Biomagnetic Approaches to Studying the Brain
Recent Advances in Three Techniques for Understanding Human Memory and Cognition

Biomedical approaches to understanding the functional organization of the human brain include 1) transcranial magnetic stimulation (TMS), 2) magnetoencephalography (MEG) by superconducting quantum interference devices (SQUIDs), and 3) the imaging of electrical currents and impedance distributions of the head based on new principles of magnetic resonance imaging (MRI) techniques. These techniques are noninvasive and very useful for studying higher brain functions of humans such as memory and cognition. This article discusses these techniques, including the histories, principles, advantages, and disadvantages of each method, by using examples from studies recently conducted primarily in the author's laboratory.

Transcranial Magnetic Stimulation
Transcranial magnetic stimulation has become an important tool for studying the functional organization of the human brain [1]. Most of the studies using TMS are related to mapping of the cerebral cortex. Mapping studies are carried out by a method of localized and vectorial magnetic stimulation using a figure-eight coil [2]. The basic principle is to concentrate induced eddy currents locally near a target by using a pair of opposing pulsed magnetic fields produced by a figure-eight coil. This method facilitates stimulation of the motor cortex of the human brain within a 5 mm resolution [3, 4]. Vectorial stimulation can be attained because the concentrated eddy currents at the target under the intersection of the figure-eight coil flow parallel to the tangent of the two circular coils. Based upon this principle, functional maps of the human motor cortex related to the hand, arm, and foot areas were obtained. The functional maps showed that an optimal direction of stimulating induced currents for neuronal excitation exists in each functional area of the cortex [4]. These vectorial characteristics in TMS reflect, in part, anatomical and functional organization of the neurons and neuronal fibers of the brain [5].

The introduction of nerve-activation models has widened our understanding of the mechanisms of nerve excitation elicited by magnetic stimulation [6, 13]. The theoretical nerve activation models have shown that for neuronal excitation, a negative peak of the spatial gradient of induced electric fields, the activating function, contributes to the depolarization of the membrane.

The site of neuronal excitation corresponds to the site of the maximal value of the activating function. Therefore, the relationship between the coil position and the target depends on several factors such as spatial distribution of the activating function and anatomical structures of neuronal fibers [14, 15]. The spatial distribution of the activating function is determined by the geometry of the volume and electrical inhomogeneities [16, 17]. However, specific neurons cannot be selected because the region of excitation in magnetic stimulation cannot be selectively restricted.

The relationship between the direct (D) wave and the indirect (I) wave in motor evoked potential (MEP) responses to TMS of the motor cortex is still a matter of debate among researchers [18-22]. TMS of the motor cortex generates multiple descending volleys, which consist of the direct activation of the pyramidal tract neuron (D-wave) and the trans-synaptically indirect activation of a pyramidal neuron (I-wave). However, detailed mechanisms of the D-wave and I-wave following TMS have not yet been clarified.

Nevertheless, TMS has many advantages. For example, it is noninvasive and
a concentrated manner. The maximum current density is attained beneath the coil and, in principle, the current density is zero at the center. When a figure-eight coil is used, flow patterns of induced currents create two vortices that merge at the point beneath the intersection of the figure-eight. Computer simulation shows that the current density at the merge point is three times greater than that in the surrounding areas. Hence, localized stimulation is attained. For TMS of the human brain, transient magnetic fields in the order of 1 T and duration of 0.1-0.2 msec are generally used. These transient magnetic fields contribute to the depolarization of nerve cells in the brain.

In order to investigate motor-nerve functions, MEPs were recorded from the peripheral muscles that responded to TMS of the target cortex area that innervates the corresponding muscles. The results of magnetic stimulation of the human motor-cortex area are shown in Fig. 2. Surface electromyograph (EMG) signals were recorded at the left abductor pollicis brevis (APB) muscle. A figure-eight coil was positioned at point “A,” from which the greatest response was recorded at the APB muscle. The direction of the induced current was oriented postero-anteriorly. The stimulus intensity was slightly above the threshold. When the coil was moved 5 mm from point “A,” little or no response was observed. In other words, it was possible to selectively stimulate the motor cortex of the human brain within 5 mm resolution.

In addition to the coil position, the direction of induced eddy currents is important for TMS. By rotating the figure-eight coil at the intersection, as shown in Fig. 3, point “A” was stimulated in eight directions. Peak-to-peak EMG responses were measured in all directions. In this case, the greatest response was observed when the induced current direction flowed postero-anteriorly. This suggests that peripheral muscle response to magnetic stimulation of the cortex is affected by both the stimulation point and the direction of induced eddy currents.

