

The role of neuroelectric and neuromagnetic recordings in assessing learning and rehabilitation effects

Claude Alain and Bernhard Ross

Introduction

- The functional organization of the adult sensory system is dynamic and modifiable by training.
- Scalp recording of EEG and extra-cranial MEG recording are noninvasive techniques for investigating neuroplastic changes in humans.

Learning and rehabilitation can result in improvement in motor controls, general cognitive functioning including attention and memory, and improvement in observers' ability to discriminate differences in the attributes of sensory stimuli. In this chapter, we focus our review of the literature on studies that examine neuroplastic changes associated with behavioral improvement in perceptual skills. This is a research area with great cross-pollination between basic neurophysiological studies revealing fundamental properties of neurons and cortical reorganization following extended training, and neuroimaging studies in humans showing neuroplastic changes in larger intertwining systems or networks rather than a specific sub-population of neurons.

It is now well accepted that the adult brain is malleable and shows an amazing ability to adapt to a novel environment or the drastic changes caused by injury. Indeed, during the last decade converging evidence from animal neurophysiology and human neuropsychological and neuroimaging research has revealed a remarkable degree of brain plasticity in the sensory and motor systems during adulthood. In hindsight, such plasticity is no

surprise given that the adult brain needs to meet the processing demands of an ever-changing environment: learning-induced changes in mature sensory cortices may occur in a task-dependent manner, and can include rapid and highly specific changes in the response properties of cells (Edeline *et al.*, 1993; Fritz *et al.*, 2003). For instance, changes in the receptive fields of ferret auditory cortex can occur within the first minutes of a tone discrimination task that was previously learned (Fritz *et al.*, 2003, 2005a, 2005b). However, these neuroplastic changes were smaller or absent when the animal listened passively to the same sounds. Such rapid changes in the receptive fields of sensory neurons have been observed in a wide variety of situations including classical conditioning (Bakin & Weinberger, 1990; Edeline *et al.*, 1993), instrumental avoidance conditioning (Bakin *et al.*, 1996) and auditory discrimination learning (Fritz *et al.*, 2003). These findings suggest that learning and memory are not static but rather allow for dynamic adjustments that likely depend on various factors like goal-directed behavior, experience or injury. These changes can occur quickly with only a few trials. However, as the training regimen or rehabilitation continues, more permanent changes are likely to take place.

Evidence from single cell recordings suggests that extended training involving daily practice sessions over a long period is associated with changes in the topographical organization representing the trained sensory attributes (Recanzone *et al.*, 1992, 1993).

These more permanent changes in sensory and/or motor representations following extended training may involve the expression of new synaptic connections, thereby resulting in an enlarged cortical representation of a specific stimulus after training (Recanzone *et al.*, 1993; Rutkowski & Weinberger, 2005). For example, extensive frequency discrimination training of tactile vibration stimuli applied to a digit in nonhuman primates was found to enhance stimulus representation that was restricted to the trained skin location compared with control digits (Recanzone *et al.*, 1992). In a subsequent study, Recanzone *et al.* (1993) trained nonhuman primates to make fine pitch discriminations over several daily training sessions and found enlarged cortical maps and sharper tuning of receptive fields at the trained frequency, which correlated with increased perceptual acuity. Although such topographical changes in auditory cortices have been reported for various animals including rats (Polley *et al.*, 2006) and barn owls (Bergan *et al.*, 2005), other studies have failed to find topographical changes in the auditory cortex following extended training (e.g., Brown *et al.*, 2004; Witte & Kipke, 2005). The lack of enlarged representation could be related to several factors such as the species (e.g., cats, Brown *et al.*, 2004; Witte & Kipke, 2005), the duration of training (Witte & Kipke, 2005) and/or different stimulus configurations and training paradigms. The way the enlarged areas are calculated may have been a factor given that the total size of a sensory map may not always have been enlarged but rather a region responding to a particular frequency may expand at the expense of another. Notwithstanding sporadic discrepancies in the literature, evidence from animal research strongly supports the notion that functional reorganization after training can take place in the adult's brain.

In spite of the tremendous progress made in understanding the neural underpinnings associated with animal learning, there remain major gaps between basic animal learning and memory research and more applied research on behavioral and cognitive rehabilitation in individuals suffering from psychiatric or neurological diseases.

Researchers and clinicians are challenged by the constant need to monitor and enhance the effect of rehabilitation. Electroencephalography (EEG) and magnetoencephalography (MEG) recordings of neuroelectric and neuromagnetic activity respectively are increasingly used in investigating the neuroplastic changes associated with extended training and may prove to be valuable tools in assessing the impact of rehabilitation techniques on structural and functional brain activity in humans. Both recording methods are completely noninvasive and provide a means to evaluate the activity of the human brain, as we perceive stimuli, make decisions and generate motor commands. Electroencephalography and MEG can be used in multiple repeated sessions, and they are less expensive than other imaging techniques such as functional magnetic resonance imaging (fMRI).

Moreover, EEG and MEG provide very accurate temporal information about the sequence of neural events underlying perception and cognition as well as response selection, preparation and execution. Such temporal resolution is particularly helpful when investigating the level at which training regimens modulate brain activity. Because brain responses can be recorded for stimuli presented either within or outside the focus of attention, these techniques may contribute important information in assessing the impact of top-down controlled processes in brain plasticity and rehabilitation. Lastly, recent advances in brain electrical and magnetic source analysis have improved our understanding of the neural generators of sensory (exogenous) and cognitive (endogenous) evoked responses, making these techniques ideal for assessing the impact of learning and rehabilitation programs on functional brain reorganization.

