

Magnetoencephalography (Neuromagnetism)

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The same fluctuating electrical currents from the brain that produce the electroencephalogram (EEG) also produce a magnetic field over the head, called a neuromagnetic field. A measurement of this field is called a magnetoencephalogram (MEG). Because the MEG is produced by the same currents that produce the EEG, some types of MEG recordings resemble EEG recordings. For example, a single MEG trace (a recording of the fluctuating magnetic field versus time at one location on the head) roughly resembles an EEG trace recorded at a related location. However, an MEG spatial map over the head is quite different from the corresponding EEG spatial map, where each map shows the magnetic field or EEG potential over a large region of the head, frozen at one instant in time. They are different because the MEG spatially samples the currents differently than does the EEG. This difference in sampling allows the MEG map to provide some different information about electrical sources in the brain than does the EEG map. In that sense the MEG is complementary to the EEG, and both are necessary to obtain maximum information about the electrical sources in the brain. Thus, the MEG is now grouped together with the EEG among the non-invasive techniques for looking at the human brain; the MEG and EEG are unique in that they look at fast electrophysiological brain events (milliseconds). This is in contrast to functional magnetic resonance imaging (fMRI), positron emission tomography (PET) and single photon emission tomography (SPECT) which look at events in seconds or minutes, and magnetic resonance imaging (MRI), and computer assisted tomography (CAT) which only look at anatomic structures.

The fluctuating neuromagnetic field is very weak, with an amplitude typically below 10^{-12} tesla, or 10^{-8} gauss in the older magnetic units; this is much weaker than the urban fluctuating magnetic noise background of about 10^{-7} tesla or 10^{-3} gauss, and weaker yet than the earth's steady field of about 0.5×10^{-4} tesla, or one-half gauss. Therefore the two main requirements for measuring the MEG are a magnetic detector of high sensitivity, and the suppression of the fluctuating magnetic background (the steady background usually presents no problem). The sensitive detector used is the SQUID (Superconducting Quantum Interference Device) which operates at cryogenic temperatures; a SQUID sensitive enough to measure the brain requires the low temperature of 4° K, and is contained in a liquid helium dewar. The recent MEG dewars are helmet-shaped and enclose most of the head;

a dewar of this type contains many SQUIDs, mostly arrayed on a spherical section over the head, typically at grid points 2 or 3 cm apart. This spherical section is at an average distance of about 2 cm from the scalp, where some of the separation is due to the vacuum space in the dewar. The many SQUIDs allow simultaneous magnetic field measurements at the many corresponding points over the head.

The fluctuating background is suppressed in two ways. In the first way, a magnetically shielded room is used, in which the measurements are made; the room excludes almost all of the fluctuating external fields. Examples are shown in Figs 1 and 2; the degree of shielding varies with the number of wall layers, in the range of 2-8 layers. In the second way of excluding background, the gradient of the magnetic field is measured instead of the field itself, where the gradient is the difference in field measurements between two different locations. These can be neighboring locations along the scalp, or they can be radially-separated locations, one close to the scalp and the other some distance away. The background is suppressed because the gradient of the background is much reduced compared with that of the brain; the background source is much further away, and the gradient falls off very rapidly with distance from the source. Advanced gradiometers can yield further improvements by taking "the gradient of the gradient", involving a double radial separation. A gradiometer system of this type is used in Fig. 2. A good, multi-layer room can eliminate the background almost completely but adds expense, while the gradiometer method, although less expensive, cannot eliminate background as well. A combination of a gradiometer MEG system in a modest two or three layer room is now usually used. The cost of the entire MEG system, including shielded room, is in the range of \$2-\$3 million (US).

