Neurocognitive Methods in Higher Cognition

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Abstract

The methods of cognitive neuroscience, notably functional neuroimaging and cognitive neuropsychology, are becoming increasingly important in efforts to understand the processes responsible for human higher cognition. Given the complexity of human thinking and reasoning, it is frequently the case that multiple theories can explain behavioral results. By utilizing the constraint of neural plausibility, some of these possibilities can be eliminated. These tools are thus beginning to help us to understand how thinking and reasoning actually occur in the brain. In this chapter we discuss a number of the techniques most frequently used to investigate higher cognition, including cognitive neuropsychology, scalp electroencephalography (EEG), functional magnetic resonance imaging (fMRI), and transcranial magnetic stimulation (TMS). We briefly survey a number of examples of how these techniques have contributed to our understanding of higher cognition, particularly the functions of the human prefrontal cortex.

Key Words: neuropsychology, neuroimaging, functional magnetic resonance imaging (fMRI), electrophysiology, event-related potentials (ERPs), prefrontal cortex

Introduction

For the past 40 years, neuroscience methods have played an increasingly important role in the study of cognition. It is now commonplace for cognitive scientists to connect cognitive processes to their underlying neural substrates. The explosive growth in the field of cognitive neuroscience, particularly in perception and memory, is blurring distinctions between cognitive psychology and neuroscience. Neuroscientists are now recognizing that higher cognition, including the study of thinking and reasoning, are also tractable areas for research, which could greatly benefit from attention to the constraint of neural plausibility.

The development of the field of cognitive neuroscience is a natural consequence of the fact that "cognition is what the brain does." Recent years have seen unprecedented development in both the study of cognition and of the brain. The development

of neuroimaging techniques, chiefly functional magnetic resonance imaging (fMRI), has clearly accelerated this convergent growth. Because methodological developments have fueled advances in the cognitive neuroscience approach, this chapter is organized in terms of how different methodologies are informing the field.

Findings in cognitive neuroscience fall into two basic categories. In one category, researchers elucidate brain–behavior relationships; that is, they assign cognitive functions to specific brain regions or circuits. In the other category, neuroscience data are brought to bear in order to constrain cognitive theories, or they are used to provide a resolution between two theories that are both plausible based on behavioral data alone. This second category of findings is typically of more interest to cognitive scientists; however, the famous 19th-century neurologist Bernhard Von Gudden was wise to caution,

"*Faced with an anatomical fact proven beyond doubt, any physiological result that stands in contradiction to it loses all its meaning…So, first anatomy and then physiology; but if first physiology, then not without anatomy*" (as cited by Brodmann, 2006, p. 262). Thus, understanding the functional neuroanatomy of the brain is the first step in determining how the physical matter of the nervous system gives rise to human thought. Ultimately, this is one of the fundamental questions in life science. Thus, cognitive neuroscience is useful in that it provides additional methods for cognitive science, but it is also an important pursuit in its own right.

Methods of Cognitive Neuroscience

Building upon a long history of work in cognitive neuropsychology,[1] the methods of cognitive neuroscience are constantly evolving. In addition to functional neuroimaging techniques sensitive to the temporal dynamics or spatial localization of cognitive processes, researchers have also made extensive use of computational modeling to capture brain network architecture or functions, recently augmented by the methods of cognitive neurogenetics (see Green & Dunbar, Chapter 7). Here we introduce several of the techniques currently being used to study higher cognition, and we provide examples of their use (see Table 6.1 for a summary of methods).

Cognitive Neuropsychology

While modern "cognitive neuroscience" may have officially begun with the coining of the term in the late 1970s by Michael Gazzaniga and George Miller (D'Esposito, 2010), the precursors of this field can be traced to 19th-century studies of brain-damaged patients. The great controversy of the time was between *localizationism*, the view that specific cognitive functions could be ascribed to particular brain regions, versus an *aggregate field theory*, according to which cognitive abilities are distributed throughout the neocortex. Under the first view, restricted damage to specific brain regions should disrupt specific cognitive processes while leaving others intact. Under the second view, the extent of damage to the brain is more important than the location of damage, with all cognitive functions proportionately affected by damage. Some of the most compelling data from this period arguing for localizationism came from two patients studied by Paul Broca (Lee, 1981). These patients (Leborgne and Lelong) became unable to speak more than a few words. After the death of each patient, Broca

examined their brains and determined that for both patients the language difficulties were due to damage in the left inferior frontal lobe, a region now named Broca's area (see Fig. 6.1). Interestingly, subsequent work has shown that patients with lesions limited to Broca's area do not actually exhibit the kind of profound deficits in language production described in Broca's original cases. Recent examination of Leborgne and Lelong's brains with modern methods in fact demonstrate that the damage was much more extensive than originally described (Dronkers, Plaisant, Iba-Zizen, & Cabanis, 2007). Nevertheless, these case studies indicated that a complex cognitive function like language production could be selectively affected by brain damage that generally spared other functions.

Broca's dissociation-based approach (see Fig. 6.2), which looks for commonalities in spared and impaired function with associated brain damage across subjects, has continued to be used in modern cognitive neuroscience. The power of the cognitive neuropsychological approach is that it can tell us whether a specific brain region is *necessary* for a particular cognitive function, and whether remaining regions are *sufficient* to support functions that are spared (i.e., single dissociation). In addition, even in situations where the location of damage is unclear, much can be learned about the organization of cognition by studying how it breaks down. For example, the apparent relative sparing of language comprehension in patients Leborgne and Lelong, despite their severe difficulties with language production, support models of language in which these abilities are independent. Another example is the distinction between declarative and procedural memory systems. The strongest evidence that memory is organized into such systems comes from the fact that amnesic patients are able to learn skills and procedures normally despite extremely poor memory for practice episodes (Cohen & Squire, 1980; Knowlton, Mangels, & Squire, 1996).

The neuropsychological approach depends on a careful analysis and characterization of behavior (see Feinberg & Farah, 2003). Dissociations between cognitive functions can be interpreted in different ways depending on the underlying psychological theory. Although a straightforward interpretation of the findings from Broca's patients suggested a double dissociation between language production and comprehension, subsequent research has shown that similar patients have difficulty with comprehension based on grammar. It appears more accurate to describe these patients as "agrammatic." To

Table 6.1. Summary of Experimental Methods in Cognitive Neuroscience

Method	Temporal Resolution		Spatial Resolution	Advantages	Disadvantages	Methods amd Examples
	Temporal Lag	Sampling Rate				
Cognitive neuropsychology (Behavioral Neurology)	NA	NA	10^{-3}–10^{-2} m	Can access whether a particular brain region is necessary for a particular cognitive function; can be combined with structural and/or functional imaging and be used to test computational models	Depends on the "experiments of nature"; requires precise characterization of damage (structural imaging) and careful testing to establish dissociations	**Feinberg & Farah (2003);** Waltz et al. (1999); Morrison et al. (2004); Huey et al. (2009); Sonty et al. (2007)
Computed axial tomography (CT)	NA	Can be repeated over days to years	10^{-2}–10^{-1} m	Excellent vascular detail; availability in all major medical/research centers	Poor detail except for vascular structures	
Structural magnetic resonance imaging (MRI, cortical thickness, VBM)	NA	Can be repeated over days to years	10^{-3}–10^{-1} m	Excellent gray/white matter detail; can be used to measure cortical thickness or used with techniques like voxel-based morphometry (VBM) to make group comparisons; can be correlated with behavior	Claustrophobic; cannot currently be used in individuals with medical implants; difficult to use with infants and children	**Raichle (1994); Fichl & Dale (2000); Ashburner & Friston (2000);** Dumontheil et al. (2010); Rosen et al. (2002)
Diffusion tensor imaging (DTI)	NA	Can be repeated over days to years	10^{-3}–10^{-1} m	Used to measure white matter integrity (DTI); can be correlated with behavior	Expensive; claustrophobic; difficult to use with infants and children	**Filler (2009);** Rogalski et al. (2009)
Single- or multi-unit recording	Instant	ms	10^{-5}–10^{-3} m	Superior spatial and temporal resolution	Invasive! (animals and very selective brain-damaged humans); moderate startup and per-participant costs in animals	**Humphrey & Schmidt (1990);** Fuster & Alexander (1971); Cromer, Roy, & Miller (2010)

(Continued)

