



Cognitive Reserve impact on neurodegenerative disorders

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CR is a universal predictor of performance, yet its capacity to buffer cognition against brain volume loss is diagnostic-specific.

I. INTRODUCTION

Cognitive reserve (CR) may mitigate cognitive decline with various neurodegenerative conditions. This study aims to investigate the effects of CR on cognitive impairment and whole brain volume, as well as their associations across different neurodegenerative disorders.

II. METHODS

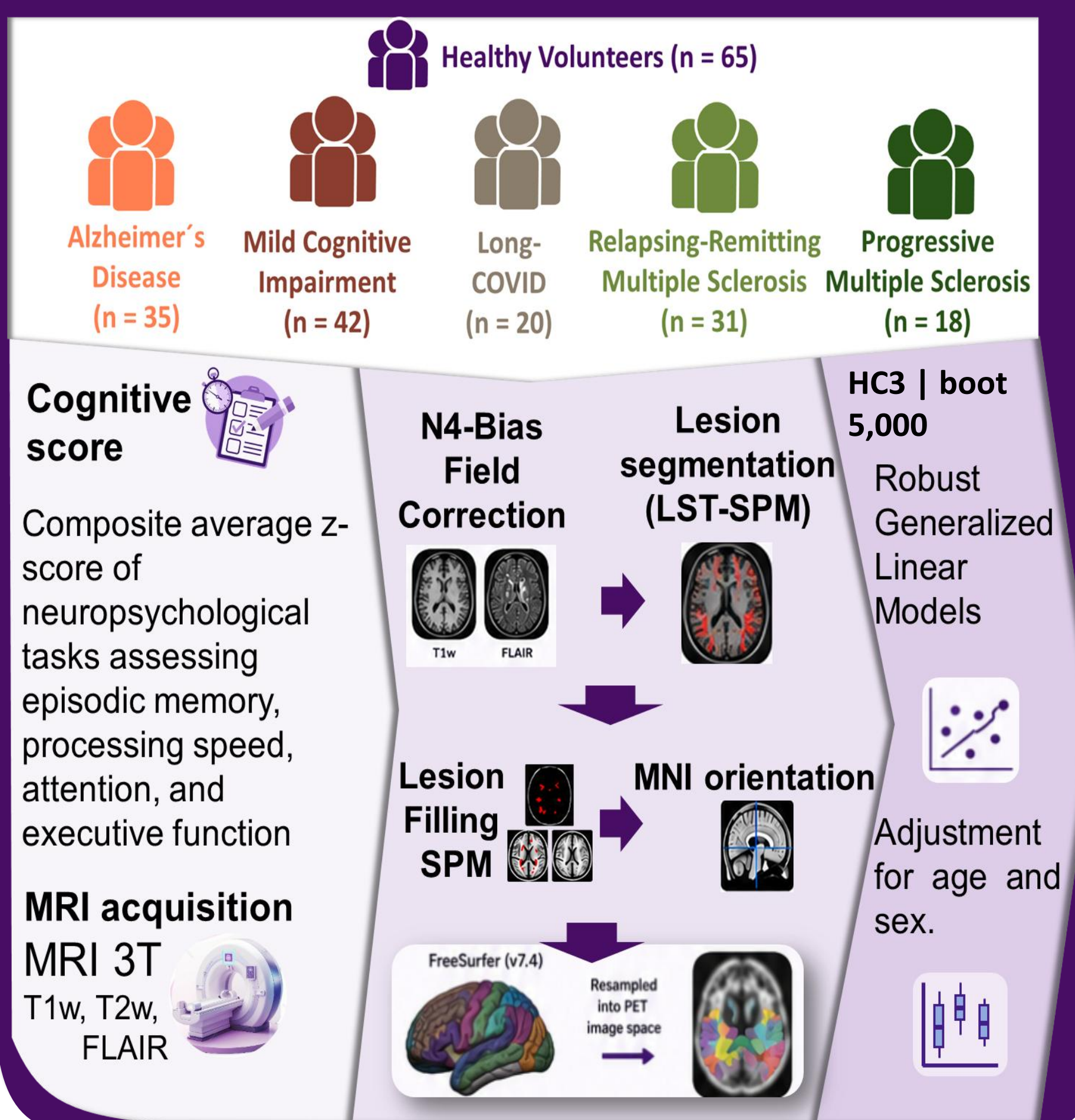


Figure 1. Moderation of cognitive reserve score on cognition and whole brain volume.

Panels A and C display the simple slopes analysis representing the moderating effect of CR (raw scale) on predicted outcomes across groups, adjusted for age and sex. Panels B and D show the adjusted pairwise comparisons of estimated marginal means with corresponding standard errors (SE) and individual predicted values (jittered points).