MEG data and instantaneous maps are produced in the following way. First, in preparation for the recording session, all magnetic material on the subject's body is removed or demagnetized, and he or she changes into magnetic-free clothes. Fiducial locations on the head are accurately noted. Then the subject, seated or in the prone position, is placed with their head in the helmet dewar, as in Fig. 2. A bite-bar is occasionally used to minimize head motion. Next, the raw recordings are made, which consist of MEG traces on all channels, due either to evoked neural activity or to spontaneous activity, depending on the purpose of the session. Then, either online or offline, a sequence of spatial maps are

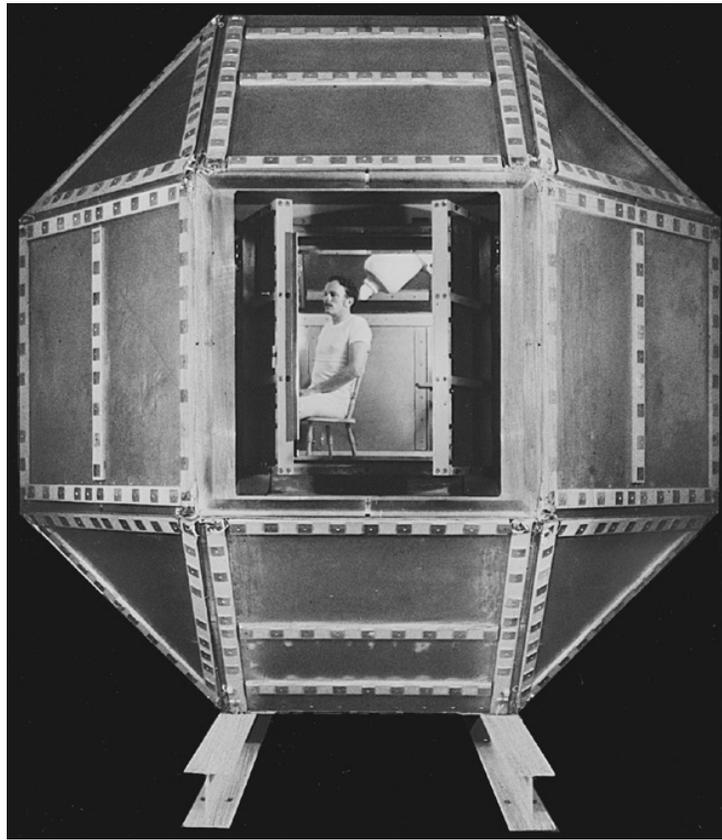


Figure 1. *The magnetically shielded room at the Massachusetts Institute of Technology, of historical interest, where the first MEG measurements with the SQUID were made (Cohen, 1972). The walls contain five layers of shielding; three are of the common high- μ shielding material called moly permalloy, and two are of pure aluminum, for eddy current shielding. This is an example of an effective room which removes almost all urban background, but is expensive to build. A subject is shown positioned for recording his MEG with an early SQUID system; the liquid helium dewar (large white cylinder) contains only a single SQUID. The subject wears clothes that contain no magnetic materials (no zippers, shoes), which could cause magnetic fluctuations. The room is roughly spherical because of the magnetic efficiency of this shape. Newer rooms are box-shaped and larger, to accommodate the new larger MEG dewars, as in Fig.2.*

extracted from the trace maps, each for a different instant in time; these are the crucial data for estimating the current sources in the brain.

Unfortunately, there are many different arrangements of current sources that can produce any given MEG map. This is because MEG (and EEG) maps have no unique solution. However, in the special case where the map arises from a single localized source, called a current dipole, then a simple inverse solution can be performed to locate the position and orientation of the dipole; maps due to two far-apart dipoles can also be treated this way, but more complex maps need more advanced treatment (also maps that appear dipolar may in fact be due to more complex sources). This treatment often consists of using extra information to restrict the source locations, usually a three-dimensional map of the subject's cortex, obtained from a separate MRI scan. Thus the solution becomes more, but not completely, unique. It is also possible to restrict the solutions yet further, biasing them toward cortical areas which have been found to be activated by the same stimuli, using hemodynamic measures such as fMRI (functional MRI) which have high spatial resolution but poor temporal accuracy (Dale et al, 2000). Finally, the sources, either dipoles or more complex continuous sources, are

displayed as an overlay on the subject's MRI map, to see where they are actually located in the brain. For example, if the purpose of the session is to investigate the activity in normal visual cortex due to a visual stimulus, one or two dipoles would be overlaid onto the visual cortex. As another simple example, if the session is a clinical search for epileptic spikes, a dipole for each type of spike might be overlaid onto the MRI of the temporal lobe. Often the EEG is recorded simultaneously with the MEG, for comparison or for complementary information; to do this, electrodes are pasted on the scalp during the subject's preparation.