Table 6.1 Continued

Method	Temporal Resolution		Spatial Resolution	Advantages	Disadvantages	Methods amd Examples
	Temporal Lag	Sampling Rate				
Electrocortiography (ECOG)	Instant	ms	10^{-3}–10^{-2} m	Good spatial and temporal resolution	Invasive! (very selective brain-damaged humans); high startup and per-participant costs	**Miller et al. (2007);** Canolty et al. (2006)
Scalp electroencelphalography (EEG/ERP/ERO)	Instant	ms	10^{-2}–10^{-1} m ?	Noninvasive; excellent temporal resolution; low cost; can be used with children and infants	Undefined satial resolution; sensitive to movement and eye artifacts	**Luck (2005); Sauseng & Klimesch (2008);** Knight et al. (1989); Vogel et al. (2005); Jung-Beeman et al. (2004); Kounios et al., (2006)
Positron emission tomography (PET)	2 m	?	10^{-2}–10^{-1} m	Can be used either structurally or functionally; can be tuned to different metabolic processes; limited availability	Invasive (radiation); very expensive per-participant costs	**Raichle (1983);** Cabeza & Nyberg (2000); Villemagne et al. (2011)
Functional magnetic resonance imaging (fMRI)	1–2 s	250 ms - 1 s	10^{-3}–10^{-1} m	Noninvasive; available at major medical/research centers; excellent spatial resolution	Expensive; loud and claustrophobic; cannot currently be used in individuals with medical implants; limited movement, poor participant contact, high per-participant cost	**Brown, Perthen, Liu, & Buxton (2007); Raichle & Mintun (2006);** Cabeza & Nyberg (2000); Kroger et al. (2002); Goel & Dolan (2004); Monti, Parsons, & Osherson (2009); Sonty et al. (2007)
Magnetoencephalography (MEG)	Instant	ms	10^{-2}–10^{-1} m ?	Noninvasive, provides high temporal resolution and moderate spatial resolution in one technique; can be used with children and infants	Not widely available in United States; high startup costs; moderate operating costs—much lower than fMRI	**Hansen, Kringelbach, & Salmelin (2010);** Ciesielski, Ahlfors, Bedrick, Kerwin, & Hamalainen (2010)

| Technique						References
Near infrared spectroscopy (NIRS)	1–2 s	ms	10^{-3}–10^{-2} m	Noninvasive; low-startup and low per-participant costs; can be used with infants and young children	Can only be used with cortical surface structures near scalp	**Villringer & Chance (1997);** Tsujii & Watanabe (2010)
Event-related optical signal (EROS)	100 ms	ms	10^{-3}–10^{-2} m	Noninvasive; low-startup and low per-participant costs; can be used with infants and young children	Can only be used with cortical surface structures near scalp; very limited availability	**Gratton et al. (1997)**
Transcranial magnetic stimulation (TMS)	Instant	NA	10^{-3}–10^{-2} m	Noninvasive virtual lesion method; relatively low cost but usually done with fMRI	Cannot be used with people with tendency to have seizures	**Pascual-Leone, Bartres-Faz, & Keenan (1999);** Tsujii et al. (2010)
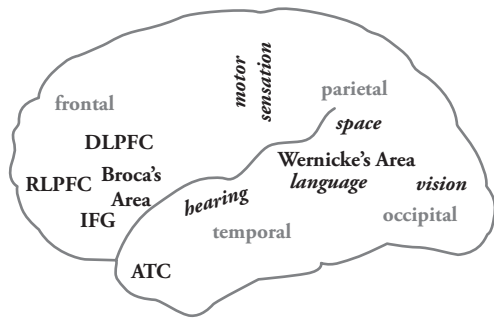
Fig. 6.1 Functional neuroanatomy in higher cognition. The human cerebral cortex is traditionally divided into four lobes (light gray labels) based on neuroanatomical landmarks (e.g., the horizontal fissure). These lobes are then frequently further partitioned with respect to smaller anatomical divisions (e.g., prefrontal cortex [PFC], rostrolateral PFC [RLPFC], dorsolateral PFC [DLPFC], inferior frontal gyrus [IFG], anterior temporal cortex [ATC]). However, sometimes brain regions are labeled with the name of the scientist who originally ascribed their function (e.g., Broca's or Wernicke's area), the type of information they process (e.g., auditory, sensation, visual), or by their dominant function (e.g., motor movement, language, spacial processing).

the extent that they can produce language, they will produce content words, but not function words that would indicate the use of grammar (Kean, 1977). Thus, more extensive examination of behavioral findings along with the development of new theoretical perspectives can lead to reinterpretations of neuropsychological data.

In the domain of thinking and reasoning, patients with frontal lobe damage are of interest because of the clear involvement of the frontal lobes in complex cognition (see also Holyoak, Chapter 13). Focal lesions to the frontal lobes (e.g., following a stroke) are very common; however, they are likely to be unilateral and restricted, making it likely that spared regions can take over lost functions. In addition,

the location and the extent of the lesions often vary between patients, making it difficult to generalize across cases (see Duncan & Owen, 2000). In investigations of neural mechanisms of reasoning, a great deal of attention has recently focused on patients with frontotemporal lobar degeneration (FTLD; e.g., Huey et al., 2009; Krawczyk et al., 2008; Morrison et al., 2004; Waltz et al., 1999; Zamboni, Huey, Krueger, Nichelli, & Grafman, 2008).[2] Although these patients are much rarer than those with focal frontal lobe damage, their damage is more encompassing of prefrontal cortex and can thus provide a good picture of its role in higher cognition.

FTLD can present with different clusters of symptoms depending on the regions of initial involvement (Mesulam, 2007; Miller, 2007). Although the disease ultimately progresses to involve multiple brain regions, in early stages it can affect specific regions of the brain more selectively. Those patients in the frontal-variant (also referred to as behavioral-variant) category exhibit executive problems early on in the disease course. Another group of patients, with early involvement in the left temporal lobe, exhibit deficits in semantic knowledge (i.e., semantic dementia). These two patient groups have been studied in the context of thinking and reasoning, as they exhibit a contrasting set of deficits. Using the technique of voxel-based morphometry to quantify the regional extent of damage, it is possible to correlate the extent of degeneration with specific cognitive abilities (Huey et al., 2009; Rosen et al., 2002). These studies have generally shown correlations between degeneration in the anterior frontal lobe and standardized tests of problem solving, whereas degeneration in other regions is strongly associated with other aspects of higher cognition. For example, degeneration in the dorsolateral prefrontal cortex
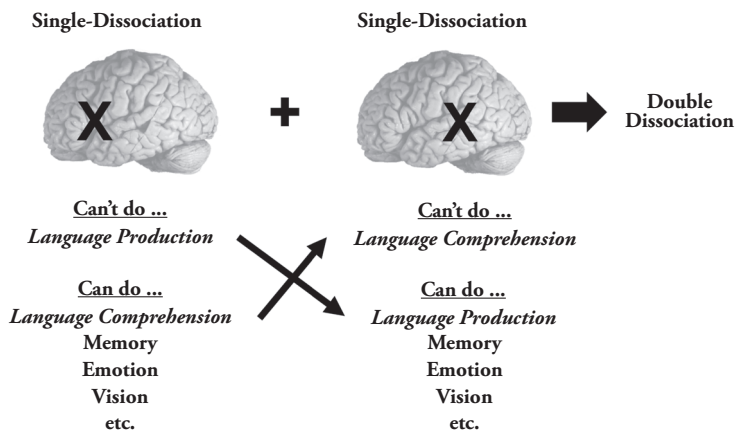

Fig. 6.2 Cognitive neuropsychology. Patient-based methods are typically based on the logic of single or double dissociations.

(DLPFC) is correlated with apathy, while degeneration in the right posterior temporal lobe is related to the patient's insight into his or her own behavioral problems (Zamboni et al., 2008).

Despite the widespread deficits in executive function shown by frontal-variant patients, there is also evidence that there is some selectivity in these deficits. For example, in tests of inductive and deductive reasoning, frontal-variant patients can perform within normal range when solving the problem requires only a single relation to be kept in mind (e.g., a Raven's Progressive Matrix problem that can be solved by considering a change across a single dimension, such as a shape getting larger across a row). However, when the subject must consider multiple relations simultaneously to find the answer (e.g., the shape is getting larger across rows and darker across columns), frontal-variant patients perform at chance levels. These results suggest that relational integration is one of the key contributions to reasoning made by the prefrontal cortex (Waltz et al., 1999).

