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Structural brain alterations in hemifacial spasm: A voxel-based morphometry and diffusion tensor imaging study

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HIGHLIGHTS

- We aimed to provide evidence that patients with hemifacial spasm (HFS) had brain abnormalities.
- Grey matter abnormality was detected within brain regions associated with motor control in patients with HFS.
- White matter microstructural disruption was not detected in patients with HFS.

ABSTRACT

Objective: Hemifacial spasm (HFS) is characterized by involuntary, irregular clonic or tonic movement of muscles innervated by the facial nerve. We evaluated structural reorganization in brain gray matter and white matter and whether neuroplasticity is linked to clinical features in HFS patients.
Methods: High-resolution structural magnetic resonance imaging and diffusion tensor imaging data were acquired by 3.0T MRI from 42 patients with HFS and 30 healthy subjects. The severity of the spasm was assessed according to Jankovic disability rating scale. Voxel-based morphometry (VBM) and tract-based spatial statistics (TBSS) analysis were performed to identify regional grey matter volume (GMV) changes and whole-brain microstructural integrity disruption measured by fractional anisotropy (FA), mean diffusivity (MD), axial diffusivity (AD) and radial diffusivity (RD).
Results: The VBM analysis showed that patients with HFS reduced GMV in the right inferior parietal lobule and increased GMV in the cerebellar lobule VIII, when compared with healthy subjects. Furthermore, within the HFS disease group, GMV decreased with the disease duration in the right inferior parietal lobule. TBSS did not identify group differences in diffusivity parameters.
Conclusions: While no white matter integrity disruption was detected in the brain of patients with HFS, our study identified evident GMV changes in brain areas which were known to be involved in motor control.
Significance: Our results suggest that HFS, a chronic neurovascular conflict disease, is related to structural reorganization in the brain.

1. Introduction

Hemifacial spasm (HFS) is a neuromuscular disease that is characterized by irregular, involuntary muscle contractions on the face (Wang and Jankovic, 1998). It is generally believed that HFS caused by vascular compression at the root exit zone (REZ) of the facial nerve (Moller, 1991). Patients with HFS often undergo rapid spasm reliefs following microvascular decompression (MVD) surgery.

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Recent studies show that HFS may also be associated with the compression of distal portions of the facial nerve (Campos-Benitez and Kaufmann, 2008; Kawashima et al., 2009).

The effects of physical training or exercise on brain morphology in animal models have been extensively reported in histological studies. For example, adult rats with free access to running-wheels exhibit marked changes in cortical thickness in motor cortex (Anderson et al., 2002; Markham and Greenough, 2004; Voss et al., 2013). A longitudinal study using voxel-based morphometry (VBM) showed regional GMV increased in motor and somatosensory areas of exercised rats (Sumiyoshi et al., 2014). Human neuroimaging studies have also shown regional GMV/cortical thickness and white matter microstructural changed after intensive exercise training (Killgore et al., 2013; Fuss et al., 2014; Drijkoningen et al., 2015; Huang et al., 2015; Tamura et al., 2015; Zhu et al., 2015). Additionally, persistent nerve compression can also cause neural plasticity in the brain. The whole-brain structural MRI and diffusion tensor imaging (DTI) have revealed alterations in GMV/cortical thickness and white matter integrity in the cases of persistent nerve compression conditions, such as, carpal tunnel syndrome, trigeminal neuralgia (Maeda et al., 2013; Obermann et al., 2013; Parise et al., 2014; DeSouza et al., 2015).

Modern neuroimaging techniques have been employed previously to investigate the brain metabolic and functional changes in patients with HFS. By using the positron emission tomography (PET), it was found that HFS patients had glucose hypermetabolism in the bilateral thalamus before and after Botox injections, when compared with healthy controls (Shimizu et al.). By using the resting-state magnetic resonance imaging (fMRI) scan, we recently report that there are regional homogeneity abnormalities across cortical areas in HFS patients, which are involved in facial movement and motor control such as precentral cortex, pons, cerebellum (Tu et al., 2015).

VBM with diffeomorphic anatomic registration through exponentiated lie algebra (DARTEL) is an automated technique for assessing brain structures, which requires no *a priori* locational assumptions. It is becoming a popular approach for identifying GMV changes in neurological and neuropsychiatric diseases (Asami et al., 2012; van der Velde et al., 2014). Compared to structural MRI, diffusion tensor imaging (DTI) provides information on the white matter integrity by measuring the motion of water molecules (Mori and Zhang, 2006). Tract-based spatial statistics (TBSS) analysis has been employed for assessing white matter integrity by means of fractional anisotropy (FA), and mean/axial/radial diffusivity (MD/AD/RD) (Smith et al., 2006). Generally, low FA is a result of demyelination, axonal loss and inflammation. AD helps to identify axonal damage or degeneration, whereas RD reflects myelin injury selectively (Alexander et al., 2007).

