The contribution of single case studies to the neuroscience of vision

Running title: Single case studies

Josef Zihl[1] and Charles A. Heywood[2]

[1]Department of Psychology, Ludwig-Maximilian-University, Munich, Germany,

[2]Department of Psychology, Science Laboratories, Durham University, UK

Keywords: visual neuroscience, case studies, neuropsychology of vision

Correspondence:

Josef Zihl, Department of Psychology, Ludwig-Maximilian-University, Leopoldstrasse 15, 80802 München, Germany

Phone: int + 89 2180 3119

e-mail: zihl@psy.lmu.de

Abstract

Visual neuroscience is concerned with the neurobiological foundations of visual perception, i.e. the morphological, physiological and functional organisation of the visual brain and its co-operative partners. One important approach for understanding the functional organisation of the visual brain is the study of visual perception from the pathological perspective. The study of patients with focal injury to the visual brain allows conclusions about the representation of visual perceptual functions in the framework of association and dissociation of functions. Selective disorders have been reported for more "elementary" visual capabilities, for example, colour and movement vision, but also for visuo-cognitive capacities, for example visual agnosia or the visual field of attention. Because these visual disorders occur rather seldom as selective and specific dysfunctions, single cases have always played, and still play, a significant role in gaining insights into the functional organisation of the visual brain.

Neuroanatomical and behavioural evidence in dogs and primates had already suggested that the posterior brain is indispensable for vision, including higher visual capacities, such as visual recognition (for a review, see Polyak, 1957). In 1887, Wilbrand had summarized the available empirical clinical evidence. He argued for functional specialization in the visual brain, albeit within the different cortical layers of the same area, i.e. the light, colour and form "senses" being tied to "relatively separate cell clusters in the centre of optic perception" (p. 73; author's translation). However, notwithstanding evidence from clinical reports of selective disorders in, for example, colour vision (Verrey 1888), the concept of functional specialization in the visual brain was rejected, not only by Henschen and Holmes, but by influential figures such as von Monakow (1914), and later by Holmes (1945) and Teuber et al. (1960; for a comprehensive review and discussion, see Zeki, 1993).

Cases showing a visual loss of, for example, colour (achromatopsia), motion (akinetopsia), depth (astereopsis), or stimulus recognition (visual agnosia) are rare and seldom occur in a selective form. The evidence they provide is necessarily gleaned from

the study of single cases. The scepticism about visual functional localization arose, not only from entrenched views about whether the 'visual receptive centre' is confined to striate cortex, but also from the paucity of cases demonstrating, unequivocally, a selective deficit as a consequence of a more or less strictly localizable injury to the visual brain. Alfred Walter Campbell (1868-1937), the prominent Australian neuroanatomist, neuropathologist and later a clinical neurologist, has succinctly explained the reason for this: "It is almost impossible for nature to restrict a damaging lesion to the cortex, and to the cortex only, in question" (1905, p. 145). Thus, association of visual disorders after acquired brain injury is the rule, and dissociation the exception.

The discovery in the late 1960s and early 1970s of a patchwork of visual cortical areas beyond striate cortex, in New and Old World monkeys, argued persuasively for specialized visual functions. Alongside this, detailed examination of single neurological cases began to extend these findings to the human brain. The complete loss of a visual function following brain damage constitutes strong evidence for functional localization, suggesting a spatial segregation of different functions in different cortical regions. In contrast, the partial degradation of a function might suggest an alternative model whereby different visual functions are represented by, for example, different populations in an assembly of neurons. Evidence for and against these alternative accounts of visual brain organization may be derived from association and dissociation of visual functions. This approach was taken by Pöppel et al. (1978) in a comprehensive single case study. Their patient had suffered bilateral occipital infarction and, as a consequence, showed severe bilateral visual field restriction. Within the spared visual field, which also included the macular region, the patient showed a selective impairment

of colour vision and loss of stereopsis and face recognition, while object, letter and (short) word recognition were at least partly preserved, although very slowed. The authors interpreted their results in the framework of, first, a segregation of different visual functions (Zeki, 1974a) and, second, by representation of different visual functions within the same neuronal network. The former would explain the selective visual impairment, the latter would explain the "unspecific" loss of visual capacities, resulting from the effect of "mass action" (Lashley, 1931) causing a marked slowing of visual processing and responding. The case study by Pöppel et al. (1978) not only exemplifies a successful methodological approach to the question of dissociation and association of visual function, but also demonstrates the difficulty of interpreting a pattern of association and dissociation of visual functions within a single model of functional organization.

In this mini-review, we present a number of single case studies, regarded as classic cases, because they have provided essential insights into the functional organization of the visual brain and added significant knowledge to the neuroscience of visual perception. We will focus on two visual-perceptual disorders (achromatopsia and akinetopsia), and two visual-cognitive disorders (visual agnosia and bilateral loss of the field of attention).

The case of cerebral achromatopsia

A salient attribute of our visual experience is colour, and the search for its neural basis has played a pivotal role in gaining insights into the functional organization of the visual brain. While Henschen, Von Monakow and others were charting the extent of the 'visuo-sensory cortex', a Swiss ophthalmologist reported a striking case. Verrey (1888) described a 60-year-old woman, Madame R, who, following a stroke, was unable to see

colours in her right hemifield, a condition we now know as hemiachromatopsia. Post-mortem examination revealed lesions in the fusiform and lingual gyri, beyond the 'cortical retina' of Henschen. The, for some, unpalatable suggestion that a separate cortical region subserved colour was at odds with the unity of visual experience and countered the claim that the visual receptive area received all 'visual impressions', including colour, form and motion. It provoked a fierce debate (reviewed by Zeki, 1990) which was finally resolved when advances in physiology, neuroanatomy and neuroimaging revealed multiple visual areas in extrastriate cortex of monkey and man. The proposal that one of them, cortical area V4 in the monkey, contains a relatively high proportion of cells that code colour (Zeki, 1973) lent credence to the notion of a 'colour centre' beyond striate cortex. Shortly thereafter, an influential review appeared (Meadows 1974) describing fourteen cases of cerebral achromatopsia with damage to the medial occipito-temporal cortex. In agreement with Verrey (1888), in each case of cortical colour blindness the lesion included the lingual or fusiform gyrus or both. The advent of neuroimaging confirmed a region of activation in the same vicinity when observers passively viewed chromatic, compared with achromatic, displays (Zeki et al., 1991).

The appearance of Meadows' review coincided with the publication (Newcombe and Ratcliff 1975) of a case of associative visual agnosia. The patient MS, in addition to difficulties in object recognition, was deficient in naming, matching or sorting coloured tokens and it is this subsidiary finding that was to become of central interest as a case of complete achromatopsia. MS, a 22 year old police cadet suffered idiopathic herpes encephalitis resulting in bilateral brain damage, described in detail elsewhere (Heywood et al., 1991). Damage in the right hemisphere was more extensive than the left. The

calcarine cortex was present in the left hemisphere but the mesial and lateral aspects of the occipital lobe of the right hemisphere were destroyed, accounting for a left hemianopia with macular sparing. In the left temporal lobe the damage included the temporal pole, the fourth temporal and hippocampal gyri and the area of the mesial occipitotemporal junction. The ventromedial location of the brain damage was consistent with other cases of achromatopsia. However, MS remains a particularly informative patient because of the severity of his colour impairment.

