Neurophysiological and Neuroimaging Techniques

Robin Nusslock, Christina B. Young, Narun Pornpattananangkul, and Katherine S. F. Damme
Northwestern University, U.S.A.

There has been a growing movement over the past three decades to place models of psychiatric disorders into a biological framework. This movement has recently been championed by the National Institute of Mental Health with the development of the Research Domain Criteria Initiative (RDoC), which calls for new ways of classifying psychiatric illness based on core brain–behavior dimensions (Insel et al., 2010). Examining these brain–behavior dimensions can inform our understanding of the pathophysiology of psychiatric illness, facilitate the identification of biological markers that can aid scientific investigation and differential diagnosis, and generate targeted treatment protocols.

This movement has been spearheaded by methodological advancements in the field of neuroscience and bioengineering. Three techniques for investigating brain function that have made important contributions to clinical psychological research are quantitative electroencephalography (EEG), event-related potentials (ERPs), and functional magnetic resonance imaging (fMRI). Each of these techniques has pros and cons, largely involving a trade-off between spatial and temporal resolution. *Spatial resolution* involves the ability to identify the biological source of a particular signal and to distinguish two separate structures close to each other in space. *Temporal resolution* refers to the ability to determine the order of occurrence of two events close to each other in time.

Quantitative Electroencephalography

The first EEG recording in humans was performed in 1924 by a German psychiatrist named Hans Berger. Using two electrodes, Berger observed spontaneous rhythmic activity oscillating at approximately 10 Hz during relaxed wakefulness in the absence of sensory input. This rhythmic activity would become known as alpha activity, and Berger was among the first to relate fluctuations in human EEG to different psychological states. The field of human neurophysiology has come a long way since Berger's landmark observation. It is now established that scalp-recorded EEG oscillations are generated by the summation of both excitatory and inhibitory postsynaptic potentials in tens of thousands of cortical pyramidal neurons. Placing electrodes at the scalp allows measurement of these small but reliable potentials.

Over the decades, researchers have developed techniques for reducing raw EEG signals into metrics that reflect the activation or deactivation of various brain regions. These techniques, referred to as spectral analyses, typically summarize EEG data into conventionally defined frequency bands. The delta band reflects low-frequency activity (1–4 Hz) typically associated with the deepest stages of sleep in healthy humans, also known as slow-wave sleep. Theta activity involving EEG activity within the 4–8 Hz range is also prominent during sleep. Elevated activity in the alpha band (8–13 Hz) is indicative of less cortical neuronal activity. Support for this claim comes from research combining EEG and positron emission tomography (PET) that demonstrates an inverse relationship between glucose metabolism (an index of neuronal activity) and alpha activity in cortical regions underlying the specified EEG electrode. Both beta (13–30 Hz) and gamma

The Encyclopedia of Clinical Psychology, First Edition. Edited by Robin L. Cautin and Scott O. Lilienfeld.

DOI: 10.1002/9781118625392.wbecp557

(36–44 Hz) activity reflect increased neuronal activity, arousal, and attention.

Clinical psychological research involving quantitative EEG frequently compares individuals with and without clinical disorders on one or more of these frequency bands. A topic in mood and anxiety disorder research that has received considerable attention over the past three decades involves asymmetrical activity in the alpha frequency band over the frontal cortex. Investigators conducting this research often use a difference score, ln(Right) −ln(Left) alpha power, to conveniently summarize the relative activity at homologous right-hemisphere and left-hemisphere electrodes. Given that alpha power is inversely related to cortical activity, this asymmetry index provides a unidimensional scale in which greater values indicate greater relative left hemispheric cortical activity and lower values indicate greater relative right hemispheric cortical activity. The approach–withdrawal model of frontal alpha asymmetry argues that increased relative left-frontal cortical activity reflects an elevated sensitivity to reward-relevant cues and a propensity to approach or engage a stimulus (Coan & Allen, 2004). By contrast, increased relative right-frontal cortical activity reflects decreased reward sensitivity and a propensity toward reduced approach-related motivation. In line with this view, over two dozen studies have reported that individuals with depression display increased relative right-frontal cortical activity (Thibodeau, Jorgensen, & Kim, 2006). These data are in line with clinical and epidemiological research indicating that depression is associated with decreased sensitivity to reward-relevant cues and decreased approach motivation and goal-directed behavior. Furthermore, these data have been interpreted in the context of a vulnerability–stress framework in which elevated right-frontal cortical activity reflects a preexisting risk factor for depression onset. Consistent with this view, elevated right-frontal cortical activity has been observed in the offspring of depressed individuals who have yet to experience a depressive episode themselves. Collectively, these data suggest that increased relative right-frontal cortical activity may be a neurophysiological marker of depression risk status.