A functional map of the motor cortex relating to the hand and foot areas was obtained, as shown in Fig. 4. Muscle responses from the APB, the brachioradial, and the abductor digiti minimi (ADM) muscles of the hand were recorded, as were EMGs from the abductor hallucis and the ADM muscles of the foot. The area corresponding to each muscle was
selectively stimulated, and the optimal eddy current was observed. The arrows indicate the optimal eddy current directions for eliciting the MEPs in each muscle of the subject.

These vectorial maps may reflect functional and anatomical information of neural structures in the brain. The neuronal fibers are easily excited when they are stimulated by the eddy currents that flow parallel to them, in contrast to the case where the currents flow perpendicular. Nerve-excitation models and computer simulations have shown these vectorial characteristics, even though the excitation mechanisms of the brain require further research.

**Paired Transcranial Magnetic Stimulation**

Paired TMS is useful for noninvasive investigation of dynamic connections of neurons in the cortex. This study involved the investigation of cortical excitatory and inhibitory systems, using the technique of paired TMS, as shown schematically in Fig. 5. Stimuli were applied with a circular coil and a figure-eight coil. The conditioning stimulus was delivered by the circular coil with the intensity set at 88% of the motor threshold. The test stimulus was delivered via a figure-eight coil with the intensity set at 130% to 140% of the motor threshold. Motor-evoked responses to the test stimulus were recorded at the contracted left-first dorsal interosseous muscle. The contraction level was about 10% of the maximum, as monitored by audio-visual feedback. MEPs for the test stimulus and the control response were recorded first. A conditioning stimulus that had various interstimulus intervals (ISIs 1, 2, 3, 4, 5, 6, 7, 10, and 15 msec) was added prior to the test stimulus.

The control responses to the test stimulus that were delivered by a figure-eight coil are shown in Fig. 6(a). Polyphasic MEPs with two negative and two positive peaks were recorded, labeled as N1, P1, N2, and P2. The N1 and N2 amplitudes were calculated as well. When the weak conditioning stimulus was added by a round coil, the MEPs changed depending on the ISI [Fig. 6(b)]. When the ISI was 1 msec, the N2 components were suppressed. Increasing the ISIs caused an increase in the N2 components. However, N1 components were stable at all ISIs.

The relationship between the interstimulus intervals and N1 and N2 amplitudes for all 10 subjects is shown in Fig. 7. The amplitudes are presented as the percentage of the control responses. The N2 components were significantly suppressed at ISIs from 1 to 5 msec, and facilitated at ISIs of 10 and 15 msec. However, the N1 components were not significantly suppressed or facilitated at any ISI.

These experimental results suggest that TMS initiates the excitation of both cortical interneurons and pyramidal tract neurons. Once the pyramidal tract neurons generate a D-wave, the excitation is unaffected by a conditioning stimulus, which

4. Functional distribution of the human cortex related to the hand and foot areas. The arrows show current directions for neural excitation. The distance between grid points is 5 mm.

5. Schematic illustration of paired transcranial magnetic stimulation.
encephalopathy, damage to the spinal cord, etc.

Modulation of Neuronal Plasticity
If neuronal plasticity can be modulated by repetitive magnetic stimulation, new horizons can be opened for the treatment or re habilitation of motor and sensory dysfunctions in the central nervous system, as well as for the treatment of mental illnesses; e.g., depression and schizophrenia. It is important to understand the effects of transient and long-term modulation of electrical excitability or inhibition of neurons by repetitive stimulation.

Transcranial Magnetic Stimulation and ECT
Electroconvulsive therapy (ECT) is argued to be the most effective treatment for depression as well as many other types of mental illnesses; e.g., mania, schizophre nia, delirium, etc. However, rapid-rate TMS is fast becoming an alternative approach for the treatment of depression, since selective stimulation of brain sites involved in depression can be achieved with fewer side effects [23].

Transcallosal Stimulation
The neuronal information that interacts between the two hemispheres, across the corpus callosum, is not well understood. The transcallosal magnetic stimulation will broaden knowledge of the dynamic neuronal mechanisms of the brain. Also, transcallosal magnetic stimulation may be medically applied for the diagnosis and treatment of central-nervous-system diseases [28-31]. Stimulation of multiple areas in the ipsilateral and contralateral cerebral cortices are also important for dynamic brain research.

