Estimates of Cerebellar, Thalamic, and Basal Ganglia Circuits Using Functional Connectivity From 1000 Subjects


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Introduction

The cerebral cortex forms spatially organized circuits with the cerebellum, thalamus, and striatum. The organization of these circuits in the human has been estimated through tract tracing and physiological studies in the monkey and cat (for review see Haber 2003; Jones 2007; Strick et al. 2009). Details of the organization, especially the topography of projections arising from association cortex, remain incompletely understood.

The present study explored the organization of subcortical circuits using resting-state functional connectivity MRI (fcMRI). fcMRI is not a direct measure of anatomical connectivity but is sufficiently constrained by anatomy to provide insights into properties of circuit organization (Fox & Raichle 2007; Van Dijk et al. 2010). Prior studies have provided estimates of organizational properties of subcortical structures that serve as a basis for the present work (e.g., Barnes et al. 2010; Di Martino et al. 2008; Habas et al. 2009; Krienen & Buckner 2009; O’Reilly et al. 2010; Zhang et al. 2008). Here we applied fcMRI to comprehensively map the cerebellum, thalamus, and striatum in a sample of 1000 participants using hybrid surface- and volume-based registration.

Our analyses involved three steps. First, we examined predicted aspects of anatomical organization including cross-modal-lateralization and somatomotor topography in the cerebellum, and somatomotor topography in the striatum. These analyses were conducted to build confidence in the approach. We then mapped in detail the anatomy within each subcortical structure. These analyses yielded maps of the estimated principal cortical targets for subdivisions (at the voxel level) within each subcortical structure. Finally, we quantified the correlations of subcortical regions to multiple cortical targets, yielding functional connectivity “fingerprints” that capture more complex patterns of connectivity (Passingham et al. 2002).

Methods

Participants

• N~1000 for resting-state fcMRI (mean age = 21.3 yr, 18-35; 42.7% male; 90.9% RH).
• N=26 for task-based motor topography (mean age = 21.3 yr; 50.0% male; all RH).
• Subsets of N~500 age, sex, and SNR matched groups were used for reliability analysis.

Imaging Parameters

• All subjects acquired on 3T Siemens Tim Trio MRI scanner (12-channel coil).
• T1-weighted MultiEcho(ME)-MPRAGE (1.20 mm iso, TR=2.2s, T=1.1s, TE=1.54ms / image #1 to 70ms / image #4, flip angle=7°, TD=200ms, 4x acceleration).
• Gradient echo T2*-weighted BOLD acquisition (3.00 mm iso, transverse orientation, 47 slices fully covering cerebral cortex and cerebellum, TR=3.2s, TE=90ms).
• One or two resting-state (eyes open) runs per subject (each 6m 12s, mean = 1.7 runs).

Hybrid Surface / Volume Image Registration

• Cortex aligned between subjects using surface-based registration (Fischl et al. 1999).
• Subcortical structures aligned using non-linear volume registration (Fischl et al. 2004).
• Correspondence between surface and volume estimated from mean of all subjects.
• Surface projections visualized using Caret software (Van Essen et al. 2001; 2002).

Approach

Registration Experiments

• Group (N=1000) SNR Map

Functional Connectivity

• Preprocessing steps illustrated below (Van Dijk et al. 2010).

• Subcortical voxels were classified using a winner-take-all algorithm whereby the voxel’s principal target was defined as the most strongly correlated cortical network.

Results

Functional Connectivity Reveals Topographic Organization of Cerebellar Motor Regions

E.D. Adrian 1943

fcMRI

Task

Tongue Hand Foot

Primary and Secondary Somatomotor Maps

(Left) Adrian’s (1943) inverted somatomotor map of the monkey cerebellum. (Middle) Replicating Groud’s (2001) human somatomotor topography was estimated using task-based fMRI (foot, hand, and tongue movements) for the cerebral cortex (A) and cerebellum (B). Seed regions were constructed based on the task activations (C). Functional connectivity for the seed regions revealed clear topography in the contralateral cerebellar (D) including both the primary and secondary representations (Right, sagittal view of the right cerebellum).

A Functional Map of the Cerebellum

Maps of the estimated principal cortical targets for the thalamus (N=1000). As predicted, lateral and inferior pulvinar associate with visual cortex (purple), and the posterior ventral complex associates with sensorimotor areas (blue). The anterior and medial thalamus are coupled with multiple association networks consistent with known connections (red and orange).

A Functional Map of the Thalamus

The thalamus is mapped below in a similar fashion with several examples of correspondences between macaque anatomy and human functional connectivity illustrated.

A Functional Map of the Striatum

Maps of the estimated principal cortical targets for the thalamus including lateralization and somatomotor topography. Automated mapping to cortical networks classifies these cerebellar regions as having somatomotor cortex as their principal target.

Conclusions

1) Functional connectivity detects predicted anatomy of the cerebellum including lateralization and somatomotor topography. Automated mapping to cortical networks classifies these cerebellar regions as having somatomotor cortex as their principal target.

2) The lateral hemispheres of the cerebellum are predominantly coupled to multiple association networks that include prefrontal and parietal cortex. Like somatomotor cortex, cerebellar association circuits have multiple representations.

3) Estimates of principal targets for the striatum and thalamus also reveal functional predictions by macaque anatomy including separation of zones for motor and association cortex.

4) Mapping of principal targets for subcortical structures can be conducted comprehensively yielding results largely consistent with known aspects of topography. Certain features such as striaeomes in the stratum and fractured somatotopy in the cerebellum are not yet detected.

References


