Cortical thinning and neuropsychological changes in presymptomatic Huntington’s Disease

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Abstract

Degeneration of the striatum and striatal-frontal circuits are generally thought to cause most of the neuropsychological symptoms experienced in Huntington’s Disease (HD). Advances in cortical thickness mapping (an automated MRI method for precisely measuring the cortical thickness across the entire cortex) provide a new technique for examining changes in the brain in HD. Recent studies using this technology have reported provocative results. They found significant cortical thinning in participants with early HD (Rosas et al., 2002; Rosas et al., 2008) and even in presymptomatic HD (Rosas et al., 2005). Moreover, cortical thinning was most prominent in posterior regions of the brain, with relative preservation of the anterior frontal regions. The present study replicated Rosas et al.’s (2005) study but used a larger sample of presymptomatic HD participants (n = 19) and a control group matched for age, gender and education (n = 19). Presymptomatic HD participants were divided into two groups, PreHDclose and PreHDFar, based on their estimated proximity to clinical onset. The distribution of cortical thinning was assessed using an identical MRI method to previous cortical thinning studies with HD participants. Specific neuropsychological tests were used to assess cognitive and mood changes that may be associated with cortical thinning. It was hypothesised that cortical thinning would be more evident in posterior than frontal cortical regions. It was also hypothesised that presymptomatic HD participants would perform more poorly than controls on tests that are subserved primarily by specific posterior cortical regions, but not on tests that are subserved by anterior cortical regions. Lastly, it was predicted that poorer performance in the neuropsychological measures would be associated with greater thinning in cortical regions that are important during performance of these tasks.

Consistent with predictions, the presymptomatic HD group showed regionally-specific cortical thinning which was most prominent in the posterior cortices, particularly around the right parieto-temporal-occipital (PTO) junction. Thinning occurred in people up to 15 years before clinical onset, with little to no thinning before that. The presymptomatic HD group, and particularly the PreHDclose participants, performed significantly worse than controls in 2 of the 6 cognitive tests that are subserved primarily by posterior cortical regions (the Judgment of Line
Orientation test and modified Roadmap Test), but not in tests that are subserved primarily by frontal cortical regions. Correlational analyses showed a number of regionally-specific relationships between thinning and cognitive performance, although the distribution of these relationships did not generally support our region-of-interest predictions. The results contribute to a better characterisation of the cortical and neuropsychological changes that occur early in the development of HD, and provide tentative support for cortical thickness mapping as a valid and sensitive measure for assessing cortical changes in presymptomatic HD.
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List of Abbreviations

AD            Alzheimer’s Disease
ANOVA         Analysis of Variance
BA            Brodmann Area
CVLT          Californian Verbal Learning Test
DLPFC         Dorsolateral prefrontal cortex
DRS           Dementia Rating Scale
fMRI          Functional Magnetic Resonance Imaging
HADS          Hospital Anxiety and Depression Scale
HD            Huntington’s Disease
HVLT          Hopkins Verbal Learning Test
HVOT          Hooper Visual Organisation Test
ICV           Intracranial volume
IDAS          Irritability-Depression-Anxiety Scale
IGT           Iowa Gambling Test
JLOT          Judgement of Line Orientation Test
MMSE          Mini-Mental State Examination
MRI           Magnetic Resonance Imaging
PET           Positron Emission Tomography
QNE           Quantified Neurological Examination
ROI           Region-of-interest
SDMT          Symbol Digit Modalities Test
SoC           Stockings of Cambridge task
TBI           Traumatic Brain Injury
TFC           Total Functional Capacity Scale
ToL           Tower of London task
UHDRS         Unified Huntington’s Disease Rating Scale
VBM           Voxel-Based Morphometry
VLPFC         Ventrolateral prefrontal cortex
WCST  Wisconsin Card Sorting Test
WMS  Wechsler Memory Scale
YTO  Estimated Years To clinical Onset