Neurophysiological Approaches to Understanding Behavior

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A biological revolution is occurring in the behavioral and social sciences, with an increasing emphasis on the use of neuroscience methods to understand human behavior, especially across the various subareas of psychology. The field of neuroscience reflects the interdisciplinary effort to understand the structure, function, physiology, biology, biochemistry, and pathology of the nervous system. From a psychological perspective, however, the term neuroscience typically is used to refer primarily to the study of the brain. Of interest is how the brain gives rise to learning, cognition, and behavior. Since the late 1980s, there has been dramatic growth in the field of cognitive neuroscience, which combines cognitive psychology, computational sciences, and neuroscience to examine how brain activity gives rise to cognitive abilities (e.g., memory, emotion, attention, language, consciousness). Indeed, this approach has been quite successful in providing new insights into many of these mental functions (Gazzaniga, 2004).

Most recently, social neuroscience is an emerging field that uses the methods of neuroscience to understand how the brain processes social information. It involves scholars from widely diverse areas—such as social psychology, neuroscience, philosophy, anthropology, economics, and sociology—working together and across levels of analysis to understand fundamental questions about human social nature. Social neuroscience merges evolutionary theory, experimental social cognition, and neuroscience to elucidate the neural mechanisms that support social behavior. From this perspective, just as there are dedicated brain mechanisms for breathing, walking, and talking, the brain has evolved specialized mechanisms for processing information about the social world, including people's ability

to know themselves, to know how others respond to them, and to regulate their own actions in order to live and interact with other people in society. The problems that are studied by social neuroscience have been of central interest to behavioral and social scientists for decades, but the methods and theories that are being used reflect recent discoveries in neuroscience. Although the field is in its infancy, there has been rapid progress in identifying the neural basis of many social behaviors (Adolphs, 2003; Heatherton, Macrae, and Kelley, 2004).

We begin this paper with a brief review of the intellectual history of examining behavior from a biological perspective. We then describe the major neurophysiological and neuroimaging methods being used to understand behavior, with examples of how specific methods have provided key insights about important aspects of psychological functioning. The third short section considers conceptual and practical concerns in using the methods, and the final section presents our conclusions. Throughout this paper we focus on the vexing issue of the extent to which psychological functions are localized in discrete brain regions, which can be considered one of the major challenges in much contemporary brain research.

INTELLECTUAL HISTORY

By the beginning of the 19th century, anatomists had a reasonably good understanding of the basic structures of the brain. What was unclear, however, is how those structures worked to produce thought and behavior. The key question was whether different parts of the brain did different things or whether the entire brain acted in unison to perform its vital functions. Some of the earliest proponents of functional localization were the phrenologists, such as Franz Gall and Johann Spurzheim. Although their theory that brain functions were associated with specific patterns of bumps on the skull is now discredited, the idea that discrete regions of the brain are specialized for different tasks was quite insightful. Early case histories of individuals with brain damage—such as Broca's patient, Tan, whose left frontal lobe damage left him unable to speak or Phineas Gage's frontal injury that led to dramatic changes in personality while leaving his intellectual faculties intact—provided considerable evidence for localized functions. The evidence from these early reports seemed clear: localized brain damage causes specific impairments.

Yet psychologists such as Karl Lashley in the early 20th century continued to argue that all parts of the cortex contributed equally to mental abilities through mass action, an idea known as equipotentiality. In a series of learning studies, Lashley removed cortical tissue from rats to see if he could disrupt their ability to remember how to navigate through mazes. He found that it was the amount of tissue removed rather than where it was

located that impaired learning. However, had Lashley removed subcortical tissue he would have come to a much different conclusion: it is now well established that subcortical structures such as the hippocampus and the amygdala are critical to learning and memory.

One reason the debate about whether psychological processes are located in specific parts of the brain or distributed throughout the brain continued so long was because researchers did not have methods for studying ongoing mental activity in the working brain. The first noninvasive method of brain mapping developed for humans, electroencephalography (EEG), was used as early as the 1920s by Hans Berger, but its signals were not clear or specific enough to answer questions about the location of psychological processes. That situation changed swiftly and decidedly with the invention of brain-imaging methods in the 1970s and 1980s. Positron emission topography (PET) was invented by a team led by Michael Ter-Pogossian at Washington University in 1973, whereas magnetic resonance imaging (MRI) was invented by Paul Lauterbur in the early 1970s at the State University of New York at Stony Brook and further developed by Peter Mansfield of the University of Nottingham, for which they shared the Nobel Prize in physiology or medicine in 2003.