In contrast to the performance of frontal-variant patients, those with temporal lobe involvement do not appear to have a deficit in relational integration. Rather, these patients exhibit deficits in using semantic knowledge to make inferences (Krawczyk et al., 2008; Morrison et al., 2004), while they are often able to reason about materials for which semantic content is not important, such as the Raven's Progressive Matrices test (Waltz et al., 1999). These results suggest that different neural circuits subserve reasoning about familiar versus unfamiliar domains. One interpretation of these findings is that reasoning based on familiar information necessarily uses the semantic knowledge system—in other words, it is difficult to reason with familiar entities as if they are arbitrary (see Evans, Chapter 8). In contrast, when there is an arbitrary relationship between items, a system for applying formal logical rules is engaged. Based on the results from FTLD patients as well as neuroimaging studies, interactions between frontal and temporal lobes are crucial for reasoning when semantic knowledge is relevant (Krawczyk et al., 2008, Luo et al., 2003; Morrison et al., 2004), whereas frontoparietal circuitry plays a major role in applying formal rules of logic to arbitrary relations (Hinton, Dymond, von Hecker, & Evans, 2010; Noveck, Goel, & Smith, 2004). Because the parietal lobes remain relatively intact in FTLD, these patients are able to solve deductive and inductive reasoning problems with

arbitrary content, particularly if they involve only a limited number of relations. With arbitrary relations, patients with frontal involvement perform poorly when they must consider multiple relations simultaneously in working memory (Waltz et al., 1999) or when activated semantic information competes during reasoning (Krawczyk et al., 2008; Morrison et al., 2004). The study of patients with FTLD has provided strong support for the idea that reasoning with semantically meaningful and arbitrary relations involves different neural circuitry.

Neuroimaging

Cognitive neuropsychology continues to yield new insights into the dissociable processes within the domain of reasoning. However, while this approach emphasizes dissociation, other approaches are needed to understand how regions act cooperatively. Neuroimaging approaches have a distinct advantage over cognitive neuropsychology in that they are noninvasive and involve relatively large numbers of healthy subjects, allowing greater generalizability of their findings. As cognitive neuropsychology depends on "experiments of nature," there is unavoidable variability between patients in terms of lesion site or course of illness, which can make it difficult to make inferences about those regions responsible for observed deficits. Neuroimaging approaches, on the other hand, allow one to glimpse the intact brain at work. Neuroimaging methods vary with respect to whether they measure the structure or function of the nervous system; however, results from either type of method can be correlated with behavioral measures to provide valuable information about cognitive function. Functional methods can in turn either directly or indirectly measure neural activity. For instance, scalp electroencephalography (EEG) directly measures changes in voltage resulting from firing neurons, whereas functional magnetic resonance imaging (fMRI) indirectly measures neuronal activity by measuring increased blood flow to the area of the brain recently active. A further distinction is between methods that focus on spatial localization (e.g., fMRI) versus those that provide information on temporal dynamics (e.g., EEG).

STRUCTURAL NEUROIMAGING

Although neurologists are able to look at X-rays of the head to see damage to the skull, X-rays are inadequate to image soft tissue such as the brain. In 1974, brain imaging took a huge step forward with the development of computer axial tomography (CT or

CAT scan). This enhanced three-dimensional X-ray was able to resolve gray and white matter as well as blood and cerebrospinal fluid. As a consequence, neurologists were able to see the damage caused by tumors and different types of irregular blood flow (e.g., ischemia and aneurysms). This greatly facilitated cognitive neuropsychology because researchers did not have to wait until a patient died to know what areas of their brain were damaged. The development of magnetic resonance imaging (MRI), with its greater white/gray contrast and finer spatial resolution, allowed for precise volumetric measurement of different brain structures (Raichle, 1994). The state of the art in structural MRI allows researchers to measure cortical thickness (Fischl & Dale, 2000) or white matter integrity (Filler, 2009), correlating it with various types of behavior and even developmental change.

Comparisons can also be made across groups using techniques such as voxel-based morphometry (VBM; Ashburner & Friston, 2000), which allows researchers to spatially normalize brain images into a common stereotactic space, and then make voxel-by-voxel comparisons of the local concentration of gray matter between groups. This technique is particularly useful for demonstrating the similarities of cortical damage in different patients groups. For instance Rosen et al. (2002) used VBM to characterize structural differences in various subtypes of FTLD. Variability in a particular brain region can also be correlated with behavioral changes (see Huey et al., 2009).

In a recent developmental study of reasoning, Dumontheil, Houlton, Christoff, and Blakemore (2010) tested a large group of children using a relational reasoning task that shows major behavioral changes during adolescence. Using structural MRI with both cortical thickness and VBM analyses, they found significant reductions in gray matter but not white matter volume during adolescence in areas of prefrontal cortex functionally involved in relational reasoning. These results suggested that improvements in relational reasoning can be the result of decreases in the number of synapses, allowing for an increase in effective connectivity between brain regions necessary for reasoning.

Although structural MRI allows for excellent contrast between gray and white material, it does not directly measure the integrity of the tissue. In contrast, diffusion tensor imaging (DTI) can be used to appraise the integrity of white matter by using different settings during MRI image capture (Filler, 2009). The analysis procedure appraises the characteristics of water in the tissue. Clinically, these methods have been used to diagnosis multiple sclerosis and recently have also been potentially helpful in detecting early stages of Alzheimer's disease (Rogalski et al., 2009). Importantly, white matter (the axons of myelinated neurons) connects different regions of the brain, and it is critical for both working memory (frontal/parietal network) and language (frontal/temporal network). Thus, it is likely that differences in connectivity as measured by DTI may be useful for appreciating individual differences in thinking, as well as development.

ELECTROPHYSIOLOGICAL FUNCTIONAL NEUROIMAGING

Single- and Multi-Unit Recording

Our understanding of many basic cognitive functions has been profoundly aided by studies using electrophysiological methods with nonhuman animals. In these studies microelectrodes are inserted into precise locations in the brain and can be used to directly record the firing of either single (i.e., single-unit recording) or small groups (i.e., multi-unit recording) of neurons (see Humphrey & Schmidt, 1990). This technique produces results with excellent temporal and spatial resolution—we know exactly when and where neurons are firing when a particular cognitive process is engaged. This information is particularly useful when cognitive processes can be clearly defined. For instance, if we would like to know what neurons respond to the spatial frequency of a visual pattern, we can place electrodes in various regions in primary visual cortex and locate neurons that fire to a particular spatial frequency, but not other frequencies. Similarly, we can ask whether there are cells that are specifically sensitive to face stimuli and not other complex visual objects.

Unfortunately, it is frequently difficult to isolate cognitive processes underlying thinking and reasoning with this same degree of precision. As Penn and Povinelli argue in Chapter 27, it is very likely that humans differ from even their nearest primate relatives in the nature of relational representations and processing. Despite these limitations, electrophysiology in the macaque monkey has provided some insight into the functions of the prefrontal cortex for higher cognition. Much of higher cognition, particularly System II or explicit processing (see Evans, Chapter 8), depends heavily on the working memory system for the maintenance

and manipulation of information (see Morrison, 2005). Seminal studies in the macaque by Fuster and Alexander (1971) demonstrated that neurons in prefrontal cortex selectively fire during the delay in delayed match-to-sample tasks, in which a monkey is required to match a target to a previously displayed sample object shown before a brief delay. In an elegant study using cortical cooling to temporarily deactivate connective fiber tracts, Fuster, Bauer, and Jervey (1985) went on to demonstrate that prefrontal neurons were not simple buffers for the temporary storage of information, but rather were responsible for maintaining the activity of neurons in posterior cortex, which actually coded for the information being maintained. Consistent with Cowan's (1995) conception of working memory as a process of selective attention, Fuster's finding illustrates one central "truth" of higher cognition—brain regions dynamically collaborate to accomplish complex processes.

Electrocorticography

The invasive nature of single- and multi-unit recording typically prevents its use in humans. One exception is in patients with intractable epilepsy. These patients frequently have surgery to remove parts of the brain (usually in the temporal lobe) responsible for initiating or propagating seizures. In preparation for surgical resection, patients frequently have electrodes placed directly on the brain under the skull and dura matter. In some cases electrodes capable of single- or multi-unit recording are even inserted into the cortex (i.e., depth electrodes). Patients are monitored for up to several weeks waiting for seizures to occur. During this period patients typically participate in a variety of cognitive studies, which allow researchers to correlate brain activity with function (see Miller et al., 2007). Although this provides an excellent opportunity for directly recording the activity of neurons in humans, caution must be exercised in interpreting results because of the pathology associated with epilepsy in these patients.

One recent example of how electrocortiography (ECOG) can be used to constrain cognitive models, demonstrated that different areas of cortex communicate with each other during behavioral tasks by precise timing of different populations of neurons firing at different frequencies (Canolty et al., 2006). It was hypothesized that these communication patterns may be regulated by GABAergic inhibitory neurons in the basal forebrain. In general, it appears that local, domain-specific neural circuits communicate using high frequencies (e.g., *gamma*) while more distant cross-domain circuits use lower frequencies (e.g., *theta*; Canolty & Knight, 2010). These observations are consistent with those symbolic-connectionist accounts of higher cognition (see Doumas & Hummel, Chapter 5) that use temporal synchrony as a binding mechanism for representing explicit relational structures necessary for relational thinking and reasoning.

