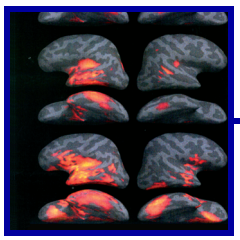

6

Electroencephalography, Event-Related Potentials, and Magnetoencephalography

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In this chapter I discuss the use of electroencephalography, event-related potentials, and magnetoencephalography in psychiatry. Of these three measures, electroencephalography is the only one that is currently used in standard psychiatric clinical practice, and even here, its main use is to exclude certain neurological disorders in the differential diagnosis of psychiatric disorders. Event-related potentials and magnetoencephalography currently have no direct clinical applications in psychiatry. Nonetheless, they are both the focus of intense research interest. This is because these methods, of all the noninvasive neuroimaging techniques, provide the most direct measure of neurocognitive function with the greatest temporal resolution.

The main aim of this chapter is to serve as in introduction to each of these techniques. Each section begins with a description of how the relevant signals are extracted, followed by a summary of some of the technique's applications in psychiatric clinical practice or research.

The Electroencephalogram

Generation of Signal

Conventional Electroencephalography

If a pair of electrodes is attached to the surface of the scalp and connected to an amplifier, the output of the amplifier shows a variation in voltage over time. This pattern of voltage variation is known as the electroencephalogram (EEG). The amplitude of the normal EEG varies between approximately –100 and +100 micro-

volts, and its frequency ranges to 40 Hertz (Hz) or more. Figure 6–1 shows a standard placement of electrodes over the scalp.

The EEG signal does not arise from individual action potentials; rather, it derives from the extracellular current flow that is associated with excitatory postsynaptic potentials (EPSPs) and inhibitory postsynaptic potentials (IPSPs). These current flows are of much lower voltage than action potentials. They are, however, distributed across a large surface area of membrane and are of longer durations than action potentials, allowing summation. Even with summation, however, the fields produced by individual neurons are much too weak to be detected by the EEG at the surface of the scalp. In order to generate externally detectable signals, the neurons within a volume of tissue must be aligned, and their synaptic current flows must be correlated in time. Of all the neurons in the human brain, the cortical pyramidal cells are particularly well suited to generate externally observable electric fields. This is because of their elongated apical dendrites, which are systematically aligned in a columnar fashion, perpendicular to the cortical sheet.

Although much of the amplitude of the brain electrical activity derives from cortical neurons underlying the scalp electrodes, the synchronicity of the recorded activity is largely regulated by subcortical sites. For example, pacemaker neurons within the thalamus normally oscillate synchronously, producing an alpha rhythm that characterizes the EEG of an awake healthy person at rest. Such synchrony is reduced by arousal. Desynchronization of electrical activity is thought to be mediated by afferent projections from the reticular formation and basal forebrain. These effects may be modulated by noradrenergic, cholinergic, and γ-aminobutyric acid (GABA)ergic neuronal systems. Brain electrical frequencies are generally reported in the delta (0–4 Hz), theta (4–8 Hz), alpha (8–13 Hz), and beta (>13 Hz) bands. Figure 6–2 shows examples of alpha and beta activity.

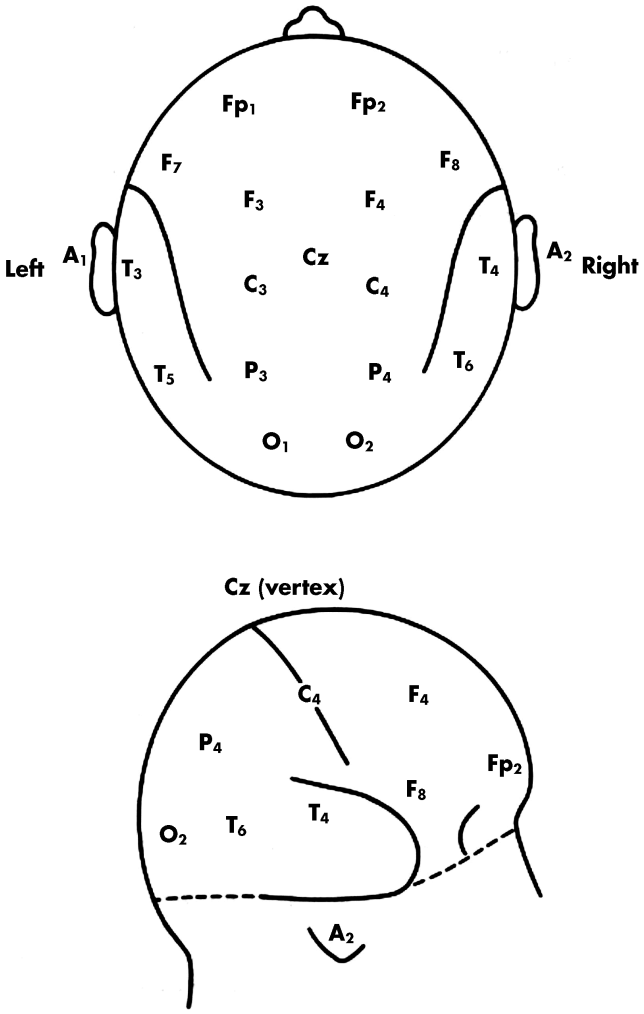

Figure 6–1. Standard placement of EEG recording electrodes at the top and sides of the head. Abbreviations for electrode placements: A = auricle; C = central; Cz=vertex; F=frontal; Fp=frontal pole; O = occipital; P=parietal; T=temporal. The multiple electrode placements overlying a given area (e.g., temporal) are indicated by numerical subscripts. Placement C_4 overlies the region of the central sulcus. *Source.* Reprinted from Kandel ER, Schwartz JH, Jessell TM (eds.): *Principles of Neural Science,* 3rd Edition. New York, McGraw-Hill, 1991, p. 779. Copyright 1991, The McGraw-Hill Companies. Used with permission.

