

Three postulates to help identify the cause of Alzheimer's disease

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After more than 100 years following its pathologic description, the cause of Alzheimer's disease (AD) remains unknown. To test the validity of present and future proposals related to the probable cause of AD, three postulates, or necessary conditions, are recommended by Jack de la Torre, MD, PhD, Adjunct Professor of Psychology at the University of Texas, Austin, in an article published in the *Journal of Alzheimer's Disease*.

"Knowing what causes AD is critically important because it would allow more effective therapy to specifically prevent new cases and apply interventions to slow down the [mental decline](#) in people who already have this [dementia](#)," commented Dr. de la Torre. "In search of the Alzheimer cause, a considerable number of hypothetical proposals have been published, but no proposal so far has reached a consensus of agreement by experts in the field. Proposals regarded as weak and insubstantial by evidence-based medicine not only cost lots of money and effort, they also hinder clinical progress."

Dr. de la Torre believes that any likely cause of AD would need to satisfy the criteria established by the three postulates when hypothetical proposals are submitted to explain the [pathogenesis](#) of AD. The first postulate requires that the cause of AD precedes the [cognitive decline](#) and neurodegenerative pathology that characterize AD. This rule identifies a primary event from a neuropathological effect generated by the disease process. The second postulate stipulates that interventions aimed at the proposed causal event should prevent or reverse the

cognitive and neurodegenerative pathology associated with AD prior to disease onset. This postulate emphasizes prevention or reversal of emerging neurocognitive pathology considerably before AD onset. If the first and second postulate requirements are met, the third postulate follows that interventions targeting the causal event should significantly lower the incidence of AD.

To evaluate the potential usefulness of the three postulates, Dr. de la Torre examined seven mainstream proposals offered as the cause of AD and explored their relative merit or lack of merit on Alzheimer patients. Proposals included the amyloid- β , cell cycle, cholinergic, inflammatory, oxidative stress, tau, and vascular hypotheses.

Dr. de la Torre analyzed evidence of efficacy for each proposal obtained from high-quality clinical trials, then assessed whether such evidence met the requirements posed by each postulate. Only two of the seven proposals examined, the vascular hypothesis and the oxidative stress hypothesis, partially met the requirements of one or two but not all three postulates.

Dr. de la Torre concludes that "By questioning or helping validate a proposed cause-effect relationship to AD, the three postulates I have described may serve as a primary instrument in targeting efficient therapeutic initiatives designed to prevent, reverse, or slow down the likely cause of this dementia."

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