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Apraxia, Neglect, and Agnosia

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ABSTRACT

PURPOSE OF REVIEW: In part because of their striking clinical presentations, disorders of higher nervous system function figured prominently in the early history of neurology. These disorders are not merely historical curiosities, however. As apraxia, neglect, and agnosia have important clinical implications, it is important to possess a working knowledge of the conditions and how to identify them.

RECENT FINDINGS: Apraxia is a disorder of skilled action that is frequently observed in the setting of dominant hemisphere pathology, whether from stroke or neurodegenerative disorders. In contrast to some previous teaching, apraxia has clear clinical relevance as it is associated with poor recovery from stroke. Neglect is a complex disorder with many different manifestations that may have different underlying mechanisms. Neglect is, in the author's view, a multicomponent disorder in which impairment in attention and arousal is a major contributor. Finally, agnosias come in a wide variety of forms, reflecting impairments ranging from low-level sensory processing to access to stored knowledge of the world (semantics).

SUMMARY: The classic behavioral disorders reviewed here were of immense interest to early neurologists because of their arresting clinical phenomenology; more recent investigations have done much to advance the neuroscientific understanding of the disorders and to reveal their clinical relevance.

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INTRODUCTION

Interest in higher functions of the nervous system, including those discussed in this article, figured prominently in the early days of neurology as the field diverged from psychiatry. Phenomena such as apraxia and agnosia became the subjects of intense interest in the latter part of the 19th century and early 20th century; these and other disorders were noteworthy at the time in part because "psychiatric" explanations of the disorders were not considered to be viable, necessitating brain-based (ie, neurologic) explanations of the disorders. This article reviews three of the disorders of higher brain function described by early neurologists that continue to be of clinical and neuroscientific relevance—apraxia, neglect, and agnosia—to assist neurologists in recognizing and treating these important and fascinating disorders.

APRAXIA

Apraxia is a disorder of skilled action and tool use that cannot be attributed to weakness, tremor, or other primary sensorimotor deficit or generalized cognitive impairment. The term *apraxia* is sometimes extended to include a wide range of disorders that have little or nothing to do with skilled action; *dressing apraxia*, *oculomotor apraxia*, and *constructional apraxia*, for example, are not relevant to this discussion as this article uses the term *apraxia* to refer specifically to disorders of skilled action, most commonly involving the upper extremity.

KEY POINT

- ***Ideomotor apraxia*** **is conceptualized as a loss of knowledge regarding skilled action. *Ideational apraxia* is often considered to be a disorder of planning and sequencing that is most apparent in multistep actions, such as preparing a letter to be mailed.**

History

Liepmann[1,2] was the first to systematically explore disorders of skilled action. In his landmark manuscript published in 1908, he reported data from 89 patients with chronic stroke, 47 with left-brain damage and 42 with right-brain damage.[1] He noted for the first time that apraxia was associated with left hemisphere lesions and that the disorder was usually evident in both the right and left hands. He also demonstrated that, although apraxia and aphasia often co-occur, they are dissociable. Finally, he noted that patients with apraxia typically performed least well when asked to pantomime the use of a tool, somewhat more reliably when asked to imitate the use of a tool (as demonstrated by the examiner), and best when provided the object to use. All these observations have been confirmed in many subsequent studies.

Liepmann described three different types of apraxic disorders. The first is *limb kinetic apraxia*, a disorder in which even simple movements lack precision and fluency. Whether this represents a disorder of stored motor knowledge or a primary low-level sensorimotor disorder has been debated. The second form of the disorder noted by Liepmann is *ideomotor apraxia*, which Liepmann believed reflects a failure to access stored kinematic patterns or "space-time engrams" that specify the activation parameters and timing of the contraction of muscles that would generate the desired movement. Finally, Liepmann described *ideational apraxia*, in which errors are not typically observed with simple movements but in the setting of complex multistep sequences, such as addressing and mailing an envelope. In contrast to ideomotor apraxia and limb-kinetic apraxia, this disorder is not specific to the body part used for the task. Ideomotor apraxia and ideational apraxia may co-occur. Geschwind[3] resurrected the study of apraxia in the 1960s in the context of disconnection syndromes and provided an anatomic model of the disorder. Geschwind proposed that action knowledge was supported by the temporoparietal cortex and that this information was transmitted to the left premotor cortex, where the action plans were implemented. Like Liepmann, he attributed the fact that most patients with apraxia show deficits in both hands to the belief that the motor plans are communicated from the left premotor cortex to the right premotor cortex by means of transcallosal fibers. Support for this assumption comes from the phenomenon of *callosal apraxia* (CASE 5-1).[4]

