CNS 2017 ANNUAL MEETING
BOSTON, MASSACHUSETTS
OCTOBER 7–11, 2017

Tractography-defined Subregions of Human Nucleus Accumbens Predict Acute Anxiolytic Response to Selective Stimulation

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Introduction

The nucleus accumbens (NAc) serves as a key node in reward processing underlying motivated behavior, and its dysfunction is implicated in a host of psychiatric disorders that are amenable to deep brain stimulation (DBS). On the basis of histochemical and structural connectivity data most thoroughly conducted in animals, the NAc is divided into two primary subregions, core (dorsolateral) and shell (ventromedial), which have dissociable afferent and efferent connections and functions. To characterize NAc subregions, the current study used high-resolution diffusion tractography to delineate core and shell and assessed the immediate clinical implications.

Methods

Multimodal MRI data from 245 healthy, unrelated subjects was obtained from the Human Connectome Project database (1). Freesurfer-generated brain regions were used to perform probabilistic tractography using every NAc voxel as seed and every other Freesurfer region as target (2). NAc voxels with similar connectivity fingerprints were grouped using k-means clustering. This procedure was also performed retrospectively on two other datasets of lesser quality, including that of one patient with obsessive-compulsive disorder who underwent bilateral DBS lead placement targeting the NAc. The final position of the DBS leads relative to tractography-defined subregions was determined, and the effect of monopolar stimulation on self-reported anxiety utilizing subregion-specific contacts was assessed utilizing a Likert scale.

Results

Tractography-based segmentation of the NAc produced ventromedial and dorsolateral subregions across subjects and datasets, consistent with prior histochemical evidence from humans. At electrical currents as low as 1.6 mA, monopolar stimulation of dorsolateral but not ventromedial subregions produced an acute reduction in self-reported anxiety.

Conclusions

NAc subregions that resemble histologically defined core and shell with dissociable acute clinical effects can be produced with tractography -based segmentation. These results have implications for DBS targeting of the NAc, and may help to explain variances in clinical outcome among patients receiving NAc DBS to date.

Learning Objectives

1) Understand utility of diffusion tractography.

2) Improve NAc DBS targeting.

3) Understand location of NAc subregions.

References

1. Glasser MF, Sotiropoulos SN, Wilson JA, et al. The minimal preprocessing pipelines for the Human Connectome Project. NeuroImage. 2013;80:105-124

2. 1. Fischl, B. (2012). FreeSurfer. NeuroImage 62, 774-781.

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