



**Paul Newhouse, M.D.**

Vanderbilt University  
Nashville, Tennessee

2018 The Part the Cloud to RESCUE Brain Cell Degeneration in Alzheimer's Disease-  
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**M1-PAM VU319 Effects on Network Connectivity in Mild Cognitive Impairment: A Proof-of-Concept Study**

*This is a Phase 2a clinical trial to test if a novel drug that stimulates specific brain cell proteins could improve memory and attention in people with Mild Cognitive Impairment.*

**PI**

- M.D., Loyola University Stritch School of Medicine, 1977
- Director of the Vanderbilt Center for Cognitive Medicine and the Division of Geriatric Psychiatry
- Diplomat of the American Board of Psychiatry and Neurology
- Frequent consultant to pharmaceutical and biotechnology companies

**STUDY**

- CADRO category: Translational Research and Clinical Intervention
- Past Association funding helped Dr. Newhouse understand the effects of estrogen in preserving cognitive function in aging women.

**Background**

Nerve cells in the brain communicate by releasing and sensing signaling molecules called neurotransmitters. One neurotransmitter, called acetylcholine, is particularly important for attention and memory. People with Alzheimer's tend to have a decreased number of nerve cells that sense and respond to acetylcholine. This limits the amount of nerve cells connections in the brain and can make it harder for brain cell networks to communicate.

Drugs that broadly increase acetylcholine could help improve brain cell connectivity, but have only proven modestly successful in people with Alzheimer's. Drugs that target specific proteins on brain cell surfaces (called "receptors") that sense acetylcholine might offer a more focused and effective strategy. Dr. Paul Newhouse and colleagues have been studying a drug, M1-PAM VU319 that stimulates a specific acetylcholine receptor protein. Selectively targeting this particular protein could be one way to help restore brain cell connections in people with Alzheimer's.

**Research Plan**

Dr. Newhouse and colleagues are currently conducting Phase 1 safety and tolerability studies in healthy volunteers using M1-PAM VU319 and have now proposed a Phase 2a clinical trial to study the drug's efficacy in people with mild cognitive impairment, a stage of cognitive decline that precedes Alzheimer's. Dr. Newhouse will study whether a 28-day regimen of the new drug can improve memory or attention in this population.

**Impact**

If successful, this study could provide additional support for a novel therapeutic designed to reduce Alzheimer's symptoms. Brain scans collected during the study may also reveal how brain connectivity correlates with a person's attention and memory. This multi-pronged approach multi-modal data collection approach could help to predict success of the drug M1-PAM VU319 in larger trials in the future.