

Non-invasive ultra-high-frequency light stimulation preserves entorhinal cortex integrity in Alzheimer’s Disease

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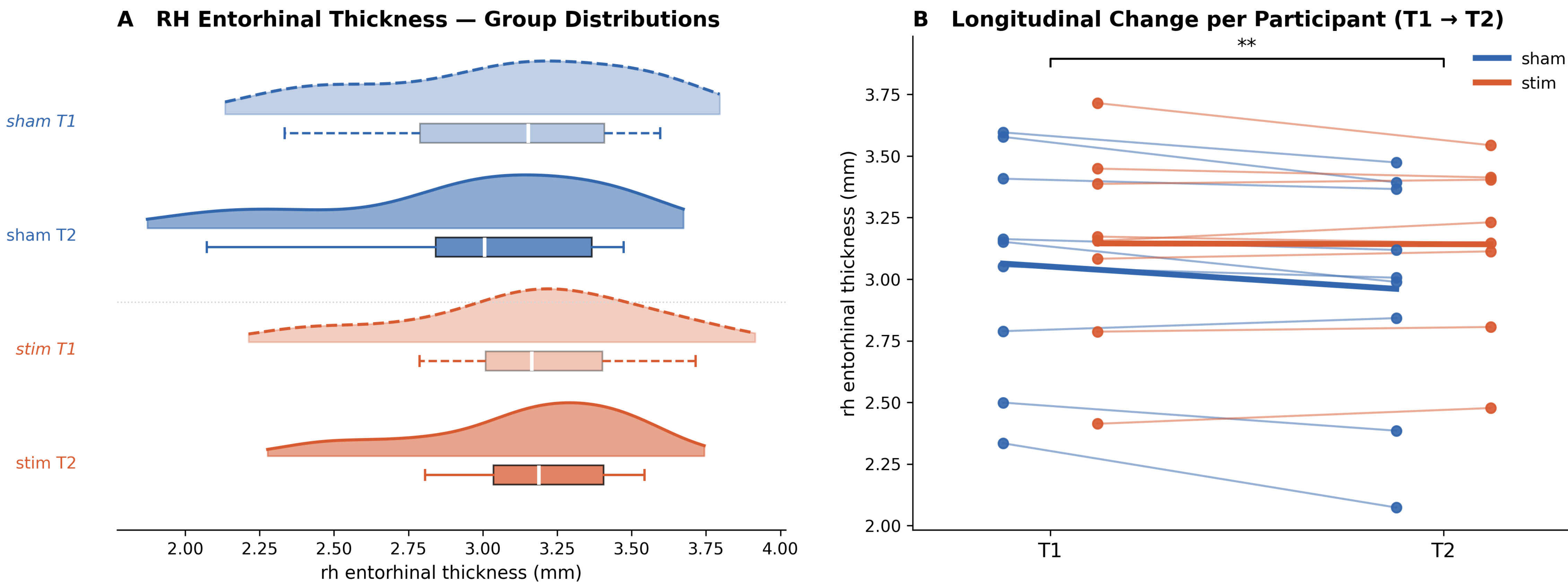
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Alzheimer's disease (AD) represents one of the most pressing public health challenges of our time, with global prevalence continuing to rise [1,2]. Despite recent regulatory approvals, broadly effective disease-modifying treatments remain elusive[3,4]. The urgent need for novel therapeutic strategies has driven interest in non-pharmacological approaches targeting the neural mechanisms underlying memory consolidation. In this randomized, sham-controlled trial, we test whether ultra-high-frequency light stimulation that induces sharp wave ripples can thereby slow disease progression in a mild cognitive impairment (MCI) cohort. Participants received one hour of daily home-based stimulation over six months.

We focus on the entorhinal cortex (EC) as our primary region of interest. It is the principal gateway between neocortex and hippocampus, and one of the earliest, most reliable structural markers of AD progression. Here, we report MRI outcomes evaluating entorhinal integrity as a biomarker of treatment response.

Right Entorhinal Cortex Thickness by Treatment Group



Ongoing single-center study at Charité, Berlin.

Target: 36 participants across 6 months

MRI: Siemens Prisma 3T

Processing: freesurfer longitudinal pipeline

ANCOVA: EC thickness (T2) ~ EC thickness (T1) + age + sex + education + group

3 months – interim (N=17):

Sham (n = 9): age 65.7 ± 9.2 years | 5 female, 4 male | education 7.2 ± 2.3 years

Stim (n = 8): age 70.0 ± 6.9 years | 4 female, 4 male | education 6.5 ± 2.6 years

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The interim results of the current study show that the stimulation group preserved right entorhinal cortex thickness while the sham group declined. This pattern is consistent with the hypothesis that entrainment of sharp wave ripples via non-invasive sensory stimulation may confer neuroprotective effects in memory-relevant cortical regions. Given the preliminary sample size of n=17, replication in a larger pre-registered trial is warranted. These results nonetheless support the feasibility of home-based light stimulation as a non-pharmacological intervention in MCI and motivate further investigation.