Visual agnosias and related disorders: beyond Lissauer

A. García-Molina[1,2,3], J. Peña-Casanova[4,5]

[1]Institut Guttmann. Institut Universitari de Neurorehabilitació (UAB), Badalona, Spain.
[2]Fundació Institut d'Investigació en Ciències de la Salut Germans Trias i Pujol, Badalona, Spain.
[3]Universitat Autònoma de Barcelona, Bellaterra, Spain.
[4]Behavioural neurology research group. Fundación Institut Mar de Investigaciones Médicas (FIMIM), Barcelona, Spain.
[5]Psychiatric and Legal Medicine Department. Universitat Autònoma de Barcelona, Barcelona, Spain.

ABSTRACT

Introduction. In 1878, Hermann Munk associated visual processing with the occipital cortex. Twelve years later, Heinrich Lissauer proposed a stage model of object recognition, constituting the basis for the study of visual recognition disorders.

Development. This article describes the development of the study of visual recognition disorders, focusing on four main concepts: *1) Seelenblindheit* (mind-blindness) and Lissauer's stage model; *2)* visual perception as a multicomponent cerebral process, whose alteration causes specific symptoms (eg, shape agnosia, central achromatopsia, prosopagnosia, simultanagnosia, and akinetopsia); *3)* cognitive neuropsychology and object constancy; and *4)* dual visual processing (dorsal and ventral streams).

Conclusions. In clinical practice, Lissauer's stage model is the most widely used reference framework for the classification of visual agnosia. Contributions made from different scientific disciplines over the 20th century have opened new paths to understand the complexity of disorders of visual recognition, beyond Lissauer.

KEYWORDS

Agnosia, perception, vision, occipital lobe, ventral stream, dorsal stream

Introduction

The history of the localisation of cerebral functions can be divided into three periods. The first focused on identifying what part of the human body is the seat of the essence of being ("the soul"); the second aimed to determine the localisation of mental processes in the brain (ventricular system vs brain parenchyma); and the third focused on how these processes are organised in the cerebral cortex (equipotentiality vs cortical localisation). Proponents of equipotentiality believed that all mental activity involved the participation of extensive brain regions, whereas localisationists maintained that specific brain functions are developed in specific cortical regions. While the literature prior to 1800 includes a handful of examples of specialised brain regions,[1] localisationist theories were not recognised as valid until well into the 19th century.[A] In 1861, Paul Broca (1824-1880) contributed one of the first empirical demonstrations of the correspondence between a cognitive process and a specific area of the cerebral cortex, relating impairment of articulated language to

[A]Phrenology may be considered to be based on localisationist principles: phrenologists maintained that the brain is made up of mental organs, each of which is dedicated to a specific function.

Corresponding author: Dr Alberto García-Molina
E-mail: agarciam@guttmann.com

Received: 18 January 2022 / Accepted: 11 March 2022

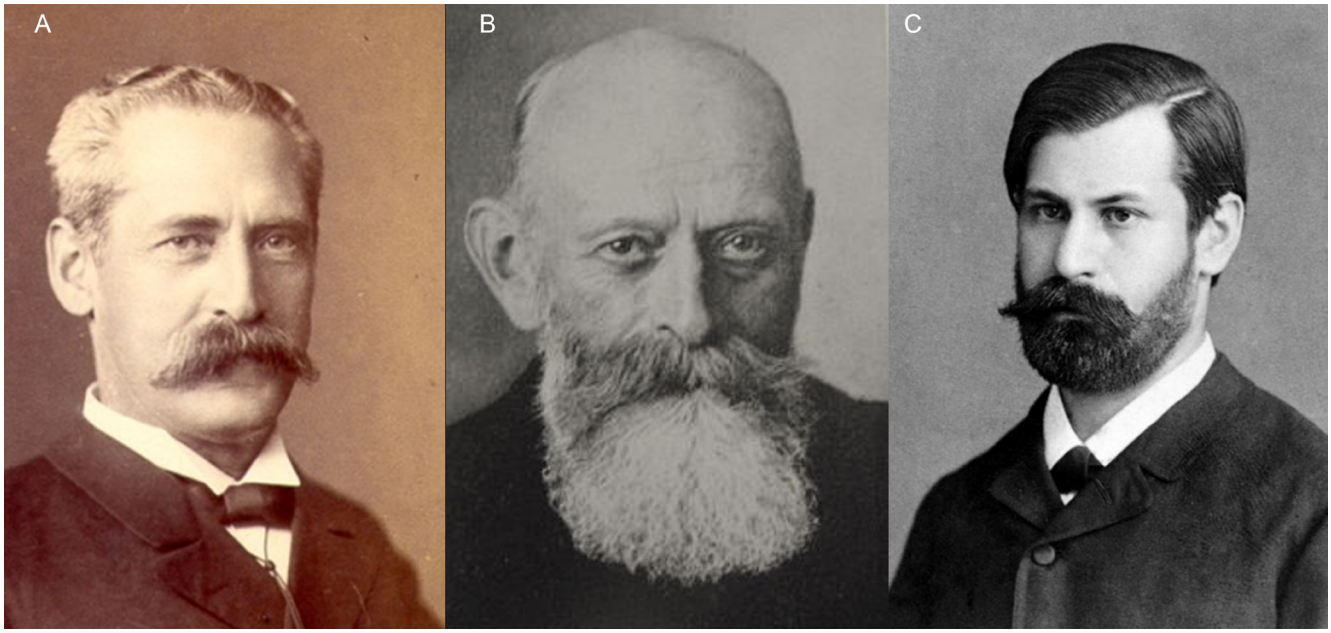

Figure 1. A) Hermann Munk (1839-1912). B) Hermann Wilbrand (1851-1935). C) Sigmund Freud (1856-1939).

lesions circumscribed to the third left frontal gyrus.[2] Nine years after Broca's discovery, Eduard Hitzig (1838-1907) and Gustav Fritsch (1838-1927) associated the posterior frontal lobe with movement.[3] In the 1870s and 1880s, David Ferrier (1843-1928) and Edward Albert Schafer (1850-1935), respectively, made remarkable contributions to the localisation of cortical sensory areas.[4,5] Hermann Munk (1839-1912) (Figure 1A) did the same for the neuroanatomical substrate of vision, linking visual processing to the occipital cortex.[B]

The 1880s saw greater acceptance of the idea that multiple brain processes may be involved in vision.[6,7] These ideas led to speculation about the functional organisation and neurobiological basis of visual perception. In 1884, the ophthalmologist Hermann Wilbrand (1851-1935) (Figure 1B) argued in favour of the existence of autonomic cortical centres responsible for the recognition of individual qualities of vision: "The sense of light, the sense of space, and the sense of colour are located in spatially separate cortical areas of the occipital lobe of each hemisphere."[8(p2)]

In the early 20th century, Pierre Marie[9] (1853-1940) and Gordon Morgan Holmes[10] (1876-1965) questioned the existence of dissociations in visual perception. Although numerous researchers defended the dissociative hypothesis, the holistic paradigm became the dominant theory until the 1950s. In subsequent decades, the contributions of cognitive neuropsychologists revived the idea that visual perception is a cognitive process with a multicomponent structure. This article aims to summarise the history of visual disorders associated with brain alterations in the period from 1880 to 1990.

