Cognitive Neurology

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Cognitive neurology is a discipline that draws on cognitive neuroscience to reveal the nature of both clinical disorders and the functional architecture of the mind in an experimentally testable way (Cappa, Abutalebi, Demonet, Fletcher, & Garrard, 2008). It is informed by theories of neural and cognitive mechanisms that underlie mental processes and their behavioral manifestations and, like all bridging disciplines, comprise a broad range of methods and approaches. Central to this approach, however, is the reciprocal and ongoing relationship whereby cognitive neuroscience can inform neurology and clinical findings can enlighten cognitive research. Moreover, as a recent addition to the cognitive neurosciences, cognitive neurology is well placed to exert a powerful influence on basic science, clinical research, and rehabilitation by integrating complimentary strengths and methods from a number of key cognitive fields.

As a testament to its interdisciplinary nature, cognitive neurology connects knowledge and methods from cognitive neuropsychology, where patterns of performance produced by brain damage are used to develop and evaluate theories of normal function (Caramazza & Coltheart, 2006); behavioral neurology, a subspecialty of neurology concerned with understanding the phenomenology, pathophysiology, diagnosis, and treatment of cognitive, emotional, and behavioral disturbances in individuals with recognized neurological disorders (Silver, 2006; see Chapter 66); and cognitive neuroscience, including localization methods, which harness the powerful spatial and temporal resolution afforded by modern technologies such as event-related potentials (ERP), Positron emission tomography (PET), functional Magnetic Resonance Imaging (fMRI), Magnetoencephalography (MEG) and Transcranial magnetic stimulation (TMS) (Gazzaniga, Ivry, & Mangu, 2002).

Like its related subfields, cognitive neurology has its roots in the cognitive revolution of the 1960s and 1970s, where the success of information processing theories of the mind provided a framework for linking behavior and psychology to identifiable brain networks. From a conceptual point of view, cognitive systems are best viewed as a series of related functional systems (e.g., language, memory, attention executive) all of which can be impaired differentially (depending on age, location, and extent) following acquired brain damage. Although extensive neurological damage following stroke or head injury typically impairs several interacting cognitive systems, relatively discrete neuropathologies produce more selective impairments. The observed associations and dissociations in the patterns of impairments are subsequently used to infer the functional architecture of brain, together with converging evidence from other behavioral and anatomical studies from normal participants and neurological patients.

Cognitive neurology is characterized by the twin focus on clinical and basic (cognitive) research questions. By considering traditional clinical and neurological syndromes in terms of damage to known cognitive systems, investigators can move beyond mere description of symptomatology and attempt to meaningfully link cognitive deficits to impaired neural processes. This was well described by Basso and Marangolo (2000, p. 228) who wrote:

The most important contribution of cognitive neuropsychology . . . lies in the massive reduction of the theoretically motivated choices left open to the therapist. Clearly articulated and detailed hypotheses about representations and processing of cognitive functions allow rejection of all those strategies for treatment that are not theoretically justified. The more detailed the cognitive model, the narrower the spectrum of rationally motivated treatments; whereas the less fine-grained the cognitive model, the greater the number of theoretically justifiable therapeutic interventions.

Consequently, clinical terms such as dyslexia, dysphasia, amnesia, or visual neglect are not explanations in themselves but rather shorthand descriptions for different types of behavior that stand in need of a cognitive explanation. A major focus of cognitive neurology is the development of theories of how healthy system break down with the intention of using the observed impairments to inform mechanisms,
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diagnosis, assessment, and potential interventions. This approach holds considerable promise for advancing the fields of functional cognition (Donovan et al., 2008), clinical diagnosis (Cappa et al., 2008), and selectively targeted interventions (Halligan & Wade, 2005).

Given that several areas related to cognitive neurology are covered elsewhere in the handbook (e.g., language/language disorders—VIII 6, stroke and recovery—IX 7, memory—V 3, attention—IV 1, 3, spatial perception—III 6 and consciousness—IV 7) the aim of this chapter is to provide a broad conceptual overview interspersed with several selective and in-depth considerations of common clinical conditions. For a comprehensive review the interested reader is directed to Cappa et al. (2008), Hodges (2007), Halligan, Kischka, and Marshall (2004) and Mesulam (2000).

LEARNING FROM NEUROLOGICAL DISSOCIATIONS

Cognitive neuropsychology has achieved considerable understanding of the functional architecture of cognitive systems by charting dissociations between cognitive tasks in patients with selective brain damage (Shallice, 1988). When attempting to understand complex cognitive systems, examples of robust dissociations (where neurological damage A affects cognitive process X but not cognitive process Y) provide a useful tool. Examples of double dissociation are considered evidence of two functionally independent processes.

Naturally occurring dissociations between task performances in neurological patients have provided valuable insights into the intact and damaged mechanisms in language (Margolin, 1991), amnesia (Cermak, 1982), dyslexia (Coslett & Saffran, 1989), prosopagnosia (Young, 1994), and neglect (Halligan & Marshall, 1994), to name but a few.

Some of the most striking and theoretically important dissociations in neuropsychology result from disconnections between conscious or explicit awareness (e.g., what the patient reports) and nonconscious or implicit processing (e.g., how the patient performs), and these merit particular consideration. Recording patient reports is a relatively straightforward process in most cases, but evidence for implicit psychological processing has traditionally been ascertained using a combination of at least three different methods: (1) forced choice methods—where the patient is requested to guess or indicate a preference, (2) evaluating the extent to which selective primes or cues in the affected modality modulate or interact with responses on the nonaffected side, and (3) by directly measuring the physiological or autonomic responses.

Traditionally, the method most commonly used to demonstrate dissociations involve comparing a patient’s subjective report with their behavioral or physiological performance. For example, in the case of prosopagnosia (a disorder of face perception where the ability to recognize faces is impaired), some patients demonstrate differential electrical skin conductance or evoked potentials to familiar faces despite being unable to explicitly identify them (Bauer, 1984; Tanel & Damasio, 1985). In the case of memory, amnesic patients may show significant improvements in overall accuracy when a test is repeated (practice effects), despite failing to explicitly recall the test or its content. Such distinctions make it necessary to qualify amnesia as an impairment of conscious recollection rather than as a global failure to retain it (Moscovitch, Winocur, & McLachlan, 1986). In aphasia, patients who fail tests of comprehension may show normal semantic priming and semantic context effects on lexical decision tasks (Milberg, Blumstein, & Dworetzky, 1987); in dyslexia, patients who cannot read when tested explicitly can nevertheless guess correctly what the words denote using drawings (Shallice & Saffran, 1986).

Blindsight is one of the better known dissociations of consciousness reported in a small number of patients who show impressive intact visual processing in their blind visual field (at levels significantly above chance) despite a lack of phenomenological awareness for the location of stimuli when requested to guess (Stoerig, 1996; Weiskrantz, 1986). Until the 1970s, it was typically assumed that brain injury involved damage to the primary visual areas and consequently produced permanent loss of vision for selective parts of the visual field. Assessing visual field deficits involved asking the patient to report with their eyes fixated on a central target what they could see when stimuli at different locations were presented in the peripheral fields. Although demonstrably unaware of targets in their affected field, some patients were able to indicate by pointing or moving their eyes (when requested to guess in a forced choice experiment), the location of targets in their blind field (Weiskrantz, Warrington, Sanders, & Marshall, 1974). Although such patients clearly perceive more than might be expected, blindsight does not appear to confer any functional benefit for the patient (Weiskrantz, 1991).

Evidence of blindsight has also been found using skin conductance performance (Zihl, Tretter, & Singer, 1980) and altered pupil size (Weiskrantz, 1990). Rafael, Smith, Krantz, Cohen, and Brennan (1990) demonstrated that unseen stimuli presented to the blind hemifield had the effect of inhibiting the latency of saccades to the seen stimulus in the intact field. Studies of blindsight indicate that the processing of visual stimuli can take place even though there is no phenomenological awareness by the
subject. Anatomical and physiological evidence suggest that some forms of blindsight may rely on intact residual visual ability that is mediated subcortically (Stoerig, 1996; Weiskrantz, 1986). Other forms may be explained in terms of a disconnect between specialized areas in the visual cortex (Zeki, 1993).

ASSESSMENT, NEUROPSYCHOLOGICAL TESTING, AND NEUROIMAGING

Central to cognitive neurology is the assessment and quantification in terms of the impact to known cognitive structures of neurological disturbance. This requires understanding how neuropsychological testing and clinical neuroimaging complement each other to inform a comprehensive clinical picture. Importantly, there is no fixed contribution that each method makes because the scope of each procedure changes with the arrival of new conceptual and technological developments. For example, neuropsychological testing is no longer the primary method for localizing brain lesions owing to the wide availability of structural and functional brain imaging, although the advent of the clinical applications of functional neuroimaging has meant that well-designed psychometric tasks are now key to uncovering meaningful functional brain networks in the latest brain scanners.