MEG-EEG differences

There are three differences between MEG and EEG instantaneous spatial maps that allow the MEG to give different information than the EEG. These differences are predicted from physics theory, when the head is idealized as a system of concentric spherical shells representing scalp and skull, etc. Also, the current source generating the MEG and EEG is idealized to be a dipole, the simplest source possible; a more complex neural source can always be synthesized as a sum of dipoles. In the following discussion, the theoretical

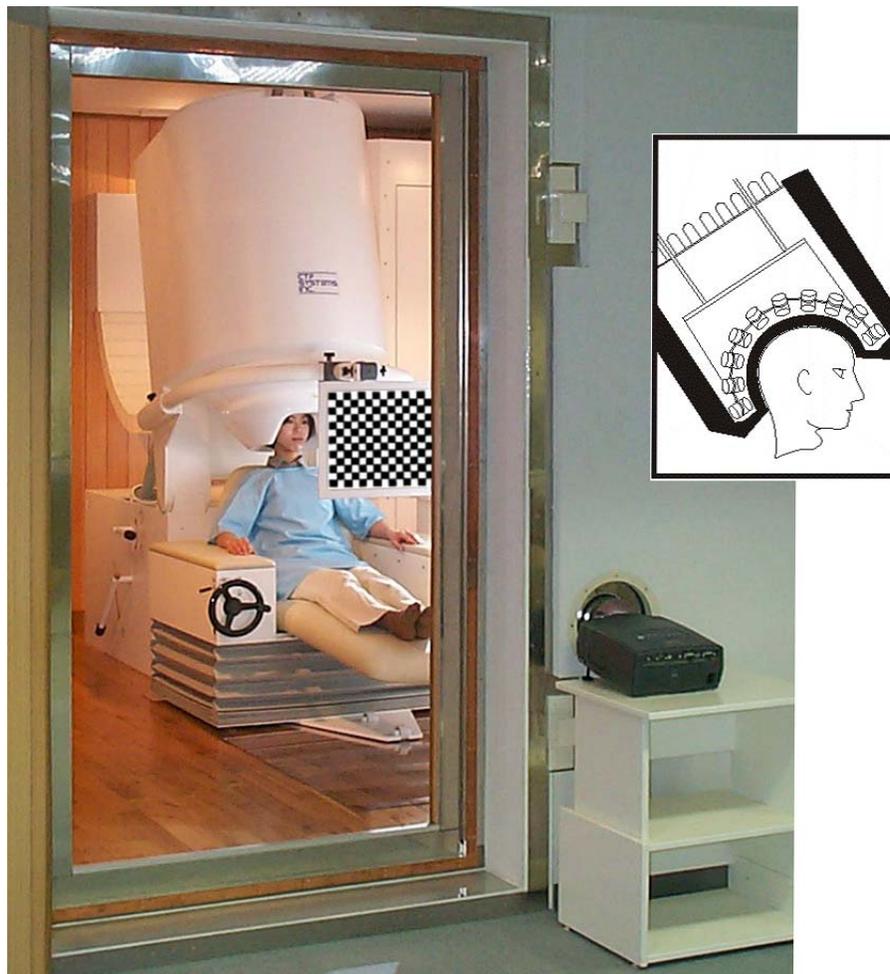


Figure 2. An example of a new MEG system. A larger shielded room contains a large helmet dewar which encloses most of the subject's head. The inset is a cutaway showing some of the 275 gradiometer coils in the dewar. In this case each coil is made of three in-line groupings, measuring "the gradient of the gradient", and is connected to a SQUID higher up, not shown here. The black areas in the dewar are the vacuum space. The checkerboard pattern in front of the subject, illuminated by the projector at the outside hole, is viewed by her in a visual evoked response study. This system, in use by Riken (Japan), is made by CTF Systems, Port Coquitlan, BC, Canada (see [www site below](http://www.ctfsystems.com)).

