

# SQSTM1 mutations in frontotemporal dementia are associated with asymmetrical focal temporal lobe atrophy

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## Background

FTD is a common cause of young onset dementia and in around a third of cases is genetic. Recently mutations in SQSTM1 have been shown to be a rare cause of familial FTD. Little is known about the clinical or neuroanatomical phenotype at present. In this study, we investigated the pattern of grey matter atrophy in a group of patients with SQSTM1-associated FTD.

## Methods

From the UCL FTD DNA cohort (n=440), we investigated four patients with the SQSTM1 mutation variant: two P392L, one E155K and one E396 frameshift mutation. The clinical diagnoses in the patients were behavioural variant FTD, FTD with motor neurone disease, corticobasal syndrome and primary progressive aphasia. The mean (standard deviation) age at onset was 59.0 (5.9).

All patients had undergone a T1-weighted magnetic resonance imaging scan acquired on a 3T Siemens Trio scanner: age at scan 65.8 (6.4). Their imaging was compared with 24 age- and gender-matched healthy controls (age: 66.5 (5.2)). We undertook a voxel-based morphometry (VBM) analysis comparing the SQSTM1 mutations carriers and the controls, correcting for age, gender and total intracranial volume. Statistical parametric maps were thresholded at  $p < 0.05$  after family-wise error correction and rendered on a study-specific average group T1-weighted MRI template image in MNI space.

Groups	n	Gender (male)	Age
SQSTM1	4	50 %	65.8 (6.4)
Controls	24	50 %	66.6 (5.2)

Table 1. Demographic and clinical variables for SQSTM1 patients and controls.

## Results

Grey matter atrophy was asymmetrical with three patients having right-sided dominant atrophy and one left-sided. For the analysis we flipped the scan in the midsagittal plane of the patient with left-sided atrophy so that the hemisphere in which there was predominant atrophy was the same in all four cases.

The VBM analysis showed evidence of focal involvement of the antero-inferior-medial temporal lobe, particularly affecting the temporal pole, amygdala, hippocampus, entorhinal cortex, parahippocampal gyrus, and fusiform gyrus. There was an anterior-posterior gradient of atrophy as well as inferior-superior and medial-lateral gradients.

