Thalamocortical Connectivity Predicts Level of Awareness in Disorders of Consciousness

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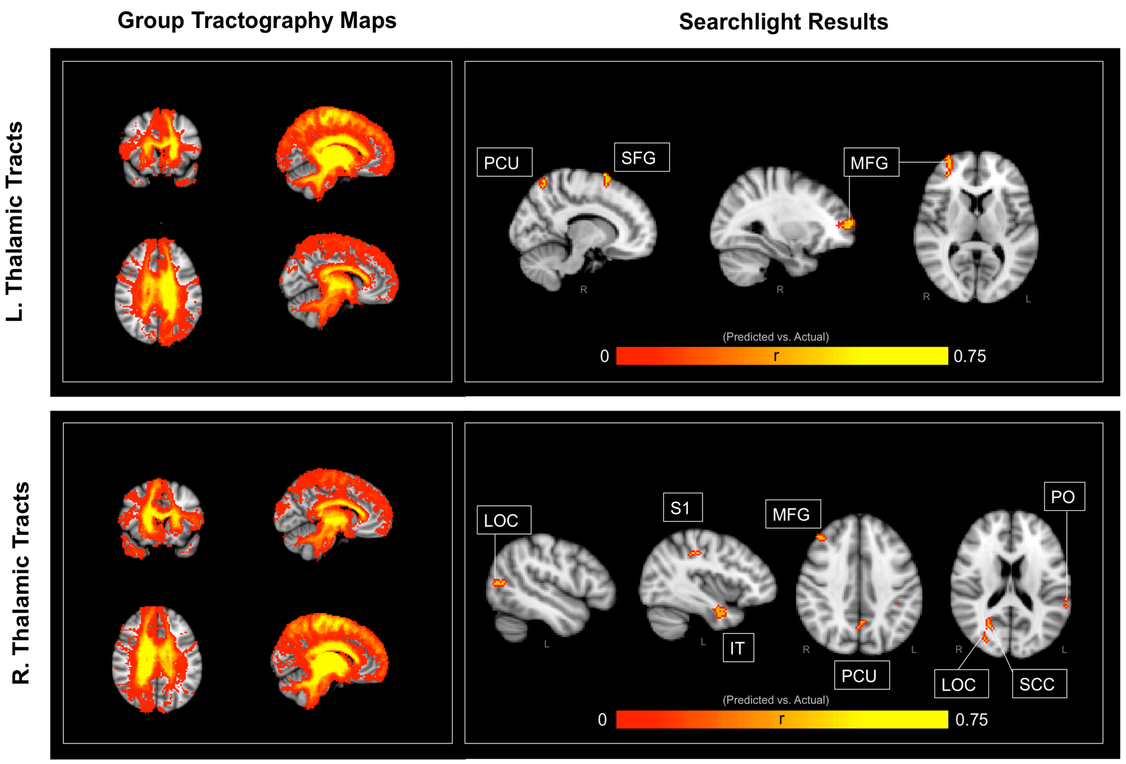
Introduction

- Previous research has suggested that disorders of consciousness (DOC), including vegetative state (VS) and minimally conscious states (MCS), may result from disconnections of thalamocortical loops[1].
- The thalamocortical system has been implicated in central aspects of consciousness, including arousal and awareness[2].
  - Disruption to this system can lead to loss of consciousness[3], and, in turn, its restoration has been associated with recovery from VS[4].
  - Increased thalamic atrophy has been associated with poorer 6-month recovery from severe TBI[5].
- We used a combination of probabilistic tractography and machine learning algorithms to identify a subset of thalamocortical projections that have significant power in predicting the varying levels of consciousness in severely brain-injured patients.

Methods

- 23 DOC patients (8 VS, 7 MCS-, 8 MCS+) were evaluated using the Coma Recovery Scale-Revised (CRS-R) by trained clinicians.
- The CRS-R spans six subscales aimed at assessing overt consciousness: auditory, visual, motor, oromotor, communication, and arousal. Collapsing across the 6 subscales, we obtained a total CRS-R score for each patient. While individual subscales directly differentiate between levels of consciousness, total CRS-R is significantly correlated with the subscales.
- Probabilistic tractography, which allows fibre tracking into the gray matter, was carried out using left and right thalami as seeds. The output of this workflow generated whole-brain thalamic connectivity maps, where each nonzero voxel contained a *structural connectivity index* with the thalamic seed.
- We then employed a searchlight mapping procedure by centering a 5mm sphere at each voxel in the brain. The thalamic-connectivity-index values of voxels within each sphere were used as predictors in a support vector regression (SVR). The predictive power of our model was assessed by a leave-one-patient-out cross-validation.

Results



Abbreviations: MFG=Middle Frontal Gyrus, SFG=Superior Frontal Gyrus, PCU=Precuneus, PO=Parietal Operculum, S1=Postcentral Gyrus, IT=Inferior Temporal, LOC=Lateral occipital cortex, SCC=Supracalcarine Cortex

- When using connectivity indices from the left thalamic tracts as predictors, the predicted CRS-R scores correlated with the actual CRS-R scores most strongly when the searchlight was centered in right frontal and parietal regions.
  - Connectivity values between L. Thal and R. MFG and R. PCU allowed for predictions that accounted for upwards of 44% of the variance in CRS-R scores.
- When the searchlight spheres drew from right thalamic tractography maps, regions from all four lobes provided connectivity values that yielded significant predictive models. Regions with particularly high predictive power were found in bilateral occipital areas.
  - These occipital regions included bilateral LOC, which accounted for as high as 56% of the variance, and R. SCC, in which 49% of the variance in CRS-R was accounted for.

Conclusions

- Differential patterns of thalamocortical connectivity are associated with gradations in total CRS-R scores.
- These results demonstrate that DOC are at least partially accounted for by the strength of long-range connections of the thalamocortical system.
- Particularly, contralateral thalamocortical connections may be more informative in predicting level of awareness.
- Probabilistic tractography combined with machine learning algorithms may facilitate the identification of neuroanatomical markers underlying DOC.

References

1. Schiff, N.D., 2010. Recovery of consciousness after brain inury: a mesocircuit hypothesis. Trends Neurosci. 33, 1-9.
2. Van der Werf, Y.D., Witter, M.P., Groenewegen, H.J., 2002. The intralaminar and midline nuclei of the thalamus. Anatomical and functional evidence for participation in processes of arousal and awareness. Brain Res Brain Res Rev. 39, 107-40.
3. Kim, S.P. Hwang, E., Kang, J.H., Kim, S. & Choi, J.H. Changes in the thalamocortical connectivity connectivity during anesthesia-induced transitions in consciousness. *Neuroreport* 23, 294-8 (2012).
4. Laureys S. et al. Restoration of thalamocortical connectivity after recovery from persistent vegetative state. *Lancet* 355, 1790-1 (2000).
5. Lutkenhoff, E.S., McArthur, D.L., Hua, X., Thompson, P.M., Vespa, P.M., & Monti, M.M. Thalamic atrophy in antero-medial and dorsal nuclei correlates with six-month outcome after severe brain injury. *NeuroImage: Clinical*, *3*, 396-404. (2013)

Acknowledgments

This study was funded by the James S. McDonnell Foundation and this material is based upon work supported by the National Science Foundation Graduate Research Fellowship under Grant No. DGE-1144087.