Similarly, the fact that pathology can be characterized entirely at the cognitive level (e.g., dysexecutive syndrome), the neurological level (e.g., glioma), or a mixture of both (e.g., vascular dementia), means that the contribution of each approach to the diagnosis or conceptual formulation of the disorder depends partly on the presenting clinical problem and reasons for assessment.

One of the key functions of assessment is to formulate a working hypothesis regarding the areas of intact strength and weakness in functioning that in turn provides for setting appropriate goals for effective intervention (Byng, Kay, Edmundson, & Scott, 1990; Howard & Hatfield, 1987). While this is not the sole role of assessment, the adequacy of assessments for characterizing the underlying condition in cognitive terms and informing the rehabilitation process is clearly critical. The clinical aims of both neuropsychological testing and neuroimaging typically focus on three main areas:

1. **Diagnosis** to determine the nature and extent of the underlying problem in both clinical and cognitive terms.
2. **Impact** to gage the effect of the impairment on everyday functioning and cognitive ability.

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3. **Course/outcome** to measure and predict change over time, either from premorbid levels or throughout the progression of the recovery.

When attempting to answer these questions, the clinical team will typically integrate the patient’s history and presentation with the results of neuropsychology and relevant neuroimaging assessments to arrive at a well-rounded formulation based on a set of well-defined clinical questions, although clinical reality dictates that the assessment might need to be based on the best available evidence and often proceeds in an iterative manner.

Key aspects of a patient’s history include their social and medical history, paying particular attention to any personal or family history concerning educational attainment, employment, developmental or idiopathic neurological disorder, dementia, or psychiatric illness. Similarly, the onset and course of the problem in an individual patient is noted alongside any results of earlier assessments and previous experience of the tests, assessments, or environment. Key aspects of presentation include the signs (behavioral indicators suggestive of underlying disease) and symptoms (subjective reports of ill health by patient), mental state, insight, other medical problems, understanding of the purpose and possible outcomes of the assessment, comprehension of the test instructions and expressive language, level of concentration, level of motivation during each test, current mood, and ongoing pain. Simple cognitive screening tests (such as the Minnesota Mental State Examination, MMSE) or simple bedside tests may be conducted by most suitably trained clinicians but more thorough cognitive testing requires the involvement of a clinical neuropsychologist. A general overview of the types of clinical assessment employed by cognitive neurologists is provided in Cappa (Chapter 2: 2001) in addition, excellent guides to neuropsychological testing are available (Hodges, 2007; Snyder, Nussbaum, & Robins, 2005) as well as more comprehensive handbooks (Lezak, Howieson, Loring, Hannay, & Fischer, 2004; Strauss, Sherman, & Spreen, 2006).

In combination with neuropsychological test results, structural scans are important for inferring links between cognitive deficits and detectable lesions in individuals (see Figure 59.1), and can also be useful for constraining test interpretation (e.g., an individual who performs poorly on an executive test but has only posterior lesions might suggest that the deficit is one that involves early vision rather than the executive system). Functional neuroimaging offers accessible reliable measures of hemodynamic changes—blood flow in the case of positron emission tomography (PET) and blood oxygenation in the case of functional magnetic resonance imaging (fMRI)—in response to selective cognitive task engagement. Both FMRI and PET...
provide indirect measures of synaptic activity and neural firing and are extensively used to characterize the neural bases of intact and impaired neural systems underlying different sensory and cognition tasks (see Figure 59.1). Resting state functional scans (typically using Positron emission tomography (PET) or Single photon emission computed tomography (SPECT), and more recently perfusion MRI) can similarly provide information on whether there are disturbances of cerebral perfusion, suggesting areas which might be consistently under- or overactive. Due to individual variation in the neuroanatomical areas that support particular cognitive functions and the fact that not all neurocognitive impairments are detectable on standard clinical scans, there has been an increased interest in applying task-based functional neuroimaging, more typically used in research on normal cognition, for addressing clinical problems in individual patients.

Much research has focused on replacing the Wada test for establishing language lateralization and postoperative outcome assessment. The Wada test, or the intracarotid sodium amobarbital procedure (ISAP), involves neuropsychological testing of specific hemispheric functions while one, and subsequently the other, hemisphere of the brain is functionally impaired by the injection of a barbiturate into the ipsilateral carotid artery. The Wada test is also commonly used to determine likely memory impairment after a proposed unilateral temporal lobectomy in cases of intractable epilepsy. Although effective, the procedure is expensive and carries an approximate 1% morbidity risk (Baxendale, 2000) so the development of noninvasive alternatives offers significant advantage. The application of neuroimaging methods has been promising but, so far, none are in a position to replace the Wada test. This is partly because of a lack of research data, but partly because activation patterns can be influenced by task, analysis technique, and noise in the data (Abou-Khalil, 2007).

Related difficulties affect all such attempts to apply functional neuroimaging to individual patients, which has largely been developed to determine average activation over a group of people. Data acquisition artifacts that are likely to be of minor influence when data is averaged across participants (such as head movement or minor anatomical differences) have a much larger impact when only one person is being scanned. Similarly, analyses used for groups of young healthy participants, such as the reliance on a constant blood oxygenation level dependent (BOLD) signal response, may not apply so readily to children or older patients, for whom cerebral blood flow rate is known to be significantly related to age (Ackerstaff, Keunen, van Pelt, Montauban van Swijndregt, & Stijnen, 1990; Schöning & Hartig, 1996).

To overcome similar sorts of issues, neuropsychological tests commonly employ standardized scoring and norm-referenced performance comparisons, so that an individual’s performance can be seen alongside a relevant age, education, ethnicity, and/or gender matched comparison group. However, similar data for clinical function neuroimaging assessments is still rare and clinicians are encouraged to make their data available to others so these essential data sets can be created.

Although neuropsychological tests typically provide an estimate of the performance level in different cognitive domains, equally important is the process by which individuals complete the task. For example, patients with differing pathologies may not differ in their final test score, but may show remarkable differences in the way they complete the test (Kaplan, 1988). A related pattern has also been observed in functional neuroimaging studies, where a difference in behavioral measures but not activation, or vice versa, has been found (Wilkinson & Halligan, 2004). Some tests may have a measure of process built-in, and others do not. Careful observation during testing may be the key to uncovering relevant cognitive deficits in these cases.

When considering in-scanner clinical assessments, Desmond and Chen (2002) make several recommendations: (a) experimental tasks designed for research participants may be too taxing for patients, so recommend that a middle-ground compromise between collecting relevant data points and creating a valid task needs to be reached; (b) cognitive tasks may need practice outside the scanner;
(c) to draw valid clinical conclusions, the tasks need to be norm referenced; and (d) standardization of image analysis methods need to be adopted.

ACQUIRED DISORDERS OF ATTENTION

Attention—the mental process of selectively focusing on aspects of our environment including one’s body while ignoring or disattending from other things—is probably one of the most important cognitive processes given that it pervades all aspects of cognitive life and, when compromised, provides for a wide range of debilitating consequences. The range of deficits stems from the fact that attention is not a single process but rather a set of interacting, albeit relatively autonomous, subprocesses vulnerable to damage with differing consequences. As assessments have been refined over the past decade, the negative impact of impaired attention for recovery and outcome has become increasingly clear. Consequently, the development of interventions designed to enhance natural recovery in these systems remains a pressing clinical goal (Robertson & Halligan, 1999). Clearly, a framework for understanding the functional organization of attention is vital for both the clinic and research laboratory. One influential model proposed by Posner and Peterson (1990) suggests three key specific functions of attention:

1. **Spatial attention**: The capacity to distinguish incoming signals from one spatial location.
2. **Selective or focused attention**: The ability to prioritize some types of information and to restrain others on the basis of an existing planned goal or a stored representation of a target.
3. **Arousal/sustained attention**: The ability to maintain an alert, ready state.

Although these and similar taxonomies (e.g., Mirsky, Anthony, Duncan, Ahearn, & Kellam, 1991; Raz & Buhle, 2006; Van Zomeren, Brouwer, & Deelman, 1984) are capable of further fractionation, it is clear that one of the most important functional consequences is that attention modulates or “gates” activity in primary sensory areas of the brain (Desimone & Duncan, 1995) including vision (Moran & Desimone, 1985), audition (Woldorff et al., 1993), and somatosensory perception (Drevets et al., 1995).

Attention as a cognitive process cannot be observed directly but rather its presence is detected by monitoring the systematic variation in performance of different attention-demanding tasks. Posner (1980), using visual cueing paradigms, employed a simple but highly influential example of this approach. Here subjects were asked to maintain their gaze at the center of a screen and only press a button when they observed a designated target to appear. Subjects had no information where on the screen this target would be, although on a number of informative trials they received a directional or spatial cue as to probable location. These attentional cues, when accurate, produced significant reductions in overall reaction time, but when inaccurate, produced significant increases. Given that all other aspects of the task remained constant, the temporal differences were attributed to the movement or allocation of spatial attention (Figure 59.2; Posner, 1980).

