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Tau Positron Emission Tomography with [18F]RO948 in Frontotemporal Dementia

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Positron Emission Tomography (PET) tracers targeted at the protein tau could potentially separate tau-positive and tau-negative frontotemporal dementia (FTD) in vivo. We examined the tracer [18F]RO948 retention in FTD, aiming to include cases were underlying protein pathology can be predicted with certainty. 35 patients with FTD underwent [18F]RO948 PET and MRI: 21 behavioural variant FTD (bvFTD) cases, 11 symptomatic C9orf72 mutations carriers, one patient with non-genetic bvFTD-ALS, one individual with bvFTD due to a GRN mutation and one due to a MAPT mutation (R406W). Tracer retention was examined using a region-of-interest (ROI) and voxel-wise approaches. Comparison subjects were matched cases of Alzheimer´s disease (AD, n =13) and Aβ-negative cognitively unimpaired individuals (n =13). Two patients underwent postmortem neuropathological examination and tracer binding was also assessed using [3H]RO948 autoradiography, in six separate cases. [18F]RO948 retention across ROIs was clearly lower than in AD and comparable to that in Aβ-negative cognitively unimpaired individuals. Only minor loci of tracer retention were seen in FTD, which did not overlap with the observed cortical atrophy in the examined cases nor the expected or verified protein pathology distribution. Autoradiography did not show any [3H]RO948 binding. AD-like retention levels and specific in-vitro binding was however seen in the R406W MAPT mutation carriers. With a clear exception being specific MAPT mutations, [18F]RO948 uptake is not significantly increased in FTD patients and thus cannot predict underlying protein pathology in the majority of cases. [18F]RO948 has a promising specificity in AD vs FTD.

Conflicts of interest

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