



Preliminary Evidence for Individual Response Variability to Cerebellar iTBS Over Right Crus I Across the Aging Spectrum

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BACKGROUND

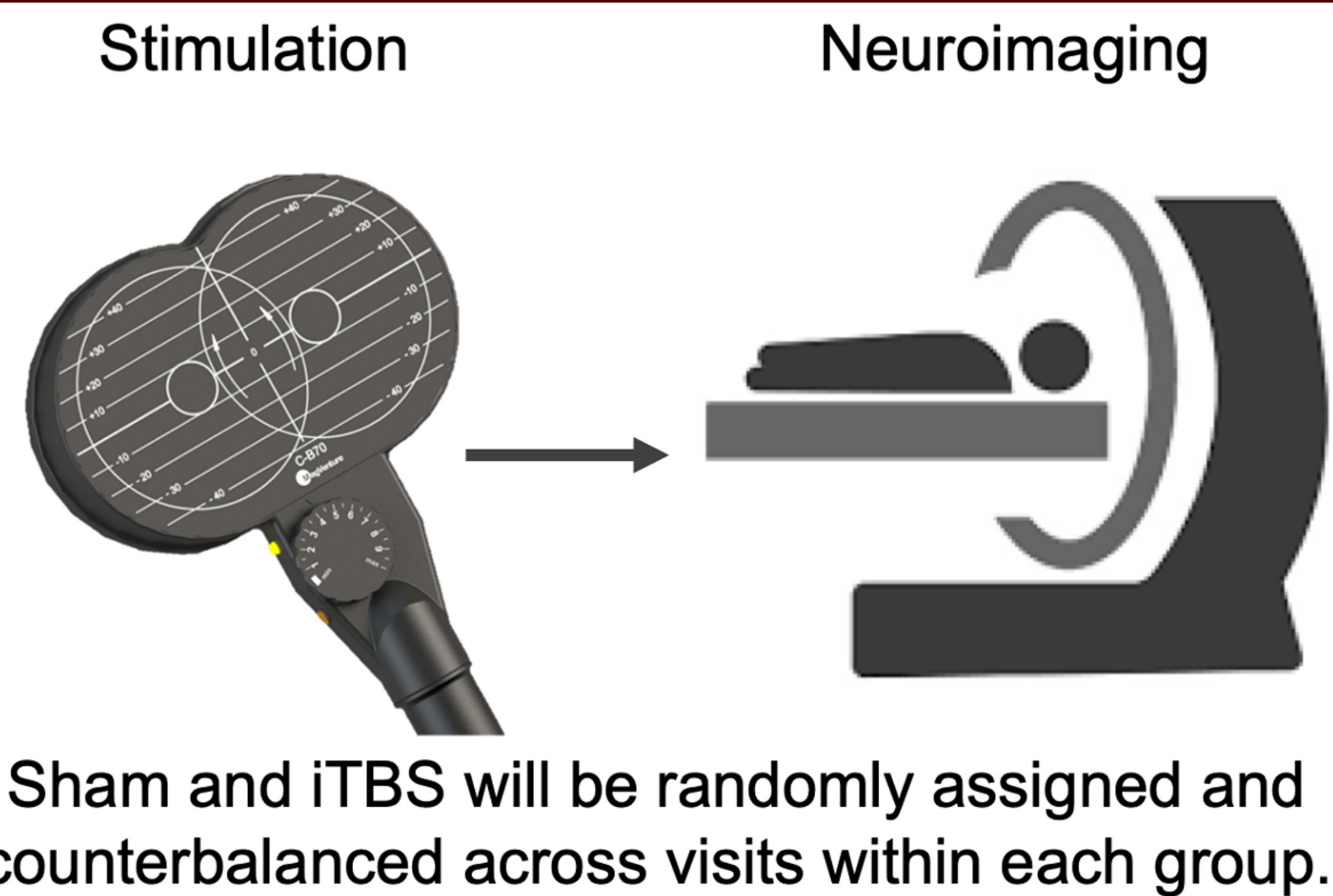
- Right Crus I (RCrusI) of the cerebellum has emerged as a key node in cerebello-cortical networks underlying cognitive function, with network-selective vulnerability to Alzheimer's disease (AD) pathology¹
- Intermittent theta burst stimulation (iTBS) targeting the lateral cerebellum has shown promise for modulating these networks, including the default mode network²
- However, substantial interindividual variability in iTBS response remains a critical barrier to clinical translation³, particularly in aging populations with cognitive impairment.
- This study examines RCrusI-targeted iTBS response across the aging spectrum using a responder framework, as a first step toward a precision medicine approach to cerebellar neuromodulation in AD

