Disorder of higher visual function

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Current Opinion in Neurology 2011, 24:1–5

Purpose of review

Both monkey and human neuroimaging studies show that visual processing beyond the striate cortex involves a highly complex network of regions with modular functions. Lesions within this network lead to specific clinical syndromes. In this review we discuss studies on blindsight, which is the ability of remaining regions to support vision in the absence of striate cortex or visual awareness, recent work on 'ventral stream' syndromes such as object agnosia, alexia, prosopagnosia, and topographagnosia, which follow damage to medial occipitotemporal structures, and simultanagnosia, the classic 'dorsal stream' deficit related to bilateral occipitoparietal lesions.

Recent findings

We highlight work on the anatomic basis of blindsight, the recent description of the new disorder developmental topographic disorientation, and studies contrasting global and local perception in simultanagnosia.

Summary

These studies advance our understanding of the mechanisms of complex visual processing and provide an important neuropsychological complement to our expanding knowledge about vision from functional neuroimaging.

Keywords

alexia, blindsight, object recognition, prosopagnosia, simultanagnosia

Curr Opin Neurol 24:1–5

1350-7540

Introduction

This review discusses the advances made in understanding disorders of vision created by cortical lesions affecting processing after the stage represented by striate cortex. It begins with a discussion of the nature of processing that remains in the absence of striate cortex, then reviews discoveries concerning disorders of object recognition, related to lesions of the ventral occipitotemporal procesing stream, and finishes with a discussion of simultanagnosia, the classic deficit after lesions of the dorsal occipitoparietal stream.

Function in the absence of striate cortex: blindsight

One of the most intriguing questions in vision research over the last few decades is whether and what type of visual ability remains after lesions causing blindness, the loss of awareness of visual stimuli, particularly after striate damage. A comprehensive review of blindsight has been published [1••]. This includes a detailed discussion about the problem of artifacts, which continue to be illustrated by a report that used manipulations of stimulus luminance and functional MRI (fMRI) recordings to conclude that the 'blindsight' in one patient was due to cues from intra-ocular scatter [2]. In addition to the importance of artifact control, debates remain about what it means to be 'unaware' in blindsight, and how we can be certain of unawareness. A wager paradigm has been introduced as a means of assessing the patient's confidence in their response, with the idea that the trials on which patients were hesitant to bet would be more representative of unconscious vision. However, the validity of this reasoning has been questioned [3].

The review also discussed conjectures about the anatomic substrate of blindsight. One prominent theory proposes that blindsight is mediated by retinal projections to the superior colliculus, and from there to extrastriate cortex, possibly via the pulvinar. A monkey study using rabies virus showed labeling in the colliculus after injections of this trans-synaptic tracer into areas V3 and V5, regions involved in motion processing, but not after injections into V2 and V4 [4•]. In humans, diffusion tensor imaging suggested the possibility of a connection between the lateral thalamus and area V5, although this technique cannot determine the direction of information flow [5]. There were more studies capitalizing on the fact that the superior colliculus has limited input from S-cones, but these produced contradictory results regarding whether blindsight could still occur with stimuli invisible to L-cones and M-cones [6,7]. A second theory is that blindsight depends upon projections from the lateral geniculate nucleus to extra-striate cortex. To assess this, one study injected a $GABA_A$ agonist to inactivate the

lateral geniculate nucleus in monkeys with permanent striate lesions [8•]. After the V1 lesion, monkeys were still able to make saccades to high contrast targets within the resulting scotoma and showed fMRI activation in extrastriate cortex, but both of these effects were lost after the geniculate inactivation.

Saccades are among the earliest and most frequently used responses to show residual processing in the blind fields of humans. A study of monkeys with V1 lesions showed that several months were required before saccades to blind stimuli emerged, and that these lacked the usual on-line trajectory corrections that improve accuracy to visible targets [9]. In humans, studies have capitalized on the 'indirect' technique of examining whether stimuli in the blind field alter responses to stimuli in the seeing field. In addition to prior work showing that distractors cause saccadic trajectories to curve away from either blind or seen stimuli [10], a follow-up study examined the 'global effect', in which a nearby distractor causes saccades to land at a position intermediate between the target and the distractor. Such studies were motivated by models that propose that these effects reflect activity in the superior colliculus. However, in hemianopic patients an anomalous global effect was found, with saccades landing on the side opposite to the distractor, raising questions about our understanding of the anatomic basis of the global effect [11].

The ventral occipitotemporal stream

This discussion includes various disorders of object recognition, as follows.

Visual object agnosia

Studies of perceptual processing in object recognition have usually focused upon shape. However, surface properties such as color and texture can also provide important information. Functional imaging studies have suggested an anatomic dissociation, with lateral occipital cortex involved in shape processing and inferior occipital cortex with texture analysis [12]. A study of two patients with general visual agnosia provided corroborative evidence [13•]: one patient with bilateral lateral occipital lesions was impaired at shape but normal at texture discrimination, while another with bilateral posterior collateral sulcus lesions showed the converse.

