

# Nicotinic acetylcholine receptors in the pathophysiology of Alzheimer's disease

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Nicotinic acetylcholine receptors (nAChRs) have been pursued for decades as potential molecular targets to treat cognitive dysfunction in Alzheimer's disease (AD) due to their demonstrated role in processes underlying cognition such as synaptic facilitation, and theta and gamma wave activity. Historically, activity at these receptors is facilitated in AD by use of drugs that increase the levels of their endogenous agonist acetylcholine, and more recently nAChR selective ligands have undergone clinical trials.

In this article, we discuss recent findings suggesting that the expression and function of nAChRs in AD may be regulated by direct [interactions](#) with specific proteins in the brain, including Lynx proteins, NMDA-receptors and the Wnt/ $\beta$ -catenin pathway, as well as  $\beta$ -amyloid sheets. The ability of protein interactions to modify nAChR function adds a completely new level of complexity to cholinergic signaling in the brain that may be specifically altered in AD. It is currently not known to what degree current nAChR ligands affect these interactions, and it is possible that the difference in the clinical effect of nAChR ligands in AD is related to differences in their ability to modulate nAChR protein interactions, rather than their effects on ion flow through the receptors. Drugs designed to target these interactions may thus provide a new avenue for drug development to ameliorate cognitive symptoms in AD.

Notably, the development of experimental drugs that specifically modulate these interactions may provide the opportunity to selectively affect those aspects of nAChR function that are affected in AD.

**More information:** Morten Thomsen et al, Nicotinic Acetylcholine Receptors in the Pathophysiology of Alzheimer's Disease: The Role of Protein-Protein Interactions in Current and Future Treatment, *Current Pharmaceutical Design* (2016). [DOI: 10.2174/1381612822666160127112357](https://doi.org/10.2174/1381612822666160127112357)

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