In the following sections, we review the evidence from various paradigms and approaches suggesting that the recording of neuroelectric and neuromagnetic activity can provide objective markers of recovery of cortical mechanisms, with an emphasis on perceptual learning. Perceptual learning occurs when two stimuli that at first appear identical, become differentiated with practice. This is a true

change in perception – not just a change in strategy or a change in response criterion. Importantly, the presence and characteristics of ERPs (event-related potentials, obtained by averaging EEG segments time-locked to the stimulus onset) and ERFs (event-related fields, the complement to ERP obtained with MEG) in terms of latency and amplitude can be quantified during the course of training and recovery following a stroke or closed head injury. In conjunction with behavioral measures, recording of neuroelectric and neuromagnetic activity can highlight neuroplastic changes associated with the recovery of motor, perceptual and cognitive functions. We propose that the recording of ERPs and ERFs can be particularly useful in the framework of cortical remodeling following training procedures and as a monitor of cortical repair that parallels clinical improvements. The goal of this chapter is to assess the role of neuroelectric and neuromagnetic measurements as potential tools in assessing the brain plasticity associated with training and/or following brain damage. This review may assist in the development of more effective ways to assess and monitor the impact of training regimens during rehabilitation by evaluating the role of EEG and MEG in identifying neuroplastic changes in human observers. We now consider some of the methodological considerations with respect to the application of these techniques in basic and applied research, before going on to discuss studies that used these techniques in investigating neuroplastic changes following extended training in various perceptual and cognitive tasks.

Methodological and technical considerations

- The EEG/MEG signal is directly related to the number of synchronously activated cortical neurons.
- Relevant measures for training induced plasticity include changes in amplitude and latency of sensory evoked responses, oscillatory activity, intra-cortical coherence and source localization.

- Dipole source analysis aims at explaining the scalp-recorded data with a small number of generators.

Introduction to neuroelectric and neuromagnetic signals

Common primary sources of neuroelectric and neuromagnetic signals are current flows within apical dendrites of pyramidal neurons in the cerebral cortex. The intracellular currents are associated with magnetic fields that propagate through the brain tissue and the skull and are detected extra-cranially using MEG. Corresponding extra-cellular electric currents spread through the conductive brain tissue, the cerebrospinal fluid, the skull and the skin and result in voltage differences at the scalp surface, which are recorded with electrodes attached to the head using EEG. Since the dendrites of adjacent cortical neurons are aligned in parallel, the magnetic fields of single neurons are superimposed and result in a larger measurable magnetic field. The corresponding volume currents superimpose in a similar way and contribute to the expression of the voltage distribution on the scalp surface. Consequently, the EEG and MEG signals can be viewed as direct and complementary measures of the number of synchronously activated cortical neurons at the time of recording. Some 1000 to 100 000 neurons must be synchronously active in order to be registered with EEG or MEG (Williamson *et al.*, 1991).

Modern MEG systems measure brain activity simultaneously at 150 to 300 positions above the head. The detection coils of 10 to 20 mm diameter are equidistantly spaced on a helmet-shaped array. Participants are required to keep their head in a fixed position inside the helmet and to minimize as much as possible any head movement during the measurement. Most MEG systems measure the difference of magnetic flow through two coils, which are either arranged in an axial direction or side by side in the plane. Such axial or planar gradiometers measure the magnetic field gradient perpendicular to the head or in tangential direction,

respectively. The exceptionally high sensitivity for detecting small magnetic field changes is achieved by using superconducting quantum interference devices (SQUID), which convert magnetic field changes into recordable voltage changes. The SQUID devices operate near absolute zero temperature and need continuous cooling with liquid helium. Typical whole-head MEG systems are mounted in a large dewar positioned above the head of the participant. The size of detectable magnetic fields of brain activity is one to several hundred fT (femto Tesla, 10^{-15} T), which is 8–10 orders of magnitude smaller than the earth's magnetic field. To reduce the effects of environmental magnetic fields, MEG systems need special magnetically shielded rooms and noise cancellation techniques. Because the strength of the magnetic field decreases with increasing distance from the sensors, MEG is more sensitive to cortical sources than “deeper” subcortical sources. Furthermore, MEG is more sensitive to magnetic fields perpendicular to the coils (tangential sources). For example, a source at the center of the sphere (i.e., the head) produces magnetic fields almost in parallel with all sensor coils (radial sources) and is almost not visible in MEG. This is in contrast with EEG, which is sensitive to both radial and tangential sources, highlighting the importance of combining EEG with MEG recordings, especially in cases where complex source configurations are suspected.

Modern EEG systems contain 32–256 electrodes, which are usually mounted on a cap. High-density integration of the EEG amplifier makes the system portable. This is important given that clinical studies may require measurements at the bed site. Also, some of the new developments in using biofeedback techniques and EEG for assistance of individuals suffering from language and motor impairment depends on the portability of the EEG system.

The most common data analysis technique for separating relevant neuroelectric and neuromagnetic activity from the background neuronal activity consist of averaging epochs of brain waves that are time-locked to either external sensory events such as auditory, visual or somatosensory stimuli or

internal events such as perception and decision-making processes. Some of these brain waves are exogenous (i.e., obligatory) in the sense that they occur regardless of the observer's intention and motivation, reflecting the physical properties of the external events, whereas others are endogenous because they are determined by psychological factors such as attention and expectation. The amplitudes of the event-related brain waves index the strength of the response, whereas the latency refers to the amount of time, in milliseconds (ms), that is taken to generate the bioelectrical response following the onset of the event. The latency of sensory responses is therefore related to neural conduction time and site of excitation; the time it takes for the sensory input to travel through the peripheral sensory system to the place of excitation in the sensory cortex.

