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Interactions of intracellular amyloid beta peptides and biomarkers of Alzheimer disease in cerebrospinal fluid

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Ideal biomarker of Alzheimer disease (AD) does not exist yet. Cerebrospinal fluid (CSF) levels of amyloid β 1-42 (Aβ 1-42), τ and phospho-τ are often used standards (senzitivity > 85% and specificity > 75-85% are expected for a good biomarker). We evaluated new biomarkers based on interactions of Aβ and its intracellular binding partners (mitochondrial 17β-hydroxysteroid dehydrogenase type 10 (17β-HSD10) and τ) and on abilities of amyloid peptides/proteins to oligomerize/aggregate. In young patients with neuroinflammatry diseases, no changes in Aβ were found. Increased concentrations of 17β-HSD10 were observed only in people with multiple sclerosis in later stages probably as a compensatory response to attacts of immune system. In old patients with neuroinflammatory diseases, changes in Aβ (but not in τ/phospho-τ or 17β-HSD10) were similar to those in AD. Results can be interpreted by age- and neuroinflammation-dependent alterations in extracellular Aβ and a key role of Aβ in interactions. Changes observed in MCI-AD (Aβ, τ/phospho-τ, Aβ – τ complexes, 17β-HSD10, thioflavinT-based to intrinsic amyloid fluorescence signals ratio) were similar to those in AD. Results suggest early changes in intracellular Aβ and accumulations of amyloid peptides/proteins in the brain, in addition to increased oligomerization/aggregation. Both fluorescences are probably based on different amyloid structures (ThioflavinT-based on oligomers, instrinsic amyloid fluorescence on aggregates partly accumulated in the brain). Characteristic of new biomarkers of AD are as follows: Aβ – τ complexes (senzitivity 68.6% and specificity 73.3%), 17β-HSD10 (80.0% and 73.3%), 17β-HSD10 – Aβ complexes (66.7% and 68.8%), ThioflavinT-based to intrinsic amyloid fluorescence signals ratio (61.1% and 70.8%).

Biography

Zdenka Kristofikova studied at Czech Technical Univerzity in Prague (Ing., Department of Nuclear Chemistry) and at Univerzity of Defence, Faculty of Military Health Sciences in Hradec Kralove (PhD, Department of Toxicology), both in the Czech Republic. She works at National Institute of Mental Health (as a senior researcher and a head of working group) and is interested in Alzheimer disease. She has published many publications based on neurochemical analyses of the human or rodent brain tissue (e.g. validations of various pharmacological and genetic animal models of Alzheimer disease) and of cerebrospinal fluid (evaluations of new biomarkers of Alzheimer disease).

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