Research using EEG has also made important contributions to understanding sleep disturbances in clinical disorders. Given the noninvasiveness of EEG systems, neurophysiological data can be recorded while participants sleep either in their own home or in a sleep laboratory. Relevant to this research, sleep architecture refers to a specific type of EEG patterning and is typically divided into rapid eye movement (REM) and non-REM sleep. Non-REM sleep is further categorized into four stages, with stages 1 and 2 considered lighter sleep stages and stages 3 and 4 referred to as slow-wave, delta, or deep sleep. REM sleep is characterized by rapid and random eye movements and vivid dream recall. REM latency refers to the interval of time from sleep onset to REM onset, and REM density is the ratio of REM activity to the total duration of REM sleep recorded during a night. Clinical disorders such as major depressive disorder are associated with an increase in both REM activity and REM density as well as a decrease in both REM latency and delta-wave sleep.

Advantages and Disadvantages of Quantitative Electroencephalography

Quantitative EEG has a number of advantages for clinical psychological research. First and foremost, it is feasible and cost-effective. Unlike MRI, once an investigator has purchased an EEG system, there are minimal costs associated with maintenance and data collection. Accordingly, EEG technology is very amenable for use in more clinical or treatment-oriented settings. Second, EEG technology is noninvasive and relatively resistant to movement- and muscle-related artifacts. This advantage is particularly relevant when studying children or clinical conditions such as mania or attention deficit hyperactivity disorder (ADHD), where it can be challenging for participants to sit still for extended periods of time. Lastly, given that EEG involves recording electrical activity of

neuronal assemblies, it has the potential to provide temporal resolution on the order of milliseconds as opposed to seconds afforded by fMRI.

The primary limitation of EEG is that it provides poor spatial resolution. Considering that the diameter of EEG electrodes is orders of magnitude larger than single neurons and that the area of an electrode covers approximately 250,000 neurons, it is clear that many neurons must be activated to detect an EEG signal at the scalp. The distorting effects of the head volume, low signal-to-noise ratios, and the limited spatial sampling due to practical limits on the number of electrodes that can be employed also contribute to poor spatial resolution in EEG. Perhaps most troubling, however, is what is typically referred to as the inverse problem. The inverse problem is the fact that there are an infinite number of neuronal source configurations that can explain a given set of scalp-recorded signals. Thus, we cannot know with certainty the correct configuration, and there is no way of generating a reliable margin of error for any attempt to localize the source configuration. Given that one objective of clinical neuroscience is to link clinical symptoms to specific neural processes, EEG is limited in this capacity.

Despite these challenges, researchers have developed mathematical techniques that attempt to model the neuronal generators of scalp-recorded signals. These source localization techniques are relatively robust to noise and informed by anatomy, neurophysiology, MRI, and volume conduction physics. Common source localization techniques include low-resolution brain electromagnetic tomography (LORETA) and brain electrical source analysis (BESA). Although promising, these techniques are typically restricted to cortical gray matter given that scalp-recorded EEG oscillations reflect postsynaptic potentials in cortical neurons. Thus, many of the subcortical neural regions implicated in clinical disorders (e.g., amygdala) are not accessible by source localization or EEG more generally. Researchers have also raised conceptual and technical concerns about source localization and the assumptions underlying these techniques (Luck, 2005).

A second limitation of quantitative EEG relates not to the technique itself, but to how researchers frequently process and analyze EEG-related data. The spectral analyses frequently used in quantitative EEG research to compute power estimates for resting data average across a series of 1 min epochs or time windows. Task-related spectral analyses frequently involve 6–7 s epochs. Thus, despite measuring electrical activity of neuronal assemblies on the order of milliseconds, the spectral analyses typically employed in clinical research provide surprisingly poor temporal resolution. In fact, the temporal resolution afforded by these analytic strategies is equivalent to the limited temporal resolution of fMRI. Fortunately, researchers have begun to address this issue by developing EEG modeling techniques such as event-related spectral perturbation (ERSP) that take full advantage of the millisecond temporal resolution that EEG data are able to provide.

