

WILL THERE EVER BE A VALID BIOMARKER FOR AD? NO

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Alzheimer Disease (AD) is a dementia disorder with a wide range of symptomology. It is a “spectrum disorder”! This is underlined by the occurrence of at least three subtypes of hereditary AD, APP-, PS1- and PS2-mutations and early as well as late onset sporadic AD. Variation exist with regard to risk factors, like life style, physical activity, education, diabetes type II, blood pressure problems, cholesterol, age, depression. They are contributing or may even cause AD. Such variation is reflected by the fact that “mild cognitive impairment (MCI)” in only half of such cases is preceding AD. Also even in specialized clinical centres the rate of exact diagnosis is not better than 85% indicating the clinical problems of symptom specificity and selectivity.

From the various molecular genetic clinical studies, including GWAS-studies, it is evident that the outcome of significant genetic parameters varies and is not reproduceable. The reasons are understood only in part but may simply reflect the enormous variation in genetic subsets that may causative for sporadic AD.

Similarly, there is an enormous overlap in the neuropathology of AD:

- AD with white matter lesions or not
- AD with or without plaques and tangles
- AD with plaques only
- AD with or without capillary/endothelial pathology

Agreeing with this the rate of disease progression varies and the neurochemical pathology of each such parameter like cholinergic, glutamatergic, serotonergic, noradrenergic, dopaminergic, peptidergic ones shows a wide range between patients.

Although it would be of great value to establish “a” valid biomarker for AD in order to identify the disorder at a presymptomatic stage and to establish an early treatment it is – as outlined above - impossible, to reach this goal with a single biomarker. If so, “personalized AD” needs “personalized biomarker(s) in order to develop “personalized treatment strategies”.