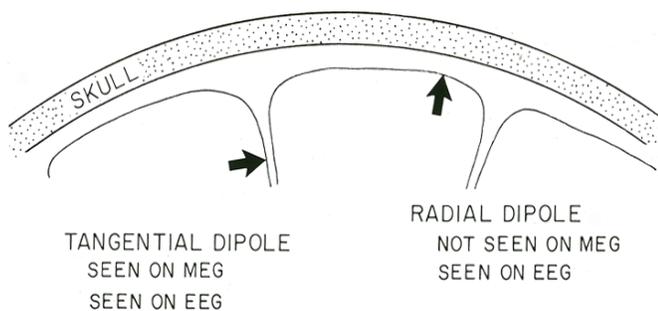


Figure 3. Two sources in the cortex; one is oriented tangentially to the skull, and the other is oriented radially. Each is represented as a current dipole, shown as a heavy arrow. Because sources in the cortex are generally oriented perpendicularly to the cortical surface, tangential sources are located in the sulci while radial sources are in the gyri (an exception is where the cortex turns away from the skull, so that gyri and sulci are reversed). Although the EEG sees both sources, it is dominated by the radial sources in the gyri.

MEG and EEG maps are considered for the task of determining the orientation of the dipole with respect to the skull, and the task of spatially locating the dipole source

The first difference is due only to the orientation of the dipole. Theory shows that *there is zero magnetic field over the scalp, hence no MEG signal whatever, for a dipole oriented radially to the skull*. This is due to the symmetry and cancellations which take place in perfectly spherical conductors. There is only an MEG signal for a dipole oriented tangentially, where there are no such cancellations. Because electrical sources in the cortex which are tangential to the skull are usually located in the sulci and radial ones are usually on the gyri, as shown in Fig. 3, it follows that the MEG is usually due only to the sources in the sulci; the EEG is due to both (an exception to this rule is noted in the caption). Therefore, one consequence of this first difference is that the MEG should see those tangential sources which, on the EEG, may be dominated or masked by strong radial