Event-Related Potentials

In their raw form, EEG data are a rather coarse measure of brain activity that are difficult to use for the assessment of specific cognitive and affective neural processes that are often the focus of clinical neuroscience. Embedded within EEG data, however, are neural responses associated with specific sensory and cognitive events, and it is possible to extract these responses from overall EEG by means of simple averaging techniques. These specific responses are called ERPs to denote the fact that they are electrical potentials that occur in preparation for, or in response to, discrete events, whether they are internal or external to the participant. Conceptually, ERPs are regarded as neural manifestations of specific psychological functions. Like EEG, ERPs are generated predominately from postsynaptic potentials in cortical pyramidal neurons, and the recorded voltage

reflects the sum of many underlying ERP components that overlap in time. The advantage of ERP is that it provides arguably the best temporal resolution of any neurophysiological or neuroimaging method utilized in clinical psychological research. ERPs have a temporal resolution of 1 ms or better under optimal conditions, leading this to be referred to as the "reaction time for the 21st century" (Luck, 2005).

Although the first sensory ERP recordings from humans were performed in the 1930s, it was not until the advent of digital computers in the 1960s that ERPs gained traction. The procedures used to derive ERPs begin with the same electrodes and amplifiers used to obtain EEG data. The experimental questions and analytical procedures, however, are very different between EEG and ERP. The ERP is small (a few microvolts) in comparison to EEG (about 50 mV). Thus, analysis generally begins with procedures to increase the discrimination of the signal (ERP) from the noise (background EEG). The most common of these procedures involves averaging samples of EEG data that are time-locked to repeated occurrences of a particular experimental event. The resulting averaged ERP waveforms consist of a sequence of positive and negative voltage deflections, which are called peaks, waves, or components. Figure 1 displays a typical ERP. In this figure, the peaks are labeled P1, N1, P2, N2, and P3. P and N are traditionally used to indicate positive-going and negative-going peaks, and the number simply indicates a peak's position within the waveform (ERP waveforms are sometimes plotted with negative voltages upward and positive voltages downward, as this was the convention among early physiologists). Importantly, the latency of a peak in milliseconds is often approximately 100 times the ordinal position, so that P1 is often referred to as P100, N2 as N200, P3 as P300, and so on. The sequence of ERP peaks reflects the flow of information through the brain. Thus, ERP affords researchers the ability to examine the temporal unfolding of neurocognitive processes to specific stimuli or manipulations.

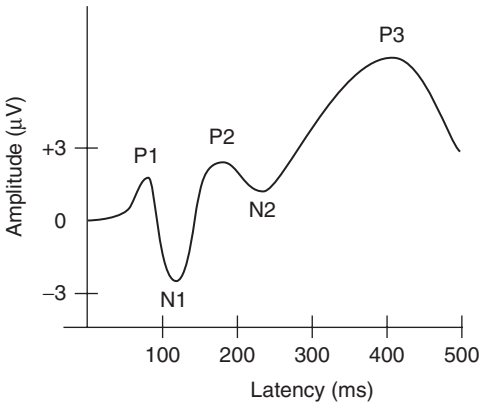

Figure 1 Example of an event-related potential (ERP) component.

Early or initial ERP components that occur within approximately 100 ms of the stimulus (e.g., P1 and N1) are typically referred to as "sensory" or "exogenous" components because they will always be generated if the stimulus is perceived. These early sensory evoked potentials index automatic attention to stimuli and are frequently used in the diagnosis of neurological diseases, such as multiple sclerosis and congenital deafness. Subsequent ERP components (e.g., N2 and P3) typically do not depend on the physical properties of the eliciting stimulus but on the task performed by participants and the sustained allocation of attention to emotional stimuli. These components are typically referred to as "endogenous" components to indicate their dependence on internal rather than external factors.

