Disentangling Disorders of Consciousness: Insights from DTI and MVPA

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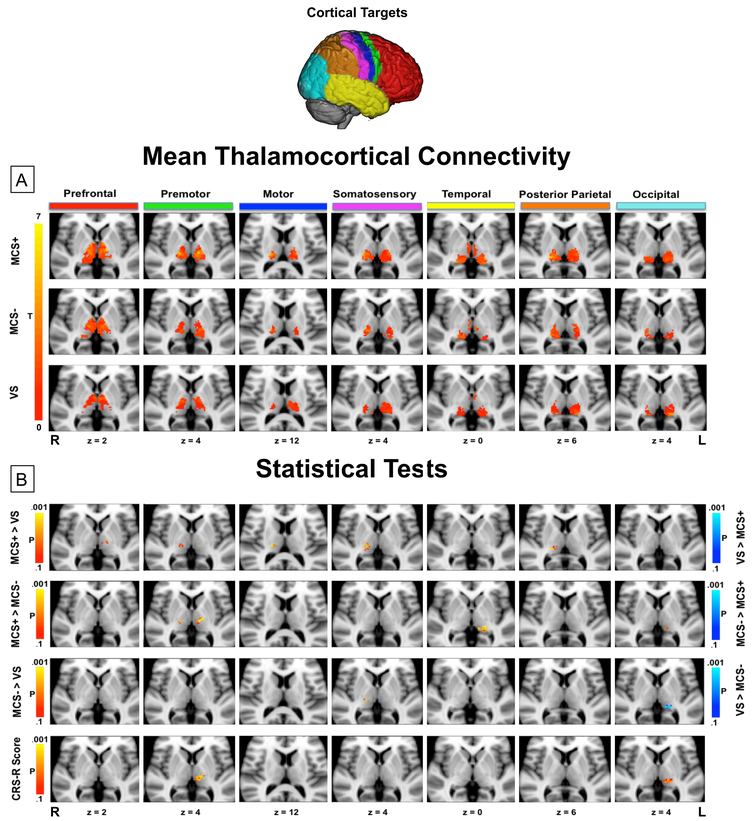
Introduction

- The stratification of patients suffering from disorders of consciousness (DOC), including vegetative state (VS) and minimally conscious states (MCS), is entirely based on behavioral criteria.
- This approach is problematic for 2 reasons:
  1. What if a patient were aware but unable to respond?
  2. Diagnosis is blind to the underlying pathology.
- The thalamocortical system has been implicated in central aspects of consciousness, including arousal and awareness[1].
  - Disruption to this system can lead to loss of consciousness[2], whereas its restoration has been associated with recovery after severe brain injury from VS[3].
  - Increased thalamic atrophy has also been associated with worse 6-months outcome in severe TBI[4].
- We assessed connectivity patterns between the thalamus and cortex using diffusion tensor imaging (DTI) in MCS+ (patients exhibiting high-level behavioral awareness), MCS- (low-level awareness), and VS (awake but not aware) patients.

Methods

- 23 DOC patients with varying etiology (8 MCS+, 7 MCS-, 8 VS)
- Probabilistic tractography was used to:
  - segment the thalamus into clusters containing specific ipsilateral connections with each cortical target (7 per hemisphere).
  - generate whole-brain tractography maps by tracking connections from the thalamus to every voxel in the brain.
- Univariate analysis: pairwise statistical comparisons were carried out between VS, MCS-, and MCS+ for each ipsilateral thalamocortical cluster. Moreover, coma recovery scale-revised (CRS-R) scores were used to test for any positive linear relationship with each thalamocortical cluster.
- Multivariate classification: we employed a searchlight mapping approach by centering a 5mm sphere at each voxel in the brain. The thalamic-connectivity-index values of voxels within each sphere were used as features in a support vector machine (SVM) classification scheme. SVM classifier accuracy was assessed in a leave-2-subjects-out cross-validation fashion. The achieved accuracy was assigned to the voxel that the sphere was centered around, yielding whole-brain accuracy maps.

Results: Univariate



A. Connectivity-based probabilistic tractography revealed clusters within thalamus with target-specific connections.

B. MCS+ contained more thalamocortical connections as compared to VS in all except for temporal and occipital systems. For MCS+ > MCS-, more thalamocortical connections were found in premotor, temporal, and occipital cortices. MCS- had more connections in somatosensory cortex relative to VS, but the opposite contrast revealed greater connectivity in occipital cortex. A positive linear relationship was found between CRS-R scores and thalamo-premotor and thalamo-occipital connectivity.

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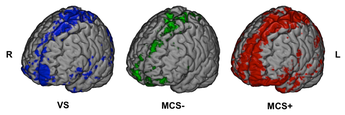
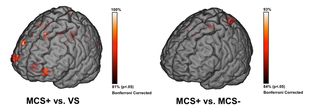
Results: Multivariate

Left Thalamus to Whole-Brain Tractography Patterns



Classification Accuracy



- Whole-brain tractography projections from the left thalamus were used as features for classification:
  - MCS+ vs. VS: widespread thalamocortical networks were identified, with large clusters primarily in the thalamo-frontal, parietal, and sensorimotor circuits, with 100% accuracy in the superior frontal gyrus and cingulate gyrus.
  - MCS+ vs. MCS-: while small clusters were found in the prefrontal and sensorimotor cortices, a large cluster was observed in the precuneus.
  - MCS- vs. VS (not shown): similar to MCS+ vs. VS, widespread thalamocortical networks were seen, with the highest accuracies in sensorimotor cortices and angular/supramarginal gyri.

Conclusions

- DTI combined with machine learning classification may facilitate the diagnostic distinction between different states of DOC.
- Different patterns of disruptions in thalamocortical circuits underlie different levels of disorders of consciousness.
- The main distinction between the different states of DOC may involve higher-order cognitive systems such as thalmo-frontal and/or parietal circuits, along with the integrity of the sensorimotor systems.
- CRS-R scores are sensitive to changes in thalamo-premotor and thalamo-occipital systems.

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