Dystonia related disease pattern using ICA and resting state fMRI

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Target Audience  Neuroscientist, brain imager, dystonia researcher, resting state fMRI analyst.

Purpose  Dystonia is characterized by sustained or intermittent muscle contractions resulting in abnormal movements or postures. Several studies have reported that dystonia-related abnormalities in patients with genetic or sporadic form using functional neuroimaging, but there are no reports of network-level analysis based on resting state fMRI (rsfMRI). The purpose of this study is to use rsfMRI to determine disease affected brain networks in dystonia patients compared to controls.

Methods  We studied 23 primary dystonia subjects (10 M/13 F; mean age 47±17 years; 6 DYT1/6 DYT6 manifesting the disease and 11 sporadic dystonia) and 23 healthy controls (13 M/10 F; mean age 50±13 years). Subjects were divided into two sets of training (12 controls and 12 DYT1/DYT6) and testing (11 controls and 11 sporadic dystonia patients). Resting state fMRI were acquired on a 3T clinical scanner, 5 mins, 150 volumes, FOV = 24 cm, TE = 28.3 ms, TR = 2 sec, flip angle 77 degrees, 40 slices of 3 mm. In addition, a T1-weighted structural images was acquired for each subject with FOV = 24 cm, TE 2.9 ms, TR = 7.6 ms, TI = 650 ms, flip angle 8 degrees, 176 slices of 1 mm. Clinical MRIs were normal in all subjects. rsfMRI preprocessing was performed using FMRIB software library (www.fmrib.ox.ac.uk/fsl). The preprocessing included motion correction, brain extraction, spatial smoothing with FWHM kernel of 10 mm, and temporal high-pass filtering with a cutoff frequency of 1/300 Hz. The fMRI volumes were registered to the individual subject’s structural T1 volume and then to the standard Montreal Neurological Institute (MNI) template. rsfMRI data from all subjects were then analyzed using spatial group independent component analysis with GIFT software, in which 50 independent components (ICs) were determined and subject spatial maps and temporal dynamics were estimated using dual regression. The number of components was estimated from the data set using minimum description length criterion. We then calculated subject expression values for each IC by taking the dot product of the mean group map with the subject’s spatial map using the previous method for making group inferences. Multivariate logistic regression (JMP software, SAS Institute Inc., Cary, NC) using a forward-selection method was then utilized to identify a subset of independent components (ICs) that yielded a maximum separation between control and dystonia groups in the training dataset. Disease pattern was computed by a linear combination of independent components in this subset using estimated parameters of nominal logistic model. Individual subject scores were z-transformed with respect to corresponding healthy control values in training dataset.

Results  Four components representing independent contributions from cerebellar/pons, thalamic and premotor/prefrontal regions achieved maximum separation between control and dystonia groups in training dataset (χ² = 18.71; df = 4, p < 0.001) when combined into a disease pattern (Fig.1). This pattern was also applied on the testing data set (see Fig.2). Subject scores representing the mean expression of the dystonia-related pattern were abnormally elevated (p<0.001, Fig. 2, left) in the DYT1 and DYT6 patients of the training cohort. Moreover, prospectively computed pattern expression values were also elevated (p<0.05, Fig. 2, right) in the sporadic dystonia patients of the testing cohort. Thus a replicable dystonia-related network method for making group inferences from functional MRI data using independent component analysis. Hum Brain Mapp 14:140–151. 4. Speirs P et al (2006). Highly automated computer-aided diagnosis of neurological disorders using functional brain imaging. Proc SPIE: Medical Imaging6144: 61445M. 5. Carbon M et al (2004). Regional metabolism in primary torsion dystonia. Neurology, 62, 1384-1390.

Discussion/ Conclusions  We identified dystonia-related disease pattern based on resting state fMRI data and IC analysis. The expression of this pattern was abnormally elevated in patients. This spatial pattern was characterized by increased areas of premotor/prefrontal and cerebellum/pons, decreased area of mediodorsal thalamus, and these regions corresponded to the results of previous studies that utilized FDG PET imaging.

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