Source analysis

Determining the intra-cerebral sources for neuroelectric and neuromagnetic activities measured outside the head is referred to as the bioelectromagnetic inverse problem. For this analysis, the head is modeled in first approximation as a spherical volume (Sarvas, 1987). Often the cerebral sources can be modeled with only a small number of dipoles, for example single sources in the left and right auditory cortices. For estimation of the dipole location, orientation and strength, the difference between the measured magnetic or electric field and the calculated field is minimized by varying the dipole parameters (Hämäläinen *et al.*, 1993). Since the magnetic and electric fields sum linearly, more complicated source configurations may be composed by adding the contributions of several dipoles. More general approaches modeling brain activity with spatially distributed sources can be accessed with methods like minimum-norm solutions (Lin *et al.*, 2006) or beamformer techniques (Hillebrand & Barnes, 2005). For minimum-norm source estimation, the field of a large number of dipoles at fixed positions, for example equally spaced on the cortical surface, is approximated to

the measured field with the constraint of minimal current densities (Wang, 1993). Beamformer methods are spatial filters that identify for each volume element in the brain the unique contribution of a source, which is not coherent with other sources (Sekihara *et al.*, 2001; Vrba & Robinson, 2001).

After localizing the sources, time-series of brain activity at the source location can be calculated to illustrate the time course of neural activity (Figure 11.1). This source space projection method transforms the hundreds of electric and magnetic field waveforms into a small number of source waveforms. This improves the signal-to-noise ratio by reducing the overlap from other possible sources and filtering out the effect of sensor noise (Ross *et al.*, 2000; Tesche *et al.*, 1995). Although the source space projection method is more commonly used for analysing MEG data, a similar approach has also been applied to EEG data (Heinrich *et al.*, 2004; McDonald & Alain, 2005).

Summary

Electroencephalography and magnetoencephalography are powerful techniques for investigating neuroplastic changes associated with learning and rehabilitation because they permit the opportunity to study brain activity with precise temporal resolution. Moreover, scalp recordings of ERPs or ERFs can be used to examine both exogenous (sensory representation) and endogenous (attention and learning) aspects of information processing. The development of new dipole source modeling algorithms can help localise the neural generators allowing researchers to identify which brain areas support behavioral improvement following training and rehabilitation programs. We now turn to the effects of training and expertise on sensory evoked responses as measured by EEG and MEG.

Perceptual learning and neuroplastic changes in sensory evoked responses

- Perceptual learning modulates amplitude and latency of sensory evoked responses.

- Practice-related changes in sensory evoked responses could be expressed as:
 - (1) increase in the size of cortical areas representing the trained attribute;
 - (2) higher degrees of synchronization within a particular neural ensemble;
 - (3) sharpening the tuning of cells for the task-relevant (trained) attributes; and
 - (4) changes in cortical maps (locus) representing the trained attribute.

In the past 10 years, there has been a growing interest in using EEG and MEG techniques to investigate brain plasticity in human adults. In this section, we review several studies that have used EEG and/or MEG to reveal neuroplastic changes in auditory, visual and motor systems in normal healthy adults. Then, we examine studies that have used these techniques to assess and monitor recovery following a stroke or closed head injury.

Measuring neural activity during auditory learning

The effects of practice on auditory processing have been extensively studied by comparing amplitude and latency of auditory evoked potentials (AEPs) and auditory evoked fields (AEFs). Auditory evoked potentials and AEFs are comprised of sequences of several positive and negative deflections (i.e., waves). Each deflection reflects synchronous activity from large neuronal ensembles that are time-locked to sound onset. The sequence of AEPs tracks neuronal processing as the information ascends the auditory system from the cochlea, through early brainstem response (1–10 ms after sound onset) to the primary auditory cortex (middle-latency evoked responses, 10–50 ms) and onto higher auditory cortical areas. Long-latency evoked potentials take place after 50 ms and include the P1, N1 and P2 waves. The P1-N1-P2 complex is related to signal detection and is present only when a transient auditory stimulus is audible (Hillyard *et al.*, 1971; Martin *et al.*, 1997). However, the conscious discrimination of an auditory event is often associated with an

