Supplementary Material

Methods

Network connectivity parameters

Degree

The degree of a particular node is defined as the total number of edges that are connected to that specific node, i.e., nodal degree is a measure for the local connectivity of a particular node with its nearest neighbours. Let Z represent the set of all nodes in the network. The degree (g) of a specific node e was calculated using the Eq. (1).

$$g_e = \sum_{f \in Z} h_{ef} \tag{1}$$

where h_{ef} is the link (connection) between nodes e and f.

Modularity

The entire brain network can be divided into non overlapping modules. In a module, the nodes are densely connected with each other, while maintaining sparse connections with nodes in other modules [1]. The modularity of a network (Q) was calculated using Eq. (2).

$$Q = \frac{1}{i} \sum_{ef \in Z} \left[h_{ef} - \frac{g_e g_f}{i} \right] \delta_{m_e m_f} \tag{2}$$

where i is the actual number of links, m_e is the module containing a node e, and $\delta_{m_e m_f}$ =1 if $m_e = m_f$, and 0 otherwise.

Clustering

The clustering is a measure of the degree to which nodes in a graph are part of a cluster. It is a parameter of the local network organization that reflects the number of connections between neighboring nodes [2]. The highly connected neighbors form a cluster around the node, while sparsely connected neighboring nodes do not. The clustering coefficient (C) of a node e is given by Eq. (3).

$$C_e = \frac{2t_e}{g_e(g_e - 1)} \tag{3}$$

where t_e is the number of triangles around node *e*.

Local efficiency

The local efficiency quantifies local network integration and local network performance. A fully connected network has maximal local efficiency since all distances are minimal, while a disconnected network has minimal local efficiency since certain distances are infinite [3, 4]. The local efficiency (E_{loc}) of a network was calculated using Eq. (4).

$$E_{loc} = \frac{1}{z}\sum_{e \in Z} E_{loc,e} \tag{4}$$

where $E_{loc,e}$ is the local efficiency of a node e.

Path length

The path length of a network is a measure of how long (i.e., passing how many nodes) information has to travel through the network to reach its destination [2]. The path length (L) of a network is calculated using Eq. (5).

$$L = \frac{1}{z}\sum_{e \in Z} L_e \tag{5}$$

where L_e is the average distance between the node e and all other nodes.

Global efficiency

The global efficiency reflects the global network integration and the efficiency of information flow through the entire network. It also reflects the network performance and the network's capacity to efficiently perform the global tasks [3]. The global efficiency of the network (E) is calculated using the Eq. (6).

$$E = \frac{1}{z}\sum_{e \in Z} E_e \tag{6}$$

where E_e is the efficiency of the node e.

Results

Regional network differences between patients (BSP, and HFS) before treatment and HC

Compared to the HC, the patients group showed higher degree and clustering in the motor cortex, parietal and temporal regions, while lower mainly in the parietal regions and cerebellum (Supplementary Figure 1) (all at $p < 0.05$).

[**insert Supplementary Figure 1.**]

Global network differences between patients with BSP and HFS after treatment

After the treatment, patients with BSP relative to patients with HFS showed higher modularity, and path length, while lower clustering, local efficiency and global efficiency ($p < 0.001$) (Figure 1A-E). These results show that patients with BSP relative to HFS had higher segregation and lower integration even after BoNT treatment.

Regional network fingerprints of dystonia and facial hyperkinesia after treatment

After the treatment, BSP patients relative to HFS patients showed an increased degree and clustering in temporal regions, while mainly we demonstrated a decrease in the cerebellum ($p < 0.05$) (**Supplementary Figure 2A**). BSP patients relative to HC exhibited a heightened degree and clustering in the occipital, parietal, and temporal regions, while there was a decline in the frontal and cerebellum regions ($p < 0.05$) (**Supplementary Figure 2B**). After the treatment, HFS patients relative to HC showed increased degree and clustering in the temporal and parietal regions, while there was a reduction in the cerebellum ($p < 0.05$) (**Supplementary Figure 2C**). These results further highlight the decreased connectivity in the cerebellum in patients with BSP relative to patients with HFS after treatment.

[**insert Supplementary Figure 2.**]

GMV changes

The GMV differences between BSP and HFS before the treatment did not survive the cluster level FDR correction. However, whole brain VBM analysis found the differences for voxel-level uncorrected $p < 0.001$. Prior to the treatment, BSP patients relative to HFS patients showed increased GMV in right superior temporal region (**Supplementary Figure 4A**, Supplementary Table 2), while decreased GMV in the bilateral supplementary motor, left superior parietal, and right postcentral (**Supplementary Figure 4B**, Supplementary Table 2).