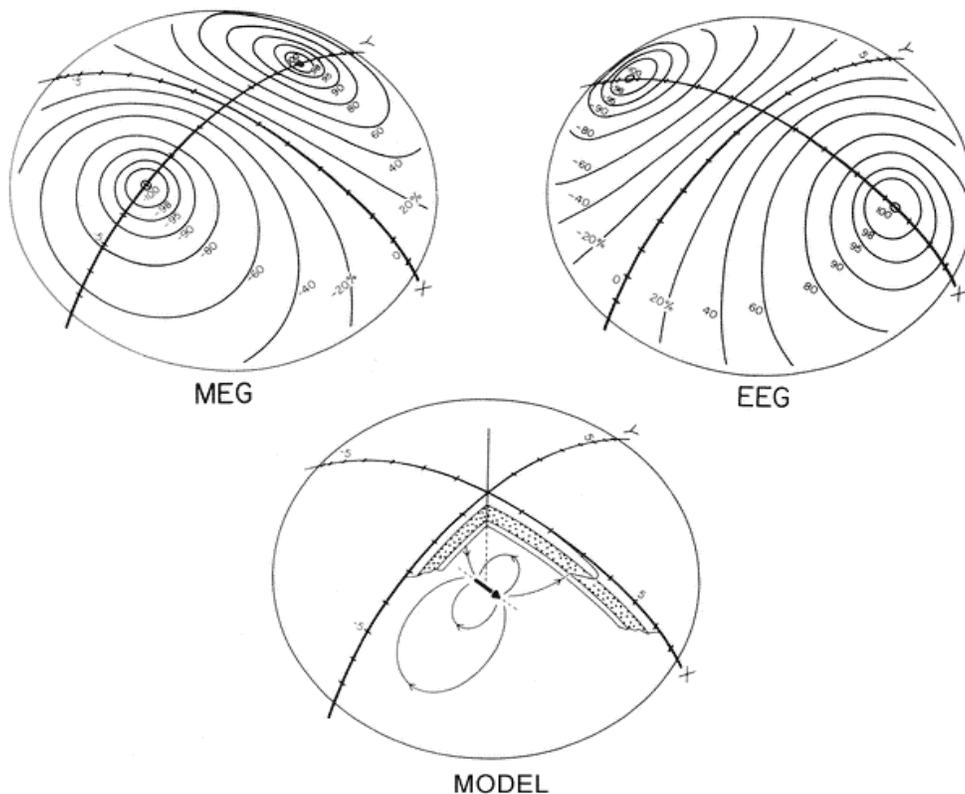


Figure 4. Computed theoretical MEG and EEG maps, shown as contour maps, due to a tangential dipole source in a spherical model of the head (Cohen and Cuffin, 1983). They are shown on a spherical “cap”, which has x and y coordinates with ticks at each cm; a model with concentric spherical shells representing brain, CSF, skull and scalp is used for the computation, and is shown with the same cap. The EEG map is of the surface potential with contour lines every 20% while the MEG map is of the component of magnetic field vector normal to the scalp, also with 20% lines. The neural source generating the MEG and EEG is approximated as a tangential dipole (heavy arrow) at a depth of 2.7 cm. It is seen that the MEG pattern is oriented at 90° to that of the EEG, and is somewhat tighter (by about 30%).

sources. Indeed, radial sources tend to dominate the EEG because, on the gyri they are closer to the electrodes on the scalp. Another consequence of this difference is that the MEG should not see sources near the center of the head because a dipole at the center of a sphere is always a radial source. Thus, the MEG map is due to a sub-group of the sources seen on the EEG.

The second and third MEG-EEG map differences involve actual map patterns, due to a tangential dipole. These are illustrated in Fig. 4, where the MEG contour-map pattern is seen to be oriented perpendicularly to the EEG pattern, and is also seen to be somewhat smaller than the EEG pattern. The perpendicular difference is due to a basic orthogonality between magnetic and electrical fields. Its consequence is that the MEG localizes a source better in the y direction, while the EEG localizes better in the x direction. The reduced size of the tighter MEG pattern compared with the EEG pattern is largely due to the smearing, by the high-resistivity skull, of the surface current measured by the EEG; the MEG mostly sees currents at the sources, hence is not much affected by the surface smearing. The consequence of this size difference is that the MEG should localize a tangential dipole somewhat better in its best direction (y), in comparison to the EEG in its best direction (x), if all other factors were equal, such as

modeling errors and measurement noise. Although there had been a belief that the MEG can localize far better than can the EEG, say to within 2 mm because of reduced modeling errors, the one reported experiment with implanted dipoles in the actual living human head has shown only a minor advantage, yielding 8 mm accuracy for the MEG vs 10mm for the EEG (Cohen et al, 1990). Also, advanced theoretical modeling has shown no great MEG localization advantage (Mosher, 1993; Liu et al, 2002). A full discussion of the MEG-EEG localization issue is beyond the scope of this article. The MEG has, however, contributed to EEG source localization in an unexpected way. Because the MEG was developed in physics labs, advanced techniques were used for inverse solutions on the maps to find the sources. But EEG maps had usually been interpreted by visual inspection, occasionally with large errors. However, the EEG manufacturers began duplicating the MEG inverse solutions, and now include such software in EEG systems, so that EEG localization is now more accurate.