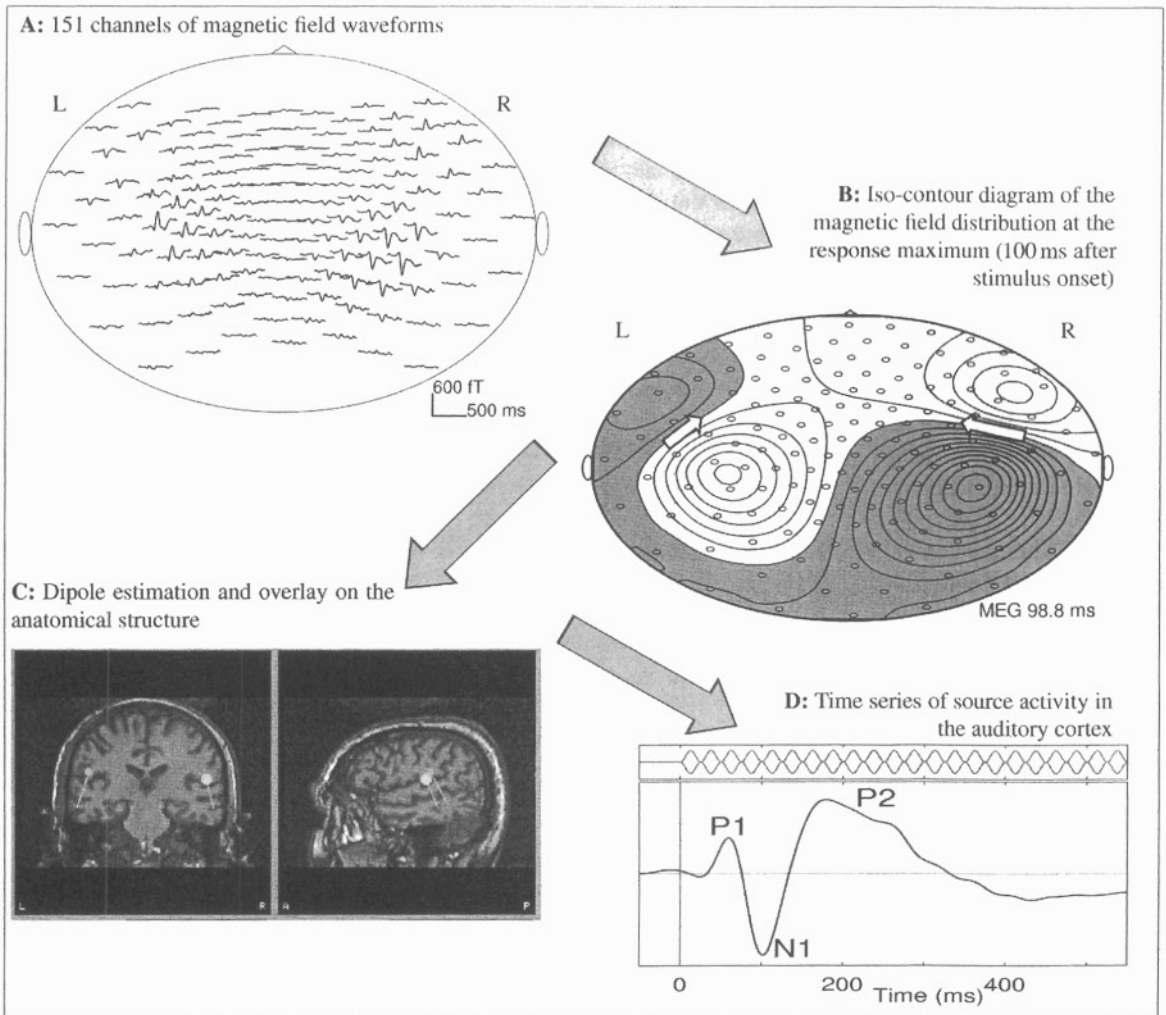


Figure 11.1. (This figure is reproduced in the color plate section at the front of this volume.) Example of data transform during magnetoencephalography (MEG) analysis. (A) This panel shows an average auditory event-related field recorded in a representative participant. The evoked response comprises a negative wave that is maximal over the left (L) and right (R) hemispheres. (B) Iso-contour maps illustrating the amplitude distribution of this negative wave peaking at about 100 ms (i.e., N1m). The shaded areas indicate the outgoing field. (C) The amplitude distribution can be accounted for by a pair of dipoles located in the temporal lobe near Heschl's gyrus. The dipoles are superimposed on the magnetic resonance image (MRI) obtained from the participants. (D) This panel shows the source waveform activity from the right auditory cortex. The source waveform comprises an early positive peak at about 50 ms (P1), followed by the N1 and P2 wave peaking at about 100 and 180 ms post-stimulus, respectively. The red drawing at the top of the panel illustrates the amplitude-modulated tone used to elicit the response.

additional late positive wave peaking between 250 and 600 ms post-stimulus, referred to as the P300 or P3b (Hillyard *et al.*, 1971; Martin *et al.*, 1997; Parasuraman & Beatty, 1980).

One way to assess the impact of extended training on brain plasticity is to compare individuals that differ in terms of their expertise with the material presented, such as in the case where musicians and non-musicians are presented with auditory stimuli. Shahin *et al.* (2003) examined the effects of long-term musical training on ERPs and found larger N1c amplitudes (~140 ms) to pure tone, piano tones or violin tones in musicians relative to non-musicians. The N1c is an ERP component thought to reflect the activation of the lateral portion of the superior temporal gyrus. This effect of musical training on the N1c was accompanied by enhancement of the P2 (~185 ms) wave, an ERP component that is maximal at central sites (Shahin *et al.*, 2003). The enhanced P2 amplitude in musicians compared with non-musicians was recently replicated using MEG (Kuriki *et al.*, 2006). Musicians also showed enhanced early cortical activity (19–30 ms), which was paralleled by an increase in gray matter volume (Schneider *et al.*, 2002). Larger N1m (the magnetic counterpart of the electric N1) has also been found for piano tone compared with pure tone in musicians, whereas no such difference in brain response was found in non-musicians (Pantev *et al.*, 1998). Neuromagnetic recordings have also revealed enhanced N1m that was specific to the principal instrument played by the musician (Pantev *et al.*, 2001b). Although such findings are in accordance with the notion that timbre-specific enhancements in cortical representation are attributable to musical practice rather than a predisposition to music (Pantev *et al.*, 2001a), subsequent studies could not consistently demonstrate differences in N1m amplitude elicited by piano tones and pure tones between musicians and non-musicians (Hirata *et al.*, 1999; Lütkenhöner *et al.*, 2006; Schneider *et al.*, 2002). This discrepancy in the literature may reflect procedural differences. Studies that revealed enhanced N1 amplitude in musicians usually adjusted sound intensity on an individual basis based on hearing

thresholds for each stimulus type (Pantev *et al.*, 1998) whereas those failing to show differences between musicians and non-musicians presented stimuli at the same intensity level for all participants (Hirata *et al.*, 1999).