Risk Assessment
Risk and safety aspects of rTMS with pulse trains of high frequencies need to be investigated [26, 27]. Repetitive electrical stimulation at high frequencies over focal brain regions, such as stimulation of the hippocampus and amygdala, causes epileptic seizures under certain conditions. This phenomenon is called the kindling effect. It is necessary to identify which conditions cause the kindling and other undesirable effects, before applying rTMS to human subjects.

Magnetoencephalography
Ionic currents associated with brain electrical activity produce weak magnetic fields around the head as well as the electroencephalogram (EEG) at the scalp. These magnetic fields, called magnetoencephalograms, were first measured by Cohen [32, 33]. MEG has proven to be a useful noninvasive method for the localization of circumscribed regions of brain activity. During the past decade, many studies of functional organization of the human brain have been made through a technique of MEG topographic mapping. Most of these investigations have an inhibitory effect on excitability of pyramidal tract neurons.

Medical Applications and Risk Assessment
Potential applications and problems associated with magnetic stimulation are as follows:

Estimation of Brain Function and Structure
Since it is possible to investigate the functions and structure of the brain by applying localized and vectorial magnetic stimulation to targets in the cerebral cortex, magnetic stimulation is expected to become an increasingly important method in the field of brain research.

Assessment of Motor Functioning in Neurological Disease
Magnetic stimulation has many potential medical applications. For example, it can be applied to the assessment of cerebral infarct, multiple sclerosis, amyotrophic lateral sclerosis, demyelinating

7. Relationship between the interstimulus intervals and N1 and N2 amplitudes in 10 subjects (8 males, 2 females).

8. Territories of MEG, fMRI, and PET for their temporal and spatial resolutions.
were concerned with the estimation of source localization from measured data obtained from the surface of the head [34-45]. Compared with EEG, MEG is primarily sensitive to intracellular currents that flow parallel to the scalp surface. These current sources represent pyramidal cell activation in the fissural cortex and can be localized within 1-2 mm accuracy for transient brain events.

In recent years, several noninvasive techniques for imaging brain function, such as MEG, fMRI (functional magnetic resonance imaging) and PET (positron emission tomography) have advanced significantly. From the time of the first successful application of fMRI [46], the relationships between MEG and fMRI have been studied to clarify the origin of brain electrical activity [47-51]. Use of fMRI provides high spatial resolution (less than a few mm), but poor temporal resolution, since this technique is susceptible to local changes in cerebral blood flow. In contrast, MEG can measure electrical activity of populations of neurons, and it provides good temporal resolution. Figure 8 shows territories of MEG, fMRI, and PET for their temporal and spatial resolutions. The current study will focus on the development of a new imaging technique that combines information from the two methods to produce a better temporal and spatial description of neural activity.

Source Localization of Somatosensory-Evoked Response Using MEG and Functional MRI

Activation of the primary somatosensory cortex was investigated using MEG and fMRI [52]. A right thumb and a ring finger were stimulated by electrical current pulses. Both MEG and fMRI identified expected anatomical regions of the primary somatosensory cortex. When the thumb and ring finger were stimulated simultaneously, it was possible with fMRI to discriminate between the area of the thumb and the ring finger in the primary somatosensory cortex. Using MEG, a single-dipole current model might fit with a sufficiently large correlation coefficient, because the two sources are closely located (within 10 mm). It is difficult to discriminate between two closely located dipoles if no initial information is given.

Figure 9 shows the waveforms of somatosensory-evoked fields in the electrical stimulation of the thumb. Figure 10 shows the superposition of all 37 curves.

9. Somatosensory-evoked magnetic fields following the right thumb stimulation. The sensor array was centered near P3 based on the international 10-20 system.

10. The superposition of all 37 curves of sensory-evoked magnetic fields in the stimulation of the thumb and topographies of magnetic field distributions for N20m, P30m, N40m and P55m. The magnetic fields penetrating and exiting the skull are represented by solid and dashed lines, respectively. The bold lines indicate zero lines.
Two short-latency magnetic components and two middle-latency components were recorded. These components were referred to as N20m, P30m, N40m, and P55m, respectively. Figure 11(a) shows the source locations that were superimposed on the MRI scan. Dipoles were obtained in the contralateral primary somatosensory cortex, with the goodness of fit better than 99%. Although the exact positions of the four dipoles for each component differed, they were all located within a 15 by 15 mm area. The fMRI image was also obtained, as shown in Fig. 11(b). The activated area was observed in the contralateral primary somatosensory cortex, distributed along the central sulcus in the left hemisphere. The distances between the nearest point of distributed fMRI activation and the MEG location of each component were 5.3 mm, 4.1 mm, 5.5 mm, and 6.0 mm, respectively. These differences mainly appeared in the z-direction. The differences on the x-y plane are only a few millimeters. Distributed fMRI areas are explained by the plots of the dipoles, which are estimated in each component of the magnetoencephalogram. These results show that fMRI provides temporal information over relatively long periods of activation, while the magnetoencephalogram provides accurate temporal information.

