Mapping subcortical functional connectome of the default mode network for targeted neuromodulation

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Introduction

Recent advances in functional connectivity analysis create new opportunities for therapeutic neuromodulation of human brain networks. For patients with disorders of consciousness (DoC), connectome mapping can be used to identify widely-connected network hubs that could be therapeutic targets for stimulation[1]. Although the optimal therapeutic targets for neuromodulation have not been defined, evidence shows that the default mode network (DMN) plays a crucial role in modulation of consciousness in humans[2]. However, the subcortical connectome of the DMN, which includes many regions of interest (ROI) targeted by neurostimulation, has not been well characterized. In this work, our goal is to identify the subcortical functional connectome of the DMN and explore which regions are strongly connected to the cortical DMN nodes. To do so, we applied a Nesterov-Accelerated SCAlable and Robust (NASCAR) tensor decomposition method[3], in conjunction with the BrainSync algorithm[4], to a group of 7T resting-state functional MRI (rs-fMRI) data.

Methods

Eighty-four healthy control subjects with 7T rs-fMRI scans from the Human Connectome Project[5] were analyzed. We used the first session of the minimally preprocessed grayordinate-represented rs-fMRI data to avoid inter-subject misalignment due to imperfect distortion correction. Each session lasted 15 minutes. We applied a group BrainSync algorithm to temporally align the rs-fMRI data[4,6], Fig. 1 (a). The synchronized data were then arranged along the third dimension, forming a 3D data tensor, Fig. 1 (b). We extracted low-rank components of this 3D tensor using the NASCAR algorithm[3,7], where each component represents a brain network, Fig. 1 (c). The DMN was identified as the second strongest network from the decomposition. The cortical and subcortical section of the DMN spatial map were separated from the grayordinate representations and defined as the "cortical map" and the "subcortical map", respectively, Fig. 1 (d). The cortical map was plotted on the tessellated (inflated) surfaces, while the subcortical map was converted into a 3D volume for visualization, Fig. 1 (e). Quantitatively, we computed and visualized using violin-plots the values of the subcortical map within each ROI, where the ROIs were defined using three co-registered atlases: a subcortical atlas provided by the automated segmentation tool (aseg atlas) in FreeSurfer; a probabilistic atlas for sub-segmentation of the thalamus (PTN atlas)[8] and the Harvard ascending arousal network atlas (AAN atlas)[9] for segmentation of brainstem arousal nuclei.

Results

Fig. 2 (a)-(b) show the subcortical maps of the DMN overlaid with the segmentation atlases on a T1-weighted image. Fig. 2 (c)-(e) show the violin plots of the values in the subcortical map of the DMN in each ROI. We found that the thalamus and brainstem are highly positively interconnected with the canonical cortical DMN (yellow-red in (a) and (b)). Thalamic nuclei known to modulate consciousness, such as CL, CeM, and Pf, show strong positive correlations with the DMN, while the strongest brainstem correlations with the DMN were observed within DR and MnR. We also found that activities in the putamen and globus pallidus are negatively correlated with the cortical DMN nodes (blue in (a)). These observations provide evidence for the proposed "mesocircuit" model[10] in humans, whereby downregulation of a striatopallidal feedback system is crucial in maintaining normal anterior forebrain function via disinhibition of the central thalamus.

Conclusion

We identified the subcortical functional connectome of the DMN using a tensor framework NASCAR. Results were well aligned with the mesocircuit model, and several sub-regions within the thalamus and brainstem show higher impact on the DMN, which could provide guidance for precise neuromodulatory targeting in applications such as transcranial focused ultrasound stimulation of deep brain structures to promote recovery from DoC.