In a series of influential manuscripts, Rothi and colleagues[6] developed a cognitive model of apraxia reminiscent of the information-processing reading models of the 1980s. They proposed distinct auditory verbal, visual object, and visual gestural inputs to "lexicons" that included distinct types of stored representations, including an action input lexicon that was assumed to contain motor engrams (stored motor programs specifying a familiar action) that specified object-specific actions. Gesture production was accomplished by activation of

CASE 5-1

A 45-year-old right-handed man with a history of recent stroke presented with weakness and clumsiness of his right leg and difficulties in using his left hand. Examination showed moderate spastic weakness of the entire right leg, with increased reflexes and a Babinski sign. His right and left hands exhibited normal dexterity, power, and tone, and his language was normal. MRI demonstrated a stroke in the left anterior cerebral artery territory with involvement of the deep white matter tracts in the frontal lobe, consistent with the right leg upper motor neuron deficit.

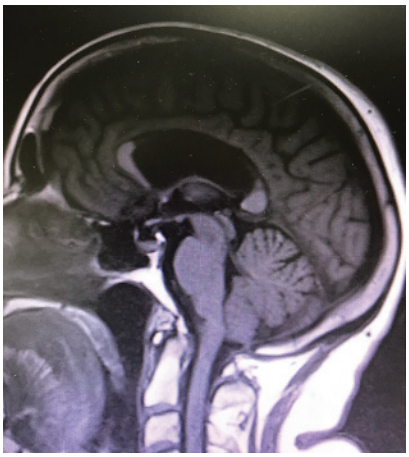

FIGURE 5-1
Sagittal T1-weighted MRI showing infarction of the corpus callosum in a patient with callosal apraxia.
Reprinted with permission from Watson RT, et al, Brain.[5] © 1985 Oxford University Press.

To evaluate his difficulty is using his left hand, the patient was first asked to demonstrate the use of a hammer and how to flip a coin with his right hand. He performed these and similar gestures to command flawlessly. When asked to do the same with left hand, he waved his hand purposelessly in the air and indicated verbally that what he was doing was not correct. When again asked to execute the same gesture with his right hand, he did so perfectly while appearing bemused. He was shown a hammer and asked to demonstrate its use with his left hand but again waved his hand randomly.

COMMENT

What does such a case reveal about the anatomic bases of knowledge of skilled action? First, as noted by Liepmann,[1] Geschwind,[3] and Watson and Heilman,[4] this and similar patients demonstrate that stored information supporting skilled action is lateralized to the dominant hemisphere. This case also demonstrates that this knowledge reaches the premotor cortex of the right hemisphere via fibers that connect premotor regions by means of the anterior body of the corpus callosum. The role of the white matter tracts connecting the premotor regions of the hemispheres in the transmission of knowledge regarding skilled action is demonstrated by the development of callosal apraxia in a patient with an infarct largely limited to the corpus callosum (FIGURE 5-1[5]).

entries in the output lexicon that specified the timing of the innervation of limb effectors. This model has been further developed in recent years.[7]

Building on the dual-route framework that distinguishes between a ventral route for object recognition and a dorsal or "how to" route for visuospatial processing and action, Binkofski and colleagues[8] elaborated an influential theory of apraxia that distinguishes between two components of the dorsal stream: dorso-dorsal and ventrodorsal. In this theory, the dorso-dorsal pathway, which is supported by superior parietal/intraparietal sulcus regions connecting to the dorsal premotor cortex, is considered crucial for reaching and grasping. In contrast, the ventrodorsal pathway, supported by the posterior temporal lobe and inferior parietal lobule and projecting to the inferior prefrontal cortex, is considered crucial for object use; this system specifies the representations of object-specific actions, precisely the type of information postulated by Liepmann to be disrupted in patients with apraxia. Support for this theory is found in studies of patients as well as in anatomic studies in primates.[8] Although beyond the scope of this article, it should be noted that an extensive literature is emerging regarding the neural basis of tool use, a topic closely related to apraxia.[9]

KEY POINTS

- The ventrodorsal and dorso-dorsal streams are particularly important in the production of meaningful and meaningless gestures, respectively.
- Apraxia is best assessed by asking the patient to execute an action to command or, if unable to do so, to imitate a meaningful gesture made by the examiner.

Clinical Assessment

Apraxia is often, but not always, associated with aphasia; thus, to assess for apraxia, the examiner must first demonstrate that the patient understands what he or she is being asked to do and has sufficient movement capacity to execute the requested movement. Comprehension permitting, the patient should first be asked to pantomime a specific movement, such as flipping a coin, hammering a nail, or pouring water from a pitcher into a glass. If the patient does not understand or is unable to execute the command, the examiner should demonstrate the gesture and the patient should be asked to copy the action precisely. If the patient is unable to do this, he or she should be asked to perform the action with the appropriate object (ie, the patient should be offered a screwdriver, for example, and asked to demonstrate its use).