Development

Seelenblindheit (mind-blindness)

In 1878, Hermann Munk conducted a series of experiments in which he surgically removed different

[B]History treatises attribute to Munk the discovery of the relationship between vision and the occipital lobes; however, the first contribution on the subject was made by the Italian physician Bartolomeo Panizza (1785-1867).

cortical regions in dogs.[11,12] When the procedure was performed near the posterior pole of the occipital lobe, he observed a peculiar change in the animals' visual behaviour. Their ability to move through space without colliding with or tripping over objects remained intact. However, they did not "understand" the function of the drinking trough they had previously used. Similarly, they did not recognise their handler and could not find the place where their food bowl was usually kept (unless guided by other senses, such as smell). Munk concluded that the animals were able to see but could not understand the meaning of the objects they saw. They had lost their *Erinnerungsbilder* (stored visual images) and developed *Seelenblindheit* (mind-blindness).[C] According to this researcher, the animals had lost their memory images of previously perceived stimuli. Consequently, they were unable to relate current and past experience, and therefore could not understand the meaning of the perceived stimuli. Six years after Munk presented his experimental findings, John Hughlings Jackson (1835-1911) published one of the first descriptions of an acquired disorder of visual processing.[13] He presented the case of a patient who was unable to recognise places and individuals: "at one time he did not know his own wife […] and having wandered from home was unable to find his way back."[13(p153)] Hughlings Jackson proposes the hypothesis that the deficits were caused by a defect in the sensorimotor processes involved in the recognition of objects (not in seeing them).

Munk's term *Seelenblindheit* became popular among clinical professionals after the publication of Wilbrand's[14] monograph *Die Seelenblindheit als Herderscheinung und ihre Beziehungen zur homonymen Hemianopsie, zur Alexie und zur Agraphie* (1887) (Mind-blindness as focal symptom and its relationships to homonymous hemianopia, alexia, and agraphia). In this study, he describes how the mind establishes relationships between visual forms and their meanings. Among the patients reported, he highlights the case of Fräulein G: "when people stood at my bedside and spoke with pity of my blindness, I thought to myself: you can't really be blind because you are able to see the table-cloth over there, with the blue border, spread out on the table in the sick-room."[14,D] The autopsy study[15] showed significant depression of the right fusiform gyrus, forming a flaccid, membranous sac extending to the pole of the occipital lobe, with the ipsilateral cuneiform segment being diminished and softened. In the left hemisphere, Wilbrand observed a small cavity between the first and second occipital gyri, bordering on an area of chronic softening at its frontal edge.

Three years after the publication of Wilbrand's monograph, the neurologist Heinrich Lissauer[16] (1861-1891) published the article "Ein Fall von Seelenblindheit nebst einem Beitrag zur Theorie derselben" (A case of mind-blindness and a contribution towards a theoretical explanation). In this study, he posited a stage model of object recognition, based on his observations of the patient Mr Gottlieb.[E] According to Lissauer, the process of recognition (*wiedererkennen*) involves a perceptual stage and a second associative stage. Alterations in the perceptual stage result in what Lissauer terms *apperceptiven Form der Seelenblindheit* (the "apperceptive form of mind-blindness," caused by involvement of perceptual mechanisms or the connection between sensation and perception). He refers to alterations in the associative stage as *associativen Form der Seelenblindheit* (the "associative form of mind-blindness," caused by disconnection between perception and stored conceptual associations). The associative stage underpins the ability to recognise the meaning and nature of a visual object.

Lissauer questioned Munk's theory that *Seelenblindheit* was associated with the presence of occipital lesions. Based on the associationist ideas of his mentor Carl Wernicke (1848-1905), he proposed that:

> […] when a sensory impression is recognised, the cortex responsible for perception is the first to act. However, it must subsequently follow the chain of associative images that recall the different memory images determining the object in question. […] This process must be mediated by the transcortical tracts of the visual cortex […] blockage would prevent

[C]Munk drew a distinction between *Seelenblindheit* and *Rindenblindheit* (cortical blindness). In *Rindenblindheit*, the animal was unable to see any object presented to it.

[D]Translator's note: English translation taken from Solms M, Kaplan-Solms K, Brown JW. Chapter 8: Wilbrand's case of "mind-blindness". Code C, Wallesch CW, Joanette Y, Lecours AR, eds. Classic cases in neuropsychology, Vol I. Hove (GB): Psychology Press; 1996.

[E]Lissauer first presented this theory on 28 November 1888 at the conference of the Association of East German Neurologists.

> the link between perception and the associations needed for the process of recognition, which would give rise to *Seelenblindheit*."[16(p258)]

Findings from the post mortem examination of Mr Gottlieb at least partially confirmed these hypotheses.[17] The left posterior cerebral artery was occluded, with the corresponding left occipital lesions. Lissauer also detected lesions to the corpus callosum with evident contraction of the splenium and demyelinating lesions in the occipital white matter bilaterally.

The replacement of the term *Seelenblindheit* with agnosia is attributed to Sigmund Freud (1856-1939) (Figure 1C). In his 1891 monograph *Zur Auffassung der Aphasien: eine kritische Studie*[18] (On the conception of aphasia: a critical study), he distinguishes between three types of aphasia: *1) verbale Aphasie* (verbal aphasia), *2) asymbolische Aphasie* (asymbolic aphasia), and *3) agnostische Aphasie* (agnostic aphasia). In Freud's classification, agnostic aphasia is defined as a unimodal disorder of object recognition in which the central language area remains intact but cannot be accessed via object associations within a given sensory modality. Several years later, authors including Karl Ludwig Bonhoeffer[19] (1868-1948) and Constantin von Monakow[20] (1853-1930) began using the word *Agnosie* (agnosia) to refer to *Seelenblindheit*.[F]

In 1908, Hugo Liepmann[21] (1863-1925), a disciple of Wernicke and colleague of Lissauer, suggested that mental processes may disintegrate through dissolution or disjunction. With respect to perceptual processes, he suggested that these two mechanisms would cause *dissolutorischen Agnosie* (dissolutory agnosia) and *disjunktive* (*ideatorische*) *Agnosie* (disjunctive [ideational] agnosia), respectively. Dissolutory agnosia is defined as a perceptual alteration of a specific modality (visual, auditory, or tactile) associated with focal brain lesions. According to Liepmann, visual dissolutory agnosia would encompass both the apperceptive and the associative forms of mind-blindness described by Lissauer. Disjunctive (ideational) agnosia, secondary to diffuse brain lesions,[G] hinders multimodal recognition of stimuli, causing disintegration of concepts (*Zerfall der Begriffe*): "A patient stated that a child's trumpet was a pistol. When asked about its purpose, she replied 'for shooting.' When it was placed in her hand, she also used it as a weapon. When she brought it to her mouth and was asked to blow it, the effect translated into a joyous recognition."[21(p667)]

Selective disorders of visual perception

In the final decades of the 19th century, there was growing support for the idea that visual perception is a brain process involving multiple components. Thus, alterations to these components could cause selective disorders of visual perception, such as difficulties recognising shapes, discriminating colours, perceiving movement or depth, or locating objects in space.

