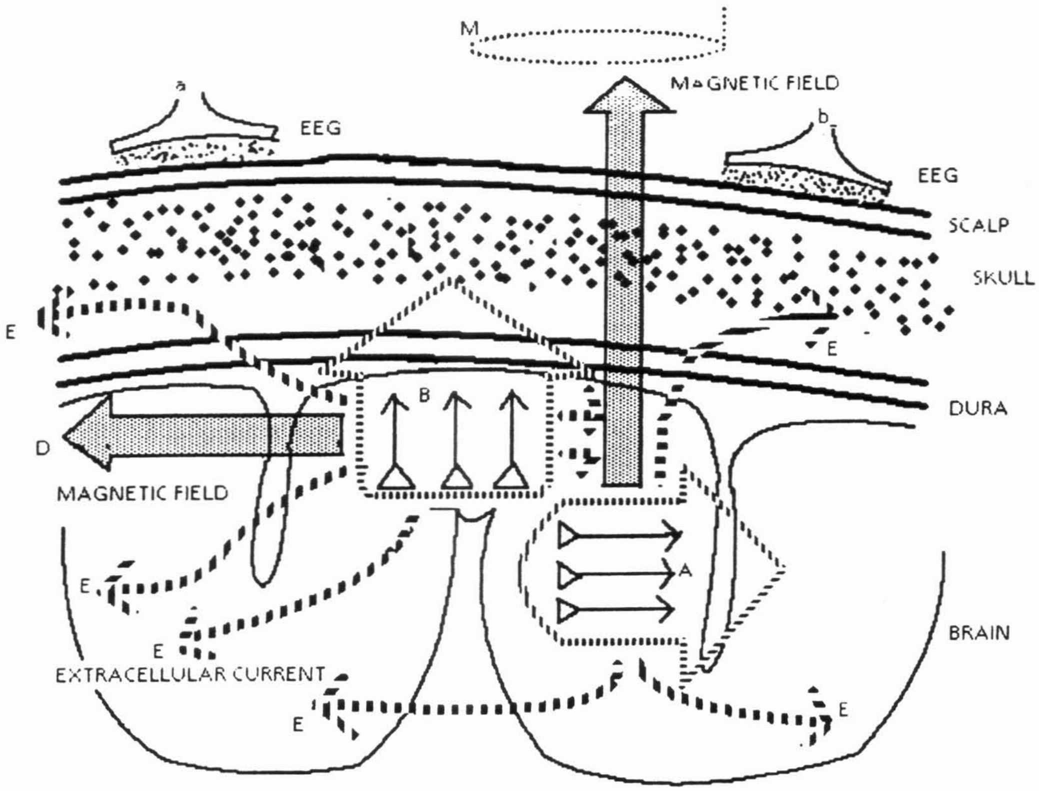

FIG. 1. EEG is recorded between two electrodes (a and b) placed over the scalp, whereas MEG records the magnetic fields emanating from a tangential source (A). The magnetic field (C) is not distorted by the scalp, skull, and dura, but the EEG signal is dispersed, attenuated, and distorted by them (E). A radial dipole (B) generates magnetic fields (D) parallel to the detection coil (M), and they may not be detected.

rents; they are easily attenuated, diverted, and distorted by the dura, skull, and scalp, whereas the magnetic fields are not affected by these structures (Fig. 1). However, it is well known that the magnitude of the magnetic fields decays at a rate of $1/r^2$ to $1/r^3$ (where r = distance from the source). Therefore, there is some concern about the ability of MEG to detect deeper sources (Cuffin and Cohen, 1977*a*). Electrodes and conductive gel are used in EEG, but not in MEG. The quantity measured by EEG is a relative value, namely, a potential difference between two electrode positions, whereas MEG measures an absolute value when the distance of a source is within the baseline of the detection coil (Wikswo and Roth, 1988) and a relative value when a source is deeper than the baseline distance. The EEG contour maps are often monopolar and occasionally dipolar. The MEG maps are usually dipolar or multipolar and rarely monopolar. The MEG pattern is rotated by 90° from the EEG pattern, and the MEG maps are about one-third tighter that the EEG maps (Cohen and Cuffin, 1983). EEG is known to measure the field potentials of current sources oriented in all directions, with radially oriented current sources measured somewhat preferentially. MEG measures chiefly the radial component of the magnetic fields, assuming that the head is spherical, because of the configuration of the magnetometer. This peculiarity of MEG has been interpreted to mean that MEG measures tangential current sources located in sulci; because about two-thirds of the cortex is in sulci, it is thought that loss of information due to MEG's inability to measure current sources in the gyri is minimal (Hari and Kaukoranta, 1985).