The Farnsworth-Munsell 100-Hue test, an effective means of testing perceptualcolour deficiency, requires patients to place a number of equiluminant coloured chips in chromatic order between two endpoints. The higher the number of misplacements, the larger the total errors score. In an extensive review of published cases, Bouvier and Engel (2006) reported a mean score of 582 achieved by 46 cases of achromatopsia. MS' score of 1245, no better than that which results from random ordering, exceeds that of any published case. The incomplete nature of the colour disorder in the majority of other cases makes it difficult to reveal the contribution of spectral processes beyond assigning colour to surfaces. For example, MS is quite unable to select the odd-one-out of three patches, i.e. two reds and an equiluminant green, even at the extremes of the colour gamut of a visual display. Yet a patch embedded in a background of an otherwise discriminable colour (e.g. red on green) can be readily discerned. That is, MS is able to see borders between two, for him, phenomenally indistinguishable colours. This surprising ability to detect chromatic contrast between two apparently perceptually identical surfaces would, of course, be impossible to demonstrate in observers where, albeit impoverished, colour differences between surfaces persist, as in casesof incomplete achromatopsia.

It may be tempting to relate the preserved ability to segment the visual scene on the basis of unseen colour differences to the well-known role of the colour-opponent P- and K- channels and the broad-band M-channel of primate vision. The division of labour between the colour-opponent channels and broadband channel is such that the former have been assigned a role in colour and fine detail vision whereas the latter, responding well to low contrast and to rapid spatial and temporal fluctuations, has been assigned a role in motion (and low-contrast) vision (Shapley & Hawken, 2011; Lee, 2015). Perhaps, then, MS has lost the colour opponent pathways and is reliant on a surviving M-channel. It is known that cells in the broadband channel can signal chromatic contour without coding information about the colours of which the contours are composed (Saito et al., 1989). This property may mediate MS' preserved ability to detect equiluminant contour. However, there is persuasive evidence that this is not the case and that MS retains colour opponent channels. He continues to detect chromatic borders even when confronted with a chromatic visual display into which rapid and spurious spatial and temporal luminance fluctuations are introduced. The robust response by the M-channel to such rapid luminance variation renders it unable to signal wavelength variation and provides strong evidence for the integrity of colour-opponent pathways in patient MS (Heywood et al, 1994). This has been confirmed by measurements of spectral sensitivity (Heywood et al, 1991). M.S. does not show the single peak of sensitivity to wavelengths of ~550nm, characteristic of the sensitivity of the broad-band M-channel. Instead, his sensitivity peaks at three different wavelengths, indicative of colour-opponent mechanisms of the P-channel (Sperling & Harwerth, 1971). Moreover, a consequence of colour-opponency, as seen in the profile of spectral

sensitivity, is that a patch of light created by a mixture of red and green light appears yellow but also appears conspicuously dimmer than would be expected on the basis of simple brightness additivity (Guth, 1965). While unable to discern the colours, MS experiences a similar reduction in perceived brightness of the colour mixture.

While the contribution of chromatic signals to motion processes is uncertain, neuroimaging suggests that cortical area MT, a region specialized for visual motion, is activated by chromatic motion (Ffytche, Skidmore, & Zeki, 1995). Cells in area MT of the macaque monkey respond to equiluminant gratings where, from moment to moment, the phase of the grating is stepped by 90o (Dobkins & Albright, 1994). Each step results in the replacement of one border (e.g. red/green) with another of opposite sign (e.g. green/red). The direction of motion should thus be ambiguous to a cell or an observer blind to the sign of the colour. Nevertheless, M.S. effortlessly reported the 'correct' direction of apparent movement, but was quite unable to discriminate the constituent colours of the grating (Heywood et al., 1994). While the capacity to use wavelength variation to signal colour is abolished, spectral differences continue to signal not only visual form but direction of visual motion.

In summary, the loss of colour vision in achromatopsia can leave other wavelength-based, spectral processes intact. These surviving abilities to detect form or motion direction from wavelength variation are not mediated by what remains of a damaged 'colour centre' - a possibility in cases of incomplete achromatopsia - but by independent spectral processes which use wavelength differences to derive other visual attributes. While each of these remaining processes has a consciouscorrelate, i.e. the contours are visible to MS and he experiences visual motion, it is far from certain how the visual world appears to such an achromatopsic observer.

Cases of achromatopsia are frequently reported where patients are said to complain that their visual world is drained of colour or consists of 'dirty' shades of grey. However, MS shows a noticeable reluctance to provide a description of his phenomenal experience. When asked about the properties of surfaces with which he is confronted, he will never spontaneously use colour terms, including achromatic terms such as ‘black’, ‘white’ or ‘grey’. Moreover, he is evidently mystified when asked to describe the colour or property of a single surface, but more willing to compare two surfaces and assign comparative terms such as ‘brighter’ or ‘darker’. Perhaps, a commentary on the appearance of surfaces is only possible in cases with incomplete achromatopsia. Perhaps, in cases of complete achromatopsia it is impossible to provide a commentary on the absence of a perceptual property of a surface when the cortex that normally is responsible for providing the percept is missing. In the same manner, it is not uncommon for a substantial field loss, as a consequence of damage to striate cortex, to go unreported. In support of this, von Arx et al. (2010) have reported a longitudinal study of a patient with cerebral achromatopsia from stroke, who was initially entirely unaware of his deficit. In the course of recovery, the patient’s subjective complaints about his condition paradoxically increased as colour vision returned. Awareness of the deficit, and hence the capacity to describe the appearance ofsurfaces, was presumably coupled with the recovery of the cortical machinery responsible for colour perception. The authors suggest that a common neural substrate underlies both visual processing and conscious perception.

In accordance with this, the loss of the perceptual experience of hue has been interpreted by some as a failure of colour constancy, namely those mechanisms essential for the 'synthesis' or 'construction' of colour (Zeki, 1990a; Bartels & Zeki, 2000). Surfaces are composed of different materials that reflect light of different wavelengths with different efficiencies. It is the proportion of light of different wavelengths that reaches the eye that signals the properties of that material. However, there can be considerable variation in the light illuminating the world, for example over the course of the day, or as a result of shadows. The wavelength composition of the reflected light from a surface therefore depends on the spectral power distribution of the illuminant and the spectral reflectance function of a surface. If the perceived colour were simply determined by the wavelength composition of light reflected from a surface, then, as the nature of the illuminant changes, we would live in a world of shifting colours. Our perception of an object as having an invariant colour despite changes in its illuminant requires that we successfully 'discount the illuminant' (Helmholtz, 1911). This is called colour constancy and the visual system appears adapted to achieving it (albeit not perfectly). Many cues may be used heuristically to estimate illumination within a scene, for example in the manner described by the Retinex colour-constancy algorithm developed by Edwin Land (Land & McCann, 1971).

