

Network Disconnection Explains Domain-Specific Cognitive Impairment After Ischemic Stroke

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Background

- Higher cognitive functions depend on distributed brain networks; focal stroke produces remote, network-level effects beyond the lesion site.
- Indirect lesion-network mapping (LNM) projects lesions onto a normative connectome, but predicts cognitive outcomes poorly — and direct rs-fMRI is infeasible in acute stroke.

Aim

- Determine why conventional LNM fails for post-stroke cognitive impairment (PSCI), and devise modifications that recover domain-specific, network-level signal.

Methods

- 1,431 ischemic stroke patients (two hospitals, Meta VCI Map consortium); normative connectome from the GSP dataset (1,000 healthy adults); lesions in MNI152.
- Five cognitive domains: impaired < -2 SD, unimpaired > -1 SD (age/sex/education-adjusted).
- Three analyses: (1) lesion-network overlap, (2) lesion-network contrast mapping (LNCM; impaired vs unimpaired), (3) ridge-PCR over varying numbers of PCs; virtual-lesion simulation tests cross-network contamination.

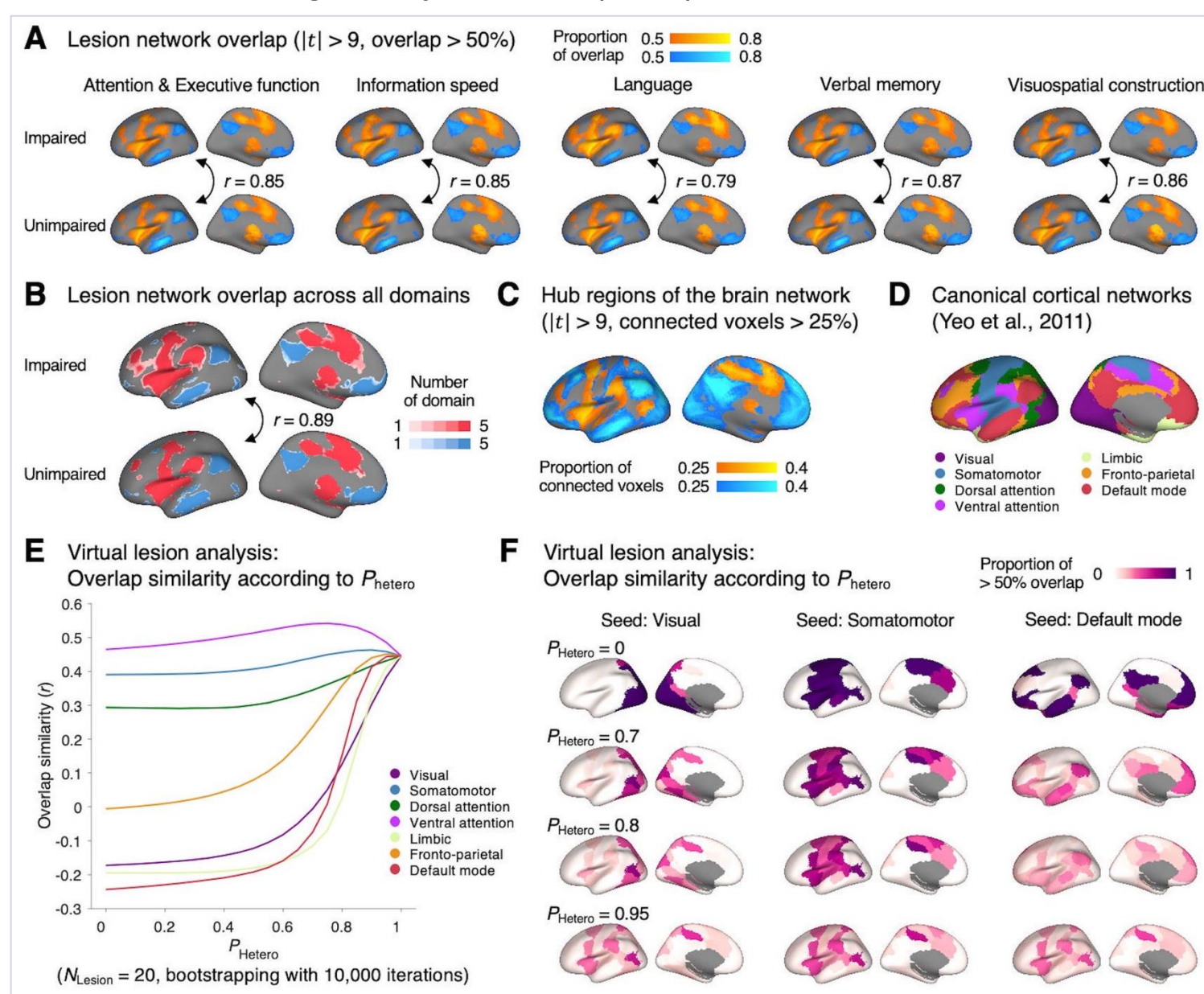
Study population

- N = 1,431; mean age 67.8 ± 11.6 y; median NIHSS 3 (mild); median MMSE 26.
- Stroke-to-assessment 106.6 ± 71.2 d; impaired 15.1% (language) – 29.4% (visuospatial).

KEY RESULT

Hub-localization bias

Figure 2. Overlap maps converge on connectome hubs (A–D); virtual-lesion simulation shows convergence grows with cross-network heterogeneity, P_{hetero} (E–F).



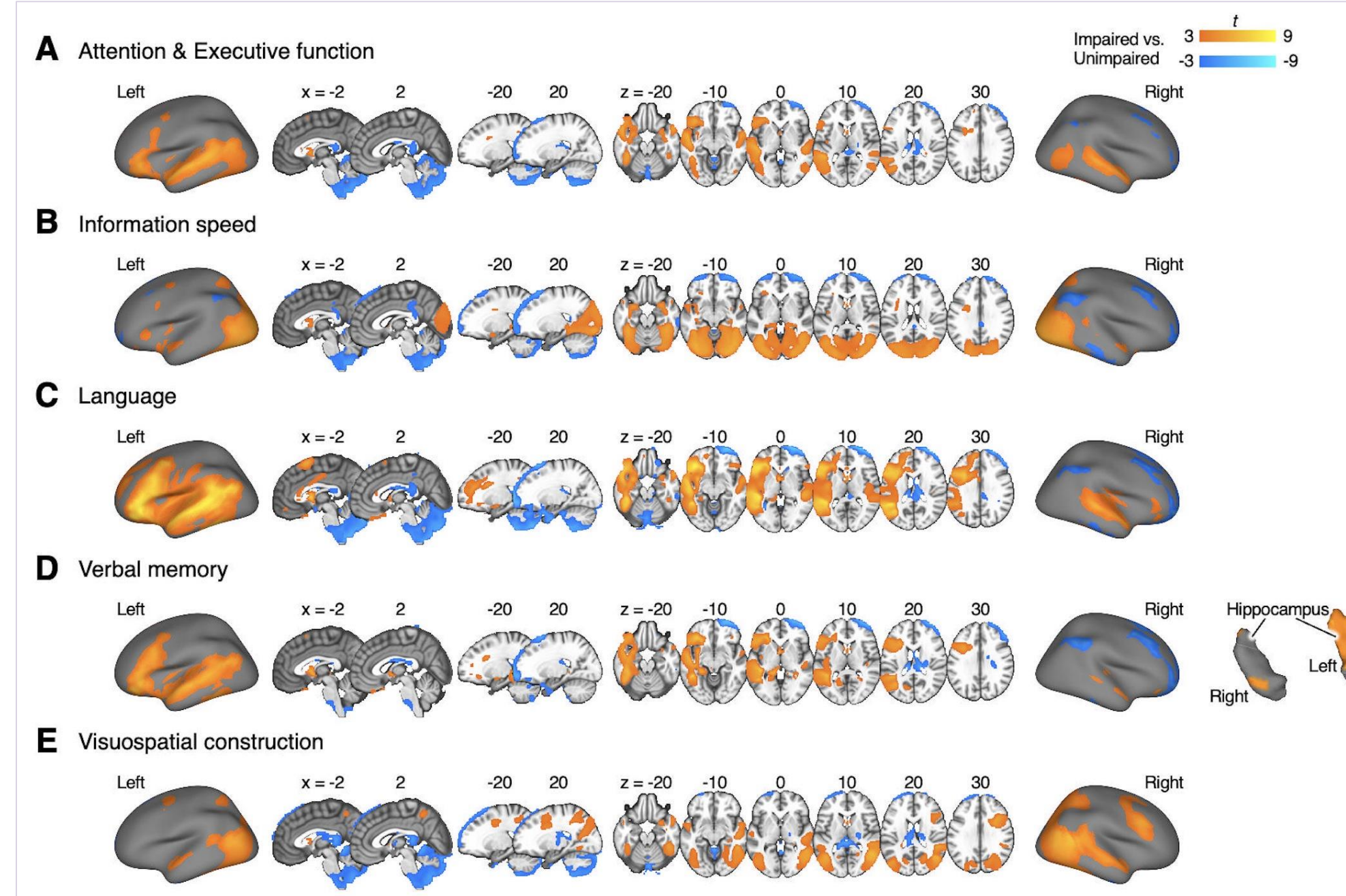
Overlap collapses onto hubs — not domain-specific.

