Decreased temporal dopamine D2/D3 receptor binding in temporal lobe epilepsy: an ^{18}F-Fallypride PET study

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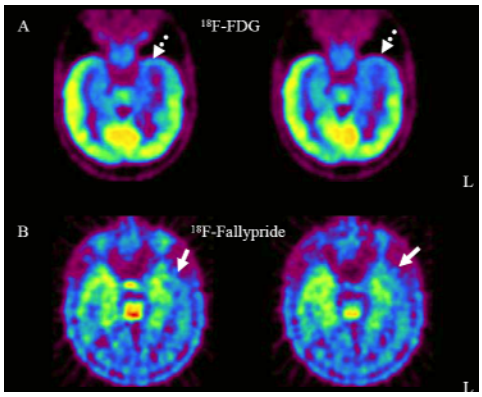
The role of dopamine in focal epilepsy is controversial. In animal models of temporal lobe epilepsy (TLE) activation of D1-receptors has a pro- and of D2-receptors an anticonvulsant effect. Evidence for an alteration of the extrastriatal dopaminergic system in human focal epilepsy is missing. To quantify D2/D3 receptor density we studied seven patients with mesial TLE and 7 aged-matched control subjects by PET using the high affinity dopamine D2/D3 receptor ligand ^{18}F-Fallypride ([^{18}F]FP) suitable for imaging extrastriatal binding. Mesial TLE was defined by interictal and ictal Video-EEG, MRI and ^{18}F-Fluorodesoxyglucose ([^{18}F]FDG) PET and was due to hippocampus sclerosis. Anatomical regions of interest (ROIs) were drawn on MRIs. PET data were quantified using the simplified reference tissue model to assess binding potential (BP) values in each ROI, with cerebellum as reference. For each patient, a normalized percentage BP change was calculated as the relative variation of BP in each ROI on the epileptogenic compared with the unaffected hemisphere. In addition, a voxel-based analysis was performed using statistical parametric mapping (SPM). Results were correlated with [^{18}F]FDG PET and MR-volumetry data. Compared to the controls, [^{18}F]FP BP was significantly decreased in the epileptogenic temporal lobe. This reduction was particularly evident in areas surrounding the seizure onset zone in the pole (- 34%) and lateral aspects (- 33%) of the temporal lobe. The decrease of [^{18}F]FP BP in these areas was significantly greater than the decrease of [^{18}F]FDG uptake. In contrast, in the hippocampus there was no significant decrease of [^{18}F]FP binding whereas [^{18}F]FDG uptake was significantly reduced and correlated with hippocampus atrophy (- 33%). Reduction of [^{18}F]FP BP did not correlate with seizure or spike frequency, and hippocampal atrophy as measured by MR-volumetry. Our findings are consistent with the hypothesis of reduced D2/D3 binding in the temporal pole and lateral aspects of patients with mesial temporal lobe epilepsy with hippocampus sclerosis.



Static [^{18}F]FP (A) and [^{18}F]FDG PET (B) data in patient with left mesial temporal epilepsy and hippocampus sclerosis on histology as an illustrative example.
L = left.
The arrows point to areas of decreased [^{18}F]FDG uptake or [^{18}F]FP binding in the mesial and lateral left temporal lobe ipsilateral to the side of seizure onset

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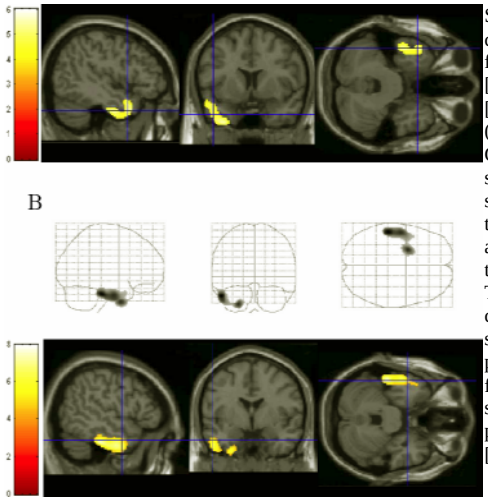
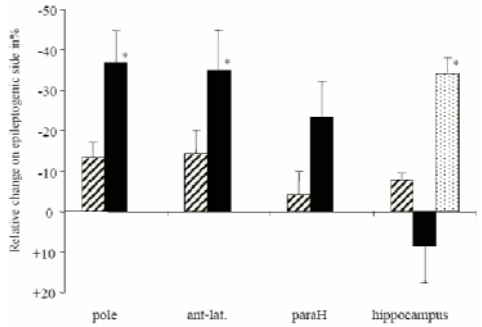


SPM results (contrast controls – patients) for all patients.
[^{18}F]FP BP in (A) and [^{18}F]FDG uptake in (B).
Glass brain of the statical map (top) and superposition of statistical maps onto an averaged MRI (bottom).
The colour scale indicates *t* scores. The statistical threshold is $p < 0.001$ (corrected for multiple comparisons) for [^{18}F]FP and $p < 0.0001$ for [^{18}F]FDG data.



Mean (± SEM) relative changes of [^{18}F]FP BP (black), [^{18}F]FDG uptake (dashed) and hippocampus volume (dotted bars) comparing ROIs in the epileptogenic versus unaffected hemisphere in patients with hippocampus sclerosis (n = 6, Pat. No. 4 excluded). Pole = temporal pole, ant-lat. = anterior-lateral temporal lobe, paraH = parahippocampal gyrus. * $p < 0.05$ in two-sided paired t-test.