

HIGHER CORTICAL VISUAL DISORDERS: CASE-BASED REVIEW

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Introduction

The diagnosis of disorders of higher visual processing often poses a considerable clinical challenge.^{1, 2} Routine evaluations of visual function may not readily yield a diagnosis; a refined examination of visual function is necessary to correctly localize and identify these otherwise elusive syndromes. The original descriptions of these conditions depict how careful clinical observation, coupled with study of anatomical pathology at autopsy, yielded tremendous insights that were the foundation of the development of modern neurology. More recently, neuroimaging techniques including functional magnetic resonance imaging (fMRI) and positron emission spectrography (PET) have allowed further insights into complex structure-function relationships. Disorders of visual processing not only have significant clinical importance, but also shed light on neuroscientific questions regarding normal visual processing in the brain.

The Dorsal and Ventral Streams

The concept of the dorsal (“Where”) pathway and ventral (“What”) pathway was put forth by Ungerleider and Mishkin in their 1982 paper entitled “Two Cortical Visual Systems.”³ They proposed that occipitotemporal areas are selective for processing the identity of visual objects. Specific regions in the ventral stream are specialized for identifying faces, objects, or visual scenes. Meanwhile, the occipitoparietal areas are selective for visuospatial processing; previously, subcortical areas such as the superior colliculi were thought to be the main contributors to these aspects of vision.

Ungerleider and Mishkin supported their idea with several converging lines of evidence, relying heavily on experiments previously published by Walter Pohl in which macaque monkeys had selective lesions in the frontal, parietal, or temporal lobes.⁴ The Landmark test relied on spatial relationships between objects, and performance was severely impaired in monkeys with parietal lesions. Conversely, performance on an object identification task, which did not rely on spatial relationships, was impaired in monkeys with temporal lobe lesions.

Many of the disorders described below highlight the ways in which higher visual functions may be separable, with certain aspects of visual processing impaired while others are preserved. The “What/Where” concept of visual processing provides a useful framework with which to localize these clinical syndromes.

Anton Syndrome

Anton Syndrome refers to cortical blindness without awareness of the deficit. Patients have complete visual loss from bilateral occipital lesions, yet they do not directly complain of the deficit. Gabriel Anton, from Graz, Austria, described this condition in 1899 in a paper entitled “On the Self-Awareness of Neurologic Deficits in Patients with Cortical Blindness and Cortical Deafness.”⁵ He described a 56-year-old woman who “could not distinguish light and darkness,” yet was “almost unaffected by the visual deficit.” At autopsy he found that the patient had “cystic necrosis primarily affecting the gray and white matter of the right and left occipital lobes.” He concluded by suggesting, “it is undoubtedly possible that the function of some parts of the brain, which are not damaged themselves, can become altered through damage to other parts.” Here, he advanced the powerful concept of network connections in the brain, addressing the fact that occipital lesions would understandably produce visual loss, but disturbances in other associated networks presumably play a role in the prominent anosognosia characterizing this condition.

Apperceptive Visual Agnosia

Visual Agnosia refers to the impaired ability to identify, recognize, or interpret visually presented information even though elementary aspects of vision remain intact. Patients cannot name objects presented visually, but they can identify objects perceived through touch or sound. They cannot read because of the severe impairment in processing visual forms, so a standard eye chart cannot be used to measure the visual acuity. The actual spatial acuity is intact, however, and this can be demonstrated with tests such as the Preferential Looking Test, in which a patient simply looks at black-and-white gratings including stimuli with very high spatial frequency approximating 20/20 vision.

Heinrich Lissauer described this syndrome, at the age of 27, in an 1889 paper entitled "A Case of Visual Agnosia, With a Theory About the Same."⁶ He described an 80-year-old man who "was quite incapable of visually recognizing the most common objects." Yet when his vision "was assessed by showing him small dots on a white background, his visual acuity was essentially normal."