In 1888, the ophthalmologist Louis Verrey[22] (1854-1916) published the article "Hémiachromatopsie droite absolue" (Absolute right hemiachromatopsia), in which he described a woman who had presented a haemorrhagic stroke in the left occipital lobe. The main sequela was the inability to perceive colour in the right visual field. Other cases had been described of patients with central achromatopsia,[23] but Verrey's was the first to include post mortem data. Based on the anatomical pathology findings, he concludes that "the centre of the chromatic sense would lie in the most inferior part of the occipital lobe, probably in the posterior part of the lingual and fusiform gyri."[22(p298)] In 1945, Justo Gonzalo Rodríguez-Leal[24] (1910-1986) described an unusual chromatic alteration in a patient (case M) with lesions to the left parieto-occipital convexity: "When he picks up a coloured object or touches with his hand a coloured surface, the patient has the visual impression that he is grasping the colour, or submerging his hand into it. Therefore, colours are not attached to the surface of the object […] but rather appear frontally as a plane, producing the appearance of a coloured film."[24(p220)H] From a neuroanatomical perspective, Gonzalo suggests that "influenced by the doctrine of cerebral localisation, we attempted to identify in the occipital lobe the localisation of colour vision […] these localisations are inadmissible."[24(p196)]

[F]The term *Seelenblindheit* continued to be used by German-speaking authors until the 1950s, whereas it disappeared from the English-language literature in the early 20th century.
[G]Liepmann indicated that disjunctive agnosia is associated with diffuse atrophic processes, progressive paralysis, senile dementia, and general cerebral atherosclerosis.
[H]Gelb published one of the first descriptions of the "film colour" phenomenon in 1920.

In 1909, Rudolf Bálint[25] (1874-1929)[I] described a patient with ischaemic stroke involving the bilateral posterior parietal region, who was able to visually identify objects in isolation but had difficulties processing combinations of visual elements. When he was shown a letter and a triangle, he saw only the letter; when he was told there was a second object, he said he could see the triangle but not the letter. In 1924, Ilja Wolpert[26] (1891-1967) coined the term *Simultanagnosie* (simultanagnosia)[J] to refer to this perceptual disorder. Henry Head[27] (1861-1940) described an inability to combine details into a coherent whole, while Oliver Zangwill[28] (1913-1987) spoke of "piecemeal perception." Independently of the terminology used, patients with this visual perception disorder have no difficulties perceiving individual elements or details of a complex visual stimulus, but cannot appreciate its overall meaning.

In 1911, Otto Pötzl (1877-1962) and Emil Redlich[29] (1866-1930) published one of the first descriptions of akinetopsia (difficulty perceiving movement). The patient presented a bilateral occipital lesion, and was unable to detect moving objects or to fix her gaze on them when they moved towards her. Kurt Goldstein (1878-1965) and Adhémar Gelb[30] (1887-1936) reported similar alterations in the patient Schn: he was able to perceive objects "here or there" (ie, at the start or end point), but could not see the translation. George Riddoch (1888-1947) studied numerous cases during the First World War, suggesting that "movement may be recognised as a special visual perception."[31(p15)] Holmes refutes Riddoch's work, arguing that "the condition described by Riddoch should not be spoken of as a dissociation of the elements of visual sensation, since it is only a condition of visual hypoaesthesia in which the stronger and more adequate stimuli alone excite sensations […] occipital lesions do not produce true dissociations of function."[10(p379)] Decades later, Gonzalo reported how his patient M, instead of seeing an object's movement, perceived a series of objects: "a kind of decomposition of the movement of the object, which transformed into a series of successive, static images along the path travelled."[24(p290)] In 1983, Zihl, von Cramon, and Mai[32] presented the patient LM, contributing evidence supporting a specific, selective alteration of movement vision after an acquired brain injury.[K] LM explained that she had difficulty pouring a cup of coffee because the liquid appeared to be frozen, like a glacier. She was unable to stop pouring at the correct time as she could not perceive the movement in the cup as the fluid rose. She also reported difficulty crossing the street due to her inability to judge the speed of approaching vehicles: "When I'm looking at the car first, it seems far away. But then, when I want to cross the road, suddenly the car is very near."[32(p315)L]

In 1917, Friedrich Best[33] (1871-1965) attended a soldier (patient 38) with a bullet wound to the head. The patient recognised shapes, sizes, and colours, but was unable to determine the direction of movement. He also presented optic ataxia and impairment of the eye movements involved in visual exploration. In addition to these symptoms, he presented a noteworthy deficit: he was able to recognise any stimulus presented to him, regardless of its spatial orientation, but was unable to determine its orientation. Best describes the patient as follows: "this case shows that the neuronal centres for characterising spatial characteristics are very distant from the centres that process the recognition of all other characteristics of these objects."[33(p122)] The patient died several days after the examination. The autopsy study showed an entry wound affecting the upper section of the left angular gyrus and the exit wound slightly above the right angular gyrus (in the posterior part of the inferior parietal lobe). Gonzalo's[24(p264)] patient M "occasionally perceived objects as leaning or even inverted. Men working on scaffolding appeared to be upside-down." Another patient (patient T) examined by the same author explained that he "could read an upside-down newspaper as easily as if it was upright, without noticing any difference, and stated that the letters were always in the normal position."[24(p267)] In accordance with his hypothesis about

[I] In the early 20th century, Bálint described a symptom complex characterised by the presence of psychic gaze paralysis, optic ataxia, and a spatial attention disorder. This triad is now known as Bálint syndrome or Bálint-Holmes syndrome.

[J] Kulcsár and Szatmári (1939) used the term *Wolpertsche simultane Agnosie* (Wolpertian simultaneous agnosia), while Klimes and Mészáros (1942) refer to *Wolpertsche Agnosie* (Wolpertian agnosia).

[K] Semir Zeki's (b. 1940) experimental studies in the 1970s on area V5 and its role in movement perception contributed to confirming the theories on the functional specialisation of the visual cortex.