ERP research has made important contributions to our understanding of the neurophysiology of clinical disorders such as depression, anxiety, and schizophrenia. With respect to depression, there is increasing evidence that individual differences in reward sensitivity can be measured using the feedback negativity (FN), an ERP component elicited by stimuli that indicate monetary gain versus loss. In gambling tasks, the FN appears as a relative negative deflection in the waveform approximately 300 ms following feedback indicating monetary gain versus loss, and it is thought to reflect

early, binary evaluation of outcomes as either better or worse than expected. In line with the approach–withdrawal model's hypothesis that depression is characterized by a reduced sensitivity to reward-relevant cues, individuals with depression display decreased amplitude of reward-related FN. Furthermore, lower FN amplitude prospectively predicts depression onset. Thus, both quantitative EEG and ERP research suggest that reduced reward-related brain activity may represent a neurophysiological marker of depression risk status (Bress, Foti, Kotov, Klein, & Hajcak, 2013).

ERP research has also contributed to our understanding of cognitive and attentional deficits in depression and anxiety. Both depression and anxiety are associated with a hypervigilance to negative stimuli, as reflected in an enhanced early ERP component (P1) to negative or threatening stimuli (Weinberg & Hajcak, 2011). There is also considerable behavioral and neuroimaging evidence that both depression and anxiety are associated with impairment in an executive control system that might account for patients' difficulties with cognitive tasks. In line with these data, ERP research has identified neural deficits in depressed and anxious individuals during executive control tasks involving both error processing (error-related negativity, or ERN) and response inhibition (N2 during response inhibition) (Holmes & Pizzagalli, 2010; Weinberg, Olvet, & Hajcak, 2010).

Lastly, there has been considerable interest in using ERP to examine deficits in sensory gating in psychotic disorders such as schizophrenia. Sensory gating is a neurological process of filtering out redundant or unnecessary information. Individuals with schizophrenia have a deficit in attending to stimuli and are often overloaded by attended stimuli. The P50 ERP test of sensory gating involves measuring the amplitude of the P50 component in response to two auditory clicks separated by 500 ms. In normal participants, the second P50 wave is suppressed or "gated" due to the inhibitory effects of the first click. Impaired suppression of the P50 wave has been identified as a vulnerability marker for sensory-gating deficits in schizophrenia and is one of the most established biological traits of schizophrenia (Clementz, Geyer, & Braff, 1998).

Advantages and Disadvantages of Event-Related Potentials

As noted, ERPs can provide temporal resolution of 1 ms or better under optimal conditions. This is a 1,000-fold advantage over the temporal resolution afforded by hemodynamic measures such as fMRI, which is also described in this entry. Furthermore, ERPs provide a continuous measure of the neural processing of stimuli that allows researchers to examine specific neurocognitive deficits (e.g., attention, error detection, and response inhibition) associated with clinical disorders. Unlike behavioral measures, ERPs provide an online measure of stimuli processing in the absence of a behavioral response. This allows researchers to covertly monitor neurocognitive processes that are outside the scope of conscious awareness. Many ERP components, such as the P3, have a test–retest reliability on the order of .8 or greater, which is comparable to many leading psychological tests. Lastly, like EEG, ERP is highly cost-effective, noninvasive, and resistant to movement and muscle-related artifact.

Like EEG, the primary limitation of ERP is that it provides poor spatial resolution and that, due to the inverse problem, we are unable to know with certainty the neuronal source configuration for a set of scalp-recorded signals. Furthermore, ERPs are generated largely by postsynaptic potentials in cortical pyramidal neurons that have a very specific spatial organization (i.e., open-field organization). Thus, ERPs represent just a portion of the brain's electrical activity in response to a particular event or stimuli. This limitation is relevant to clinical psychological research as many of the neural regions implicated in clinical disorders (e.g., amygdala and ventral striatum) are located in subcortical portions of the brain that cannot be indexed by ERP techniques. For this reason, some caution should be used in

the interpretation of ERP data. For instance, if an experimental manipulation has no effect on ERP profiles, we cannot be certain that it has no effect on the brain. Likewise, if two experimental conditions have the same effect on ERP, we cannot conclude that they influence identical neuronal processes. Thus, ERP is suited to answer a subset of questions, and it is important for researchers to be clear about what those questions are prior to conducting an ERP study.