Calculation of three-dimensional coordinates from EEG data requires six parameters: three for location, one for magnitude, one for orientation, and one for conductivity, whereas MEG does not require a parameter for conductivity (Stok, 1986).

Because of the tissue-induced attenuation and diffusion of the EEG, the dipole depth calculated by EEG mapping may turn out to be deeper than the actual depth. The direction of current flow estimated by evoked magnetic fields is opposite the direction estimated by evoked potentials, suggesting that the magnetic fields are generated by high-density intracellular current, whereas the electrical potentials are produced by volume current (Kaufman and Williamson, 1982).

These comparisons suggest that MEG may have a somewhat better spatial resolution than EEG (Cohen and Cuffin, 1983).

MODELING IN MEG

A knowledge of the so-called forward and inverse problems is essential for understanding biomagnetism and its analysis, but there is no unique solution to the inverse problem. For MEG analysis, information concerning the geometry of the head and the current source or sources must be obtained. A simple spherical model with a single current dipole has been used most commonly, although other models may be more appropriate in some situations. These subjects have been reviewed by Nunez (1981), Ilmoniemi et al. (1985), Hari and Ilmoniemi (1986), Stok et al., (1986, 1987), Sarvas (1987), and Williamson and Kaufman (1987).

Head Geometry

The simplest model of the head is the homogeneous half-space model with a single dipole (Williamson and Kaufman, 1987), in which the magnetic field at any point is easily predicted by Biot-Savart's law, allowing estimation of the location and direction of such a dipole from the magnetic field map and the interextrema distance. In practice, the head is most commonly modeled as a uniform conducting sphere, in which radial current dipoles are assumed to have no measurable external magnetic field (Cohen and Hosaka, 1976; Cuffin and Cohen, 1977*b*). In this model, it is also assumed that volume currents make no contribution to the field and that simple relations exist between field maxima and the dipole location and depth. This is probably the most frequently used model in MEG; however, there are important problems with this model. Such a simple model does not represent the temporal lobe well, causing an angulation problem between the sensors and the inner surface of the skull, and the results are susceptible to the effects of volume currents (Barth et al., 1986; Rose et al., 1987*b*, 1989*a*).

More precise models based on the actual skull shape obtained by magnetic resonance imaging (MRI) have been suggested (Meijs et al., 1987; Meijs and Peters, 1987) and give more accurate localization in in vitro models, although at some computational expense. Such a model was recently applied to localization of scalp-recorded spike discharges in the temporal region and appeared to give reasonable accuracy of discharge localization compared with that obtained by subdural electrodes (Ducla-Soares et al., 1989).

Source Models

Modeling spike foci as a current dipole source is simplistic; the foci are probably more distributed. Nunez (1986) discussed possible effects of multiple dipole sources, and Barth et al. (1989) attempted to solve the sources of interictal activity with multiple current dipoles, each with its own temporal properties. A more complicated distributed current source is probably more representative of the epileptogenic focus, and work is underway on the interpretation of MEG sources with respect to such a model (Clarke et al., 1989; Ioannides et al., 1989; Kado et al., 1989), although this has not yet been applied to the field of epilepsy.