Scalp Electroencephalography

The ability to directly record electrical activity from the brain began long before the advent of single- and multi-unit recording. In 1929 Hans Berger first used electrodes on the scalp to record the summation of voltage changes associated with the firing of millions of neurons. This early method of neuroimaging showed rhythmic patterns associated with different states of consciousness. For instance, cycles of approximately 10 times per second (10 Hz, *alpha*) were detected in electrodes over the occipital lobe during sleep or periods when an individual's eyes were closed. The method of scalp electroencephalography (EEG) was used for many years to diagnose a number of different medical conditions, including epilepsy.

Event-Related Potentials

The true power of EEG for neuroimaging was not realized until computing advances allowed for large numbers of measurements to be summed (Galambos & Sheatz, 1962). The resulting event-related potentials (ERPs) can be time locked to particular events, such as the presentation of a stimulus, or a button press in response. Averaging many time-locked trials increases the signal-to-noise ratio, resulting in a smooth waveform with characteristic positive and negative peaks (see Fig. 6.3). Over thousands of experiments, researchers have associated many of these peaks with particular cognitive processes (For a detailed introduction to EEG/ERP methods, see Luck, 2005; Luck & Kappenman, 2012).

Typically, researchers compare ERPs from different within-subject conditions to isolate particular neural components; however, ERPs can also be used to compare different groups as well. Here we briefly consider two different studies showing the power of ERPs to elucidate the function of prefrontal cortex. In general, one important function of prefrontal cortex is to filter information. The filtering can either take the form of tonic gating, serving
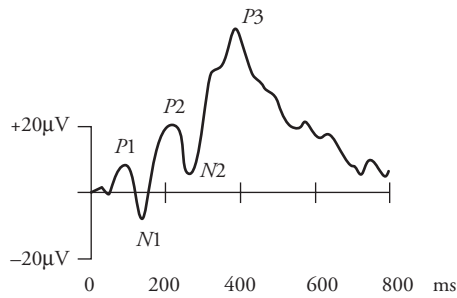
Fig. 6.3 Sample ERP. Averaging many trials from the same condition in an experiment improves the signal-to-noise ratio of time-locked EEG signal, resulting in an event-related potential with positive and negative peaks, which can sometimes be associated with particular cognitive processes.

to down-regulate sensory input from the outside world, and thereby avoiding distraction (Knight, Scabini, & Woods, 1989); or dynamic filtering to manage the contents of working memory for a current goal (Vogel, McCollough, & Machizawa, 2005). These are both essential aspects of executive functioning necessary for higher cognition that rely on prefrontal cortex.

Knight, Scabini, and Woods (1989; see also Knight & Grabowecky, 1995) provided one early example of how ERPs can be used in conjunction with cognitive neuropsychology. They exposed patients with damage to DLPFC, or age- and education-matched control participants, to a sound recording of simple auditory clicks. These sounds produce positive deflections in the ERP within 30 ms of the click (P30). A group analysis revealed that patients and controls showed similar P30 ERPs when recorded from posterior electrode positions, whereas patients showed much more positive P30s than controls when the ERP was measured from parietal-, temporal-, or frontal-positioned electrodes. This pattern suggests that a functioning DLPFC serves to protect the higher cortical areas from sensory distraction by down-regulating signals.

A second ERP study investigating this issue explored how the ability to dynamically filter information can determine effective working-memory capacity. Numerous studies have linked individual differences in working-memory capacity with the ability to reason (Conway, Kane, & Engle, 2003). Vogel et al. (2005) used a delayed match-to-sample paradigm, similar to that used by Fuster in monkeys, in humans who were divided into two groups based on their individual working-memory spans (Conway et al., 2005). In Vogel et al.'s task participants had to remember the exact location and orientation

of several color bars over a delay. There were three different task conditions: *(1)* remember two bars of one color, *(2)* remember four bars of two different colors, or *(3)* remember two bars of one color and ignore two bars of a different color. Thus, the two latter conditions (2 and 3) had identical stimuli, with only the task differing. Vogel et al. isolated a contingent negative variation (CNV) in the EEG signal that began when the sample stimuli disappeared and persisted during the delay before participants were to respond to a target. The CNV thus appears to be an analog to the neural activity observed by Fuster using single-unit recording in nonhuman primates. Vogel and colleagues demonstrated that the CNV was modulated by working-memory load, with greater loads (remember-four) resulting in a more negative CNV than smaller loads (remember-two). However, they found that for people with low working-memory span, the remember-two and ignore-two condition produced the same CNV as the remember-four condition, while for high working-memory span people, the CNV for the remember-two and ignore-two condition looked like that for the remember-two condition. Thus, it appears that people with greater working-memory spans do not have greater working-memory capacities; rather, they simply manage the capacity they have more efficiently via dynamic filtering as regulated by prefrontal cortex.

Event-Related Oscillations

While the vast majority of EEG studies in cognitive neuroscience to date have used ERP analysis techniques, ERPs collapse the voltage data in such a way as to obscure the true nature of neuronal firing patterns. Clusters of neurons found in neural circuits tend to fire in oscillatory waves with characteristic frequencies. To capture this information, an increasing number of EEG studies in cognitive neuroscience have begun to employ what we term here event-related oscillation analyses (ERO; see Sauseng & Klimesch, 2008). These analyses are based on mathematical techniques (Fourier transform or wavelet analysis) that transform the recorded voltage changes into a frequency spectrum. Thus, researchers can estimate the relative populations of neurons firing at different rates. This is the type of analysis used in the ECOG study described previously (Canolty et al., 2006), but it can also be used with standard EEG recording as well.

Van Steenburgh et al. (Chapter 23) describe several different studies using time-frequency analysis to investigate the role of insight in problem

solving. In one study, Jung-Beeman et al. (2004) found two notable differences between problems that participants solved with or without insight. First, in problems solved with insight, they measured a sustained burst of low-alpha (around 10 Hz) EEG activity over the right parietal-occipital cortex beginning 1.5 seconds before the participant reported an answer. Low-alpha activity over visual cortex is understood to reflect visual sensory gating; thus, the brief deactivation of visual cortex may reflect a reduction of distracting sensory inputs needed in preparation for insight. Second, just 300 ms before answering, a burst of higher frequency gamma (30–80 Hz) activity over the right anterior temporal cortex was measured. The anterior temporal cortex is believed to be important for semantic integration, so it is likely that this burst is the signature for this cognitive process.

Although time-frequency analyses are frequently performed time-locked to stimuli or responses, they can also be used as a more general appraisal of cognitive state. In addition to the time-locked findings mentioned in the previous paragraph, Kounios et al. (2006) found that low-alpha EEG activity (8–10 Hz) prior to problem solving predicted whether a participant would solve the ensuing problem with insight, with greater alpha signifying a greater likelihood of a solution with insight. Likewise, many researchers have found that frontal asymmetries in low-alpha EEG activity also predict trait tendencies with respect to a general withdrawal or avoidance system (Davidson, 1993).

This type of analysis will likely prove increasingly useful as researchers in higher cognition seek to model the temporal dynamics of neuronal circuits. Changes in these dynamics have already been shown to provide parsimonious accounts for changes in reasoning associated with cognitive development (Morrison, Doumas, & Richland, 2011), aging (Viskontas, Morrison, Holyoak, Hummel, & Knowlton, 2004), and brain damage (Morrison et al., 2004).

SPATIAL FUNCTIONAL NEUROIMAGING

Spatial functional neuroimaging techniques make it possible to locate regions of activity in the brain with a greater level of precision than is possible with noninvasive electrophysiological techniques, such as EEG (see Table 6.1). Despite advances in source localization, there is nevertheless some ambiguity as to the brain regions that are contributing to an EEG signal because voltage is measured on the scalp, far from the many potential source generators. As a

result, a given pattern of electrical activity as measured on the scalp can arise from activation in many different areas of cortex. Techniques such as positron emission tomography (PET) and functional magnetic resonance imaging (fMRI) can be used to link cognitive functions with specific locations in the brain (see Cabeza & Nyberg, 2000). Both of these techniques measure biophysical changes associated with metabolic activity and exploit the fact that neural activity requires energy. Thus, locations where there is more neural activity should be the source of greater metabolic activity. Thus, unlike EEG these techniques provide an indirect measure of neural activity; however, the greater spatial resolution they provide has been a key factor in the growth of cognitive neuroscience.

Positron Emission Tomography

In the 1980s, positron emission tomography (PET) became the first widely used functional neuroimaging technique providing adequate spatial resolution (see Raichle, 1983). In the most commonly used PET procedure, blood flow is measured using a radioisotope of water. Participants must be injected with this radioactive material, but the short half-life (about 123 seconds) renders it relatively safe. Blood flow (and thus the water isotope) is increased to regions that are metabolically active, and it can be detected by sensors outside the head. Complex mathematics implemented in a computer are used to build a three-dimensional map of where the changes in metabolic activity are located in the brain. A similar method, single-photon emission computed tomography (SPECT scan) is frequently used diagnostically by neurologists to characterize potential brain damage in patients showing abnormal behavior. Early studies using the PET procedure studied memory and perception. For example, regions that were determined to be involved in vision based on recordings from neurons in animal models were shown to have increased blood flow during visual tasks. Confirmatory studies such as these provided support for the validity of the PET technique.