Quantitative Electroencephalography

EEGs have traditionally been evaluated by visual inspection of paper tracings. To quantify measurements of the frequency content of the EEG, the digitized signal can be recorded on magnetic or optical media. The quantitative EEG (qEEG) provides information that cannot reliably be extracted from visual inspection of the EEG. It has been argued that such qEEG estimates improve intra- and interrater reliability and yield reproducible estimates that can be compared over time in single individuals. Once digital data are recorded, they can be transformed through use of the Fourier transformation algorithm from the domain of "amplitude versus frequency" to a domain of "power versus frequency." The qEEG gives rise to a number of different measures. For example, *absolute power* is a measure of the intensity of energy measured in microvolts

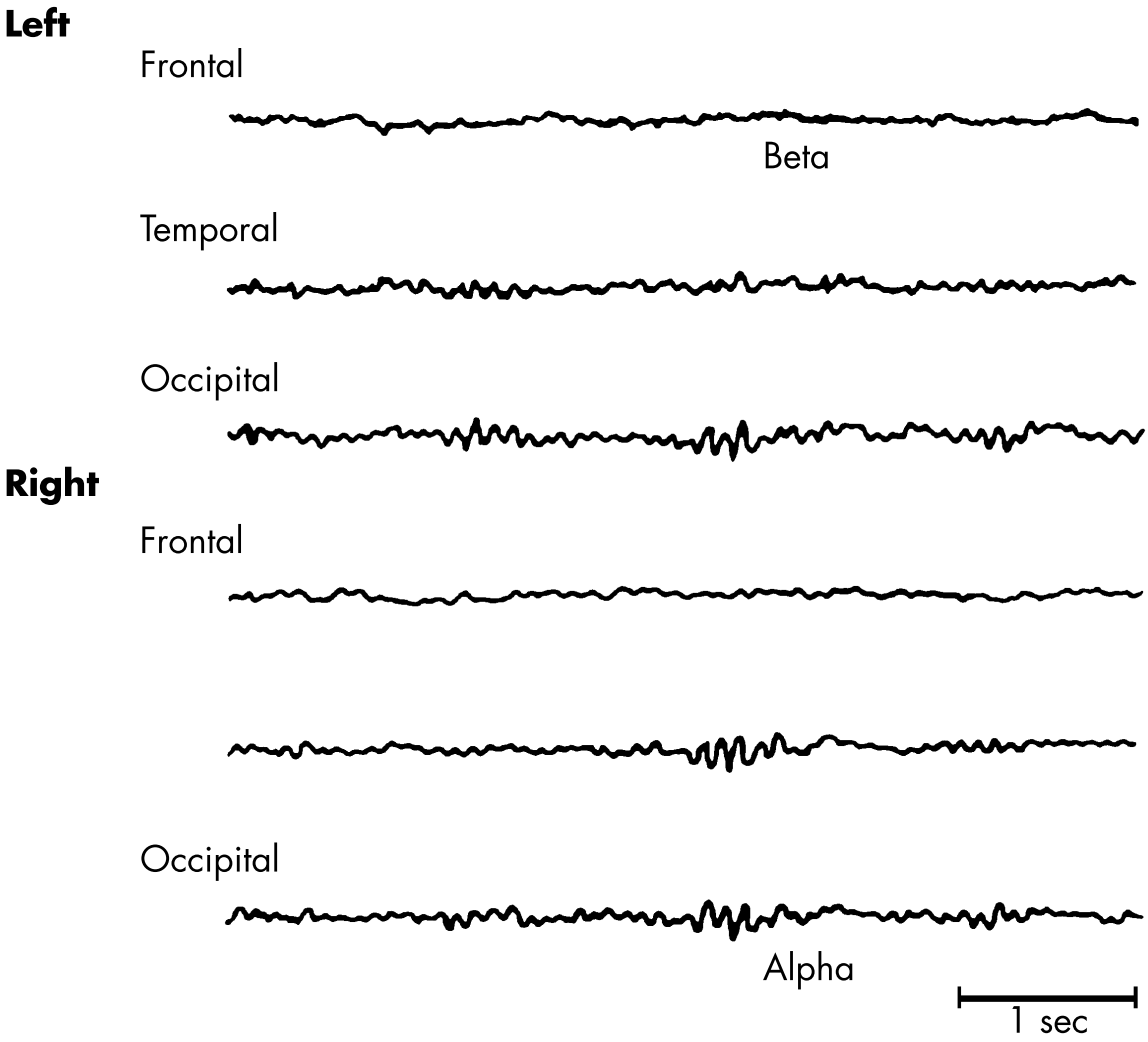

Figure 6–2. Electroencephalogram (EEG) recorded in a human subject at rest from the scalp surface at various points over the left and right hemispheres.
Three pairs of EEG electrodes are positioned so as to overlie the frontal, temporal, and occipital lobes. Beta activity—the EEG activity with the highest frequency and lowest amplitude—is recorded over the frontal lobes. Alpha activity—a signature of a brain in a relaxed and wakeful state—is recorded in the occipital and temporal lobes. The presence of alpha activity in the occipital lobe suggests that the subject's eyes were closed.
Source. Reprinted from Kandel ER, Schwartz JH, Jessell TM (eds.): *Principles of Neural Science,* 3rd Edition. New York, McGraw-Hill, 1991, p. 778. Copyright 1991, The McGraw-Hill Companies. Used with permission.

squared and calculated in a series of frequency bands (the *power spectrum*) for approximately 25 seconds. Another important measure is *coherence*—a measure of the *phase consistency* of two signals (i.e., the extent to which EEG signals from different brain regions have frequency components that are time-locked to each other). Coherence varies between 0 and 1 and is analogous to a correlation coefficient of the signal between two brain areas. It is thought to reflect the degree of functional connectivity between brain regions, although its functional physiological significance remains unclear.