Functional brain imaging, the use of imaging techniques to observe ongoing mental activity, was pioneered in the mid 1980s by Marcus Raichle and his colleagues (including Peter Fox, Michael Posner, and Steven Petersen). Although early imaging work used PET, functional MRI (fMRI) was developed in the early 1990s and now serves as the dominant brain imaging method. In the past decade there has been an explosion of research linking specific brain areas with particular behaviors and mental processes (for reviews, see Posner and DiGirolamo, 2000; Gazzaniga, Ivry, and Mangun, 2002). It is now clear that there is some localization of function, but that many different brain regions participate to produce behavior and mental activity. That is, although there is considerable support for the general idea of specialization, virtually every behavior involves the joint activity of many brain regions. As we discuss below, identifying specific functions for discrete brain structures remains an ongoing challenge for neurophysiological approaches to studying behavior.

The ability to study the working mind through neurophysiological methods relies on understanding how the nervous system works. In the late 19th century, Santiago Ramón y Cajal proposed that individual neurons are genetically and metabolically distinct units that serve as the building blocks of the nervous system. This neuron doctrine was a challenge to the prevailing belief that the nervous system was a continuous mass of connected tissue. By using staining methods developed by Camillo Golgi, Ramón y Cajal not only was able to visualize neurons, but also went on to discover that electrical signals moved along the neuron from the dendrites down

to the axon. That neurons operate by electrical activity allows one way to examine the working brain, namely by recording the electrical activity of neurons, either singularly or collectively.

Although it was initially believed that communication between neurons also occurred electrically, in the early 20th century it was discovered that chemical signals sent across the synapse in the form of neurotransmitters formed the basis of neuronal communication. It was initially and long believed that no more than a handful of neurotransmitters were involved in brain activity, but it is now known that hundreds of different substances act in diverse ways to affect mental activity and behavior. Interestingly, it is now known that cells other than neurons also affect thought and behavior. For instance, glial cells that were once considered little more than part of the physical structure of the brain have been found to modulate neural activity.

Understanding the chemical processes of the brain has provided many new insights into mental activity and behavior and has also been useful for developing treatments to help people with various psychological disorders. Some recent methods for understanding brain function capitalize on their ability to measure the actions of specific neurotransmitters within the nervous system.

NEUROPHYSIOLOGICAL METHODS

The principles of how cells operate in the brain to influence behavior have been studied with great progress for more than a century, but it is only recently that researchers have been able to study the working brain as it performs its vital mental functions. Although a multitude of different methods have been developed, they tend to group into two categories. The first group relies on measuring the electrical activity (and its associated magnetic consequences) in the brain. These methods are optimized for assessing the timing of brain activity (i.e., they are high in temporal resolution), but they are limited in their ability to localize the origins of the brain activity (i.e., they are low in spatial resolution). The second category is based on tracking blood flow (and its correlates) that accompanies neuronal activity. Methods such as PET and fMRI are relatively high in spatial resolution, but because of the rather sluggish nature of blood flow, they are low in temporal resolution. This section describes the major neurophysiological and neuroimaging techniques.

Electroencephalography (EEG) and Event-Related Potential (ERP)

Electroencephalography (EEG) is based on the principle that neural activity produces electrical potentials that can be measured and that the sum

of these potentials indicates the relative activity of the brain. EEG records these electrical signals in real time through electrodes that are strategically placed on the scalp (with an additional reference electrode placed on an electrically neutral area, usually the earlobe). Electrical potentials from the electrodes are expressed in terms of the difference between the scalp electrodes and the reference electrode.

EEG provides a wealth of information about global brain activity and is therefore commonly used in clinical settings to study sleep cycles and diagnose neurological disorders, such as epilepsy. However, because EEGs register all brain activity, the signal is noisy, and it cannot provide information about specific changes in brain activity in response to a stimulus or cognitive task. This problem is remedied by using event-related potentials (ERP), an offshoot of EEG. During ERP experiments, the time period following the onset of a stimulus or cognitive task is extracted from the ongoing EEG signal. In order to reduce background noise, the trials are repeated numerous times, and the EEG signals that follow those trials are averaged together in order to create an average waveform of the brain's response to the experimental event. ERPs are expressed in terms of the polarity of their signal (P for positive deflecting ERPs and N for negative), and the latency at which they are expressed. That is, a negatively deflecting ERP occurring 400 milliseconds after an event is termed an N400. Perhaps the most important feature of ERP is that it provides a relatively precise record of brain activity.

The majority of ERP research has focused on categorizing ERPs elicited by visual, auditory, and verbal stimuli. Recently emerging ERP research has begun to consider more socially relevant stimuli, such as identifying ERPs that are uniquely responsive to human faces (e.g., N170) (Bentin, Allison, Puce, Perez, and McCarthy, 1996) and human bodies (N190) (Thierry et al., 2006). However, these findings are not without controversy. For instance, although the typical N170 response for face recognition is absent in patients with face recognition disorders such as prosopagnosia (Bentin and Deouell, 2000), emerging evidence suggests that the N170 may reflect expert object recognition, of which face processing is only one example. Indeed, animal experts have been shown to elicit an N170 to images of their favored animal (Tanaka and Curran, 2001). Nonetheless, the use of ERP methods has provided psychologists with insights about a number of important social behaviors, including identifying unique patterns that are associated with perceiving members of an outgroup, at least for those who score high on measures of racial prejudice (Ito, Thompson, and Cacioppo, 2004).