Although fMRI has since eclipsed PET for the purpose of localizing cognitive functions to particular brain regions, PET remains an important technique for examining the role of neurotransmitters in cognitive function. These can be radiolabeled so that the uptake of the specific neurotransmitter in different brain regions can be localized (e.g., Okubo et al., 1997). Using specialized isotopes, PET has also found important diagnostic applications, including

the early detection of Alzheimer's disease (e.g., Villemagne et al., 2011).

Functional Magnetic Resonance Imaging

There are several advantages to the use of functional magnetic resonance imaging (fMRI) compared to PET. Rather than using radiation, fMRI measures the oxygenation level of blood in particular regions of the brain, and it exploits the fact that a magnetic field is disturbed differently based on the amount of oxygen in the blood. Because there is more oxygenated blood in regions where there is more neural activity, the BOLD (blood oxygenation level dependent) signal can be used to indirectly assess relative activity of brain regions (see Fig. 6.4). With PET, the exposure to radiolabeled compounds limits the frequency with which subjects can be tested, thus making it difficult to test changes across time or practice in individuals.

A major advantage of fMRI is that it has far greater spatial and temporal resolution than PET (Brown, Perthen, Liu, & Buxton, 2007; Raichle & Mintun, 2006). The BOLD signal can resolve changes in regions as small as a cubic millimeter using some specialized techniques. This enables researchers to test more precise anatomical hypotheses than are possible with PET or EEG measures. fMRI also is more temporally precise than PET, although the hemodynamic response still takes many seconds to develop. With fMRI, it is possible

to measure BOLD signal associated with individual trials (Glover, 1999). This advance enabled a much wider range of experimental paradigms than were possible with PET. For example, one could intermix trials with varying demands or eliminate trials in which the subject made an error. However, it remains the case that fMRI cannot provide the kind of millisecond temporal resolution that is possible with direct neural activity measures such as EEG or ECOG.

Ongoing work using fMRI methods may be able to gain leverage on issues that have proved difficult to resolve through behavioral experimentation alone. For example, there have been two general approaches to understanding how humans solve reasoning problems (see Evans, Chapter 8). According to one view, humans reason based on innate logical rules. According to another view (see Johnson-Laird, Chapter 9), we form a mental model of the premises of a problem and then identify solutions by scrutinizing the model. If we assume that mental logic rules are linguistic and propositional in nature (Braine, 1998; Rips, 1994), one might expect that reasoning should engage left hemisphere regions that are active during syntactic processing. By the mental models view, solving problems that involve relations that can be represented spatially (taller-than, better-than) should activate visuospatial regions in the right hemisphere (Knauff, Fangmeier, Ruff, & Johnson-Laird, 2003; Knauff & Johnson-Laird,
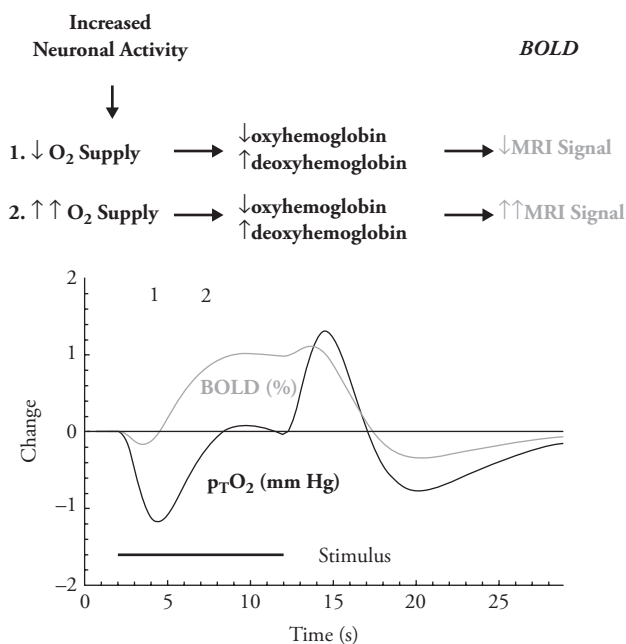

Fig. 6.4 Function magnetic resonance imaging (fMRI) is based on the hemodynamic response resulting from increases in metabolism in active neurons.

2002). At this point, existing fMRI data do not unequivocally support one view over the other, as the regions that are active during reasoning vary considerably depending on the task and the content of the reasoning problem. For example, solving syllogisms that are devoid of semantics such as (if P then Q, there is P, is there Q?) results in activation in left frontal-parietal pathways, whereas similar problems that use meaningful terms (If it is sunny, I ride my bike; I did not ride my bike today, is it sunny?) activate frontal and temporal lobe regions involved in semantic processing. Interestingly, when semantic knowledge or perceptual features of the problem are incongruous with the logical conclusion (If it is snowing, I ride my bike; I did not ride my bike today, is it snowing?), activation is also seen in right lateral midfrontal regions and the anterior cingulate (Goel & Dolan, 2003; Prado & Noveck, 2007), two areas that are implicated in cognitive control and conflict resolution. The fact that people often make errors when the logical conclusion of a problem is inconsistent with prior knowledge (the belief-bias effect, discussed later) can be viewed as a failure of engagement of these control circuits.

Overall, data from fMRI studies suggest that reasoning does not engage a dedicated neural circuit. Reasoning does not necessarily activate the right hemisphere regions involved in visuospatial processing, nor does it necessarily involve the same left hemisphere regions that are active during language processing (Kroger, Nystrom, Cohen, & Johnson-Laird, 2008; Noveck et al., 2004). However, these regions are engaged in some studies, supporting the possibility that rule application and visuospatial mental models can both support reasoning performance.

A view that is consistent with the mixed fMRI findings is that deductive reasoning involves a set of fractionated neural systems, each supporting different forms of relational reasoning (Goel, 2007). For example, although conditional reasoning (such as if-then problems) about unfamiliar information appears to rely on left frontoparietal regions, relational reasoning (e.g., Abe is to the left of Bill, and Bill is to the left of Charles; is Abe to the left of Charles?) relies in part on bilateral regions of the brain that have been implicated in visuospatial function, including the temporal-parietal-occipital junction (Goel & Dolan, 2004; Prado, Van Der Henst, & Noveck, 2010). Reasoning problems that involve semantically meaningful materials engage left temporal lobe storage sites for semantic information

(Goel, Buchel, Frith, & Dolan, 2000), consistent with the specific deficits in semantically meaningful problems exhibited by temporal-variant FTLD patients described earlier (Krawczyk et al., 2008; Morrison et al., 2004). The picture that appears to be emerging from these studies is that humans did not evolve a single reasoning system, but rather multiple systems suited to different problem domains are involved. Humans may have several reasoning systems at our disposal, including both rule-based mental logic and visuospatial mental models, and rely on whichever corresponding neural system is best suited for the problem (Prado et al., 2010).

Although fMRI studies to date do not seem to support any general theory of human reasoning, these studies together have consistently shown that deductive reasoning engages regions distinct from those involved in linguistic processing (Monti, Osherson, Martinez, & Parsons, 2007). While left hemisphere regions, including Broca's area in the inferior frontal gyrus (IFG), are often activated during deductive reasoning (Goel & Dolan, 2004), it is unclear if this is because language processing is required to understand the premises of a problem, or because these regions are generally important for syntactic processing that is common to both linguistic processing and logical reasoning. Based on fMRI approaches that allow the hemodynamic activity to be identified as the subject is processing different phases of the problem, it appears that although language areas in the frontal lobes are active for the initial interpretation of the premises, this activation quickly recedes to baseline, and nonlinguistic frontoparietal areas become active while the subject is actually solving the problem (Monti, Parsons, & Osherson, 2009). Thus, linguistic and logical rules used during reasoning appear to depend on distinct regions that occupy neighboring regions in left hemisphere, and fMRI data are at least making a good case that reasoning and thought can operate independently at the neural level. In addition, the existence of right hemisphere activation in several reasoning studies also suggests nonlinguistic processes may be engaged. For example, the involvement of right superior parietal lobule in these studies (Eslinger, et al. 2009; Goel & Dolan, 2003) is consistent with the idea that reasoning often involves the mental representation and manipulation of spatial information.

