

# "Non-invasive brain modulation in MCI patients: effects on executive functions through a randomized controlled trial of rTMS and fMRI"

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## Introduction

Executive functioning deficits are frequently observed in prodromal phase of Alzheimer's Disease (AD) similarly to the episodic memory impairment.<sup>1</sup> They are associated with conversion of Mild Cognitive Impairment (MCI) to dementia AD-related, functional decline and clinical progression of dementia. The "executive control" depends on the integrity of cross-cortical (frontal-temporo-parietal) and cortico-subcortical (frontal) networks, early impaired in MCI neuroimaging studies, revealing a "disconnection syndrome".<sup>2</sup> Repetitive Magnetic Transcranial Stimulation (rTMS), a non-invasive brain stimulation technique, can modulate cortical excitability inducing long-lasting cumulative modifications of synaptic plasticity, even at brain sites distant from those stimulated.<sup>3</sup>

## Methods

Within the AIRalzh-Coop<sup>®</sup> network, a randomised, double-blind, sham-controlled trial was performed, enrolling 30 patients newly diagnosed with MCI (Albert 2011). They were randomly assigned to receive 20 consecutive sessions of either active TMS or sham, over the dorsolateral prefrontal cortex bilaterally (10Hz rTMS at 80% of motor threshold, 2000 pulses per session). Neuropsychological (NPS) and Functional Magnetic Resonance Imaging (fMRI) assessments were performed at baseline, after the last TMS session and after six months.

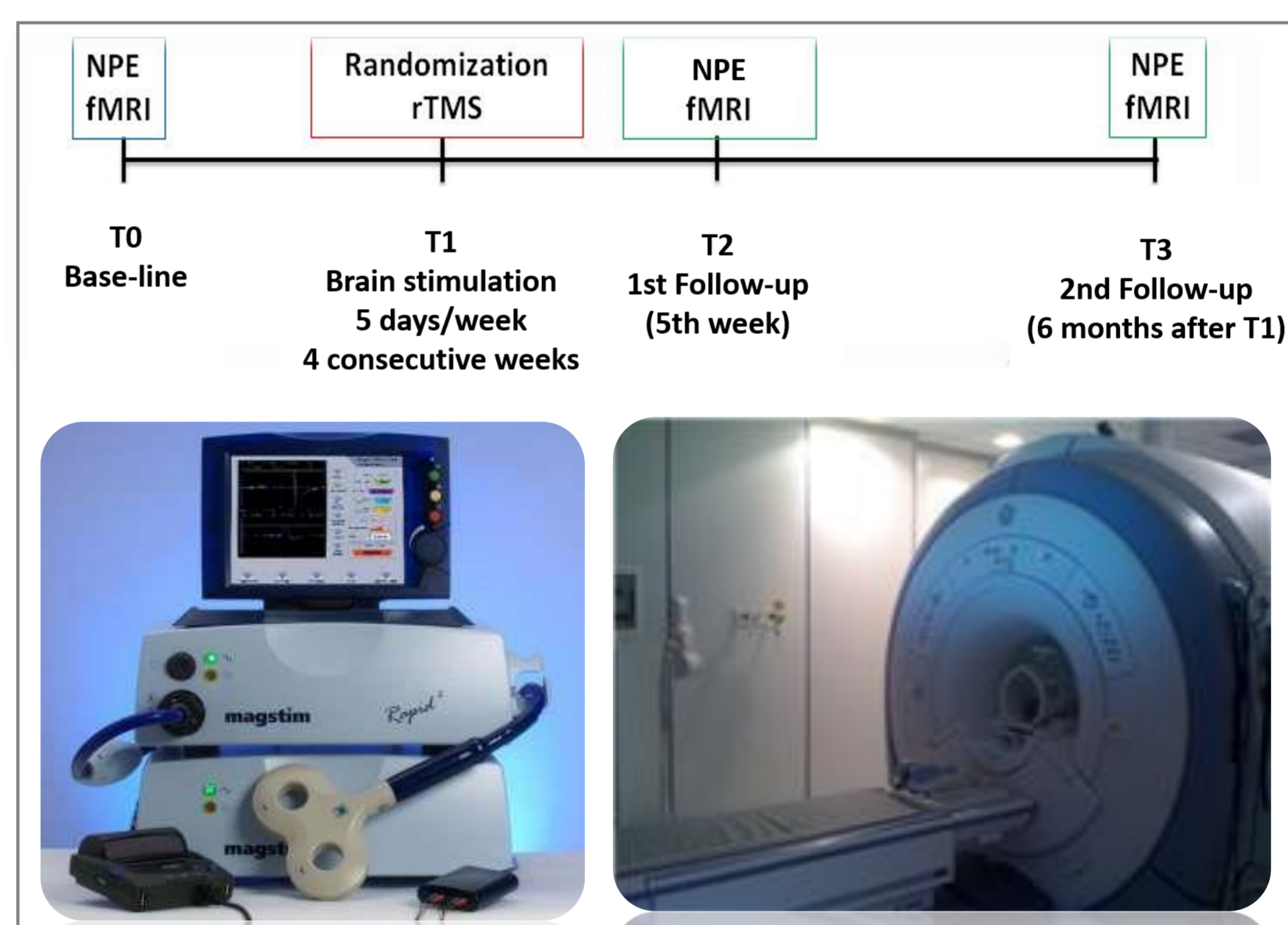
## Expected Results

To detect in treated patients:

1. Possible NPS improvements, in particular of executive functions, episodic memory and attention (skills needed to preserve ecological functioning).
2. Changes in the resting-state functional connectivity of the networks underlying the executive functioning (such as Executive, Salience, Fronto-Parietal, and Default Mode Networks).
3. Evidence of short- and long-lasting effects on cognition and brain networks.

## Conclusions and future implications

The main aim of such study was to demonstrate effectiveness and efficiency of a non-invasive therapeutic intervention on executive functions of MCI patients. rTMS may be a promising strategy to delay conversion of MCI to dementia and disease progression, through the improvement of the executive control and than preserving functional abilities. Given the individual and social costs of Dementia, the encouraging data regarding the safety of rTMS, and the manageability of the technique in terms of human and professional resources, we might hypothesize to translate our research model into clinical practice, to support the currently routine treatments.



## Bibliografia

1. Harrington MG, et al. Executive Function Changes before Memory in Preclinical Alzheimer's Pathology: A Prospective, Cross-Sectional, Case Control Study. *PLoS One*. 2013.
2. Yuan P, et al. Prefrontal cortex and executive functions in healthy adults: a meta-analysis of structural neuroimaging studies. *Neurosci Biobehav Rev*. 2014.
3. Lefaucheur JP, et al. Evidence-based guidelines on the therapeutic use of repetitive transcranial magnetic stimulation (rTMS). *Clin Neurophysiol*. 2014.