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Neuronale Korrelate der kognitiven Defiziten bei Patienten mit leichter kognitiver Beeinträchtigung und bei Patienten mit Alzheimer Demenz

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Doktorvater: Prof. Dr. med. J. Schröder

Aoife Hunt Dr. med. Neuronale Korrelate der kognitiven Defiziten bei Patienten mit leichter kognitiver Beeinträchtigung und bei Patienten mit Alzheimer Demenz- Eine klinische und FDG PET Studie Geboren am 01.07.1969 in Dublin, Ireland Final Medical Examination im Mai 1992 at the University of Dublin, Trinity College Promotionsfach: Psychiatrie Doktorvater: Prof. Dr. med. J. Schröder Alzheimer's disease (AD) is the commonest neurodegenerative disease in the elderly, and is associated with metabolic changes in various brain structures, which can be detected in vivo using positron emission tomography (PET).

PET studies have consistently demonstrated a reduced glucose uptake in temporal and parietal association cortices extending to the frontal cortex with disease progression in patients with manifest AD compared to healthy controls. Aging-associated cognitive decline (AACD) is characterised by consistent cognitive impairment with normal activities of daily living, and is associated with an increased risk of progression to AD. Groups of individuals with mild cognitive impairment have been shown to have reduction in glucose metabolism in temporal and parietal cortices. Although PET has been applied in dementia research for more than two decades; there is a surprising paucity of prospective longitudinal data on PET in AACD. In the present study 14 patients with AACD, 14 controls, and 44 patients with AD were investigated using PET with ^{18}F -2-deoxyglucose as a tracer. Patients with AACD were followed up clinically to determine conversion to AD, and to examine baseline metabolic changes in converters compare to controls. Cerebral metabolic deficits might directly cause the observed neuropsychological symptoms in AD and AACD and/or indirectly influence symptoms through functional

connectivity. To clarify this question, the present study correlated cerebral glucose metabolism with scores on subtests of the Consortium for the Establishment of a Registry for Alzheimer's disease (CERAD) neuropsychological test battery.

The voxel-based comparison and correlation of the PET images was done using the MatLab-based statistical software package SPM. The study yielded the following results:

- Patients with AACD showed reduced cerebral glucose metabolism compared to controls in right precuneus, right angular gyrus, left posterior cingulate gyrus and bilateral middle temporal cortices. Patients who subsequently converted to AD showed reduced cerebral glucose metabolism at baseline in right precuneus, right angular gyrus and bilateral middle temporal cortices.
- The regions involved in AD were similar but more extensive to those affected in AACD. Thus patients with AD showed bilateral reduced cerebral glucose metabolism compared to controls in fronto-temporo-parietal and posterior cingulate cortices compared to controls
- The findings of the present study support the hypothesis that AACD could be regarded as a preclinical state of AD. There is a hierarchy of cerebral metabolic changes in AD, with precuneus, bilateral middle temporal cortices, and right angular gyrus being first affected, followed by temporal and parietal cortices, and frontal cortex.
- There were significant correlations between cognitive deficits reflected by the CERAD neuropsychological test battery and reduction in cerebral glucose metabolism in AD and AACD patients, indicating that PET with FDG reflects neuronal damage, and that this damage corresponds to the typical neuropsychological deficits.

AACD patients show a distinctive pattern of reduction of glucose metabolism in right precuneus, right angular gyrus, middle temporal cortices and posterior cingulate cortex. This finding suggests AACD to be a prestate of AD

Furthermore, the neuropsychological deficits found in AD and AACD and tested by the reliable and valid instrument CERAD correlate with the glucose metabolic deficits found on PET scanning. This is the first time that PET has been used in such a large and heterogeneous group of patients with mild and moderate AD and AACD to examine the neuropsychological correlates of CERAD. The results of this study provide further evidence that not only memory function but also functions of

language and constructional praxis involve different brain areas in patients with AD. Compared to scores of immediate memory performance, delayed memory test performance showed an additional correlation with frontal association cortices indicating a large network of brain regions involved in delayed memory performance