Attention has also been shown to operate on stimuli at differential levels of analysis depending on processing demands (Lavie, 1995). Such methods have led to clearer accounts of the capacities and limitations of normal human attention. When combined with the study of brain damaged patients, neuroimaging or neurophysiological techniques provided a working hypothesis regarding the neural basis of some cognitive abilities.

**Hemi-Inattention (Visuo-spatial Neglect)**

The most common and striking neurological condition to follow brain damage involving attentional processes is visuospatial or hemispatial neglect (Karnath, Miller, & Vallar, 2002). The neglect syndrome has become an established clinical entity that features prominently in most current texts of behavioral neurology and cognitive neuropsychology (Heilman & Valenstein, 2003). Not surprisingly, it is
also the area where rehabilitation is also well developed (Luaute, Halligan, Rode, Rossetti, & Boisson, 2006).

Visual neglect refers to a person’s difficulty in detecting, acting on, or even thinking about information on one side. People with visual neglect often fail to notice food on the left side of their plate, fail to dress or wash the left side of their body, have difficulty in imagining the left side of familiar objects, and, in some cases, even deny ownership of their own left limbs (Figure 59.3).

A number of basic clinical observations have been established that inform our understanding of the brain’s representation of space, attention, and action (Buxbaum, 2006). The condition has been reported in the visual, auditory, tactile, and olfactory modalities (Halligan & Marshall, 1993), although the most extensive investigations typically concern visuospatial neglect (Figure 59.4). Left neglect after right hemisphere lesions are more frequent, severe and long lasting than right neglect after left hemisphere lesions. Neglect can affect personal (or body) space, peripersonal space (stimuli within reaching and grasping distance), and extrapersonal space (stimuli within walking distance). Although lateralized (left-right) visual neglect has attracted most research interest, comparable phenomena have been observed for the other two dimensions of space (radial and altitudinal neglect). Although classically associated with lesions to the right posterior parietal cortex (Heilman & Watson, 1977; Vallar & Perani, 1986), neglect has been observed following damage to a variety of brain structures including the right prefrontal cortex and subcortical areas (Damasio, Damasio, & Chui, 1980; Mesulam, 1981; Karnath, Ferber, & Himmelbach, 2001; Samuelsson, Jensen, Ekholm, Naver, & Blomstrand, 1997).

Figure 59.3  Illustration of left-sided visual neglect when copying.

Figure 59.4  Cortical anatomical correlates of visuospatial neglect. Note: Cortical anatomical correlates of unilateral visuospatial neglect. Most anatomo-clinical correlation studies show that the lesions responsible involve right inferior parietal lobule (Brodmann areas BA (regions of the cortex defined based on their cytoarchitecture) 39 and 40, highlighted in black) and in particular the supramarginal gyrus, at the temporo-parietal junction (black–grey area). Neglect after right frontal damage although less common is usually associated with lesions to the frontal premotor cortex, particularly BA 44 and ventral BA 6. Neglect has also be associated with damage to the more dorsal and medial regions of the frontal prefrontal cortex, and to the superior temporal gyrus. (from Halligan, Fink, Marshall, & Vallar, 2003).

Visuospatial neglect is often diagnosed on the basis of simple (bedside) tests such as cancellation, line bisection, copying, spontaneous drawing, reading, and writing; in many patients, the verbal description of complex visual images and topographic routes (generated from long-term memory) can also show lateralized neglect (Bisiach, Brouchon, Poncet, & Rusconi, 1993). Even with such relatively simple tasks as copying or spontaneous drawing, many qualitatively distinct patterns of impairment can present as lateralized neglect (Halligan & Marshall, 2001).

Research over the past 30 years has convincingly shown that neglect is a protean disorder whose symptoms can selectively affect different sensory modalities, cognitive processes, spatial domains, and coordinated systems (Buxbaum, 2006; Halligan, Fink, Marshall, & Vallar, 2003). Deficits of attention, intention, global-local processing, spatial memory, and mental representation make it unlikely that this clinical syndrome can be traced back to the disruption of a single supramodal cognitive process (Vallar, 1998). Many of these clinical findings have been used to better understand the anatomical and functional architecture of the premorbid subsystems of spatial cognition, in particular: (a) neuropsychological structure of space, (b) relevant spatial frames of reference used prior to recognition, and (c) selective preservation of preattentive processes.
Neuropsychological Structure of Space

Although space extends seamlessly in three dimensions, it does not appear to be homogeneously represented in the brain. Embodied space can be behaviorally divided into at least three different regions: personal space, peripersonal space, and extrapersonal space (see Figure 59.5; Robertson & Halligan, 1999). Personal space involves the body and body surface: the space in and on where one can feel touch and within which one can comb one’s hair or scratch an itch. Peripersonal space is the working space beyond the torso but within arm’s reach. Extrapersonal space is beyond arm’s reach but one can obviously bring objects within peripersonal space by moving there or by deploying a tool. One can orient the eyes toward an object in extrapersonal space, point to it, or throw something at it. Evidence for the neurobiological distinction between peripersonal (near) and extrapersonal (far) space comes from a wide range of animal and human studies (Caramazza & Hillis, 1990; Previc, 1990) but some of the clearest evidence comes from patients with left neglect after right hemisphere lesions (Buxbaum, 2006; Rizzolatti, Berti, & Gallese, 2000).

Personal Space

Neglect of left personal space can occur without neglect of left peripersonal space (Guariglia & Antonucci, 1992) and vice versa (Beschin & Robertson, 1997). One of the first demonstrations of dissociation was reported by Brain (1941) in a case of right hemisphere glioblastoma where the patient was impaired in pointing to objects in near space without comparable difficulty for objects in far space. Typical manifestations of left personal neglect include failure to shave or groom the left side of the face, failure to adjust spectacles on the left side, and failure to notice the position of the left limbs and use them appropriately even when no significant motor weakness is present. By contrast, the ability to use left personal space without difficulty can be seen in the context of severe left neglect of peripersonal space as assessed by visual search tasks where the targets are displayed within arm’s reach (Beschin & Robertson, 1997). This double dissociation of personal and peripersonal neglect suggested that distinct neuronal circuits underlie how the two spaces are represented in the human brain. Performance difference in different space has also been shown to include imaginal or representational space (Beschin, Basso, & Della Sala, 2000; Ortigue, Mégevand, Perren, Landis, & Blanke, 2006).

Peripersonal and Extrapersonal Space

Similar double dissociations have been discovered between left neglect in peripersonal and in extrapersonal space. When lines of constant visual angle are bisected by a laser pen in near versus far space, some patients show accurate performance in far space but a significant rightward deviation in near space (Halligan & Marshall, 1991), while other patients show the reverse dissociation: far left neglect without near left neglect (Vuilleumier, Valenza, Mayer, Reverdin, & Landis, 1998). A study by Viaud-Delmon, Brugger, and Landis (2007) shows how back space is also represented in patients suffering from spatial neglect and further underscores the distinction between motor and nonmotor space. It appears that acting in a particular spatial domain involves distinct neuronal representations of near or far space to become active. Nevertheless, a study by Pitzalis, Di Russo, Spinelli, and Zoccolotti (2001) employing both perceptual and motor versions of line bisection in near and far space argues against this view. The same patients were tested in all conditions. In both the perceptual and the motor tasks, some patients showed near left neglect without far left neglect and others the reverse dissociation. Thus, different accuracy of performance between spatial domains can be revealed by purely perceptual tasks. Furthermore, the patients showed similar degrees of impairment on the motor and the perceptual versions of line bisection.

The coding of space as extrapersonal and peripersonal is not solely determined by the hand-reaching distance and can depend on how the brain represents action capabilities. Berti and Frassinetti (2000) showed that in a patient with demonstrable peripersonal space neglect, previously intact far space bisection (using a laser light pen) became as severe as neglect in the near space when the patient
performed the task using a stick as an artificial extension of the patient’s body and appeared to undergo a remapping of extrapersonal space as peripersonal space.

Weiss et al. (2000) used PET to determine the functional anatomy implicated when volunteers were requested to bisect lines and point to dots in peripersonal or extrapersonal space (see Figure 59.6). Twelve healthy right-handed male volunteers bisected lines or pointed to dots in near or far space using a laser pen. When performing either task in near space, the subjects showed neural activity in the left dorsal occipital cortex, left intraparietal cortex, left ventral premotor cortex, and left thalamus. In far space, subjects showed activation of the ventral occipital cortex bilaterally and the right medial temporal cortex. These findings provide physiological support for the clinically observed dissociations even when the motor components of the tasks were identical when performed in both spaces.

Spatial Frames of Reference

Systematic analysis of visual neglect over the past 2 decades has revealed significant insights into how attention can be allocated to objects- and space-based representation in terms of differential spatial coordinate frames used in normal cognition. There is compelling evidence that egocentric space can be coded in different viewer-centered frames.
of reference, including eye, head, torso, shoulder, arm- and hand-centered coordinates (Beschin, Cubelli, Della Sala, & Spinazzola, 1997). The terms left or right are consequently relative, since they can be defined with respect to different reference points (Buxbaum, 2006).

