

DEBATE: WITH 25 YEARS' HINDSIGHT, WERE THE CHOLINERGIC DRUGS WORTH DEVELOPING?

Görsev G. Yener

Professor of Neurology, Dokuz Eylül University and Istanbul Kultur University, Turkey

As the world is aging rapidly, dementia is one of the more prevalent syndromes. So far, cholinergic drugs have been the most widely accepted and proven approach to the treatment of mild to moderate Alzheimer's disease, vascular dementia and Lewy body dementia. The only other option for symptomatic treatment of moderate to severe Alzheimer's dementia has been an NMDA receptor antagonist, with less efficient results. The expected benefit from either active or passive immunization agents have been proved to be not useful for symptomatic dementia cases. The positive effects of cholinergic drugs on cognition, behavior and caregiver burden of dementia or pre-dementia phase make these agents worth developing. Either decreasing their side effects or searching their other mechanisms of action, or combination therapies with other potential drugs can be main area of research on cholinergic drugs. Besides its well-known action on the synapse, ACh is also found outside the synapse where, among other activities, it plays a role in controlling inflammation and might impact on pathological changes. A re-analysis of one of the clinical trials displayed a significant delay in progression to AD with dual cholinesterase inhibition over 3 to 4 years. Therefore, it is plausible that cholinesterase inhibition might contribute to disease modification and elucidation of these mechanisms involved could provide insights for their usage in disease modifying treatment of dementia.