Another way to assess the neuroplastic changes associated with learning and rehabilitation involves comparing performance and brain activity prior to and after training in discriminating stimuli that originally appear very similar. Training-related changes in auditory evoked responses have been reported for a wide range of tasks requiring a discrimination between tones of different frequencies (Bosnyak *et al.*, 2004; Brattico *et al.*, 2003; Menning *et al.*, 2000), consonant vowel stimuli varying in voice onset time (Tremblay *et al.*, 1997, 2001), as well as in tasks requiring segregation and identification of concurrent vowels (Reinke *et al.*, 2003). Prior studies focusing on auditory perceptual learning have shown a decrease in N1 latency (Bosnyak *et al.*, 2004; Reinke *et al.*, 2003) as well as an augmentation of N1m amplitude (Menning *et al.*, 2000) following extended training. The training-related enhancement in N1m may either indicate that more neurons are activated or that neurons representing the stimulus were firing more synchronously. In addition, the N1c component showed an increase in amplitude with extended practice (Bosnyak *et al.*, 2004). Interestingly, the N1c amplitude continued to increase over 15 training sessions (Bosnyak *et al.*, 2004). In addition, extended training has been found to enhance the amplitude of the P2 wave (Atienza *et al.*, 2002; Bosnyak *et al.*, 2004; Reinke *et al.*, 2003; Tremblay *et al.*, 2001) which can appear after two (Atienza *et al.*, 2002) or three (Bosnyak *et al.*, 2004) daily test sessions. Figure 11.2 shows the effects of four daily training sessions on N1 and P2 waves elicited by two vowels presented simultaneously. In that study, the enhanced P2 amplitude paralleled behavioral improvement in identifying both vowels presented concurrently (Reinke *et al.*, 2003). The enhancement in P2 amplitude was preceded by rapid neuroplastic changes over the right auditory cortex during the first hour of testing, which occurred only when listeners were

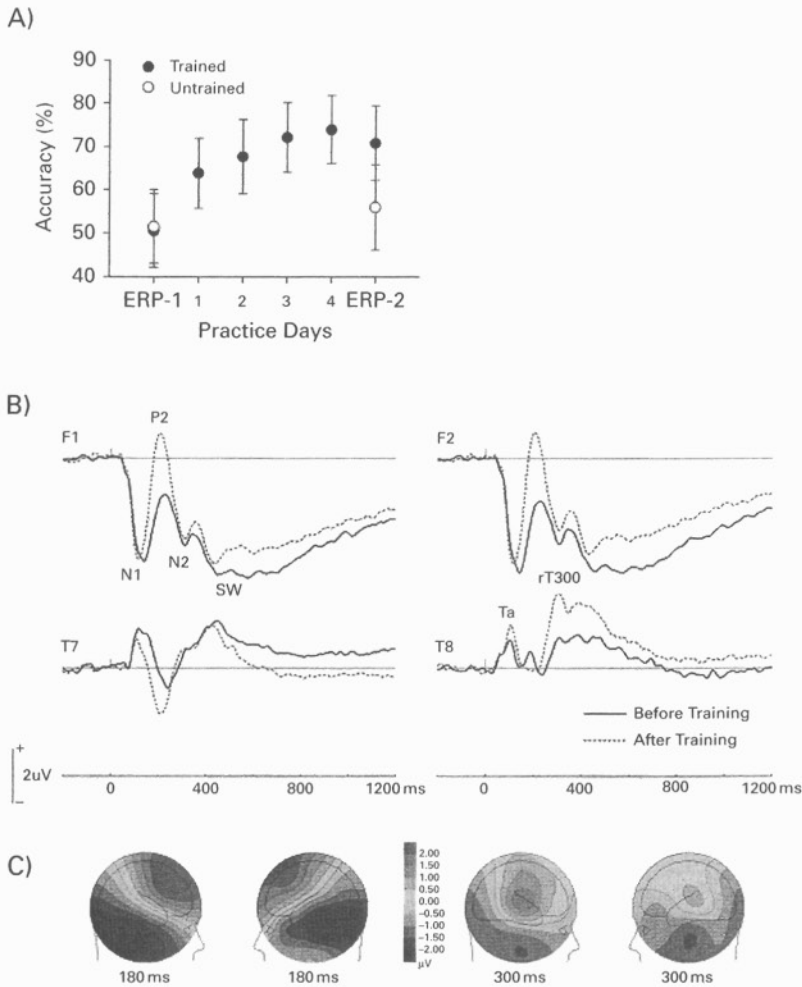


Figure 11.2. (This figure is reproduced in the color plate section at the front of this volume.) Effects of training on auditory ERPs. (A) Group mean accuracy in identifying two vowels presented simultaneously during the first (ERP-1) and second ERP (ERP-2) recording sessions in trained and untrained individuals as well as during the four daily training sessions in the trained group. Error bars reflect standard error of the mean. (B) Group mean ERPs recorded before and after 4 days training period in the trained group. Note the large increase in P2 amplitude over the frontal electrodes (i.e., F1 and F2). Behavioral improvement was also paralleled by an increase in amplitude recorded over the right temporal cortex (i.e., T8). F1 = Left Frontal; F2 = Right Frontal; T7 = Left Temporal; T8 = Right Temporal. (C) Isocontour maps of the difference in ERP amplitude between the first and second ERP testing sessions. Adapted with permission from Reinke *et al.* (2003).

attending to the stimuli (Alain *et al.*, 2007). There was no significant increase in P2 amplitude within the first hour of testing (Alain *et al.*, 2007), suggesting that the P2 effects index a relatively slow learning process that may depend on consolidation over

several days. However, it has been reported that exposure to the stimulus material without discrimination training can also result in P2 amplitude changes (Sheehan *et al.*, 2005). In summary, the majority of EEG and MEG studies show that

learning-related changes in sensory evoked responses (i.e., N1, N1c and P2) can be observed in a wide range of carefully designed auditory tasks.

Another auditory ERP component that has been used to investigate the impact of training on sensory representation is the mismatch negativity (MMN). The MMN is elicited by infrequent deviant stimuli embedded in a sequence of otherwise homogenous stimuli (Picton *et al.*, 2000). Sounds that deviate in terms of their pitch, spatial location, duration, and intensity from repeating standard stimuli elicit an MMN wave. Also, infrequent disruptions in the temporal organization of sounds such as in a sequence of sounds that alternate in pitch (Alain *et al.*, 1994, 1999) or during the violation of musical contours or intervals (Fujioka *et al.*, 2004; Trainor *et al.*, 2002) generate MMN waves. The MMN is thought to index automatic detection of stimulus invariance, with its amplitude and latency increasing and decreasing respectively, as the deviant stimulus becomes more discriminable (Alain *et al.*, 1994, 2004; Javitt *et al.*, 1998; Sams *et al.*, 1985).