Impaired vs unimpaired maps are nearly identical ($r = 0.79$ – 0.89).

As $P_{\text{hetero}} \rightarrow 1$, overlap localizes to hubs: it reflects lesion topography $\times$ connectome structure, not symptom-specific disconnection.

Lesion-network contrast mapping

Figure 3. Lesion-network contrast across five cognitive domains (impaired vs unimpaired) — domain-specific, spatially resolved disconnection.



Domain-specific disconnection

- Attention / executive — left IFG + bilateral superior/middle temporal gyri.
- Information speed — bilateral early visual pathways (V1–V3) + posterior thalamic relay nuclei.
- Language — left fronto-temporal; extends to left SFG + right STG/IFG.
- Verbal memory — left hippocampus + precuneus (posterior medial system).
- Visuospatial — right-lateralized $\rightarrow$ bilateral dorsal stream (occipital, superior parietal, premotor).

Contrast subtracts non-specific multi-network involvement, yielding domain-specific, bilaterally distributed disconnection maps — biologically more plausible than hub-centric overlap.

Prediction — ridge-PCR

- Retaining only PCs $\leq 95\%$ variance (PC95) gave low accuracy (R^2 0.02–0.08).
- Adding higher-order PCs (PCopt; all thresholds > 98%) improved accuracy (R^2 up to 0.11 language, 0.08 verbal memory) and localization.
- Higher-order weights align with LSM (fine-grained), lower-order with LNCM (network-level) — complementary, supporting biological validity.

Limitations

- Normative connectome from healthy young adults vs older patients; limited individual specificity; WMH disconnection not fully modeled; -2 SD cutoff may miss subtle deficits; cross-domain impairment may blur specificity.

Conclusions

- Overlap-based LNM suffers hub-localization bias and cannot dissociate domains.
- Lesion-network contrast reveals domain-specific network disconnection underlying PSCI.
- Optimizing PC selection improves prediction; overall R^2 remains modest — room to improve.

Key message

Contrast-based network disconnection — not focal tissue loss — explains domain-specific post-stroke cognitive impairment.

Figure 1. Analysis overview: (A) lesion-network overlap, (B) lesion-network contrast, (C) ridge-PCR prediction.