Clinical Use in Psychiatric Practice

When electroencephalography was first introduced by Hans Berger in 1929, the hope was that it would directly aid the diagnosis of the major mental disorders—schizophrenia, depression, and anxiety. This hope has long since been abandoned. Nonetheless, the EEG remains a valuable part of psychiatric clinical practice. It is mainly helpful in the diagnosis of neurological disorders—such as delirium, dementia, and epilepsy—that must often be ruled out in the differential diagnosis of many "nonorganic" psychiatric disorders.

Although the EEG does not play a direct role in the diagnosis of psychiatric disorders, the EEGs in such disorders often do show abnormal (although nonspecific) features. In the following sections, I summarize some characteristic features of the EEG in dementia, delirium, schizophrenia, and other psychiatric disorders.

Dementias

In general, the EEG in patients with dementia is characterized by relatively low-frequency rhythms with an increase in the amount of delta and theta waves and a relative decrease in the amount of high-frequency beta activity. In addition, the alpha rhythm is slowed, and in some individuals its normal suppression to eye opening is not observed. These features may be particularly helpful in distinguishing dementia from depression in elderly persons.

It is thought that at least half of the individuals with minimal impairment on the Mini-Mental State Examination show some EEG abnormalities. It has therefore been suggested that the EEG may aid the diagnosis of dementia at an early stage in the disease course. Moreover, increased slow activity is correlated with cognitive impairment and measures of clinical severity in Alzheimer's disease. qEEG studies in dementia are consistent with conventional EEG findings, confirming increased delta and/or theta power.

Although the etiology of dementia cannot be determined by use of the EEG alone, certain types of dementia are characterized by particular EEG features. For example, focal EEG abnormalities are more common in vascular dementias (although not in diffuse white matter ischemic disease [Binswanger's disease]) than in primary degenerative dementias. In frontotemporal dementias such as Pick's disease, the posterior dominant background rhythm is relatively well preserved, whereas increases in slow waves are less pronounced and, when they occur, tend to be distributed anteriorly. In Creutzfeldt-Jakob disease, the EEG is characterized by frontally distributed triphasic waves and paroxysmal epileptiform discharges.

Delirium

The hallmark of the EEG in delirium is a slowing of the background rhythm. The exception to this is delirium tremens, in which the EEG is characterized by fast rhythms. The appearance of generalized slow-wave activity during a delirium often parallels the severity and time course of alternations in consciousness. In addition to increased slowing, other specific EEG patterns are associated with particular metabolic encephalopathies. For example, frontal triphasic waves at a frequency of 2 or 3 per second are particularly characteristic of a hepatic encephalopathy and may also occur in patients with chronic renal failure.

Schizophrenia

There are no EEG changes that are specific to schizophrenia. Nonetheless, across a large number of studies, there is some consensus that patients with schizophrenia show a high incidence of EEG abnormalities, including increased delta and theta rhythms. Evaluation of the EEG in schizophrenia is complicated by the heterogeneity of the disorder itself and by the effects of medication. Indeed, the incidence of EEG abnormalities may be particularly high in patients taking atypical antipsychotic drugs such as clozapine and olanzapine.

Other Psychiatric Disorders

The incidence of abnormal EEG findings in mood disorders is thought to range from 20%–40%. Small sharp spikes and paroxysmal events have been described, and there are numerous reports of abnormal sleep patterns. Several studies have also suggested a high incidence of EEG abnormalities in anxiety disorders, including panic disorder and obsessive-compulsive disorder. There is no marked consistency across studies, however, in the precise patterns of abnormalities.

Event-Related Potentials

In the following subsections, I consider the issue of how an ERP component is defined and provide a brief overview of some of the better known ERP components that have been studied in psychiatric disorders.

Generation of Signal: Selective Averaging of EEG to Derive ERPs

Event-related potentials (ERPs) are voltage fluctuations, derived from the ongoing EEG, that are time-locked to specific sensory, motor, or cognitive events (Figure 6–3).

Suppose a stimulus is presented to a subject during EEG recording. Some of the voltage changes may be specifically related to the brain's response to that stimulus. In most cases, the voltage changes occurring