An interesting application of ERP has been to investigate the neural correlates of deception. The majority of research in this area focuses on two ERP components: the P300, which typically indexes the subjective novelty

of an item (Friedman, Cycowicz, and Gaeta, 2001), and another component commonly referred to as the "parietal old/new effect," which distinguishes true from false recognition (Curran, Schacter, Johnson, and Spinks, 2001). For instance, Rosenfeld and colleagues (1999) have demonstrated that differences in the amplitude of the P300 can be used to distinguish between truly novel items and previously seen items in people who are feigning amnesia. More recently, Johnson, Barnhardt, and Zhu (2003) conducted a deception study in which participants were asked to provide truthful responses on some trials and deceptive ones on others. Interestingly, the authors found that the amplitude of the parietal old/new effect was largest for previously seen stimuli regardless of whether the participant responded truthfully or deceptively. The authors argue that this parietal old/new effect can be used as an objective measure of true recognition that is independent of a person's behavioral response, thereby providing a measure of guilty knowledge.

Magnetoencephalography (MEG)

EEG and ERP have the advantage of being relatively inexpensive, and they have submillisecond temporal resolution. Their potential for localizing function, however, is severely limited due to the possibility that there are multiple generators of the ERP signal that cannot be distinguished. A technique related to ERP that also provides better spatial resolution is magnetoencephalography (MEG), which measures magnetic fields that are produced by the electrical activity of the brain. Unlike EEG, MEG does not require electrodes; rather, it uses special sensors that detect magnetic fields. MEG has the same temporal resolution as ERP because it is basically measuring the same neural activity measured by EEG; however, because magnetic signals are not distorted by the skull, as are EEG signals, the MEG signal localization is far superior. In fact, MEG can localize the magnetic current within 2-3 millimeters under favorable conditions (e.g., when the target cortical structure is near the scalp). The one disadvantage of MEG is that it is much more expensive than ERP.

Despite its superior spatial resolution, MEG does not provide structural or anatomical information. It is therefore predominantly used to provide temporal information about known cortical structures. Language research, for instance, has relied on MEG to provide information about the time course of events by which speech is generated (which occurs in Broca's area) and understood (which occurs in Wernicke's area). In one study, participants were presented with pictures of simple objects (e.g., a house, dog, or cat) that they were told to identify silently in their minds (Kober et al., 2001). They then read simple words silently. The results suggested that, for most participants, activation in Wernicke's area occurred before activation

in Broca's area in both the silent naming and reading tasks. Not only has MEG provided insight about the time course of language comprehension, it also has contributed to understanding how quickly and effectively the brain processes visual cues. For instance, Amano, Nishida, and Takeda (2006) asked participants to attend to a visual target and press a button when its velocity changed. The authors found that the faster that participants were able to press a button to indicate that the target's velocity had changed, the higher their MEG responses.

As these examples show, MEG provides useful information about the time course of neural activity and even about specific anatomical regions when that region is known. In many studies, however, the underlying cortical structure that gives rise to a specific cognition or behavior is unknown. MEG is thus often combined with imaging techniques, such as fMRI, that identify the discrete cortical regions engaged in specific cognitive tasks. MEG can then glean temporal information about those regions. For instance, research on the fusiform face area, a region of the temporal lobe, has benefited greatly from both fMRI and MEG research (Downing, Liu, and Kanwisher, 2001). First, fMRI studies are used to identify the fusiform face area as an area that responds selectively to faces (Kanwisher, McDermott, and Chun, 1997). Subsequently, MEG is used to map the time course of face recognition (Liu, Harris, and Kanwisher, 2002). This combination of techniques has provided insights into the psychological processes underlying face perception.

Positron Emission Tomography (PET)

The brain imaging methods that have produced the greatest scientific enthusiasm in recent times measure metabolic processes rather than electrical activity. Brain activity is associated with changes in the flow of blood as it carries oxygen and nutrients to activated brain regions. Brain imaging methods track this flow of blood to understand which areas of the brain are most active for a given task. Positron emission tomography (PET), the first imaging method developed, involves a computerized reconstruction of the brain's metabolic activity by using a relatively harmless radioactive substance that is injected into the blood stream. A PET scanner detects this radiation as blood travels through the brain and therefore can be used to map out brain activity in real time in three-dimensional space. The resulting image identifies the neural structures engaged in specific cognitive tasks.