[L] The literature includes very few descriptions of patients with akinetopsia. In 2019, Heutink et al. presented the case of the patient TD. Source: Heutink J, de Haan G, Marsman JB, van Dijk M, Cordes C. The effect of target speed on perception of visual motion direction in a patient with akinetopsia. Cortex. 2019;119:511-8.

the non-existence of a cortical colour centre, Gonzalo underscored that "optical direction is disturbed from any location in the sensory brain. […] Therefore, we must not seek localisations of any type."[24(p270-1)]

Wigan[34] (1844), Quaglino and Borelli[35] (1867), Charcot[36] (1883), and Wilbrand[14] (1887) describe patients with various disorders of visual perception, including difficulties recognising faces. In the late 1930s, Hans Hoff (1897-1969) and Otto Pötzl[37] proposed the existence of a specialised brain function for processing faces; in 1947, Joachim Bodamer (1910-1985) conducted one of the first systematic analyses of this deficit. Bodamer characterised prosopagnosia as a specific visual agnosia affecting the ability to visually recognise faces, with an intact ability to recognise individuals by other means (eg, voice, gait, or clothing).

Brain lesions and visual illusions

The German- and English-language scientific literature from the first half of the 20th century includes cases of patients with posterior brain lesions who presented an exaggerated or distorted visual perception of the external world.[38,39] Against the framework of Jackson's distinction between negative and positive neurological symptoms, Macdonald Critchley[40] (1900-1997) classes these phenomena as "positive" disorders, as opposed to "negative" disorders that cause difficulties with the formation and recognition of visual stimuli (with agnosias being the most paradigmatic example).

In 1908, Giovanni Mingazzini[41] (1859-1929) published one of the first descriptions of polyopsia (the perception of multiple images of an object). In the 1930s, Hoff and Pötzl[42,43] documented additional cases, including that of a patient with a tumour in the right occipital convexity who saw his room-mate's bed copying itself: "The beds appeared to be forming a row to the left […] the figure of the patient lying in the bed also multiplied. The first beds were lighter and the others further to the left were darker."[43(p435)] Hoff and Pötzl propose using polyopsia in the differential diagnosis between tumours affecting the base of the temporal lobe and those involving the occipital lobe. In 1945, Morris Boris Bender[44] (1905-1983) described four new cases of this unusual anomaly. In one patient:

> Everything around him seemed to be quadruple, no matter in which direction he looked. The four images were arranged in two parallel pairs, one above the other. Everything seemed to be indistinct, and he was unable to differentiate the true from the false images. They all appeared to be of the same size.[44(p325)]

Holmes reports the case of a patient with an angioma in the right occipitoparietal region:

> She stated that on three occasions, at intervals of about half an hour on the one day, after someone had walked past the foot of her bed from left to right, she had for a moment or two the impression of the same person as before walking past, but when she looked carefully the person was not there. The dress, size, and distance of the person appeared exactly the same, but the image was more shadowy."[45(p472)]

In 1944, Alexandra Adler[46,47] (1901-2001) reported the case of the patient HC, who presented visual agnosia after carbon monoxide poisoning. When HC attempted to read, "previously seen words impose themselves on subsequent ones and interfere, regardless of whether these words have been recognised or not."[46(p258)] According to Adler, this demonstrates that the patient was "caught by previous optic impressions, which superimpose themselves on subsequent ones, with resulting misinterpretations."[46(p258)] In 1951, Critchley[40] reported additional examples of this unusual phenomenon associated with occipitoparietal lesions, in which the patient continued seeing a stimulus after it had disappeared from the visual field. He considered this to be a type of visual perseveration in time, which he refers to as paliopsia. Critchley also describes an anomaly characterised by an illusory extension of visual perception over a larger than expected area. In this case, he suggests a visual perseveration in space, coining the term illusory visual spread. According to this author, illusory visual spread is a phenomenon that "takes the form of a metamorphopsia whereby objects appear elongated in one dimension only."[40(p268)]

Positive disorders have classically been considered to include visual illusions, such as those described above, and hallucinations (perceptions produced in the absence of an external sensory stimulus). With respect to hallucinations associated with posterior brain lesions, the contributions of Jacques Jean Lhermitte[48,49] (1877-1959) and Henri Hécaen[50] (1912-1983) are particularly relevant.

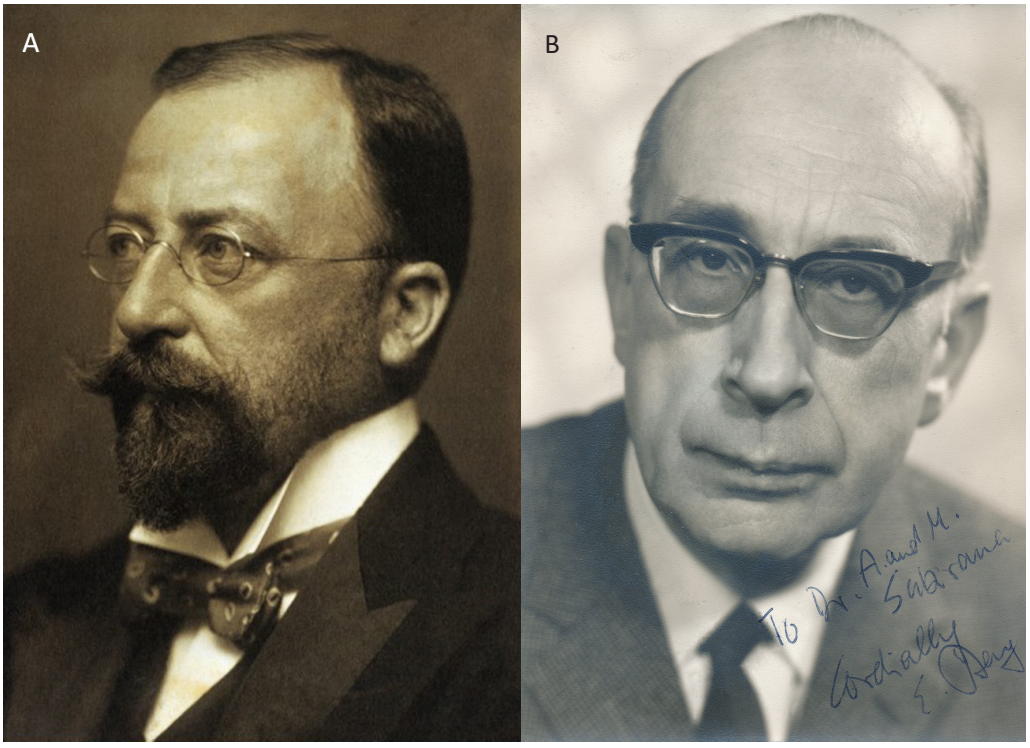

Figure 2. A) Henry Head (1861-1940). B) Eberhard Bay (1908-1989; Historical Archive of the Spanish Society of Neurology).

Do visual agnosias exist?

Over the 20th century, distinguished neurologists openly questioned the existence of visual agnosias. In his *Studies in neurology*, Henry Head[51] (Figure 2A) argues that because most, if not all, cases of agnosia are associated with primary visual field defects and mental alterations, valid interpretation of this disorder is not possible. Morris Boris Bender and Hans-Lukas Teuber[52] (1916-1977) note that the variability of symptoms observed in patients invalidates the concept of agnosia as a clinical entity.