If achromatopsia is a failure of constancy mechanisms, then it certainly should not be assumed that the visual experience of an achromatopsic observer is of a world stripped of colour, in the same manner that a normal observer may experience a monochrome display. Indeed, the cortical mechanisms required to assign a colour to a surface on the basis of its reflectance properties are no different for the assignation of greys than for any other hue. While a failure of colour constancy remains a plausible

explanation of achromatopsia, there are reports of defective colour constancy without any accompanying impairment in colour matching (Clarke et al., 1998) or hue discrimination (Rüttiger et al., 1999). Such dissociations are not consistent with the view that deficient hue discrimination is a consequence of a failure of colour constancy. Moreover, a recent report (Norman et al., 2015) suggests that, in normal observers, colour constancy mechanisms operate in the absence of awareness and are not, by themselves, sufficient to give rise to phenomenal colour experience.

The study of a case of complete cerebral achromatopsia has uncovered some surprising dissociations in the visual processing of wavelength variation. Apart from deriving the colours that make up our visual experience, such processes contribute to signalling other perceptual attributes such as form and motion. The loss of phenomenal colour experience has also repeatedly been shown to be quite distinct from other disorders of colour such as disorders of colour naming (Oxbury et al., 1969), colour agnosia (Beauvois & Saillant, 1985), and deficits of colour imagery and memory (Kinsbourne & Warrington, 1967; Luzzatti & Davidoff, 1994). Cerebral achromatopsia, and its partner, cerebral akinetopsia, to which we now turn, serve as striking examples of selective visual disorders.

The case of cerebral akinetopsia

The functions of motion vision are ubiquitous; apart from conveying information about the trajectories of objects in the world, motion vision can aid, for example, postural and locomotor control, image segmentation, and the perception of depth and distance.

In classical psychophysics, visual movement perception was long understood in physical terms, i.e. as a derivate of a calculation based on the distance a stimulus has

passed in a given time period, which allows the judgment of speed, and the consideration of successive stimulus positions, which allows the judgment of direction of movement. In 1931, Brown evaluated the state of scientific knowledge on movement vision and concluded that there is a "lack of correlation between the velocity of the stimulating movement and the phenomenal velocity. … Velocity is perceived directly" (p. 199; 231). Many years later, Gibson (1954) came to the same conclusion. "Visual motion is a 'sensory' variable of experience. It has a kind of intensity (speed) and a kind of quality (direction). … But more than any sensory impression, it fails to correspond to the physical stimulus presumed for it. … It cannot be assumed, that a movement is the same thing in the object, the retina, the brain, and consciousness" (pp. 310-311).

While visual motion perception has long been studied with the tools of psychophysics, by the 1960s this was supplemented with a wealth of physiological findings. For example, Carlson (1962) and Sekuler and Ganz (1963) used selective adaptation, a psychophysical technique assessing the effects of the repeated presentation of one stimulus on a subsequently presented stimulus, to dissociate perception of the direction and speed of moving visual stimuli, and found evidence for a dissociation. Such findings were interpreted in the context of current knowledge of primate visual cortical neurophysiology. The discovery of striate cortical cells that explicitly represent the direction of motion of a moving retinal image was followed by a report (Zeki, 1974b) of an apparent specialisation for visual motion analysis in an extrastriate cortical area in the posterior bank of the temporal sulcus in the rhesus monkey (area V5). It became clear that a neurological case with selective loss of movement vision after brain injury would provide a persuasive argument for movement vision as a discrete and localizable visual capability.

In 1911, Pötzl and Redlich had published a report on a patient who presented with a difficulty in seeing visual stimuli in motion, while colour and form vision were intact. Unfortunately, this patient suffered a severe concentric visual field restriction. Therefore, the difficulty with movement vision was probably selective, but not specific, because the severe visual field restriction may have impaired the patient's ability to visually grasp the moving stimulus. Riddoch (1917) published several cases who showed preserved vision of moving stimuli in homonymous field regions, in which patients were unable to see form or colour. This observation has often been used as a complementary argument for the existence of a brain mechanisms particularly engaged in the analysis of visual movement. However, because a moving visual stimulus has a higher salience, it can be more readily detected even in amblyopic regions of the visual field. It was not until 1983, that the first report on a patient, LM, with selective and specific loss of movement vision appeared (Zihl et al., 1991). The term cerebral akinetopsia was coined by Zeki (1991) to describe this condition.

LM was a 43-year-old woman who, following bilateral posterior brain injury, had nearly completely lost the ability to see visual stimuli in motion. She was articulate in her description of her difficulties, for example, that everything appeared "restless", walking people and dogs "jumped forth and back", without a clear direction, cars "appeared and disappeared, with nothing in between", fluids (milk, water, coffee, tea) appeared like "frozen liquids". A very detailed analysis revealed cognitive slowing as an unspecific symptom (which is a common functional consequence of brain injury; Bashore & Ridderinkhof, 2002), but normal visual fields, visual acuity, contrast sensitivity, colour and form vision, stereopsis, object and face perception and recognition, and reading. Spatial and temporal resolution, as well as visual localization,

were not impaired. LM could discriminate between moving and non-moving stimuli, and could indicate the direction of movement, provided single stimuli were used, and speed did not exceed ~ 6 deg/s. Her cognitive abilities (attention, memory, executive function) were not impaired. Thus, LM showed a selective visual disorder, because all other visual functions and capabilities were intact. Furthermore, her visual disorder was also specific, because other visual or non-visual deficits could not explain it. As expected, visual movement blindness secondarily impairedvisually guided eye- and hand-movements when the stimulus was moving (e.g., pursuit eye-movements or catching a moving object). Interestingly, her akinetopsia also affected perception of facial expressions and of lip reading, indicating that both capabilities are reliant on perception of visual motion. The observations on LM, together with reports of other authors and of experimental work in primates (for a comprehensive review, see Zihl & Heywood, 2015) strongly support the idea that movement vision is a genuine visual perceptual capability, which has its own representation in extrastriate visual cortex. Thus, LM's case contributed significantly to the understanding of the functional organisation of the visual brain in general, and of the cortical representation of movement vision in particular.

The case of visual agnosia

The quest for the cortical seat of vision and its topographic representation of the retina had preoccupied neurologists and physiologists during the close of the 19thC. The correspondence of injury to the afferent, postchiasmatic visual system and resulting homonymous visual field defects was used as basis for the understanding of the topographic representation of the visual field. In pursuit of this goal the German physiologist Hermann Munk (1881) had produced various cortical lesions in dogs and