Although most fMRI studies of higher cognition have aimed to elucidate the various brain areas important for processing, there has been increasing

interest in understanding how these regions work together. In fact, the temporal dynamics of brain networks may be equally as important in higher cognition as simple activation. A dramatic example involving human language processing is a study by Sonty, Mesulam, Weintraub, Parrish, and Gitelman (2007), who used fMRI in conjunction with the cognitive neuropsychology approach. Patients with primary progressive aphasia (PPA; Mesulam, 2007; see also note 2), a neurodegenerative disease, show progressive loss of language functions, including the ability to name words and to appreciate the semantic relationships between concepts. Sonty et al. had patients with PPA, and age- and education-matched control participants, perform a semantic matching task (identify synonyms) and a letter-matching task (match nonword letter strings). Patients were less accurate than controls at the semantic task and slower on both tasks. Using fMRI, Sonty et al. found that several brain regions in the left hemisphere frequently associated with language (posterior fusiform gyrus, posterior superior temporal sulcus [Wernicke's area], IFG [anterior Broca's area], inferior parietal lobule, intraparietal sulcus, and ventral premotor cortex) were more active in the semantic than the letter task. Interestingly, these areas were not less active in patients than in controls, despite the poorer performance in patients. However, when Sonty et al. examined effective connectivity between these regions using dynamic causal modeling (DCM; Friston, Harrison, & Penny, 2003), a different story emerged. DCM uses a Bayesian decision algorithm to make estimates of how different brain regions affect each other via mono or polysynaptic interregional connections. Sonty et al. found that when patients were compared to controls, a significant decrease was found in connectivity between posterior superior temporal sulcus (Wernicke's area) and IFG (anterior Broca's area), and this decrease correlated with reduction in performance. Thus, in PPA it was not a change in activation *per se* that was responsible for changes in behavior, but rather the effectiveness of communication between areas. It is likely that connectivity patterns affect capabilities throughout higher cognition and may in part explain the dramatic individual differences and developmental patterns seen in cognitive abilities.

NEW METHODS FOR FUNCTIONAL NEUROIMAGING

Although EEG and fMRI currently dominate the neuroimaging methods used to study thinking and reasoning, two new methods offer exciting possibilities for the future given their lower cost and better temporal resolution (relative to fMRI) and their superior spatial resolution (relative to EEG).

Magnetoencelphalography

Like EEG, magnetoencelphalography (MEG) directly measures neural activity; however, instead of measuring voltage, it utilizes the electromagnetic properties of the electrical charge associated with neurons to measure minute magnetic forces resulting from increases in neuronal firing (see Hansen, Kringelbach, & Salmelin, 2010). According to Faraday's Law, magnetic forces exist perpendicular to current flow and as a result the magnetic forces do not spread as much as the voltage differences measured by EEG. Thus, the potential source generators for MEG signal are better constrained than those potentially responsible for EEG signal. Like EEG, MEG can be sampled with millisecond resolution. Also like EEG, the participant experience is quite noninvasive, allowing some participant movement during testing and good experimenter access to the participant. Like fMRI, MEG can also be used to examine when different brain regions tend to sequentially activate via DCM (Kiebel, Garrido, Moran, Chen, & Friston, 2009). As a result, MEG is rapidly becoming the preferred functional neuroimaging technique for imaging young children and infants. Thus, MEG will likely be important for understanding early changes in language and reasoning. For example, MEG has recently been used to compare 10-year-old children and adults in terms of the engagement of frontoparietal networks during working-memory processes (Ciesielski, Ahlfors, Bedrick, Kerwin, & Hamalainen, 2010). Even though the children and adults exhibited the same level of performance on an n-back task, differences in MEG signal in the two groups indicated that the children were relying on different neural mechanisms compared with adults.

Functional Optical Imaging

Functional near infrared spectroscopy (fNIRS) involves placing infrared light emitters and detectors on the scalp (see Villringer & Chance, 1997). The light penetrating the scalp is absorbed by oxy- and deoxyhemoglobin in the blood. The reflected wavelengths can then be measured, and the concentration changes as a result of neuronal activity can be estimated. Unlike fMRI, the NIRS response can measure both oxy- and deoxyhemoglobin,

with millisecond accuracy; however, just as with fMRI there is a delay in the beginning of the signal, because both techniques rely on measuring the hemodynamic response. NIRS equipment is relatively inexpensive, and unlike fMRI it costs very little to run the equipment. Thus, it is possible to run a larger number of participants in a study and thus potentially capture smaller behavioral effects. However, one problem with NIRS is that it can only detect neuronal activity in gray matter within approximately 1 cm of the scalp surface. While this limitation may prevent using NIRS to study the functions of subcortical structures, regions of the prefrontal cortex involved in working memory and reasoning are readily accessible using this technique. Like MEG, NIRS is being used in populations who cannot be tested in fMRI, including infants and young children.

An even more recently developed technique, event-related optical signal (EROS; Gratton et al., 1997), uses infrared light like fNIRS, but instead of measuring the hemodynamic response like fMRI it takes advantage of the light scattering qualities of neurons undergoing action potentials. Thus, EROS has a temporal latency (100 ms) closer to EEG and MEG than the multisecond latency of fMRI and fNIRS. Like NIRS, EROS can be sampled with millisecond frequency.

Tsujii and Watanabe (2010) recently used fNIRS to investigate the belief-bias effect, which has been explained using dual-process theory (Evans, Chapter 8). In this paradigm participants are asked to solve syllogisms in which the logical conclusions are either true (congruent) or not true (incongruent) about the world. The general finding is that participants are more likely to make reasoning mistakes when the logical conclusions are not factually correct—an effect that is enhanced when reasoning is speeded. Explanations based on dual-process theory argue that when resources (e.g., time) are limited, participants defer to a fast System I heuristic based on whether they believe the conclusion, rather than assessing whether it is logically correct. In contrast, when time is plentiful, participants use slower System II analytic processing. Tsujii and Watanabe used fNIRS to look at activity in right and left IFG, an area of the prefrontal cortex frequently associated with cognitive inhibitory functions, and an area they believed would be necessary to inhibit System I heuristic processes in order to choose the logically correct solutions when solving incongruent syllogisms. Their results were consistent

with this hypothesis. Specifically, they found that right IFG increased in activity on long-incongruent trials relative to short-incongruent trials, and that right IFG activity was correlated with the accuracy of individual participants on incongruent trials. These findings are broadly consistent with previous findings of right lateral prefrontal activation during incongruent trials (Goel & Dolan, 2003), and they extend these results in that they demonstrate a relationship between IFG activity and performance, and the ability to overcome belief-bias with time on each trial. The effects sizes in the Tsujii and Watanabe (2010) experiment were very modest, and they tested 48 participants in the study, something that would not have been feasible in an fMRI experiment due to expense.

Virtual "Lesions" Using Transcranial Magnetic Stimulation

Approaches such as EEG and fMRI seek to measure the output of the brain, and then correlate this activity with concurrent cognitive functions. Thus unlike cognitive neuropsychology, these approaches are unable to demonstrate whether this activity is necessary for the observed cognitive function. It is always possible that the activity that is measured is in fact supporting some incidental cognitive process. For example, activity associated with performance of a reasoning task could be related to incidental learning of the responses, or mental imagery, rather than the reasoning processes in question. Transcranial magnetic stimulation (TMS) allows the experimenter to alter function in a brain region and then measure the extent to which various cognitive functions are affected (see Pascual-Leone, Bartres-Faz, & Keenan, 1999). TMS relies on the fact that a magnetic field will induce an electric current orthogonal to the direction of the field. This induction is not impeded by the scalp or skull, so an electromagnetic coil held at the surface of the head can induce current in the brain tissue below. When TMS is administered as repetitive pulses, the effects of the current can be long lasting. In most experimental studies, TMS is used to disrupt function. However, if different stimulus intensities are used, it can also be used to enhance function. TMS given for extended periods over several sessions has been shown to be an effective treatment for some neurological and psychiatric disorders, as it appears to induce functional changes in activity (Wassermann & Lisanby, 2001).

Similar to the limitations of NIRS and EROS, a major disadvantage of the TMS technique is that

it is currently only possible to apply stimulation to regions on the surface of the brain that are accessible to the field generated by a coil. While thinking and reasoning certainly make use of subcortical structures, the frontoparietal network is clearly of great importance and accessible to TMS. For example, Tsujii et al. (2010) were able to follow up their NIRS study described previously using repetitive TMS to disrupt the region in the right IFG they found to be active when subjects needed to inhibit semantic-based heuristic processing to solve reasoning problems. As predicted, repetitive TMS applied to the right IFG interfered with performance on incongruent trials, thus enhancing the belief-bias effect.

TMS can be used in conjunction with neuroimaging techniques to examine whether regions of activation detected are in fact necessary for task performance. However, several important questions may be impossible to address with TMS, such as the interactions between cortical and subcortical structures in thinking (e.g., cortico-striatal loops) or the influence of emotion on thinking mediated by the amygdala.