Neuroimaging

Whereas neurophysiology assesses EEG oscillations or electrical potentials emitted from the skull, neuroimaging techniques are able to generate maps of underlying neuronal organization and function. Neuroimaging is broadly classified into structural and functional imaging. The most common structural imaging technique for human research is MRI. MRI uses a series of changing magnetic gradients and oscillating electromagnetic fields. Depending on the frequency of the electromagnetic fields, energy may be absorbed by atomic nuclei. MRI scanners are tuned to the frequency of hydrogen nuclei, which are the most common in the human body due to their prevalence in water molecules. After the electromagnetic energy is absorbed, it is later emitted by the nuclei, and the amount of emitted energy depends on the numbers and types of nuclei present. Using this emitted energy, researchers are able to generate high-resolution images of underlying biological tissues.

Structural MRI research has made important contributions to our understanding of the neural pathophysiology of clinical disorders. More than 300 peer-reviewed articles have delineated subtle neuroanatomic abnormalities in schizophrenia. These abnormalities include increased lateral ventricular size and reduced gray matter density in a distributed network of neural regions relative to healthy controls. Meta-analytic research indicates that these structural abnormalities may be present before the onset of a first psychotic episode and may be predictive of the development of psychosis within high-risk participants. Other structural MRI research has identified volumetric reductions in prefrontal regions involved in emotion regulation and volumetric enlargement in subcortical regions involved in emotion generation (e.g., amygdala) in multiple psychiatric disorders, including depression, bipolar disorder, and ADHD. This work is in line with the perspective that many clinical disorders involve an excess of "bottom-up" emotion generation and deficits in "top-down" prefrontal regulation of emotion. Lastly, structural MRI may help delineate neurodevelopmental processes associated with clinical disorders. For example, whereas adults with bipolar disorder typically display enlarged amygdala volume relative to healthy controls, children with bipolar disorder often display reduced amygdala volume relative to healthy controls. This discrepancy either suggests that child and adult bipolar disorder are distinct disease processes, or suggests that there are important neurodevelopmental processes associated with the course of bipolar disorder.

Structural MRI research in clinical neuroscience has focused predominately on gray matter that contains neural cell bodies. More recently, however, clinical neuroscientists have begun to employ diffusion MRI techniques such as diffusion tensor imaging (DTI) and diffusion spectrum imaging (DSI) to examine white matter pathways in clinical disorders. White matter consists mostly of glial cells and myelinated axons that serve as the anatomical pathways through which information is transmitted between different parts of the brain. Diffusion MRI techniques use radiofrequency and magnetic field gradient to measure the strength and direction of water diffusivity in brain tissue. The diffusivity of water molecules in white matter is modulated by axonal membrane thickness and diameter, the degree of myelination, and/or the amount of parallel organization of axons. Summary statistics of water diffusivity serve as an indicator of white matter pathway strength and integrity. There is growing evidence that multiple clinical

disorders, including depression, anxiety, and bipolar disorder, involve altered white matter microstructures in neural pathways connecting the prefrontal cortex to subcortical regions involved in emotion generation, such as the amygdala, which potentially underlies mood and emotional dysregulation.

Despite providing detailed information on neuronal tissue, structural imaging is limited by its static representation of the brain. Functional neuroimaging provides a powerful complement to structural imaging by generating maps of neuronal activation that can be linked to dynamic mental processes. Using functional neuroimaging, researchers are able to measure changes in brain function while participants perform experimental tasks or during a resting state. Researchers in the area of clinical neuroscience are then able to determine which profiles of neuronal activation relate to clinical symptoms or best distinguish individuals with and without a clinical disorder.

Two established functional neuroimaging techniques are PET and fMRI. PET is a nuclear medical imaging technique that involves injection of radioactive isotopes or tracers to image the tissue concentration of molecules. If the chosen tracer is fludeoxyglucose (FDG), an analog of glucose, the concentration of the imaged tracer indexes the level of neuronal activation in a given region. This is because the more active a brain region is, the more glucose that region requires for metabolic purposes. An advantage of PET is that the use of different tracers allows researchers to examine the tissue concentration and distribution of receptors of a variety of different molecules and neurotransmitters. For example, using PET, clinical neuroscientists have made important contributions to our understanding of the role of dopamine activity in a number of clinical and neurological disorders, including depression, bipolar disorder, substance abuse, and Parkinson's disorder. PET is limited, however, by relatively poor spatial and temporal resolution (typically, overall intervals of a minute or longer) and the invasiveness of injecting radioactive isotopes.