One of the primary functions of PET was to isolate neural regions that are involved in certain physical or cognitive processes. One such interesting application of PET was to identify the extensive neural network involved in perceiving pain. Coghill, Sang, Maisog, and Iadarola (1999) administered thermal stimulation to participants during a series of PET scans to

isolate the global organization of brain mechanisms involved in processing pain. The authors identified an extensive network in pain perception that includes the anterior cingulate cortex, insula, and cerebellum.

In addition to identifying the specific underlying mechanisms that motivate physical and psychological processes, PET provided investigators with a powerful method for addressing research questions that are difficult to study using behavioral methods. Memory researchers, for instance, long debated whether different forms of memory (e.g., encoding new memories or retrieving old ones) originate from the same or different neural systems. This debate was intensified by the famous case of patient H.M. In 1953 H.M. underwent a radical surgery in which his hippocampus was removed bilaterally in an attempt to cure his severe epileptic seizures. Following the surgery, H.M. suffered from profound amnesia and was unable to form new memories (Scoville and Milner, 1957). The surgery sparked a debate over whether the removal of the hippocampus impaired H.M.'s ability to form memories, retrieve memories, or both. Results from PET studies resolved this issue by demonstrating that different cortical networks are engaged during encoding and retrieval (Fletcher et al., 1995; Kapur et al., 1995). Using a classic memory paradigm, Tulving et al. (1996) had participants evaluate photographs during a PET scan that they had either previously viewed (old) or were novel (new) to identify neural regions involved in encoding (e.g., viewing a novel stimulus) and retrieving (e.g., viewing a previously presented photograph) information. For encoding, the researchers found that greater activation occurred in the hippocampus; for retrieval, they found greater activation in the prefrontal cortex.

PET has one major disadvantage. The use of radioactive substances places an inherent limitation on the number of trials and accordingly tends to have low power. Moreover, it can take a long time to image the entire brain and so trials need to last for an extended period. These features of PET require modification of many of the standard paradigms used in cognitive psychology. Thus, for reasons of safety as well as the ability to use many trials, most current brain imaging is conducted using fMRI.

Functional Magnetic Resonance Imaging (fMRI)

Functional magnetic resonance imaging (fMRI), like PET, measures brain activity by tracking metabolism associated with blood flow, but it does so noninvasively (i.e., nothing is injected into the blood stream). Thus, a single fMRI study can contain hundreds of trials, thereby greatly enhancing the power of the study. For instance, in fMRI it is possible to alternate continuously between experimental and control conditions. (In PET, a break is needed between conditions in order for the radioactive tracer to clear the system.) Moreover, fMRI provides superior spatial resolution, 1-2

millimeters in comparison with PET's resolution of 5-10 millimeters; thus, fMRI permits exploration of smaller brain structures (e.g., the amygdala) that tended to be overlooked in PET research.

In fMRI, blood flow is not measured directly. Rather, fMRI uses a strong magnetic field to assess changes in the blood-oxygen level dependent (BOLD) response at particular cortical sites after they have become active, which is an indirect measure of blood flow. Specifically, the BOLD signal is derived from the ratio of oxygenated to deoxygenated blood at cortical locations throughout the brain. Neural substrates that are active during a cognitive task have a greater repository of oxygenated hemoglobin than regions that are at rest. Deoxygenated hemoglobin is paramagnetic and distorts the magnetic field created by fMRI. Oxygenated hemoglobin, however, is diamagnetic and thus does not distort the magnetic field. The degree to which the magnetic field is distorted at a given location forms the fMRI image.

During the past decade, the advent of fMRI has led to increased research on cognition, behavior, and emotion. The superior spatial resolution of fMRI enables researchers to investigate smaller, subcortical regions, such as the amygdala. Indeed, a wealth of information has become available on the amygdala, implicating it in such tasks as perceiving emotion (Whalen, 1998), emotional memory (LeDoux, 1993), and evaluating stigmatized others (Krendl et al., 2006; Phelps et al., 2000). Research using fMRI has provided insight on the modulatory role of the prefrontal cortex over subcortical regions, such as the amygdala. For instance, Ochsner, Bunge, Gross, and Gabrieli (2002) provided compelling evidence that the prefrontal cortex increases activation during tasks that require overriding prepotent responses. In their study, the authors showed participants highly negative scenes and asked them either to attend to the pictures or to reappraise them so that the pictures became unemotional. During the reappraisal trials, the authors observed heightened activation in the medial and lateral prefrontal cortex and decreased activation in the amygdala and orbitofrontal cortex (regions implicated in processing emotion).

