# Cortical Excitability in Alzheimer's Disease: Meta-Analysis of Transcranial Magnetic Stimulation Studies

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## What is transcranial magnetic stimulation (TMS)?

TMS is a non-invasive brain stimulation technique based on Faraday's principle of electromagnetic induction (i.e., changing magnetic field induces a changing electric field and vice versa). TMS has been closely investigated as a therapeutic tool for a number of clinical conditions (Chou et al. 2015; Chou et al., 2020). It is also a valuable neuro-scientific method that can be used to characterize cortical excitability in healthy adults and patients with neurodegenerative disorders.

## What is the purpose of this meta-analysis?

To quantify alterations in cortical excitability associated with Alzheimer's disease (AD) and mild cognitive impairment (MCI)

## How did we perform the meta-analysis?

We searched PubMed and Web of Science using combinations of the following terms: Alzheimer's disease or mild cognitive impairment and transcranial magnetic stimulation. Standardized mean difference (i.e., Cohen's *d*) was used to express the effect size of group differences.

## What did we find?

Twenty-two studies comprising 839 participants (421 AD; 74 MCI; 344 controls) were included in this analysis. Patients with AD and MCI exhibited significantly (1) lower motor threshold (MT), effect size $d = 1.08$, (2) reduced short-latency afferent inhibition (SAI), $d = 1.09$, and (3) reduced short-interval intracortical inhibition (SICI), $d = 0.62$. All the comparisons had $p$ values $< .0001$.

## How to interpret the findings?

Previous pharmaco-TMS studies (Ziemann, 2013) show that (1) MT is associated with function of voltage-gated sodium channels, which are essential for regulating axonal excitability; (2) SAI can be used to probe central cholinergic function; and (3) SICI is a measure of $GABA_A$ receptor-mediated inhibitory neurotransmission. Thus, the pooled evidence from our meta-analysis suggests the existence of cortical hyper-excitability as documented by decreased MT as well as reduced inhibition and impaired cholinergic function as measured by the the SICI and SAI, respectively. Future studies will be needed to examine whether these cortical excitability measures can be used to differentiate prodromal dementia from normal healthy aging.

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