# Global and Regional Brain Morphology in Subjects with Huntington's Disease Prior to Diagnosis

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## Introduction:

Huntington's Disease (HD) is an autosomal dominant degenerative brain disorder.

The discovery of the CAG repeat expansion in the huntingtin gene has allowed a unique opportunity to study participants who undergo predictive testing for presence of the expansion.

The length of the CAG repeat expansion is highly correlated with age of diagnosis, making possible the prediction of the approximate time to diagnosis for persons with the expansion but no symptoms (referred to as preHD)

The PREDICT-HD study is an international 32-site study of preHD.

In previous analyses, we have found that total cortical volume in preHD participants is reduced compared to controls.

However, as the cortex is functionally and structurally divided into distinct regions, a global assessment is insufficient to assess the regional morphology of the cortex.

The current study was designed to use cortical thickness mapping to assess detailed regional cortex morphology in preHD participants.

## Methods:

The sample consists of 693 participants: 170 gene-non-expanded and 468 gene-expanded participants.

Gene-expanded participants are divided into three prognostic group:
1) far- from-diagnosis (>15 years)
2) midway-to-diagnosis (9-15 years)
3 )near-to-diagnosis (<9 years)

Table 1 shows demographics

Scans were obtained using a standard multi-mode protocol with an axial 3D volumetric spoiled gradient echo series and a dual echo PDT2 series. All sites used a General Electric 1.5 Tesla scanner (with the exception of two sites using a 1.5 Tesla Siemens scanner).

Cortical thickness maps were generated using the program Freesurfer. Comparisons were made between each prognostic group and controls. Effects of age and gender were accounted for. There were no significant age by group or gender by group interactions.

## Results:

As displayed in the series of figures to the right, the far from diagnosis group showed no significant difference in cortical thickness compared to controls.

Subjects midway to diagnosis showed a pattern of diffuse thinning with posterior and superior regions being somewhat more prominent.

Subjects near diagnosis had diffuse, widespread cortical thinning as well as an area within the anterior cingulate that was significantly thicker compared to controls.