As ideomotor apraxia is often body-part specific, performance should be assessed with each hand, the face, and the body. In the case of the extremities, both transitive (object-related) and intransitive gestures should be assessed as performance on the two types of actions may dissociate. Transitive gestures include demonstrating the use of a tool (eg, a comb), whereas intransitive gestures do not use objects and include gestures such as waving or saluting. To assess oral-buccal-facial praxis, patients may be asked to blow out a candle or drink through a straw. Praxis for midline body movements may be assessed by asking patients to show the posture of a boxer or dancer.

The adequacy of the patient's response is assessed at the bedside based on the precision, timing, and location of the movements. For example, when asked to pantomime brushing one's teeth, patients should exhibit back-and-forth movements of the arm and hand at the mouth with the teeth bared and with fingers curled as if gripping the object. A commonly observed error is the "body part as object" response. When asked to pantomime brushing one's teeth, the patient may extend the index finger and mimic using the finger as the utensil. Gesture substitutions may also be observed. In this case, when asked to pantomime hammering a nail, a patient may incorrectly pantomime using a saw; many of these errors are semantically based.

The ability to understand gestures should also be assessed. To this end, patients may be shown a gesture, such as hammering a nail, and asked to indicate what act is being performed. Alternatively, for patients with aphasia, language requirements may be minimized by asking them to simply match a verbal label to a gesture. Patients should also be asked to produce meaningless gestures. To assess this, patients may be instructed to assume random body postures or execute an unfamiliar sequence of specific finger, hand, and arm movements; for example, a patient may be asked to imitate the examiner's posture, in which the right index finger is placed at the top of the head and the left thumb over the sternum. A double dissociation between the ability to produce meaningful and meaningless gestures may be observed. Some patients demonstrate apraxia (ie, an impairment in producing familiar, meaningful gestures); as noted above, this may be seen in patients with a lesion of the ventrodorsal pathway. Other patients do not demonstrate apraxia but are impaired in the production of meaningless movements; this may be observed in patients with a lesion of the dorso-dorsal pathway. It should be noted that the inability to copy meaningless movements or assume static body positions is not considered to be apraxia because it reflects a deficit in translating visual information into motor coordinates rather than a deficit in stored knowledge of action sequences. Several short screening tests appropriate for bedside testing have been developed, including the Short Screening Test for Ideo-motor Apraxia (STIMA)[10] and the Short Test for Apraxia.[11]

Neural Correlates

Liepmann[1,2] reported that in right-handed individuals, apraxia was associated with left hemisphere lesions, particularly involving the parietal lobe. Although more recent studies have refined and extended this picture, left hemisphere lateralization has been persistently reported. Studies that evaluated groups of patients using the lesion-symptom mapping approach have demonstrated that tool use deficits and imitation of meaningless gestures are associated with lesions in a fronto-temporo-parietal network.[7,9] Impaired recognition of action has been associated with damage to the left posterior temporal lobe[12] and left inferior frontal gyrus.[13]

NEGLECT

Neglect is an acquired asymmetry in the processing of information from one side of the body or space. The deficit is typically manifested on the contralesional side of the body or space and is typically more severe and persistent after right cerebral lesions. Neglect is a heterogeneous and multicomponent disorder with protean manifestations. For example, neglect can involve one side of the body, one side of peripersonal space (roughly the space to which one can reach), or one side of extrapersonal space (beyond peripersonal space). Additionally, neglect may be evident for all objects in a region of space or may be stimulus-centered, involving one side of an object or word regardless of its location. These different forms of neglect may be observed alone or in combination. Neglect may also be observed in mental imagery for locations or arrays.[14,15] Although most investigations have emphasized the sensory manifestations of neglect, the disorder may also be manifest in action; motor neglect is a disorder in which patients do not use the contralesional limbs despite having the power to do so. The following sections

review these and other aspects of the syndrome as well as theoretical models of the disorder.

Spatial Neglect and Frames of Reference

The world around a person can be divided into the right and left sides (or *hemispaces*). The distinction between the right and left may be based on at least three different frames of reference centered on the body midline, head midline, and visual field. In the classic anatomic position with the head and eyes directed forward, the three hemispaces are aligned; in many activities, however, they are dissociated. For example, if a person's head is turned 45 degrees to the left while sitting at a dining service, the fork is in left body hemispace but right head hemispace.