distinguished between Rindenblindheit (cortical blindness) and Seelenblindheit (psychic blindness). The complete loss of vision in the former was in contrast to the latter, where dogs were unable to remember the meaning of objects they had encountered, yet retained the visual capacity to navigate and avoid obstacles. Influenced by Munk and others (Ferrier 1876), clinical visual neuroscience turned its attention to so-called higher visual abilities including colour vision, visual space perception and, in particular, identification and recognition of visual stimuli. The first detailed report of the latter which, following Munk, was described as a case of 'psychic blindness', was published by Wilbrand in 1887 (for an English translation, see Solms, Kaplan-Solms, & Brown, 1996). The more recent term 'visual agnosia', meaning 'without knowledge', was coined by Freud in 1891 to describe the condition of visual sensation without recognition. The patient Mrs. G, a 63-year-old female, had suffered a sudden brain injury (presumably bilateral occipital stroke), with transient loss of consciousness and loss of vision. Vision recovered, but was restricted to the central visual field. In addition, the patient was aware of her persisting difficulties with the recognition of familiar people and with her topographical memory. Wilbrand examined Mrs. G in detail four years after her brain injury. She showed an incomplete left-sided homonymous hemianopia and a right-sided lower quadranopia in the right hemifield. Visual acuity, colour, form vision and reading were normal. The most striking visual disorder was a total loss of recognition of familiar objects and faces, including her own face when looking in a mirror; the physiognomy of familiar faces looked indistinct. Furthermore, she could never remember new faces. In contrast, she could "recall to mind the sound of a voice or the dialect of my visitors and could easily recognise them thereafter" (Solms, Kaplan-Solms, & Brown, 1996, p. 95). Interestingly, she was also

able to evoke correct visual impressions of everyday objects from memory when she could touch them. In summary, this case shows that visual recognition of objects and faces was severely impaired despite preserved visual acuity, sufficient (although restricted) visual fields and preserved colour and form vision. Furthermore, visual imagination, either elicited by auditory (voices) or tactile (touching of objects) stimuli, was prompt and correct. Thus, detailed analysis with an emphasis on systematic observation and investigation led Wilbrand to the correct conclusion. Visual agnosia in this patient occurred as a selective visual disorder, which is not explained by impaired elementary visual sensory abilities that are necessary, but not sufficient, prerequisites for visual recognition. Furthermore, the preservation of visual object and face imagery can dissociate from visual recognition, i.e. they are not lost because of visual agnosia, or cause visual agnosia when lost (for a detailed discussion, see Solms, Kaplan-Solms, & Brown, 1996).

Three years after Wilbrand's seminal case, Lissauer (1890) published the first comprehensive account of visual agnosia, including the single case, Mr. L. Lissauer's approach differed in two principal aspects from that of Wilbrand (1887). He was the first to make use of an a priori definition of visual agnosia as a genuine disorder of visual recognition, which cannot be explained by visual-sensory, cognitive, or aphasic deficits. In addition, he deduced his methodological approach and assessment from a theoretical framework, where visual recognition is understood as an integrative process ('synthesis') at the perceptual level. Lissauer differentiated between visual agnosia at the perceptual and the semantic level; the first he named apperceptive agnosia and the second, associative agnosia. In addition, Lissauer did not rely only on the patient's subjective reports concerning his visual difficulties, but used a simple, experimental

approach. In the first experimental condition, he presented various everyday objects, which the patient should recognize visually. In a second condition, his patient had access to tactile (form, material) or acoustic information (sound) of the same object. The main outcome was that his 80-year-old male patient could recognize individual visual object features (e.g., size, form, details), but was unable to grasp objects as a whole. For Lissauer's definition, the sparing of the visual sensory prerequisites ('sensations'), which are essentialfor visual perception (=recognition), was a crucial issue. Mr. L showed a complete right-sided homonymous hemianopia; visual acuity was about 0.6, colour matching was correct, visual localization, line bisection and size and distance perception were normal; stereoscopic vision was moderately reduced. Copying of simple objects was not impaired, which also indicated that basic visual abilities were intact. From these observations, Lissauer concluded that the integration of object parts or features was the chief underlying difficulty, i.e. the visual 'synthesis' of visual sensations, was the main underlying impairment. Interestingly, the patient could correctly name objects based on non-visual information and from verbal description, indicating that the associative (semantic) system was intact. The observation that the patient could select the correct colour or object according to a verbally given name was consistent with this. In contrast to Wilbrand's patient, topographical orientation and recognition of familiar (famous) faces were normal in Lissauer's patient. Lissauer went well beyond Wilbrand's theoretical framework by developing a two stage-model of visual identification, the first entailing visual perception and the second, visual recognition. Moreover, he defined unequivocal exclusion criteria to rule out nonspecific (so-called secondary) disorders of visual recognition. Despite the proposal that visual

recognition is a two-stage process, Lissauer did not expect ‘pure’ forms of apperceptive or associative agnosia. Instead, he emphasized their intimate interplay.

Riddoch and Humphreys (1987) reported a similar case of visual agnosia, patient HJA, who also showed this piecemeal kind of object processing and description, but with intact visual form imagery. Because this type of visual processing was not limited to objects and faces but also occurred in a parallel search condition, indicating that the patient was unable to group visual stimuli, these authors preferred the term ‘integrative agnosia’ to denote the special character of this type of visual agnosia. Failures of ‘synthesis’ or ‘integration’ both denote difficulties in spatial and/or feature-based visual grouping operations to enable the observer to establish a mental gestalt of single stimuli or parts of a more complex visual stimulus. Thus, the very detailed single case study of Riddoch and Humphreys (1987), with much more sophisticated methods of visual analysis, are consistent with both Lissauer’s findings, based on comparatively simple methods of assessment and his concept of visual agnosia (for a detailed report and discussion, see Humphreys, 1999).

It is essential, but not straightforward, to distinguish between cases of genuine agnosia and those where difficulties in visual identification result from impaired ‘lower’ visual capacities such as visual acuity, contrast or form vision. This is best exemplified by the case of Goldstein and Gelb (1918), who reported a 24-year old male patient who suffered a traumatic brain injury caused by shrapnel. Binocular visual fields were restricted to about 30 degrees horizontally in each hemifield; binocular visual acuity was 0.50, but showed marked fluctuations (possibly because of pathological fatigue). Colour vision and depth perception were intact; movement vision was impaired. He could recognise familiar objects and reported details of other complex visual stimuli,

but failed completely to copy figures, although he could draw simple forms from memory. He could not read, but could write. However, by using kinaesthetic information (e.g. by tracing outlines with a finger), he could identify forms, objects and letters. Visual identification of forms and letters improved when the patient used head movements as a compensatory strategy. Interestingly, he could 'see' illusory figures, for example the Müller-Lyer illusion. Goldstein and Gelb (1918) interpreted their observations in the framework of Gestalt Psychology. They assumed that their patient had lost the perception of Gestalten, sparing the perception of colours, size and location, but impairing the integration of object properties leading to a Gestalt. In a comprehensive theoretical paper, Poppelreuter (1923) discussed the details of this study and, based on the outcome of experiments with normal subjects, demonstrated that similar difficulties can be 'simulated' by restricting the field of visual processing and thereby limiting 'simultaneous' (i.e. parallel) processing of multiple visual stimuli arrays. He concluded that the patient of Goldstein and Gelb (1918) did not demonstrate genuine visual agnosia, but a kind of 'pseudoagnosia' as a result of impaired visual functions that serve as crucial prerequisites for visual recognition. This single case study provoked a spirited discussion, lasting some 40 years, without reaching a satisfactory conclusion (see Grüsser and Landis, 2000). There may well be alternative explanations for the pattern of impairments. Some characteristics of the case, for example the frequent use of head movements to overcome a limited overview or the inconsistency of responses to the same or similar visual stimulus configurations, may point toward either a more severe visual field defect or a restriction of the field of attention (so-called Balint syndrome, see below). In addition, visual field examination was performed with light stimuli only; thus, it is not clear whether form and colour vision were preserved in the