Computational Modeling of Neural Systems

Computational modeling has greatly contributed to the development and testing of theories of thinking and reasoning at the computational and algorithmic levels of analysis (see, e.g., Doumas & Hummel, Chapter 5; Rips et al., Chapter 11; Buehner & Cheng, Chapter 12; Holyoak, Chapter 13; Koedinger and Roll, Chapter 40). Relatively little effort, however, has focused on understanding thinking and reasoning at the implementation level. Most implementation-level modeling of brain circuits has been based on connectionist architectures (e.g., Braver, Barch, & Cohen, 1999; O'Reilly, 2006), sometimes augmented with Bayesian decision rules. While these architectures and algorithms can capture many System I types of learning, they fail to capture many System II forms of thinking and reasoning that require explicit representation of relations (see Doumas & Hummel, Chapter 5). Notable exceptions include Anderson and colleagues (Anderson, Albert, & Fincham, 2005; Anderson et al., 2004) ACT-R model of problem solving, and Hummel and Holyoak's (1997, 2003) LISA model of relational reasoning.

ACT-R is a symbolic production system computer model of human cognition, including problem solving. ACT-R serves as a high-level programming language, including many basic assumptions about how cognition works but also allowing users to add additional task-specific assumptions. ACT-R can make predictions for such indicators of task performance as response time or accuracy. Although ACT-R was not designed with brain architecture in mind, researchers have recently attempted to map several of ACT-R's basic functions to brain areas, and then to use this information to match fMRI activation patterns to the functioning of the model as it solves a complex problem, such as the Tower of Hanoi (see Bassok & Novick, Chapter 21). In a series of studies that attempted to isolate cognitive processes in ACT-R with relatively simple tasks, Anderson et al. (2005) associated a posterior parietal brain region with changes in problem representation, a prefrontal brain region with retrieval of task-relevant information, and an area in primary motor cortex with programming of manual responses.

Hummel and Holyoak's LISA model (1997, 2003; see also Doumas & Hummel, Chapter 5, and Holyoak, Chapter 13) is a symbolic-connectionist model that aims to provide a unified account of analogical retrieval, mapping, inference, and relational generalization. LISA solves the relational binding problem by a form of dynamic binding implemented via temporal synchrony. Temporal synchrony is a fundamental property of neural circuits, as evidenced by the rhythmic oscillations evident in raw EEG signals. The use of temporal synchrony as a binding mechanism was first demonstrated via single-cell recording in cat visual cortex (Gray, Engel, Konig, & Singer, 1992), and it has been proposed as a general binding mechanism in the brain (see Singer, 1999). LISA uses temporal synchrony to bind relational representations in working memory. Specifically, propositional structures like *chase* (cat, mouse) are "thought about" in LISA by firing semantic units capturing what it is to chase, and to be a cat, at the same time; and conversely firing units capturing what it is to be chased, and to be a mouse, at the same time, but out of synchrony with *chase* (cat). See Morrison, Doumas, and Richland (2011) for a recent detailed description of LISA's functioning using these types of representations.

While the early papers on LISA remained agnostic regarding the neural substrate of different functions in the model, cognitive neuroscience studies provide a basis for some conjectures (see Fig. 6.5). Based on the previously discussed study by Fuster, Bauer, and Jervey (1985), it appears likely that DLPFC is involved in activating representations for objects and relations that are maintained in posterior cortex (Fig. 6.5b). This process
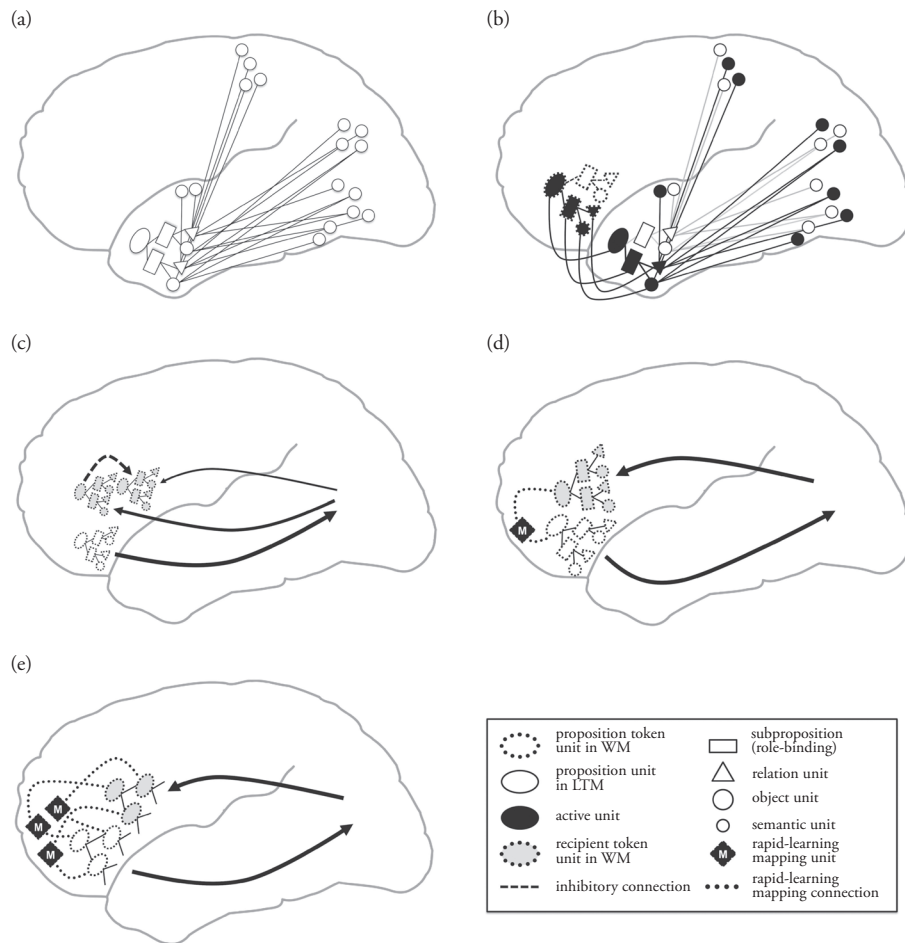
Fig. 6.5 LISA in the brain. (*a*) Networks responsible for relational representations in long-term memory are likely located in anterior temporal cortex, with their distributed semantic units found in regions responsible for sensation and perception, language, and spatial processing. (*b*) Thinking about a proposition (e.g., *loves* (Bob, Debbie)) in LISA entails forming dynamic proxy units (Duncan, 2001) in prefrontal cortex (PFC). LISA fires separate subpropositions (e.g., *lover*+ Bob) and their connected object (e.g., Bob) and relation (e.g., *loves*) units synchronously. These units pass activation to their static counterparts in long-term memory, effectively bringing long-term memory representations into active working memory (Cowan, 1995; Fuster et al., 1985). Subpropositions for a given proposition alternate being activated in working memory through a process of reciprocal activation and inhibition (i.e., black-and-white units in figure would oscillate out of synchrony with one another). (*c*) An analog's activation is computed by the rapid-learning mapping units by integrating (over time) the activations of all propositions in that analog. Because of the distributed nature of representations in LISA, more than one potential recipient analog may initially be activated. The probability that a given analog will be retrieved from long-term memory is proportional to its activation divided by the sum of the activations of all analogs. (*d*) During the pattern of synchronous firing, activation spreads through semantic units in posterior regions of the cortex and gradually activates analogous units in the recipient. Once again dynamic proxy units form in prefrontal cortex. Rapid-learning mapping units in prefrontal cortex (Assad et al., 1998; Cromer, Machon & Miller, 2010) track synchronously active units between the driver and recipient analogs via Hebbian learning and thus learn analogical mappings. Although in this figure only proposition units are shown connected via a rapid-learning mapping unit, all dynamic proxy units in prefrontal cortex (i.e., proposition, subproposition, object, relation) are hypothesized to connect to analogous units via these mapping-unit neurons. (*e*) Higher order relations (propositions taking propositions as fillers) activate more anterior regions of prefrontal cortex (e.g., Kroger et al., 2002), most likely because of the greater need to track analogical mappings via rapid-learning mapping units.

likely also requires the involvement of IFG to inhibit competing representations (Cho et al., 2010). LISA assumes that propositions are stored in long-term memory as conjunctive codes, perhaps in anterior temporal cortex (Morrison et al., 2004), with the hippocampus serving to form and later retrieve the conjunctive codes. The process of analogical mapping appears to be dependent on rostrolateral prefrontal cortex (Fig. 6.5d; Bunge, Helskog, & Wendelken, 2009; Bunge, Wendelken,

Badre, & Wagner, 2005; Nikitin & Morrison, 2011). The role of the rostrolateral prefrontal cortex (RLPFC) in reasoning appears to increase with the complexity of the task-relevant relations (Fig. 6.5e; Kroger et al., 2002). The anterior cingulate is also important for conflict monitoring, particularly in preparation of a decision concerning mapping (Cho et al., 2010; Kroger et al., 2002; Kroger et al., 2008).