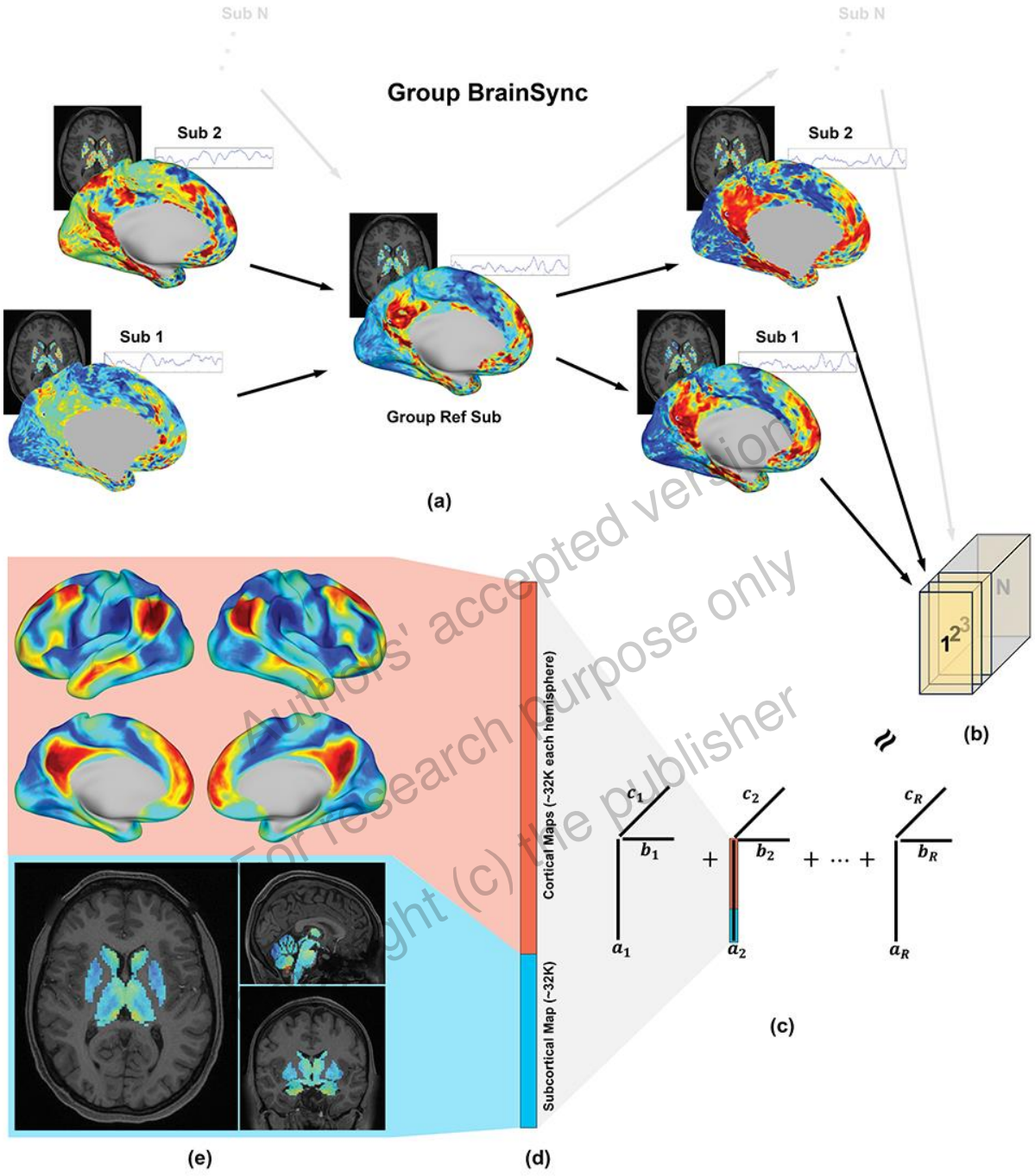

Figure 1: Brain network identification pipeline. (a) Group BrainSync transform for temporal alignment; (b) 3D Tensor formation (space x time x subject); (c) Tensor decomposition using NASCAR; (d) Grayordinate representation of the spatial map of the default mode network (DMN); (e) The cortical map and the subcortical map of the DMN.