Figure 12 shows the location of estimated dipoles of N20m and P30m in the stimulation of the thumb, the ring finger, and both the thumb and the ring finger. The dipole in the ring-finger stimulation exists 10 mm superior to the location of the thumb’s area along the central sulcus. Dipole locations of N20m and P30m in the stimulation of both fingers are estimated to be deeper than the location of the thumb’s dipole. Because spread areas, including regions of the thumb and the ring finger in the somatosensory cortex, are active at the same time, it is impossible to fit the single-dipole model.

Figure 13 shows the fMRI in the stimulation of the thumb, the ring finger, and both the thumb and the ring finger. When the thumb or the ring finger was stimulated, the activated areas of fMRI were separately observed in each expected anatomical region of the sensory cortex. These areas are in the same sulcus that is identified by MEG. In the stimulation of both fingers, activated areas are clearly separated as to the thumb and the ring finger.
TMS is noninvasive and less painful than direct electric stimulation through surface electrodes placed on the scalp.

These results indicate that fMRI is able to resolve somatosensory cortex areas with a resolution better than 10 mm.

MEG Activities Associated with Short-Term Memory Tasks
Studies on data processing in the brain associated with short-term memory in human subjects are interesting and important themes in brain science. MEG studies on short-term memory have been reported that are mostly concerned with auditory-evoked MEG [53, 56]. In our study, visually evoked magnetoencephalograms associated with a delayed-match paradigm were measured to obtain functional information related with short-term memory processes [57]. The delayed-match paradigm consisted of four-color stimuli: a pair of circles with four differently colored regions. The magnetoencephalograms were measured by a 122-channel whole-head-type (SQUID) system. A DC-like slow wave was observed in the period between latencies of 900 msec and 1,500 msec during the short-term memory task. The source localizations of the DC-like slow wave were estimated as being localized either in the occipital or postero-temporal region.

Figure 14 shows the schematic illustration of a stimulus sequence. In the delayed-match experiment, four-color stimuli—a pair of circles with different colors in each quadrant (blue, red, green, and orange) generated by an LCD projector—were presented on a screen in a shielded room. The visual angle of the stimulus was 6.7°. The interstimulus interval between the first stimulus (SAMPLE: duration 50 msec) and the second stimulus (TEST: duration 50 msec) was constant at 3.0 sec. The inter-trial interval varied randomly between 1800 and 2200 msec. In the memory task, subjects were requested to move the index finger quickly when the TEST was identical to the SAMPLE, and the middle finger when it was not identical. In the control task, the subjects were instructed to ignore the SAMPLE, and to move the index or middle finger alternately when the TEST was presented.

Figure 15 shows the results of averaged magnetic-field waveforms. The...
solid lines denote the magnetic fields for the memory tasks and the dashed lines denote the magnetic fields for the control task. The magnetic data were sampled at 497 Hz, after bandpass filtering between 0.03 Hz and 100 Hz, and digitally lowpass filtered at 40 Hz after averaging more than 100 times. This type of DC-like slow wave was also observed in different subjects.

Figure 16 shows the estimated source locations of three subjects for the memory task, from 900 msec to 1500 msec after the onset of visual stimuli. The source locations are overlaid on each subject’s MR images.

MEG has proven to be a useful noninvasive method for the localization of circumscribed regions of brain activity.

