

《招待講演》

PET Study in Dementia

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Measurement of local cerebral glucose metabolism (ICMRGlc) by positron emission tomography (PET) and ^{18}F -2-fluoro-2-deoxy-D-glucose (FDG) has become a standard technique during the past 20 years and is now available at many university hospitals in all highly developed countries. Many studies have documented a close relation between ICMRGlc and localized cognitive functions, such as language and visuoconstructive abilities.

Alzheimer's disease (AD) is characterized by regional impairment of cerebral glucose metabolism in neocortical association areas (posterior cingulate, temporoparietal and frontal multimodal association cortex), whereas primary visual and sensorimotor cortex, basal ganglia, and cerebellum are relatively well preserved. Recently the diagnostic accuracy of FDG PET in AD has been confirmed by comparison with autopsy in 138 cases (Silverman et al. *JAMA* 2001; 286: 2120–2127).

We performed a multicenter study comprising 10 PET centers (Network for Efficiency and Standardisation of Dementia Diagnosis, NEST-DD*) which collected a data base of 639 PET studies of normals, patients with depression, mild cognitive impairment (MCI) and dementia. With an automated voxel-based analysis of FDG PET images, the distinction between controls and AD patients was 93% sensitive and 93% specific, and even in very mild dementia (at MMSE 24 or higher) sensitivity was still 84% at 93% specificity. Significantly abnormal metabolism was also found in most MCI patients, similar to mild AD, but only rarely in depression. Follow-up data suggested a constant rate of progression of the metabolic deficit. It was estimated that reduced neocortical glucose metabolism can be detected with FDG PET in AD on average one year before onset of subjective cognitive impairment. There was some overlap of the AD metabolic pattern with that of other dementing diseases such as fronto-temporal dementia, dementia with Lewy bodies, and vascular dementia. Differences among these diseases are now being analyzed using image decomposition into principal components in a prospective study.

In addition to glucose metabolism, acetylcholine esterase (AChE) activity is of interest for differentiation among dementia subtypes. Parametric images of AChE activity in standard

stereotactic space were generated by use of C-11-labeled *N*-methyl-4-piperidyl-acetate (MP4A). AChE activity was significantly lower in AD patients even at an early stage than in age-matched normal controls. In contrast to regional cerebral glucose metabolism, which was relatively well preserved in primary motor and primary visual cortex, reduction of AChE activity was more widespread in neocortex. It was most severe in temporobasal and temporo-occipital cortex.

In summary, standardized FDG PET has the potential for more widespread use in a clinical context for diagnosis of dementia at a very early stage. Measurement of local AChE activity by PET detects impairment of the cholinergic system in AD also at an early stage.

* Participants of NEST-DD: MPI/Univ. Köln, K. Herholz, Coordinator; HSR/Univ. Milano, D. Perani; CRC/Univ. Liege, E. Salmon; INSERM Caen, J.C. Baron; Univ. Firenze, S. Sorbi; Univ. Dresden, V. Holthoff; Univ. Graz, F. Fazekas; Univ. Frankfurt, L. Frölich; Univ. Heidelberg, H. Schröder; NILS, Obu, Japan, K. Ito
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