

# Long-Term Nicotine Treatment of Mild Cognitive Impairment

<https://www.neurodegenerationresearch.eu/survey/long-term-nicotine-treatment-of-mild-cognitive-impairment/>

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### Country

USA

## Title of project or programme

Long-Term Nicotine Treatment of Mild Cognitive Impairment

## Source of funding information

NIH (NIA)

## Total sum awarded (Euro)

€ 8,720,526.61

## Start date of award

15/09/2015

## Total duration of award in years

3

## The project/programme is most relevant to:

Alzheimer's disease & other dementias

## Keywords

Acquired Cognitive Impairment... Aging... Alzheimer's Disease... Alzheimer's Disease including Alzheimer's Disease Related Dementias (AD/ADRD)... Behavioral and Social Science... Brain Disorders... Clinical Research... Clinical Research - Extramural... Clinical Trials and Supportive Activities... Dementia... Neurodegenerative... Neurosciences... Prevention... Translational Research

## Research Abstract

? DESCRIPTION (provided by applicant): Precursor conditions to Alzheimer's disease (AD) such as Mild Cognitive Impairment (MCI) are now a target of patient identification and potential treatment, as studies clearly showing that the risk of progression to dementia is very high. Despite attempts to develop new treatments for AD and its precursor, MCI, methods of interrupting the course of illness and preventing progression have proven elusive. Treatment strategies for AD based on molecular pathologies (such as A $\beta$ ) have thus far produced equivocal or negative results. Investigation is thus shifting to the potential treatment of precursor conditions, including MCI, pre-MCI, and subjects at risk with identification via genetics or other biomarkers. Losses of cholinergic neurons and particularly nicotinic cholinergic receptors have been shown to be principally related to cognitive decline in AD. However, approved treatments for AD have not significantly improved MCI, despite clear evidence of alteration of cholinergic function at this stage. Thus nonspecific enhancement of cholinergic function does not appear to be a fruitful strategy for either enhancing long-term cognitive functioning in MCI, nor retarding the progression to AD. There is a continuing search for new treatments that will improve cognitive symptoms while potentially be disease modifying. Nicotine may be one of those molecules and is easily available, inexpensive, and easy to use. We have performed a double-blind 6 month pilot trial showing that nicotine treatment significantly improved cognitive performance in the areas of attention and episodic memory, showed improving global ratings of functioning and self-rated memory problems, and was well tolerated with an impressive safety profile and no abuse liability (Newhouse, P., K. Kellar, et al. (2012). *Neurology* 78(2): 91-101). We now propose a definitive 2-year multi-center clinical trial to test whether daily transdermal nicotine will produce sustained cognitive, clinical, and functional benefits in patients with MCI. Our primary hypothesis is that transdermal nicotine will enhance cognitive performance and symptoms of cognitive dysfunction compared to placebo and that this difference will be sustained over two years. We also plan to test in a smaller sub study whether there is evidence that nicotine treatment will affect the underlying biology related to MCI/AD by monitoring biological markers including structural and functional brain imaging and measures of AD pathology in spinal fluid. This proposed study has broad clinical and scientific significance. If the hypotheses were validated, these findings would support a novel, broadly available, and inexpensive intervention for MCI and would encourage early treatment intervention to improve symptoms and/or retard progression of cognitive impairment. This would be the longest trial of nicotine or nicotinic agonists to date and if successful would lead to combined trials with other symptomatic agents and/or agents that might directly interact with A $\beta$  or tau- related mechanisms.

### **Lay Summary**

**PUBLIC HEALTH RELEVANCE:** Mild cognitive impairment (MCI) is a condition in which patients experience a decrease in memory and attention and often precedes Alzheimer's disease. We previously showed in a six-month long study that treatment with transdermal nicotine patches improved symptoms in MCI. In this longer, definitive two-year study, our primary hypothesis is that nicotine will enhance attention and memory in 300 patients with MCI, that this improvement will improve overall functioning, and that this difference will be sustained over two years.

**Further information available at:**

### **Types:**

Investments > €500k

**Member States:**

United States of America

**Diseases:**

Alzheimer's disease & other dementias

**Years:**

2016

**Database Categories:**

N/A

**Database Tags:**

N/A