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2 Rethinking the Neuropsychology of g: Structural and Functional Lesion Network Mapping of General Cognitive Ability

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Objective: General cognitive ability (g) is central to our understanding of human cognition, as it accounts for nearly half of individual differences in performances on diverse cognitive tests. There is growing interest in the brain networks necessary for g because such knowledge could elucidate neural mechanisms of g. Prior work highlighted the association between g and frontoparietal functional networks. However, the specificity of this relationship has been questioned. Moreover, no studies have compared the relative importance of structural and functional networks for g, and most studies have relied on data from neurologically healthy individuals, which limits causal brain-behavior inference. Lesion network mapping (LNM) can overcome such limitations. LNM integrates lesion location and structural and functional brain network data, and allows for inference upon networks necessary for cognitive functions. Here, we used data from three cohorts of patients with focal brain lesions to perform a large-scale LNM study of g. We also compared the relative value of lesion-behavior mapping, and structural and functional LNM, for predicting g across cohorts.
Participants and Methods: Using data from 402 individuals with chronic, focal brain lesions from the Iowa Neurological Patient Registry, we created a bifactor model to estimate g from the shared variance across neuropsychological tests. To create "cognitive comparisons," we also estimated the unique aspects of domain-specific abilities (visuospatial processing, memory, and processing speed) by removing domain-general variance from each. Next, we used multivariate lesion-behavior mapping to create statistically weighted maps linking deficits in g and domain-specific abilities to regions of focal brain damage. To perform LNM, the local maxima of the lesion-behavior maps were used as seeds for structural and functional connectivity analyses based on normative diffusion-weighted imaging and resting-state functional connectivity data, respectively. The resulting maps were collapsed using principal components analysis (PCA). We quantified the overlap between each map and the lesion volumes of patients from two validation cohorts (n = 101, n = 100). We used these scores to predict observed g in the validation cohorts while controlling for lesion volume. We also compared the relative predictive value of the lesion-behavior maps, and the structural and functional LNMs.
Results: Lesion-behavior mapping indicated that lesions of left frontal white matter, bilateral frontal operculum/insula, and a region of white matter in the posterior left hemisphere were associated with impairments in g. Across all lesion-behavior mapping and LNM results, only two of the structural LNM maps linked to g were statistically significantly predictive of g in both validation cohorts: a map corresponding to the anterior thalamic radiation, and another corresponding to left frontal pyramidal projections. Both added value beyond lesion-behavior mapping and functional LNM.
Conclusions: The results are notable in several respects: they highlight the importance of structural networks for g, de-emphasize the relevance of functional networks for g, and suggest novel brain circuitry involved in g. Our findings are consistent with animal studies implicating anterior thalamic nuclei in working memory, a cognitive function central to g. Clinically, our study highlights the importance of considering domain-general deficits and the effects of focal lesions on distributed cognitive networks.

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