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Rethinking Cognitive Reserve in fMRI research: a Meta-analytic investigation on the neural consistency of Proxy measures

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Introduction: Cognitive reserve (CR) refers to the capacity of the brain to sustain cognitive performance despite age-related changes or pathophysiological conditions. Human brain mapping techniques, particularly task-based functional magnetic resonance imaging (tb-fMRI), have been instrumental in exploring its underlying neural correlates. CR is traditionally assessed through socio-behavioral proxies such as education, intelligence quotient, or composite indices, with considerable variability in their definitions and applications, which challenges their validity and consistency across studies. This study systematically explores the heterogeneity of brain activation patterns associated with CR proxies in healthy adults. Methods: A literature search identified 12 eligible tb-fMRI experiments, encompassing 802 healthy adult participants, that reported whole-brain CR-related activation. A coordinate-based meta-analysis using Permutation of Subject Images–Signed Differential Mapping (PSI-SDM) was conducted to assess consistent activation patterns across experiments. To further explore potential subgroupings or hidden similarities among experiments, hierarchical clustering and one-class support vector machine (SVM) analyses were applied. Results: The PSI-SDM meta-analysis did not yield any significant clusters of activation, and multivariate models revealed high dissimilarity across activation patterns, with over 30% of experiments classified as outliers. A qualitative synthesis of individual experiments further highlighted a lack of topographical consistency, with both CR-related increases and decreases in task-related activation observed across widespread cortical and subcortical regions. Conclusion: These findings indicate that current proxy-based approaches may struggle to capture the complex nature of CR. Advancing the study of CR will require a multifaceted approach, a focus on network-level brain function, and deeper investigations into the neural mechanisms of cognitive compensation.

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