METHODS

- Young adults (YA; 18-35 yrs; n = 29-33), cognitively healthy older adults (OA; 60+ yrs; n = 7-10), and OA with cognitive decline (CD; 60+ yrs, Montreal Cognitive Assessment ≤ 26 ; n = 9-10) completed a randomized, double-blind crossover design receiving active and sham iTBS to RCrusI at 100% active motor threshold
- Responders were quantified within each group using Cohen's d effect sizes on active-minus-sham change scores. Profiles were explicitly classified as Responders (d > 0.5), Non-responders ($-0.5 \leq d \leq 0.5$), Negative Responders (d < -0.5), using OA sham performance as a behavioral rescue benchmark for CD.
- Paired and Welch t-tests examined within- and between-group differences in Responder/Non-responder profiles

RESULTS

- iTBS produced distinct Responder, Non-responder, and Negative Responder profiles within each group (Fig 1-3)
- 2-Back: CD participants showed a higher proportion of Negative Responders with more pronounced accuracy declines relative to YA (Fig 1)
- Stroop: Responder/Non-responder divergence was significant across all three groups (ps < .004), despite no consistent group-level direction of effect (Fig 2)
- Sequence: no CD participants met Responder criteria for reaction time, though CD Accuracy Responders diverged significantly from Non-responders (p = .0002); YA showed significant divergence across both reaction time (RT) and accuracy (ps < .001; Fig 3)



Scans	
High-resolution structural image (anatomy)	
Diffusion tensor imaging (white matter)	
Resting state connectivity (networks)	
Task-based (function)	
Task	Control
Stroop incongruent	Stroop congruent
Verbal 2-back	Verbal 0-back
Finger sequencing	Simple tapping

