

Chapter 1

Introduction

Virtually everything we know about the brain functions underlying human cognition has been learned by one of two methods: studying brain-lesioned patients and functional neuroimaging. The two methods tend to yield reassuringly consistent evidence. Yet they have significantly different strengths and weaknesses, to be discussed later in this chapter, and for this reason neither method is dispensable.

Disorders of visual object recognition following brain damage are known as visual agnosias. There is amazing diversity to the ways in which object recognition can break down, from visual form agnosia in which patients with normal acuity cannot recognize something as simple as a circle or a square, to topographic agnosia in which patients with normal face, object, and word recognition cannot recognize locales. In each case the patterns of preserved and impaired abilities put useful constraints on our theories of how the normal visual recognition system works.

1.1 A Brief History of Agnosia

For much of its history, the study of agnosia focused on the question of whether there *is* such a thing as agnosia. Researchers began with this most basic of questions, and perhaps in retrospect stayed with it too long, because the syndrome seemed so counterintuitive and contradictory. How could someone be able, in the words of Humphreys and Riddoch's (1987b) book title, *To See but Not to See?* Repeatedly over the years, the concept of visual agnosia has met with skepticism. First Bay (1953), and then Bender and Feldman (1972), argued that visual agnosia, in the sense of a selective impairment in visual recognition per se, does not exist. Bay proposed that

the appearance of a selective impairment in object recognition was invariably the result of a combination of two more general characteristics of agnosic patients. First, he suggested that these patients always have subtle impairments in elementary visual functions, which may be less apparent under the conditions of standard tests of visual fields, acuity, and so on, than when they are being used for object recognition under natural conditions. Second, he claimed that these patients suffer from a general intellectual decline. According to Bay, impairments in elementary vision and general intelligence may occasionally conspire to produce disproportionate difficulties with object recognition, but there is no such thing as an impairment in object recognition *per se*. Bender and Feldman (1972) supported Bay's claims with a systematic review of a large number of neurological patients. They searched all of the patient records from a twenty-year period at New York's Mount Sinai Hospital and found relatively few cases with visual recognition difficulties. What they took to be more damaging to the concept of agnosia was the fact that all of these cases also had some significant elementary visual and/or general intellectual impairments.

Bay, and Bender and Feldman won over many influential neuropsychologists to their point of view on agnosia (e.g., Critchley, 1964; Teuber, 1968), but their skepticism was not shared by everyone. Even though a "pure" case of agnosia (a patient with impaired visual object recognition and perfectly normal elementary visual and intellectual capabilities) would disprove the skeptics' position, the absence of such a case does not prove it. Neuropsychologists know far too well that "nature's experiments" are executed rather sloppily, and they would have very little to study if they confined themselves to pure cases of anything. With this in mind, Ettliger (1956) made the important point that finding a "pure" agnosic was not the only way to settle the issue empirically. Just as effective would be the demonstration that agnosic patients were no more impaired in their intellectual and elementary visual capabilities than many non-agnosic patients. He demonstrated that this was true by systematically assessing a variety of elementary visual functions in patients already screened for generalized intellectual decline. Although only one of his cases had a true agnosia, and this case did have elementary visual impairments, he found other patients with more severe elementary visual impairments who were not agnosic. More recently, De Haan, Heywood, Young, Edelstyn,

and Newcombe (1995) carried out a more stringent test of Ettlenger's hypothesis with three severe visual agnosics and a more comprehensive and sophisticated battery of visual tests. Their data supported Ettlenger's conclusion that whatever elementary visual impairments the agnosic patients had, they were not the cause of the agnosia. Patients with equally impaired elementary visual function were not agnosic.

The impulse to "explain away" agnosia can be understood in terms of the theories of vision available to agnosia's skeptics in the mid-twentieth century. If one views object recognition as taking place in two relatively undifferentiated stages—(1) seeing the object and (2) associating general knowledge with the visual percept—then the only possible way to disrupt object recognition is by disrupting vision or general knowledge. If object recognition difficulties seem disproportionate to difficulties of vision or general knowledge (as is the case, by definition, with visual agnosia), then this must be due to a synergistic interaction of minor difficulties in both vision and general knowledge. However, with the advent of single unit recording in visual cortex (e.g., Gross, Rocha-Miranda, & Bender, 1972; Hubel & Weisel, 1962) and computational modeling of vision (e.g., Marr, 1982), a different view of visual object recognition emerged. According to this latter view, object recognition is accomplished by repeatedly transforming the retinal input into stimulus representations with increasingly greater abstraction from the retinal array and increasingly greater correspondence to invariant properties of objects in the physical world (see Farah, 2000). Within such a system, brain damage affecting just the later stages of vision would create a "pure" visual agnosia.