Revisiting the ideas explored by Head, Eberhard Bay[53] (1908-1989) (Figure 2B) proposes that impaired object recognition is the result of a combination of *1)* subtle deficits in elementary visual functions, and *2)* general intellectual deterioration. According to Bay, both characteristics may conspire to cause disproportionate difficulties with object recognition, although there is no deficiency in object recognition per se: "The mind-blindness, or visual agnosia for objects, is due to an impaired primary visual system combined in most cases with general mental deterioration."[53(p544)] Bay also writes that: "The so-called mind-blindness being the base for the classical concept of visual agnosia, we see no reason for retaining any other type of visual agnosia which was originally derived from mind-blindness."[53(p545)] Bay's statements are corroborated by Bender and Feldman.[54] These authors did not identify a single case of visual agnosia without elementary visual deficits and/or general intellectual deterioration among the patients attended at Mount Sinai Hospital in New York in the 1950s and 1960s: "In every patient who showed inability to recognise a common object visually, though able to do so by touch or by sound, there were also alterations in vision, and often in other sensory functions and in mentation."[54(p174)]

Critchley[55(p281)] notes that "cases of visual agnosia, though a commonplace in medical text-books, represent —let us admit— an extreme rarity in clinical practice. The validity of most of the handful of recorded cases is indeed open to serious criticism." He also questions Lissauer's distinction between apperceptive and associative agnosias, arguing that patients' subjective experiences and the diversity of visual dysfunction described lead to the idea that this distinction lacks a theoretical basis and has no relation to clinical experience.

Object constancy

In the late 1960s, the nascent discipline of cognitive neuropsychology contributed new perspectives in the approach to disorders of visual perception. Particularly relevant contributions were made by Elizabeth Kerr Warrington (b. 1931) (Figure 3A), Glyn William Humphreys (1954-2016), and Jane Riddoch (b. 1948) (Figure 3B).

In 1973, Warrington[56] observed that patients with right parietal lobe lesions could easily identify photographed objects as long as the photographs were taken from a conventional (prototypical) perspective. However, they were unable to do so when photographs were taken from an unusual (non-prototypical) perspective.[M] In the author's opinion, this deficit in the recognition of objects shown from non-prototypical perspectives or in unusual lighting conditions originates in a failure of perceptual classification or, in other words, in the assignation of equivalent stimuli in the same perceptual category.[57] David Marr[58] (1945-1980) made a similar interpretation: he posits that visual object recognition fundamentally relies on constructing and accessing a representation centred on the object, independently of the viewer. Humphreys and Riddoch[59,60] propose that object constancy[N] is achieved through the identification of distinctive features of an object, and the description of its structure in relation to its principal axis of elongation.

In 1978, Warrington[61] formulated an object recognition model analogous to Lissauer's stage model. This model is based on the behaviour of patients with left or right parietal lesions in two categorisation tasks: a perceptual and a semantic task. In the perceptual task, patients were asked to match objects photographed from a prototypical perspective to images of the same objects photographed from a non-prototypical perspective. In the semantic task, patients were shown groups of three dissimilar objects and asked to identify which two had the same purpose. Patients with right parietal lesions displayed difficulties with the perceptual but not with the semantic task (as long as objects were shown from a prototypical perspective). Patients with left-sided lesions, in turn, made mistakes in the semantic task and correctly performed the perceptual task (independently of the perspective from which the object was shown). Warrington's sequential model thus identified two postsensory categorical stages in visual object recognition. The first stage (postsensory semantic system) enables perceptual categorisation, whereas the second is involved in semantic categorisation. The visual analysis that gives rise to a structural perception, normalised for size and luminance, occurs in the visual cortex (with no lateralisation at this level of analysis). The perceptual categorisation system, located in the right hemisphere (specifically in the right-posterior cortex) processes information from the bilateral primary visual cortex. The semantic categorisation system, located in the left hemisphere, processes the output from the perceptual categorisation system. Years later, Warrington reformulated this sequential model after observing that some patients presented intact semantic visual processing despite significant deterioration of perceptual processing.[62,63] In the updated model, perceptual categorisation is an optional resource, rather than an obligatory stage in semantic categorisation.

In 1890, Lissauer sketched out a stage-based model of visual recognition, distinguishing between *apperceptiven Form der Seelenblindheit* (apperceptive form of mind-blindness) and *associativen Form der Seelenblindheit* (associative form of mind-blindness). A hundred years later, Humphreys and Riddoch[64] argued that the visual perception disorders described in the literature do not fit into this synthetic sequential model and proposed a new taxonomy comprising five types of visual agnosia,

[M]Although objects may be observed from an infinite number of perspectives, some are more familiar (or prototypical) than others.
[N]Object constancy is a perceptual process enabling recognition of an object independently of its orientation, lighting, or distance from the viewer.
[O]Benson and Greenberg (1969) refer to this as visual form agnosia. Warrington (1995) considers it not to be a form of agnosia, but rather a pseudoagnosia.

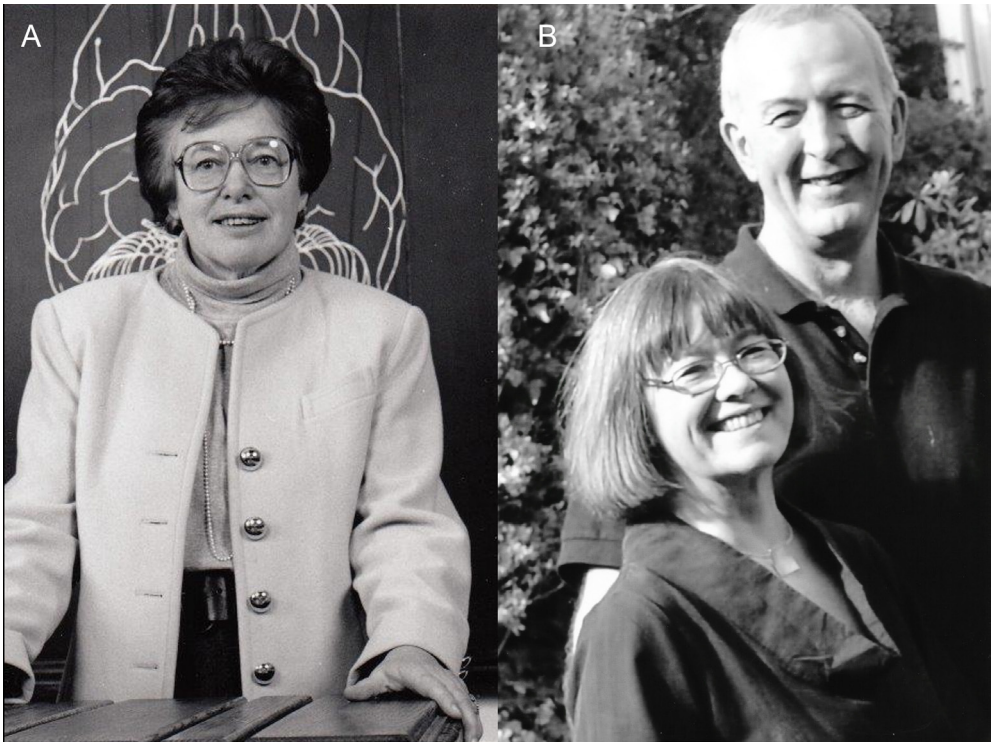

Figure 3. A) Elizabeth Warrington (b. 1931). B) Jane Riddoch (b. 1948) and Glyn Humphreys (1954-2016).

