# Effects of Theta Transcranial Alternating Current Stimulation Over Fronto-temporal Cortex on the Efficacy and Neural activity of Patients with Alzheimer's Disease

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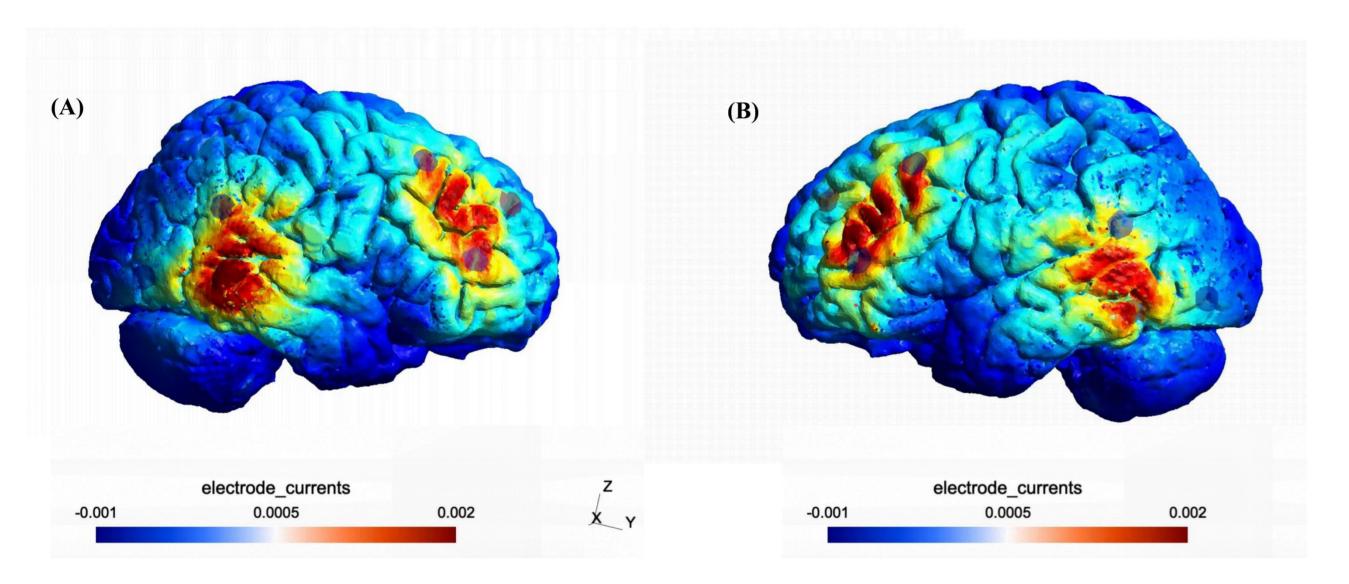
## **BACKGROUND:**

Alzheimer's disease (AD), as an irreversible progressive neurodegenerative disease, is pathologically manifested by amyloid  $\beta$  (A $\beta$ ) deposition and synaptic transmission dysfunction<sup>1</sup>, resulting in dysfunction of central executive network (CEN) and default mode network (DMN) with fronto-temporal lobe as the hub nodes<sup>2</sup>. Studies have shown that theta oscillations impaired is a neurological marker of memory impairment in AD<sup>3</sup>. Therefore, we apply dual-site fronto-temporal high-density transcranial alternating current stimulation (HD-tACS) to improve brain functional connectivity and cognitive dysfunction by modulating the theta oscillation of the cognitive network.

### **METHODS:**

10 AD patients received 40min 6Hz dual-site high-density tACS treatments for 12 sessions targeting bilateral fronto-temporal lobes. Cognitive assessments, including the Mini Mental State Examination (MMSE), Montreal Cognitive Assessment (MoCA) and Alzheimer's Disease Assessment Scale, Cognitive Subscale (ADAS-Cog) were assessed before treatments(W0), at the end of treatments (W4), and at 8-week follow-up (W12). The resting state functional MRI was collected before and after treatments to evaluate the changes of degree centrality and brain functional connectivity in AD patients.

Electrode Montage Using the sim NIBS software simulates the theoretical electric field and current intensity to ensure the efficiency of the electrode montage. A:Simulated electric field diagram of the right fronto-temporal region. B:Simulated electric field diagram of the left fronto-temporal region.



