Effects of donepezil on cortical metabolic response to activation during (18)FDG-PET in Alzheimer's disease: a double-blind cross-over trial.

RATIONALE: Cholinergic enhancement is among the best established treatments of Alzheimer's disease (AD). The cognitive effects of treatment are thought to be mediated by improvement of neuronal transmission. Positron emission tomography using 18F-fluorodeoxyglucose (FDG-PET) by measuring cortical metabolic response to activation assesses integrity of neuronal transmission in vivo. OBJECTIVE: To determine the effects of treatment with donepezil, a centrally selective acetylcholinesterase inhibitor, on cortical metabolism in AD using 18FDG-PET. METHODS: We enrolled 23 patients, 18 of which completed the study, with mild to moderate probable AD (mini-mental status exam scores of 15-28, inclusive) in a double-blind cross over trial of 8 weeks donepezil compared to 8 weeks placebo with repeated double 18FDG-PET examinations during passive audio-visual stimulation. Effects of treatment on cortical metabolic response to stimulation were determined with a linear model on a voxel level using Statistical Parametric Mapping (SPM 99, Wellcome Department of Imaging Neuroscience, London). RESULTS: Effects of treatment on cognitive measures were not different between donepezil and placebo. During passive audio-visual stimulation, patients showed activation in posterior visual and auditory areas.
and decreased activation in frontal cortex and basal ganglia. Resting state metabolism was increased with donepezil in left prefrontal cortex and decreased in right hippocampus. Cortical response to activation was increased in right hippocampus with donepezil compared to placebo. CONCLUSION: Donepezil treatment shows a spatially limited functional effect on right hippocampus and left prefrontal cortical metabolism, independently of clinical response to treatment.