

Understanding brain function could lead to breakthrough Alzheimer's treatment

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Synaptic plasticity, one of the neurochemical foundations of learning and memory, is predominantly controlled by NMDA receptors. One of the hallmarks of Alzheimer's disease is a neurological dysfunction caused by nerve cell damage, which in turn is caused by the overactivation of NMDA receptors.

Currently, clinically available treatments for the disease are drugs that stimulate the actions of acetylcholine - a neurotransmitter in the nervous system - or inhibit the function of NMDA receptors.

Published this month in <u>Nature Neuroscience</u>, a team led by Professor Kei Cho from Bristol's Faculty of Medicine and Dentistry, detail how



they discovered a novel interaction between NMDA receptors and muscarinic acetylcholine receptors (mAChRs), whereby activating the latter can depress NMDA receptor function. This novel form of synaptic plasticity was located in the hippocampus, a centre of learning and memory in the brain.

Their findings suggest that this <u>molecular mechanism</u> could be targeted for new drug developments for the treatment of Alzheimer's disease - stimulating mAChRs would reduce the strength of synaptic transmission mediated by the activation of NMDA receptors. This could be beneficial in targeting the excitotoxicity caused by NMDA receptors, thereby potentially reducing the widespread <u>cellular damage</u> seen in the brains of people with Alzheimer's disease.

However, Prof Cho cautioned that while there are several mAChR agonists available for research purposes, they would require further evaluation using various Alzheimer's disease models, including clinical trials, before they could be readily translated into a usable treatment.

Professor Graham Collingridge FRS, Director of the MRC Centre for Synaptic Plasticity and a member of the research team, said: "Basic research such as this is vital if we want to understand the causes of Alzheimer's disease and other devastating <u>brain disorders</u>," yet added a note of caution, saying "we are still a long way from finding a cure; more investment in basic research, not less as advocated by Government, is desperately needed."

Professor Stafford Lightman, co-founder of Bristol Neuroscience, added: "This is yet another example of how Bristol Neuroscience has brought together teams from different faculties within the University of Bristol to tackle some of the most important challenges facing society."



Provided by University of Bristol

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