The topography of subcortical impact on cortical connectivity aligns with neuroanatomical hierarchy

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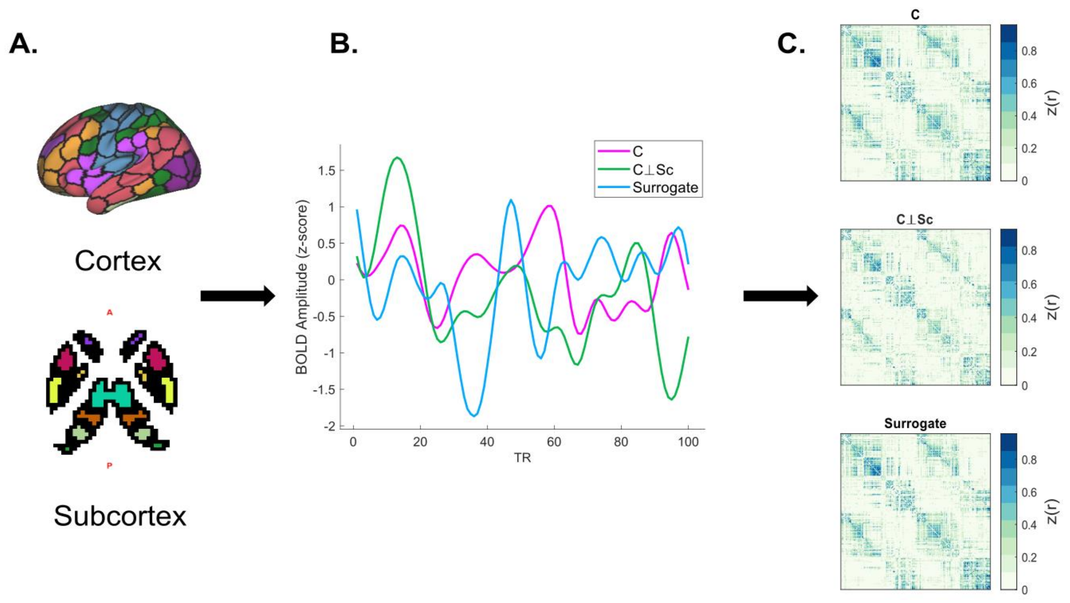
BACKGROUND:

- Recent research reemphasizes contributions of subcortex (Sc) to cognition by influencing cortical dynamics [1]
- Sc integrates information from diverse cortical networks [2]
- Open question: How does cortico-cortical connectivity look like after precise statistical control for Sc influences?
- Prediction: Cortical networks should become more segregated from each other after controlling for Sc effects on their cortico-cortical connectivity profiles.

METHODS:

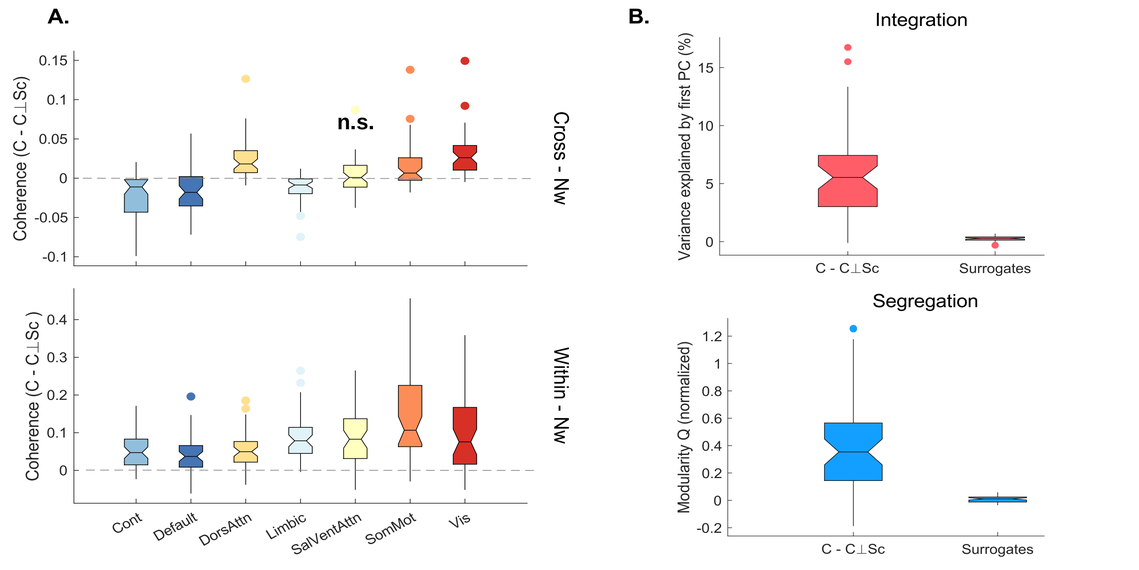
- Data: Resting state session (14.4 min) from 50 unrelated subjects of the Human Connectome Project [3]
- After parcellation each cortical area is assigned to one of seven canonical resting-state networks (RSNs) [4]
- To estimate Sc influences on cortical nodes and networks three cortical correlation matrices (C, C⊥Sc, Surrogate) are obtained per subject:



- **Fig.1 Single subject workflow.** **A:** Cortical and subcortical (Sc) regional timeseries (Ts) are extracted. **B:** Ts for an exemplary cortical parcel: C (magenta) is the normal Ts, C⊥Sc (green) is the residual Ts of C with linear Sc effects regressed out, and Surrogate (blue) is equivalent to C⊥Sc, but phase shuffling is applied to C before the regression procedure (simultaneously to all cortical parcels) . **C:** The three corresponding cortical FC matrices resulting from correlating the (differentially processed) signals and omitting negative correlations.

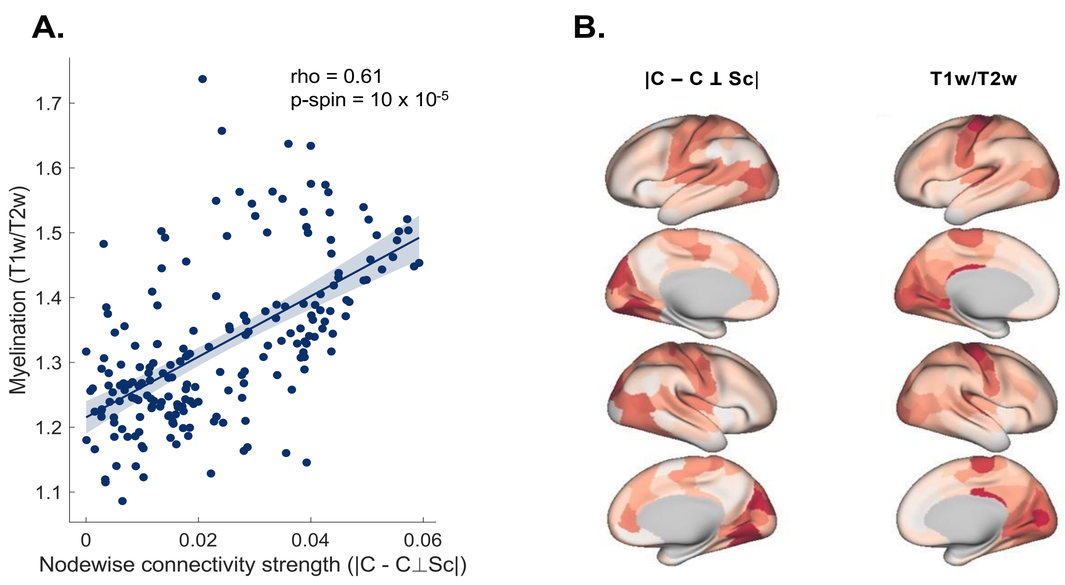
- Subsequently, within- and across RSN-coherence is estimated by averaging the corresponding entries in the matrices
- Global integrative/segregative effects of Sc on cortex are assessed with principal-component analysis and modularity maximization [5]
- For all outcome measures we take the difference between C and C⊥Sc, with the difference between C and surrogate data serving as null distribution.

RESULTS:



- **Fig.2 Network level- and global effects.** **A:** Controlling for Sc leads to significant increases in terms of Cross-Nw coherence for default-mode-, control-, and limbic networks, and significant decreases mainly for sensory networks (top). Significant decreases in Within-Nw coherence occur for all seven RSNs (bottom). **B:** Removal of Sc effects results in a significantly less integrated cortical landscape (top), while (cortical) modularity is also significantly reduced (bottom).

- Convergent with the observed patterns of change in Cross-Nw coherence (Fig.2 A, top), a transition from sensory to higher order RSNs can be seen for absolute changes in connectivity strength (|C - C⊥Sc|) at the node level (Fig.3 B, left)
- To investigate structural correlates of this gradient we correlate it with the corresponding spatial map approximating intracortical myelin levels [6] :



- **Fig.3 Node level effects.** **A:** Degree of myelination (T1w/T2w) correlates with absolute difference in average connectivity strength for cortical nodes (|C - C⊥Sc|). **B:** Cortical surface maps for |C - C⊥Sc| (left), and T1w/T2w (right). Warmer colors indicate higher values.

CONCLUSIONS:

- Significant changes in cortical network integration and segregation after removal of Sc effects, in line with recent evidence [1, 7]
- Removal of Sc influences has divergent effects on the Cross-Nw coherence of different RSNs
- The extent of Sc influence on a cortical region's connectivity profile aligns closely with its estimated myelin content, a proxy for anatomical hierarchy [8]

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