Lissauer divided visual agnosia into two types, proposing that "there may exist both apperceptive and associative agnosia." With apperceptive visual agnosia, vision is disrupted at a very early stage of processing; these patients cannot perceive even the most basic geometric relationships creating the contours of a visual object. With associative visual agnosia, basic visual perception is preserved but a percept cannot be associated with semantic knowledge; in the words of Teuber, the normal percept is "stripped of its meaning."⁷

Further insights into the origin of apperceptive visual agnosia have emerged from studies of patient D.F., a 35-year-old woman who suffered severe carbon monoxide poisoning in 1988. She demonstrated severe deficits in shape recognition and orientation, despite preserved acuity, color vision and tactile discrimination.⁸ High resolution MRI study of her brain revealed near complete destruction of the lateral occipital cortex (LO), a fundamental component of the ventral stream.⁹

In their 1992 paper entitled "Separate Visual Pathways for Perception and Action,"¹⁰ Goodale and Milner used this case to refine the traditional concept of the What/Where framework. When D.F. was shown a mail slot, although she could not describe or match its orientation, she had no difficulty reaching forward to put a card correctly through the slot. Similarly, she could not describe the dimensions of a visually presented object, but her grip aperture scaled perfectly when she actually reached to pick it up. Goodale and Milner used these data to suggest that the dorsal stream should be recognized as a 'How' pathway to emphasize its role in using visual information to guide limb movements that allow a person to interact with and manipulate the environment. In accord with their theory, fMRI studies of D.F. have revealed loss of activity in area LO with preserved activity during visually guided motor actions in regions of the dorsal stream.¹¹

Central Hemiachromatopsia

Central Hemiachromatopsia arises when a lesion in inferior occipital cortex diminishes or abolishes color vision in the contralateral hemifield. If the lesion includes the inferior bank of the striate cortex, then a contralateral superior field defect is also seen, and the color vision impairment will be seen only in the contralateral inferior quadrant.

In 1888, Verrey first reported hemiachromatopsia in an article entitled "Absolute Right Hemi-Achromatopsia, with Partially Spared Perception of Light and Shapes, Due to Chronic Hemorrhagic Cyst of the Left Occipital Lobe."¹² Describing a 60-year-old woman, he said "in half the binocular visual field color perception is abolished, producing a sensation of gray." At autopsy, he found that the lesion "occupies the third occipital gyrus," and concluded that "the center of the color sense appears to be in the inferior occipital lobe." An autopsy study of a patient with hemiachromatopsia showed damage involving the fusiform gyrus¹³ so it is not surprising that many patients with the disorder also suffer from prosopagnosia.

For many years, the notion of a cortical center for color was controversial (if not heretical), until 1973 when Samir Zeki used single cell recordings to identify neurons in the macaque whose responses were purely selective for color.¹⁴ He named this cortical region area V4, and shortly afterward, the same color area was identified in humans using functional neuroimaging.¹⁵

Alexia Without Agraphia

Alexia Without Agraphia refers to the loss of the ability to read, although the ability to write remains spared. Remarkably, patients will not be able to read a sentence that they have written themselves. This defect is limited to the perception of written language; production and comprehension of spoken language is fully preserved.

The syndrome of alexia without agraphia was first described by M.J. Dejerine in an 1892 paper entitled “Different Types of Word Blindness: Pure Word Blindness, With Intact Writing, Spontaneously and to Dictation.”¹⁶ His patient was a man named Courriere, who was walking in Paris when he suddenly noticed that he could no longer read. Dejerine described that his “writing is perfectly preserved . . . but reading what he has written is absolutely impossible.” The patient had a right homonymous field deficit, as occurs in most (but not all) patients with this syndrome. At autopsy, Dejerine found a lesion involving the left occipital lobe, extending anteriorly to involve the splenium of the corpus callosum. Normal reading requires that vision be linked to language areas in the dominant hemisphere. In this case, Dejerine reasoned that the patient lost the ability to read because visual information that was retained, in the right visual cortex, was disconnected from intact language areas in the contralateral hemisphere.

More recently, MRI tractography in a patient with alexia without agraphia has confirmed a reduction of inter-occipital fibers and left occipital-temporal fibers.¹⁷ A pure form of alexia without agraphia, in which right homonymous hemianopia is not present, may result from a lesion in the ‘visual word form area’ in the fusiform gyrus.¹⁸ Conversely, agraphia without alexia may occur in the setting of a left angular gyrus lesion.¹⁹

Riddoch Syndrome

The Riddoch Syndrome describes preserved ability to detect motion in an otherwise blind visual field.²⁰ There is ‘statokinetic dissociation,’ in which the patient can perceive an object only if it is moving. Form and color cannot be appreciated. A similar phenomenon is also termed “blindsight,” in which patients lack conscious awareness of vision, yet their actions indicate awareness of some aspects of visual information, such as motion alone.

George Riddoch described this phenomenon in 1917 in a paper entitled “Dissociation of Visual Perceptions Due to Occipital Injuries, With Especial Reference to Appreciation of Movement.”²¹ He described 10 patients, all soldiers in World War I who had been injured with shrapnel from bullets. For example, he described a Lieutenant Colonel who “quickly perceived finger movements in the whole left half field, though when the fingers were kept stationary he saw nothing.” Riddoch assessed the localization of the lesion by looking at entry wounds and X rays, concluding that the “bullet entered the right occipital lobe just on the occipital pole.” He reasoned that primary visual cortex was affected, but nearby motion processing areas were spared.