How do patients with object agnosia scan the world when they cannot recognize the objects in that world? Healthy subjects tend to fixate regions with high 'relevance' related to ongoing tasks, goals or their understanding of the scene: in visual agnosia, scanpaths are directed more at regions with high stimulus 'saliency', areas that attract attention based on properties like contrast, color, and brightness [14].

Key points

- After striate damage there can still be some residual visual processing: evidence from monkeys suggests that this 'blindsight' may be mediated by direct projections to extrastriate cortex from the lateral geniculate nucleus.
- There remains controversy over whether patients with developmental prosopagnosia have cortical abnormalities in the fusiform gyrus or anomalous projections and connectivity of such occipitotemporal face processing areas with other regions.
- Developmental topographic disorientation is a newly described disorder, in which patients have a life-long problem with forming mental maps of their environment.
- Simultanagnosic patients also have a problem with seeing both local and global frames of reference in a scene at the same time: with some stimuli they show 'local capture', seeing only the trees but not the forest, but with other stimuli they can show 'global capture', seeing only the forest but not the trees.

A patient with a rare form of developmental object agnosia was described [15]. Unlike more typical cases, she had no trouble telling different categories of objects apart – for example, distinguishing a cat from a chair – but had trouble with visual memory for different examples of the same category, such as types of horses or cars, a 'within-category recognition deficit'. The notable exception was normal performance with faces. Hence she contrasts with cases of developmental prosopagnosia, who perform better with recognition of other objects, reinforcing conclusions about the modular specificity of face versus object recognition processes.

Prosopagnosia

This is the inability to recognize familiar faces. It was emphasized that the ability to recognize people through other routes such as their names and voices should be proved intact with formal testing [16], particularly in patients with anterior temporal lobe damage, to avoid confusion between associative prosopagnosia and a multimodal person recognition deficit [17].

More innovative studies were done on patient PS to try to confirm that she has a specific problem with a 'holistic' style of face processing [18–20]. However, a study of another patient showed that the processing of individual facial features can also be affected in prosopagnosia [21]. A holistic defect may be specific to faces, as PS showed normal influence of global information in the perception of hierarchical letters [22], confirming a prior report in other patients. Similarly another study showed that, while prosopagnosic patients struggled with the spatial configuration of dot patterns, they still retained evidence of whole object influences in their performance [23].

A range of perceptual tests with a variety of nonface objects were used to make the argument that the processing deficit in patient PS is limited to faces, promoting the view that this patient may have a 'pure prosopagnosia' [24•]. However, given that humans vary in their expertise and interest in other objects, it can be difficult to know what level of recognition a certain prosopagnosic subject should show for other objects like cars and horses. One study tested patients for their knowledge about cars, and used this semantic score to adjust their visual car recognition scores. Prosopagnosic patients scored lower for visual car recognition than predicted [25•], and the results underlined the point that 'normal' recognition scores may actually be abnormal for patients when their premorbid expertise is taken into account.

Developmental prosopagnosia has received much interest, and there were more claims that 2% of the population may have it [26], though it remains unclear if this prevalence figure merely reflects the end of the bell curve for normal variation or if it is truly that of a pathological entity. Potential heterogeneity within this diagnosis was also underscored by a report that some patients referred for face recognition problems had autistic spectrum disorders or broader problems with object recognition [27]. Autistic traits likely cannot be attributed to a primary prosopagnosic deficit, as a questionnaire study of 10 patients with developmental prosopagnosia found only one showing social impairments [28].

Impoverishment of facial representations in memory can be reflected in poor mental imagery for faces. This is seen in acquired prosopagnosia and now has been shown in the developmental variant [29]. While lack of facial memories has been blamed for the absence of covert face recognition in developmental prosopagnosia, two case studies used priming or forced-choice methods to show some residual face recognition in this condition [30,31].

The anatomic basis of developmental prosopagnosia remains an enigma. A volumetric study reported reductions in grey matter in the right middle fusiform and inferior temporal gyri that correlated with behavioral performance in developmental prosopagnosia [32•]. However, prior reports have shown normal activation of the occipitotemporal face-processing network, including the fusiform face area, but suggested reduced structural connectivity of this network with anterior temporal and frontal cortex. In support of this, an fMRI-adaptation study found normal sensitivity to the identity of faces in the occipitotemporal network, but no such sensitivity in anterior paracingulate cortex or the precuneus [33•].

Pure alexia

Patients with left occipital lesions may have alexia with relatively preserved writing ability. While older accounts have proposed a disconnection of visual input from left hemisphere reading mechanisms, alexia could also reflect a selective visual agnosia from damage to left fusiform structures, particularly the visual word form area, or even a type of ventral simultanagnosia, in which patients have trouble processing multiple elements of text. In support of the agnosia account, two reports of alexic patients with left fusiform lesions showed impairments in reading efficiency for even single letters and digits, not just words with multiple letters, and there were also subtle deficits in recognition of other objects, indicating a problem with creating stable sensory representations [34,35•].