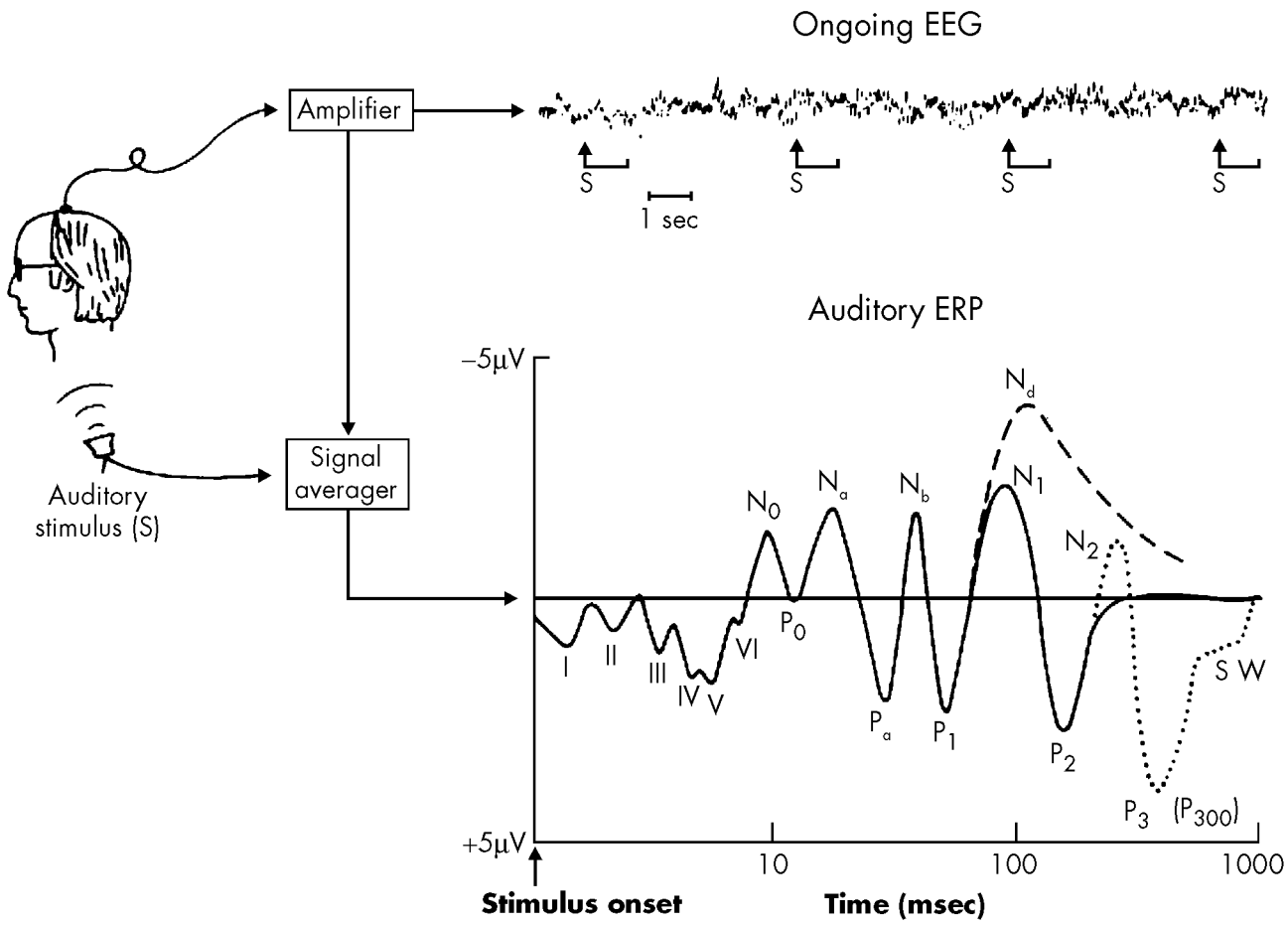

Figure 6–3. Idealized waveform of computer-averaged auditory event-related potential (ERP) elicited to brief sound.
The ERP is generally too small to be detected in the ongoing electroencephalogram (EEG) *(top)* and requires computer averaging over many stimulus presentations to achieve adequate signal-to-noise ratios. The logarithmic time display allows visualization of the early brain-stem responses (waves I–VI), the midlatency components (N_0, P_0, N_a, P_a, and N_b), the "vertex potential" waves (P_1, N_1, and P_2), and the task-related endogenous components (N_d, N_2, P_3, and slow wave [SW]). S=auditory stimulus; μV=microvolts.
Source. Reprinted from Hillyard SA, Kutas M: "Electrophysiology of Cognitive Processing." *Annual Review of Psychology* 34:33–61, 1983. Copyright 1983, Annual Reviews (www.annualreviews.org). Used with permission from *The Annual Review of Psychology,* Volume 34.

within a particular *epoch* (time period) of EEG following an event are on the order of microvolts and are therefore too small to be reliably detected. The most common way of extracting the signal is therefore to record a number of EEG epochs, each time-locked to repetitions of the same event (or type of event), and to derive an average waveform. EEG activity that is not time-locked to the event will vary randomly across epochs; thus, this background activity will disappear to zero in the averaging procedure.

In early research, the term *evoked potentials* was used to describe these waveforms, because it was believed that they reflected brain activity that was directly "evoked" by the presentation of stimuli. Many of these waveforms, however, are now thought to reflect processes that arise from the cognitive demands of the situation—hence the use of the more neutral term *event-related potentials.*

What Is an ERP "Component"?

Particular regions or temporal windows of the ERP waveform have been differentiated and labeled according to their polarity (positive [P] or negative [N]), their peak latency, and/or their ordinal position. These are called ERP components. ERP components have traditionally been classified as either *exogenous* (i.e., generally occurring within 200 msec of stimulus onset and

determined by the physical nature of the eliciting stimulus) or *endogenous* (i.e., sensitive to changes in the state of the subject, the meaning of the stimulus, and/or the processing demands of the task). The question of what constitutes a distinct ERP component remains controversial. Most researchers define components on the basis of their polarity, their scalp distribution, their characteristic latency, and their sensitivity to experimental manipulations.

