

Consistent tACS Gains in MCI: A Meta-analysis Across the Aging and Alzheimer’s Spectrum

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KEY TAKEAWAY: tACS produces consistent, statistically homogeneous cognitive gains in MCI ($g = 0.59$; $I^2 = 0\%$) — the most stable clinical window for standardized neuromodulation across the aging and Alzheimer’s spectrum.

INTRODUCTION

- Cognitive decline (healthy aging, MCI, AD) is a major public-health challenge.
- tACS: non-invasive, low-cost; modulates neural oscillations (theta) linked to memory.
- Efficacy debated — high methodological heterogeneity.
- **OBJECTIVE:** First tACS meta-analysis in adults ≥ 60 y to find stable clinical signals.

METHODS

Figure 1 - PRISMA Flow Diagram

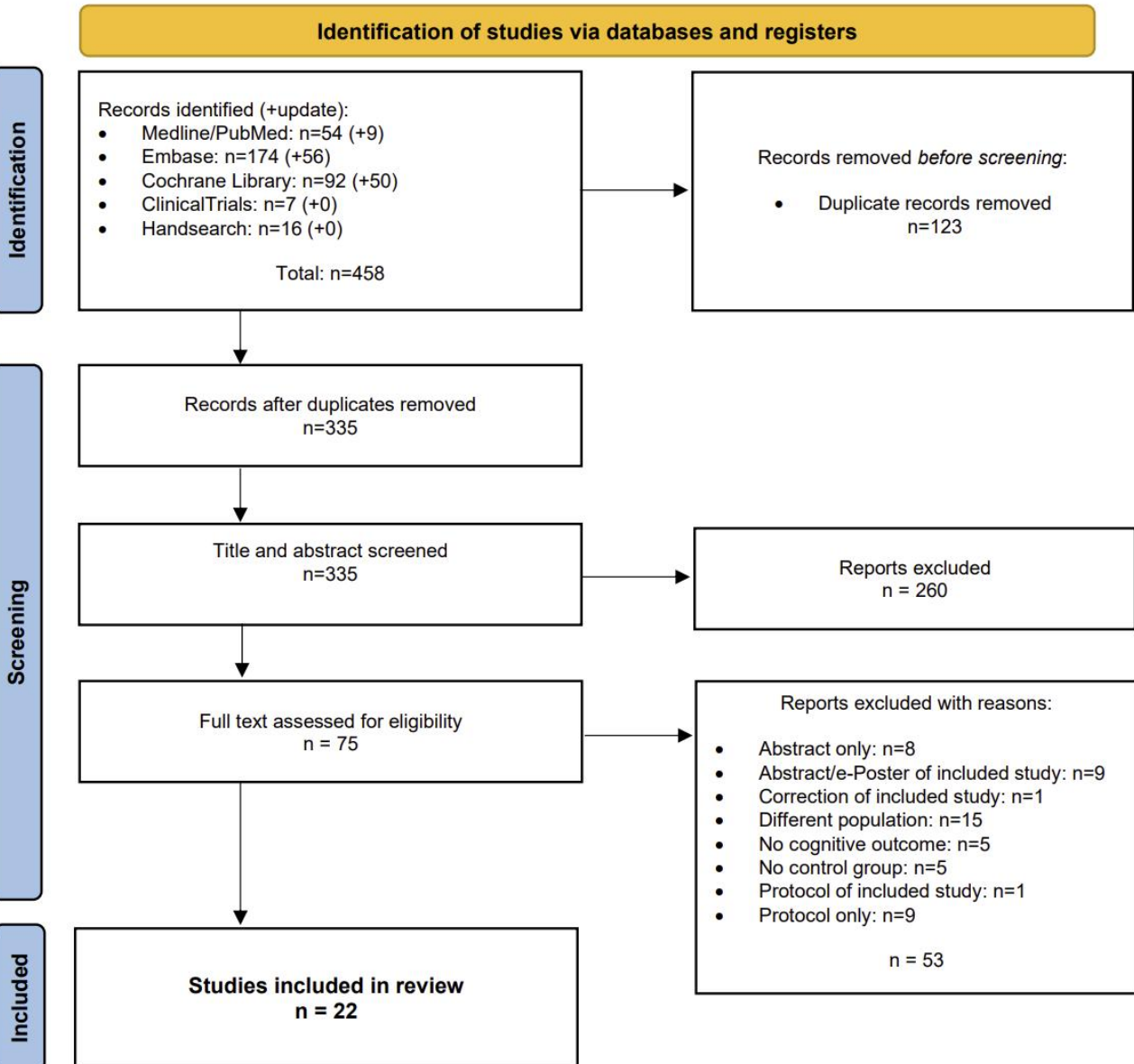


Figure 2 - Forest plot of all included studies-effects and pooled estimates (with and without the outlier)