The neuroimaging technique that has arguably garnered the most attention over the past decade is fMRI. fMRI provides reasonable temporal resolution and exquisite spatial resolution, allowing researchers to localize brain activity on a second-by-second basis within millimeters of its origin. In fact, if a researcher's primary aim is to examine profiles of neural activation or deactivation to experimental manipulations, fMRI is currently the gold standard. The physics of fMRI is based on the assumption that information-processing activity of neurons increases their metabolic requirements. The vascular system supplies energy to meet these requirements in the form of two fuel sources, glucose and oxygen, the latter bound to hemoglobin molecules. Once supplied, oxygenated hemoglobin converts to deoxygenated hemoglobin. Given that deoxygenated hemoglobin has magnetic field gradients that alter the properties of nearby hydrogen nuclei, changes in the concentration of deoxygenated hemoglobin provide a measure of the level of neuronal activation. Thus, fMRI does not directly assess neuronal activity but rather generates an estimate of neuronal activation by indexing the metabolic correlates of neuronal activation.

Many significant contributions in clinical neuroscience have emerged from fMRI research. This research typically involves examining abnormalities in core brain–behavior dimensions in individuals with clinical disorders or the relationship between these dimensions and specific symptom profiles. A dimension that has received considerable attention in clinical neuroscience is threat processing or threat-related brain function. The amygdala is a neural region that is integral to threat processing and fear acquisition. fMRI research has identified amygdala hyperactivity to emotional stimuli in numerous clinical disorders, including depression, bipolar disorder, anxiety disorders, and personality disorders such as borderline personality disorder. This hyperactivity is in line with behavioral and clinical data indicating that these disorders are characterized by elevated negative affect and

general distress. In contrast, disorders characterized by reduced fear such as psychopathy have frequently been associated with reduced or blunted amygdala activation to emotional stimuli.

A second brain–behavior dimension relevant to clinical research is reward processing and reward-related brain function. As indicated, both EEG and ERP research indicate that depression is associated with reduced approach-related motivation and reward-related brain function. In line with this perspective, fMRI research demonstrates that individuals with, and at risk for, major depressive disorder display decreased ventral striatal activity to reward-relevant cues (Forbes, 2009). The ventral striatum is a core component of the neural circuitry underlying reward processing, and these data provide further support for the notion that depression is characterized by abnormalities in reward-related brain activity. fMRI research has made additional contributions to our understanding of abnormalities in brain–behavior dimensions such as cognition, attention, memory, and self- and emotional regulation in multiple other clinical disorders.

Historically, fMRI-based research has examined activation in one brain region in isolation from its relationship to other brain regions. This *localization of function* approach, however, is limited by the fact that no brain region exists in isolation. An active area of neuroimaging research involves examining the functional connectivity between spatially remote areas in the brain. Connectivity analyses allow researchers to characterize the relationships between distinct neural regions during cognitive, affective, or motoric tasks or from spontaneous activity during rest. Connectivity analyses have important implications for understanding the etiology of clinical disorders. This is due to the fact that clinical disorders may be characterized as much by abnormalities in the communication between brain regions, as they are by abnormalities in any one specific area of the brain. Future research is needed to test this hypothesis, and connectivity analyses will likely play an important role in clinical neuroscience for the foreseeable future.

Advantages and Disadvantages of Neuroimaging

Structural and functional neuroimaging provide researchers with a powerful set of techniques to examine abnormalities in both brain tissue and function in clinical disorders. Functional neuroimaging is able to circumvent the inverse problem encountered in neurophysiology and generate precise maps of underlying brain function. Furthermore, functional neuroimaging is able to index neuronal activation in subcortical regions such as the amygdala and ventral striatum that are typically inaccessible to neurophysiology. fMRI provides very strong spatial resolution and is most suited for examining a spatial range from millimeters to centimeters. Lastly, recent developments in both structural (DTI) and functional connectivity analyses allow researchers to move beyond examining neural regions in isolation and instead examine the relationships and communication pathways between brain regions. The more integrative systems approach that structural and functional connectivity analyses afford promises to be an important direction for clinical neuroscience.