As a rule of thumb, differences in the polarity and/or scalp distribution are usually interpreted as reflecting the activity of distinct neuronal populations subserving qualitatively different neurocognitive processes. This is not necessarily the case, however, because a waveform observed on the surface of the scalp may result from the summation of electrical activity that may be generated by several different sources in the brain. Thus, an ERP peak may not necessarily reflect activity of a single neuronal generator but rather the combined activity of two (or more) generators maximally active before or after that peak, but with fields that summate to a maximum at the time of the peak.

Because ERPs are time-locked to specific events and their measurement does not require an overt response by the subject, they provide important information about the relative time course of cognitive events. Once again, however, it is difficult to extrapolate from the waveform seen at the surface of the scalp to the underlying neurocognitive process. For example, is it the timing of a peak itself that is more informative about cognitive processing, or is the timing of the peak's onset of most relevance? Does a peak appear when a particular cognitive process is complete? Or does it indicate that enough information has accumulated to cross threshold and trigger the onset of a cognitive operation?

Abnormalities in Specific ERP Components in Psychiatric Disorders

In this section, I briefly review four of the ERP components studied in psychiatric research—the contingent negative variation (CNV), the mismatch negativity (MMN), the P300, and the N400. I first provide a brief description of the paradigms that elicit each of these components, and then summarize studies that have examined these components in different psychiatric populations.

The Contingent Negative Variation

The CNV was first described by Walter and colleagues in 1964. In their original paradigm, a warning click was presented, followed by a flashing light. The subject was required to press a button in response to the light. During the interval between the click and the light, a slow negative wave was observed that reached its peak at around the time of the light presentation—the CNV. The CNV was not evident when the click or the light was presented alone or when they were paired without the response requirement. Although it was originally described as an "expectancy" wave, more recently the CNV has been linked with the motor or goal-directed preparatory processes. Several studies have reported a reduced amplitude of the CNV in patients with schizophrenia and patients with depression. These findings have generally been interpreted fairly nonspecifically as reflecting abnormalities in attentional processes.

The Mismatch Negativity

At about 200 milliseconds (msec) following the presentation of auditory events that deviate in some way from the surrounding events, a negative component is observed—the N200 or N2. The difference waveform between the improbable events (signals) and the surrounding events (standards) is called the MMN. The MMN is observed in response to events that are improbable with respect to a number of factors, such as frequency and duration. It is seen in association with both attended and unattended events.

Several studies have reported that the MMN is reduced in patients with schizophrenia, particularly in response to events that are deviant in duration. A reduced MMN has been reported in both medicated and unmedicated patients as well as in unaffected first-degree relatives of patients. Functional magnetic resonance imaging (fMRI) findings suggest that patients with schizophrenia show abnormally reduced activity of the superior temporal cortex in association with mismatch events. It has been hypothesized that the reduced MMN in patients with schizophrenia reflects a specific deficit in auditory sensory memory. The specificity of MMN deficits to schizophrenia remains controversial; some (but not all) studies have also reported a reduced MMN in association with depression.

The P300

The P300 is probably the best-studied of all ERP components, both in healthy volunteers and in psychiatric populations. The standard paradigm eliciting the P300 is similar to the one described above in relation to the MMN: a series of events are presented of which one class is rarer than the other—hence the name *oddball*

task. Subjects are required to respond in some way to the rarer of the two events. The ERP elicited consists of a positive deflection that is maximal over the parietal/central scalp electrodes and has a latency of at least 300 msec and as much as 900 msec. In simple oddball tasks, the amplitude of the P300 depends on probability: the rarer the event, the larger the P300. It has been proposed that the P300 reflects the process by which contextual information is updated within memory. Several investigators, however, have noted that the P300 does not appear to be a unitary component. Indeed, recent fMRI studies that used oddball paradigms revealed widespread brain activation, distributed throughout many cortical and subcortical regions.

There have been numerous investigations of the P300 in patients with a variety of psychiatric disorders, particularly schizophrenia. The most robust finding in schizophrenia patients is of an abnormally reduced P300 amplitude. In some studies, the P300 latency is increased. The reduced P300 amplitude is particularly robust when auditory rather than visual stimuli are presented. The reduced P300 amplitude has been described in patients having their first episode of psychosis and in patients who are not taking medication. Some studies have suggested that the reduced P300 amplitude is associated with negative symptoms and with positive thought disorder (disorganized speech). Moreover, there is some evidence that the P300 amplitude becomes larger as symptoms ameliorate in the same patients over time, although it does not appear to normalize completely. These findings suggest that the reduced P300 may be both a state and a trait marker in schizophrenia.

A reduced P300 has also been reported in individuals who are at risk for developing schizophrenia and in healthy individuals who have loosening of associations similar to that observed in schizophrenia patients with positive thought disorder. Some studies, but not all, have reported a greater reduction of the P300 amplitude on the left than the right side in schizophrenia. Several studies also have linked structural gray matter deficits in temporal regions with a reduced P300 in schizophrenia.

Although an abnormal P300 is a very reliable finding in schizophrenia, it is not specific to schizophrenia. Studies have also reported abnormalities in the P300 waveform in association with dementia, substance abuse, depression, anxiety disorders (panic disorder, obsessive-compulsive disorder, and posttraumatic stress disorder) and in association with some personality disorders (schizoid, antisocial, and borderline).

