**Supplementary Materials**

**Methods:**

*Image acquisition:* All structural MR images were performed on Siemens Trio 3T scanner at the University of California, San Francisco Neuroscience Imaging Center. A volumetric magnetization prepared rapid gradient echo sequence obtained a T1-weighted image (repetition time: 2300 ms; echo time: 2.98 ms; flip angle 9°; 160 sagittal slices; matrix size 240 x 256; voxel size = 1 mm3).

*Voxel-based morphometry:* We compared the patient to a group of 30 healthy controls matched for age, sex, handedness, and scanner type. VBM was performed using the SPM8 VBM8 toolbox (SPM8 <http://www.fil.ion.ucl.ac.uk/spm>). T1-weighted images were preprocessed using VBM8 default estimation settings, spatially normalized using standard spatial normalization with light clean up (to remove non-brain tissue from data), modulated and normalized for non-linear warping, then segmented into gray and white matter images. Gray matter images were smoothed using an 8 mm full-width at half-maximum isotropic Gaussian kernel. We used multiple regression compare smoothed gray matter maps of patient to the control group, with age and total intracranial volume used as nuisance regressors in the model. Significant clusters were defined using a t-threshold corrected for family-wise error at p<0.05 with a minimum cluster size of 50 voxels.

Positron Emission Tomography (PET) imaging with [18F] fluorodeoxyglucose (FDG-PET) and beta-amyloid ligand [11C]PiB (PIB-PET) were performed on a Siemens ECAT EXACT HR scanner at Lawrence Berkeley National Laboratory. 15 mCi of [11C]PIB was injected intravenously, and four 5 min frames were acquired at t=50-70 min post-injection. Following PIB acquisition, 5 mCi of [18]FDG was injected, and six 5 min frames were acquired at t=30-60 min post-injection. Image reconstruction and attenuation correction were performed as previously described (Rabinovici et al., 2011). 2011). PET frames were summed and normalized to mean activity in cerebellar gray matter (PIB) or pons (FDG).

*Genetic testing: C9ORF72* repeat expansion mutations were determined using the repeat-primed PCR reaction as described in DeJesus-Hernandez et al. 2011 (Dejesus-Hernandez et al., 2011). PCR products were run on an ABI3730 DNA Analyzer and analyzed using the Peak Scanner Software. The characteristic "saw-tooth" pattern is indicative of the presence of a repeat expansion.

Table 1. Regions significantly atrophied in voxel-based morphometry comparison of patient < 30 healthy controls

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Region containing peak voxel** | **BA** | **Extent** | **x,y,z** | **Peak T** |
| L Hippocampus | 20 | 954 | -26,-15,-21 | 13.90 |
| Vermis | -- | 1474 | 2,-72,-21 | 12.80 |
| L Caudate | 25 | 10124 | -5,8,-5 | 12.10 |
| R Lingual | 19 | 2798 | 23,-56,2 | 11.00 |
| R Cerebellum | 30 | 4974 | 21,-33,-20 | 10.60 |
| L Middle temporal gyrus | 21 | 809 | -62,-27,-5 | 9.90 |
| L Calcarine sulcus | 17 | 314 | -15,-56,5 | 9.56 |
| R Middle temporal gyrus | 21 | 544 | 63,-21,-6 | 9.48 |
| R Superior temporal gyrus | 48 | 146 | 45,-14,18 | 9.29 |
| R Insula | 48 | 142 | 38,-11,-2 | 9.14 |
| L Anterior mid cingulate | 24 | 211 | -6,17,33 | 9.05 |
| R Posterior mid cingulate | -- | 81 | 11,-26,42 | 8.84 |
| L Middle occipital gyrus | 19 | 58 | -44,-84,3 | 7.98 |
| L Middle temporal gyrus | 21 | 72 | -63,-12,-23 | 7.87 |
| R Superior temporal gyrus | 48 | 62 | 50,-9,-3 | 7.54 |