Journal of Alzheimer's Disease & Parkinsonism

Kayser, J Alzheimers Dis Parkinsonism 2021, 11:S9

Short Communication Open Access

Note on Biomakers in Alzheimer's Disease

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Received: December 06, 2021; **Accepted**: December 20, 2021; **Published**: December 27, 2021

Citation: Kayser K (2021) Note on Biomarkers in Alzheimer's Disease. J Alzheimers Dis Parkinsonism S9: 036.

About the Study

Research in the field of Alzheimer's disease and particularly in the area of Alzheimer's disease biomarkers, continues its extraordinary growth with support from federal and nongovernmental funding sources, alongside stunning technological advances in imaging and diagnostics. Waves of neurobiological discovery in Alzheimer's disease research have influenced new thinking on how to detect the disease earlier so it can treat earlier to improve the lives of patients. In the last three decades, a rich array of new ideas, new discoveries and new technologies have accelerated AD biomarker research. Even in the last few years, we have witnessed an explosive increase in the discovery, validation and application of AD biomarkers for diagnosis, assessment of prognosis, longitudinal tracking, evaluation of therapeutic efficacy and clinical trials. Despite this increase in our understanding about AD neurology and disease biomarkers, an integrated and cohesive summary of the field has been sorely lacking.

In an attempt to consolidate the history of Alzheimer's disease biomarkers and new discoveries into a comprehensive collection, collecting every testing modality and biomarkers and their applications and including a critical evaluation of each and the need for ongoing biomarker research. It is important to know what we have learned about Alzheimer's disease biomarker from various disciplinary perspectives including imaging, genetics, biochemistry, physiology and neurology [1,2]. An unbiased and comprehensive understanding of all Alzheimer's disease biomarkers including neuroimaging biomarkers, cerebrospinal fluid biomarkers, genetic biomarkers and biomarkers in peripheral fluids and cells is important.

A 10-country survey of 10,000 adults found that three quarters of respondents would like to know whether they have a particular neurological disorder, even in the absence of a cure. This survey also reported that 81% of the respondents would like to know whether their partner has a neurological disease. In addition, a majority of survey respondents indicated that diagnosis should have either government or private health insurance companies. The size of the survey and results reinforce the urgent need for early diagnosis of Alzheimer's disease. Currently available diagnostic tests have moved the field closer to early diagnosis of Alzheimer's disease; however, a definitive diagnosis is made only with the development of clinical dementia later in the disease progression and the presence of amyloid plaques and neurofibrillary tangles at autopsy [3]. At the present time, there are no biomarkers of early-stage Alzheimer's disease that are ready for testing in clinical trials or application in primary care.

Sporadic LOAD is often not diagnosed until later stages when cognitive deficits become clinically significant. In the past two decades, researchers have focused on the identification of biomarkers that can provide an earlier diagnosis of Alzheimer's disease or assess the risk of developing Alzheimer's disease. There are several biomarkers currently being investigated for the diagnosis of Alzheimer's disease, including markers in the CSF, PET and MRI neuroimaging markers and markers detected in peripheral tissues such as blood and skin. An ideal antemortem Alzheimer's disease biomarker should meet the ability to detect the fundamental features of Alzheimer's disease neuropathology that can be validated at autopsy. It should have the ability to differentiate Alzheimer's disease from non-Alzheimer's disease dementias. It should detect early stages of Alzheimer's disease and differentiate between the stages of Alzheimer's disease progression to guide therapy. Highly reliable, easy to perform, inexpensive and use minimally invasive sample collection, such as peripheral tissues, without requirement for lumbar puncture or other invasive sampling procedures.

There is a significant correlation between the decline in memory function and synaptic loss but no clear correlation between memory decline and the presence of amyloid plaques and neurofibrillary tangles at autopsy; this suggests that synaptic dysfunction is the primary indicator of Alzheimer's disease pathology. The newly revise criteria for Alzheimer's disease emphasize that the Alzheimer's disease pathophysiological process starts years or decades before clinical symptoms appear [4,5]. Decades of fundamental research have generated substantial evidence that a silent pathophysiological process of Alzheimer's disease as well as by aging studies. A meaningful and actionable diagnosis of Alzheimer's disease should be made during early stages of Alzheimer's disease, when Alzheimer's disease pathological changes start but clinical symptoms have not yet developed. Preclinical diagnosis of Alzheimer's disease would allow therapeutic intervention to be initiated before neurons and connectives are lost. The last-stage treatment timing, after the loss of synapses has already occurred, is one of the reasons why almost all therapeutic clinical trials in patients with severe Alzheimer's disease failed. Early-stage biomarkers of Alzheimer's disease will allow the identification of people still in the preclinical stage of Alzheimer's disease and who will benefit from therapeutic intervention, prior to synaptic loss. Therapeutic intervention at later stages of Alzheimer's disease may be less effective, once synaptic loss has begun.

The scope should not be limited to only a few well-studies Alzheimer's disease biomarkers, but covers all modalities and biomarkers from neuroimaging to cell-biased bioassays [6]. A comprehensive study is required to illustrate the current and potential applications and their utility in the detection of Alzheimer's disease, prognosis and guiding therapeutic intervention in the everyday care of patients.

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