Neuropsychologia 79 (2015) 138–146

Contents lists available at ScienceDirect

Neuropsychologia

journal homepage: www.elsevier.com/locate/neuropsychologia

The impact of occipital lobe cortical thickness on cognitive task performance: An investigation in Huntington's Disease

Eileanoir B. Johnson [a], Elin M. Rees [a], Izelle Labuschagne [b,c], Alexandra Durr [d], Blair R. Leavitt [e], Raymund A.C. Roos [f], Ralf Reilmann [g], Hans Johnson [h], Nicola Z. Hobbs [a], Douglas R. Langbehn [i], Julie C. Stout [b], Sarah J. Tabrizi [a], Rachael I. Scahill [a,*], The TRACK-HD investigators

[a] UCL Institute of Neurology, University College London, UK
[b] School of Psychological Sciences, Monash University, Clayton, Victoria, Australia
[c] School of Psychology, Australian Catholic University, Melbourne, Victoria, Australia
[d] Department of Genetics and Cytogenetics, and INSERMUMR S679, APHP, ICM Institute, Hôpital de la Salpêtrière, Paris, France
[e] Centre for Molecular Medicine and Therapeutics, Department of Medical Genetics, University of British Columbia, Vancouver, BC, Canada
[f] Department of Neurology, Leiden University Medical Centre, Leiden, The Netherlands
[g] George-Huntington-Institute, Germany
[h] Department of Psychiatry, University of Iowa, Iowa City, IA, USA
[i] Department of Biostatistics, University of Iowa, Iowa City, IA, USA

ARTICLE INFO

Article history:
Received 5 June 2015
Received in revised form
7 October 2015
Accepted 26 October 2015
Available online 28 October 2015

Keywords:
FreeSurfer
Huntington's Disease
MRI
Occipital lobe
Visual cortex

ABSTRACT

Background: The occipital lobe is an important visual processing region of the brain. Following consistent findings of early neural changes in the occipital lobe in Huntington's Disease (HD), we examined cortical thickness across four occipital regions in premanifest (preHD) and early HD groups compared with controls. Associations between cortical thickness in gene positive individuals and performance on six cognitive tasks, each with a visual component, were examined. In addition, the association between cortical thickness in gene positive participants and one non-visual motor task was also examined for comparison.

Methods: Cortical thickness was determined using FreeSurfer on T1-weighted 3T MR datasets from controls ($N=97$), preHD ($N=109$) and HD ($N=69$) from the TRACK-HD study. Regression models were fitted to assess between-group differences in cortical thickness, and relationships between performance on the cognitive tasks, the motor task and occipital thickness were examined in a subset of gene-positive participants ($N=141$).

Results: Thickness of the occipital cortex in preHD and early HD participants was reduced compared with controls. Regionally-specific associations between reduced cortical thickness and poorer performance were found for five of the six cognitive tasks, with the strongest associations in lateral occipital and lingual regions. No associations were found with the cuneus. The non-visual motor task was not associated with thickness of any region.

Conclusions: The heterogeneous pattern of associations found in the present study suggests that occipital thickness negatively impacts cognition, but only in regions that are linked to relatively advanced visual processing (e.g., lateral occipital, lingual regions), rather than in basic visual processing regions such as the cuneus. Our results show, for the first time, the functional implications of occipital atrophy highlighted in recent studies in HD.

1. Introduction

The occipital cortex is primarily viewed as the visual area of the brain, with topologically-distinct regions believed to manage different aspects of visual processing (Wandell et al., 2007). In Huntington's Disease (HD), a progressive genetic neurodegenerative disease, atrophy in the occipital cortex has been identified as an early and prominent element of neurodegeneration, although this atrophy in the occipital lobe has not been the focus of research to date (Rosas et al., 2002; Tabrizi et al., 2012). The regional specificity of occipital changes in HD is unknown, as are the functional implications of occipital cortex thinning on cognition. As most

* Correspondence to: Huntington's Disease Research Group, UCL Institute of Neurology, Queen Square, London WC1N 3BG, UK.
E-mail address: r.scahill@ucl.ac.uk (R.I. Scahill).

http://dx.doi.org/10.1016/j.neuropsychologia.2015.10.033
0028-3932/

cognitive tasks involve a visual component, for example written responses or symbol identification, impaired visual processing due to occipital cortex pathology could manifest as poorer performance on these tasks. This study used an HD sample to describe the regional pattern of cortical thickness in the occipital cortex, across the spectrum from premanifest (preHD) to early HD, and the associations between occipital atrophy and performance on cognitive tests involving a visual component.

The visual system is a complex integrative system, with a ventral steam thought to process colour and discriminate shapes and objects, and a dorsal stream that processes spatial information, motion and visually-guided grasping and reaching (Hebart and Hesselmann, 2012). It has long been thought that specific regions of the occipital cortex are associated with different visual processing functions that make up these two streams (Hebart and Hesselmann, 2012). Consequently, the location of occipital cortex pathology is likely to affect the manifestation of any visual deficit. Current understanding of the functional topology of the occipital cortex, which is derived from visual field mapping and supported by functional imaging studies (see Cabeza and Nyberg (2000)), divides the occipital cortex into a number of processing areas that extend over the occipital gyri. Briefly, the primary visual area (V1), also called Brodmann Area (BA) 17, is located within the pericalcarine region and maps the signals received from the retina in a topographic manner (Tootell et al., 1998; Wandell et al., 2007). This visual information is also projected to higher-level processing regions (Roe and Ts'o, 1995), known as V2, V3 and V4. Visual area 2 (V2, BA18) is spread across part of the cuneus above V1, and the lingual gyrus below V1. V2 is thought to process basic visual characteristics such as colour and orientation (Roe and Ts'o, 1995; Zeki, 1978). Visual area 3 (V3), believed to play a role in motion perception (Gegenfurtner et al., 1997; Larsson and Heeger, 2006), is also located within the cuneus but extends laterally. The lateral occipital cortex (LOC) can refer to a small sub-region of the lateral side of the occipital cortex, but for the current study it refers to the entire lateral side of the occipital cortex. This region is thought to integrate visual information, especially shape information, along with visual and tactile object recognition (Beauchamp, 2005; Grill-Spector et al., 2001; Larsson and Heeger, 2006). The LOC also plays a role in tasks involving the performance of motor actions and tactile stimulation, especially movements involving the limbs (Amedi, 2002; Astafiev et al., 2004). Within the lingual gyrus is visual area 4 (V4), a colour processing area also thought to identify words and letters (Mechelli et al., 2000; Tootell et al., 2003). To summarise, regions of the occipital cortex, (described here in relation to the pericalcarine, cuneus, lingual and LOC) perform topologically-specific functions in visual processing. It is currently unclear what effect pathology within these regions has on performance levels for cognitive tasks with visual components.

