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The visual cortex and visual cognition in Huntington's disease: An overview of current literature

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ABSTRACT

The processing of visual stimuli from retina to higher cortical areas has been extensively studied in the human brain. In Huntington's disease (HD), an inherited neurodegenerative disorder, it is suggested that visual processing deficits are present in addition to more characteristic signs such as motor disturbances, cognitive dysfunction, and behavioral changes. Visual deficits are clinically important because they influence overall cognitive performance and have implications for daily functioning.

The aim of this review is to summarize current literature on clinical visual deficits, visual cognitive impairment, and underlying visual cortical changes in HD patients. A literature search was conducted using the electronic database of PubMed/Medline.

This review shows that changes of the visual system in patients with HD were not the primary focus of currently published studies. Still, early atrophy and alterations of the posterior cerebral cortex was frequently observed, primarily in the associative visual cortical areas such as the lingual and fusiform gyri, and lateral occipital cortex. Changes were even present in the premanifest phase, before clinical onset of motor symptoms, suggesting a primary region for cortical degeneration in HD. Although impairments in visuospatial processing and visual perception were reported in early disease stages, heterogeneous cognitive batteries were used, making a direct comparison between studies difficult. The use of a standardized battery of visual cognitive tasks might therefore provide more detailed information regarding the extent of impairments in specific visual domains. Further research could provide more insight into clinical, functional, and pathophysiological changes of the visual pathway in HD.

1. Introduction

Many regions of the human brain are involved in processing visual stimuli, from the retina to cortical brain areas. The organization and function of the visual cortex has been extensively studied in primates, both in macaques and healthy human adults [1,2]. Visual field mapping using functional Magnetic Resonance Imaging (fMRI) showed that approximately 20–30% of the human brain is directly or indirectly involved in visual processing [3,4]. Incoming visual stimuli are transmitted from the retina through the afferent visual pathway via the optic nerve and optic tract, to the lateral geniculate nucleus in the thalamus [5]. Then, via the optic radiation, signals reach the primary visual cortex in the occipital lobe and eventually the associative (secondary and tertiary) visual cortices for further processing [5].

The primary visual cortex (also known as V1, striate cortex or Brodmann area 17) is located around the edges of the calcarine fissures on the medial and dorsolateral surface of the occipital lobe [3,6]. The visual association areas (also known as the extra-striate cortices) are responsible for the interpretation of the visual input, such as color discrimination, motion perception, depth, and contrast [3]. The secondary visual cortex (V2 or Brodmann area 18) processes basic visual characteristics such as color perception and orientation [2,7]. On the medial occipital lobe surface, V2 is located in the cuneus above V1 and in the medial occipito-temporal gyrus (e.g. lingual gyrus) below V1, whereas on the lateral surface, V2 is located in the occipital gyrus anterior to V1 [2]. From V2 onwards, visual processing proceeds along

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Table 1
Visual cortex and higher visual function.

Visual area	Brodmann area	Cortex	Function
V1	17	Calcarine fissure Occipital pole	Mapping and processing visual stimuli
V2	18	Cuneus Lingual gyrus	Color discrimination
V4	19 (medial)/37 20	Fusiform gyrus Inferior temporal gyrus	*Ventral 'what' pathway:* Object recognition
V3	19	Lateral part of cuneus	*Dorsal 'where' pathway:* Movement and spatial perception
V5	19 (lateral)/7	Superior occipital gyrus Posterior parietal cortex	

two parallel pathways, the ventral (occipito-temporal) pathway, and the dorsal (occipito-parietal) pathway [8]. The ventral stream is also known as the 'what' visual pathway, and is involved in the recognition of objects, faces and shapes and color processing [2,7]. The dorsal stream is known as the 'where' visual pathway and it is suggested that this area is necessary for depth (three-dimensional vision) and movement perception in relation to objects in space in the frontal eye fields [1,2,9,10]. A summary of the visual cortical areas and their function is presented in Table 1 and Fig. 1.

Any alteration in the visual pathway may result in clinical visual deficits and changes in cognitive performance. In Huntington's disease (HD), a hereditary neurodegenerative disorder, cortical degeneration of visual brain regions is suggested to be present in early disease stages, in addition to striatal atrophy [11–13]. HD is autosomal dominantly inherited and caused by a cytosine-adenine-guanine (CAG) repeat mutation of the Huntingtin (HTT) gene on chromosome 4 [14]. The estimated prevalence of the disease is 5–10 per 100.000 in the Caucasian population [15]. The manifest phase of the disease is generally characterized by progressive motor disturbances, cognitive decline, and behavioral changes [15]. However, clinical signs can vary considerably among patients during the course of the disease as well as time of disease onset. Typically, the mean age of disease onset is between 30 and 50 years (range from 2 to 85 years) and the mean disease duration is between 17 to 20 years [15].