## **KEY WORDS:**

Alzheimer's disease, High-Density transcranial Alternating Current Stimulation, Theta Oscillations, Degree Centrality, Functional connectivity.

#### **RESULTS:**

1. Cognitive scale improvements in AD patients after 6Hz dual-site tACS treatment

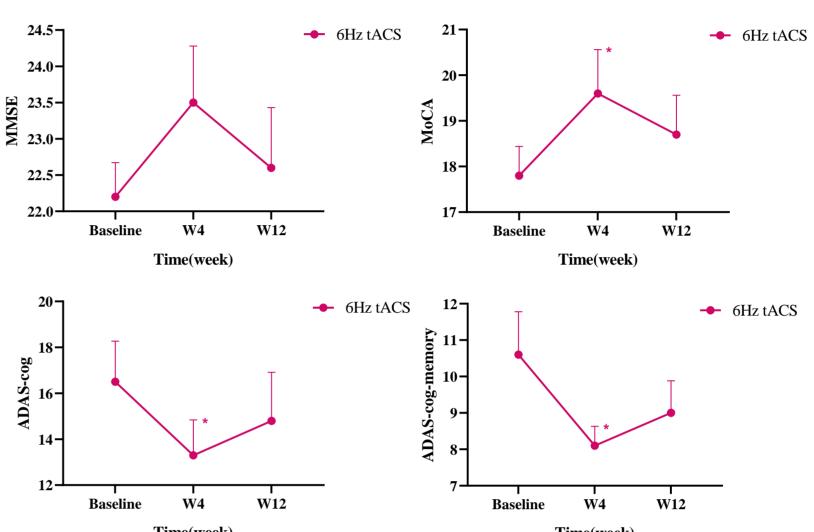
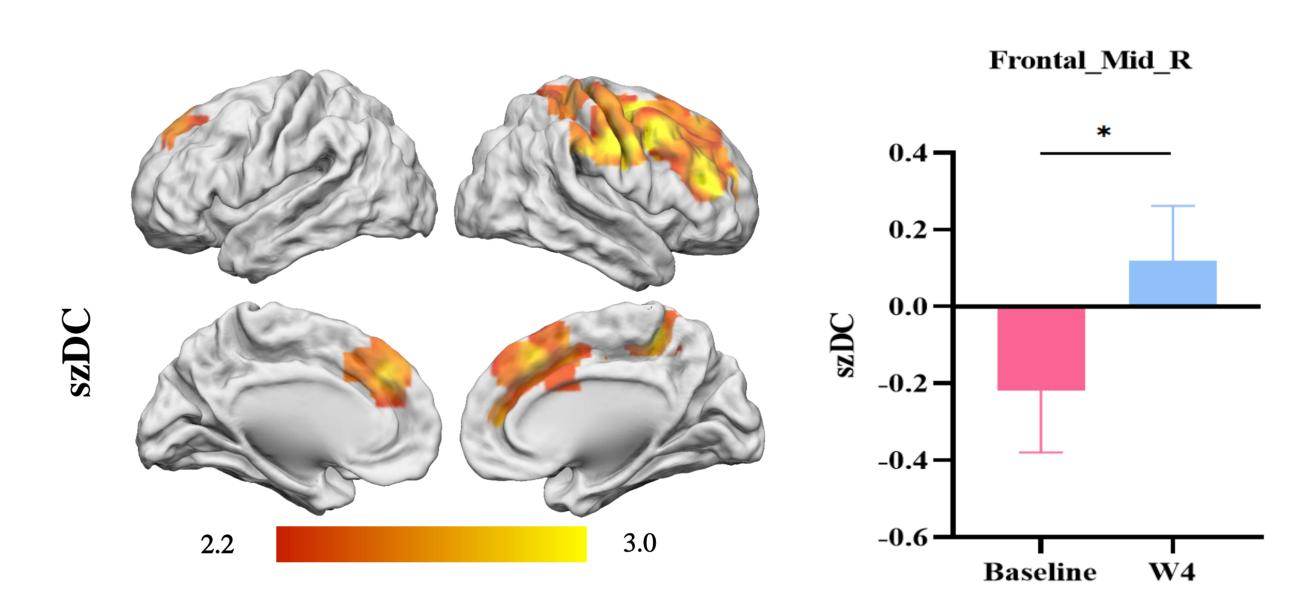