HD has an onset in mid-adulthood and is characterised by progressive motor, cognitive and psychiatric symptoms. There is a long premanifest period (referred to as preHD) during which subtle signs of the emerging disease are detectable (Paulsen et al., 2008; Tabrizi et al., 2009). The neuropathology of HD is primarily focused within the striatum of the basal ganglia, although extra-striatal and cortical regions are also affected (Tabrizi et al., 2012; Vonsattel and DiFiglia, 1998). Brain atrophy has been shown to begin many years before disease onset and progresses from preHD to manifest disease with increasing disease burden (Tabrizi et al., 2011, 2009). Several imaging studies have detected occipital cortex atrophy in both pre- and manifest HD (Rosas et al., 2008; Stoffers et al., 2010; Tabrizi et al., 2011, 2009; Wolf et al., 2014) and there is a marked reduction in number of neurons in the occipital cortex in HD (Lange, 1981; Rüb et al., 2015). In addition, performance deficits on cognitive tasks involving a visual component have been widely reported in both preHD and early HD (Paulsen et al., 2014; Tabrizi et al., 2013) and a small number of studies have identified difficulties with visual processing, although this is not reported as a common feature of the disease. Early HD participants suffer from motion discrimination deficits, but not deficits in static contrast sensitivity, and preHD participants generally show no deficit in these tasks (O'Donnell et al., 2008, 2003). An HD cohort ranging from pre- to manifest disease would therefore be expected to exhibit varying levels of both cognitive impairment and occipital cortical thickness, with some possible deficits in motion processing.

In addition, previous studies have also found significant relationships between cognitive performance and brain volume in HD. Occipital grey matter volume was found to be significantly related to time to complete a visual discrimination task (Gomez-Anson et al., 2009), and emotion recognition (Scahill et al., 2013). Cortical thickness of the occipital region has been associated with performance on the Symbol Digit task and a Stroop Colour Reading task, although these analyses were whole-brain studies with no correction for multiple comparisons (Rosas et al., 2008, 2005). These studies suggest that there is a relationship between occipital lobe thickness and cognitive performance in HD, however a regional analysis allowing for in-depth characterisation of the specific relationship between sub-regions of the occipital lobe and cognitive performance across varying disease stages has not yet been performed. Furthermore, without controlling for other factors likely to contribute to cognitive performance, such as disease progression and education, it is unclear whether the occipital lobe uniquely contributes to cognitive performance.

This study aimed to test unique associations between thickness of the visual cortex and cognitive test performance in HD. Cortical thickness in four occipital regions (pericalcarine, cuneus, lingual and LOC) was compared between healthy controls, preHD and manifest HD participants, and the relationship between occipital cortex thickness and cognitive impairment was examined in the HD gene-carriers. It was hypothesised that the thickness of the cuneus, lingual region and the LOC, which are areas known to be involved in functions such as motion detection, visual memory, integration of visual information and object recognition, would be associated with cognitive test performance. In contrast, as visual field deficits are not known to occur in HD, it was hypothesized that that the pericalcarine (V1) would not show such associations.

2. Materials and methods

2.1. Participants

Participants were recruited across four study sites as part of the TRACK-HD study (Tabrizi et al., 2009), 313 participants from the 2010 time-point were included in the present investigation of the occipital cortex (107 controls, 116 preHD and 90 HD individuals). The preHD cohort was separated into two groups based on the median expected years to disease onset; those estimated to be more than 10.8 years from disease onset (Langbehn et al., 2010) were classified as the preHD-A group and those less than 10.8 years from estimated onset, preHD-B. Using the Unified Huntington's Disease Rating Scale (UHDRS;(Huntington Study Group, 1996)) the HD cohort was classified based on their Total Functional Capacity (TFC) scores as HD1 (TFC=11–13) or HD2 (TFC=7–10); HD2 being the more advanced group. The control group was comprised of partners, spouses and gene-negative siblings of the gene-carriers. Full selection criteria and data collection processes have been published previously (Tabrizi et al., 2009).

Participants were tested for visual function using a Snellen Visual Acuity equivalent, the Low-Contrast SLOAN Letter Charts (Balcer et al., 2000). This provided a score ranging from 1–12, with 1 representing poor visual acuity (20/200 vision) and 12 representing high acuity (20/16 vision). Participants with a score of less than 11, which is equivalent to below the average 20/20 vision, were excluded from the current study. The remaining cohort for group cortical thickness comparisons comprised 275 participants (97 healthy controls, 51 preHD-A, 58 preHD-B, 40 HD1 and 29 HD2 participants). A subgroup of gene-positive participants was then used to relate cognitive performance to occipital lobe thickness. Participants who had manually measured caudate volumes already available and a score on the