Most reported behavioral and psychiatric symptoms in HD include apathy, depression, irritability, and obsessive-compulsive behavior [16]. Visual hallucinations or other psychotic symptoms are rarely seen in HD patients. In a study of 1993 HD gene mutation carriers, mild psychosis was only observed in 2.9% of the study population and only 1.2% scored moderate to severe psychosis, but no visual hallucinations were reported [16].

Early cognitive deficits in HD mainly involve impairments in executive functioning, such as attention and planning difficulties, and cognitive inflexibility, which gradually progresses over time and eventually results in dementia [15,17]. Executive dysfunction can already be present in the premanifest phase, before motor symptoms occur [17,18]. Although deficits in visual acuity or visual dysfunction are not typical clinical features of HD, visuospatial deficits are reported in HD patients. Such visuospatial deficits are of clinical importance because they can influence overall cognitive performance and may have major functional implications, for example the impact on driving a car or using electronic devices such as mobile phones and computers. Also, visual deficits should be taken into account when conceptualizing cognitive assessments for measuring drug efficacy in clinical trials. By providing an overview regarding the brain structure and function of the visual cortex in patients with HD, we propose to provide novel information on disease progression and cortical degeneration. Therefore, the aim of this review is to summarize the current literature regarding visual cognitive impairment and identify the posterior cortical changes

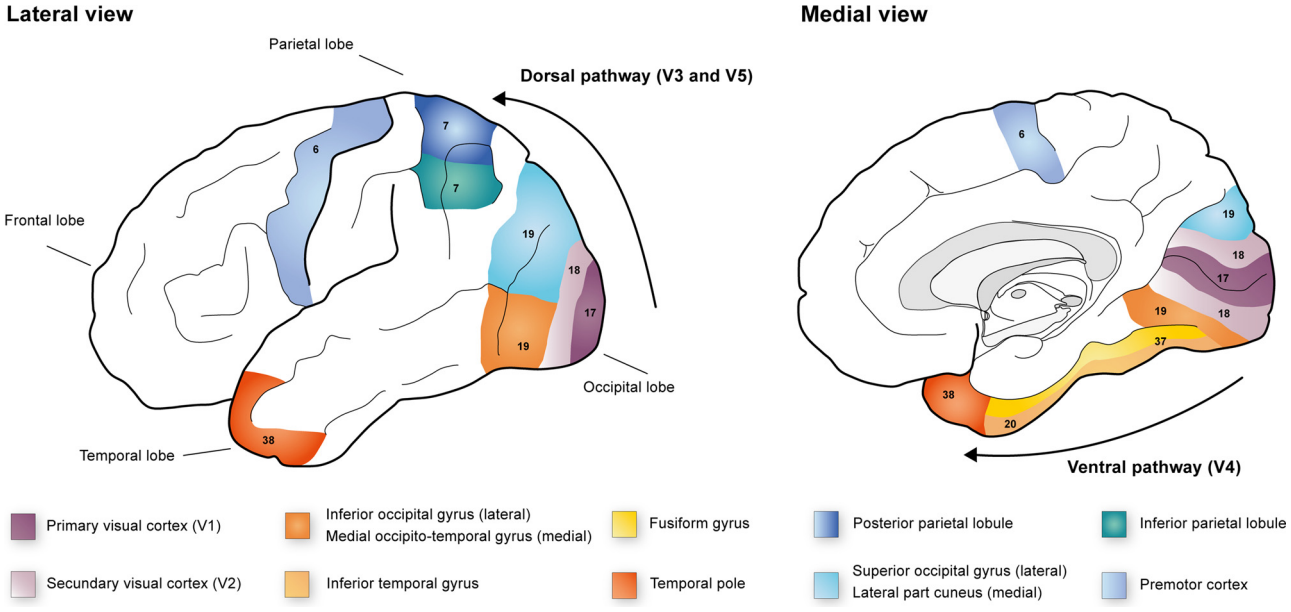

Fig. 1. Visual cortex in human brain.
Schematic lateral and medial overview of cortical regions involved in the processing of visual stimuli in the human brain. Stimuli pass the retina via the optic tract to the primary visual cortex (V1) and secondary visual cortex (V2) for basic processing (i.e. shape and contrast). Although there are no clear demarcations among the regions of the posterior cortex, it is clear that higher-level visual processing occurs in the regions surrounding the primary visual cortex, which are divided into visual areas V3, V4 and V5. The ventral pathway runs through the medial part of Brodmann area 19, located in the anterior medial occipito-temporal gyrus, towards Brodmann area 37 (or V4) which is located in the caudal two-thirds of the lateral occipito-temporal gyrus (e.g. fusiform gyrus). V4 projects to Brodmann area 20, located in the inferior temporal gyrus, to Brodmann area 38, located in the anterior temporal pole, and to the limbic system. The dorsal pathway (V3 and V5) conveys visual information to the posterior parietal cortex (Brodmann area 7) and the premotor cortex (Brodmann area 6).
In general, the ventral pathway in the temporal-occipital region is involved in object recognition and color processing, whereas the dorsal pathway processes depth and movement perception. Numbers in each cortical region depict corresponding Brodmann areas.