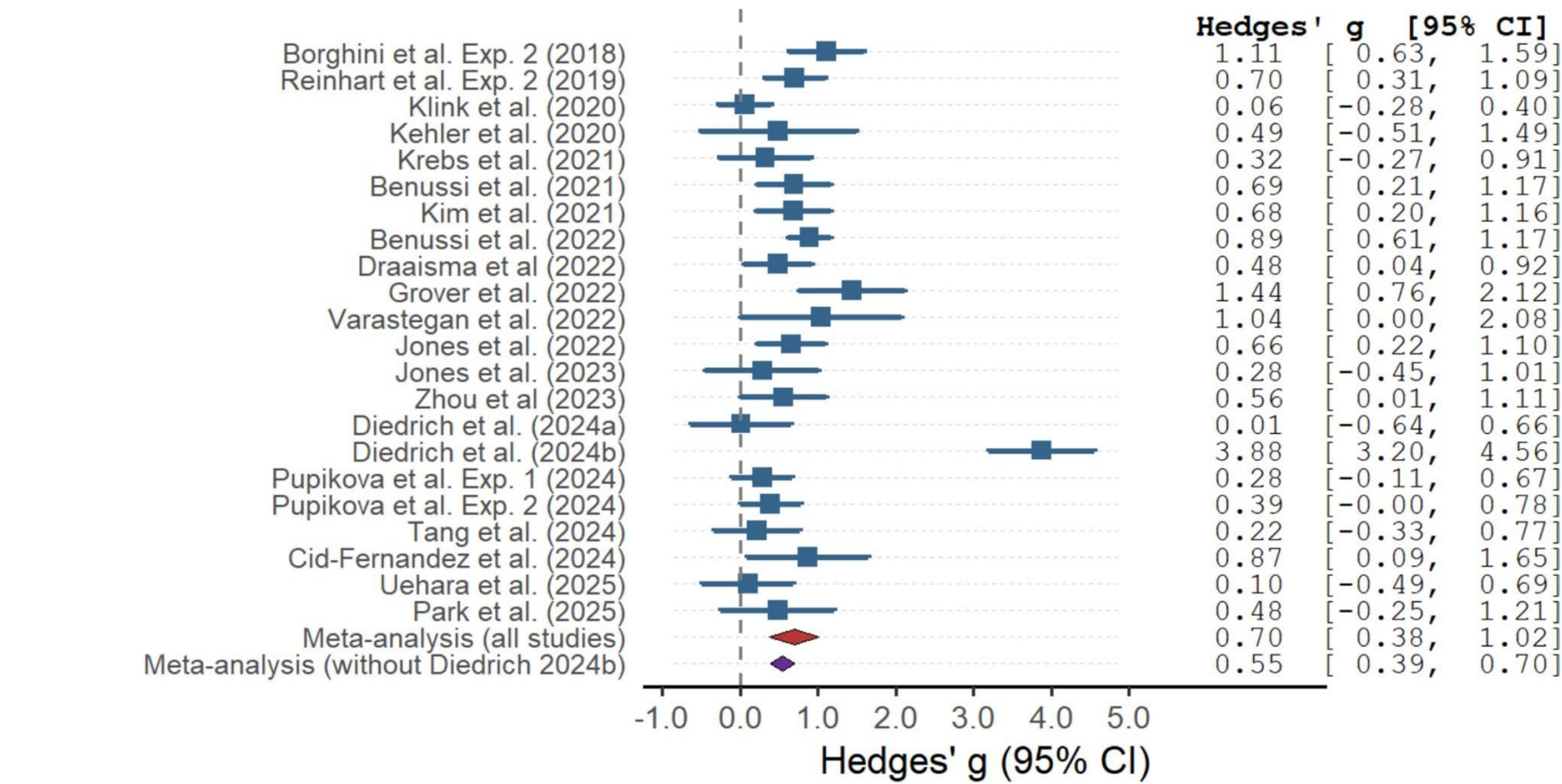


Fig. 2 - Squares show the study-specific standardized mean differences (Hedges' g) and horizontal bars their 95% confidence intervals (CI). The vertical dashed line marks the null ($g = 0$). Positive values indicate better cognitive performance with tACS; outcomes for which lower scores reflect improvement (e.g., reaction time) were sign-reversed so that all effects are aligned in the same direction. Diamonds summarize the random-effects meta-analytic estimates: the red diamond is the pooled effect including all 19 studies ($g = 0.70$, 95% CI 0.38–1.02; heterogeneity $I^2 = 88.5\%$, $\tau^2 = 0.495$; $p < .0001$) and the purple diamond is the pooled effect from the sensitivity analysis excluding the influential outlier (Diedrich et al., 2024b), yielding a smaller but still significant estimate ($g = 0.56$, 95% CI 0.39–0.70; $I^2 = 47.1\%$, $\tau^2 = 0.056$; $p = .0053$) and improved model stability. The outlier (Hedges' $g = 3.88$) was flagged by influence diagnostics as highly influential (studentized residual = 7.81, Cook's distance = 0.868, DFBETAs = 1.96); see Methods/Results for details. Exp = Experiment.

- 22 studies | 826 participants.
- Overall effect: $g = 0.70$ (95% CI 0.38–1.02); $I^2 = 88.5\%$. Outlier-robust $g = 0.55$ (0.39–0.70).
- MCI: $g = 0.59$ (0.32–0.87), $I^2 = 0\%$ — homogeneous, stable signal.
- Healthy: $g = 0.83$ ($I^2 = 94.9\%$) | AD: $g = 0.50$ ($I^2 = 62.2\%$) — high variability.
- Memory = most responsive domain. No serious adverse events.

RESULTS

Figure 3 - Population-specific effects of tACS on cognition in older adults: subgroup random-effects meta-analyses (REML–Hartung–Knapp)