In summary of the three above differences: *the MEG sees less than the EEG, but sees it somewhat more clearly.*

There are other MEG-EEG differences which are of a more practical nature. One difference, favorable to the EEG, is the nuisance of embedded magnetic material in the subject,

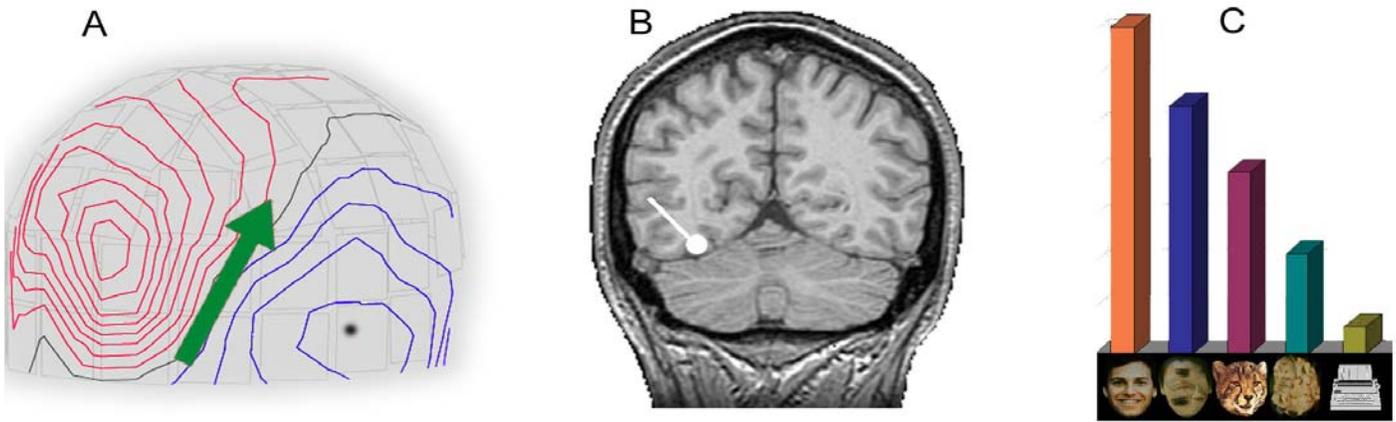


Figure 5. *Use of MEG in face-recognition research. (A) MEG contour map (50 fT step/line), drawn on the head of the subject and sampled at 165 msec after a photo has been viewed. The head is viewed from the right-rear; the dark spot marks the right ear. The pattern is seen to be roughly dipolar, hence a single dipole was assumed for the source; an inverse solution located the dipole, shown as the green arrow, where the depth is not seen here. (B) Same dipole source superimposed on the subject's MRI, seen from the front. The dipole is here a white dot, for accurate location, shown in the right fusiform gyrus. The attached rod gives the dipole direction and amplitude. (C) The dipole amplitudes after viewing any of five face photographs and controls, averaged over 10 subjects. The normal human face evokes the largest response. MEG can thus be used to estimate the location, timing and strength of a neural process associated with face encoding (Halgren et al 2000).*

such as magnetic dental work, which creates large interfering magnetic signals; but this material can often be demagnetized with a hand-held magnetic eraser. However, there are differences which are favorable to the MEG. Perhaps the most obvious of these is that the MEG requires no pasting of electrodes on the head, as does the EEG. Another, more profound difference, concerns dc. The EEG cannot record dc signals from underlying neural tissue, because of large dc skin potentials, which necessitate the blocking of dc into the EEG system so that it only responds to ac. But the MEG does not usually see dc from the skin, perhaps due to the high skin resistivity and radial dc sources, and it can therefore be used as a true dc instrument, to see underlying dc neural sources. These could be, for example, from migraine headache, or injury currents due to stroke. However, the MEG measurements of dc are currently in their early phases.