The cortical area specialized for processing motion is called V5 and is situated dorsal to the primary visual cortex in the occipital lobe. It remains controversial how visual inputs may arrive at this area to give rise to the statokinetic dissociation seen in the Riddoch Syndrome. Some researchers have assessed fMRI responses in a patient with this disorder and, failing to find responses in V1, have suggested that there are additional direct subcortical projections to area V5.^{22, 23} Furthermore, tractography of patients with blindsight has shown an intact connection between the lateral geniculate nucleus (LGN) and V5, but not in those patients without blindsight.²⁴ On the other hand, other investigators have found small ‘islands’ of activation within the lesioned portion of primary visual cortex.²⁵ Impoverished inputs at any level of the visual system may compromise most aspects of visual processing – such as shape, color, and form – and yet leave coarse motion perception intact.

Balint Syndrome

The Balint Syndrome is a profound disruption of visual attentional mechanisms resulting from bilateral parietal lesions. Although elementary aspects of vision, including acuity and object recognition, remain preserved, patients are profoundly affected by an inability to disengage and shift their attention to various parts of a visual scene. One component of the Balint syndrome is optic ataxia, referring to impaired reaching under visual guidance. Unlike cerebellar ataxia, the movement back to touch one’s nose remains accurate with optic ataxia, since visuospatial attention is not required for this action. Another component is ocular apraxia, which describes the abnormal eye movements that are made when a patient tries to shift gaze from one object to another target in the environment. A third component is simultanagnosia, which refers to the perception of local elements of a scene, but inability to perceive its global elements. In colloquial terms, this is described as “missing the forest for the trees.” This may be tested using a Navon figure, which is a large letter (for example, E) composed of many smaller letters (for example, A); the patient with simultanagnosia will see the large letter but be unable to see the smaller ones.

In 1909 the Hungarian physician Rudolph Balint described this clinical presentation in a paper called “Paralysis of Gaze, Optic Ataxia, and Disturbance of Spatial Attention.”²⁶ He described an engineer who could no longer assemble models due to a profound inability to manipulate spatial attention, although visual acuity, strength, and dexterity were normal. He tried to light a cigar in the middle rather than the end, and could not cut a steak as he directed his knife outside the plate. At autopsy, he was found to have bilateral parietal infarcts.

In 1918, Gordon Holmes expanded on Balint's concept of "psychic paralysis of gaze," now referred to as "ocular apraxia," by describing 5 patients who could direct their eyes accurately to the location of a sound or to a region verbally described by the practitioner, but not to a target that appeared in the visual field.²⁷

To be precise, simultanagnosia was not explicitly mentioned in Balint's report; it was described shortly thereafter in a paper by I. Wolpert in 1924.²⁸ His patient was asked to describe the events in a scene, and "in contrast to the almost perfect description by normal individuals, the patient saw only details that he could not sum up."

The Balint syndrome typically occurs in the setting of bilateral parieto-occipital lesions, most often seen in the setting of cardiovascular disease, posterior cortical atrophy, posterior reversible leukoencephalopathy syndrome (PRES) and progressive multifocal leukoencephalopathy (PML). Functional imaging studies suggest that optic ataxia stems from damage to the pathways connecting the "parietal reach region" and medial interparietal area to the dorsal premotor cortex, while ocular apraxia results from disrupted connections from the lateral interparietal area to the superior colliculus and frontal eye fields.²⁹

Prosopagnosia

Prosopagnosia is a specific form of visual agnosia in which face perception is impaired, while other aspects of vision are intact. Patients may be unable to recognize even their own face when looking at a photograph or in the mirror. Typically, patients identify individuals using other clues, such as gait, physical mannerisms, clothing, or voice.

Human beings are expert at extracting information from a face in order to accurately and effortlessly identify it. This expertise is the result of a specialized group of neurons in the ventral processing stream, known as the Fusiform Face Area. Nancy Kanwisher and her colleagues first identified this area of the brain using fMRI in 1997.³⁰ The concept that face identification has a privileged status in the visual system was not unique, however. For example, 460 years before the discovery of the FFA, the Italian artist Giuseppe Arcimboldo created a popular series of paintings of objects such as fruit bowls; but when these paintings were inverted, they took on a configuration that could be expressly processed by the FFA, making it easy to see a face 'hiding' in the picture.³¹

Although cases of patients with impaired face perception were described in the 19th century by Charcot and others, the term Prosopagnosia was first used in 1947 by Joachim Bodamer in a paper entitled, "On Prosopagnosia: The Agnosia of the Cognition of Faces."³² He described three patients who lost the ability to identify faces after sustaining injury to the occipitotemporal lobes. In most cases of prosopagnosia, these lesions occur bilaterally, but in some cases they may affect the right hemisphere alone.

