Aniko Egerhazi: The early diagnosis and differentialdiagnosis of Alzheimer's disease with clinical methods

SUMMARY

Several different clinical techniques were evaluated for the early diagnosis of Alzheimer's disease (AD). The brain has the capacity to compensate for the smaller damages and to retrieve small lesions, therefore the disorder can have a long preclinical phase before the clinical symptoms are present. There is a need for sensitive biological markers to detect AD pathology. The recognition of prodromal and early phase of AD opens possibility for the prevention (i.e. elimination of the vascular risk factors), and for the early treatment.

The Cambridge Neuropsychological Test Automated Battery (CANTAB) showed characteristic changes in early AD and amnestic MCI, which suggests that aMCI may be a prodromal phase of AD. The cognitive deficit appears to be similar in major depression (MD), so it does not give a determined help to differentiate it from AD. There are less cognitive deficits in the remission phase of MD than in the depressed phase. Presumably the underlying process of the cognitive deficit in depression might be rather functional disturbance than structural damage in the brain. Some advantages of CANTAB compared to the other neuropsychological methods are the following: it is independent from language, useful in case of aphasia, and requires shorter time to perform.

The late component of auditory evoked potential, P300, is not widely used in psychiatry, althought it may be a sensitive marker of cognitive impairment. P300 has less value in the differentiation of AD from vascular dementia (VD), because the changes are similar in these two disorders. The longer latency of P300 in amnestic MCI might predict the conversion to AD, and a more extensive use is offered.

The altered serum paraoxonase (PON) activity, a defect in the antioxidant capacity beside lipid metabolism, and the increased oxidative stress all play important role in the pathomechanism of AD and in atherosclerosis, which suggests an overlap in the pathogenesis of AD and VD. The altered PON activity can be a sensitive marker of the defect in antioxidant capacity.

The transglutaminase activation is a marker of apoptosis and elevated isodipeptide concentrations in the body fluids might correlate with the intensity of apoptotic cell turnover.

The determination of N^{ε}(γ-glutamyl)lysine isodipeptide (IDP) concentration in the cerebrospinal fluid offers a novel method for measurement of neurodegeneration in primary and mixed dementias.

There is not enough evidence to recommend one specific technique for the prediction and early detection of AD. A combined use of cognitive tests, ApoE genotype, functional and structural neuroimaging techniques, the serum and cerebrospinal fluid measurements is probably the best option.