SPONTANEOUS ACTIVITY

Alpha Rhythm

In 1968, alpha rhythm was magnetically measured with an induction coil for the first time (Cohen, 1968). There is a good correlation between MEG and EEG alpha rhythm (Hughes et al., 1976; Cohen, 1979; Cohen and Cuffin, 1979; Modena et al., 1982). The amplitude of alpha rhythm is largest over the parieto-occipital regions (Reite et al., 1976), and the largest magnetic flux of alpha rhythm occurs over the longitudinal midline (Cohen, 1979). The maximum amplitude of the magnetic alpha rhythm is 2.5 pT peak to peak (Carelli et al., 1983). Many investigators have attempted to localize the sources of alpha activity, and some have suggested that the alpha activity has multiple sources in or near the visual cortex (Vvedensky et al., 1986; Carelli et al., 1989). Recent work suggests that magnetic alpha rhythm arises from many discrete sources, oscillating one after another and occasionally overlapping temporally. These sources are clustered near the midline, extending to a depth of several centimeters (Williamson et al., 1989).

Sleep Spindles

Sleep spindles were initially difficult to record with MEG (Hughes et al., 1976; Freedman, 1981). With a laboratory-built single-channel magnetometer, however, sleep spindles (12.5–16 Hz) were recently detected at the central vertex, predominantly as a radial magnetic component, in three normal volunteers (Nakasato et al., 1990).

Epileptiform Activity

The use of MEG in epilepsy research has been reviewed by Rose et al. (1987*c*). A worldwide surge of interest in MEG occurred when investigators from the United States and Italy published their results on localization of epileptiform discharges in 1982 and 1984 (Barth et al., 1982, 1984*a*; Modena et al., 1982; Ricci et al., 1984). MEG is used to study interictal and ictal discharges and also background activity, because all of them are important for localization of the seizure origin.

Interictal Activity

Hughes et al. (1977), followed later by Modena et al. (1982), first reported that the spike component of epileptiform discharges was well defined magnetically, but the slow-wave component was not. Simultaneous MEG and EEG recordings showed that EEG slow waves and MEG multiple spikes often occurred together or that EEG changes occurred without accompanying MEG signals or vice versa (Ricci, 1983; Sutherling et al., 1988*a*).

Spike averaging. At each sensor position, as many as 10–20 similar EEG spikes are sampled, and their magnetic signals are averaged using an EEG channel as a trigger. Then a map of the magnetic field is constructed and used for calculation of equivalent current dipole sources for spike discharges. The purpose of spike averaging is to improve the signal-to-noise ratio, and the eventual localization is usually expressed as a point or central point (centroid) (Sutherling et al., 1988*a*). Even though the epileptogenic focus is physiologically not a point, dipole source modeling is an important step toward further understanding of a complex problem such as epileptic seizures (Barth et al., 1982, 1984*a,b*; Sutherling et al., 1988*a*). Unfortunately, spike-averaging methods may result in loss of spatial and temporal information and of details concerning individual spike types. The template method (Salustri and Chapman, 1989) can be used to find similar spikes for averaging. With a larger MEG system, such as a 37-channel machine, this process becomes easier or unnecessary because the magnetometer does not have to be moved around to scan the patient's head.

Single-spike analysis. Individual spikes can be mapped and their location estimated without averaging (Sato et al., 1985; Rose et al., 1987*a*). With this method, important information riding on "waves" will not be "averaged out." Although individual EEG spikes appear somewhat dissimilar in morphology, amplitude, and distribution, it nonetheless seemed possible to group spikes according to their similarities, thereby yielding several different types of spikes (Rose et al., 1987*a*). With a single-channel or seven-channel system, the entire head cannot be measured simultaneously, causing difficulties in combining events dispersed in time. Therefore, the selection of signals with a good signal-to-noise ratio becomes essential but is tedious. The method of identifying spike types is typically visual, although other methods are available (Salustri and Chapman, 1989). Nevertheless, less information may be lost with single-spike analysis than with averaging techniques. With a 37-channel magnetometer, consecutive spikes can be analyzed with good results on localization (Sato et al., 1990).