Evidence exists that hemispace defined by all three coordinate frames can influence neglect. Many investigators have demonstrated that phenomena such as line bisection are influenced by the location of the stimulus to be bisected[16] defined with respect to the body midline, with performance better on the right than the left side of the body. Additionally, tactile extinction may be influenced by the location of the hands being tested: patients with neglect may show less neglect of the left hand when both hands are placed on the right side of the head or body. Similarly, bisecting a line in the midline may be improved by turning the patient's head to the left, thereby putting the line in the right head hemispace. Finally, even visual field deficits may be modulated by head and body position. Kooistra and Heilman[17] reported a patient who appeared to have a left hemianopia with head and eyes directed ahead but demonstrated much improved visual detection when the eyes were deviated to the right and much of the left visual field was in the right head and body hemispace. Hemispatial effects may also be observed in patients without overt neglect. The author has reported hemispatial effects on motor and language processing in patients with right and left parietal lesions, sometimes in the absence of other manifestations of neglect.[18] Although the effects of head, body, or eye position on neglect are not observed in everyone, they are common, occurring in approximately 25% of patients in the author's experience.

Associated Deficits

A number of deficits are often seen in association with neglect but are not clearly part of the syndrome, because they may not be present in patients with hemispatial neglect or may be observed in the absence of other manifestations of the disorder. The most common of these is extinction (the tendency to report only one of two stimuli presented simultaneously). Although it is most commonly seen in the setting of neglect and many patients with clear neglect will exhibit extinction as they improve, extinction is considered by many to be independent of neglect.[19]

Disorders of the body schema, such as somatoparaphrenia, are most frequently encountered in patients with right hemisphere lesions, many of whom have neglect. In this condition, patients may deny ownership of a part of the body, usually the left arm. Often patients will treat the body part as foreign, sometimes demanding that the left arm be removed from their bed. Disorders such as somatoparaphrenia may be more common than previously reported. Antoniello and Gottesman[20] reported that 61% of patients with acute right middle cerebral artery stroke exhibited disorders of limb misidentification acutely; the phenomenon was observed in 15% of patients at 1 week. When evaluating patients with neglect, it is often useful to ask specifically if they feel

KEY POINTS

- Inability to imitate meaningless body postures or gestures is not a disorder of skilled action but reflects an impairment in the procedures for translating visual information into motor coordinates.
- *Hemispace* refers to the side of a person's environment and may be defined with respect to at least three axes: head, body, and eye position. Manifestations of neglect may be influenced by all three coordinate frames.
- Results of tests for neglect are very frequently influenced by the location of the stimulus or response; for example, patients may extinguish tactile stimuli on the left hand when it is located in left hemispace but not when it is in right hemispace.
- A wide range of phenomena, such as extinction, are commonly observed in neglect but may dissociate and are not considered by many to be a core part of neglect.

that their body is well formed, as some patients are reluctant to mention that their body feels distorted for fear of appearing unhinged.

Finally, anosognosia for hemiparesis or spatial deficit is commonly observed in patients with neglect. In the former condition, patients may be unaware of frank hemiplegia[21]; they may develop elaborate explanations for their deficits. Furthermore, even if patients acknowledge their weakness or sensory deficit, their behavior may not reflect this insight. Patients may, for example, concede that they cannot move the left side but immediately thereafter attempt to walk to the door.

Theoretical Models of Neglect

Perhaps because the manifestations are so variable, no satisfactory theoretical model of neglect exists; work in recent years is converging on the view that the clinical syndrome of neglect is not a single disorder but a combination of disorders, perhaps with differing pathophysiologies.[22] Several of the major theories to explain at least some aspects of the disorder are reviewed here.

Many theories attribute neglect to a failure of attention, a broad and often ill-defined theoretical construct. One theory attributes neglect to failure to direct attention to or to act in the contralateral hemispace.[22,23] The fact that neglect is more commonly observed after right hemisphere lesions is attributed to the fact that the right hemisphere mediates attention to both the right and left sides, whereas the left hemisphere mediates attention only to the right side.[23] An alternative view first proposed by Kinsbourne[24] suggests that each hemisphere manifests a vector of attention toward the contralateral side; the hemispheres differ in that the left hemisphere vector of attention is strongly lateralized to the right, whereas the right hemisphere vector of attention is only weakly lateralized to the left. In this theory, each hemisphere is inhibited by the opposite hemisphere. Left neglect is explained by hypothesizing that a right hemisphere lesion reduces inhibition of the left hemisphere, thereby unmasking the left hemisphere's strong rightward bias of attention. In contrast, Bisiach and Luzzati[25] suggested a "representational deficit" in neglect. They reported patients who, when asked to imagine the establishments on the Piazza Del Duomo in Milan, reported primarily landmarks on the right when facing the cathedral at one end of the square.[25] When asked to imagine the square while facing in the opposite direction, however, the patients again reported the landmarks on the right, ignoring the previously reported landmarks.