The use of fMRI has also proven effective for resolving conflicting theories that cannot be addressed by traditional behavioral methods. One example is the use of brain imaging to understand the self-reference memory effect. In the realm of cognition, one's self receives preferential access to attentional resources, and there is a selective advantage for remembering stimuli evaluated with reference to the self (Rogers, Kuiper, and Kirker, 1977). However, the basis of this advantage was long debated in social psychology, with the argument that either the self is somehow special or that the self is not special but simply encourages more elaborative encoding (Greenwald and Banaji, 1989; Klein and Kihlstrom, 1986). Which view is right? A frustrating feature of these competing accounts is that they are dif-

ficult to evaluate using purely behavioral measures as they make identical predictions—enhanced memory for self-relevant material. Herein lies the tremendous advantage of using brain imaging. An initial attempt to examine the neural substrates of the self-reference effect used PET. Unfortunately, there is a limit to the number of trials that can be presented using PET, and the researchers did not obtain a statistically significant self-reference effect (Craik et al., 1999). Nonetheless, their results were intriguing in that during self-reference processing trials, they did find distinct activations in frontal regions, notably the medial prefrontal cortex (MPFC) and areas of right prefrontal cortex.

Observing the limitations of PET, Kelley et al. (2002) used fMRI in an attempt to identity the neural signature of self-referential mental activity. In the task, participants were asked to judge 270 trait adjectives in one of three ways: self ("Does the trait describe you"?); other ("Does the trait describe George Bush"?); and case ("Is the trait presented in uppercase letters"?). Following two encoding runs, participants were given a "surprise" recognition memory test: participants viewed both trait adjectives that had been presented during the encoding scans and novel trait adjectives that had not been presented. The large number of trials (an advantage of fMRI over PET) allowed for the replication of previous behavioral findings that trait words encoded for one's self were better remembered than trait words encoded for George Bush or words for which participants made case judgments. More importantly, a direct comparison revealed that "self" trials produced significantly greater activation than "other" trials in a number of different brain regions, most notably the MPFC.

These findings provide preliminary evidence that the MPFC is involved in self-referential processing, but a question remains: How can one determine if this brain activity is responsible for the increase in memory for material encoded with reference to self? That is, activity in the MPFC accompanies self-referential processing, but does this activity contribute to the formation of memories in the brain? To investigate this question, Macrae et al. (2004) measured brain activity while participants judged the relevance of a series of personality characteristics. Afterwards, memory for the items was tapped in a surprise recognition task. By contrasting brain activation elicited by items that were later remembered with those that were later forgotten, it was possible to identify brain regions that predict successful recognition. Importantly, this research showed that the level of activity in the MPFC during self-referential judgments predicted which items would be remembered on the surprise memory test (i.e., the greater the MPFC activity, the more likely an item was to be remembered). Thus, not only does activity in the MPFC track with self-referential processing, but it also contributes to the formation of self-relevant memories. The important point for this paper is that brain imaging allowed researchers

to test competing hypotheses that could not be discriminated by standard behavioral testing.

Although fMRI has advanced scientific research in many domains, it is important to note that, like PET, fMRI is not without its limitations. Primarily, fMRI sessions are expensive (costing at minimum several hundred dollars per participant). Furthermore, fMRI has inferior temporal resolution, particularly in comparison with ERP and MEG. An fMRI detects cortical activation on the basis of changes in the BOLD signal, but the BOLD signal changes only after a cortical region has become active. In an attempt to circumvent this limitation, many researchers have begun to conduct fMRI studies in conjunction with ERP and MEG to minimize the temporal limitations of fMRI (Foucher, Otzenberger, and Gounot, 2004). To date, much of the initial research has focused on validating the method, and it remains to be seen whether it will prove more useful in studying cognition than either technique alone. There are also interpretive issues related to brain imaging in this work, which we discuss below.

Morphometry

In the above sections we have explored methods that index brain activity; however, with the advent of high resolution MRI, it has also become possible to noninvasively measure the shape, size, and orientation of white and gray matter in the brain. The study of brain morphometry allows for the identification of structural features of the brain that can be correlated with pathology or behavior. The study of morphometry has had a tremendous impact on identifying brain abnormalities associated with neuropathological conditions, such as autism, Parkinson's disease, and epilepsy (Abell et al., 1999; Bernasconi et al., 2004; Nagano-Saito et al., 2005). For instance, two recent morphological studies of autism revealed reduced grey matter volume and cortical thickness in areas of the brain known to be important for social and emotional functioning: this finding may help explain the well known social and empathetic deficits characteristic of autism (Hadjikhani, Joseph, Snyder, and Tager-Flusberg, 2006; McAlonan et al., 2005). Research has also demonstrated direct links between brain morphometry and experience. For instance, Maguire et al. (2000) found that the posterior hippocampus, an area important for spatial memory, was larger in a population of London taxi drivers than in matched controls; in addition, the size of this area correlated with driving experience.