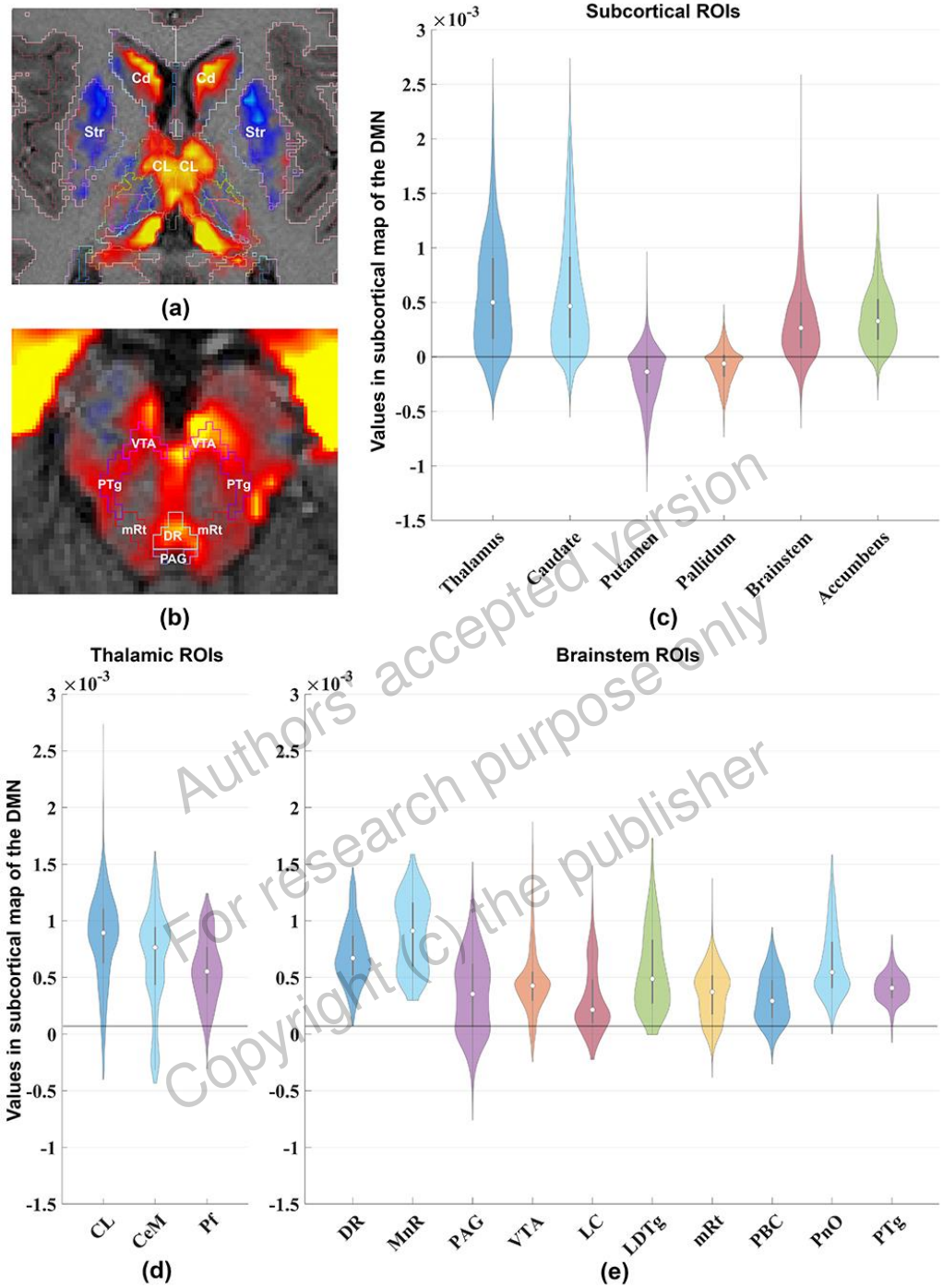

Figure 2: Subcortical functional connectome of the DMN. (a) Subcortical map in an axial slice through thalamus, caudate, and striatum, overlaid with the segmentation atlases and the T1-weighted image; (b) Similar to (a) but through brainstem; (c) Violin plot of each subcortical ROIs in aseg atlas; (d) Similar to (c) but for ROIs in PTN atlas. (e) Similar to (c) but for ROIs in AAN atlas.

CL - Central Lateral Nucleus; CeM - Central Medial; Pf - Parafascicular; DR - Dorsal Raphe; MnR - Median Raphe; PAG - Periacqueductal Grey; VTA - Ventral Tegmental Area; LC - Locus Coeruleus; LDTg - Laterodorsal Tegmental Nucleus; mRt - Midbrain Reticular Formation; PBC - Parabrachial Complex; PnO - Pontis Oralis; PTg - Pedunculotegmental Nucleus.

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