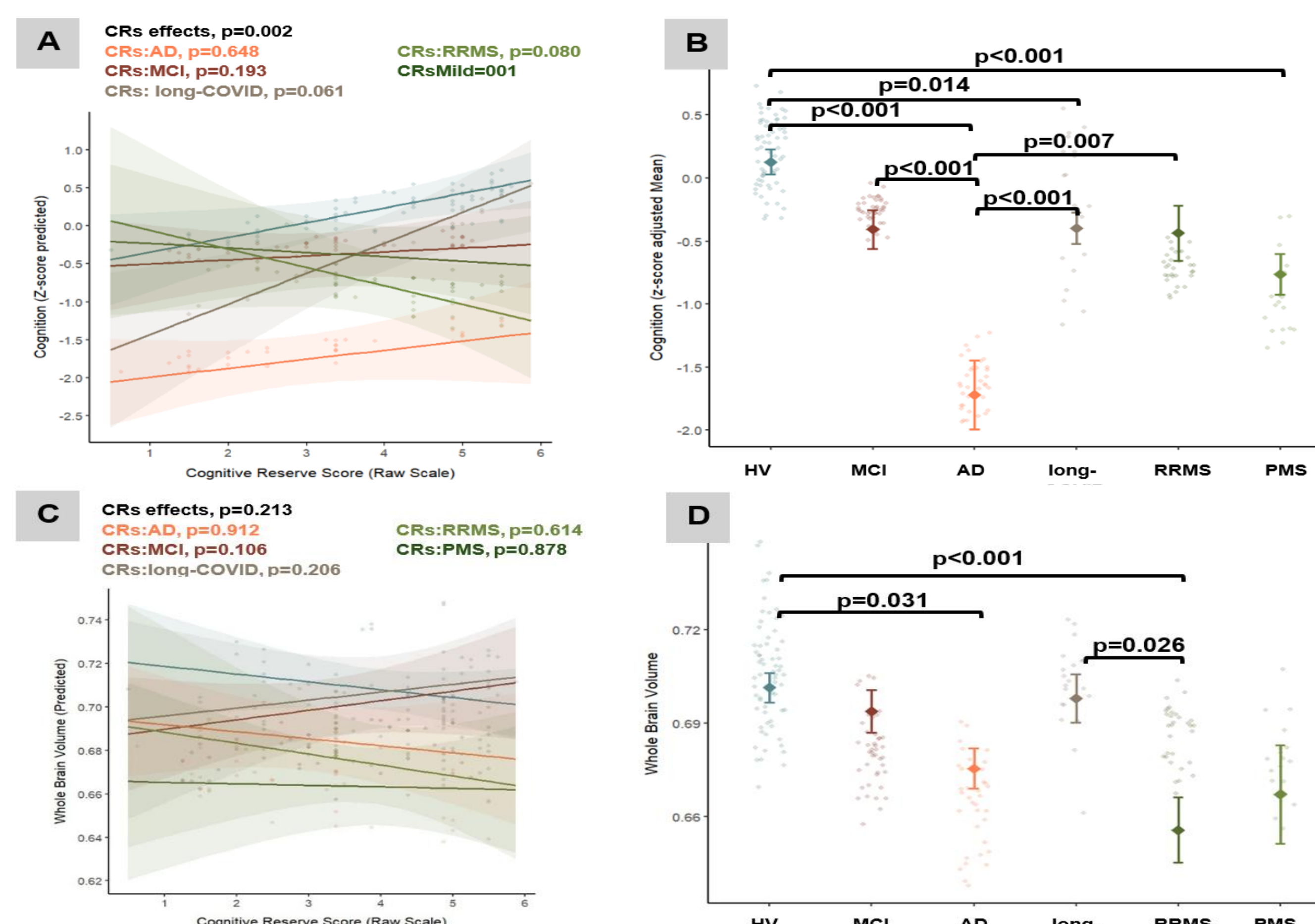
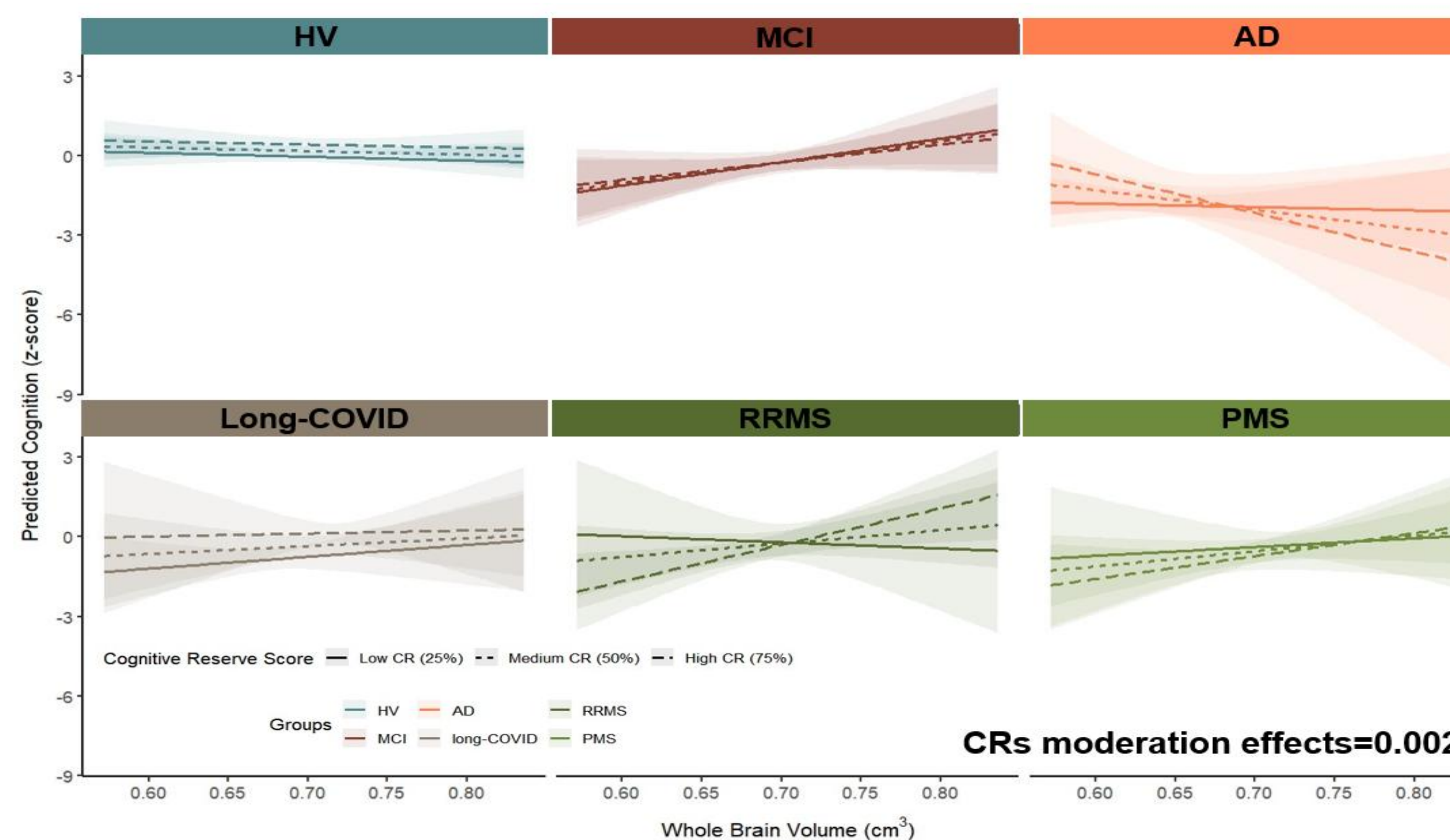