Some individuals demonstrate a developmental prosopagnosia from childhood, without any apparent cortical injury. In some of the patients, fMRI studies³³ have shown a loss of the face-specific activation of the FFA while evoked potentials have demonstrated loss of face-selective increase in the N170 waveform over the right posterior temporal cortex, which contains the FFA, superior temporal sulcus (STC) and lateral occipital cortex.³⁴ Barton and colleagues have demonstrated deficits in the perception of spatial arrangement of features in both patients with acquired³⁵ and developmental prosopagnosia.³⁶ Prosopagnosia has widely been seen as incurable, but certain rehabilitative efforts, including those aimed at training subjects to categorize faces by the spatial relationships of their features, have demonstrated modest improvement.³⁷

Charles Bonnet Syndrome

Charles Bonnet Syndrome refers to "release" hallucinations that occur in the context of visual loss. The hallucinations are typically nonthreatening, and patients often describe seeing small people, animals, or flowers. It is important to recognize this syndrome and correctly differentiate it from other causes of hallucinations, including psychotic disorders. One distinguishing feature is that auditory hallucinations are not typically part of the Charles Bonnet syndrome.

The syndrome is given its eponym because it was described by Charles Bonnet, a Swiss naturalist and lawyer, in his 1760 work entitled, "Analytic Essay on the Faculties of the Soul."³⁸ In it, he described "a respectable man, with full health, candor, judgment, and memory, who in plain day and irrespective of any outside stimulus, from time to time perceives before him figures of men, women, birds, cars and buildings." In fact, the man he described was actually his own 87-year-old grandfather who was nearly blind from cataracts.

Functional imaging studies have shown spontaneous increases in activity in visual association areas in the ventral extrastriate cortex that temporally correlate with the reported hallucinations.³⁹ These findings lend credence to the idea that in the absence of receiving external sensory information, the visual system can generate internally formed hallucinations instead.

Lhermitte's Peduncular Hallucinosis

Lhermitte's Peduncular Hallucinosis describes vivid, dream-like hallucinations that occur during normal wakefulness. This condition was described in 1922 by M.J. Lhermitte in a paper entitled "Syndrome of the Top of the Cerebral Peduncle: Psycho-sensory Disturbances in Lesions of the Mesencephalon."⁴⁰ He described a 72-year-old woman who saw "different animals walking on the floor. They are cats, chickens looking a little strange, their pupils dilated, possessing a strange radiance." He inferred that the lesion "is caused by a vascular lesion of the pedunculo-pontine region." Although he did not have a confirmatory autopsy in this case, the clinical examination showed that "paralysis of nerves III, IV, and VI is the proof." He explained the occurrence of bizarre, vivid hallucinations by saying, "it is therefore possible to interpret the psycho-sensual disturbances as a dream state intruding upon wakefulness." Five years later, L Van Bogaert described a similar patient with the sudden onset of vivid hallucinations, and showed at autopsy that there was indeed infarction of regions of the midbrain.⁴¹

A lesion that produces the syndrome of peduncular hallucinosis may be in the midbrain or thalamus. In these regions, the reticular activating system and thalamic intralaminar nuclei regulate the state of wakefulness of the brain, permitting vivid dreams to occur during REM sleep. Analysis of network connectivity shows that lesions producing peduncular hallucinosis are functionally anti-correlated with visual association areas.⁴² The complexity of the visual hallucinations in PH also implicates dysregulation of visual association areas, rather than of primary occipital cortex, since stimulation of the latter produces more basic hallucinations of flashes and colored lights.⁴³ These findings support Lhermitte's original proposal that mesencephalic and diencephalic lesions may impair the normal regulation of internally generated dream imagery so that it occurs not just during sleep but during wakefulness as well.

Conclusion

In this course and accompanying syllabus, we have looked carefully at several cases showing the dramatic manifestations of cortical visual disorders. Timely diagnosis and optimal management of patients with disorders of visual processing are important challenges faced by the practicing neurologist. The study of these disorders provides a framework to consider important neuroscientific concepts regarding the functional organization of the brain.

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