Visuospatial attention can also operate in coordinate frameworks independent of the position of the observer. In object-based neglect, the left side of an object is ignored (Umilta, 2000). Some of the most convincing evidence for selective damage to object-based attention deployment can be found in the drawing and copying performance of neglect patients (see Figure 59.7).

By contrast, object-centered coding (Driver & Halligan, 1991) of left and right concerns the intrinsic laterality of an object (e.g., English words have an intrinsic left to right sequence of letters). Examples of this form of coding in neglect have been elegantly demonstrated by Caramazza and Hillis (1990) in a left brain damaged patient with right neglect dyslexia. When reading, her errors were always located on the right side of the word irrespective of whether the words were presented horizontally, vertically, or even mirror-reversed.

Finally, neglect findings have been used to both support and question features of Kosslyn’s (1994) analog theory of visual mental images, that is, representations that produce the experience of seeing in the absence of sensory input. Within cognitive science, the debate about the depictive representational format of visual mental imagery clearly differentiates analog (picture-like images with intrinsically spatial representational properties) from the propositional account (linguistic descriptions without inherently spatial properties) championed by Pylyshyn (1981). Moreover, a defining assumption of the former account is that perceptual and imagery processes share the same mental operations and neural structures (Kosslyn & Thomson, 2003). Clinical accounts of visual neglect such as those by Bisiach and Luzzatti (1978) and others involving neglect of visual images in parallel with deficits in perception (Marshall & Halligan, 2002) have been used to support the analog claim, however, subsequent case reports describing selective lateralized breakdown of imaginal representation or imagery without corresponding deficits in perceptuo-motor performance question the close functional overlap of imagery and perception processes (Bartolomeo, 2002; Behrman, Winocur, & Moscovitch, 1992).

Knowing without knowing

Investigations of neglect have contributed to the fascinating debate regarding the processing locus of attentional selection (Kanwisher & Wojciulik, 2000). Several studies of visual neglect have shown that different levels of preattentive processing up to the level of meaning can take place in the neglected field without conscious awareness (Driver & Vuilleumier, 2001). Even on line bisection (a traditional clinical measure), patients with left neglect show implicit sensitivity to manipulations of both stimulus and the visual background (Shulman, Alexander, McGlinchey-Berroth, & Milberg, 2002) confirming that preattentive visual capacities of figure ground and stimulus can influence explicit visual motor performance.

Informally, many students of visuospatial neglect consider the condition to be a classic disorder of visual awareness—where awareness is equated to the psychological construct of attention (Posner, 1978). Unlike blindsight, which is elicited experimentally, left neglect occurs spontaneously and remains a major negative prognostic factor associated with poor performance on most functional recovery measures (Halligan & Robertson, 1992). However, with blindsight, there is considerable evidence that when tested indirectly, many patients can show some degree of information processing for the stimulus of the affected side (Berti & Rizzolatti, 1992; Marshall & Halligan, 1988; McGlinchey-Berroth, Milberg, Verfaellie, Alexander, & Kilduff, 1993; McIntosh et al., 2004).

Evidence for this possibility of nonconscious perception in the case of neglect can be traced back to Kinsbourne and Warrington (1962) who reported a length effect in neglect dyslexia; reading errors maintained the length of words presented. Moreover, A. W. Ellis, Flude, and Young (1987) who replicated this finding suggested that although neglect selectively affected the coding of the identity of the left most letters, patients are still capable of coding letter position and overall length. A clinically similar but less well known phenomenon occurs in line bisection. When requested to bisect a line located in the center of a page.

Figure 59.7 Illustrations of object-centered visual neglect in copying.
most patients with neglect show a displacement of absolute magnitude that is linearly related to line length (Halligan, 1995; Halligan & Marshall, 1988). This linear performance may be explained in terms of implicit processing of the visual information on the neglected side. Thus, the neglected end of the stimulus line may covertly influence the patient’s performance in deciding the subjective center of the line.

In one of the first clinical cases reported by Marshall and Halligan (1988), patient PS, who had sustained a right hemisphere stroke, was presented with two line drawings of a house (see Figure 59.8) simultaneously, one of which had red flames emitting from the left side window. Requested to make same/different judgments between the two simultaneously presented pictures, PS reliably judged the two drawings identical. When asked several minutes later to select the house she would prefer to live in, she reliably chose the nonburning house with a high level of statistical significance, commenting that it was a “silly question” since both houses were identical. In other words, although PS was unable to perceive the crucial differences between the two houses (despite free movement of the head and eyes), she nevertheless appeared able to process some information in the hemispace contralateral to lesion that influenced her preference judgment (cf. Manning & Kartsounis, 1993). Later, more detailed studies by Berti and Rizzolatti (1992) and McGlinchey-Berroth et al. (1993) using cross field matching and priming experiments showed that implicit perception, up to the level of meaning, was possible in some patients with neglect. In the case of Berti and Rizzolatti (1992), patients who denied seeing anything in the left visual field nevertheless showed significantly shorter reaction times to the right field stimulus for the congruent rather than the noncongruent conditions.

Marshall and Halligan (1994) showed evidence of a further type of dissociation between two forms of conscious perceptual awareness—again in a free vision task (Figure 59.9). In a series of experiments, they showed that a patient with neglect had a selective inability to analyze and copy accurately the left contours of geometric nonsense figures. These results were present even when there was a single vertical contour (to be copied) that divided a rectangle or a circle into two subfigures. A physically identical boundary was copied more accurately when it was cued as the right edge of the left subfigure than when it was cued as the left edge of the right subfigure. The results were interpreted in terms of demonstrating the presence of intact preattentive (global) figure-ground parsing despite gross impairment when focal attention was demanded and the right side of an object was only coded as a figure.

In most cases, however, global processing of the visual world can no longer be used to direct automatic focal attention to spatial locals that require further focal analysis. Without this ability, local attention which is usually biased to the right will always represent too little of the visual

Figure 59.8 Illustration of covert processing in visual neglect.

Figure 59.9 Preserved figure-ground segregation in visual neglect.

Note: When asked to copy the top display, the patient only drew the right side of the black figure (C). However if requested to copy the left side of the same object when it was cued as the right side of the left white subfigure (previously ground), the left side could be accurately copied (A). Copies of the left side for the same right white subfigure (previously ground) always showed neglect of the details of the contour (B) (see Halligan, Fink, Marshall, & Vellai, 2003).
world. However, once attention has been focused, the panoramic or global view is lost to conscious awareness. When focal attention is biased to the right as in the case of neglect, the patient is in no position to observe the absence of left-sided input. Even if selective attention can be voluntarily moved leftward, the necessary guiding framework provided by the global scale is no longer available.

Consequently, patients no longer have any reason to continue to explore leftward. In these and other examples (Marshall & Halligan, 1995) where performance within an individual patient can be normal on one aspect and grossly impaired on another involving the same stimulus seconds later, left neglect may be regarded as a partial disconnection of conscious visual awareness where residual processes of the impaired right hemisphere cannot be used to constrain the performance of the intact left hemisphere in performing the designated task.

Collectively, these findings from visual neglect highlight the danger of equating phenomenological conscious experience with the operation of the perceptual mechanisms involved. In the absence of apparent phenomenological awareness, there is evidence that many patients, when tested indirectly, may show some degree of information processing for the stimulus of the affected side in the case of neglect or blindsight.

Although adequate cognitive accounts of awareness still remain to be developed (see Clare & Halligan, 2006; Dehaene & Naccache, 2001; Farah & Feinberg, 1997), productive contributions toward the emerging cognitive neuroscience of consciousness rely on pathologies of awareness and the tasks used to reveal them (Babinski, 1914; Bisiach & Berti, 1987; Forstl, Owen, & David, 1993; Prigatano & Schacter, 1991). These have also included examples from nonvisual modalities. For example, in the tactile modality, reports of blind touch (Lahav, 1993; Paillard, Michel, & Stelmach, 1983; Rossetti, Rode, & Boisson, 1995) or “numbsense” (Perenin & Rossetti, 1996) and “deaf hearing” (Michel, Peronnet, & Schott, 1980) have also been recorded. These reports lend further support to the concept of multichanneling sensory information already well established in the visual system and the realization that perception is not a unitary process but one subserved by several separable modules.

While most theoretical studies have been concerned with showing what a patient can do without explicit awareness of their clinical condition using experimental task performance (Berti & Rizzolatti, 1992; Bisiach & Rusconi, 1990; Marshall & Halligan, 1988), many other clinical studies are primarily concerned with diagnostic issues (Cutting, 1978; S. J. Ellis & Small, 1994; Levine, Calvanio, & Rinn, 1991; Nathanson, Bergman, & Gordon, 1952) and characterizing the anatomical and functional consequences of their reported and behavioral unawareness (Pia, Neppi-Modona, Ricci, & Berti, 2004; Samuelsson et al., 1997; Stone, Halligan, & Greenwood, 1993).