Relative covariance method. MEG and EEG are recorded simultaneously, the EEG activity of interest (frequency band) is identified by Fourier transform techniques, and then MEG and EEG are digitally filtered to a narrow band surrounding the frequencies of interest. The covariance of the filtered MEG and EEG signals at each sensor site is calculated and divided by the variance of the filtered EEG, giving the "relative covariance." This calculation is performed at all MEG locations, and the EEG channel or channels used are consistent for all MEG locations, although different EEG channels may be compared (Ricci et al., 1984, 1985, 1987; Romani and Leoni, 1985; Chapman, 1989). It is claimed that the relative covariance is proportional to the value of the magnetic field perpendicular to the head at a given location (Ricci et al., 1985). A contour map of the relative covariance is constructed, and an equivalent dipole current source may be localized. The localization step is typically based on a spherical model assuming that only radial magnetic components are measured (Ricci et al., 1985).

The relative covariance method is important, because it allows analysis of background activity and localization in the absence of a spike focus if there is detectable abnormal rhythmic activity. In principle, a similar analysis could be applied to stereotyped seizures with rhythmic activity.

Ictal Activity

The capturing of an ictal event with MEG is difficult, particularly with the single-channel and seven-channel systems. Nevertheless, ictal recording is not entirely precluded, because the patient usually does not move for 5–10 s during the initial phase of the seizure (Sutherling et al., 1987) or during simple partial seizures (Rose et al., 1989*b*). Simple recordings of ictal events such as 3/s spike-and-wave discharges were done early in the development of MEG (Modena et al., 1982), but detailed studies to determine spatial localization of sources are difficult inasmuch as events would have to be recorded at many locations (in the absence of large multichannel magnetometers) and the information from different seizures combined. In patients with jacksonian seizures, MEG was thought to provide localizing information despite the absence of abnormal EEG findings (Modena et al., 1982; Ricci, 1983).

Migraine

Spreading cortical depression, which is a slowly changing potential, has been implicated in migraine to explain the evolution of the clinical manifestations associated with the disorder. Although spreading cortical depression has never been observed spontaneously in humans, biphasic waves lasting for less than 10 s with amplitudes ranging from 800 fT to 13 pT were recorded with MEG in patients with migraine (Tepley et al., 1989). This area of research requires further investigation and confirmation of results.

EVOKED RESPONSES

While studies of evoked magnetic responses have not yet provided unique clinical information, they do provide information on cerebral functional processing and, when combined with imaging information, establish interesting functional–anatomical correlations. The information provided by MEG complements and in some cases resolves ambiguities remaining in comparable studies of evoked potentials. All modalities may be studied by MEG, but stimuli must not generate significant magnetic fields.

Auditory Evoked Responses

Short-Latency Evoked Responses

The detection of brainstem-evoked fields is technically quite difficult. When signals somewhat above background noise were recorded in a shielded room, using a magnetometer (not a gradiometer) and averaging from 12,000 to 96,000 sweeps (Erne et al., 1988), waveforms corresponding to brainstem-evoked potential waves V and VI could be recorded, and their amplitudes were different at different recording locations.

Middle- and Long-Latency Evoked Responses

The auditory stimulus is generally led by plastic tube to the patient to avoid interference from the magnetic field generated by the usual transducers or headphones. Table 1 shows recording parameters and details of stimuli from a sample of studies. Responses to approximately 100 stimuli are usually recorded at each magnetometer position. The magnetometer is moved (by some investigators randomly) over the region of interest in order to avoid systematic bias resulting from a change in state, which has a significant effect on responses. Filter settings given in Table 1 reflect the final bandpass; the signals typically are recorded through analog filters with a wider bandpass and are subsequently filtered digitally.

Reite et al. (1978) demonstrated the feasibility of recording magnetic fields to auditory stimuli. Hari et al. (1980) described the time course and spatial distribution of auditory evoked responses. In particular, major peaks at a latency of 100 ms (N100) and 200 ms (P200) were described in addition to a subsequent slow sustained field. For the most part, when source localization has been attempted, simple models such as a single equivalent dipole in half space (Pantev et al., 1988) or a single equivalent dipole in a spherical conductor (Papanicolaou et al., 1990) have been used.