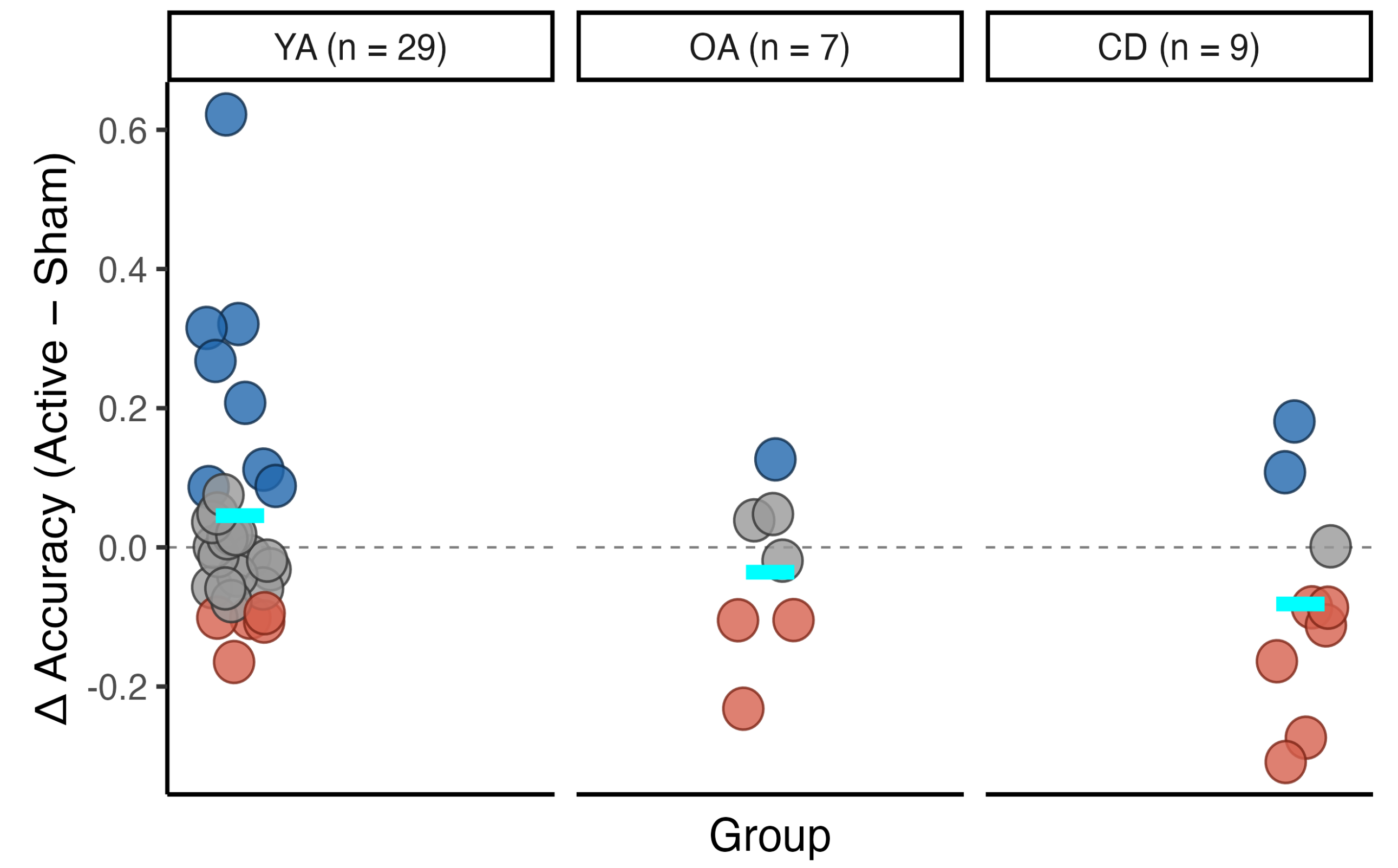
CONCLUSIONS

- Preliminary findings reveal substantial individual variability in RCrusI iTBS responses across tasks, with CD participants showing the most consistently negative profiles, including a complete absence of Sequence RT Responders
- Divergence in Responder/Non-responder profiles across tasks and groups underscores the need for a precision medicine approach to neuromodulation in aging and AD
- Data collection and neuroimaging analyses ongoing (target n = 40/group); upcoming analyses will examine whether RCrusI structural and functional integrity predicts iTBS response, potentially informing patient stratification in future clinical trials

REFERENCES

1. Guo et al., 2016, Brain. 139(5), 1527–1538.
2. Halko et al., 2014, J. of neurosci. 34(36), 12049–12056.
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Fig 1. 2-Back Accuracy Change



