

Commentary

Risk Factors Versus Alzheimer's Disease *or* Symptoms Associated with Alzheimer's Disease

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Alzheimer's disease (AD) is in general described by certain symptoms; there is generally no consensus for the case definition of AD. Although the symptoms are considered to be the 'hallmark' of AD, there are more people having the hallmarks with no disease than with the disease!

Regardless of this seemingly inconsistent and rather confusing definition of AD, there should be no inconsistency or confusion in considering AD to be a disease. We, in general, have studied the symptoms and hallmarks of the disease more than the disease process itself. Drs. Chen and Fernandez are presumptuous and have treated AD and its hallmarks interchangeably when discussing the roles of risk factors.

As stated by the authors, age is a prerequisite and hence a causal factor for hallmarks of AD. But I do not extrapolate this statement to AD. Age is certainly correlated with histopathological symptoms of AD, such as senile plaques and

neurofibrillary tangles, as well as with clinical symptoms of AD, such as memory loss and cognitive impairment, but these symptoms do not necessarily correlate with AD.

It is of interest to note that the authors have characterized their approach as revisiting AD. As far as I am concerned, we have never left it. The debate is very much alive and a conclusion has yet to be reached.

Another point is that the authors have given special attention to a possible physiological symptom of AD, namely Ca^{2+} signaling potency. They link its decline, caused by aging, to the cause of senile plaque and neurofibrillary tangle formation and hence the cause of AD. It seems we are all guilty of selective prejudices.

Let us recognize AD as what it is: a disease. Regardless of the debate on what the risk factors are or what the cause and effects are, there should be a common path to the pathophysiology of this fatal neurodegenerative process and certainly there should be common targets for affecting or modifying the process to be used in drug discovery approaches. We can all help to reach the goal of treating the disease process by maintaining an open-minded approach and avoiding finality in our conclusions.