MEG Activities Associated with Mental-Rotation Tasks

A mental-rotation process requires rotation and matching of a pair of mental images [58, 59]. Mental-rotation processes were shown to activate the parietal region by PET and fMRI methods [60, 61]. Although these methods simply show the temporal integration of brain activation during entire processes, they actually require the cooperative interaction of multiple areas in the brain. Dynamic properties of the electrical-current distribution in the human brain that correspond to the early mental rotation processes were investigated. A current-reconstruction algorithm was used that was based on the weighted minimum-norm estimation (WMNE) with weighting factors [62] calculated from the results of simplified multiple signal classification (MUSIC) scan [63]. In this method, along with the depth-normalization technique, weighting factors of the WMNE are determined by the cost-value distribution previously calculated by the MUSIC scan, which contained the temporal information of the measured data [64]. This method is able to handle the noisy data without introducing large distortion into the source estimation. It is also able to suppress the large estimation error related to the temporal correlation of the multiple source activation. In the calculation of the cost value, a multiple-source model method [65] and a generalized Wiener estimation model [66] are introduced. This calculation reflects the probability of source localization. Source-current distributions in the mental-rotation and the control tasks were estimated from the MEG signals for five
subjects, in the latency range between 100 and 250 msec after the stimulus onset. Activation of the right lateral posterior temporal region at about 200 msec was observed in three out of the five subjects in the mental-rotation task, while only the primary visual cortex was activated continuously up to about 200 msec in the control task.

Figure 17 shows a schematic diagram of the mental-rotation task performed in this study. A pair of simple line drawings was shown for 1000 msec in the left and right positions. The drawings were separated by a visual angle of 1.5° from a fixation point on the screen. The subjects were required to discriminate the rotation-symmetric pair (True) from the mirror-reversed pair (False), and to react by moving the right index (True) or middle (False) finger. MEG signals were recorded from 200 msec before the visual stimulus onset to 2500 msec after the onset.

Figure 18 shows typical waveforms of the MEG signals measured during the mental-rotation task and the control task of a subject. The difference in the intensity of the MEG signals between two conditions was observed in the right lateral posterior area in this subject.

Source-current distributions in the mental-rotation task and the control task were estimated in the latency range between 100 and 250 msec after the visual stimulus onset of 2 msec intervals. In this study, time length, which was required for the MUSIC prescanning, was set to 15 msec for each estimation.

Figure 19 shows that estimated sources for the same subject during: (a) the mental-rotation task and (b) the control task, superimposed on an MR image of the subject’s head. The size of the red dots in each MRI slice indicates the estimated source-distribution density. The right lateral posterior region was activated about 200 msec after the onset of the visual stimuli during the mental-rotation task, whereas the primary visual cortex was continuously activated about 200 msec after the onset of the visual stimuli during the control task.

**Impedance MRI**

Since electrical properties are important characteristics of living organisms, techniques for impedance tomography to visualize impedance distribution have been developed with great interest. The previously proposed techniques require that electrodes be attached to the surface of the human body [69, 70].

When conductive tissues are subjected to an excitation RF field in MRI, eddy currents are induced. In this article, a new method for impedance tomography is introduced, based on MRI techniques. The basic idea is to use the shielding effects of induced eddy currents on spin precession. Two methods are proposed.

![Schematic diagram of the mental-rotation task procedure.](image)

18. Typical waveforms of the measured MEG signals during the mental-rotation task and the control task.
19. Estimated sources for subject "KY." during (a) the mental-rotation task and (b) the control task.

20. Series of image projections of water and saline-solution phantom obtained with excitation power increased stepwise from left to right.

21. Series of image projections of a mouse head obtained with the excitation power increased stepwise from left to right.

22. Image of a mouse head obtained with an excitation flip angle of 180°.

One proposed method to visualize the conductivity distribution of living organisms is to use very large flip angles. The method is used to obtain conductivity-enhanced MR images at the given Larmor frequency.

The other proposed method is to apply an additional time-varying magnetic field parallel to the main static field, $B_0$. This added magnetic field is produced by a third coil, the "$B_1$" coil. This method is used to obtain conductivity-enhanced MR images at an arbitrary frequency. Experiments have been carried out to verify these concepts using a 7.05 T, 18.3 cm system.

When conductive tissue is exposed to RF magnetic fields, eddy currents are induced, which results in the reduction of the net RF fields into the tissue. By the shielding effects, the flip angles, i.e., mutation angles of the macroscopic magnetization of excited spins from the axis of the main static field, $B_0$, are reduced in varied degrees, depending on the electrical characteristics of the tissue.

When a precise 180°, 360°, or 540° excitation pulse is applied to conductive tissue, the tissue does not yield a signal, due to absence of the transverse component of magnetization. Meanwhile, resistive tissue yields a signal, because it is less electrically shielded than conductive tissue and simultaneously undergoes a different flip angle. Also, resistive tissue maintains a transverse component, with magnitude determined by the sine-wave function of the flip angle. The difference in signal, therefore, reflects the conductivity of tissue. By applying very large flip angles, conductivity-enhanced MR images can be obtained, but only at the given Larmor frequency, and in the direction perpendicular to the applied RF field.