2-Back RT Change

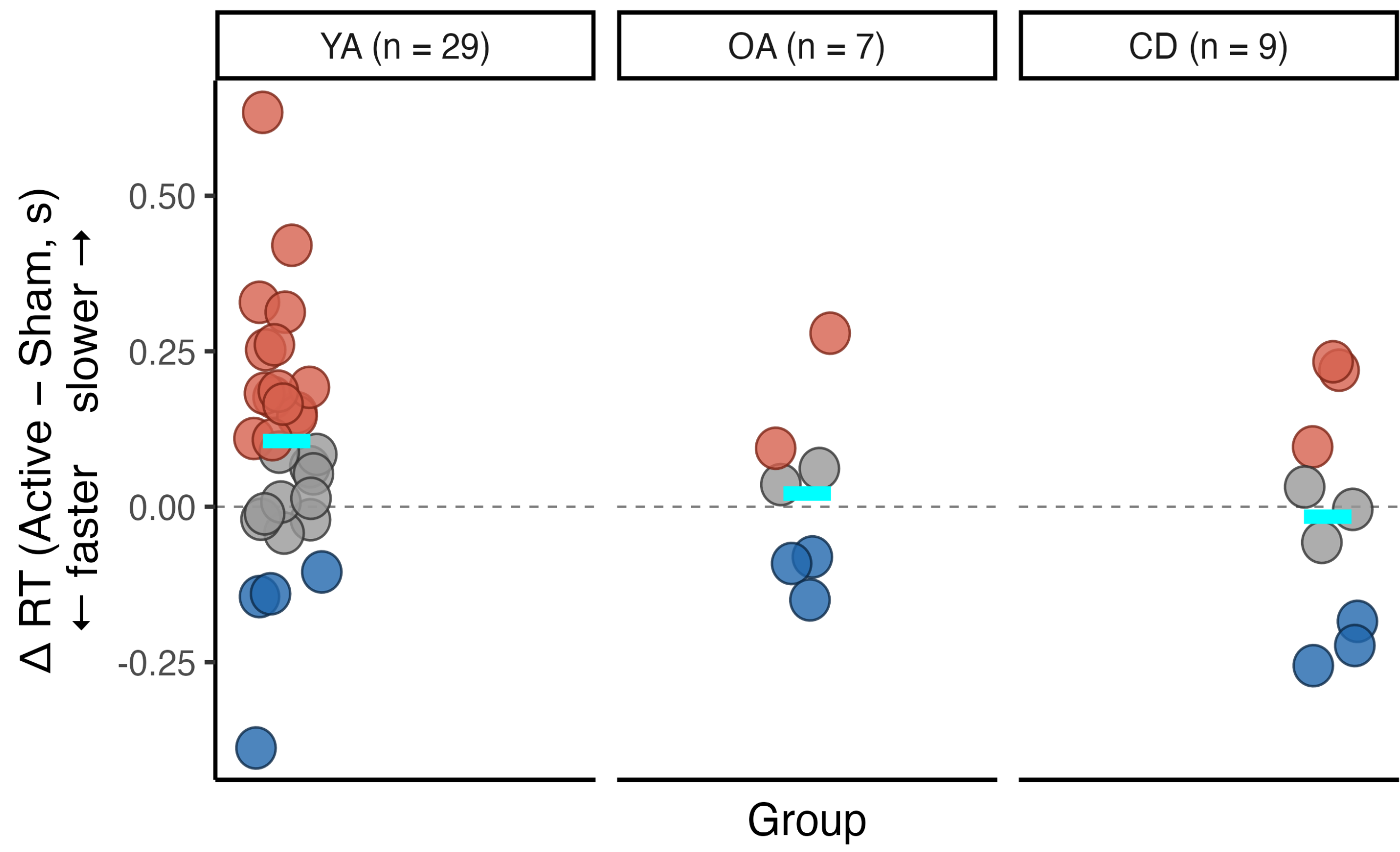
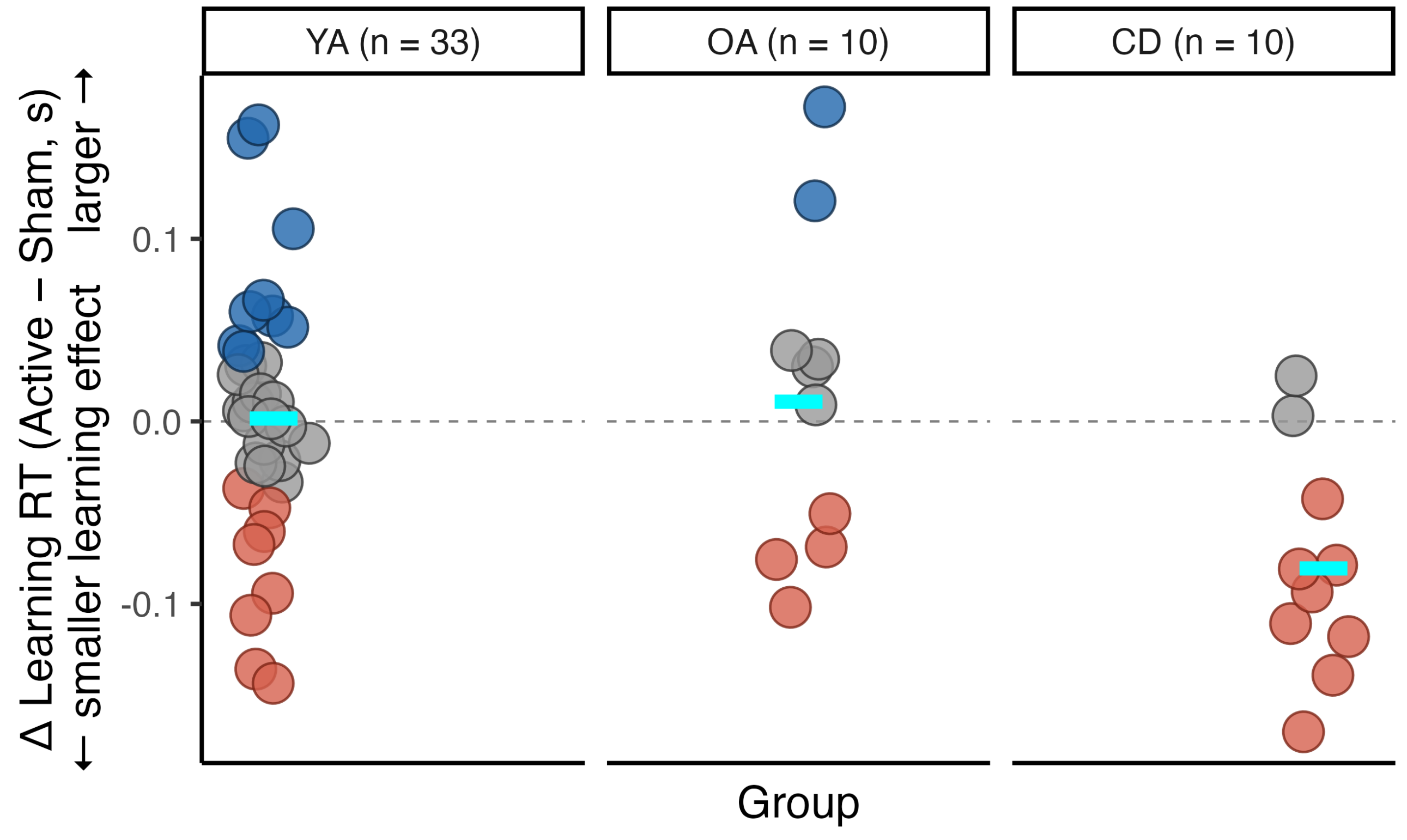