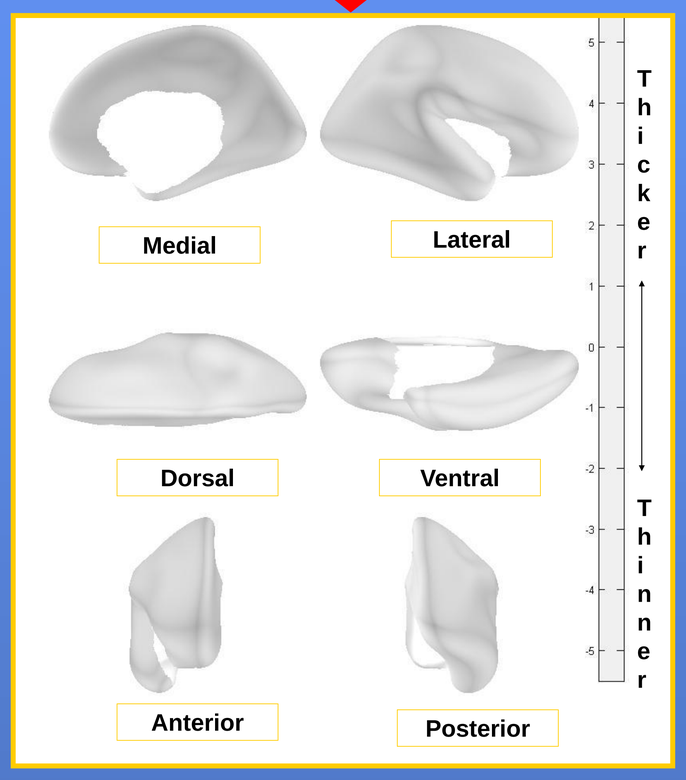
**Table 1: Demographic Information**

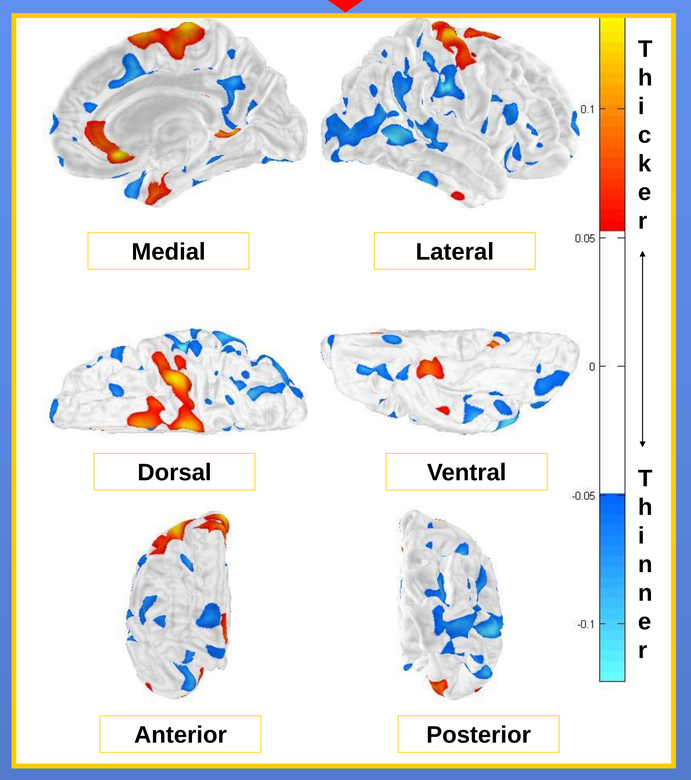
| | Controls | Far from Diagnosis | Midway to Diagnosis | Near Diagnosis |
|---|---|---|---|---|
| N | 170 | 180 | 184 | 127 |
| Gender M/F | 62/108 | 57/113 | 54/109 | 55/80 |
| % Female | 63.5% | 66.5% | 66.9% | 59.3% |
| Age [Mean (SD)] | 44.90 (12.1) | 38.1 (8.4) | 44.1 (10.1) | 47.1 (9.5) |

**Inflated Surface Significance Maps: Regions that are significantly different compared to controls**

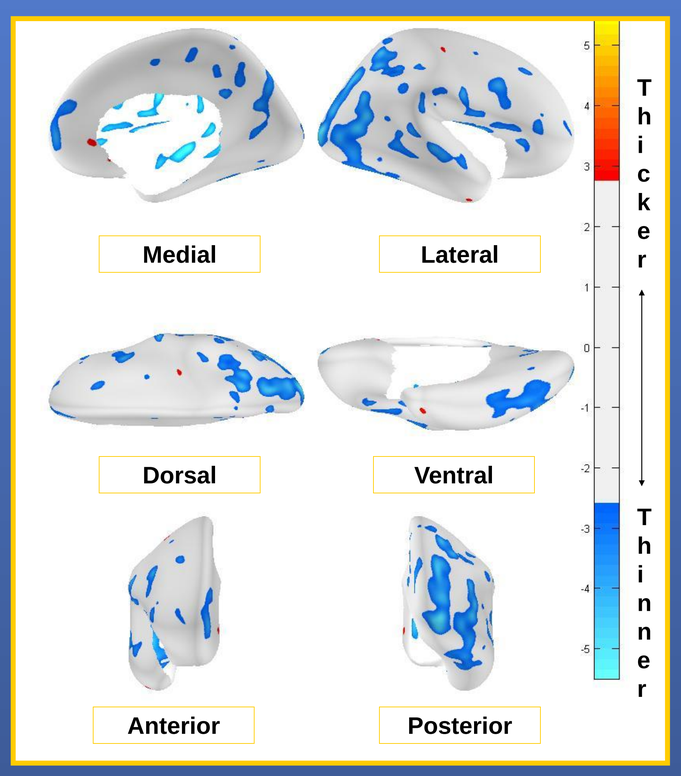
**Pial Surface Thickness Maps: Relative thickness between preHD subjects and controls, not thresholded for significance**