Previous research has shown that musical expertise is associated with enhanced MMN amplitude (Fujioka *et al.*, 2004, 2005; Lopez *et al.*, 2003; Nager *et al.*, 2003; Tervaniemi *et al.*, 1997). Moreover, studies of language processing in healthy adults have found enhanced MMN amplitude in response to phoneme changes that are relevant to listeners' native language (Näätänen *et al.*, 1997; Ylinen *et al.*, 2006), providing further support that MMN amplitude is sensitive to observers' expertise. The MMN latency decreases and its amplitude increases following pitch (Menning *et al.*, 2000) and speech (Kraus *et al.*, 1995) discrimination training. Enhanced MMN amplitude has also been reported within a single daily training session (Atienza *et al.*, 2002; Gottselig *et al.*, 2004; Tremblay *et al.*, 1997). In these studies, the MMN was recorded during passive listening prior to and after a brief training session that involved an active listening task. Although the MMN is thought to index a pre-attentive change detection process (Näätänen, 1992), evidence from many studies has suggested that attention to auditory stimuli enhances the MMN amplitude (Alain &

Izenberg, 2003; Alain & Woods, 1997; Arnott & Alain, 2002; Woldorff *et al.*, 1991, 1998). Therefore, it is still debated whether an enhanced MMN amplitude following training is related to learning per se or whether it indexes participants' increased attention to recently learned auditory material. However, the fact that training-related changes in MMN amplitude are seen in response to speech stimuli that share the trained acoustic cue but were *not* used in the training session suggests that attention alone might not be responsible for training-related changes in MMN (Tremblay *et al.*, 1997). The effects of training on MMN occur quickly, being present after 105 minutes of practice (Tremblay *et al.*, 1998). This rapid training-related change in MMN amplitude was followed by behavioral improvement in speech discrimination. Together, these findings suggest that the MMN wave could be used to assess the efficacy of training in the absence of a behavioral response. This is particularly important in cases where the effectiveness of auditory training can be difficult to assess using behavioral methods such as in infants, young children and individuals with aphasia.

Although studies employing the MMN as the dependent measure may provide important insights into the physiological processes underlying stimulus representation, auditory discrimination and learning, this ERP/ERF component is not necessarily suitable to assess the impact of recovery and rehabilitation on a single patient basis. The MMN is relatively small in amplitude and elicited by infrequent events thereby requiring relatively long recording sessions in order to obtain a reliable signal/noise ratio. Also, there is no one-to-one relationship between behavioral improvement and neuroplastic change in stimulus representation because the MMN is recorded during passive listening and changes in amplitude may reflect stimulus exposure or top-down modulations as mentioned earlier.

In summary, ERPs or ERFs can be used to assess the impact of auditory training regimens. Notwithstanding some inconsistencies in the literature, the bulk of the research comparing musicians and non-musicians, as well as those directly

assessing neuroplastic changes during the auditory perceptual learning, reveals reliable changes in sensory evoked responses that parallel behavioral improvement. Moreover, our review of the literature shows that rapid and slow perceptual learning is associated with a distinct pattern of neural activity, with the training-related P2 enhancement requiring several daily practice sessions. The extent to which these neuroplastic changes are modality-specific is examined by reviewing the effects of practice and expertise on visual evoked responses.

Visual evoked responses

Visual evoked potentials are comprised of positive, negative, positive deflections peaking at about 100 (P1), 170 (N1) and 240 (P2) ms respectively after stimulus onset over the occipital and inferior parietal regions. The amplitude of the P1 wave is sensitive to spatial attention (Woldorff *et al.*, 2002), whereas the N1 amplitude is modulated by the nature of the visual input such as a face or an object (Itier & Taylor, 2004).

The fact that the N170 is larger for some classes of stimuli over others may reflect the viewer's expertise with the material. Indeed, larger N170 has been observed in bird watchers for bird stimuli (Tanaka & Curran, 2001), and for car experts viewing cars (Gauthier *et al.*, 2003). Similarly, when English readers were presented with Roman and Chinese characters, Chinese characters elicited smaller N170 than Roman characters (Wong *et al.*, 2005). This language-specific effect was not present in Chinese-English bilinguals. These findings suggest that the visual N170 reflects long-term experience with visual material and, perhaps, could be used to assess the integrity of long-term representations following brain injury.

In comparison with hearing research, fewer studies have examined the impact of an explicit training regimen on visual evoked responses and those that examine training-induced plasticity have yielded mixed results. For instance, some studies reported

an enhancement of visual N170 amplitude elicited by nonface objects (e.g., greebles, vernier stimuli) following extended training (Rossion *et al.*, 2004; Shoji & Skrandies, 2006). However, other studies found reduced N1 amplitude over the parietal region (Song *et al.*, 2002, 2005) that was generalised over differently oriented stimuli (Ding *et al.*, 2003). Learning to detect degraded images, which were not recognized unless previously associated with its nondegraded version, also resulted in enhanced amplitude of induced gamma oscillation at about 250 ms after stimulus onset (Goffaux *et al.*, 2004).

In addition, training on a simple visual discrimination task has been associated with enhanced P2 amplitude, which was paralleled by a decrease in response time (Ding *et al.*, 2003; Song *et al.*, 2005). Both the P2 enhancement and RT training-related improvement were specific to the trained stimuli (Ding *et al.*, 2003). The P2 enhancement was not present when participants were trained with slightly more complex stimuli (e.g., arrow as opposed to line segments) (Song *et al.*, 2005). For the arrow stimuli, training resulted in an increased P3 (350–550 ms) amplitude over the central/parietal areas (Song *et al.*, 2005). These findings suggest that perceptual learning modifies the response at different levels of visual cortical processing related to the complexity of the stimulus. The neuronal mechanisms involved in perceptual learning may depend on the nature (e.g., the complexity) of the stimuli used in the discrimination task.