integrating the theories of classical neurology and those of cognitive neuropsychology:

- Shape agnosia[O]: inability to discriminate shapes with normal sensory functions. The patient has problems recognising objects, copying them, and pairing them according to shape.
- Integrative agnosia: adequate discrimination of the details of the shape with inability to aggregate them to generate a coherent perceptual whole. The patient is able to match and copy shapes (though poorly) but does not recognise them.
- Transformation agnosia[P]: codification of the perceptual whole is correct, but there is an alteration in object constancy. The patient experiences difficulty recognising objects depending on their spatial orientation or illumination.
- Semantic agnosia: the visual process enabling the construction of a perceptual whole is preserved, but there are alterations to the process responsible for creating memory images. The patient displays normal perceptual abilities but is unable to recognise objects.
- Semantic access agnosia: alteration to the connection between the perceptual whole and its memory image. The patient experiences no difficulty in matching and copying tasks or in the semantic tasks, but is unable to identify the visually presented objects.

[P]Farah (1990) proposes the term perceptual categorisation deficit rather than transformation agnosia.

Agnosias and dual visual processing

The emergence of cognitive neuropsychology in the 1960s helped to strengthen the idea that visual processes have a multicomponent structure. In parallel to this,

the accumulation of experimental, electrophysiological, and clinical data suggested that these processes involve hierarchically organised functional pathways.[65]

In 1968, Colwyn Trevarthen[66] (b. 1931) suggested that the midbrain is responsible for ambient vision, a type of vision that guides body movement (eg, locomotion), whereas the geniculostriate system is responsible for focal vision, guiding fine motor actions (eg, manipulation). In 1969, Gerald E. Schneider[67] published his article "Two visual systems," decisively contributing to the departure from the monolithic view of visual processing. Schneider notes that, in lower mammals, visual information represented in the midbrain informs the animal about the spatial location of a stimulus, whereas the retinothalamocortical pathway is responsible for recognition of the stimulus. Around the same time, Freda Newcombe (1926-2001) published her results from studies with veterans of the Second World War.[68] She observed that patients with parietal lesions had difficulty in the execution of visuospatial tasks (eg, line orientation and maze learning) but performed normally in tasks involving the visual recognition of objects or faces. Patients with temporal lesions presented the opposite pattern. Newcombe's experimental procedure, called double dissociation, which is widely used in cognitive neuropsychology and animal experiments, is based on the proposition that, if a lesion involving a specific brain structure is demonstrated to impair function X but not function Y, and a lesion to a different structure affects function Y but not function X, then we may infer specific conclusions about the function and its neuroanatomical localisation. Ironically, Hans-Lukas Teuber, one of the main champions of double dissociation, explicitly questioned the existence of visual agnosia.

In the early 1980s, Mortimer Mishkin (1926-2021) and Leslie Ungerleider (1946-2020) observed that in primates, the cortex not only participates in visual discrimination, but also plays an important role in the visual determination of positional information. They found that the "striate cortex in the monkey is the source of two multisynaptic corticocortical pathways."[69(p414)] Specifically, "one courses ventrally, interconnecting the striate, prestriate, and inferior temporal areas, and enables the visual identification of objects. The other runs dorsally, interconnecting the striate, prestriate and inferior parietal areas, and allows instead the visual location of objects."[69(p414)] Lesions to the ventral stream (the "what pathway") affect the capacity for visual discrimination, whereas lesions to the dorsal stream (the "where pathway") leave discrimination capacity largely intact, affecting the visual determination of spatial relationships.[70] The model developed by Mishkin and Ungerleider is fundamentally corticocortical, whereas those formulated by Trevarthen and Schneider include both cortical and subcortical structures. Mishkin and Ungerleider also place the "where pathway" in a perceptual framework, rather than (like Schneider) identifying it as a system for spatial control of motor orientation. This feature was subsequently revisited by Melvyn Alan Goodale (b. 1943).

In 1992, Goodale and Milner[71] published their influential article "Separate visual pathways for perception and action," in which they propose an alternative interpretation of the role of the dorsal stream described by Mishkin and Ungerleider. Rather than emphasising distinctions in input (the location, rather than the qualities, of the object), they place greater importance on output characteristics, suggesting that the dorsal stream serves to guide interactions with objects:

> We propose that the ventral stream of projections from the striate cortex to the inferotemporal cortex plays the major role in the perceptual identification of objects, while the dorsal stream projecting from the striate cortex to the posterior parietal region mediates the required sensorimotor transformations for visually guided actions directed at such objects.[71(p20)]

They also suggest a terminological change based on their reinterpretation of visual streams, renaming Mishkin and Ungerleider's "where pathway" the "how pathway." Milner and Goodale[72] note that alterations to posterior segments of the ventral stream may entail failure to construct a perceptual whole (causing apperceptive visual agnosias). When anterior segments are affected, impaired recognition is associated with an alteration to the semantic system (causing associative visual agnosias). They argue that spatial processing is associated with both the dorsal and the ventral streams. The dorsal stream is involved in egocentric codification, enabling real-time programming and control of the movements needed to perform an action. The ventral stream, in turn, is responsible for allocentric codification of space, essential to the relative and categorical location of objects.

The dorsal-ventral functional distinction proposed by Milner et al.[73] is based on data from animal models and individual case reports. Regarding the latter, a noteworthy example is the patient DF, who in 1988 developed visual agnosia due to accidental carbon monoxide poisoning. The particular interest of this case lies in the fact that "despite DF's poor performance on shape recognition tasks, she had little difficulty in everyday activity such as opening doors, shaking hands, walking around furniture, and eating meals. It was further observed in informal testing that she could accurately reach out and grasp a pencil orientated at different angles."[73(p418)] In the experiments, she "was able to modify the posture of her hand to match the orientation of a slot towards which she was reaching, yet she was unable to *perceive* the orientation of the slot."[73(p424)] Based exclusively on behavioural data, Goodale and Milner suggest that DF's visual agnosia resulted from an extensive bilateral lesion to the occipitotemporal cortex and that her ability to precisely manipulate objects was explained by the lack of structural alterations to the dorsal stream. In 2003, James et al.[74] corroborated these interpretations in a comprehensive neuroimaging study of the same patient.[Q]