spared field regions. It has been known since the work of Wilbrand and Saenger (1892), Poppelreuter (1917/1990) and Riddoch (1917) that visual field regions may show a loss of colour and form vision, while light vision is preserved or only depressed (see also Zihl, 2011). Thus, the patient of Goldstein and Gelb (1918) may have suffered loss of colour and form vision in the perifoveal field regions, while light vision was preserved more peripherally. In addition, the observed pathological fluctuations in visual acuity and visual performance after brain injury, with and without defective accommodation, have been reported by others (Poppelreuter, 1917/1990; Zihl & Schmid, 1989). These secondary factors could explain difficulties with processing complex, larger visual stimuli. The difficulty in attributing impaired identification and recognition to visual agnosia, without due consideration of the possibility that low-level sensory disturbances are a cause, is illustrated by a recent study. Serino et al. (2014) have shown, in a detailed single case study, that a homonymous central scotoma, combined with a severe deficit in line orientation processing, can impair visual recognition to an extent that corresponds well to the neuropsychological entity of visual agnosia.

The single cases reported by Wilbrand (1887) and Lissauer (1890) had shown that agnosia might comprise all or only some visual categories (objects, faces, letters, surroundings). The early idea of the functional specialization of the visual brain considered mainly "lower" visual capabilities, e.g. colour, form and movement vision. Wilbrand and Lissauer went beyond and assumed, based on their single cases, that visual perception and visual recognition can dissociate, but did not address a further fractionation within visual recognition. The first authors to report a case of particularly selective agnosia, and suggest a cerebral specialization for face processing, were Hoff and Pötzl in 1937. In the acute phase, their patient showed a global form of visual

agnosia, i.e. recognition in all categories was affected. However, the patient recovered fully from agnosia for letter (pure alexia), and partly from object agnosia, but showed no recovery for his agnosia for familiar faces, including his own face. It was the German ophthalmologist Bodamer who pursued the idea of faces being a particular visual category. His argument for this was based on research on the presence of face perception in babies (Bühler, 1934) showing its fundamental biological relevance. In 1947, Bodamer reported on two patients with severe persistent failures in recognizing familiar faces, and coined the term 'Prosop-Agnosie' (prosopagnosia) (from Greek 'prosopos' and 'agnosia' = 'agnosia for faces'). Bodamer's patients exhibited various visual impairments, including reduced visual acuity, homonymous uni- or bilateral visual field defects with impaired overview, cerebral dys- or achromatopsia, and impaired visual recognition of objects. However, the most severe visual disorder affected the recognition of familiar faces. Both patients used a feature-by-feature analysis, and appeared to have difficulties with integrating the single features into a whole face, in a manner similar to Lissauer's patient. The caveats of ruling out elementary sensory disturbance as a causal factor also apply to these cases and prosopagnosia was not selective, i.e. not the only visual category affected. Nevertheless, it remains to Bodamer's credit that he stressed that visual face perception is a special visual capability. De Renzi (1986) reported several single cases with rather 'pure' prosopagnosia, but in no case did prosopagnosia appear highly selective, probably because the brain injuries encroached on cortex beyond those subserving the brain mechanism in question. It is now apparent that visual face perception has its own representation in the visual brain, which has been shown in numerous brain mapping studies (e.g., Parvizi et al., 2012).

As counterparts to Lissauer's distinction, prosopagnosia can also occur in an apperceptive and associative (amnesic) form (De Renzi et al., 1991). A further dissociation, particular to the role that faces play in social communication, was evident in Bodamer's cases who complained of being unable to understand facial expressions. Such cases of dissociation of face identification and recognition of facial expressions have repeatedly arisen (Calder & Young, 2005), indicating that independent processing mechanisms underlie the two visual capacities. It is important to note, however, that patients with prosopagnosia have no difficulties in saying that a face is a face, and to discriminate faces, indicating that this level of processing is intact.

Bodamer's theoretical, developmental perspective on the particular nature of visual face recognition is also supported by reports of single cases with developmental, congenital prosopagnosia. The condition is characterized by a child's inability to learn to recognise faces, while recognition performance for other visual categories is less affected, although not normal (e.g., Ariel & Sadeh, 1996; Barton et al., 2003). Identification of facial expressions is more often preserved in developmental compared with acquired prosopagnosia (Humphreys et al., 2007).

The case of visual impairment because of loss of spatial attention

Severe restriction of the overview is typically observed in patients with bilateral homonymous hemianopia, also called tunnel vision, because the visual field is limited to a few degrees of visual angle, and visual scanning is usually severely impaired (Zihl, 2011). Patients may behave indistinguishably from people suffering complete blindness and may chiefly be reliant on acoustic and tactile information to guide their behaviour. There exists, however, a condition, where patients do not exhibit bilateral loss of the visual field, yet behave as if they have lost their sight. Balint (1909) stressed the

importance of (spatial) attention for the ability to process stimuli appearing within the visual field. His patient, an older male (age not reported) had suffered a bilateral stroke. Visual acuity was normal, but during acuity testing the patient showed a strange phenomenon. He read only the letters on the right end of the line, and was completely unaware that he omitted all the other items. After instruction to look to the left, he searched for other letters and read them correctly, but it took him much effort and time to find the items. He commented that he reads the letter he can see when he is looking at the acuity chart, then moves on to the next line, and reads the new letter, etc. Visual perimetry did not reveal any visual field defect, either for light or for colour and form stimuli. Themain problem was that the patient could only see a visual stimulus when it (a form, figure, picture, or word) appeared in his line of sight. However, even in this condition he seemed to have a rather small field of visual processing, because he could only see a stimulus if it did not exceed a particular size, and if it was presented as a single stimulus. Balint showed his patient pairs of stimuli. Apart from a difficulty in seeing stimuli to the left or right of his line of sight - in which case the patient found it more difficult to detect stimuli on the left side - he could perceive only one stimulus at a time in the spared field of vision. The size of this field was somewhat flexible and depended on the size of the stimulus. If a smaller and a larger stimulus were presented together, for example a small circle in the centre of a larger triangle, the patient reported only the circle. If the circle was removed, the patient reported the triangle. Thus, the patient could somehow adjust his field of attention to the size of the stimulus within given limits. If asked to shift his gaze to the left or right from the fixation position, the patient could do so; he never shifted his gaze spontaneously to get a more complete overview. The patient also had great difficulty with visual localization; for example, he

was unable to light a cigar on the very end, but lighted it always somewhere in the middle. The restriction of his field of attention, the lack of spontaneous visual exploration, and the impaired visual localization understandably represented a severe visual handicap for the patient's activities of daily living. He stayed in the hospital until he died three years later.