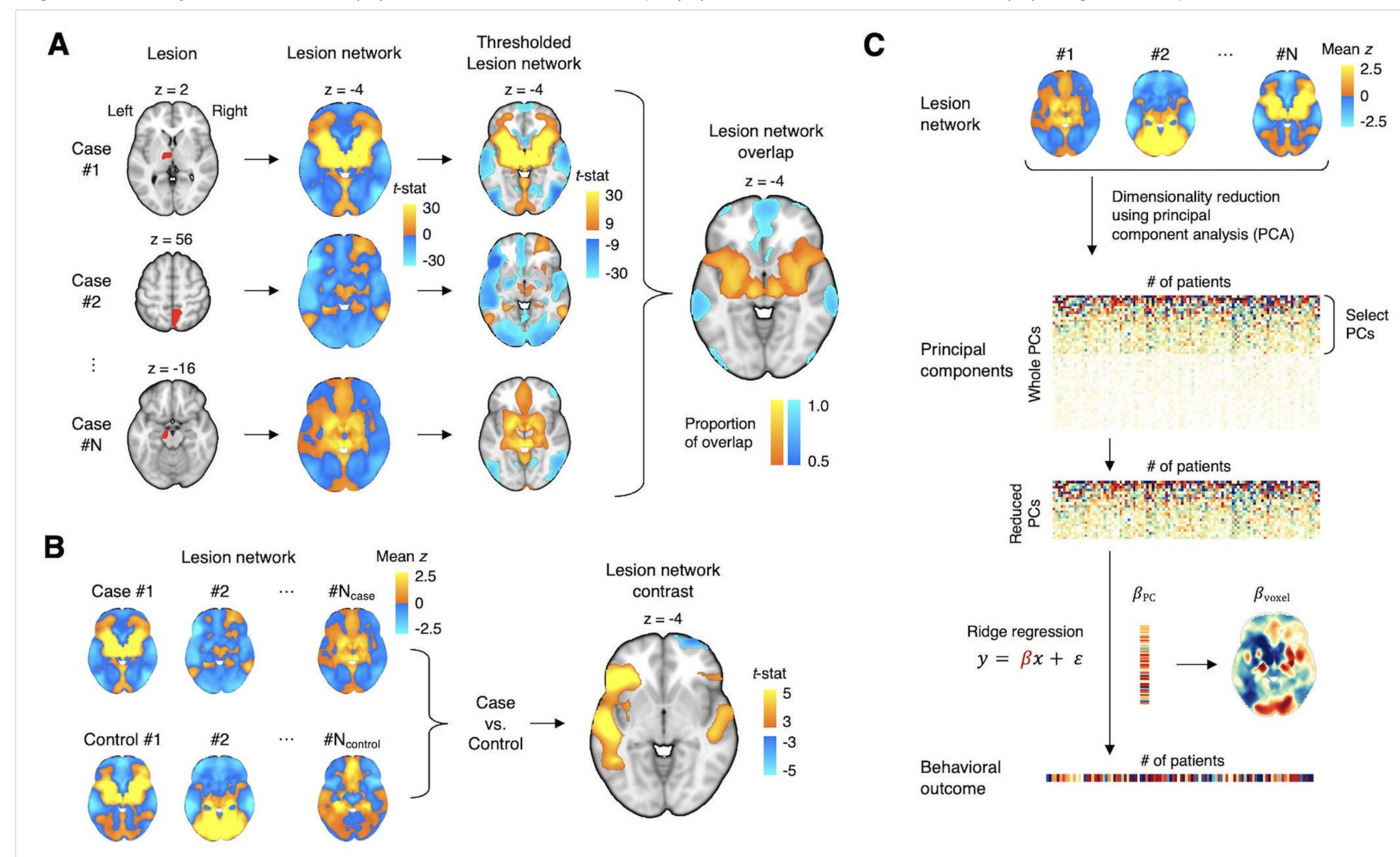


Figure 4. R^2 vs number of PCs (A); predictive weight maps, PC95 vs PCopt (B–F).