There are a number of logistical challenges associated with neuroimaging. First, relative to neurophysiological techniques, neuroimaging is quite expensive and requires a significant infrastructure. Second, MRI requires participants to lie in a fairly small tube-like structure, referred to as the MRI bore. The confined nature of the MRI bore can be restrictive for participants with claustrophobia or weight-related issues. Third, MRI is very sensitive to movement-related artifacts, which can make it challenging to scan individuals prone to engage in significant motor or muscle-related movement (e.g., individuals in a manic episode, individuals with Parkinson's disease, individuals with elevated anxiety or panic, and children). Lastly, compared to ERP,

functional neuroimaging techniques that index hemodynamic activity such as fMRI provide relatively slow temporal resolution. The temporal resolution of fMRI is largely limited by the fact that the hemodynamic response that it indexes does not occur until 1–2 s after neuronal firing. Thus, the constraint on the temporal resolution of fMRI is as much biological as it is related to the capabilities of MRI technology.

It is clear that the strengths and limitations of neurophysiology and neuroimaging techniques are often complementary. That is, the strength of one technique is frequently the limitation of another, and vice versa. Accordingly, many researchers are moving toward a multimodal approach in which multiple assessment tools (e.g., EEG, ERP, and fMRI) are used within the same study. This approach allows researchers to assess clinical pathology at multiple levels of analysis along the continuum of spatial and temporal resolution.

SEE ALSO: Molecular Genetics

References

Bress, J. N., Foti, D., Kotov, R., Klein, D. N., & Hajcak, C. (2013). Blunted neural response to rewards prospectively predicts depression in adolescent girls. *Psychophysiology, 50,* 74–81.

Clementz, B. A., Geyer, M. A., & Braff, D. L. (1998). Poor P50 suppression among schizophrenia patients and their first-degree biological relatives. *American Journal of Psychiatry, 155(12),* 1691–1694.

Coan, J. A., & Allen, J. J. B. (2004). Frontal EEG asymmetry as a moderator and mediator of emotion. *Biological Psychology, 67,* 7–49.

Forbes, E. E. (2009). Where's the fun in that? Broadening the focus on reward function in depression. *Biological Psychiatry, 66,* 199–200.

Holmes, A. J., & Pizzagalli, D. A. (2010). Effects of task-relevant incentives on the electrophysiological correlates of error processing in major depressive disorder. *Cognitive, Affective & Behavioral Neuroscience, 10(1),* 119–128.

Insel, T., Cuthbert, B., Garvey, M., Heinssen, R., Pine, D. S., Quinn, K., … Wang, P.W. (2010). Research Domain Criteria (RDoC): Developing a valid diagnostic framework for research on mental disorders. *American Journal of Psychiatry, 167,* 748–751.

Luck, S. J. (2005). *An introduction to the event-related potential technique.* Cambridge, MA: MIT Press.

Thibodeau, R., Jorgensen, R. S., & Kim, S. (2006). Depression, anxiety, and resting frontal EEG asymmetry: a meta-analytic review. *Journal of Abnormal Psychology, 115(4),* 715–729

Weinberg, A., & Hajcak, G. (2011). Electrocortical evidence for vigilance-avoidance in generalized anxiety disorder. *Psychophysiology, 48,* 842–851.

Weinberg, A., Olvet, D. M., & Hajcak, G. (2010). Increased error-related brain activity in generalized anxiety disorder. *Biological Psychology, 85(3),* 472–480.

Further Reading

Fabiani, M., Gratton, G., & Federmeier. (2007). Event-related brain potentials: Methods, theory, and application. In J. Cacioppo, L. G. Tassinary, & G. G. Berntson (Eds.), *The handbook of psychophysiology* (pp. 85–119). New York: Cambridge University Press.

Huettel, S. A., Song, A. W., & McCarthy, G. (2008). *Functional magnetic resonance imaging*. Sunderland, MA: Sinauer.

Pizzagalli, D. A. (2007). Electroencephalography and high-density electrophysiological source localization. In J. Cacioppo, L. G. Tassinary, & G. G. Berntson (Eds.), *The handbook of psychophysiology* (pp. 56–84). New York: Cambridge University Press.