However, it is clear that a patient does not need to be explicitly unaware of their cognitive or neurological deficit at the level of verbal reporting to continue to demonstrate significant pathologies of awareness on formal testing. Several patients with intractable chronic neglect show what appears to be considerable conceptual and experiential insight into their deficit and its consequences while continuing to demonstrate neglect on selective tasks (Cantagallo & Della Sala, 1998). Moreover, stroke patients with anosognosia may verbally admit to being hemiplegic yet appear to ignore the consequences of such statements when planning and programming their functional motor activities (House & Hodges, 1988; Marcel, Tegnér, & Nimmo-Smith, 2004).

**DISORDERS OF READING AND WRITING**

**Acquired Reading Disorders**

Reading is a complex process that involves visual processing, access to semantics and phonology, and control of articulation. Since Marshall and Newcombe’s (1966, 1973) landmark studies on two patients with reading disorders after brain injury, knowledge of both the diversity of reading deficits and of how reading occurs in the normal brain has grown exponentially. Notably, while the literature makes clear distinctions between different reading deficits, they are rarely observed as totally distinct syndromes in individual patients and are often accompanied by other language or visual processing difficulties (Patterson & Lambo Ralph, 1999). This section focuses on acquired reading disorders because they have been the focus of most research in cognitive neurology, although developmental dyslexias are now being increasingly studied in the same context (Temple, 2006).

Two neuropsychological models of normal reading currently form the basis of acquired dyslexia theories. The dual route model and its variations (Coltheart, Rastle, Perry, Langdon, & Ziegler, 2001; Rapcsak, Henry, Teague, Carnahan, & Beeson, 2007; Figure 59.10a) are largely based on observed post-brain injury dissociations between reading regular words (that follow the standard rules of pronunciation – such as ‘drink’), irregular words (that are exceptions to the normal rules of pronunciation – such as ‘chord’), and nonwords (pronounceable but meaningless letter strings – such as ‘lart’). These models suggest that there are two main routes for determining the identity of a word or letter string. The first lexical route is where a word...
is recognized by matching the letter string to a directory of familiar words stored in memory, called the visual word form system. Once the visual word form is activated, this can activate the phonology (pronunciation) of the word either via the word’s meaning (the lexical-semantic route) or direct link to its phonological representation (the direct-lexical route). Alternatively, the nonlexical route derives the pronunciation of words by working out letter-sound associations. The triangle model of reading (Plaut, 1997; Seidenberg & McClelland, 1989; Figure 59.10b) takes a radically different approach using a connectionist model with three interconnected systems that represent the recognition of orthography (vision), phonology (pronunciation), and semantics (meaning). This model suggests that both nonwords and regular words are read aloud via the vision to phonology route, while reading aloud irregular words requires both the vision to semantics route and the semantics to phonology route. This latter account is notable because it suggests that disorders of reading can be understood in terms of the disruption to one or more of these processes without the need for procedures specific to reading itself. In other words, it suggests that acquired dyslexia is not a disorder or reading per se, but a result of damage to more general cognitive processes.

Acquired dyslexia is often classified into peripheral or central types. Peripheral dyslexias are characterized by perceptual deficits that prevent the affected person from matching the visual representation of the word to the stored visual word form. Central dyslexias are where the impairment affects access to meaning or speech production after the point where the visual word form is activated.

Peripheral Dyslexias

Patients with peripheral dyslexia are impaired in reading text but have intact writing, speaking, spelling, listening comprehension, and recognition of orally spelled words. Pure alexia (also called letter-by-letter dyslexia, alexia without agraphia, spelling dyslexia, verbal dyslexia, word blindness, or letter confusability dyslexia) is a visual perceptual impairment in the processing of word and letter shapes and is often considered with theagnosias (Farah, 2004). It is typically associated with lesions centered on the left occipito-temporal junction and is often accompanied by a contralateral visual field impairment (homonymous hemianopia; Leff, Spitsyna, Plant, & Wise, 2006). It may result in letter-by-letter reading, where patients have to identify each letter individually before working comprehending the word, although even this process may be impaired in severe cases (Shallice & Rosazza, 2001).

Neglect dyslexia can result from hemispatial neglect (see section on Attention) where patients miss the leftmost letters of a word, and is particularly apparent when attempting to read nonwords (di Pellegrino, Ladavas, & Galletti, 2002). Attentional dyslexia (sometimes called letter position dyslexia) is where the reading of single isolated words may be relatively well preserved, but with impaired reading of words in the context of other words or letters (Friedmann & Gvion, 2001).

Central Dyslexias

Deep dyslexia is, perhaps, the most studied of the acquired reading impairments and is often the most profound and complex (Coltheart, Patterson, & Marshall, 1987). The most striking feature is the tendency to make frequent semantic errors (reading uncle as cousin, for example) although visual errors (e.g., reading crowd as crown) are also typically present, and combined visual-semantic errors have been reported (e.g., reading earl as deaf). Patients are often also impaired in reading nonwords, function words, and are worse at reading less imageable words compared to more imageable words (e.g., trust is more difficult than tree). Furthermore, nouns are typically read better than adjectives, and adjectives better than verbs. In terms of the dual route model, deep dyslexia is likely to result from reading that is reliant on lexical-semantic route because the other pathways are impaired (Coltheart, 2006). Deep dyslexia is commonly associated with large left hemisphere lesions that cover the frontotemperoparietal area (Lambon Ralph & Graham, 2000).

Surface dyslexia is an impairment in the ability to read phonologically irregular words (such as chord or ache) while the reading of regular words (such as book or tree) and nonwords is relatively well preserved (A. W. Ellis, Lambon Ralph, Morris, & Hunter, 2000). It is most common in the dementias and particularly characteristic of semantic dementia (Hodges et al., 1999) although it is linked to left temporal damage even in acquired impairments (Vanier & Caplan, 1985).

Phonological dyslexia is a selective impairment in reading nonwords (such as wax or lart) compared to relatively intact reading of both regular and irregular real words, which suggests disruption to the nonlexical reading route that relies on working out letter-sound associations (Tree & Kay, 2006). In a review of lesion studies, Lambon Ralph and Graham (2000) noted that phonological dyslexia was most associated with damage focused on the anterior perisylvian regions with significant variation in size and extent.

Comparisons of patients with deep and phonological dyslexia have tended to show a continuum of impairment in phonology and semantics with no clear dividing line between the two, supporting the triangle model of reading (Crisp & Lambon Ralph, 2006). However, the model would predict that if dyslexia arises from damage to either
Disorders of Reading and Writing

of the three general processes (vision, semantics, or phonology), similar impairments would also be apparent in other areas that draw on the same function. In rare cases, this does not seem to be the case, as with a patient reported by Tree and Kay (2006) who presented with a clear phonological dyslexia (nonword reading impairment) despite having intact good performance on a variety of other phonological tasks. These types of cases make it unlikely that reading is based on purely general processes, although the extent to which the brain has become specialized for these relatively recently developed skills (either through selection or developmental plasticity) is still undecided. Much of the recent research is an attempt to settle this issue.

Writing Disorders

Writing is a similarly complex process involving several cognitive, linguistic, and sensorimotor processes and, although agraphia has been less studied than dyslexia, similar principles apply. Although incorporating a wide range of language processes, writing and spelling have been similarly explained using a dual route model (Rapcsak et al., 2007; Figure 59.10a) broken down into peripheral and central components (Beeson & Rapcsak, 2003): peripheral writing processes include allographic conversion (letter representations converted to letter shapes), graphic motor programs (spatial sequences for specific letters), and graphic innervatory patterns (motor commands to control relevant muscles); central writing processes include semantic representation of word meaning, orthographical output lexicon (learned spellings), and phoneme-grapheme (sound to letter) conversion, all of which are thought to converge on a common output mechanism, termed the graphemic buffer (working memory for written letter output). Furthermore a nonlexical and lexical-semantic route has been suggested to account for nonlexical phonetic spelling (creating plausible spellings from sound-to-letter conversion) and lexical-semantic retrieval of orthographic information via the activation of word meaning (Rapcsak et al., 2007).

The triangle model (Plaut, 1997) has similarly been applied to disorders of writing, suggesting that they largely arise from damage to a general three-component system of recognition of orthography (vision), phonology (pronunciation), and semantics (meaning). Recent comparisons of patients with deep dyslexia, dysgraphia, and dysphasia suggest a level of common impairment in general processes, rather than solely with task-specific abilities (Jeffries, Sage, & Ralph, 2007). Recent theories that are not so strictly tied to models of reading and which attempt more explicitly to integrate spelling processes have become more prominent (Glasspool, Shallice, & Cipolotti, 2006) partly influenced by the fact that patients with both general semantic deficits and writing specific impairments (e.g., in the graphemic buffer) have been reported, which are not adequately accounted for by the existing three-factor models of central processes (e.g., Cipolotti, Bird, Glasspool, & Shallice, 2004).

