NMDA RECEPTOR MODULATORS AS NOOTROPIC THERAPIES IN AGING BRAIN

https://neurodegenerationresearch.eu/survey/nmda-receptor-modulators-as-nootropic-therapies-in-aging-brain/

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Country

USA

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NMDA RECEPTOR MODULATORS AS NOOTROPIC THERAPIES IN AGING BRAIN

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1

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Research Abstract

? DESCRIPTION (provided by applicant): Age-related memory loss is a growing public health issue which will be magnified in the coming decades by increasing life expectancies and the aging baby boomer population. Age is the most important risk factor for developing dementia:

17% of the population between 70 and 79 has some form of dementia, 50% between 80 and 89, and 65% of those 90 or older. The therapeutic value of cholinesterase inhibitors (CIs), which are the standard form of treatment for dementia in Alzheimer's disease, is modest. CIs delay the cognitive decline by only 6-12 months, and their use is limited by cardiovascular contraindications. The NMDA receptor is a promising target for addressing age-related memory loss. Age-related decline in NMDAR protein expression and function is observed in humans and other mammals that are directly correlated with memory impairment and performance in learning-dependent tasks. However, most of the known compounds active at the NMDAR produce strong side effects, greatly limiting their clinical utility. Naurex has developed a novel class of orally bioavailable NMDAR partial agonists, based on the company's NMDAR partial agonist GLYX-13, which has demonstrated exceptional safety and efficacy in clinical trials for depression. GLYX-13 and its NRX mimetics improve learning and memory indicators in behavioral assays in rats and enhance long term potentiation in hippocampal slices. Importantly, they do not produce sedative or psychotomimetic effects. The scope of this Phase I project is to identify a lead drug candidate for age-related memory loss within the NRX library using advanced models of aging. To this end, our Specific Aims are: SA1: Perform full dose-response curves in both young and learning impaired aged rats evaluating 18 lead orally-bioavailable NRX isomers for restoring synaptic plasticity and modulating NMDA receptors in hippocampal slices from young and aging brains. SA2: Use full dose-response curves to evaluate the two best compounds screened in SA1 for the ability to enhance cognitive functioning in normal aging using the Morris water maze task. SA3: Use full dose-response curves to evaluate the two best compounds screened in SA1 for the ability to increase the total number of mature spines in dendrites of hippocampal neurons. On its completion, the proposed Phase I study will yield a lead molecule that will be advanced to IND-enabling studies and subsequent clinical trials for treating age-related cognitive decline.

Further information available at:

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