Eventually, neuropsychologists looked beyond the question of whether or not agnosia exists, to other questions about agnosia, including the possibility of different types of agnosia and their associated lesion sites. As the field of cognitive neuropsychology blossomed in the 1980s, researchers attempted to relate aspects of agnosia to theories of visual object recognition, and in the process to test those theories with data from agnosic patients (e.g., Farah, 1990; Humphreys & Riddoch, 1987b; Ratcliff & Newcombe, 1982). In the pages that follow, I will delineate a dozen or so distinct visual agnosic syndromes, and bring each of them to bear as evidence on the nature of visual object recognition. Examples of the questions to be addressed include: Are there different recognition modules, or subsystems, required for recognizing different kinds of stimuli (e.g., faces,

common objects, printed words)? Does visual selective attention operate prior to object recognition, subsequent to it, or in parallel with it? Are the long-term visual memory representations underlying recognition implemented locally or in a distributed network?

1.2 *Types of Agnosia*

Taxonomizing may appear to be a rather atheoretical enterprise that would be better replaced by analysis of the phenomena of agnosia using cognitive theories. However, we must begin with issues of taxonomy because grouping the phenomena correctly, in any area of science, is a prerequisite for making useful theoretical generalizations about them. This is all the more important—and all the more difficult—in the study of agnosia because the entire database is comprised of single cases, no two of which are exactly alike. Therefore, much of the scientific work to be done in this field involves sorting these countless variable and unique cases into a tractable number of “natural kinds.”

There is no standard taxonomy of agnosia. Everyone agrees that agnosic patients differ from each other in certain ways, but the question of which differences are differences of degree and which are differences of kind has not found a unanimous answer. On careful reading of patients’ abilities and deficits, I find that many authors have grouped patients in unhelpful ways. Their implicit taxonomies misrepresent the basic empirical phenomena, both by overinclusive categories that blur theoretically important distinctions between different syndromes, and by overfractionation of syndromes, in which differences of degree are treated as differences of kind.

Most neuropsychologists follow Lissauer (1890) in distinguishing between the “apperceptive agnosias” and the “associative agnosias.” According to Lissauer, apperceptive agnosias are those in which recognition fails because of an impairment in visual perception, which is nonetheless above the level of an elementary sensory deficit such as a visual field defect. Patients do not see objects normally, and hence cannot recognize them. In contrast, associative agnosias are those in which perception seems adequate to allow recognition, and yet recognition cannot take place. It is said to involve, in the oft-quoted phrase of Teuber (1968), a “normal percept stripped of its meaning.”

In this respect, the apperceptive–associative distinction, as defined above, includes a significant assumption about the mechanisms of agnosia: that the underlying deficit in so-called associative agnosia lies outside of the modality-specific perceptual processing of the stimulus. Whether or not this is true is an important issue that will be discussed later. Nevertheless, the grouping of agnosics into two categories—those with prominent, easily noticed perceptual deficits and those without—does seem to be empirically valid.

Within these two broad categories there is tremendous variation. For example, among the patients who have been labeled “apperceptive” are those who cannot discriminate a circle from a square, those who can recognize any one object but cannot see other objects presented at the same time, and those whose difficulty with object recognition is manifest only with objects presented at unusual orientations. Among the patients who have been labeled “associative” are those whose impairment is confined to specific categories of visual stimulus such as faces, places, or printed words, as well as those with across-the-board recognition impairments and those who seem impaired only when naming a visually presented object. The organization of this book reflects my attempt to find a happy medium between lumping distinct syndromes together and splitting the phenomena into an unmanageable and unnecessary number of separate categories. Each of the next eight chapters describes a type of agnosia, along with its relations to theories of normal visual function.

1.3 Patient-Based Cognitive Neuroscience in the Age of Imaging

The first edition of this book was written one methodological revolution ago, just before functional neuroimaging transformed cognitive neuroscience. At that time, everything we knew about the neural bases of high-level vision in humans came from studies of patients. It was therefore particularly exciting to work through the rich database of clinical studies in search of insights about normal object recognition, knowing that such insights lay waiting there and, at the time, only there.