Early work (Hari et al., 1980; Elberling et al., 1982) suggested that the generators of the N100 were probably located on or near the planum temporale. More recent studies with gross anatomical correlation (Pantev et al., 1988) or MRI correlation (Pantev et al., 1990; Papanicolaou et al., 1990) have largely confirmed this localization. The generators of a peak at 50 ms (Reite et al., 1988) are also near the planum temporale.

Reite et al. (1981) showed that the amplitude of the N100 peak is larger when the stimulus is from the contralateral side. Papanicolaou et al. (1990) found that the equivalent dipole for the N100 was located more posteriorly and medially when stimuli were contralateral. Rogers et al. (1989, 1990) suggested that successive time points in the N100 peak had generators that moved anteriorly, and this was clear when stimulation was contralateral, not ipsilateral. These and other studies, then, suggest the possibility that somewhat different cortical areas are activated by contralateral and ipsilateral stimulation.

Elberling et al. (1982), on the basis of the N100 response, suggested that equivalent dipoles over the left hemisphere are posterior to those over the right. Reite et al. (1988) made similar observations on the 50-ms response, although MRI correlation allowed localization of the equivalent dipole near the planum temporale.

TABLE 1. *Auditory evoked responses*

Reference	Acquisition [Freq (Hz), time (s)]	Final bandpass (Hz)	Repetitions	Number of positions	Magnetometer (channels)	Design (order)	Stimulation[a]	Shielding
Reite et al. (1978)	?, 0.2	5.0–15.0	516	5	1	2nd	Clicks; ISI, 0.25	Aluminum
Reite et al. (1981)	?, 0.5	0.1–30	128	1	1	1st	Clicks; ISI, 0.7	Aluminum
Elberling et al. (1982)	320, 0.8	DC–18	60	24	1	1st	Tones (1 kHz), 0.5; ISI, 1.5–4.5	No
Romani et al. (1982*a,b*)		32	1,000	40	1	2nd	AM tones (200–5,000 Hz) steady state	No
Pantev et al. (1988)	250, 1.024	0.1–30	96	50–60	1	2nd	Tones (250–4,000 Hz), 0.5; ISI, 4	No
Papanicolaou et al. (1990)	?	?	100	56	7	2nd	Tone (1 kHz), 0.05; ISI, 0.4	Yes
Hari et al. (1980)	?	0.03–15	>300	30	1	0	Tone (1 kHz), 0.8; ISI, 4	No

[a]Type of stimulus (frequency), length in seconds, interstimulus interval (ISI) in seconds.

Early studies using a steady-state technique (Romani et al., 1982*a,b*) suggested a tonotopic arrangement of the responses, and more recent work (Pantev et al., 1988, 1990) is in basic agreement; the depth of the equivalent dipole generating the N100 increases with the logarithm of the stimulus frequency. The mapping is not clear for the later waves at 160 ms.

Various paradigms involving speech elements as stimuli, or so-called oddball paradigms, have been used in studies attempting to elucidate cerebral processes underlying attention and speech perception (Sams et al., 1985; Makela et al., 1988; Hari, 1989*a,b*; Hari and Lounasmaa, 1989). This work is beyond the scope of the present review, but such studies, when combined with MRI findings, for example, should provide impressive functional–anatomical information.

Somatosensory Evoked Responses

The basic stimulation paradigms for somatosensory evoked responses are not greatly different from those used in recording somatosensory evoked potentials (SSEPs). Recordings may be successfully performed even without a shielded room (Sutherling et al., 1988*b*). The current pulse is brief enough not to interfere with subsequent recordings. An overview of methodology is given by Hari and Kaukoranta (1985); they also briefly discuss fields evoked by noxious stimuli. Huttunen (1986) has described methodology for recordings of fields evoked by tactile stimulation. The recording bandpass and sampling rate determine to a large extent whether or not early peaks corresponding to the "cortical" components of SSEPs are emphasized.