Peripheral Agraphias

Impairments in the sensorimotor aspect of writing can produce peripheral agraphias that have much in common with
Apraxic agraphia with normal praxis is a selective impairment in writing while other motor functions, sensorimotor processes, and oral spelling and typing are preserved (Roeltgen & Heilman, 1983). Visuospatial agraphia (also known as constructional or afferent agraphia) is characterized by impairment to spatial orientation during writing and can result in inability to maintain writing on a line, insertion of blank space between letters, and stroke perseveration (Ardila & Rosselli, 1993). Patients with allographic writing impairment have difficulty selecting letter shapes, often selective for one case, or sometimes producing mixed case words (e.g., *Hello*), despite having relatively intact oral spelling, praxis, and visuospatial ability (Forbes & Venneri, 2003). Writing can also be impaired following executive impairments that impact general motor planning (Ardila & Suroff, 2006) and after damage to neuromuscular control processes affected by disorders such as Parkinson’s disease (Van Gemmert, Teulings, & Stelmach, 2001).

**Central Agraphias**

Lexical or surface agraphia is where patients are not able to access whole word spelling information and so have to rely on phoneme-to-grapheme conversion and spell words as they sound. It is most commonly linked to left posterior inferior temporal cortex damage (Rapcsak & Beeson, 2004) and is thought to arise when there is damage to the lexical-semantic route leaving spelling to rely on the relatively intact nonlexical route (Macoir & Bernier, 2002). In phonological agraphia, patients have difficulty writing nonwords in response to dictation, while writing words to dictation and oral repetition of the words and nonwords are relatively preserved. Spelling errors are often based on visual similarity reflecting the presumed deficit in the phonological system (Roeltgen, 2003) and, despite considerable variability, the disorder is most commonly linked to lesions in the anterior-inferior part of the left supramarginal gyrus, although superior temporal damage has been reported (Kim, Chu, Lee, Kim, & Park, 2002). Patients with deep agraphia have similar trouble spelling nonwords, but also have a tendency to make semantic errors (e.g., writing *flight* instead of *propeller*), have more trouble with function words than with nouns, and words of low imageability (e.g., *love*) compared to words of high imageability (e.g., *lamb*). The syndrome is typically associated with large left hemisphere lesions (Rapcsak, Beeson, & Rubens, 1991).

**OBJECT PERCEPTION AND FACE RECOGNITION**

Disorders of visual perception are a relatively common result of neurological disturbance. They can include frank visual field deficits such as scotoma; acquired color-blindness (achromatopsia), motion-blindness (akinetopsia), or impairments in shape, form, or size discrimination, which can occur after visual cortex damage; or a range of visual agnosias, including object and face recognition difficulties, alexia (see earlier section on Disorders of Reading and Writing), and vision-for-action problems, usually caused by damage to either one or both of the ventral or dorsal streams (Pisella, Binkofski, Lasek, Toni, & Rossetti, 2006).

Less common, although admittedly, less studied, are perceptual disorders of other modalities, including auditory disorders that can impair specific frequency ranges or word or music comprehension, tactile disorders that can impair perception of simple sensations or semantic recognition through touch. In contrast to these disorders of functional deficit, frank hallucinations of varying complexity can be an equally distressing result of neurological disturbance that can occur in any of the perceptual modalities.

The visual system is heavily integrated with and reliant on other cognitive functions, which means that damage to the attentional system can lead to a similar behavioral syndrome, but with a markedly different cause (e.g., hemispatial neglect). Care must be taken to distinguish these using appropriate tests and clinicians must bear in mind that disorders of both attention and perception may co-exist.

Possibly owing to the influence of Marr’s (1982) sequential computational approach to visual perception, cognitive neuroscience has been better at outlining the sequential bottom-up stages, rather than the functional neuroanatomy of top-down processing (Bly & Kosslyn, 1997). However, it has been clear from lesion studies that even early perception is heavily influenced by feedback from higher-level brain areas, as illustrated by the fact that, for example, patients with left-sided lesions typically have problems perceiving detail, while patients with right-sided lesions are more likely to have problems with perceiving perceptual wholes, even when lesions are not primarily located in the visual cortex (Robertson & Lamb, 1991). Many of the syndromes detailed in the following section have been key to understanding the components of the visual perceptual system, but have been less useful in understanding the dynamics of perception. Neuroimaging methods have been particularly useful in this regard, helping to uncover the time course of perception-related brain activity (Hopfinger, Woldorff, Fletcher, & Mangun, 2001) and how bottom-up and top-down processes interact during perceptual tasks (Mechelli, Price, Friston, & Ishai, 2004).

**Disorders of the Early Visual System**

Because the visual pathway from the retina via the lateral geniculate nucleus to the primary visual cortex is
retinotopically organized, selective damage to any part of this pathway will lead to corresponding visual scotomas or, in severe cases, cortical blindness. The actual extent of the subjective visual field deficit may seem significantly smaller than the objective deficit, owing to the effects of visual completion (filling-in) and nystagmus (Valmaggia & Gottlob, 2002; Zur & Ullman, 2003). As well as selective impairment, visual cortex damage may also cause more diffuse problems of visual acuity.

The specialization of the primary visual cortex for the processing of color (V4) and motion (V5) means that lesions to this area can lead to selective deficits in these abilities. Color perception deficits most commonly occur after lesions to the ventral occipital cortex, although rarely affect color vision in its entirety and are typically accompanied by other perceptual difficulties including prosopagnosia, alexia, object agnosia, and spatial perception impairments (Bouvier & Engel, 2006). Reports of pure motion blindness are much rarer in the literature, although are more apparent if syndromes are included that present in only one part of the visual field (Vaina, Cowey, Eskew, LeMay, & Kemper, 2001), or are selective for a particular direction of motion (Blanke, Landis, Mermoud, Spinelli, & Safran, 2003).

**Visual Agnosia**

Visual agnosia is the loss of object recognition and identification in the absence of any significant damage to the early visual system and without intellectual impairment (alexia is sometimes considered among the agnosias, but is discussed earlier in the section on Disorders of Reading and Writing). Farah (2004) provides an excellent guide to the whole range of visual agnosias.

Following Lissauer (1890; translated in Shallice & Jackson, 1988) agnosia is typically divided into an apperceptive type (increasingly called visual form agnosia), where the problem concerns assembling a unified perceptual impression from its component parts—largely attributed to impairments in visual grouping, and an associative type, where the difficulty lies in attributing meaning to a correctly perceived object. Classically, the distinction between these two subtypes is made on the basis that although neither can identify objects, patients with apperceptive agnosia are additionally unable to match, copy, or distinguish between simple objects. The clinical syndromes are often indistinct, however, and agnosias with features of each major subtype have been reported (De Renzi & Lucchelli, 1993; Farah, 1990), suggesting that these are ends of spectrum rather than discrete disorders. Although a recent case has been reported (Anaki, Kaufman, Freedman, & Moscovitch, 2007), agnosia rarely presents without some form of basic visual impairment, although these are not considered sufficient to account for the wider syndrome. More specific syndromes have also been reported, such as impaired recognition when viewed as a mirror reflection (Priftis, Rusconi, Umlita, & Zorzi, 2003), when viewed from unusual angles (Warrington & James, 1986), or intact object recognition but impaired identification of its orientation (Turnbull, Della Sala, & Beschkin, 2002).

Associative visual agnosia is where an object is seemingly perceived correctly, but the patient cannot name, describe, explain, or categorize the object (even in nonverbal grouping tasks), although it is possible to do so through other senses (e.g., touch). In contrast to apperceptive agnosias, visual spatial processing tends to be relatively intact. Humphreys and Riddoch (1987) proposed that associative agnosia results from selective impairment in the integration of the largely intact high-level visual processes with memory. However, this has been challenged by Farah (1990) who reviewed the literature and found significant evidence of perceptual deficits in these cases, suggesting that the role of perception and memory in object recognition is not clearly distinct.

An illustration of an informational processing model for visual object recognition is outlined in Figure 59.11. This model charts the hypothetical information processing routes from preattentive extraction of simple structural properties, to more advanced post attentional integration of local or global processing, and finally to assignment of relevant spatial frames of reference prior to recognition and naming.