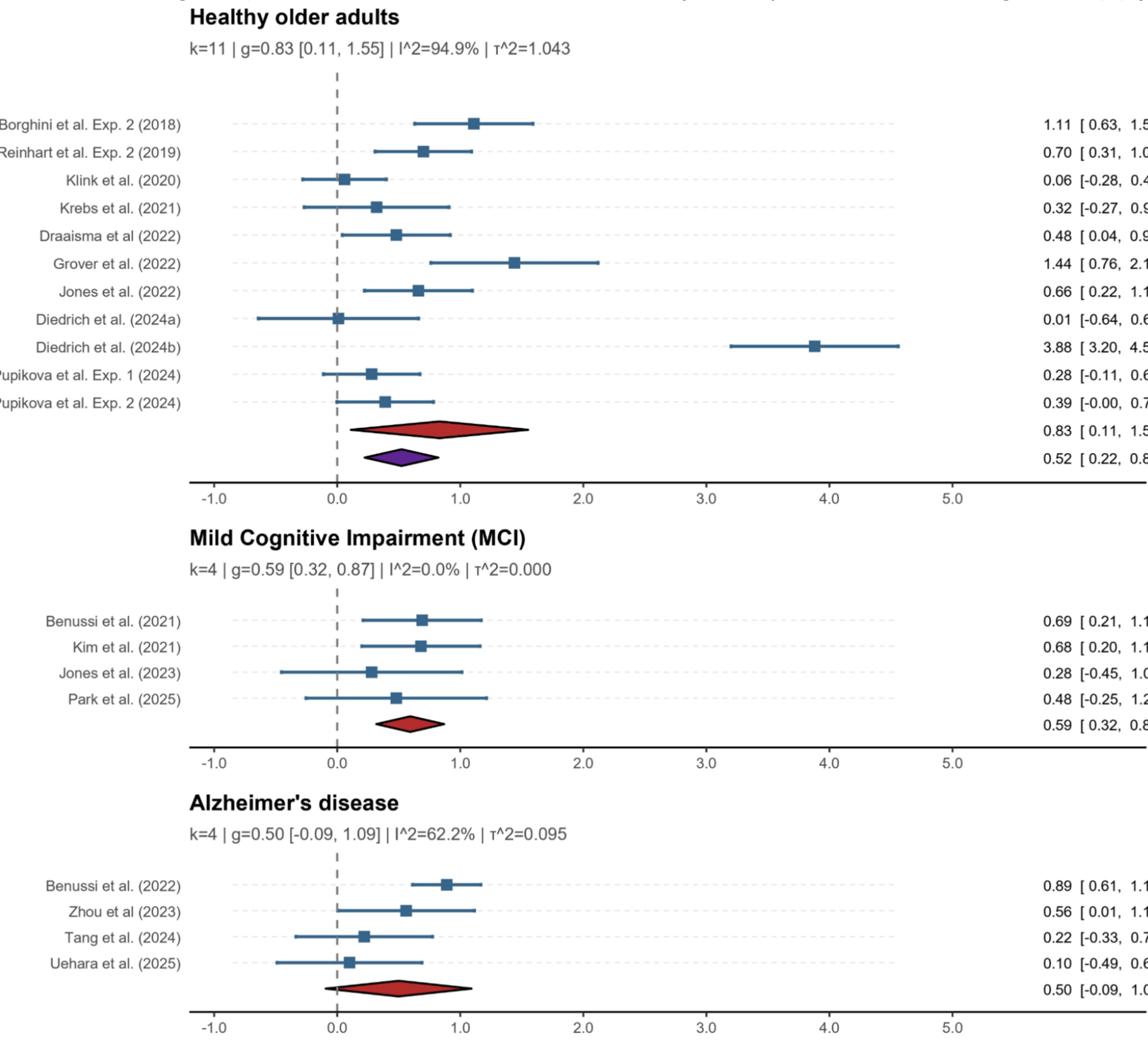


Fig. 3 - Subgroup random-effects meta-analyses (REML with Hartung–Knapp adjustments) of Hedges' g for healthy older adults, mild cognitive impairment (MCI), and Alzheimer's disease (AD). Squares show study-level effects and 95% CIs; the dashed vertical line marks the null ($g = 0$). Pooled estimates (diamonds) were: Healthy ($k = 11$), $g = 0.83$ (95% CI 0.11 to 1.55), $I^2 = 94.9\%$, $\tau^2 = 1.043$; MCI ($k = 4$), $g = 0.59$ (95% CI 0.32 to 0.87), $I^2 = 0.0\%$, $\tau^2 = 0.000$; AD ($k = 4$), $g = 0.50$ (95% CI -0.09 to 1.09), $I^2 = 62.2\%$, $\tau^2 = 0.095$. In the Healthy panel, the red diamond is the pooled estimate including all studies; the purple diamond is a sensitivity analysis excluding the influential outlier (Diedrich et al., 2024b). Three studies with mixed populations (subjective memory complaints; MCI with mild–moderate dementia; subjective memory decline/MCI/AD) were omitted from these panels but were included in moderator analyses. Abbreviations: tACS, transcranial alternating current stimulation; MCI, mild cognitive impairment; AD, Alzheimer's disease; CI, confidence interval.

CONCLUSIONS

- Consistent cognitive gains in MCI — more stable than healthy aging or AD.
- Robust memory response fits theta-band modulation.
- MCI homogeneity supports standardized neuromodulation protocols.
- Next: standardized, dose-response designs.

REFERENCES

1. Freitas da Costa B, et al. Targeting brain rhythms to support cognition in aging: a meta-analysis of tACS across healthy aging, MCI, and Alzheimer's disease. GeroScience. 2026. doi:10.1007/s11357-026-02312-w
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