Brain perfusion patterns in familial frontotemporal lobar degeneration

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Introduction
Frontotemporal lobar degeneration (FTLD) is a clinically, genetically and pathologically heterogeneous disorder. FTLD is characterized by a variable clinical presentation of progressive behavioural, language and executive dysfunction. Two major gene defects have been detected in familial FTLD; mutations in the microtubule associated protein tau (MAPT) and progranulin (GRN) genes. However, there still remain one or more familial forms of FTLD with unknown gene defect (UGD), in particular familial FTLD with motor neuron disease (FTLD-MND).

Histopathologically, MAPT is associated with FTLD with tau-positive inclusions (FTLD-tau), whereas GRN as well as familial forms with unknown genetic defect are associated with ubiquitin- and TDP-43 positive inclusions (FTLD-TDP). The aim of this case-control study was to compare clinical features and perfusion patterns on SPECT of patients with MAPT mutations and familial FTLD-TDP.

Methods
Patients were included if they had MAPT or GRN mutations, positive family history with pathologically-proven FTLD in the patient or first-degree relative, or were part of FTLD-MND families. All patients and ten age- and gender-matched controls underwent measurement of brain perfusion using 99mTc-HMPAO SPECT. We used SPM8 to perform image processing and voxel-based group analyses (p<.001). Gender and age were included as nuisance variables in the design matrices.

Results
Of the 29 patients with familial FTLD, 19 had familial FTLD-TDP (GRN mutations in six), and 10 had MAPT mutations. At clinical presentation, familial FTLD-TDP patients were older at onset (p=.030) and had more memory deficits (p=.011), whereas MAPT had more naming deficits (p<.001) and obsessive-compulsive behaviour (p=.001).

The between groups SPECT analyses revealed significantly less perfusion in the right frontal lobe, precuneus, cuneus and inferior parietal lobule in familial FTLD-TDP, whereas significantly less perfusion was found in the left temporal and inferior frontal gyri in MAPT. Post-hoc analysis of familial FTLD-TDP with unknown genetic defect versus MAPT patients revealed less perfusion in the right frontal and parietal lobe.

Conclusion
Familial FTLD-TDP shows relatively more posterior hypoperfusion, including the precuneus and inferior parietal lobule, possibly related to significant memory impairment. MAPT patients were characterised by impaired perfusion of the temporal regions and naming deficits and obsessive-compulsive behaviour.