**Simultanagnosia**

Simultanagnosia is a related condition and involves the inability to perceive complex visual scenes, or two or more objects simultaneously, despite being able to perceive single objects without significant impairment. Farah (2004) divides the syndrome into dorsal and ventral simultanagnosia based on in which of the postocipital visual pathways the lesion occurs. Dorsal simultanagnosia typically occurs in the context of Balint’s syndrome that entails an additional inability to direct eye or hand movements to visual targets. Ventral simultanagnosia differs in that patients are somewhat less impaired and can often see multiple objects simultaneously (although do not necessarily recognize them simultaneously), can manipulate objects, and can navigate without bumping into obstacles. Nevertheless, both types typically involve grossly impaired reading ability. The condition is typically explained as a form of pathological local attentional capture, although recent studies have suggested that global scene structures or unseen objects are processed implicitly (Dalrymple, Kingstone, & Barton, 2007; Jackson, Shepherd, Mueller, Husain, & Jackson, 2006).
Prosopagnosia

Prosopagnosia is a form of visual agnosia that is selective or relatively selective for the recognition of faces (Figure 59.12). (See Figure 59.8 for a cognitive model of face recognition.) It has been classified into an apperceptive type, where patients are to construct coherent face perceptions, typically detected by an inability distinguish between faces and nonface configurations of facial features; and an associative type, typically detected by an inability to recognize famous or previously familiar faces. Early research focused almost exclusively on the acquired type, typically occurring after right or bilateral fusiform gyrus lesions. It has been increasingly recognized that there is an idiopathic form (variously called congenital or developmental prosopagnosia) that more closely matches the associative type. There is some evidence suggestive of the syndrome running in families in an autosomal dominant pattern (Grueter et al., 2007; Kennerknecht, Plumpe, Edwards, & Raman, 2007) and affected individuals may not be significantly impaired in everyday life because they learn to rely on nonface cues or external face features (hair, glasses etc.) for recognition. Because this is an adaptive developmental strategy, people with this form of the condition often do not realize until quite late in life that they recognize people differently from others. There remains a considerable debate over whether prosopagnosia is the result of a face-specific deficit (McKone, Kanwisher, & Duchaine, 2007) or whether it is simply the most common result of damage to domain-general perceptual expertise system (Gautier & Bukach, 2007).

Other Perceptual Disturbances

Other visual agnosias are the most studied, they also occur in other sensory modalities. Auditory agnosia has been reported—with evidence for a dissociation between auditory
and musical recognition deficits (Vignolo, 2003), as have gustatory (Small, Bernasconi, Bernasconi, Sziklas and Jones-Gotman, 2005) and tactile agnosias (Caselli, 1991). Hallucinations with preserved insight into the false nature of the perceptions arise in a number of neurological conditions, including macular degeneration, migraine, epilepsy, and dementia (Manford & Andermann, 1998). Auditory verbal hallucinations (hearing voices) seem a relatively rare result of acquired brain injuries in the absence of psychosis (Lampl, Lorberboym, Gilad, Boaz, & Sadeh, 2005).

**LEARNING AND MEMORY**

Memory is one of the most commonly affected cognitive abilities after neurological disturbance (cross reference—v 3-8) and can be the source of the most disabling long-term effects. Learning occurs at all levels throughout the brain, and from this perspective, virtually all cognitive neurology is the study of how learned patterns are disrupted by neuropathology. However, decades of careful experimental studies on both healthy participants and neurological patients have shown us that the brain has become specialized to encode, consolidate, store, and retrieve information for certain types of tasks.

Current theories of memory make functional divisions that are not necessarily mutually exclusive, although some have been shown to rely on largely independent neural systems. Sensory memory is thought to last only a matter of milliseconds and provides a lingering impression to the senses. Working memory is considered to be a limited capacity memory system where temporarily stored information (usually less than 30 secs) can be manipulated by the executive system during cognitive tasks. Long-term memory is considered to represent semi-permanent or permanent storage and has been divided into semantic memory (for general knowledge, facts and words that can be recalled without access to the context in which they were learned), and episodic memory (the remembrance of episodes from our personally experienced past). Memory can also be divided into declarative or explicit memory, which we can consciously recall, reflect upon, and describe; and procedural memory, which is the ability to learn skills and actions. Implicit memory is not consciously accessible and includes skill learning (as per procedural memory), but also conditioning, associative learning, priming, and, in fact, anything down to Hebbian learning at the neural level. Memory can also be distinguished by the content that is being remembered, such as verbal, visual, or spatial memory.

Disorders of memory are usually categorized in a similar fashion and only the briefest outline will be given here. Brief reviews are available in Budson and Price (2005) and Kopelman (2002), or for a more in-depth treatment, Baddeley, Kopelman, and Wilson (2004) and Baddeley, Kopelman, and Wilson (2002) are excellent resources. The fact that the classification of memory disorders tends to pragmatically follow traditional classifications of normal memory is worth bearing in mind, particularly when data challenging the traditional models appears. For example, electrophysiological studies during tasks that are classically described as working memory tasks have been used as a basis to argue that there is no separable working memory system, only temporary activation of long-term memory stores (Ruchkin, Grafman, Cameron, & Berndt, 2003) and that short- and long-term memory stores are not separate (Cameron, Haarmann, Grafman, & Ruchkin, 2005). While this debate continues in the literature, both the clinician and researcher must be aware that there is a temptation to fit the complexity of clinical disorders into the traditional categories, rather than the more difficult task of adjusting the traditional categories to allow for the intricacy of impairment.
Working Memory Impairments

Working memory is a short-term, explicit, declarative memory system that is commonly conceptualized as having both a visual-spatial and an auditory short-term store. It uses a network of cortical and subcortical areas, although it is particularly reliant on the prefrontal cortex (Postle, 2006). It is increasingly thought that working memory is not a separate memory system, but the emergent property of a number of cognitive processes working together (D’Esposito, 2007). This means working memory is particularly sensitive to impairment after neurological disturbance that is largely caused by disruption to the executive system, rather than the short-term stores themselves (Muller & Knight, 2006). Disorders of working memory are likely to present as difficulties with concentration, following instructions, or general forgetting, with the impairment also impacting on encoding into long-term memory (Blumenfeld & Ranganath, 2007).

Impairments in working memory are common in a range of brain disorders, with a particular impact on the prefrontal cortex. Disorders of the frontal lobe can result in a reduction in the ability to plan, organize, and perform complex tasks, which is also known as working memory (D’Esposito, 2007). This is because working memory is heavily dependent on the prefrontal cortex for its function (Blumenfeld & Ranganath, 2007).

Long-Term Memory Impairments

Amnesia is the general name given to a range of long-term memory impairments although the classic anterograde amnesic syndrome consists of the impaired encoding of new declarative memories, intact recall of premorbid information, and intact implicit memory. Pathologies that cause anterograde amnesia typically result in a limited retrograde amnesia that follows a temporal gradient (Ribot’s law), in that memories are more likely to be intact because the memories are more distant in time. Differences between anterograde amnesia caused by medial temporal lobe and diencephalon disruption have been reported in the literature but are likely to be negligible in practice, while both have faster rates of forgetting and benefit less well from category prompts than when the syndrome is caused by prefrontal pathology (Kopelman, 2002). Because the prefrontal cortex is involved in both encoding and retrieval of memory, pathology in this area may also lead to increased memory distortion, including false memory recall, loss of context (source amnesia), and frank confabulation (Johnson, O’Connor, & Cantor, 1997).

Posttraumatic amnesia is an amnesic syndrome that occurs in the acute stage after brain trauma. The length of the amnesia is known to reflect the severity of the brain injury and typical resolution times stretch from 1 day to several weeks (McMillan, Jongen, & Greenwood, 1996). Transient global amnesia is a dense amnesic syndrome with a sudden onset that resolves within a matter of hours. It can be triggered by physical or emotional stress, and, with the exception of headaches in affected younger people, is not reliably associated with other neurological signs (Quinette et al., 2006). Transient epileptic amnesia may present in a similar fashion, although it typically lasts for a shorter duration (less than 1 hour) and patients may experience clear seizure-related sensory and motor disturbance for the duration of the amnesia.

Specific impairments in existing semantic memory take a number of forms and are particularly common after pathology of the anterolateral temporal lobes (Levy, Bayley, & Squire, 2004). Patients may present with object identification and language difficulties and so they can sometimes erroneously be assumed to have agnosia or aphasia. A presentation of a selective semantic deficit will be in the context of normal perception and intact nonsemantic language skills such as repetition, reading aloud, and writing to dictation. Alzheimer’s disease is perhaps the most common form of semantic impairment that arises from both degradation of semantic memory owing to temporal atrophy, and impairment in executive control processes due to frontal pathology (Grossman et al., 2003). Semantic dementia is a variant of frontotemporal dementia that involves focal lateral temporal atrophy and a progressive decline in semantic knowledge with little or no distortion of the phonological and syntactic aspects of language, and relative sparing of other aspects of cognition, such as episodic memory, nonverbal problem solving, and perceptual and visuospatial skills (Garrard & Hodges, 2000).

Impairments in semantic memory may be category specific, affecting knowledge of particular classes of objects. Dissociations between knowledge of animate and animate, living versus nonliving, and animals and plants (to name but a few) have been reported in the neurological literature (Gainotti, 2005). However, it is not clear whether these distinctions reflect the organization of knowledge within the semantic system, or whether there are other higher-level or emergent properties that could better explain the apparent category-specific effect (Borgo & Shallice, 2001).