An early limitation of morphometry was that it relied on manually segmenting brain regions, a method that is prone to subjective bias or error. As morphometry becomes increasingly popular, numerous automated segmentation techniques for measuring grey and white matter have developed. The main advantage of such an automated approach is that analyses are not

restricted to easily segmentable structures or prior regions of interest. By far the most common of the automated methods is voxel-based morphometry (VBM). In this method, MRI images of the brain are submitted to an automated segmentation algorithm that classifies grey and white matter on the basis of the intensity differences in the images. The resulting grey and white matter maps can then be evaluated for group differences in grey and white matter (e.g., healthy controls and patients) or to measure correlations of grey and white matter density with a continuous variable (e.g., test performance, personality measures). For instance, Sluming and colleagues (2002) used VBM to show that experienced musicians have increased grey matter density in Broca's, an area of the brain important for language.

Another popular method for studying cortical structures is analyzing cortical thickness (Fischl and Dale, 2000). This method measures the distance between segmented white and grey matter borders along the cortex. The primary difference between this and VBM is that statistical differences can be expressed in terms of the millimeter thickness of the cortex. Research using cortical thickness analysis has spanned a broad range of topics. For example, Lazar and colleagues (2005) found that experienced meditation practitioners displayed increased cortical thickness in brain areas involved in attention. In two recent studies, Rauch and colleagues (2005) measured the correlation between cortical thickness, extroversion, and ability to modulate fear. Interestingly, they found that the capacity to extinguish memory for conditioned fear was correlated with increasing cortical thickness in the orbitofrontal cortex. These findings were consistent with previous work by Rauch et al. (2003) showing that patients with posttraumatic stress disorder have reduced grey matter volume in this area of the brain, which may lie at the root of their difficulty in extinguishing fearful memories.

Although the application of morphometric techniques in nonclinical populations is still in its infancy, recent research has been successful in highlighting specific brain structures that are correlated with individual differences in personality. In one of the first studies of its kind, Pujol and colleagues (2002) used manual segmentation to measure the volume and symmetry of the cingulate cortex so that they could assess its relation to personality traits. They found that the size of the right anterior cingulate was correlated with measures of proneness to worry, shyness, and fear of uncertainty. These findings are intriguing in light of the anterior cingulate cortex's role in cognitive control and suggest that increased right anterior cingulate volume is related to a fearful temperament. More recently, a morphometric study by Pruessner and colleagues (2005) examined the relation between individual differences in stress response, self-esteem, and hippocampal volume. Interestingly, they found decreased hippocampal volume in participants with low self-esteem. Finally, Wright and colleagues (2006) found reduced cortical thickness in the inferior frontal cortex (IFC)

in participants who scored high in extraversion. These results suggest that the IFC may be an area involved in social inhibition and that the reduced thickness of this area may reflect relative disinhibition in highly extraverted persons.

Diffusion Tensor Imaging (DTI)

Despite numerous technical advances in morphometry research, it is only able to provide information about the size and location of grey and white matter regions. To understanding how different brain regions are connected, it has proven useful to examine white matter fiber tracks, which are bundles of myelinated axons that connect brain regions. The advent of diffusion tensor imaging (DTI) in the late 1990s provided researchers with the ability to detect directionality of these white matter tracts (see Basser, Mattiello, and LeBihan, 1994). DTI is based on MRI: it maps the location of white matter tracts by applying magnetic gradients to water molecules that diffuse across myelinated neuronal axons. DTI provides invaluable information about neurodegenerative disorders that target white matter (e.g., schizophrenia, Alzheimer's, stroke, and dyslexia (see Le Bihan et al., 2001)). Alzheimer's, for instance, is a disease that can only be officially diagnosed after death. However, DTI research has begun to identify differences in white matter tracts that may allow for accurate diagnosis of Alzheimer's much earlier. A recent DTI study found that 11 patients with probable Alzheimer's showed significant reduction in the integrity of certain white matter fiber tracts associated with cognitive performance, specifically, the splenium of the corpus callosum, superior longitudinal fasciculus, and cingulum (Rose et al., 2000). Interestingly, no decay was observed in white matter fiber tracts involved in motor performance, which supports the observed finding that Alzheimer's affects cognitive, not motor, ability.

DTI has also been used extensively to study schizophrenia. In the first study using DTI to examine schizophrenic brains, the researchers found that people with schizophrenia had significantly less white matter anisotropy (not having properties that are the same in all directions) in comparison with the controls, despite having equivalent white matter volume (Lim et al., 1999). Additional studies have found differences in the corpus callosum such that people with schizophrenia displayed significantly greater diffusivity, but decreased anisotropy, in the splenium than controls (Foong et al., 2000).