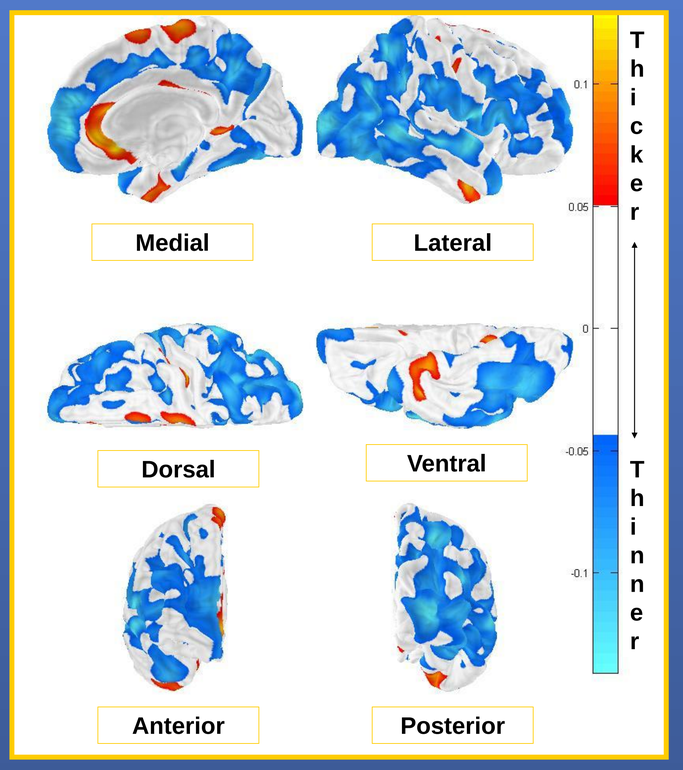
**Far From Diagnosis**



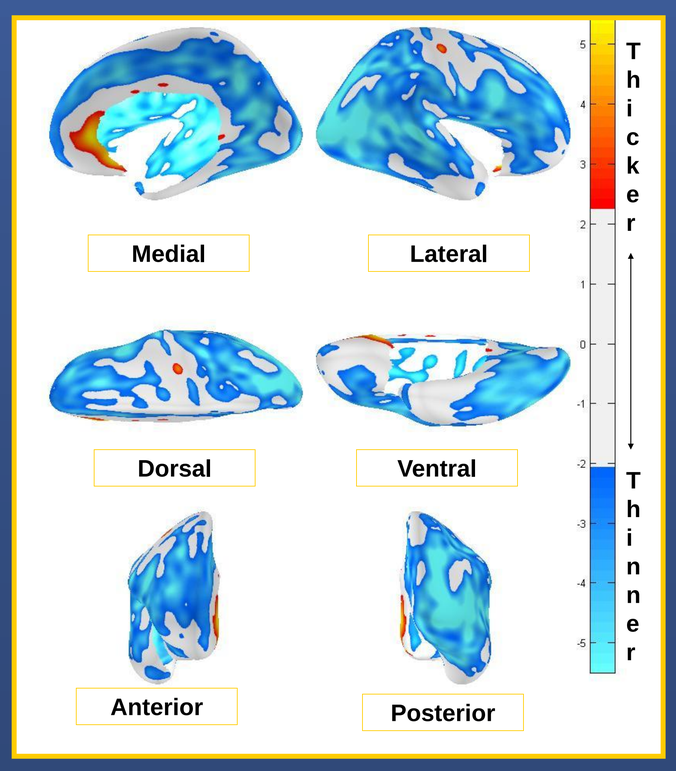



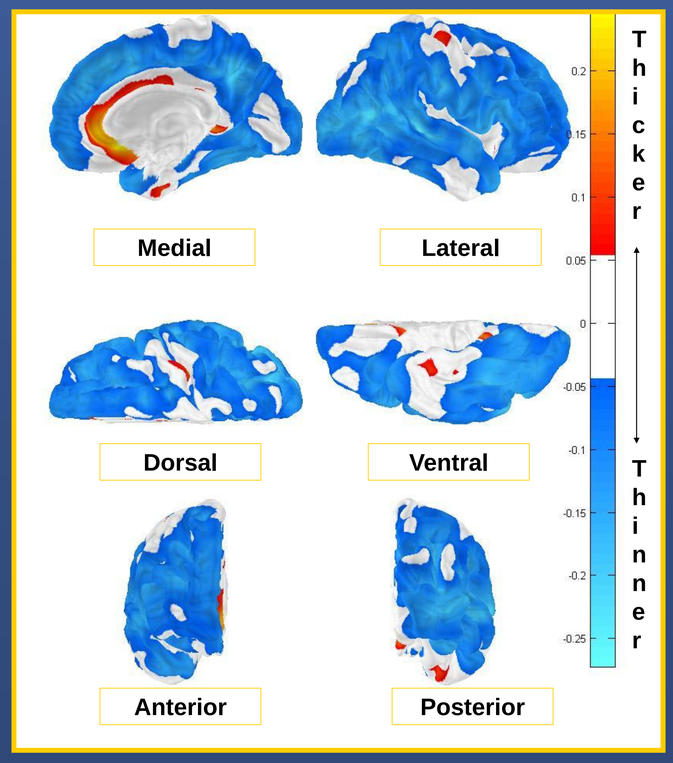

**Midway to Diagnosis**




**Near Diagnosis**




PREDICT-HD