The author and others believe that neglect should be conceptualized as a multicomponent disorder with an impairment in arousal[26] or capacity for effort[27] as a prominent feature. A number of studies show that right hemisphere lesions impair (nonspatial) tonic arousal.[26–28] In this account, the effects of lateralized attentional asymmetries are exacerbated by a decreased attentional capacity or arousal. Consistent with this view, Robertson and colleagues[28] reported that patients with neglect were impaired in judging whether a visual stimulus on the left preceded or followed a stimulus on the right. A warning sound, presented from either the right or left, eliminated neglect on a visual task, suggesting that the benefit was conferred by increasing arousal rather than enhancing processing in the neglected hemispace. Consistent with the claim that deficits in sustained attention and arousal are an important component of neglect, the author and colleagues[29] reported that the severity of nonlateralized attentional deficits correlated with the overall severity of neglect.

Clinical Examination

The assessment of neglect should commence as soon as the clinician encounters the patient. In the author's experience, neglect may often be diagnosed by observing the way patients orient to the examiner and the qualities of the patient's spontaneous movements. Many patients with neglect, for example, will show clear differences in the degree to which they attend to stimuli from the right and left. Although some neglect behaviors may be overt and unmistakable, other behaviors may be more subtle. For example, it is common for patients to be slower in turning the head and eyes to a speaker standing on the contralesional side. It is often useful for the examiner or team to address the patient from both the ipsilesional and contralesional sides to look for differences in orienting. Many patients with neglect have an associated hemiparesis that makes motor neglect difficult to observe. In patients with mild or no weakness, akinetic movements or hypometric movements, or both, are frequently encountered. For example, patients with motor neglect will often use the ipsilesional hand for grooming and gesturing even when this would not be the usual motor sequence (eg, scratching the left ear with the right hand).

A number of simple bedside tasks may also be useful in the assessment of neglect. Line bisection and cancellation tasks are often used to assess peripersonal neglect. In the former, patients are shown lines, preferably of varying lengths and locations on the paper, and asked to place a mark at the middle of the line. Except for short lines in which a "crossover" effect may be observed, patients with peripersonal neglect bisect lines to the right of the midline. Cancellation tasks require patients to identify targets displayed on a paper or screen. In general, cancellation tasks with a larger number of targets and distractors are more difficult, as are tasks in which distractors are visually similar to the targets. The stimuli for cancellation and bisection tasks may be placed in the midline or to the patient's right or left side to assess for hemispatial effects.

Personal neglect is often evident in grooming and other everyday activities. Patients may fail to dress one side of the body, shave one side of the face, or, in extreme cases, fail to recognize part of their body as their own. When asked to touch the neglected side of the body, patients may fail to do so; it is not uncommon for patients with neglect to touch the stimulated location on the ipsilesional side of the body, a phenomenon known as *allesthesia*. The fluff test and variants may be useful in the assessment of personal neglect. In these tasks, Velcro or cotton balls are attached with tape or a weak adhesive to various parts of the right and left side of the body and the patient is asked to remove the stimuli with his or her eyes closed. Patients with personal neglect may fail to remove all the stimuli from the side of the body with neglect.

Drawing tasks are also useful in the assessment of neglect. Patients may be asked to draw a house, clock, flower, or other common object from memory or to copy a figure; patients with neglect tend to omit or distort features from the contralesional side of the object. Many patients with neglect will also show a spatial distortion characterized by placing the drawn or copied object on the right side of the paper. To test for hemispatial effects, the location of the stimuli presented or action executed should be systematically varied. Finally, the examiner should manipulate the patient's posture to assess the effects of the head, eye, and body position.

KEY POINTS

- **Neglect is a heterogeneous and multicomponent disorder of which attentional asymmetries and disorders of arousal are common components.**
- **Neglect may be assessed with a wide range of bedside tasks and formal batteries. It is important to note, however, that careful observation of the patient may reveal subtle deficits that bedside tasks, such as line bisection, do not identify.**

A number of test batteries have been developed that provide quantitative measures of neglect. Perhaps the most commonly used is the Behavioral Inattention Test,[30] which includes tasks that assess cancellation, bisection, and several more naturalistic functions (eg, menu reading). The Catherine Bergego Scale[31] provides a good measure of personal neglect. In this 10-item task, an observer rates the degree to which the patient attends to the left side of the body in naturalistic tasks.