The situation is very different now. Neural systems can be visualized as they perform their functions under experimentally controlled conditions in normal subjects. This capability revolutionized all areas of cognitive neuroscience, and greatly expanded our understanding of high-level

vision in the course of just a decade of research. It therefore bears asking: Why study visual agnosia now that functional neuroimaging is available? The answer to this question involves an accounting of the strengths and weaknesses of imaging and patient-based cognitive neuroscience.

An obvious weakness of patient-based research is that naturally occurring lesions do not respect anatomical or functional boundaries. Such messiness would be less of a problem if all possible sizes and shapes of these messy lesions occurred, because different patients with overlapping lesions might permit inferences about the functions of common and distinct subregions, but this is not the case; strokes, head injury, and other etiologies of brain damage have characteristic lesions, and many possible lesion configurations do not occur. The greatest advantage of functional neuroimaging is its ability to compensate for this weakness. Although some areas of the brain are better visualized with current imaging techniques than others, imaging is hands-down the better way to probe the functions of specific anatomical regions.

Functional neuroimaging has the additional advantage of studying normal brains, which are the subject of interest. With patient-based research we are operating one inferential step away from this subject. Of course, the behavior of a damaged system is related in systematic ways to the function of the intact system. But “systematic” does not mean “simple”: reorganization following injury can greatly complicate our inferences about normal function (Farah, 1994). An additional problem with rare disorders, including most of the agnosias, is that patients provide no more than an existence proof that a certain dissociation is possible, and hence that the inferred neurocognitive organization exists. In the early days of cognitive neuroscience this was a minor worry, because of the implicit assumption that all normal human brains were wired in basically the same way. However, as our field finally begins to grapple with individual differences (Thompson, Cannon, Narr, van Erp, Poutanen, Huttunen, Lonnqvist, Standertskjold-Nordenstam, Kaprio, Khaledy, Dail, Zoumalan, & Toga, 2001; Hamer, 2002), we want to know whether the functional organization inferred from one patient applies to all humans or is just one variant. Does everyone use separate systems to recognize faces and non-face objects, or just a subpopulation, who will become prosopagnosic after certain patterns of brain damage? The ability to analyze individual subjects' images allows us to address this question by finding out what pro-

portion of subjects recruits measurably different brain regions for face and object recognition.

In weighing the advantages and disadvantages of patient-based and imaging research, there is one other drawback to patient-based research that is often overlooked: the difficulty of interlaboratory verification. Findings from patients with rare disorders like agnosia cannot be pursued by any scientist with an alternative hypothesis or a good idea for a follow-up study. This is unavoidable, at least to a degree. When a patient agrees to work with one researcher, he is not making himself available to any scientist in the field willing to travel to him at any point in the future. However, the problem is often compounded by researchers who develop a possessiveness about “their” patients. This practice is at least as dehumanizing to the patient as offering to put them in contact with other researchers, and it has impeded progress in our field. Imaging studies are much more replicable, in that a finding from one imaging lab can in principle be pursued by any other imaging lab.

These advantages of imaging over patient-based research make an impressive list. If we were to play a variant of the childhood game “would you rather” (be rich or beautiful, fly like a bird or read minds . . .) with imaging and patient-based methods, I’d be inclined to take the imaging. Happily, we do not have to choose. Patient-based methods have their own strengths, which complement those of imaging. As a result, the combination of the two approaches is more powerful than the sum of its parts.

The great advantage of studying patients is the ability to test hypotheses about mechanism. The goal of most cognitive neuroscience research to understand *how* intelligent behavior is accomplished. We are trying to describe the causal chain of events that intervene between stimulus and response. We share this goal with a number of other disciplines, from molecular neuroscience to cognitive psychology. What distinguishes these disciplines is the level of description within which they cast their hypotheses about mechanism.

The mechanistic hypotheses of cognitive neuroscience concern the information-processing functions of macroscopic neural systems. This level of description includes, at the more microscopic end of the range, the emergent behavior of populations of neurons. It is this population behavior, during learning, normal function, and after damage, that does the explanatory “work” in the computational models described in this book

(e.g., models of the word superiority effect, covert face recognition, optic aphasia, and selective semantic memory impairments). At the more macroscopic end of the cognitive neuroscience level of description are models that delineate distinct information processing components and their interrelations, such as the division of labor between form perception from static spatial cues and form from motion, and between face and object recognition.