Conclusion

In clinical practice, Lissauer's (1890) stage model is treated as the reference framework par excellence for the classification of visual agnosias. However, though it provides a useful starting point for the initial approach, this conceptualisation does not take into account the variety and specificity of visual disorders observed in clinical practice. In the early 20th century, such authors as Pötzl, Goldstein, and Riddoch studied these disorders, finding that visual perception involves multiple brain processes, whose impairment can cause specific perceptual symptoms. In the second half of the 20th century, cognitive neuropsychology and animal studies contributed new evidence corroborating these hypotheses. Nevertheless, Lissauer's theory continues to have a decisive influence on modern taxonomies of agnosias, such as that proposed by Humphreys and Riddoch (1987). The classification of visual agnosias suggested by these authors perpetuates the apperceptive/associative distinction. Thus, they divide the apperceptive form of mind-blindness into three subtypes: shape agnosia, integrative agnosia, and transformation agnosia. They also suggest that the inability to associate the visual impression to the meaning of the object (associative form of mind-blindness) may originate in the failure to generate or to access a memory image (semantic agnosia and semantic access agnosia, respectively). The anatomical-functional theories of Mishkin and Goodale constitute a departure from the dichotomy proposed by Lissauer, establishing a new model based on the duality of visual processing. These theories recover hypotheses proposed in the first half of the 20th century about the functional specialisation of the visual system, structured around two main axes: the ventral and the dorsal streams. Alterations to the ventral stream result in perceptual deficits (eg, visual agnosia, central achromatopsia, or prosopagnosia), whereas lesions to the dorsal stream cause spatial deficits (eg, akinetopsia or optic ataxia). Despite the attraction of these theories, the assumption that the visual system presents a dichotomic structure represents a simplification of the complex richness of connections in this brain network.[75] Rossetti et al.[76] question the validity of the two visual systems, dedicated to perception and action, respectively. According to these authors, the neuroanatomical structure of the visual network contradicts the existence of two independent visual systems. Following the same line of argument, Milner[77] maintains that the brain does not function through isolated subsystems and that the dorsal and ventral streams are interconnected.

Acknowledgements

We are most grateful to Dr Jane Riddoch, Dr Rosaleen McCarthey, and Dr Elizabeth Warrington for allowing us to use some of the photographs illustrating the study.

Conflicts of interest

The authors have no conflicts of interest to declare.

References

1. Gibson WC. Pioneers in localization of function in the brain. JAMA. 1962;180:944-51.

[Q]DF's lesions did not cause complete destruction of the ventral pathway. She was able to process visual information unrelated to shape, such as colour and texture.

2. Broca P. Perte de la parole; ramollissement chronique et destruction partielle du lobe antérieur gauche du cerveau. Bull Soc Anthr Paris. 1861;2:235-8.
3. Fritsch G, Hitzig E. Über die elektrische Erregbarkeit des Grosshirns. Arch für Anat Physiol und Wissenschaftliche Med. 1870;36:300 32.
4. Ferrier D. The functions of the brain. London: Smith Elder & Co; 1876.
5. Brown S, Schäfer EA. An investigation into the functions of the occipital and temporal lobes of the monkey's brain. Philos Trans R Soc Lond B. 1888;179:303-27.
6. Gowers WR. Lectures on the diagnosis of diseases of the brain. London: J. & A. Churchill; 1887.
7. Mills CK. The psychology of the visual act and the focal diseases of the visual cortex. In: Posey WC, Spiller WG, eds. The eye and the nervous system. Philadelphia (PA): Lippincott; 1906. p. 57-151.
8. Wilbrand H. Ophthalmiatrische Beitrdge zur Diagnostik der Gehim-Krankheiten. Wiesbaden (DE): J. F. Bergmann; 1884.
9. Marie P, Chatelin CH. Les troubles visuels dus aux lésions des voies optiques intracérébrales et de la sphère visuelle corticale dans les blessures du crâne par coup de feu. Rev Neurol (Paris). 1914-1915;28:882-925.
10. Holmes G. Disturbances of vision by cerebral lesions. Br J Ophthalmol. 1918;2:353-84.
11. Munk H. Weitere Mittheilungen zur Physiologie der Grosshirnrinde. Archiv für Anatomie und Physiologie. 1878;2:162-78.
12. Munk H. Ueber die Funktionen der Grosshirnrinde. Berlin: Hirschwald; 1881.
13. Hughlings Jackson J. Case of disease of the brain—left hemiplegia—mental affection. Med Times Gaz. 1872;i:513-4.
14. Wilbrand H. Die Seelenblindheit als Herderscheinung und ihre Beziehungen zur homonymen Hemianopsie, zur Alexie und zur Agraphie. Wiesbaden (DE): Bergmann; 1887.
15. Wilbrand H. Ein Fall von Seelenblindheit und Hemianopsie mit Sectionsbefund. Deutsche Zeitschrift für die Nervenheilkunde. 1892;2:361-87.
16. Lissauer H. Ein Fall von Seelenblindheit nebst einem Beitrag zur Theorie derselben. Arch fur Psychiatr. 1890;21:222 70.
17. Hahn E. Pathologisch-anatomische Untersuchung des Lissauer'schen Falles von Seelenblindheit. Arbeiten aus der Psychiatrischen Klinik in Breslau. 1895;II:105-29.
18. Freud S. Zur Auffassung der Aphasien: eine kritische Studie. Leipzig (DE): Franz Deuticke; 1891.
19. Bonhoeffer K. Casuistische Beiträge zur Aphasielehre. Archiv f Psychiatrie. 1903;37:800-25.
20. von Monakow C. Uber den gegenwärtigen Stand der Frage nach der Lokalisation im Grosshirn. Ergebnisse der Physiologie. 1907;6:334-605.
21. Liepmann H. Über die agnostischen Störungen. Neurologisches Centralblatt. 1908;13:609-17, 664-75.
22. Verrey L. Hemiachromatopsie droite absolue. Archs Ophtalmol (Paris). 1888;8:289-301.
23. Zeki S. A century of cerebral achromatopsia. Brain. 1990;113:1721-77.
24. Gonzalo J. Dinámica cerebral [Internet]. Santiago de Compostela (ES): Red Temática en Tecnologías de Computación Artificial/Natural; 2010 [accessed 1 Apr 2022]. Available from: http://dspace.usc.es/handle/10347/4341
25. Bálint R. Seelenlähmung des "Schauens", optische Ataxie, räumliche Störung der Aufmerksamkeit. Monatsschrift für Psychiatrie und Neurologie. 1909;25:51-81.
26. Wolpert I. Die Simultanagnosie: Störung der Gesamtauffassung. Zeitschrift für die Gesamte Neurologie und Psychiatrie. 1924;93:397-413.
27. Head H. Aphasia and kindred disorders of speech. Cambridge (GB): Cambridge University Press; 1926.
28. Paterson A, Zangwill OL. Disorders of visual space perception associated with lesions of the right cerebral hemisphere. Brain. 1944;67:331-58.
29. Pötzl O, Redlich E. Demonstration eines Falles von bilateraler Affektion beider Occipitallappen. Wiener Klinische Wochenschrift. 1911;24:517-8.
30. Goldstein K, Gelb A. Psychologische Analysen hirnpathologischer Falle auf Grund von Untersuchungen Hirnverletzer. Zeitschrift fur die gesamte Neurologie und Psychiatrie. 1918;41:1-142.
31. Riddoch G. Dissociation of visual perceptions due to occipital injuries, with especial reference to appreciation of movement. Brain. 1917;40:15-57.
32. Zihl J, von Cramon D, Mai N. Selective disturbance of movement vision after bilateral brain damage. Brain. 1983;106:313-30.
33. Best F. Hemianopsie und Seelenblindheit bei Hirnverletzungen. Graefes Archiv für Ophthalmologie. 1917;93:49-150.
34. Wigan AL. The duality of the mind. London: Longman, Brown, Green, and Longmans; 1844.
35. Quaglino A, Boreli GB, della Sala S, Young AW. Quaglino's 1867 case of prosopagnosia. Cortex. 2003;39:533-40.
36. Charcot JM, Bernard D. Un cas de suppression brusque et isolée de la vision mentale des signes et des objets (formes et couleurs). Le Progrès Médical. 1883;11:568-71.