Impairments of Procedural Memory

Procedural memory deficits can either take the form of marked impairments in acquiring new motor skills, or a loss of existing abilities. It can be spared in even the densest declarative memory amnesias allowing a considerable degree of implicit memory function and skill learning (Spiers, Maguire, & Burgess, 2001). Neuroimaging studies have indicated that procedural learning is associated with activation in the supplementary motor area, basal ganglia, and cerebellum (Daseelaar, Rombouts, Veltman, Raaijmakers, & Jonker, 2003) and clinical studies have shown that damage to these areas can cause selective impairments in motor learning (Halsband & Lange, 2006). Unsurprisingly, particular impairments can be seen in degenerative disorders.
such as Parkinson’s and Huntingdon’s disease that involve circumscribe pathology to these circuits (Heindel, Salmon, Shults, Walicke, & Butters, 1989).

**EXECUTIVE SYSTEM DISORDERS**

The idea of an executive system as a manager of other cognitive processes is a relatively late addition to neuropsychological theory and has largely stemmed from the discovery that neurological patients often have problems with coordinating their thoughts and actions over and above any deficits that directly impact on perception, stored memories, or motor control. One of the core ideas behind the concept of an executive system is that it is primarily involved in representing and manipulating abstract concepts, an ability that supports functions such as cognitive and emotional control, initiation and inhibition of actions, behavioral flexibility, planning, introspection, perspective taking, and social cognition. Burgess (1997) has described the executive system as lacking “process-behavior correspondence” meaning, behaviorally, the operation of this system can only be measured through other cognitive processes that are managed (or mismanaged) by the system.

Lesion and neuroimaging studies have consistently indicated that the executive system relies heavily on the prefrontal cortex and its major pathways (Duncan & Owen, 2000) and damage to this system can cause a surprisingly diverse range of behavioral abnormalities, collectively labeled the *dysexecutive syndrome.* The executive system is thought to be more fully engaged in nonroutine, effortful, and online (real life) situations and so the extent of executive impairment as measured by neuropsychological testing may not always predict day-to-day disability (Burgess et al., 2006).

Executive function is closely linked to the concept of attention, although it has traditionally been distinguished from perceptual and spatial attention that is more closely linked to the function of the parietal lobe. However, recent work has begun to question the strict distinction between these systems and the importance of the frontoparietal network in the interaction of both is now being increasingly highlighted (Collette, Hogge, Salmon, & Van der Linden, 2006; Hon, Epstein, Owen, & Duncan, 2006).

**Theories of Executive Function**

Duncan, Emslie, Williams, Johnson, and Freer (1996) have argued that the executive system is involved in constructing task plans by representing and maintaining the relevant goals and requirements, and is largely synonymous with general intelligence. Executive system impairment is described as arising from goal neglect where task requirements are disregarded despite the fact they have been remembered and understood. More recently, Duncan et al. (2008) elaborated on their theory to suggest that goal neglect reflects a limit in working memory capacity. Notably, the limiting factor is suggested to be different from the bottleneck theories of traditional capacity models of attention that concern the limits of how much perceptual or spatial information can be attended to at any one time. In this model, the limiting factor is the capacity of working memory to retain a task model—a working-memory description of relevant facts, rules, and requirements used to control current behavior. According to the theory, dysexecutive problems arise when individual task representations are lost through competition between processes that update the global task model, particularly when capacity has been limited through neurological impairment.

Norman and Shallice (1986) proposed the hugely influential supervisory attentional system (SAS) model that has two pivotal components. The contention scheduler is considered to mediate the effect of the environment (which may trigger certain actions) on the selection of automatic or routine actions. When triggered, the contention scheduling component controls the mutual inhibition of competing actions (since many actions may be triggered at once) to select the most appropriate course of action. The SAS (synonymous with the executive system in most accounts) is considered to intervene in nonroutine situations when actions have to be altered or inhibited because of a novel encounter or decision-making process. Increasingly, the supervisory system is not considered to be a single function, and there is a general consensus that it comprises of a number of anatomically and functionally independent but interrelated processes. Descriptions of the how these processes are fractionated differ and include shifting, updating, and inhibition (Miyake et al., 2000); energization, task setting, and monitoring (Stüss & Alexander, 2007) and schema selection, monitoring, memory specification, and intention setting (Shallice, 2002).

Theories of the role of reward processing in executive function have traditionally focused on the ability to respond differently to changing contingencies in the social environment (Rolls, 1996). However, more recent approaches have widened the scope of reward processing theories based on evidence that the fronto-polar cortex is involved in maintaining and prioritizing the competing demands of behavioral plans or mental tasks based on representations of reward expectations (Koechlin & Hyafil, 2007), consistent with lesion data showing patients display decision-making impairments in open-ended situations (Burgess, Gilbert, & Dumontheil, 2007).
Problems of Affect and Social Judgment

The medial frontal cortex is known to be particularly important for social cognition (Amodio & Frith, 2006) although damage to a range of prefrontal cortex areas is known to affect the ability to perceive and make judgments on social, moral, and emotional information. Two of the most popular theories of frontally related social disability include an impairment in understanding when reward contingencies for particular social behaviors have altered (Kringelbach & Rolls, 2004); and an impairment in the perception of affect-related arousal and signaling (the somatic marker hypothesis; Bechara, 2004). Common socially relevant dysexecutive symptoms include disinhibition, inappropriate social behavior, and even mania-like states (Starkstein & Robinson, 1997). At the more serious end of the spectrum, acquired sociopathy can result from damage to the orbitofrontal cortex and involves an inability to control reactive aggression and violent impulses (Blair, 2001). Similarly, impairments in the ability to reason about the acceptability of personal moral violations have been found in patients with ventromedial lesions (Ciaramelli, Muccioli, Ladavas, and Di Pellegrino, 2007). Deficits in understanding others’ emotions and mental states (Siegal & Varley, 2002) and impairments in understanding nonverbal social cues (Mah, Arnold, & Grafman, 2004) may also promote difficulties in social interaction after frontal pathology.

Deficits of Executive Memory

The executive system is most closely linked to working memory—a limited capacity memory system responsible for the temporary storage and processing of information while cognitive tasks are performed (see Learning and Memory Impairments section). However, the executive system is also involved in the retrieval and encoding of long-term memories and memory for intended actions in the future (prospective memory). As a result, executive impairment can have a potentially wide and varied impact. Distractibility undoubtedly impacts all parts of the memory process and is likely a significant factor in the impaired use of efficient organization strategies during both encoding and recall (Mangels, 1997; Parkin, Ward, Bindschaedler, Squires, & Powell, 1999). Although it is traditionally thought that executive impairment leads to a pattern of impaired recall with intact recognition, it is now well established that recognition difficulties are common, although less pronounced (Bastin, Van der Linden, Lekeu, Andres, & Salmon, 2006). One of the most dramatic pathologies of memory associated with executive impairment is confabulation, where patients produce fictitious stories without the apparent intent to deceive and are seemingly unaware that they are inaccurate. While not all confabulation can be explained by executive impairment alone, they commonly present together (Schnider, 2003).

Problems of Evaluation, Judgment, and Action Planning

Despite scoring well on measures of general cognitive function, executive dysfunction is particularly associated with the inability to make sound real world decisions. Such impairments may only be fully apparent in real world situations (Goel & Grafman, 2000) and cases have been reported of patients who seem to score within the normal range during neuropsychological testing but who make obviously unwise decisions in their everyday life (Blair & Cipolotti, 2000; Elsinger & Damasio, 1985). On the level of completing specific short-term goals, impairment to the executive system has been shown to impact on action planning, so that actions sequences may be disjointed, perseverative, or contain unhelpful or irrelevant steps (Owen, 1997). Difficulties in both judgment and action planning can arise owing to problems with acquiring rule sets (Burgess & Shallice, 1996), self-monitoring and insight, making reasonable estimates (Brand, Kalbe, Fujiwara, Huber, & Markowitsch, 2003), or multitasking (Burgess, Veitch, de Lacy Costello, & Shallice, 2000). Neuroimaging evidence suggests that control implementation and performance or conflict monitoring are linked to dissociable processes in the dorsolateral prefrontal and anterior cingulate cortices, respectively (MacDonald, Cohen, Stenger, & Carter, 2000). However, lesion maps (see Figure 59.13) of cognitive control impairment after brain injury further suggest that these processes may fractionate further (Alexander, Stuss, Picton, Shallice, & Gillingham, 2007).

SUMMARY

There is little doubt that cognitive neurology continues to contribute to our understanding of established neurological, psychiatric, affective, and related pseudoneurological and or functional disorders. There is an increasing prevalence of seemingly neurological conditions for which no organic disorder can be found to explain the patient’s hemiparesis, somatosensory loss, visual field constriction, and so on (Halligan, Bass, & Marshall, 2001). Functional neuroimaging techniques and cognitive analysis procedures have still to make a major clinical and theoretical contribution in the domain of neuropsychiatric and neurogenic disorders (Frith, 2008; Halligan & David, 2001). The rich data source of the Human Genome Project will increasingly add to our knowledge about neurological and psychiatric conditions.
Figure 59.13  Cortical lesions associated with prolonged reaction times on Stroop task.

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