The N400

The N400 ERP component is a negative shift in the ERP waveform that occurs approximately 400 msec following the onset of contextually inappropriate words. The N400 was first described in association with conceptual (i.e., semantic and pragmatic) violations in sentences (e.g., the N400 elicited in response to the word "dog" is of greater amplitude than the N400 elicited to the word "milk" when preceded by the sentence fragment, "He took coffee with sugar and ___"). Subsequent studies have established that the N400 amplitude is sensitive to the organization of semantic memory during the processing of word pairs, whole sentences, and whole discourse.

The observation that many patients with schizophrenia appear to show abnormalities in processing relationships between concepts provided the impetus for a large number of studies that have examined the N400 in schizophrenia. Some of these studies report a relatively intact N400 congruity effect in schizophrenia. Other studies, however, have reported an abnormally reduced N400 effect in both sentence and word-pair paradigms. One reason for these contradictory findings may be heterogeneity in the schizophrenia patient samples studied. Indeed, there is some evidence that the N400 effect is inversely correlated with severity of positive thought disorder in schizophrenia. Some investigators have also reported an increase in the absolute amplitude of the N400 waveform elicited in response to contextually appropriate and contextually inappropriate words, suggesting that schizophrenia patients have difficulty processing the meaning of words, regardless of the surrounding context.

Modifications of standard word association and sentence anomaly paradigms have yielded additional insights into the nature of conceptual abnormalities in schizophrenia. In a "mediated semantic priming" paradigm, an N400 congruity effect to words such as "stripes" preceded by indirectly related words such as "lion" (related to "tiger," which in turn is related to "stripes") has been reported in schizophrenia patients but not healthy control subjects. This finding is consistent with the hypothesis that activity spreads abnormally far across interconnected representations in semantic memory in schizophrenia patients. In a sentence paradigm, an N400 effect was elicited in healthy volunteers, but not in patients with schizophrenia, in response to words (e.g., "river") that were preceded by a semantically associated homonym (e.g., "bridge") when the surrounding context (e.g., "They took out their cards and started to play ___") suggested the sec-

ondary meaning of the homonym. Whereas in control subjects, the context of the whole sentence overrode the semantic associative effects of the sentence's individual words, this result did not occur in patients with schizophrenia.

Probably the most robust abnormality described across N400 studies in schizophrenia is an increased N400 latency. This abnormality has been reported in both word and sentence paradigms and suggests that the contextual integration of words may be delayed in schizophrenia.

Extracting Spatial Information: Source Localization From Multichannel Encephalography and Magnetoencephalography

The high temporal resolution of electrophysiological techniques is a clear advantage over other functional neuroimaging techniques—such as fMRI, positron emission tomography (PET), and single photon emission computed tomography (SPECT)—that look at events over the course of seconds. However, the EEG and ERPs provide very little information about the anatomic location of the neural systems that give rise to scalp-recorded voltage patterns.

In the past few years, there has been some progress toward improving the spatial resolution of EEG/ERPs by measuring over multiple channels distributed across the scalp surface and by using source localization methods to locate the underlying neural generator(s). In parallel, another technique—magnetoencephalography—has evolved from single-channel systems to multichannel systems that can monitor well over 100 channels simultaneously. The magnetoencephalogram (MEG) detects a magnetic signal that is derived from the same electrical currents that produce the EEG. Indeed, the raw MEG strikingly resembles the EEG, with alpha, mu, and tau rhythms. Similarly, the same types of signal averaging as described above that give rise to distinct ERP components also give rise to analogous waveforms when similar paradigms are used in the MEG (Figure 6–4). However, rather than focusing on the waveform itself, most MEG studies have emphasized source localization.

In the following section, I introduce the principles of source localization. I highlight implications of differences in the EEG and MEG signals and emphasize some caveats in regard to interpreting source localization data. I then summarize the potential for such methods to yield new insights into psychiatric disorders.

Source Localization

Multichannel electroencephalography and magnetoencephalography can be used to generate spatial maps of the EEG potential and the magnetic field, respectively, over the surface of the scalp at different points in time. There are important differences in the types of maps derived from MEG and EEG. These differences can be predicted from magnetic and electrical theory and have important implications for determining the underlying source that gives rise to the two types of maps. First, for a source that is oriented radially with respect to the scalp surface (including sources near the center of the head), an EEG signal, but not a MEG signal, can be detected over the scalp. In other words, the EEG sees both radial and tangential sources, whereas the MEG sees only tangential sources. Second, for sources that are oriented tangentially to the scalp surface, because of the orthogonality between magnetic and electrical fields, the MEG map is perpendicular to the EEG map. Third, the electrical conduction of currents through the brain and skull leads to *smearing*, or low-pass filtering of the voltage pattern in EEG, whereas the MEG is only minimally affected by surface smearing. Therefore, the MEG produces a somewhat "tighter" map than the EEG. For all of these reasons, MEG and EEG recordings provide different but complementary information about underlying neural sources and are therefore often collected together.

A mathematical model can then be applied from maps at the scalp surface to estimate the most likely source in the brain responsible for this surface field distribution. For a single focal source (or dipole), this mathematical model is relatively straightforward and is called a simple "inverse solution." This model must take into account neurophysiological and neuroanatomic information. For example, one would not expect to localize primary sensory sources extracerebrally or in white matter distant from primary sensory cortex. One can then apply a "goodness of fit" calculation to reflect the agreement between the known surface topography that the estimated source would produce as a function of the ideal mathematical "forward solution" and the actually measured field pattern.