Present status and future prospects

Presently, in 2003, there are about 90 whole-head MEG systems around the world, in use or on order, some with more than 300 SQUIDS per helmet. Many of these systems are grouped in Germany, Japan, U.S., Finland, and Canada. Thus, an increasing number of MEG maps are being recorded, often in combination with the EEG, due both to spontaneous and to event-related signals. The overall purpose is to see if the selectivity of the MEG can clarify the sources of the signals. The efforts are divided into two broad areas: research into the workings of the normal brain, and the search for clinical applications of the MEG.

In research into the normal brain, MEGs are being studied of responses evoked by stimulation of each of the five senses. To date the MEG has produced a variety of evidence

supporting locations of sources in the primary sensory cortices. One early example is the well-studied 20-msec somatosensory signal from the human brain in response to peripheral nerve (wrist) stimulation; from the EEG alone, the source of this signal had been ambiguous, with a choice between two radial or one tangential source. But the combination of MEG and EEG maps showed the source to be mostly a tangential dipole (Wood et al, 1985). In another example with somatosensory cortex, MEG and EEG were combined to study the finger representation in the cortex; it was found that the MEG and EEG combined gave more localization accuracy than each separately (Baumgartner et al, 1991). Some of the studies used MEG without EEG; one such study reported increased strength of cortical sources of left fingers of string players (Elbert et al, 1995); without EEG maps, however, there can be doubt that the useful information obtained was indeed due to MEG selectivity.

Overall, the MEG has demonstrated internal organization in some of the primary areas of the human brain, organization that was previously seen only in the animal brain, and has also shown the separation of activity between primary and secondary areas, for example, in somatosensory cortex and in auditory cortex.

MEGs are being studied of the later components as well. After processing in these initial sensory areas of the brain, there are further processors that decode certain classes of stimuli, such as faces. The MEG has been able to localize the face area to the same location identified with fMRI and intracranial EEG, and has been used to characterize its cognitive responses to a range of face-like stimuli (Fig. 5). The situation becomes more complicated when moving further downstream to neural activity underlying higher cognitive functions, such as understanding sentences. The fact

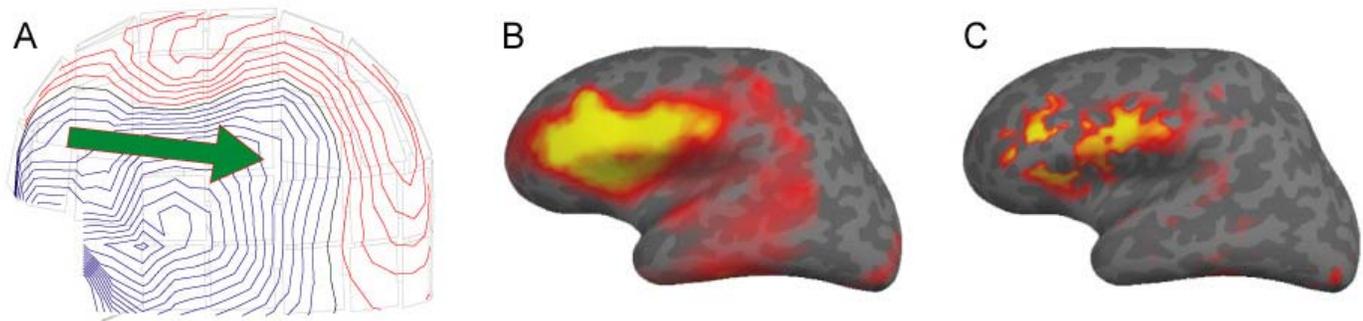


Figure 6. Use of MEG with multi-modal integration in reading research. Subjects read words and made a semantic judgment (pressing a key if the word referred to an object or animal greater than one foot in length). MEG maps were produced by subtracting the signals evoked by novel words from those evoked by words which had been read previously in the same task. (A) MEG contour map, viewed from the subject's left, at 540 msec post stimulus-onset. Again, the pattern is roughly dipolar, and the green arrow is again the computed source dipole. It appears "off-center" in this case because of the angle of view. (B) A determination of the sources, from the same contour map, using a non-dipolar advanced inverse method allowing a continuous distribution, but sources are now constrained to be on the cortical surface (Dale et al, 2000). The "inflated" left cortical surface is shown in the same view as in (A). (C) Same data as (B), except the source has been further biased by the fMRI location of activation in the same subject and task. Note the increased spatial detail revealed by the integration of the fMRI information in the same task. The MEG data thus reflect the repetition priming effect on semantic processing.