Our methods deliver information that is useful for testing hypotheses at this level of description. Current imaging techniques reveal distinguishable activations at about this scale, and the relatively more fine-grained dissociations among abilities after brain damage can also be described at this level. However, images and lesions are very different in their ability to answer questions about mechanism. Only the lesion method can reveal the causal relations among brain systems.

Imaging data are fundamentally correlational; they tell us that this area becomes active when that cognitive process is being performed. They do not tell us what causal role, if any, is played by an activation observed in this way. Not every activation is part of a causal pathway; representations may become active, in a given task context, either because they are causally involved in performing the task or because they have become associated with other representations that are causally involved. Although it may seem odd to think of the brain as activating unnecessary systems, I suspect that superfluous or only marginally useful activity is very common, and perhaps the norm. Try the following low-tech demonstration of this point: Glance at the bottom of this page and count the letters in the last word. Notice that you read and understood the word even though it was not part of your assignment. Indeed, the same thing will happen even if you *try* not to read the word. Phonological and semantic representations are so highly associated with orthographic representations that they are activated even when not necessary. This example of associated activity is intentionally obvious, but the issue is not trivial when the activated systems are less open to introspection and less well characterized cognitively.

To tease apart causal and merely associated systems, and characterize the information-processing function of each of those systems, we need to reach in and tinker. Only by seeing the consequences of removing or disabling different candidate systems can we infer their role in producing

a given behavior. Of course, with human brains we do not “tinker.” Instead, we examine the effects of naturally occurring brain damage.

How can patient-based research determine which activated systems play a causal role in implementing an ability, and which are merely associated? To answer this question, let us return to the example of unnecessary but associated activity when counting the letters in a word. Imagine that this task has been carried out in a scanner, and consistent with introspection, areas subserving visual-spatial attention are activated (as they are in counting tasks), and areas subserving orthography, phonology, and semantics are activated (as they are when words are processed). We now want to answer the question: which of these activations play a causal role in implementing letter counting, and which are merely associated? We can find out by testing patients with lesions in each of these systems on the letter counting task.

Patients with disorders of visual-spatial attention, including the dorsal simultanagnosics of chapter 3, will have difficulty with the letter counting task. This is consistent with the hypothesis that counting visual stimuli requires marking them attentionally; the movement of visual-spatial attention from item to item is not merely an associated but unnecessary process. In contrast, patients with orthographic impairments (e.g., the pure alexic patients of chapter 4), phonological impairments, or semantic impairments (e.g., the optic aphasics and semantic agnosics of chapters 8 and 9) will be able to perform the task. This is consistent with the hypothesis that the lexical processes that were reliably activated in the scanner are not in fact necessary for the behavior.

The information that patients provide goes beyond simply classifying systems as necessary or not necessary. It can also distinguish different types of processing and delineate multiple parallel chains of processing that enable a behavior. Patterns of activation in functionally parallel systems do not tell us which activations are part of the same or different pathways, or what the unique information-processing nature of each system is. By contrast, through interrupting processing at various loci we can infer just these properties of the system, through a procedure akin to trouble-shooting.

The cognitive neuroscience of object recognition has already benefited from the interplay of patient-based and imaging methods. Initial attempts to investigate visual recognition using functional neuroimaging suffered from a lack of specific hypotheses and were correspondingly quite

variable in matching experimental and baseline conditions. Many studies consisted of simply scanning subjects while they viewed pictures or performed tasks with assorted stimuli and fixation points. No wonder that, in the aggregate, this sizable literature succeeded only in establishing that visual object recognition involves the posterior half of the brain (Farah & Aguirre, 1999)! However, this changed as imagers began to test specific hypotheses about visual recognition, most of which came from the patient literature. For example, prosopagnosia and topographic agnosia suggested specific hypotheses concerning specialization in ventral visual areas, and along with more specific hypotheses came more theoretically constrained experimental designs. Imaging in turn clarified the degree of segregation among specialized recognition systems, which of course are never neatly dissociated by naturally occurring lesions.

It has recently become possible to combine imaging and patient-based research in a powerful new way, by imaging patients while they engage in the processes of interest. This approach poses many additional technical challenges beyond those of imaging a normal brain (Price & Friston, 2003), but is also uniquely well suited to understanding the anatomical and mechanistic bases of cognition. Although as yet undeveloped, the functional imaging of visual agnosics will undoubtedly play an increasingly dominant role in the cognitive neuroscience of high-level vision.