More complex mathematical models must be ap-

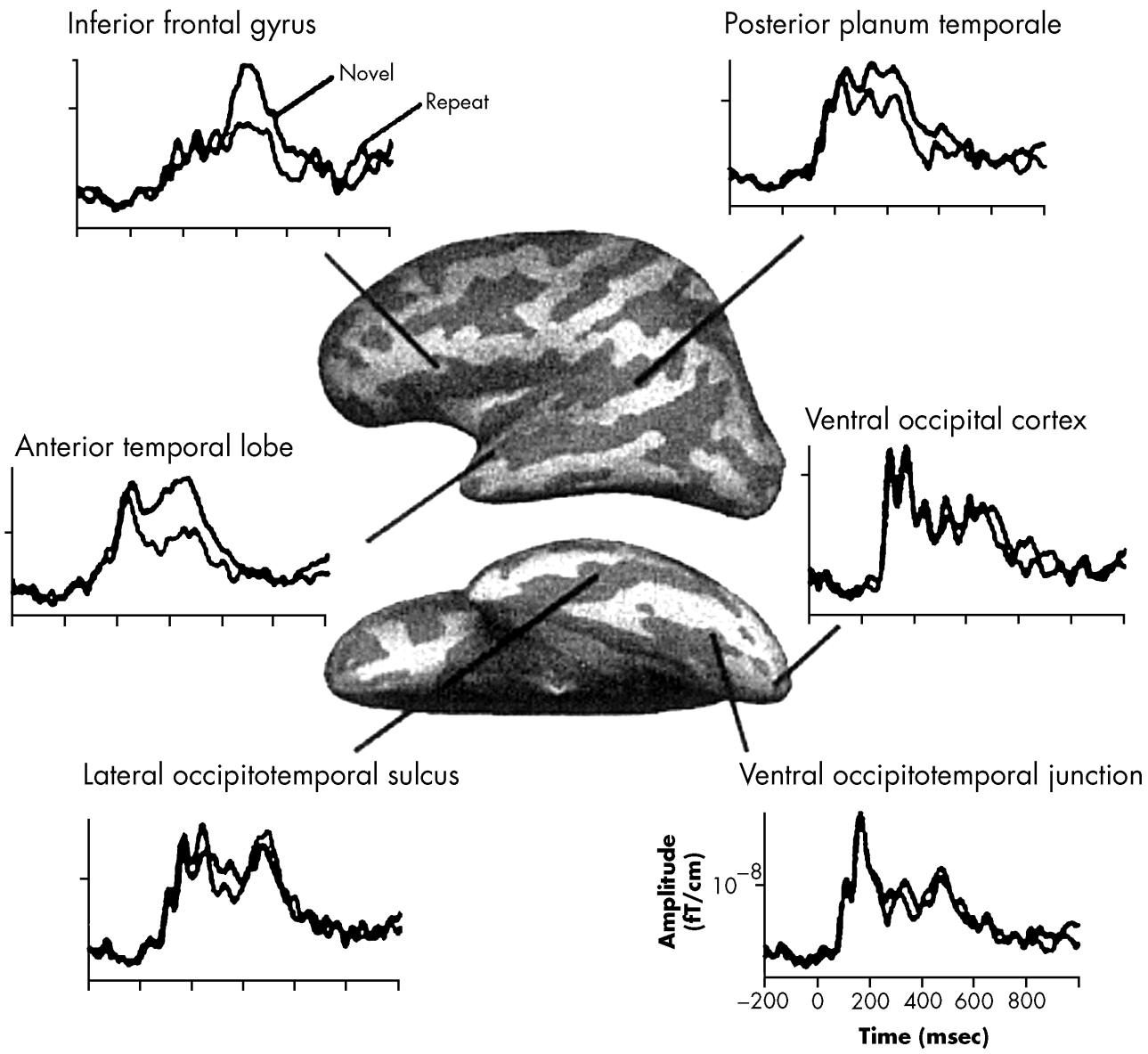

Figure 6–4. Time courses of MEG data at selected brain locations.
Waveforms show activity in response to words that are novel or repeated during a word-stem completion task. Occipital regions are activated early and do not change with repetition, whereas more anterior regions activate later and show strong replication effects.
Source. Reprinted from Dhond RP, Buckner RL, Dale AM, et al.: "Spatiotemporal Maps of Brain Activity Underlying Word Generation and Their Modification During Repetition Priming." *Journal of Neuroscience* 21(10):3564–3571, 2001. Copyright 2001, The Society for Neuroscience. Used with permission.

plied to more complex maps. For example, longer-latency endogenous complex potentials such as the N400 probably arise from multiple anatomic sources. A given spatiotemporal voltage pattern at the scalp may arise from more than one configuration of sources and is determined not only by their sites but also by their orientations. Thus, even if it is mathematically possible to calculate the inverse solution in such cases (and sometimes even to find a relatively high goodness of fit), it is important to recognize that this solution is not necessarily correct. Nonetheless, the application of such complex models has already yielded new insights into the time course of brain activity during higher-order cognitive processes such as memory and language (Figure 6–5).