The Role of the Frontal Lobes in Human Intelligence

A consistent finding across the range of methodologies employed in cognitive neuroscience is that the frontal lobes play a crucial role in high-level cognitive abilities (Cabeza & Nyberg, 2000; Duncan & Owen, 2000). But while the role of the frontal lobes in intellectual function is fundamental, it is also circumscribed. Intelligence has been typically understood as being of two different forms: crystallized intelligence, including semantic knowledge; and fluid intelligence, which supports abstract reasoning, especially in novel situations. Fluid and crystallized intelligence are differentially affected by aging and brain damage, indicating different neural substrates. Whereas patients with degenerative disease involving the temporal lobes exhibit impaired knowledge of concepts and categories (Krawczyk et al., 2008; Miller, 2007; Morrison et al., 2004), patients with frontal lobe involvement show deficits in problem solving (Holyoak & Kroger, 1995). Frontoparietal circuits are active during fMRI scanning while subjects perform fluid reasoning tasks, such as the Raven's Progressive Matrices (Kroger et al., 2002; Prabhakaran, Smith, Desmond, Glover, & Gabrieli, 1997). It appears that people with a high degree of fluid intelligence further engage regions including the DLPFC and posterior parietal lobule when problems become more complex, whereas individuals with low fluid intelligence scores activate these regions more than those with high fluid intelligence when solving easier problems but do not show this increase when problems become more complex (Perfetti et al., 2009). It is as if moderately difficult problems "saturate" this frontoparietal system in those with low fluid intelligence. High fluid intelligence may be characterized by the ability to effectively engage these circuits.

The comparative anatomy of the frontal lobes, and the fact that they are more highly developed in humans than in other animals, supports the role for the frontal lobes in cognitive abilities that are most highly developed in humans (Robin & Holyoak, 1995). The posterior part of the frontal lobes includes motor cortical regions, while more anterior, prefrontal regions have more abstract functions. Given the large size of the prefrontal cortex, it seems likely that different subregions have different functions. While there are distinct cytoarchitectonic subregions, these regions are heavily interconnected, suggesting cooperation.

Data from neuroimaging studies often show a great deal of convergence in terms of the regions that are activated in the prefrontal cortex. A number of different tasks involving cognitive control, which includes processes such as resolving response conflict, generation, working-memory manipulation, and categorization, all appear to activate a common set of regions in the lateral prefrontal cortex, dorsal anterior cingulate, and often the premotor cortex (Duncan & Owen, 2000). An increasingly popular method used to define circuits is to assess functional connectivity by measuring the correlation of BOLD signal in different brain regions (Cole & Schneider, 2007). For example, activity in the DLPFC and the anterior cingulate is correlated during task performance, and also when the subject is at rest and not performing any task. These findings indicate that these regions are interconnected and comprise part of a functional network for cognitive control. This network may subserve some process that is common to a diverse set of tasks requiring cognitive control. On the other hand, it may be that this network supports several different functions. If the latter is the case, it may prove difficult to pinpoint the cognitive functions of the prefrontal cortex because these circuits contribute flexibly to cognition.

The cognitive control network comprises a large area of cortex. According to one characterization of the prefrontal cortical control network, there is a hierarchical organization of lateral prefrontal cortex such that the more caudal regions, such as premotor cortex, are involved in response selection based on sensory stimuli, whereas more anterior regions, such as the DLPFC, are necessary when the appropriate response depends on the context. When action depends on retrieved episodic memories, the most anterior regions of the lateral cortex, including the frontal pole, are activated. By this view, the successive layers exert control over each action plan (Koechlin, Ody, & Kouneiher, 2003). In this way, behavior can be modified based on varying levels of complexity that depend on the task demands (Robin & Holyoak, 1995).

In addition to a cognitive control network, other prefrontal regions appear to be activated under other circumstances. Medial and orbital regions appear to be engaged when tasks have emotional or social components (Price, Carmichael, & Drevets, 1996). In addition, the RLPFC, the most anterior part of the prefrontal cortex, appears to have functions distinct from those of lateral prefrontal cortex. A major topic in the cognitive neuroscience of the frontal lobe is the delineation of the contribution of the RLPFC (Bunge et al., 2009; Christoff, Ream, Geddes, & Gabrieli, 2003). As discussed in the hierarchical model of cognitive control, this region becomes important when information retrieved from episodic memory is necessary for forming an action plan. This region is frequently engaged during episodic memory retrieval (Lepage, Ghaffar, Nyberg, & Tulving, 2000), but it is also active while solving reasoning problems that do not have much of a memory retrieval component. According to one view, the RLPFC becomes engaged when the problem requires the integration of multiple relations (Cho et al., 2010; Wendelken & Bunge, 2010); while according to another view, this region becomes engaged when the relations are sufficiently abstract (Christoff, Keramatian, Gordon, Smith, & Madler, 2009). As with the lateral regions, the RLPFC may play multiple roles in cognition. An important direction for future studies is the meta-analysis of neuroimaging data in order to identify commonalities in activation patterns across studies.

Conclusions and Future Directions

Methods in contemporary cognitive neuroscience range from those that have been in use for more than a century (cognitive neuropsychology) to those still undergoing development today. While each technique is better suited to address certain types of questions than others, convergent evidence from multiple methods has been most effective in moving theory forward. Because of the importance of the frontal lobes in complex cognition, their relative accessibility is a boon to researchers using techniques that are limited to the cortical surface. As a more complete understanding of the workings of the prefrontal cortex emerges, perspectives on the nature of thinking will be constrained, or perhaps new perspectives will arise.

Understanding how the brain implements human thinking and reasoning is just in its infancy. The next 10 years promise to be very exciting as the field develops with the use of new methods and analysis techniques. We believe that the fundamental challenge to this pursuit is to move beyond localist conceptions of brain function toward an understanding of how brain networks develop and operate. Thinking and reasoning are the pinnacles of human cognition and doubtless draw on many different cognitive functions. Understanding how these cognitive functions are harnessed is critical to a fuller understanding of human thought. To get to this point, we believe cognitive neuroscience needs to continue to develop in three core areas.

Cortical Connectivity

Methods for studying when and how brain regions communicate with each other are at the heart of this greater pursuit. Techniques like dynamic causal modeling have provided a way to assess connectivity using fMRI data at a macrodynamic scale; however, we need techniques to study how brain regions communicate at the temporal scale of the timing of neurons. Fortunately, methods such as EEG and MEG and possibly NIRS or EROS provide opportunities to examine real-time temporal dynamics.

Integration of Spatial and Temporal Functional Imaging

While methods like EEG and MEG provide great hope for investigating the temporal dynamics of brain circuits, they have intrinsic limitations for understanding where signals are originating in the brain. Ultimately, researchers interested in understanding brain dynamics will have to develop methods to use spatial localization techniques, such as fMRI, NIRS, or EROS, to target regions of interest, which will help to provide confidence in source localization using EEG and MEG.

Neurocomputational Approaches

Given the complexity of neural systems, we will certainly need principled ways of generating hypotheses about how they function in the service of thinking and reasoning. Computational modeling has been the great friend of thinking and reasoning in the past, helping us to develop and test models at the algorithmic and representation levels of analysis. In the coming years models will need to evolve to achieve realistic neural plausibility and thereby help to make predictions about how neural circuits work together in the service of higher cognition. This will almost certainly involve a merging of different approaches, including symbolic, connectionist, and Bayesian representations and algorithms.

Acknowledgments

Notes

1. Terminology in cognitive neuroscience is frequently rather confusing because of the interdisciplinary origins of the field. In this chapter we use the term "cognitive neuropsychology" to refer to studies of brain-damaged patients, which are frequently based on the logic of single or double dissociations (see Fig. 6.2). Cognitive neuropsychology should not be confused with the field of clinical neuropsychology, which is based on the psychometric appraisal of cognitive function. The cognitive neuropsychology approach is also sometimes referred to as "behavioral neurology."

2. Frontotemporal lobar degeneration (FTLD) is the newer nomenclature for a syndrome previously referred to as frontotemporal dementia (Miller, 2007). The umbrella of FTLD also frequently includes patients diagnosed with primary progressive aphasia (PPA; Mesulam, 2007). Patients primarily with damage in anterior to dorsolateral frontal cortex are typically referred to as either frontal-variant or behavioral-variant and have symptoms consistent with traditional frontal lobe syndromes (i.e., disinhibition, poor judgment, loss of motivation, executive and working-memory deficits). Patients with damage in anterior temporal cortex, particularly the temporal poles, are frequently referred to as temporal-variant, semantic dementia, or semantic-subtype PPA. Patients diagnosed with FTLD have a range of different postmortem pathologies, including Pick's disease, cortical basal degeneration and sometimes Alzheimer's disease.

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