In this study, we aim to assess the HFS related grey matter and white matter reorganization using VBM and TBSS approaches, and determine whether neuroplasticity is associated with disease duration and spasm severity. We hypothesized that there are changes in the GMV of motor regions and white matter tracts connecting to motor regions for HFS diseases, as they have been previously shown to be related to movement disorders.

2. Methods

2.1. Participants

A total of 72 participants were recruited in this study: 42 HFS patients and 30 age-, sex- and education matched healthy subjects from Neurosurgery Department, Ruijin Hospital, Shanghai Jiaotong University School of Medicine and local community. All subjects were right-handed according to the Edinburgh Inventory (Oldfield, 1971). The HFS diseases were diagnosed, based on clinical phenomenology, by two neurological physicians (WG Zhao, YX Wei with 27 and 5 years of experience in clinical neurosurgery, respectively). Known causes of secondary HFS were excluded on the basis of medical histories, neurological examination, and conventional MRI. All patients have no other neurological and neuropsychiatric diseases. Beck Depression Inventory-II(BDI-II) and Beck Anxiety Inventory (BAI) were used to evaluate the affective conditions of HFS patients. Patients with co-occurring symptoms of anxiety and depression were excluded. The spam severity of HFS patients was graded from grade 0 to grade 4 according to the Jankovic disability rating scale: 0–normal, 1–slight disability, no functional impairment, 2–moderate disability, no functional impairment, 3–moderate disability, functional impairment and 4–incapacitated (Jankovic, 2009). Duration of illness was calculated from onset of symptom to scan date in years.

The study was approved by the Ethics Committee of Ruijin Hospital, Shanghai Jiaotong University School of Medicine, and all participants' written informed consents were obtained prior to taking part in the study.

2.2. MRI data acquisition

All MR images were acquired using the GE Signa HDxt 3.0T scanner (General Electric Medical Systems, USA) with a standard 8-channel head coil. The 3D high resolution T1-weighted structural data were obtained using magnetization prepared rapid acquisition gradient echo (MPRAGE) sequence (TR = 5.8 ms, TE = 1.8 ms, flip angle = 12°, 196 sagittal slices, slice thickness/gap = 1.0/0 mm, FOV = 256 × 256 mm^2, matrix = 256 × 256). DTI data were acquired using a single-shot echo-planar imaging sequence, the sequence parameters were TR = 15000 ms, TE = 85.7 ms, 25 non-linear diffusion directions with $b = 1000\ s/mm^2$ and 3 additional volume with $b = 0\ s/mm^2$, 53 axial slices, slice thickness/gap = 2.5/0 mm, FOV = 240 × 240 mm^2, matrix = 96 × 96. Conventional T1 and T2 images were also acquired for radiological review in order to rule out neurological abnormalities and pathology.

2.3. MRI data preprocessing and analysis

Since 20 patients were right-sided HFS, in order to the increase consistency across the sample, the 3D high resolution structural MRI and DTI data of right-sided HFS were flipped along the mid-sagittal plane prior to preprocessing in our study.

2.4. VBM analysis

The VBM analysis was performed using Statistical Parametric Mapping (http://www.filion.ucl.ac.uk/spm/software/spm8/). The procedure included the following steps: (1) checking for scanner artifacts and gross anatomical abnormalities for each subject; (2) setting the image origin to the anterior commissure; (3) segmenting the images into grey matter and white matter images; (4) using the DARTEL toolbox on SPM8 to produce a high-dimensional normalization protocol; (5) checking for homogeneity across the sample and applying a 10 mm full width at half-maximum (FWHM) Gaussian kernel standard smoothing. After this pre-processing, modulated, smoothed, normalized images were obtained for statistical analysis. Total grey matter, white matter, and cerebrospinal fluid (CSF) volumes were calculated using Easy Volume (http://www.sbirc.ed.ac.uk/cyril/download/Easy_volume.zip) based on the segmented images, and total intracranial volume (TIV) was calculated as the sum of the volumes of grey matter, white matter, and CSF. To identify brain regions with significant group differences in GMV, a two-sample *t*-test between two groups was performed, age, gender and TIV were included as nuisance covari-