Fig 3. Sequence Learning Effect Change — Late Bin



Sequence Learning Accuracy Change — Late Bin

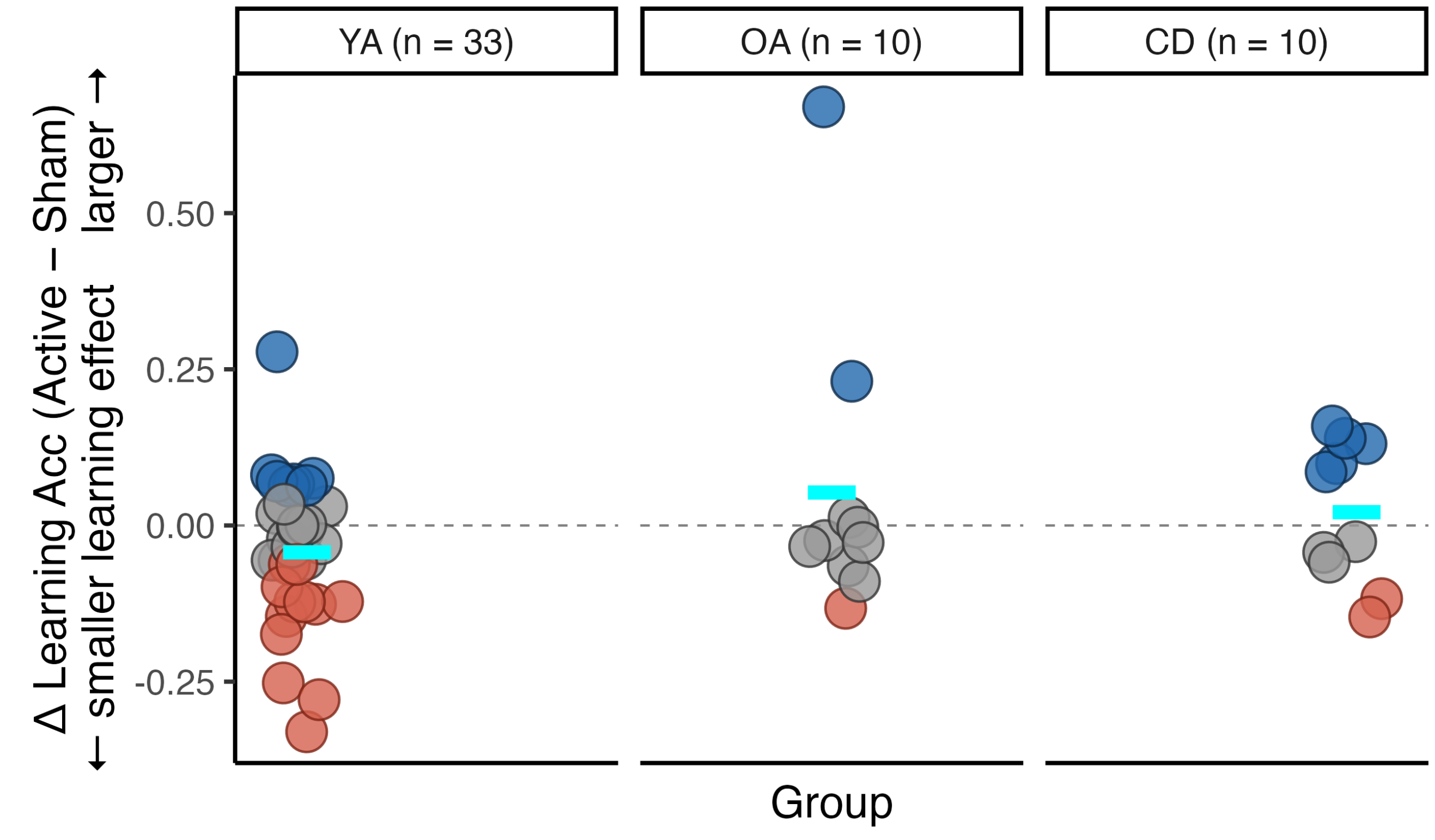