Extinction can occur in three sensory modalities: vision, touch, and audition. For all three types of stimuli, a suprathreshold stimulus is presented to the right, left, or both sides and patients are asked to point to or name the side at which the stimulus was presented. It is important to perform multiple trials of each type and to include "catch" trials in which no stimulus is presented to minimize guessing. The severity of extinction is determined in large part by the salience of the stimulus. Extinction is more likely to be evident with stimuli that are close to the detection threshold.

Anatomic Basis

Neglect has traditionally been associated with right posterior parietal lesions. If attention is mediated by large-scale distributed networks, however, one might expect neglect to be observed with lesions that involve different components of the attentional network (eg, dorsal frontal cortex, thalamus, posterior parietal cortex, posterior superior temporal gyrus), including the white matter tracts that connect them. This has been observed in animals and human subjects; for example, neglect may be associated with lesions involving subcortical structures, such as the thalamus and basal ganglia, as well as the dorsal frontal cortex. Additionally, damage to white matter tracts may underlie neglect in some patients.[16]

More recently, a number of studies have attempted to identify the pathologic substrate of distinct subtypes of neglect phenomena. Pedrazzini and colleagues,[32] for example, contend that space-based neglect is associated with lesions of the temporoparietal junction, whereas object-based neglect is associated with lesions of the posterior superior intraparietal sulcus. Although some inconsistencies between the theories may be identified, recent developments in techniques for linking lesions and behavior at a voxel level offer hope that at least some of the variability exhibited by patients with neglect will prove to be predictable from the location and size of the precipitating lesion.

Natural History and Treatment

Neglect is a disabling disorder with a poor long-term prognosis. The often-profound spatial asymmetries tend to resolve over weeks to months; for example, in a series of 166 patients with neglect, lateral attentional asymmetry was clinically apparent at 6 months after the stroke in approximately only 10% of patients.[29] Despite this improvement in the spatial aspects of neglect, the disorder has a poor prognosis and has been demonstrated to be associated with a poor functional outcome.[33]

Although considerable effort has been expended to develop treatments for neglect, all current therapies remain generally unsatisfactory. Prism therapy and noninvasive brain stimulation with transcranial magnetic stimulation and transcranial direct current stimulation have shown promise.[34]

AGNOSIA

The agnosias are a class of disorders in which a failure of recognition is present that cannot be attributed to low-level visual or sensory deficits. Perhaps the first description of visual agnosia was provided by Munk,[35] who noted that lesioning the bilateral parietooccipital cortex in dogs rendered them unable to recognize objects despite the fact that they could navigate through their environment without substantial difficulty. The first systematic discussion of the visual agnosias was provided by Lissauer,[36] who introduced the distinction between apperceptive agnosia and associative agnosia that continues to animate many discussions of the topic. This section first considers Lissauer's contribution and then briefly reviews the major types of agnosic disorders.

Agnosias as Disorders of Recognition

Visual object recognition is a process by which information presented to the retina is transformed in a cascade of processes involving the lateral geniculate and successively "higher" visual cortices to generate an internal representation of the object that permits stored knowledge of an entity to be consciously accessed. For example, when a person is presented with an apple, information about the size, shape, color, and other visual attributes of the stimulus are decoded at the retina, lateral geniculate, and primary visual cortex before being processed in a series of visual regions specialized for different visual features and attributes. This visual information is subsequently integrated in the inferior occipitotemporal cortex (the "what" system) into a mental model of an apple. The specific properties of the mental model (eg, whether it is "visual" or multimodal) continue to be the topic of research. This internal representation of an apple then contacts the totality of the individual's stored information relating to apples, including, for example, the taste, feel, color, and manner of harvesting.

Lissauer reported the first detailed description of a patient who had difficulty in this process; despite adequate vision and knowledge of objects, the patient was unable to name or otherwise show recognition of the objects. To make sense of these deficits, Lissauer proposed that two types of disorder of recognition be distinguished. The first he designated *apperceptive agnosia*, which he considered to be an impairment in the integration of visual form and feature information that precluded the generation of an internal representation of the object. The second subtype of recognition disorder he termed *associative agnosia*. In this condition, processing of the visual information is at least relatively intact but relevant stored information cannot be contacted. In Teuber's[37] apt summation, associative agnosia is characterized by a "normal percept stripped of its meaning." Lissauer's operational definition of the distinction between the apperceptive agnosia and associative agnosia relates to the ability to draw or copy a stimulus; patients with apperceptive agnosia are unable to generate a depiction of an entity, whereas patients with associative agnosia are able to copy (often in a slavish, piecemeal fashion) or draw an object but are unable to provide information about the object that they have just drawn. Although sorely lacking in detail, Lissauer's general account continues to frame the discussion of the agnosias.