As in the auditory modality, learning to discriminate between various classes of visual stimuli results in enhanced visual evoked responses. Interestingly, the P2 enhancement was also observed after daily practice sessions. While the early neuroplastic changes in N1 amplitude may reflect modality-specific effects, the later modulation occurring during the P2 interval may be reflecting more general aspects of learning common across different modalities. The pattern of changes in both auditory and visual modalities is consistent with the proposal that the P2 indexes consolidation during learning.

Somatosensory evoked responses

Tactile stimulations generate somatosensory evoked responses over the central scalp region that include early (e.g., N20, P27 and P45 wave) and late responses (N70, N140 and P220) whose latency and amplitude vary as a function of the site of stimulation (e.g., finger vs. foot). In comparison with auditory and visual evoked responses, which mainly showed changes in the response size, the effects of laboratory training on somatosensory evoked responses seems more likely to be expressed in changes in source locations than in response amplitudes. For instance, Schwenkreis *et al.* (2001) showed short-term changes in dipole location of the N20 after one hour of training, but no difference in amplitude between pre- and post-training recordings. Another MEG study examining the effect of a 30-day training regimen in discriminating the frequency of vibro-tactile finger stimulation resulted in significant improvement of behavioral performance that can even be generalized to the untrained hand, but failed to produce reliable changes in somatosensory evoked responses (Imai *et al.*, 2003). In comparison, Braun *et al.* (2002) used the more reliable within-subject, within-session measure of distance in the representation of digit 2 and 5 and found an increase in distance after vibro-tactile discrimination training without a measurable change in the amplitude of the somatosensory evoked field. Another study has shown improved discrimination performance with training that was paralleled by changes in MEG signal spectral power around 10 and 20 Hz, but found no reliable change in the amplitude of somatosensory evoked responses and their localization (Liu & Ioannides, 2004). Pleger *et al.* (2001) showed improvement in spatial discrimination thresholds, which were paralleled by a shift in the localization of the N20-dipole of the index finger that was stimulated. The distance between the dipole pre- and post-training was significantly larger on the trained side than on the control side, revealing a highly selective effect with no transfer to the index finger of the opposite, non-trained hand. The improvement in discrimination

abilities was predicted by the changes in dipole localization.

Summary

Improvement in tactile discrimination is associated with neuroplastic changes in the primary somatosensory area generating early sensory responses. These changes occur after extended training and appear to be highly specific to the trained area. The studies reviewed above demonstrate that behavioral improvement during tactile discrimination training is paralleled by changes in cortical networks. However, further work is needed to identify robust measures in the recorded EEG or MEG, which reflect reliably the training induced changes. The most promising candidates seem to be within-subject localization measures like the extension of the hand area and changes in the EEG/MEG signal spectrum.

ERP/ERF measurements during rehabilitation and treatment

- Stroke recovery and rehabilitation are associated with neuroplastic changes in sensory evoked responses and cognitive evoked potentials.
- Scalp recording of ERPs and ERFs have been used extensively in clinical research. More recently, there has been a growing interest in examining whether ERPs and ERFs could be useful prognostic tools in predicting recovery following moderate and severe brain injury (for a review see Giaquinto, 2004; Lew *et al.*, 2006). As we mentioned earlier, we believe that ERPs and ERFs could be very useful for longitudinal monitoring and assessing cortical remodeling following rehabilitation. In the previous section, we reviewed evidence supporting neuroplastic changes in the auditory, visual and somatosensory systems, revealing a high level of brain plasticity in sensory systems of healthy adults. In most studies, improvements in performance were associated with an enhancement in the amplitude of neuroelectric or

neuromagnetic activity. The latter is consistent with recruitment of additional neurons representing the trained attribute and/or higher degree of synchronization within a particular neural ensemble. Topographical changes were also observed in some studies indicating that training can also generate changes in cortical maps (loci) representing the trained attribute. More importantly, findings from these studies reveal neuroplastic changes in the adults' brain following various training regimens, which can be documented using EEG and MEG.

In spite of evidence showing training-related induced brain plasticity in healthy adults, the literature contains relatively few articles dealing with the use of ERPs and/or ERFs in assessing rehabilitation and plasticity in disordered systems. Keren *et al.* (1998) recorded ERPs from patients with closed head injury 2, 3 and 3.5 or more months after injury. Patients with severe closed head injury (significant degree of impaired consciousness greater than 24 hours) were divided into two groups according to severity using the Glasgow Coma Scale, which quantifies the level of consciousness following traumatic brain injury. Event-related potentials were elicited using the standard auditory P3 "oddball" paradigm, including targets defined by their higher pitch. At the initial test, the more severely injured group showed significantly longer P3 latencies than the less severely injured patients. In subsequent recordings, P3 latency was found to be significantly shorter compared with the initial P3 latency, and the difference in P3 latency between the two patient groups was no longer statistically significant by the time of the third recording. For the group as a whole, P3 latency decreased significantly on each repeated recording, and may reflect a decrease in stimulus evaluation time. In addition, the N2 latency was found to be significantly shorter between the first and third recordings. These changes in P3 latency correlated with improvement in neuropsychological tests such as short- and long-term story recall, word recall and Raven's progressive matrices. Although this study suggests that the P3 wave may be used as a physiologic index of brain activity that correlates with recovery from closed

head injury, this finding should be interpreted with caution since a recent study failed to find reliable changes in P3 amplitude or latency in post-stroke global aphasics as a function of recovery (Nolfe *et al.*, 2006). However, the lack of a clear relationship between ERP measurement and recovery may be attributed to the nature of the paradigm used by Nolfe *et al.* (2006), which did not emphasize focus of attention and learning.