[**insert Supplementary Figure 3.**]

[**insert Supplementary Figure 4.**]

Supplementary Table 1. Results of the between group voxel-wise comparisons of grey matter volume (GMV) of BSP and HFS patients and HC at baseline

Contrast	**Region**	**Cluster size (voxel)**	**MNI peak coordinates**			**T**	P_{FDR}
			x	**y**	**z**		
BSPpre > HC	R precentral gyrus	358	27	-21	64	10.4	0.001
	L precentral gyrus	434	-45	-16	61	9.5	0.001
	L inferior occipital	70	-51	-75	-6	8.4	0.008
HFSpre > HC	R precentral gyrus	522	29	-21	61	11.0	0.001
	R paracentral lobule	175	5	-25	72	10.2	0.001
	L paracentral lobule	1072	-6	-24	73	10.1	0.001
	L inferior occipital cortex	83	-51	-72	-8	9.9	0.004
HFSpre < HC	L crus 1 of cerebellum	261	-20	-63	-32	10.3	0.001
	L lobule 8 of cerebellum	298	-27	-58	-44	8.6	0.001
	R lobule 8 of cerebellum	152	20	-55	-48	8.4	0.001
	R parahippocampal gyrus	150	27	-16	-24	8.4	0.001

Abbreviations. L: left, R: right.

Supplementary Table 2. Results of the between group BSP and HFS before (pre) treatment voxel-wise comparisons of grey matter volume (GMV)

Contrast	**Region**	**Cluster size (voxel)**	**MNI peak coordinates**			**T**	***P***
			x	**y**	**z**		
BSPpre > HFSpre	R superior temporal gyrus	61	62	2	3	7.9	0.001
BSPpre < HFSpre	R supplementary motor area	436	6	-24	57	6.4	0.001
	L superior parietal lobule	62	-17	-54	58	8.4	0.001
	R postcentral gyrus	230	24	-37	66	7.6	0.001
	L supplementary motor area	66	-3	6	52	6.1	0.001

Abbreviations. L: left, R: right.

References

1. Newman ME. Modularity and community structure in networks. *Proc Natl Acad Sci U S A*. 2006; 103: 8577-82.
2. Watts DJ and Strogatz SH. Collective dynamics of /`small-world/' networks. *Nature*. 1998; 393: 440-2.
3. Latora V and Marchiori M. Efficient behavior of small-world networks. *Phys Rev Lett*. 2001; 87.
4. Onnela JP, Saramaki J, Kertesz J and Kaski K. Intensity and coherence of motifs in weighted complex networks. *Phys Rev E*. 2005; 71.

Figure Legends

Supplementary Figure 1. Comparison of regional structural networks between patients (BSP, and HFS) before BoNT treatment and HC: Representation of significant (FDR corrected, p < 0.05) regional between-group differences in degree (left panel) and clustering (right panel).

Supplementary Figure 2. Comparison of regional structural networks between BSP and HFS patients after BoNT treatment and HC: Representation of significant (FDR corrected, $p < 0.05$) regional between group differences in degree (left panel) and clustering (right panel) after (post) BoNT treatment for **(A)** BSPpost vs HFSpost **(B)** BSPpost vs HC **(C)** HFSpost vs HC.

Supplementary Figure 3. **Voxel-wise group comparisons of grey matter volume (GMV) between HC and BSP/HFS before (pre) BoNT treatment. (A) BSPpre > HC**: increased grey matter volume (GMV) in right precentral region (Montreal Neurological Institute peak coordinate x = 27, y = -21, z = 64) in BSP in comparison to HC before treatment. **(B) HFSpre > HC**: increased GMV in the right precentral region (x = 29, y = -21, z = 61) in HFS relative to HC before treatment. **(C) HFSpre < HC**: decreased GMV in the left cerebellum (x = -20, y = -63, z = -32) in HFS relative to HC before treatment. All these clusters survived the cluster level FDR correction ($p < 0.05$) for an extent threshold of 50 voxels. The results are superimposed on the ch2 template from MRIcron in neurological convention (left hemisphere is depicted on left).

Supplementary Figure 4. **Voxel-wise comparisons of grey matter volume (GMV) (cross-sectional VBM) between BSP and HFS patients before (pre) treatment. (A) BSPpre > HFSpre:** increased GMV in right superior temporal region (Montreal Neurological Institute peak coordinate x = 62, y = 2, z = 3) in BSP relative to HFS before treatment. **(B) BSPpre < HFSpre:** decreased GMV in the right supplementary motor area (x = 6, y = -24, z = 57) in BSP relative to HFS before treatment. The clusters that survived the uncorrected $p < 0.001$ with an extent threshold of 50 voxels are shown. The results are superimposed on the ch2 template from MRIcron in neurological convention (left hemisphere is depicted on left).