37. Hoff H, Pötzl O. Über eine optisch-agnostische Störung des Physiognomie-Gedächtnisses. Zeitschrift für die gesamte Neurologie und Psychiatrie. 1937;159:367-95.
38. Von Stauffenberg W. Über Seelenblindheit (Opt. Agnosie) nebst Bemerkungen zur Anatomie der Sehstrahlung. Arbeiten aus dem Hirnanatomischen Institut in Zürich. 1914;8:1-212.
39. Robinson PK, Watt AC. Hallucinations of remembered scenes as an epileptic aura. Brain. 1947;70:440-8.
40. Critchley M. Types of visual perseveration: "paliopsia" and "illusory visual spread". Brain. 1951;74:267-99.
41. Mingazzini G. Über Symptome infolge von Verletzungen des Occipitallappens durch Geschosse. Neurologisches Centralblatt. 1908;27:1112-23.
42. Hoff H, Pötzl O. Über cerebral bedingte Polyopie und verwandte Erscheinungen. Jb Psychiat Neurol. 1933;50:35-56.
43. Hoff H, Pötzl O. Zur diagnostischen Bedeutung der Polyopie bei Tumoren des Occipitalhirnes. Zeitschrift Für Die Gesamte Neurologie und Psychiatrie. 1935;152:433-50.
44. Bender MB. Polyopia and monocular diplopia of cerebral origin. Arch Neurol Psychol. 1945;54:323-38.
45. Holmes G. A contribution to the cortical representation of vision. Brain. 1931;54:470-9.
46. Adler A. Disintegration and restoration of optic recognition in visual agnosia: analysis of a case. Arch NeurPsych. 1944;51:243-59.
47. Adler A. Course and outcome of visual agnosia. J Nerv Ment Dis. 1950;111:41-51.
48. Lhermitte J. Les fondements anatomo-physiologiques de certaines hallucinations visuelles. Stereotactic and Functional Neurosurgery. 1948;9:43-57.
49. Lhermitte J. Les hallucinations. Clinique et physiopathologie. Paris: Doin; 1951.
50. Hecaen H, Badaraco JG. Semiologie des hallucinations visuelles en clinique neurologique. Acta Neurol Latinoam. 1956;2:23-57.
51. Head H. Studies in neurology. London: Frowde; 1920.
52. Bender MB, Teuber HL. Disturbances in visual perception following cerebral lesions. The Journal of Psychology: Interdisciplinary and Applied. 1949;28:223-33.
53. Bay E. Disturbances of visual perception and their examination. Brain. 1953;76:515-50.
54. Bender MB, Feldman M. The so-called "visual agnosias". Brain. 1972;95:173-86.
55. Critchley M. The problem of visual agnosia. J Neurol Sci. 1964;1:274-90.
56. Warrington EK, Taylor AM. The contribution of the right parietal lobe to object recognition. Cortex. 1973;9:152-64.
57. Warrington EK. Neuropsychological studies of object recognition. Philosophical Transactions of the Royal Society of London. Series B, Biological Sciences. 1982;298:15-33.
58. Marr D. Vision. San Francisco: Freeman; 1982.
59. Humphreys GW, Riddoch MJ. Routes to object constancy: implications from neurological impairments of object constancy. Q J Exp Psychol A. 1984;36:385-415.
60. Riddoch MJ, Humphreys GW. Neurological impairments of object constancy: the effects of orientation and size disparities. Cognitive Neuropsychology. 1986;3:207-24.
61. Warrington EK, Taylor AM. Two categorical stages of object recognition. Perception. 1978;7:695-705.
62. Warrington EK, James M. Visual object recognition in patients with right-hemisphere lesions: axes or features? Perception. 1986;15:355-66.
63. Rudge P, Warrington EK. Selective impairment of memory and visual perception in splenial tumours. Brain. 1991;114:349-60.
64. Humphreys GW, Riddoch MJ. To see but not to see: a case study of visual agnosia. Hove (GB): Lawrence Erlbaum Associates Ltd; 1987.
65. Ungerleider LG, Mishkin M. Two cortical visual systems. In: Ingle DJ, Goodale MA, Mansfield RJW, eds. Analysis of visual behavior. Cambridge (MA): MIT Press; 1982. p. 549-86.
66. Trevarthen CB. Two mechanisms of vision in primates. Psychol Forschung. 1968;31:299-337.
67. Schneider GE. Two visual systems. Science. 1969;163:895-902.
68. Newcombe F. Missile wounds of the brain: a study of psychological deficits. Oxford: Oxford University Press; 1969.
69. Mishkin M, Ungerleider LG, Macko KA. Object vision and spatial vision: two cortical pathways. Trends Neurosci. 1983;6:414-7.
70. Maunsell JHR. Physiological evidence for two visual subsystems. In: Vaina LM, ed. Matters of intelligence, conceptual structures in cognitive neuroscience. Dordrecht (NL): Springer; 1987. p. 59-87.
71. Goodale MA, Milner AD. Separate visual pathways for perception and action. Trends Neurosci. 1992;15:20-5.
72. Milner AD, Goodale MA. The visual brain in action. 2nd ed. Oxford: Oxford University Press; 2006.
73. Milner AD, Perrett DI, Johnston RS, Benson RS, Jordan PJ, Heeley TR, et al. Perception and action in 'visual form agnosia'. Brain. 1991;114:405-28.

74. James TW, Culham J, Humphrey GK, Milner AD, Goodale MA. Ventral occipital lesions impair object recognition but not object-directed grasping: an fMRI study. Brain. 2003;126:2463-75.
75. Felleman DJ, Van Essen DC. Distributed hierarchical processing in the primate cerebral cortex. Cereb Cortex. 1991;1:1-47.
76. Rossetti Y, Pisella L, McIntosh RD. Rise and fall of the two visual systems theory. Ann Phys Rehabil Med. 2017;60:130-40.
77. Milner AD. How do the two visual streams interact with each other? Exp Brain Res. 2017;235:1297-308.