Category-Specific Visual Agnosia

A number of patients who were more accurate in naming nonliving entities than living entities have been reported[38]; for example, they were more likely to name a hammer as compared to an elephant, even when the visual stimuli were

KEY POINTS

- **Extinction may be observed in vision, touch, and audition independently or in combination. Stimuli that are near the detection threshold are more likely to identify extinction.**
- **Neglect is most frequently associated with lesions in the right parietal lobe but may be caused by pathology in a distributed attentional network that includes the right inferior frontal lobe, thalamus, basal ganglia, and white matter tracts connecting them.**
- **In the traditional nosology, *apperceptive agnosias* result from a failure in sensory processing, whereas *associative agnosias* are caused by a failure to contact stored information about an object after an adequate perceptual representation has been constructed.**

KEY POINTS

- Prosopagnosia is a disorder of visual recognition specific to faces. In this disorder, which may be either acquired or developmental, patients often recognize a face as a face and, in some instances, derive substantial information about the stimulus such as age, gender, and emotional expression but are unable to identify the individual.
- Agnosias may be distinguished by the specific nature of the stimuli rather than the sensory modality of the input; for example, in the visual domain, material-specific agnosias are observed that selectively impair recognition of faces or words.
- Pure word deafness is a disorder in which patients can identify environmental sounds (eg, a car horn, a telephone ringing) but cannot understand speech despite at least largely normal ability to read, write, and speak.
- Modality-specific agnosias are disorders of recognition that involve one type of sensory input, such as vision, audition, or touch.

controlled for potentially confounding factors such as the visual complexity or familiarity of the stimuli. Subsequently, different performance as a function of the semantic category has been repeatedly confirmed, and many other dissociations have been reported. For example, other patients with agnosia may recognize animals better than inanimate objects, and more fine-grained distinctions, such as differential performance with fruits and vegetables, have been observed (CASE 5-2). The implications of these observations for the organization of the semantic system remain a topic of considerable interest and debate.[40]

Material-Specific Agnosia

Although impairment in the processing of visual objects is the most common type of agnosia, recognition of other classes of visual stimuli may also be impaired, sometimes selectively. Prosopagnosia is a disorder of visual recognition specific to faces. In this disorder, which may be either acquired or developmental, patients often recognize a face as a face and, in some instances, derive substantial information about the stimulus such as age, gender, and emotional expression but are unable to identify the individual. The deficit may be so profound that some patients with prosopagnosia may be unable to recognize their own faces in the mirror.

Pure alexia, sometimes designated *agnosic alexia*, is a disorder that is traditionally considered in the context of disorders of language. As patients with the disorder are typically unable to recognize words but may demonstrate no impairment with visual stimuli or auditory language, the disorder represents a type of modality-specific agnosia. *Optic aphasia* is a visual modality–specific impairment in the recognition of objects and words; patients with optic aphasia often "recognize" objects and words in the sense that they may be able to demonstrate the use of an object but are unable to name the object. Optic aphasia is distinguished from anomia by the fact that patients with optic aphasia have no problem naming objects from description or on the basis of palpation. Recent work supports previous suggestions that agnosia for words and agnosia for faces dissociate, arguing that the cognitive processes underlying face and word processing are at least partially distinct.[41]

Modality-Specific Agnosia

Agnosia is most commonly observed in the visual domain but may also be observed for auditory and tactile inputs. Generalized auditory agnosia is characterized by an inability to recognize all types of sounds in the absence of deafness. Pure word deafness is a disorder in which patients can identify environmental sounds (eg, a car horn, a telephone ringing) but cannot understand speech despite at least largely normal ability to read, write, and speak. The disorder is associated with lesions involving the primary auditory cortex bilaterally or a left superior temporal gyrus lesion. Auditory sound agnosia is a very rare but perhaps underreported syndrome in which speech recognition is largely intact but recognition of environmental sounds is poor.

Agnosia in Neurodegenerative Disorders

The most common setting in which agnosias are observed in clinical practice is in the setting of neurodegenerative diseases. Visual object agnosia is frequently seen in Alzheimer disease but may be obscured by co-occurring semantic,

CASE 5-2

A 50-year-old man awoke from cardiac surgery with difficulty recognizing people, objects, and words. After a few months, he improved, but he continued to have trouble recognizing people and objects. Except for close family members, he only recognized people based on their voices. Head CT showed a right inferior occipitotemporal infarct, which was felt to be an underestimate of the full extent of his lesions.

The patient presented for evaluation 10 months after the onset of symptoms. He exhibited a mild visual agnosia; he performed well on a wide range of spatial tasks and accurately copied complex figures but performed poorly in naming objects and faces. However, he performed differently with different types of stimuli; he was much more accurate naming drawings of nonliving objects (eg, hammer; 91% correct) than living beings (eg, dog; 41% correct) that were matched for the complexity of the visual image.