Figure 2. Interaction of Brain Volume and Cognitive Reserve score on Cognitive Performance Across Clinical Groups

Panels display predicted cognition values as a function of whole brain volume (cm^3) stratified by three levels of CRs: Low (25th percentile), Medium (50th percentile), and High (75th percentile).



III. RESULTS

CR significantly predicted cognitive performance across the entire cohort ($\beta=0.19$, $p=0.002$), acting as a robust independent predictor of better outcomes. Analysis of the moderating effect of CR on cognitive performance in clinical groups was positive only for the long-COVID group. This effect remained negative for the others, although it was significantly smaller only for the PMS group (Fig 1.A). The post-hoc analysis can be seen in fig 1.B. There was no effect of CR score on brain volume (Fig 1.C), although some differences in post-hoc analyses were observed (Fig 1.D). CR significantly predicts performance across groups ($\beta=0.19$, $p=0.002$), particularly moderates the impact of brain volume on cognition in RRMS (Fig 2).

IV. CONCLUSIONS

CR protects cognition against structural impairment in RRMS, where high reserve levels enable remaining brain tissue to maintain functional output. This protective moderation is less evident in AD or PMS, suggesting that the compensatory potential of CR is finite and contingent upon the underlying pathological mechanism and the severity of tissue damage. While CR boosts cognitive scores across groups, its role depends on the disease context and fails to offset extensive neurodegeneration in more advanced disease stages.

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