Several investigators have reliably recorded components corresponding to cortical SSEPs (Rossini et al., 1988; Sutherling et al., 1988*b*; Tiihonen et al., 1989). Tiihonen et al. (1989) found that the equivalent dipole for the 27-ms peak (P27m) was located on the average 1 cm anteromedially to sources for the 20-ms peak (N20m). Their findings were consistent with a tangential source (posterior bank of central sulcus) as the generator of the N20m. Sutherling et al. (1988*b*) compared localization of somatosensory evoked responses based on MEG, EEG, and electrocorticography (ECoG). The average distance of localization from the central fissure was 4 mm in EEG and MEG and 3 mm in ECoG. Averaging MEG and EEG distances yielded localizations comparable to those of ECoG. These results, although from only three patients, suggest that MEG and EEG may reliably and noninvasively localize somatosensory cortex. Suk et al. (1989) attempted to correlate localizations from stimulation of different fingers with MRI-based structural information. Their studies suggest that such noninvasive mapping of the sensory homunculus is possible.

Visual Evoked Responses

Teyler et al. (1975) were among the first to report on studies of visual evoked magnetic responses and described a method based on brief flashes. Because cathode-ray tubes generate large magnetic fields, more sophisticated stimuli (i.e., patterns or gratings) require the use of projection equipment and mirrors. Kouizjer et al. (1985) and Aine et al. (1989) described their techniques for stimulation and recording of visual evoked responses. As in other modalities, in the absence of large multiarray systems, obtaining field patterns requires repeating the averages at different locations. Filter settings and sampling are otherwise similar to recording visual evoked potentials. The appropriate treatment of field maps, even if apparently dipolar, is controversial. Stok et al. (1986) argued that the inverse problem should probably take into account a realistic head shape, rather than relying on spherical models. In spite of this objection, George et al. (1989), using sinusoidal grating stimuli, localized apparent equivalent dipoles that, when projected on MRI scans, were near calcarine cortex and appeared to evolve temporally. Under some conditions of stimulation and at some time points, two different dipoles appear necessary to explain the evoked fields (Aine et al., 1989).

Premotor Fields

Premotor fields are studied by recording magnetic activity preceding self-paced or triggered movements (Mizutani et al., 1989). Table 2 shows selected parameters used by several investigators. The electromyographic (EMG) burst is frequently used as the trigger to average the preceding magnetic activity. The procedure must be repeated at each magnetometer position, and the time transients then can be used to form contour maps. Depending on the resulting contours, an appropriate model can be used (i.e., dipole in a sphere) to make inferences about source localization. Great care must be taken to eliminate epochs with a large amount of eye or head movement (Antervo et al., 1983).

Slow changes in the magnetic field with topographic variation have been recorded as much as 1 s before foot (Antervo et al., 1983) and complex

TABLE 2. *Premotor fields*

Reference	Acquisition [Freq (Hz), time (s)]	Final bandpass (Hz)	Repetitions	Number of positions	Magnetometer (channels)	Design (order)	Stimulation or trigger	Shielding
Antervo et al. (1983)	175, 4	0.03–30	70	15	1	1st	EMG, foot	Yes
Cheyne et al. (1989)	?, 2	0.1–10	?	30–90	14	2nd	EMG, foot, hand, finger, face	Yes
Deecke et al. (1985)	85, 3	0.03–15	>80	11	1	3rd	EMG, fingers	No
Mizutani et al. (1989)	?, 5	0.1–20	>64	7	1	2nd	Keypress	No

hand (Deecke et al., 1985) movements. The slow-changing field preceding movement is designated the "readiness field" (RF) or "bereitschaftsmagnetfeld" (Deecke et al., 1985). There is also a large movement-related response 90–130 ms after EMG onset designated the "movement-evoked field" (MEF). Cheyne et al. (1989) found systematic variations in the location of the equivalent current dipole generators for both the RF and the MEF when face, hand, index finger, and thumb movements were studied. Their data are consistent with the motor homunculus, although explicit MRI correlation is lacking.