that neural activity can spread to distant cortical areas in about 10msec suggests that multiple widespread cortical areas may be involved in the response to words, which peaks at about 400msec. Modeling in such situations with a distributed source instead of a dipole (Fig. 6) localizes MEG activity to the same locations that have been found with hemodynamic measures and with direct intracranial EEG recordings in epileptic patients (Dale et al, 2000). Current data suggest that, in situations such as these, efforts to localize distributed generators appear to have been more successful with MEG than with EEG. If true, this may be due to the fact, as mentioned, that the MEG sees fewer sources with a somewhat tighter fields than EEG, and thus is better able to disentangle multiple distributed sources. However, it is also possible that with better forward models and inverse methods, EEG will be equally successful in localizing complex distributed generators. In any case, modeling studies and some experiments clearly suggest that the best localization will only be obtained by combining MEG and EEG.

Concerning clinical application of the MEG, efforts are being made to evaluate MEG usefulness in various areas, including pre-surgical functional mapping, head injury, and epileptic spike localization. The purpose of the pre-surgical mapping is to locate the regions of the sensorimotor strip using evoked response, in order to minimize neurological deficit due to surgery. The MEG is found to localize well in this task, as does fMRI. In some cases, the hemodynamic response near a tumor or arteriovenous malformation may be abnormal, and MEG may thus be preferable. In head injury, the MEG appears to show focal slow-wave abnormalities more reliably than does the EEG, hence shows more promise of providing localizing information. In the measurement of epileptic spikes, the MEG, when used with the EEG, is able to clarify or localize some epileptic foci better than can the EEG alone. The MEG has also shown spikes which appear to be

masked on the EEG by other spontaneous brain activity, seen less on the MEG. Definitive localization of seizure foci, adequate to guide their surgical removal, often requires the placement of intracerebral electrodes. The hope is that the non-invasive combination of MEG and EEG may allow such electrodes to be more successfully targeted, or in some cases, to be avoided altogether. MEG also appears useful when a skull defect from a prior operation severely distorts the propagation of the EEG to the scalp. MEG research studies into neuropsychiatric disorders such as schizophrenia, autism and pain appear to show promise because of its greater specificity compared with EEG, and can give insight into the neural bases of severe dysfunction in the absence of any structural abnormality. Expansion of clinical MEG use from regional referral centers to community hospitals will require further evaluation.

The future possibilities of the MEG depend on how well its advantages will balance against its practical problems and cost. The practical problems include not only the reduction of magnetic background, but also the effort in maintaining a cryogenic system that needs refilling with liquid helium every 7 days or so. A cost reduction would make the MEG more attractive for clinical diagnosis. In any case, the MEG will be used well into the future, both because the large MEG systems now in use or coming on-line will generate many years of investigations, and because there is the general, long-term need for non-invasive measurements of the brain.

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Some WWW sites involving the MEG

- www.geocities.com/Tokyo/1158/meg.
- www.berlin.ptb.de/8/82/821/
- jenameg10.meg.uni-jena.de/
- <http://www.physics.dal.ca/~medbiophys/>
- pluto.neurologie.uni-duesseldorf.de/biomag/
- bct.tn.utwente.nl/
- boojun.hut.fi/research/brain/neuromag/
- www.biomag.helsinki.fi
- psyserver.pc.rhbnc.ac.uk/vision/review.html
- www.nmr.mgh.harvard.edu/meg/
- yan.open.ac.uk/%7edbamidi/biomagnetism.html
- www.biophysics.lanl.gov/
- www.ctf.com/
- www.neuromag.com/
- www.4dneuroimaging.com/