Because of the loss of spontaneous (i.e. intentional) gaze shifts, Balint coined the term "psychic paralysis of gaze" ('Seelenlähmung desSchauens') to denote this special condition of restricted gaze, which is not observed in cases with tunnel vision. The main conclusion Balint drew from his observations was that an intact visual field by itself was not sufficient for processing visual stimuli outside the line of sight, but that attention was required too. The field of attention can be adjusted in a variable manner, depending on the region of visual interest for stimulus analysis (global or local analysis) and the intention of the observer. The loss of this flexible adaptation of the size of the field of attention causes a pathological focusing of attention to just a small region of the visual environment (scene) or object (a spotlight); stimuli or stimulus information outside this region are no longer perceived. Because gaze shifts are also restricted to this region, the patient is unable to compensate for the restricted field of attention, as is possible in the case of tunnel vision. A further feature of Balint's patient was a persistent deviation of his gaze to the right, and greater difficulty with shifting his gaze spontaneously to the left (although he could do so after instruction). This could be explained by the larger extent of the right-sided posterior parietal injury. For the anatomical interpretation of the symptoms of his patient, Balint did not only refer to the affected cortical areas in the parietal lobes. He also considered the association fibres that connect the occipital lobe with the temporal and parietal lobes, and explained the

absence of spontaneous oculomotor activities and the impaired visual guidance of hand movements by the interruption of these fibre pathways. Geschwind (1965) outlined the importance of fibre connections for the organization of sensorimotor relationships in more detail in his concept of "disconnection syndromes". Holmes (1918) added further insight to the syndrome described by Balint, in particular concerning eye-movements and visual space perception. Holmes' patients also showed difficulties with shifting their gaze on command, had impaired pursuit eye-movements, and exhibited deficits in visual depth perception. As a tribute to both neuroscientists, the syndrome is called "Balint-Holmes syndrome" in the international literature, because the research of both significantly contributed to the crucial interaction between visual perception and spatial attention and to higher-order mechanisms involved in visually-guided oculomotor and motor behaviour (De Renzi, 1996). Again, it was the methodological approach of analysing in detail affected and spared functions in the framework of association and dissociation of visual-perceptual, visual-cognitive, and oculomotor functions on the bases of single case studies, which enabled Balint and Holmes to solve a complex scientific and clinical riddle.

Comments and Conclusions

As exemplified by the cases reported in this paper, single cases have always played a prominent role in visual neuroscience. Single case analyses have helped to understand the functional organization of the visual brain in humans, which comprises the neuropsychological and neurobiological levels, i.e. visual perception and underlying brain mechanisms (Zeki & Bartels, 1998). The main reason is the fact that some visual disorders are rare and can consequently only be studied in single cases. For example, cerebral achromatopsia has been reported in many cases, albeit total achromatopsia is

rare (for a comprehensive review, see Zeki, 1990), but cerebral akinetopsia was only reported in three cases (there exist, however, many reports of impaired colour vision and movement vision in one hemifield; for a synopsis see Zihl, 2013, and Zihl & Heywood, 2015). Visual agnosia has been reported by Hecaen & Angelergues (1963) in seven (1.7%) out of 415 patients with posterior brain injury, and prosopagnosia in 22 (5.7%) out of 382 patients (Hecaen & Angelergues, 1962). Gloning, Gloning & Hoff reported visual agnosia in three (1.2%), prosopagnosia in one (0.4%), and Balint-Holmes syndrome in seven (2.9%) out of 241 patients. The very rarity of these visual disorders are a challenge not only for clinicians, because they have to detect the diagnostic symptoms, but also for the scientists, because only the detailed examination of visual and non-visual functions and capabilities allows a valid and conclusive analysis in terms of selectivity of the visual disorder in question. In addition, the association of visual symptoms is the rule, and therefore the proof for specificity is crucial, but very demanding and time consuming. Furthermore, the decision on whether a particular visual function/capability is a crucial prerequisite for colour or movement vision or for visual recognition, may be more or less arbitrary, because it depends on the model of visual perception on which the analysis of vision and the interpretation of the observations are based. In particular, the literature on visual agnosia is characterized by the polarization of theoretical frameworks, with authorities who have accepted and defended the existence of visual agnosia as a genuine visual disorder, while other authorities have questioned or even denied its existence (for a detailed discussion see Hecaen & Albert, 1978, and Grüsser & Landis, 1991). However, if one can unequivocally demonstrate that a particular visual capability can be impaired or lost selectively, and if the specificity of the disorder has been proven, then one single case is

sufficient to conclude that the visual capability in question is genuine and has its own representation in the visual brain. Conventional, standardized neuropsychological assessment is usually not sufficient to proof selectivity and specificity of a visual disorder, but experimental procedures are required, which quite often have to be developed for a valid single case analysis. This methodological challenge is, however, a hallmark of (neuro-)psychological science, and should remain so. Admittedly, earlier neuroscientists used simple methods, when compared with the technologies we have available today, but were nevertheless successful, as the enduring nature of their results and concepts is testimony. It should, however, be noted, that unequivocal demonstration of "dissociation of functions" in vision still relies crucially on the assessment of visual perception at the behavioural level. Recordings of brain activities, e.g. with fMRI, represent, of course, an interesting and important correlate, but cannot substitute for neuropsychological assessment of impaired and spared visual capabilities.

References

Ariel, R., & Sadeh, M. (1996). Congenital visual agnosia and prosopagnosia in a child: a case report. Cortex 32, 221-240. doi: 10.1016/S0010-9452(96)80048-7

Balint, R. (1909). Seelenlähmung des "Schauens", optische Ataxie, räumliche Störung der Aufmerksamkeit. [*Psychic paralysis of gaze, optic ataxia, spatial disorder of attention*]. Monatsschrift für Psychiatrie und Neurologie 25, 51-81.

Bartels, A. & Zeki, S. (2000) The architecture of the colour centre in the human visual brain: new results and a review. Eur. J. Neurosci.. **12**: 172-193. doi: 10.1046/j.1460-9568.2000.00905.x

Barton, J.J.S., Cherkasova, M.V., Press, D.Z., Intriligator, J.M., & O'Connor, M. (2003). Developmental prosopagnosia: a study of three cases. Brain and Cognition 51, 12-30. doi: 10.1016/S0278-2626(02)00516-X

Bashore, T.R., & Ridderinkhof, K.R. (2002). Older age, traumatic brain injury, and cognirtive slowing: some convergent and divergent findings. Psychological Bulletin 128, 151-198. doi:10.1037/0033-2909.128.1.151

Beauvois M.-F., & Saillant B. (1985). Optic aphasia for colours and colour agnosia: a distinction between visual and visuo-verbal impairments in the processing of colours. Cognit Neuropsychol 2, 1-48 . doi**:**10.1080/02643298508252860

Bodamer, J. (1947). Die Prosop-Agnosie. [*Prosopagnosia*]. Archiv für Psychiatrie und Nervenkrankheiten 179, 6-54.

Brown, J.F. (1931). The visual perception of velocity. Psychologische Forschung 14, 199-232. doi: 10.1007/BF00403873.

Calder, A.J., & Young, A.W. (2005). Understanding the recognition of facial identity and facial expression. Nature Reviews Neuroscience 6, 641-651. doi: 10.1038/nrn1724.

Campbell, A.W. (1905). Histological studies on the localization of cerebral function. Cambridge: Cambridge University Press.

Carlson, V.R. (1962). Adaptation in the perception of visual velocity. J Exp Psychol 64, 192-197.

Clarke, S., Walsh, V., Schoppig, A., Assal,G. & Cowey, A. (1998) Colour constancy impairments in patients with lesions of the prestriate cortex. Exp. Brain Res. 123: 154-158.

