The Structural Connectome of Isolated Task-Specific Focal Dystonia

Sandra Hanekamp, PhD1,2,3 and Kristina Simonyan, MD, PhD, Dr med1,2,3

1 Department of Otolaryngology, Massachusetts Eye and Ear Infirmary, 2 Department of Neurology, Massachusetts General Hospital, 3 Harvard Medical School, Boston, Massachusetts, USA

INTRODUCTION

Task-specific focal dystonia (TSFD) is a movement disorder, which selectively affects skilled motor behaviors, such as writing or speaking. Although its pathophysiology is unclear, it is considered a functional network disorder (Battistella et al., 2017). Several studies also point to the presence of microstructural alterations in dystonia (Simonyan et al., 2018). However, the inter-regional relationships between structural abnormalities remain less well understood. Here, we examined the organization of large-scale structural connectome in two different TSFD forms, laryngeal dystonia (LD) and writer’s cramp (WC) compared to healthy controls (HC) to determine structural network abnormalities in this disorder.

METHODS

Cohorts: Laryngeal Dystonia (N=17), Writer’s Cramp (N=15) and Healthy Controls (N=16)

Method: Diffusion-weighted MRI (3T) and graph analysis

- 116 x 116 adjacency matrix using deterministic fiber tracking
- Node centrality: nodal degree (k_i) and strength (s_i)
- Permutation testing with 10,000 iterations (p ≤ 0.05)
- Modules: normalized mutual information (NMI) using Louvain algorithm
- Hub formation: if nodal k_i/s_i 1.5 SD > mean k_i/s_i of network
- Participation index = 0.3 = provincial hubs; 0.3-0.75 = connector hubs
- Software used: AFNI, FSL, TORTOISE, Brain Connectivity Toolbox, BrainNetViewer

RESULTS

1. Modular Disorganization of Dystonic Connectome

2. Shrinkage and Expansion of Neural Communities

3. Abnormal Modular Participation

4. Abnormal Hub Formation

5. Abnormal Node Centrality

TSFD COMMON FEATURES

- Shrinkage and expansion of neural communities (Fig. 1 and 2)
- Bilateral posterior cingulate cortex upgrades from provincial to connector hub (s_i) (Fig. 2)
- Abnormal modular participation of modules II and IV (Fig. 3)
- Hub loss in left insula (k_i) (Fig. 4A)
- Hub gain in left superior frontal gyrus (k_i) and left anterior cingulate cortex (s_i) (Fig. 4B)
- Node centrality changes in regions linked to laryngeal motor functions (supplementary motor area and superior frontal gyrus) (Fig. 5A)
- Overall pattern of increased network connectivity (Fig. 5A)

LD DISTINCT FEATURES

- Hub gain in right pallidum (k_i) and left superior occipital gyrus (s_i) (Fig. 4C)
- Hub loss in left superior parietal lobule (k_i) and left precuneus (s_i) (Fig. 4C)
- Node centrality changes in cerebellar cortex and regions linked to sensorimotor integration (cingulate cortex and insula) (Fig. 5B)
- Overall pattern of decreased network connectivity (Fig. 5B)

WC DISTINCT FEATURES

- Abnormal structural connectivity architecture in TSFD suggests that dystonia is a large-scale network disorder at both structural and functional levels.
- Brain regions that show dystonia form-specific alterations may be considered as future therapeutic targets for novel drugs and invasive or noninvasive neuromodulation.

CONCLUSION