When the perturbing, or $B_1$, field is applied, slice positioning of the image is affected, and the slice selection fluctuates. Spatial information in the read-out and phase-encoded directions is also affected. Conducting tissue is less affected by the $B_1$ field because of the shielding effects. Since the frequency of the $B_1$ field is independent of the given Larmor frequency, conductivity-enhanced images can be obtained at any frequency, except in the direction perpendicular to the $B_1$ field.

Experiments were first performed on distilled-water and saline-solution phantoms. Both phantoms were columnar, 2 cm in diameter, and 4 cm long. A conventional spin echo (SE) sequence was used to obtain MR images. By varying the RF excitation power level stepwise, image projections in the read-out direction were obtained with the 7.05 T, 18.3 cm machine. The proton Larmor frequency of magnetic resonance at 7.05 T was 300 MHz. To eliminate the longitudinal T1 relaxation effects, the repetition time $Tr$ was set as $Tr = 10$ sec. A series of image projections of the head of a four-week-old mouse was obtained. The SE images were obtained by applying excitation pulses which were 160°, 180°, and 200° selective to the cerebrospinal fluid (CSF) of the head.
Techniques for impedance tomography to visualize impedance distribution have been developed with great interest.

A four-turn solenoidal coil of 6 cm diameter was fabricated as the B, coil to produce a low-frequency 1 kHz sinusoidal 10 mT magnetic field. The amplitude of the field was comparable to the amplitudes of the reading-out gradient field and the maximum phase-encoding field. An eight-week-old rat was used for the SE imaging.

Figure 20 shows a series of image projections obtained with stepwise-increasing excitation power (left to right). The larger projections, to the right of each image, are from the water phantom, and to the left are the smaller projections from the saline-solution phantom. The saline-solution phantom contained air as a marker. The maximum projection intensity resulted from a 90°, 270°, or 450° flip-angle excitation, and the minimum projection intensity resulted from a 180°, 360°, or 540° excitation. It should be noted that the saline-solution phantom requires more power for excitation than does the water phantom. Flip angles of 160°, 180°, and 200° were selective to the CSF of the head.

Figure 21 shows a series of image projections of a mouse head obtained in the read-out (F2) direction with the excitation power increased stepwise (left to right).

Figure 22 shows a head image with an excitation flip angle of 180°. Also, the flip angle was selective to the brain CSF and corresponded to that for the image projections (Fig. 21). The 180° image (Fig. 22) shows a small signal from the brain and muscle tissues because there were almost no transverse components of magnetization. On the other hand, in the same 180° image, the resistive fatty tissues, which were transparent to the RF field, yielded a specific signal. By applying 180° pulses to the conducting CSF and muscle tissue, resistive fatty tissue simultaneously received excitation of flip angles larger than 180° and produced an image signal.

Both the large flip-angle method and B, field method are sensitive to RF inhomogeneity. In addition, both the Larmor frequency B, field and the low frequency B, field are easily transmitted, absorbed, and reflected in varying degrees by biological tissue boundaries. The variability depends on the geometry of the subject, tissue properties, frequency, and the direction of the B, or B, fields. However, in spite of these difficulties, the methods of this study are useful to obtain tomographic images of electrical impedance distributions of living organisms.

Direct Neuronal-Current MRI

A new MRI technique to visualize the distribution of neuronal currents in the human brain has been developed [71]. The basic principle is to erase the effects of local spin-spin interaction T2 by subtracting MRI signals with different polarities of gradient magnetic fields. Measurements were made in a phantom of the internal magnetic-field deformation caused by an electric-current dipole moment of 10 nAmp (typical of values deduced from measurements of the evoked neuronal currents in the human brain with a SQUID magnetometer). A method based on the modified high-resolution NMR spectrometer equipped with a homemade microimaging system, at a field strength of 6.34 T and with a 3D SE sequence.

The minimum value of the current-dipole moment detected by this method was 90 nAmp. The results aid in the development of a technique that will measure focal changes in neuronal currents in the brain using this MRI technique. The application of this technique was important for obtaining maps of human brain activity using motor-stimulus paradigms. Measurements were made with an echo planar imaging (EPI) sequence at 1.5 T. Intensity changes resulting from causes other than neuronal currents were eliminated by editing functional images obtained with different polarities of the field gradients. MRI mapping of the neuronal currents in the brain during middle finger and thumb tapping was clearly observed. Signal intensity variation was roughly symmetrical around a current dipole, as expected. This is one of the strongest pieces of evidence in support of the detection of neuronal currents.

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