De Renzi, E. (1986). Current issues in prosopagnosia. In H. Ellis, M.Jeeves, F. Newcombe, & A. Young (Eds.), Aspects of face processing (pp. 243-252). Dordrecht (NL): Nijhoff.

De Renzi, E. (1996). Balint-Holmes‘ syndrome. In C. Code, C-W. Wallesch, Y. Joanette, & A. Roch (Eds.) Classic Cases in Neuropsychology (pp. 123-143). Hove (GB): Psychology Press.

De Renzi, E., Faglioni, P., Grossi, D., & Nichelli, P. (1991). Apperceptive and associative forms of prosopagnosia. Cortex 27, 213-221. doi: 10.1016/S0010-9452(13)80125-6

Dobkins, K.R. & Albright, T.D. (1994) What happens if it changes color when it moves? The nature of chromatic input to macaque visual area MT. J Neurosci. 14(8): 4854-70

Ferrier, D. (1876). The functions of the brain. London: Dawsons.

ffytche, D.H., Skidmore, B.D. & Zeki, S. (1995) Motion-from-hue activates area V5 of human visual cortex. Proc R Soc Lond B Biol Sci 260:1359: 353-8

Fishman, R.S. (1997) Gordon Holmes, the cortical retina, and the wounds of war. Documenta Ophthalmologica 93, 9-28. doi: 10.1007/BF02569044

Freud, S. (1891). Zur Auffassung der Aphasien: Eine kritische Studie. [*On the concept of aphasias: a critical study*]. Leipzig & Vienna: Deuticke.

Geschwind, N. (1965). Disconnexion syndromes in animals and man. Brain 88, 237-294; 585-644. doi: 10.1093/brain/88.2.237; 10.1093/brain/88.3.585

Gibson, J.J. (1954). The visual perception of objective motion and subjective movement. Psychological Review 61, 304-314. doi:10.1037/h0061885

Gloning, I., Gloning, K., & Hoff, H. (1968). Neuropsychological symptoms and syndromes in lesions of the occipital lobe and the adjacent areas. Paris: Gauthier-Villars.

Goldstein K., & Gelb, A. (1918). Zur Psychologie des optischen Wahrnehmungs- und Erkennungsvorganges. [*On the psychology of the optic process of perception and identification*]. Zeitschrift für die gesamte Neurologie und Psychiatrie 41, 1-142.

Guth, S.L. (1965) Luminance addition: general considerations and some results at foveal threshold. J. Opt. Soc. Am. **55**: 718-722.

Hecaen, H., & Angelergues, R. (1962). Agnosia for faces (Prosopagnosia). Archives of Neurology 7, 92-100. doi: 10.1001/archneur.1962.04210020014002

Hecaen, H., & Angelergues, R. (1963). La Cécité psychique. Paris: Masson et Cie.

Hecaen, H., & Albert, M.L. (1978). Human Neuropsychology. New York: John Wiley.

Helmholtz H. von (1909–1911) Handbuch der Physiologischen Optik [Treatise on Physiological Optics] (Leopold Voss, Leipzig, Germany); translated Warren RM, Warren RP (1968) Helmholtz on Perception: Its Physiology and Development (Wiley, New York, NY).

Henschen, S.E. (1893). On the visual path and centre. Brain 16, 170– 180. doi: 10.1093/brain/16.1-2.170

Heywood, C.A., Cowey, A., & Newcombe, F. (1991) Chromatic Discrimination in a cortically colour blind observer. Eur. J. Neurosci. 3: 802-12. doi: 10.1111/j.1460-9568.1991.tb01676.x

Heywood C.A., Cowey A., & Newcombe F. (1994) On the role of parvocellular (P) and magnocellular (M) pathways in cerebral achromatopsia. Brain. 117: 245-54. doi: 10.1093/brain/117.2.245

Hoff, H., & Pötzl, O. (1937). Über eine optisch-agnostische Störung des Physiognomie-Gedächtnisses. [On an optic-agnosic disturbance of the memory for physiognomies]. Zeitschrift für die gesamte Neurologie und Psychiatrie 159, 367-395. doi: 10.1007/BF02870681

Holmes, G. (1918) Disturbances of vision by cerebral lesions. Br J Ophthalmol 2, 353-84. doi:10.1136/bjo.2.7.353

Holmes, G (1945). The organization of the visual cortex in man. Proceedings of the Royal Society London B 132, 318-361. doi:10.1098/rspb.1945.0002

Humphreys, G.W. (1999). Integrative agnosia. In G.W. Humphreys (Ed.) Case studies in the Neuropsychology of vision (41-58). Hove (GB): Psychology Press.

Humphreys, G.W., Avidan, G., & Behrmann, M. (2007). A detailed investigation of facial expression processing in congenital prosopagnosia as compared to acquired prosopagnosia. Experimental Brain Research 176, 356-373. doi: 10.1007/s00221-006-0621-5

Grüsser, O.J., & Landis, T. (2000). Visual agnosia and other disturbances of visual perception and cognition (179-217). Boca Raton: CRC Press, Inc.

Kinsbourne, M., & Warrington, E.K. (1964) Observations on colour agnosia. J. Neurol, Neurosurg. and Psychiat. 27, 296-299. doi:10.1136/jnnp.27.4.296.

Land E., & McCann J. (1971) Lightness and Retinex Theory. J. opt. Soc. Am. 61, 1-11. doi:10.1364/JOSA.61.00000

Lashley, K.S. (1931). Mass action in cerebral function. Science 73, 245-254. doi:10.1126/science.73.1888.245

Lee, B. B. (2011). Visual pathways and psychophysical channels in the primate. J. Physiol 589.1, 41–47. doi: 10.1113/jphysiol.2010.192658

Luzzatti, C., & Davidoff, J. (1994) Impaired retrieval of object-colour knowledge with preserved colour naming. Neuropsychologia 32, 933-950.

Meadows, J.C. (1974) Disturbed perception of colours associated with localized cerebral lesions. Brain, 97: 615-632. doi: 10.1093/brain/97.4.615

Munk, H. (1881). Über die Funktionen der Großhirnrinde: Gesammelte Mittheilungen aus den Jahren 1877-80. [*On the functions of the cerebral cortex: Collected communications from the years 1877-80*]. Berlin: Hirschwald.

Newcombe, F., & Ratcliff, G. (1975) Agnosia: a disorder of object recognition. In: Michel F, Schott B, eds. *Les Syndromes de disconnexion calleuse chez l'homme.* Lyon: Colloque International de Lyon : 317-41.

Norman, L.J., Akins, K., Heywood, C.A. & Kentridge, R.W. (2014). Colour constancy for an unseen surface. Current Biology 24(23): 2822-2826. doi: 10.1016/j.cub.2014.10.009

Oxbury, J.M., Oxbury, S.M., & Humphrey, N.K. (1969) Varieties of colour anomia. Brain 92, 847-860.