Advances in Evoked Magnetic Responses

Studies of evoked magnetic fields hold promise for increasing our knowledge of cerebral sensorimotor, and possibly cognitive, processes. Localization of sources by MEG is probably less affected by volume currents than localization based on EEG. In some cases, underlying ambiguity of sources and their orientation may be better evinced with MEG because of its sensitivity to tangentially (as opposed to radially) oriented current sources. A problem with many of the studies is that responses are sensitive to changing cognitive states. The present direction of these studies includes the measurement of responses to more complex stimuli (i.e., oddball paradigms), the comparison of evoked response information with that obtained by imaging modalities, and the incorporation of greater sophistication in source modeling, as in modeling spatiotemporal sources, as described by Scherg et al. (1989) and Baumgartner et al. (1989). Future directions that seem appropriate include (1) the development of larger, multiarray systems so that responses can be recorded simultaneously over the entire head, thus avoiding the unwanted variation in cognitive state; (2) the development of algorithms to utilize EEG and MEG information for source localization; and (3) the use of more realistic source and volume conductor models (i.e., based on MRI data). The clinical utility of these advances remains to be determined, but they clearly are of importance in our understanding of the mechanisms of brain function.

PRESURGICAL EVALUATION OF EPILEPTIC PATIENTS

Although MEG has been used to study a rather large number of epileptic patients worldwide, it is not an established diagnostic tool. Furthermore, MEG currently does not influence the decision-making for the surgical treatment of epilepsy. When larger systems with faster and more realistic methods of analysis become available, the value of MEG may change significantly in this respect.

VALIDATION OF MEG

The point localization of sources predicted by MEG is unphysiological, so that the results cannot be compared with the widespread discharging region identified on ECoG recording. Invasive techniques such as depth or subdural electrode recordings are often used to validate the MEG and EEG findings (Sato et al., 1989), but spikes recorded with these methods are different from the scalp-recorded spikes in terms of amplitude, waveform, and distribution, and they cannot be compared on a one-to-one basis. Many small, independent spikes detected by depth or subdural recording may not be detected with the scalp-recorded EEG or MEG unless a wide area of the cortex fires synchronously.

An alternative way of comparing these three methods is to compare the areas explored by each method. ECoG delineates regions of epileptiform discharges on the cortical surface (Ajmone-Marsan, 1986; Rose et al., 1987*a*), whereas EEG and MEG may not easily provide regional information. Assuming that each spike represents a slightly different discharging region, analysis of many spikes will lead to an aggregate of many points, which in turn leads to a region (Sato et al., 1990). In this way, the discharging region identified with ECoG can be compared with that predicted by MEG.

FUTURE PERSPECTIVES IN MEG RESEARCH

Although the MEG localization of sources, especially deep beneath the skull surface, is not as affected by volume currents as a similar localization based on EEG mapping, MEG may have some difficulty in detecting deeper sources because of the quick decay of magnetic fields. MEG studies need to be compared with detailed EEG studies to assess the utility of each. Validation of each of the techniques must be performed in larger groups of patients treated surgically or studied with invasive techniques to assess the true utility of MEG.

A severe limitation of the currently available MEG systems in their inability to record events over the entire head simultaneously. This deficiency may introduce additional error, because nonsimultaneous events must be combined for analysis.

Without doubt, MEG is an excellent experimental tool but has yet to be proved a reliable clinical diagnostic methodology. Simultaneous EEG and MEG recording is always done to ensure that comparable signals at different locations are being compared; however, this also precludes the optimal use of MEG as an independent measurement. MEG technology is evolving, however, and a recent report from Finland (Tiihonen et al., 1990) describes a magnetometer that has seven sensors and a scanning area 93 mm in diameter. Furthermore, two 37-channel systems are now commercially available, and many other research institutes and commercial firms have expressed interest in producing even larger units to scan the entire head at once. It will be several more years until the routine clinical utility of MEG is established. Meanwhile, MEG and EEG will continue to complement each other, and both together will provide more information than either one alone.

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