One approach that has been employed to improve

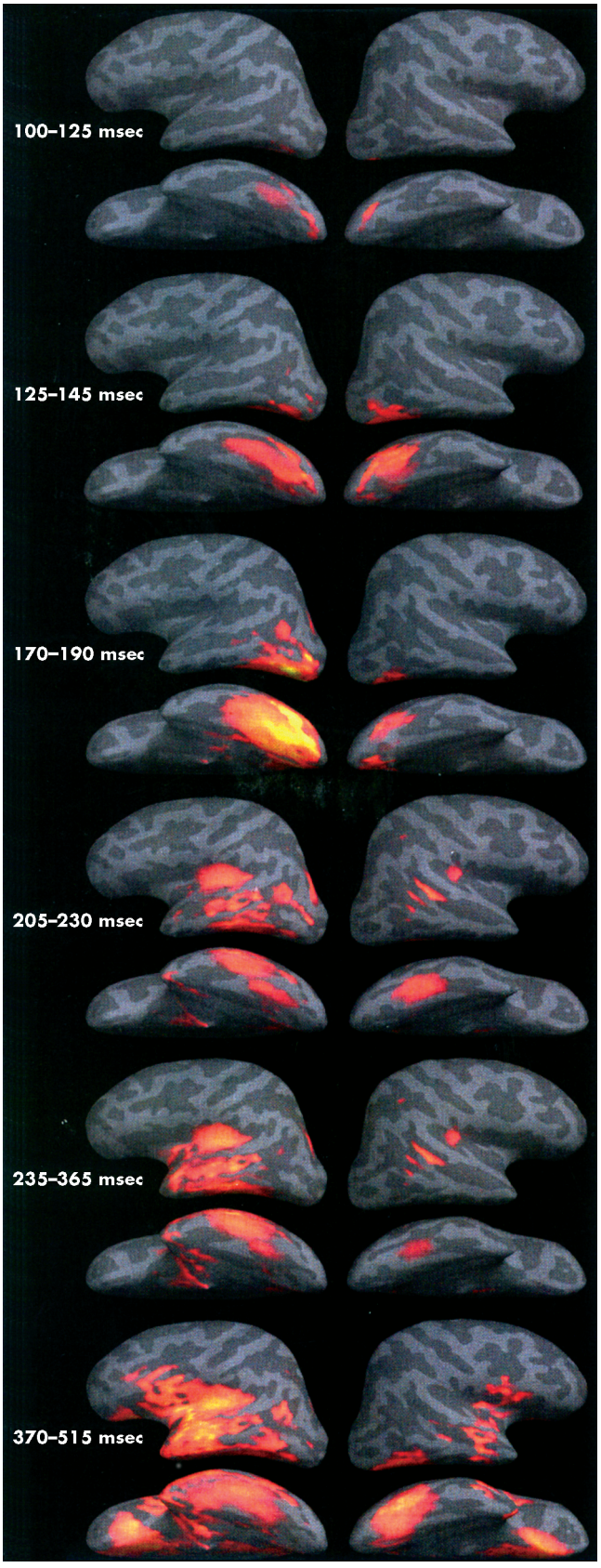

Figure 6–5. Estimated cortical activity patterns at different latencies after reading word stems, as measured with magnetoencephalography.
Activation begins with a bilateral visual response in the posterior occipital cortex (100–125 msec) and subsequently spreads forward into the ventral occipital cortex (125–145 msec) and lateralizes to the left hemisphere (170–190 msec). It then spreads to both posteroventral and lateral temporal areas (205–230 msec) and progressively extends to the anterior temporal (235–365 msec) and ventral prefrontal (370–515 msec) cortices, before fading after 515 msec.
Source. Reprinted from Dhond RP, Buckner RL, Dale AM, et al.: "Spatiotemporal Maps of Brain Activity Underlying Word Generation and Their Modification During Repetition Priming." *Journal of Neuroscience* 21(10):3564–3571, 2001. Copyright 2001, The Society for Neuroscience. Used with permission.

source modeling is to use fMRI data (collected by using identical stimulus presentation paradigms in the same subjects) as a spatial constraint. Important caveats apply to use of such an approach, however. Whereas the coupling between electrical activity in the brain and the EEG and MEG signals measured on the surface of the scalp follows from fundamental laws of physics and is relatively well understood, the coupling between neuronal activity and hemodynamic measures such as fMRI is not well understood. Thus, the precise relationships between hemodynamic signals measured with fMRI and electrical and magnetic signals measured with EEG and MEG are unclear. In particular, there are few quantitative data on how the magnitude of the hemodynamic response varies as a function of the amplitude and duration of electromagnetic activity. There is, however, increasing evidence for a strong degree of spatial correlation between various measures of local electrical activity and local hemodynamic signals. Some of the most persuasive evidence for such a correlation comes from a direct comparison of maps obtained through use of voltage-sensitive dyes, reflecting depolarization of neuronal membranes in superficial cortical layers, and maps derived from intrinsic optical signals, reflecting changes in light absorption due to changes in blood volume and oxygenation. Earlier animal studies have also shown strong correlations among local field potentials, spiking activity, and voltage-sensitive dye signals. Moreover, studies using invasive electrical recordings and fMRI to compare localization of functional activity in humans also provide evidence for a spatial correlation between the local electrophysiological response and the hemodynamic response.

Use of Magnetoencephalography in Psychiatry

The two current most common clinical uses of magnetoencephalography are in localization of epileptiform activity and presurgical mapping of sensory cortex prior to neurosurgical procedures.

The use of multichannel electroencephalography and magnetoencephalography in psychiatric research is in its infancy. Nonetheless, MEG studies have already contributed to our knowledge of specific components such as early auditory field potentials (the N100) in schizophrenia and somatosensory ERPs in affective psychoses. As discussed earlier, the development of more comprehensive models and the integration of magnetoencephalography with other functional neuroimaging techniques will enable study of the sources that give rise to endogenous ERPs. Such research will allow us to gain insight into the spatial and temporal dynamics of neural systems underlying abnormal cognitive function in psychiatric disorders.

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