Covert or implicit processing of words has long been demonstrated in pure alexia. This has been attributed by some to recognition mechanisms in the right hemisphere, and by others to residual output of a partially damaged reading network. One study asked alexic patients to categorize words they could not read and found that performance was related to the severity of alexia, a result more in keeping with the partially damaged network account [36].

There is little proven in the way of rehabilitation for pure alexia. The 'multiple oral re-reading method' requires patients to read the same passages aloud several times a day, and continues to be used clinically despite debates about its ability to improve reading efficiency beyond the practiced passages. One study with two patients with pure alexia showed that improved reading occurred only for new text that had significant overlap of words or phrases with the training text [37]. This stimulus-specificity indicates a perceptual familiarization rather than improvement in general reading mechanisms, and has significant ramifications for the implementation of this training method.

Topographagnosia

Difficulty with the spatial layout of the environment is usually manifest by getting lost in familiar places. As with all complex tasks, many processes are required for navigation, and different strategies can be used in different circumstances. Several types of topographagnosia have been described, including landmark agnosia, the failure to recognize buildings and scenes; impaired cognitive map formation, the inability to form a mental layout of scenes; and heading disorientation, a failure in discerning the relationship between objects in the environment.

A new congenital disorder, developmental topographic disorientation, was described. Studies of a woman with a life-long impairment in navigating showed impaired cognitive map formation associated with reduced hippocampal and retrosplenial activity on fMRI [38••]. A second case was described shortly afterwards [39•]. A website (www.gettinglost.ca) has been established to

study such patients and a review of the on-line test performance of the first 120 purported cases recruited in this manner was published [40].

The hippocampus is activated during cognitive map formation, and a study showed a link between aging changes in hippocampal fractional anisotropy and performance on cognitive map formation [41]. This has led to interest in assessing topographic orientation in dementia. One study found problems with landmark recognition and route description in early Alzheimer's disease [42], while a small study suggested that impaired topographical memory is present in Alzheimer's disease and mild cognitive impairment, but not in frontotemporal dementia [43].

In a different direction, another group devised a new test of heading orientation, in which patients have to learn the spatial relations of items placed around them and retain this even after their body position has changed. Performance was impaired in three patients who had right retrosplenial damage [44•].

The dorsal occipitoparietal stream: simultanagnosia

Simultanagnosia is the difficulty in detecting or perceiving multiple items in a scene, even though perception of each as single items is preserved. It often forms part of Balint's syndrome, along with optic ataxia and ocular motor apraxia. Simultanagnosia was discussed recently in a review of the anatomy of visual selection [45]. Its lesion analysis of five patients suggested that the key damage involved the medial occipitoparietal junction, cuneus, and inferior intraparietal sulcus, contrasting with prior reviews linking simultanagnosia to dorsal occipital lesions in Brodmann's areas 18 and 19.

The problem with perceiving multiple aspects of a scene is manifest not only with items at multiple spatial locations, but also in perceiving both local and global scene aspects at once. Most frequently simultanagnosic patients see the local elements but not the global whole, a phenomenon called 'local capture', although when the global structure is particularly compelling they can show 'global capture', in which case they fail to see the local elements. Local capture can be manifest in the way these patients scan social scenes [46], but is usually demonstrated with hierarchical letter stimuli, where simultanagnosic patients report the small letters but fail to see that the arrangement of these letters makes up a larger one. The frequency of local capture is related to the size of and spacing between local elements, which together influence the relative balance in salience between local and global levels [47,48,49•]. Although it may not capture all aspects of the local/global problem in simultanagnosia, one study used a gaze-contingent method to create a restricted visual window in healthy subjects, in order to simulate a hypothetical restricted 'attentional window' in simultanagnosia [50•]. This was able to reproduce the size and spacing dependencies seen in local capture.

Failure of simultanagnosic patients to report global structure is curious because, in theory, intact perception of all local elements should allow a subject to piece together the identity of the global shape eventually, using an alternate strategy of 'connecting the pieces of the puzzle'. However, the eye movements of one simultanagnosic patient showed that, on the one hand, she did not need to fixate all key elements of a global shape to report it correctly, while on the other hand, scanning of its key elements did not guarantee a correct report [48]. Furthermore, the simulation study showed that healthy subjects seeing only small portions of the screen at a time also have difficulty in retrieving the global shape [50•]. Thus this alternate strategy is not viable, likely because there are normal limitations in the ability to retain and integrate spatial information about local elements, which are particularly manifest when global perception is impaired in simultanagnosia.

Conclusion

Studies of cerebral visual processing have benefited tremendously from the sophistication of computerized visual stimuli, better structural neuroimaging, and functional neuroimaging, which is being increasingly applied to patients. We have described recent advances in the study of disorders of object recognition, including general visual agnosia, prosopagnosia, alexia, and topographagnosia, as well as simultanagnosia and blindsight.

Acknowledgements

JB has a Canada Research Chair and holds operating grants from the Canadian Institutes of Health Research and the Natural Sciences and Engineering Research Council of Canada.

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