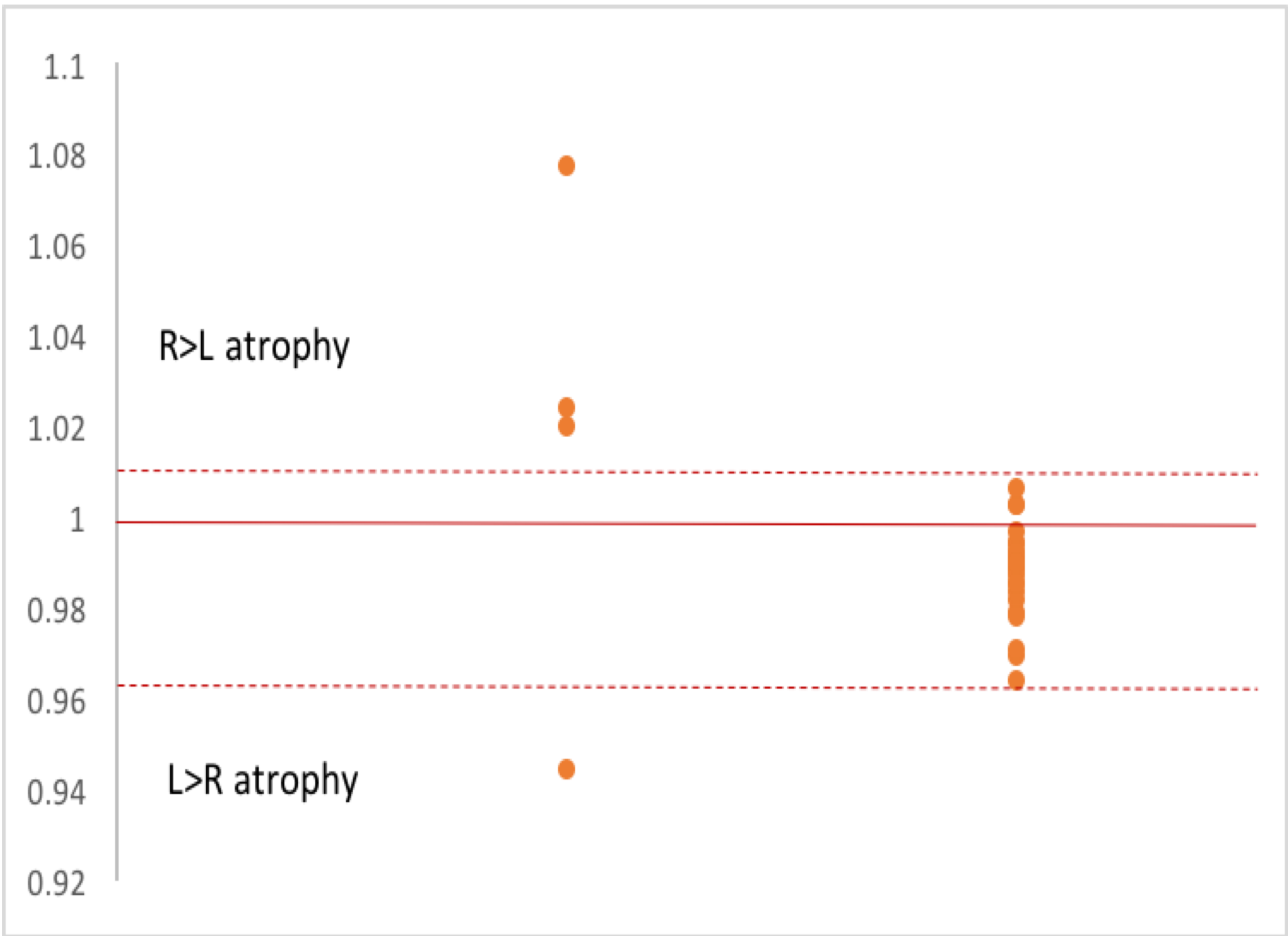
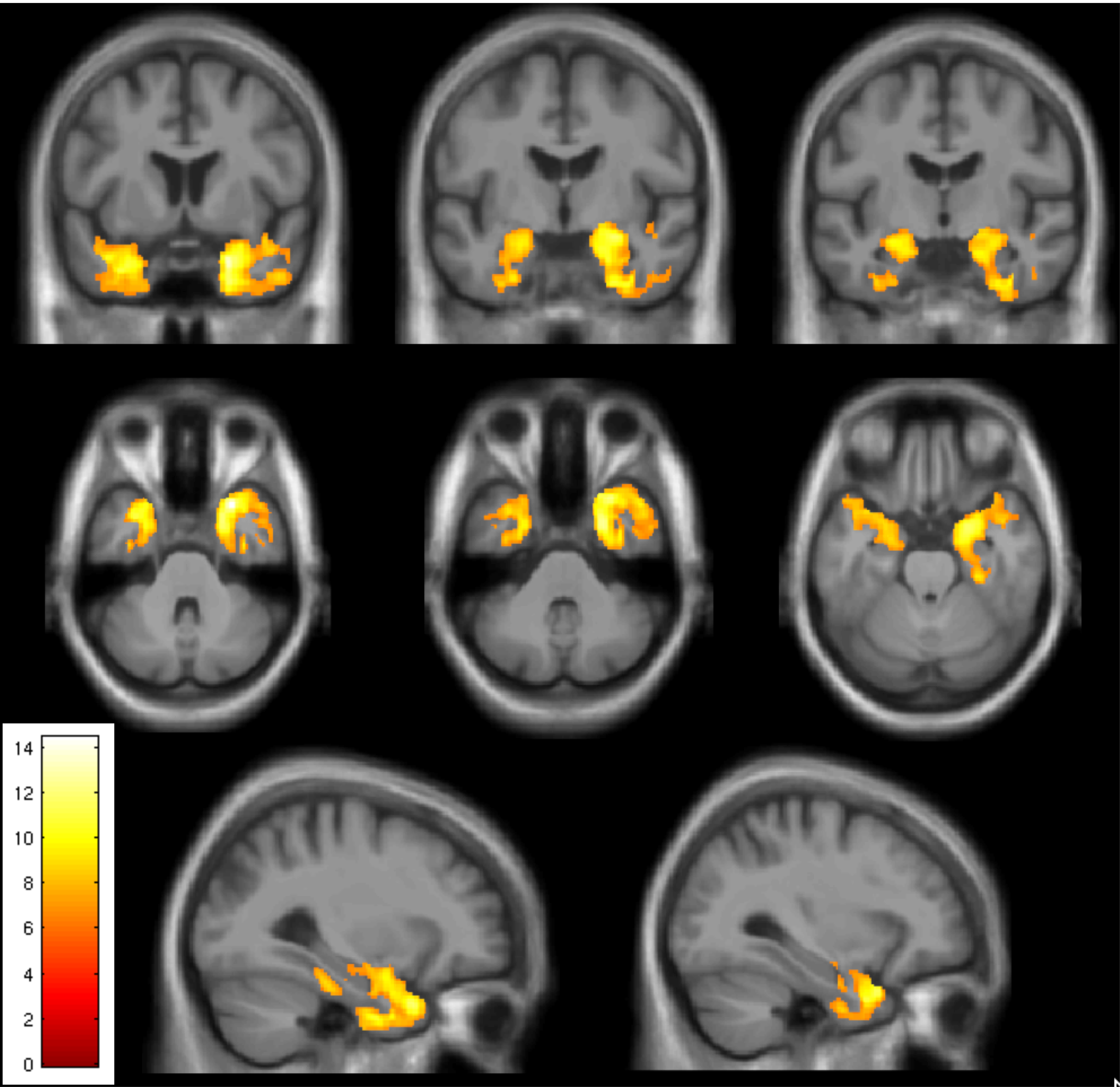


Figure 1. Asymmetrical differences between SQSTM1 patients and controls.

Figure 2. VBM analysis on GM regions. Statistical parametric maps were thresholded at  $p < 0.05$  after family-wise error correction. Analyses were adjusted for age, gender and total intracranial volume.



## Conclusions

Patients with SQSTM1 mutations can have a varied clinical phenotype but appear to be particularly associated with focal temporal lobe atrophy that can predominantly affect the right or left hemisphere.

**Acknowledgements:** The Dementia Research Centre is supported by Alzheimer's Research UK, Brain Research Trust, and The Wolfson Foundation. This work was supported by the NIHR Queen Square Dementia Biomedical Research Unit, the NIHR UCL/H Biomedical Research Centre, and the MRC UK GENFI grant. JDR is supported by an MRC Clinician Scientist Fellowship and a NIHR Rare Disease TRC Fellowship. EG is supported by an Alzheimer's Society PhD Studentship.