Transcranial Magnetic Stimulation (TMS)

It is commonly known that functional neuroimaging data only "suggest" brain regions that may be engaged during a given behavior; cor-

relations between behavior and localized brain activity cannot establish a causal brain–behavior linkage. One way to test for a causal link would be to conduct a virtual lesion study in which specific brain regions were damaged while leaving other areas relatively intact. Traditionally the establishment of causal brain-behavior links in humans has relied on the neuropsychological study of patients with damage to specific brain regions. Because head trauma or neurological disease generally causes such damage, our ability to experimentally control the location and extent of damage is severely limited. Transcranial magnetic stimulation (TMS) allows for the reversible experimental disruption of neural activity in relatively circumscribed cortical regions while study participants engage in a cognitive task (Jahanshahi and Rothwell, 2000; Walsh and Cowey, 2000; Wig, Grafton, Demos, and Kelley, 2005). Since its introduction in the mid-1980s (see Barker and Jalinous, 1985), TMS research has investigated a wide range of theoretical questions, from memory and language to epilepsy and schizophrenia. Recently, researchers have also begun investigating its therapeutic potential in treating mood-related disorders, such as depression (Loo and Mitchell, 2005).

During transcranial magnetic stimulation, a powerful electrical current flows through a wire coil that is placed on a person's scalp over the area to be stimulated. As electrical current flows through the coil, a powerful magnetic field is produced (commonly 2 Tesla or 40,000 times the earth's magnetic field), which, when rapidly switched on and off, induces an electrical current in a circumspect region of brain directly below the coil. The application of TMS interferes with neural function in discrete regions of the brain. In single-pulse TMS, the disruption of brain activity occurs only during the brief period of stimulation. If multiple pulses of TMS are given over extended time (known as repeated TMS), the disruption can carry over beyond the period of direct stimulation.

Much of the early use of TMS was in studying the motor and visual cortices. For example, TMS has been used to show a causal relationship between disruption of a region of the parietal cortex (the anterior intraparietal sulcus) and participants' ability to form the proper hand configuration for grasping an object (Tunik, Frey, and Grafton, 2005). In visual cognition, TMS has been used to selectively disrupt the perception of motion. By applying TMS over area V5 (an area of visual cortex important for processing visual motion), researchers have been able to temporarily reduce participants' ability to detect a moving stimulus (Beckers and Homberg, 1992). Recently, researchers have begun to use TMS to study the brain basis of complex social cognitive phenomenon, such as face perception and empathy for pain. Past neuroimaging research has shown that a region of the brain known as the superior temporal sulcus (STS) is often activated in the perception of biological motion (such as body movement and eye

gaze). However, it has not yet been determined whether this region is necessary to perceive biological motion. Recent studies using TMS to create a virtual lesion in the STS have demonstrated interference in the perception of eye gaze direction (Pourtois et al., 2004) and reduced accuracy in detecting biological motion from point light displays (Grossman, Battelli, and Pascual-Leone, 2005).

Although many TMS studies have sought to disrupt brain activity through repetitive stimulation, researchers have also explored the capacity of TMS to stimulate brain activity in order to improve function. An area of the brain known as the frontal eye field (FEF) has been implicated in the control of eye movements and, more recently, has been shown to be involved in the conscious detection of stimuli in primates (Moore and Fallah, 2001; Thompson and Schall, 1999). Using TMS to stimulate the FEF in humans, Grosbras and Paus (2003) were able to demonstrate increased detection of an otherwise subliminal stimulus. Thus, it seems that stimulation of FEF increases cortical excitability in the visual system and can consequently reduce the threshold needed for detecting a stimulus. More recently, Kim et al. (2005) were able to show that TMS can facilitate visual attention in one side of visual space by inhibiting brain activity in areas responsible for attending to the opposite side of visual space. By applying repetitive TMS over the posterior parietal cortex of the left or right hemisphere, thereby disrupting activity in that area, the researchers were able to show a concomitant increase in visuospatial attention in the opposite visual field. This finding demonstrates that visual attention is a resource that is shared between brain areas responsible for the left and ride side of visual space and that by inhibiting activity in one region, competition for attentional resources is eliminated and attention to the noninhibited side of visual space is increased. Whether these TMS-induced facilitation effects can exist without detriment to other facets of visual perception remains to be studied.

CONCEPTUAL AND PRACTICAL CONCERNS

In spite of the enthusiastic adoption of the methods of neuroscience to study psychological constructs, there remain important conceptual issues regarding this approach. Space limits preclude a full discussion of such concerns, but we provide a few examples in this section.

Perhaps the most central issue is that scientists do not yet fully understand the specific neural basis of brain imaging signals. Although several explanations have been proposed for the BOLD response, the precise mechanism remains unspecified at the neuronal level. Another problem (discussed above) is that most imaging methods are necessarily correlational and therefore prone to all the inherent limitations of all correlational meth-

ods. The advent of such tools as TMS may allow for examining causality, but TMS is limited to cortical areas near the skull and therefore will not be useful for many mental processes that involve subcortical structures. Assessing patients who have brain injuries can provide complementary evidence for the causal involvement of a brain region for a given psychological function.

