Can the diagnosis of AD be made solely on biomarker evidence?

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Alzheimer's disease (AD) is a devastating and relentlessly progressive neurodegenerative late onset disease, which is reaching epidemic proportions world-wide, due to the unprecedented increase of longevity. AD is defined by the progressive deterioration of memory, executive function and other cognitive domains that result in a progressive inability of patients to function within the society and their own family. All therapeutic trials of novel disease modifying therapies have failed, reflecting our significant gaps of knowledge of the precise biological mechanisms underpinning the disease aetiology. Furthermore, there is an emerging consensus that increasing and accumulating disease pathology precedes by (perhaps) decades the clinical onset. Thus, optimal intervention aimed at arresting or reversing AD seems to be in the pre-clinical stages, prior to the disease clinical onset. However, we do know that, even in the oldest old, the risk of AD does not exceed 40%, thus 60% of individuals may never develop significant cognitive decline. Identifying high-risk-for AD individuals remains a major challenge in drug development and in secondary prevention strategies. More recently, it has been suggested that the biomarker – based evidence of an abnormally high brain amyloid and tau load (patho-physiological AD biomarkers), together presence of findings suggestive of neurodegeneration, such as hippocampal atrophy, FDG-PET abnormalities or high tau can constitute sufficient basis for the diagnosis of AD, even in the absence of any cognitive decline. Thus, there is increasing popularity for biomarker – based disease diagnosis in the pre-clinical stage; similar to pre-clinical diagnosis of forms of cancer. However, there are several lines of argument against this concept. Firstly, the pathological significance of the biomarker – based profile in AD is not comparable to that of cancer diagnosis based on pathology. Secondly, the specificity and sensitivity of the proposed AD-biomarker profile remains to be validated. Thirdly, we know that ~ 30 % of clinically probable AD cases do not carry this profile and that a significant number of cognitively healthy older old individuals who do have this biomarker profile are disease free and may well never develop AD. Unlike cancer, AD is primarily a clinical distinct entity who's pathological and biological underpinning mechanisms are not, as yet, known with some precision; our understanding of AD is, probably 20 years behind other common diseases, such as cancer. Finally, it would be ethically and medically improper, in the light of our current knowledge, to suggest to a cognitively healthy individual that she/he has AD; probably the disease that they dread the most, as they grow old. This is different from suggesting high risk, although such statement must also be supported by strong and unequivocal scientific evidence.