COMMENT

How can this patient's pattern of performance be explained? Knowledge of objects comes in different forms; one not only knows what a telephone looks like but also how it feels, how it is held, how to make a call, and the sounds that it makes. Recognition of an object then may be determined not only by the degree to which the visual image matches the stored representation of the object but also by means of other kinds of information conveyed by the image. This patient, who had normal praxis and visuospatial skills, was able to use the image of the object to access information about the manner in which the object was used. If sensorimotor information about object use can supplement information about object form to aid in object recognition, one might expect objects for which the patient has sensorimotor information pertinent to the object's use to be named more accurately than objects for which no such information is available. This prediction was tested in a series of experiments, which found that this patient's ability to name visual stimuli was predicted by factors such as the manipulability of the stimulus.[39] This was true for both man-made and naturally occurring stimuli. Thus, the difference in performance between living and nonliving things exhibited by this patient was not a function of the semantic category of the stimulus but a reflection of the richness of his sensorimotor knowledge of the stimuli. While this account is not likely to explain all the category-specific agnosias, it illustrates that multiple factors influence what appears to be the straightforward task of object naming and that information from multiple types of sensory and motor representations may be integrated to influence performance. Object recognition requires not only the ability to generate an accurate mental model of an object but also access to semantic information specifying the sound, smell, action, and use of the object.

KEY POINTS

- Patients with posterior cortical atrophy may have problems recognizing faces, words, and objects and are particularly impaired in the recognition of complex scenes, often showing elements of Balint syndrome.
- Posterior cortical atrophy is caused by Alzheimer disease in approximately two-thirds of patients but is also caused by dementia with Lewy bodies, corticobasal degeneration, and prion diseases.
- Visual agnosias are frequently observed in Alzheimer disease and frontotemporal dementia.
- Recognition is a complex process that should be assessed by more than simply asking patients to name an object; patients may also be asked to point to named objects and to demonstrate the manner in which an object may be used.

language, or amnestic disorders. In the syndrome of posterior cortical atrophy, however, a visual processing disorder is the most prominent feature, and other impairments are, at least early in the course, relatively minor.[42] Patients with this disorder may have problems recognizing faces, words, and objects and are particularly impaired in the recognition of complex scenes, often showing elements of Balint syndrome. Posterior cortical atrophy is caused by Alzheimer disease in approximately two-thirds of patients but is also caused by dementia with Lewy bodies, corticobasal degeneration, and prion diseases. The pathology tends to be in the occipital, posterior parietal, or posterior temporal lobe; in different individuals, the disorder may preferentially impair visuospatial processing, object processing, or even lower-level visual processes. Prosopagnosia is not uncommon in frontotemporal dementia, particularly in patients with right anterior temporal lobe atrophy.[43]

Assessment

The hallmark of visual agnosia is impairment in naming visually presented objects. As naming deficits occur for a variety of reasons, impaired naming alone is not sufficient to support a diagnosis of agnosia. One factor that helps to distinguish aphasia from agnosia is the nature of naming; in contrast to patients with aphasia, who generally produce phonologic (sound-based) or semantic (meaning-based) errors, most errors generated by patients with agnosia reflect an impairment in the visual decoding of the stimulus; for example, a patient with agnosia may call a bicycle a pie, presumably reflecting the fact that the patient failed to "see" the entire object and misconstrued the wheel as a pie. The recognition of visual stimuli should also be assessed by asking patients to point to a named object in an array. Copying figures and drawing a familiar figure should also be assessed. Considering the category- and material-specific agnosias described earlier in this section, it is important to assess recognition for a wide range of stimuli, including animate and inanimate objects, words, faces, complex arrays, and sounds. Should patients be unable to name an object, they should be asked to indicate knowledge of the object in other ways, such as by generating the appropriate gesture or verbalizing where it might be found or its function. As patients with agnosia often perform better in naming real objects as compared to identifying line drawings, it is useful to assess performance with both types of stimuli. Two useful batteries for assessing visual object processing are commercially available: the Birmingham Object Recognition Battery (BORB)[44] and the Visual Object and Space Perception Battery (VOSP).[45]

CONCLUSION

Apraxia, neglect, and agnosia are classic neurologic disorders that continue to be of relevance to 21st century neurologists for several reasons. All three disorders are of considerable interest to cognitive neuroscientists because the patterns of deficits exhibited by patients with these disorders tell us much about the processes underlying motor planning, attention, and visual recognition. The conditions are also highly relevant to clinical practice because of their prevalence and their implications for functional recovery. It is hoped that this brief introduction to these disorders will enhance neurologists' ability to provide state-of-the-art care.

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