Another conceptual issue is the difficulty in localizing specific psychological functions to discrete brain regions. There have now been several thousand imaging studies of a variety of psychological functions. What is clear is there is no one-to-one mapping between brain region and psychological function. Indeed, some brain regions are activated across numerous cognitive tasks. Thus, when a researcher finds a particular activation in an imaging study, it is not always obvious what that activation reflects. Although the literature contains sufficient evidence that there is specialization of brain function, it can be challenging to determine the specific function associated with a particular activation. An area may be activated across a broad array of disparate cognitive tasks because those different tasks share some common psychological process (e.g., semantic processing, memory, selecting among competing stimuli). In these cases, the activation may have little to do with the research question of interest to the investigator. As in all areas of science, the value of any imaging study depends on the care with which the experimental tasks are designed. In an ideal world, the comparison conditions that are used differ from the experimental conditions in as few dimensions as possible. Researchers also have to be vigilant to the possibility that their manipulations may be confounded with other psychological processes.

Consider the following example. Given the fundamental importance of social inclusion, it was perhaps not surprising that a recent study implicated brain regions commonly associated with physical pain as crucial for the experience of social pain. Specifically, Eisenberger, Lieberman, and Williams (2003) found that a region of the dorsal anterior cingulate cortex (dACC) was responsive during a video game designed to elicit feelings of social rejection when virtual interaction partners suddenly and surprisingly stopped cooperating with a research participant. Although these findings are intriguing, they clash with prior research and theorizing on the anterior cingulate cortex. In numerous prior studies, the dACC has been most closely associated with cognitive conflict, such as occurs when expectancies are violated (Bush, Luu, and Posner, 2000), while activity in the ventral ACC (vACC) is more typically associated with social and emotional processes. The literature also indicates that the vACC is implicated in emotional disorders, such as depression (Buchsbaum et al., 1997; Drevets, et al., 1997; George et al., 1997). Indeed, in a particularly striking study, Mayberg and colleagues (Mayberg et al., 2005) demonstrated that deep

brain stimulation in vACC was effective in alleviating depression in treatment-resistant patients. Hence, the findings of Eisenberger and colleagues are intriguing, but viewed in this light somewhat surprising.

One complication in interpreting those findings is whether the method used to induce social rejection also likely violated research participants' expectations. Put simply, the participants expected to participate. When this did not happen, it violated expectancies, producing cognitive conflict. So, left unanswered is whether the activation patterns they observed in that study were produced by cognitive conflict or social rejection.

Recently, researchers sought to address that question by designing a study that allowed for an independent examination of the neural underpinnings of social rejection and expectancy violation (Somerville, Heatherton, and Kelley, 2006). Results revealed a double dissociation between dorsal and ventral ACC regions. The dACC was uniquely sensitive to expectancy violations, with greater response when feedback was inconsistent with participants' impressions. This result held regardless of whether the feedback was a rejection or an acceptance. Conversely, a region in vACC was uniquely sensitive to social feedback, with significantly greater response to negative feedback than positive feedback, irrespective of expectancy violations. The lesson from this study is that simply observing activation in a specific brain region does not necessarily identify the psychological processes that underlie that activation. An editorial in the leading journal *Nature Neuroscience* stressed that all imaging studies should be driven by hypotheses in terms of testing discrete cognitive constructs (e.g., "Is the hippocampus involved in memory?"), rather than simply brain mapping (e.g., "What happens in the brain during social influence?").

In addition to the conceptual concerns, a practical limitation to using neurophysiological methods to study behavior needs to be mentioned: the inadequacy of training opportunities to educate students about the rich traditions of psychological science along with a rigorous education in neuroscience. Consider the topic of social neuroscience. Many of the social psychologists who wish to use neurophysiological methods receive little formal training in neuroscience. At the same time, much of the work in social neuroscience is being conducted by researchers who have little awareness of the vast social psychological literature that is prized for its methodological rigor. There is a pressing need for cross-disciplinary training to facilitate theory-driven research that is methodologically sound.

CONCLUSION

The use of neurophysiological methods allows researchers to watch the working brain in action as it performs mental activities. These methods have enabled scientists to study important questions that were previously

intractable, as well as to test competing theories that cannot be distinguished based on behavioral evidence. The use of these methods in psychology is still in its early days, and there remains a great deal to be learned. It is likely that technical advances will allow researchers to better understand the significance of functional brain activity (i.e., what causes it). At the same time, there is an urgent need for cross-interdisciplinary training that allows social and behavioral scientists to use these methods in constructive and productive ways.

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