Evidence suggests that ERPs can be very helpful in assessing the reorganization of language following brain lesions even in patients with chronic aphasia. For instance, Pulvermüller *et al.* (2005) examined the impact of intense language therapy for 2 weeks on performance and brain activity elicited by visually presented words and pseudo-words. They found significant improvement in speech comprehension, which was paralleled by enhanced P2 amplitude elicited by words following treatment. Brain responses elicited by meaningless pseudo-words were not modulated by the language therapy, suggesting that the neurophysiological changes were specific to words. In an effort to determine the recovery of cortical auditory discrimination in eight aphasic left-hemisphere-stroke patients, Ilvonen *et al.* (2003) measured the MMN wave to duration and frequency changes in a repetitive, harmonically rich tone, 4 and 10 days and again 3 and 6 months after their first unilateral stroke. Relative to the initial testing session, they found increasing MMN amplitudes during the 3–6 months follow-up, which were accompanied by progressive improvement in speech-comprehension tests. This suggests that the MMN reflects spontaneous recovery and/or recruitment of auditory cortex spared by the lesion.

Perceptual training with nonlinguistic audiovisual stimuli in dyslexic children has also been found to improve sound discrimination as indexed by the MMN, which was accompanied by improvements in reading skills (Kujala *et al.*, 2001). Similar neuroplastic changes in auditory cortex were recently observed for a phonological intervention applied to preschool children diagnosed with a specific language impairment (Pihko *et al.*, 2007). These

results are very encouraging and suggest that behavioral improvements in language function during rehabilitation are paralleled by changes in the amplitude of ERP components.

Event-related potentials have also been used to assess clinical improvement associated with processing somatosensory and visual stimuli. For instance, Giaquinto & Fraioli (2003) measured the N140 and P3 waves elicited by standard and target cutaneous electrical stimuli in patients suffering from a stroke in the middle cerebral artery area. The target stimuli were presented on the elbow of the paralyzed side whereas the standard stimuli were applied on the ipsilateral shoulder. Participants indicated, by pressing a button, whenever they noticed the target stimulus. Patients in the trained group performed this discrimination task five times a week for 3 consecutive weeks whereas those in the control group were tested twice; once at the beginning and again at the end of 3 weeks. The main finding of that study was that daily practice significantly improved the recovery of N140 for stimuli presented contralateral to the paralyzed side. While 15% of the patients showed an N140 during the first testing session, the proportion increased to 80% at the end of the training regimen. In the control group, there was no difference in the proportion of patients showing the N140 response. Similarly, behavioral improvement associated with rehabilitation of chronic post-stroke visual field defects has been associated with a recovery of the P1 wave from the visual evoked responses (Julkunen *et al.*, 2003). Henriksson *et al.* (2007) examined the effects of extended training on cortical reorganization and found that weekly stimulation of the blind hemifield can induce cortical reorganization of visual areas in the intact hemisphere. These studies demonstrate that training-related improvements in the detection of sensory stimuli are accompanied by neuroplastic changes in sensory evoked responses, highlighting the fact that neuroelectric brain activity can be used to monitor and assess the impact of rehabilitation at the cortical level.

Magnetoencephalography has recently been applied to assess the impact of a rehabilitation

technique for musicians suffering from focal hand dystonia, a disorder involving cramps and uncoordinated movements of the hand and fingers. Improvement in symptoms following treatment was paralleled by alteration in the functional organization of the somatosensory cortex (Candia *et al.*, 2003). Other MEG studies demonstrated that the cortical reorganization related to the writer's cramp is task specific (Braun *et al.*, 2003) and that specific changes in cortical networks can be identified using measures of coherence between brain regions (Butz *et al.*, 2006). Magnetoencephalography is sensitive to hemispheric differences and this property is useful for observing cortical plasticity during recovery from unilateral stroke. Comparing somatosensory responses from the affected and un-affected hemisphere is a sensitive within-subject measure and gives insight into stroke-related plastic changes despite possible large inter-subject variability in the responses (Rossini *et al.*, 2001).

Summary

Recent longitudinal studies combining behavioral methods with recording of neuroelectric and/or neuromagnetic brain activity provide new insight regarding the nature and the level at which rehabilitation can impact brain function. The technique can be used to assess a wide range of treatment and shows promise in assessing the impact of rehabilitation on perceptual, cognitive and motor functions.

Overall summary and future directions

Neurophysiological studies in nonhuman primates as well as neuroimaging research in humans have revealed a remarkable degree of brain plasticity. This discovery of a highly dynamic and malleable brain in adulthood opens new areas and provides hope in treating individuals with brain dysfunctions. However, there are major challenges for research in rehabilitation. The ability to objectively assess and monitor the efficacy of rehabilitation

techniques is central for developing more effective rehabilitation programs. The evidence reviewed in this chapter suggests that EEG and MEG techniques may prove to be useful tools in assessing and monitoring brain plasticity in some situations. Recording of neuroelectric and neuromagnetic activity is versatile and easy to use in conjunction with behavioral methods. The portability of the EEG system may promote research at the bedside or in more natural settings, such as someone's house. Both techniques can be used to examine whether newly acquired skills can be generalized to other situations.

Further research is needed to explore the characteristics of this remarkably adaptable cortical activity and to uncover its boundary conditions. For instance, what are the links between early and rapid neuroplastic changes that occur within the first hours of training and those that take place following several daily practice sessions? Is the brain of middle-aged adults and/or older adults as plastic as those of young adults? If so, can such extended training be used to alleviate perceptual and cognitive "problems" that occur with normal aging? Answers to these and related questions will advance our knowledge of learning and cortical plasticity and have important implications for rehabilitation.

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