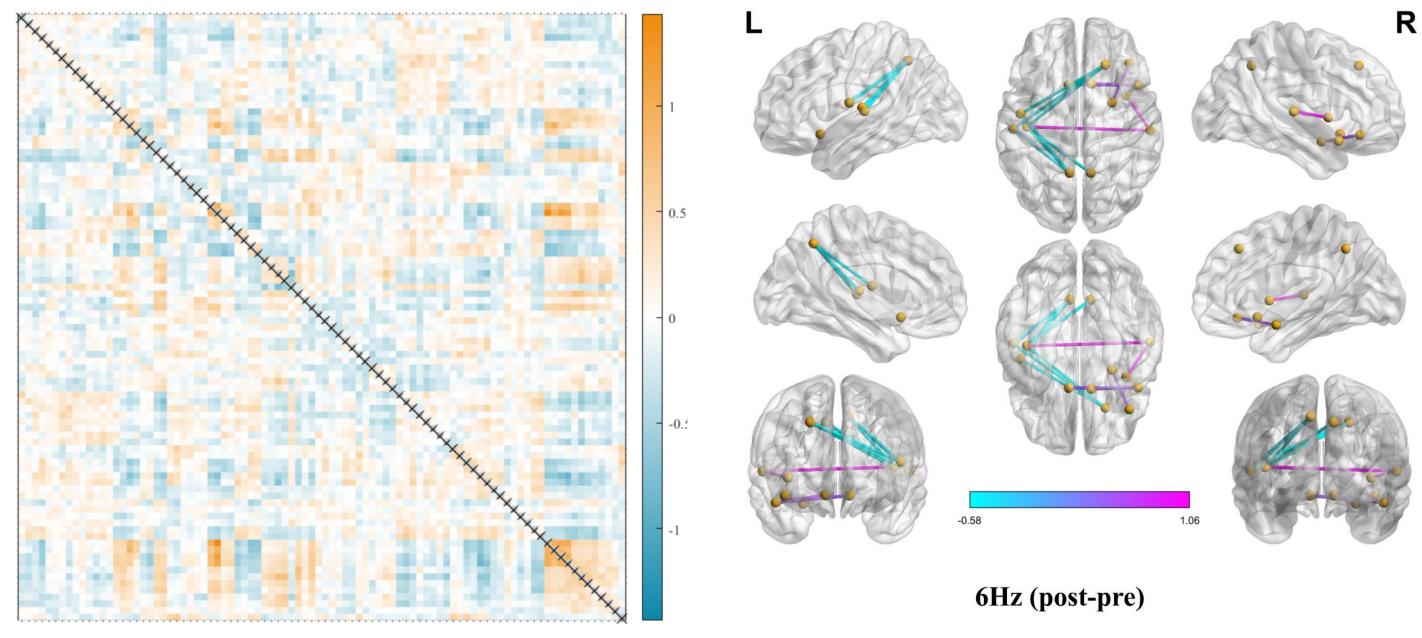
Figure 1. Scores on the cognitive scales before, after treatment, at 8-week follow-up in patients with AD. Error bars represent standard error of mean. MMSE: Mini-mental State Examination; MoCA: Montreal Cognitive Assessment; ADAS-cog: AD assessment scale cognitive subscale; tACS: transcranial Alternating Current Stimulation. W0: at baseline; W4: after treatment at week 4; W12: 8-week followup at week 12. \*P<0.025 vs pre

2. Changes of DC values in AD patients after 6Hz dual-site tACS treatment



**Figure 2. Changes of DC values before and after treatment in 6Hz dual-site -tACS group**. DC:Degree centrality. tACS: transcranial Alternating Current Stimulation.AlphaSim correction was performed. p <0.05 was considered statistically significant.

3. Functional connection changes between ROIs in AD patients after 6Hz dual-site tACS treatment



**Figure 3.** Functional connection changes between ROIs before and after treatment in 6Hz dual-site tACS group. Functional connectivities between right inferior frontal gyrus and right amygdala, right superior temporal gyrus and right insula, L-hescl increased. The functional connectivity between the L-hescl and bilateral precuneus decreased, which reflects that 6Hz dual-site tACS can improve the topological properties of CEN and DMN in AD patients. tACS: transcranial Alternating Current Stimulation. Bonferroni correction was performed. p <0.001/(90\*89/2) was considered statistically significant.

# **CONCLUSION:**

These findings demonstrate dual-site theta tACS improves cognitive function in AD patients by modulating long range brain functional connectivity in the CEN and DMN networks.

## References

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