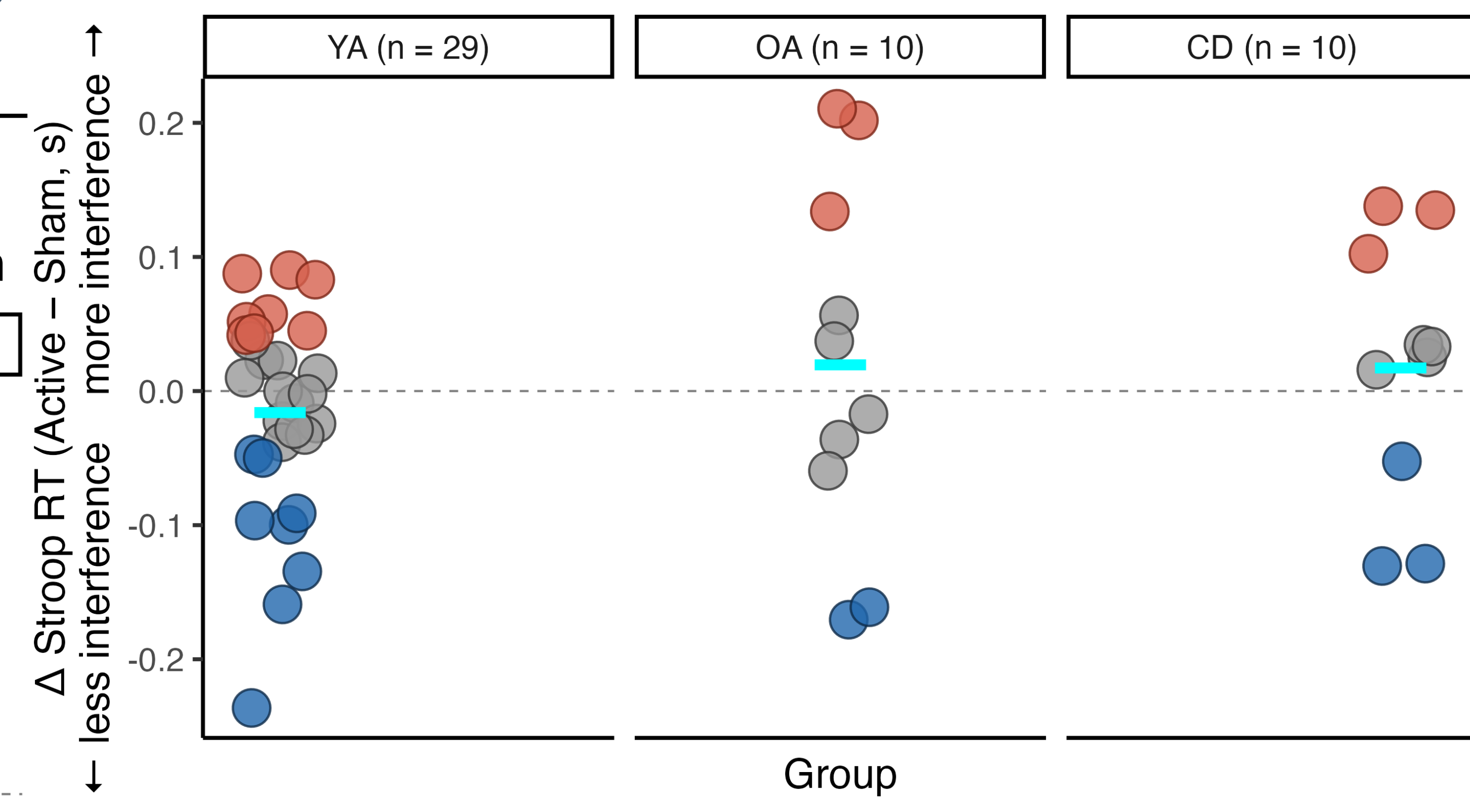


Fig 2. Stroop Interference Effect Change



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