Parvizi, J., Jacques, C., Foster, B.L., Withoft, N., Rangarajan, V., Weiner, K.S., & Grill-Spector, K. (2012). Electrical Stimulation of Human Fusiform Face-Selective Regions Distorts Face Perception. Journal of Neuroscience 32, 14915-14920. doi: 10.1523/JNEUROSCI.2609-12.2012

Pötzl, O., & Redlich, E. (1911). Demonstration eines Falles von bilateraler Affektion beider Occipitallappen. [Demonstration of a case with bilateral occipital damage]. Wiener Klinische Wochenschrift 24, 517-518.

Pöppel, E., Brinkmann, R., von Cramon, D. & Singer, W. (1978). Association and dissociation of visual functions in a case of bilateral occipital lobe infarction.

Archives of Psychiatry and Neurological Sciences 225, 1-21. doi: 10.1007/BF00367348.

Polyak, S. (1957). The vertebrate visual system. Chicago: University of Chicago Press.

Poppelreuter, W. (1917/1990). Disturbances of lower and higher visual capacities caused by occipital damage. (J. Zihl with L. Weiskrantz Trans.). Oxford: Clarendon Press.

Poppelreuter, W. (1923). Zur Psychopathologie und Pathologie der optischen Wahrnehmung. [*On the psychopathology and pathology of optic perception*]. Zeitschrift für die gesamte Neurologie und Psychiatrie 83, 26-152.

Riddoch, G. (1917). Dissociations of visual perceptions due to occipital injuries, with especial reference to appreciation of movement. Brain 40, 15-57. doi: 10.1093/brain/40.1.15

Riddoch, M.J., & Humphreys, G.W. (1987). A case of integrative agnosia. Brain 110, 1431-1462. doi: 1431-1462. doi:10.1093/brain/110.6.1431.

Rüttiger, L., Braun, D.I., Gegenfurtner, K.R., Petersen, D., Schönle, P. & Sharpe, L.T. (1999) Selective color constancy deficits after circumscribed unilateral brain lesions. J. Neurosci., 19(8): 3094

Saito, H., Tanaka, K., Isono, H., Yasuda, M., & Mikami, A. (1989) Directionally selective response of cells in the middle temporal area (MT) of the macaque monkey to the movement of equiluminous opponent color stimuli. *Exp Brain Res.* **75**: 1-14. doi: 10.1007/BF00248524

Sekuler, R.W., & Ganz, L. (1963). After-effect of seen motion with a stabilized retinal image. Science 139, 419-420.

Serino, A., Cecere, R., Dundon, N., Bertina, C., Sanchez-Castaneda, C., & Ladavas, E. (2014). When apperceptive agnosia is explained by a deficit of primary visual processing. Cortex 52, 12-27. doi: 10.1016/j.cortex.2013.12.011

Shapley, R., & Hawken, M.J. (2011) Color in the Cortex: single- and double-opponent cells. Vision Research 51, 701–717. doi: 10.1016/j.visres.2011.02.012.

Solms, M., Kaplan-Solms, K., & Brown, J.S. (1996). Wilbrand's case of "mind-blindness". In C. Code, C-W. Wallesch, Y. Joanette, & A. Roch (Eds.) Classic Cases in Neuropsychology (pp. 89-110). Hove (GB): Psychology Press.

Sperling, H.G., & Harwerth, R.S. (1971) Red-green cone interactions in the increment-threshold spectral sensitivity of primates. Science. 172, 180-184. doi: 10.1126/science.172.3979.180

Teuber, H.L., Battersby, W., & Bender, M.B. (1960). Visual field defects after penetrating missile wounds of the brain. Cambridge MIT Press.

Verrey, L. (1888) Hémiachromatopsie droite absolue. Conservation partielle de la perception lumineuse et des formes. Ancien kyste hémorrhagique de la partie inférieure du lobe occipital gauche. Archives d'Ophtalmologie 8, 289–300

von Arx, S.W., Müri, R.M., Heinemann, D., Hess, C.W., & Nyffeler, T. (2010) Anosognosia for cerebral achromatopsia--a longitudinal case study. Neuropsychologia 48(4):970-7. doi: 10.3410/f.1797961.1327060

Von Monakow, C. (1914). Die Lokalisation im Gehirn und der Abbau der Funktionen durch kortikale Herde. [The localization in the brain and the reduction of function by cortical injuries]. Wiesbaden: J.F. Bergmann.

Wilbrand, H. (1987). Die Seelenblindheit als Herderscheinung und ihre Beziehungen zur homonymen Hemianopsie. [Mind blindness as focal symptom and its relationships to homonymous hemianopia]. Wiesbaden: J. F. Bergmann.

Wilbrand, H., & Saenger, A. (1892). Über Sehstörungen bei functionellen Nervenleiden. [On visual disorders caused by functional nervous diseases]. Leipzig: F.C.W. Vogel.

Zeki, S.M. (1973) Colour coding in rhesus monkey prestriate cortex. Brain Res. 53:422-427. doi:10.1016/0006-8993(73)90227-8

Zeki, S. M. (1974a). In R. Bellairs & E.G. Gray (Eds.), Essays on the nervous system. A Festschrift for Professor J.Z. Young The mosaic organization of the visual cortex in the monkey (pp. 327-343). Oxford: Clarendon Press.

Zeki, S. (1974b). Functional organization of a visual area in the posterior bank of the superior temporal sulcus of the rhesus monkey. J Physiol (London) 236, 549-573. doi:10.1113/jphysiol.1974.sp010452

Zeki, S. (1990) A century of cerebral achromatopsia. Brain 113: 1721-1777. doi: 10.1093/brain/113.6.1721

Zeki, S. (1991). Cerebral akinetopsia (visual motion blindness). A review. Brain 114, 811-824. doi: 10.1093/brain/114.2.811.

Zeki, S. (1993). A Vision of the Brain. Oxford: Blackwell Scientific Publications.

Zeki S., Watson J.D.G., Lueck C.J., Friston K.J., Kennard C., & Frackowiak R.S.J. (1991) A direct demonstration of functional specialization in human visual cortex. J. Neurosci. 11: 641-9.

Zeki, S. & Bartels, A. (1998). The autonomy of the visual systems and the modularity of conscious vision. Philosophical Transactions of the Royal Society London B 353, 1911-1914. doi: 10.1098/rstb.1998.0343

Zihl, J. (2011). Rehabilitation of visual disorders after brain injury. Hove (GB), New York: Psychology Press.

Zihl, J. (2013). Perceptual Disorders. In K.N. Ochsner & S.M.Kosslyn, Eds. The Oxford Handbook of Cognitive Neuroscience, vol. 1 (pp. 193-211). New York: Oxford University Press.

Zihl, J., & Schmid, C. (1989). Use of visually evoked responses in evaluation of visual blurring in brain-damaged patients. Electroencephalography and clinical Neurophysiology 74, 394-398. doi: 10.1016/0168-5597(89)90007-5

Zihl, J., & C., A. Heywood (2015). The contribution of LM to the neuroscience of movement vision. Frontiers in Integrative Neuroscience 9, 6:1-13. doi: 10.3389/fnint.2015.00006.

Zihl, J., von Cramon, D., Mai, N., & Schmid, C. (1983). Selective disturbance of movement vision after bilateral brain damage. Brain 106, 313-330. doi: 10.1093/brain/106.2.313.