Investigation of local brain activity changes in restless legs syndrome using regional homogeneity: a preliminary study

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<u>Purpose</u>: Restless legs syndrome (RLS) is a common neurological disorder characterized by an urge to move the legs and paraesthesias deep in the legs.¹ The unpleasant sensations can cause severe sleep disturbances when occurred at night. Symptoms of RLS are supposed to be generated by local iron deficiency and dopaminergic dysfunction within the brain. Functional MRI has been used to study changes in regional brain activity associated with sensory symptoms.² Regional homogeneity (ReHo), a novel resting-state fMRI parameter has been raised to reflect spontaneous brain activities and the background neurophysiological process across the brain.³ In this preliminary study, we used regional homogeneity (ReHo) to investigate changes of local brain activity for RLS patients as compared to age- and gender-matched normal control (NC) subjects.

Methods: All the subjects gave written informed consent to participate the study, which was approved by the local ethical committee. Ten PLS patients (aged 43.0±12.4 years, range 28-63 years, four females) and ten age- and gender-matched NC subjects (aged 41.5±12.6 years, range 26-63 years, five females) were recruited for group comparison. All subjects were right-handed. Thirty-three axial slices covering the whole brain were acquired using a 3.0T GE Signa MR scanner (GE Healthcare, Milwaukee, WI) with an 8-channel phase array head coil (TR/TE 2000/30 ms, flip angle 90°, matrix 64 × 64, FOV 24 cm, thickness/gap 4/0mm, total 210 volumes). SPM8 (http://www.fil.ion.ucl.ac.uk/spm) was used for data preprocessing including slice timing and realignment for temporal and spatial adjustment, followed by spatial normalization to warp all the images into the same stereotactic space. An in-house software DPARSF was used for ReHo calculation (http://www.restfmri.net). All the time series were de-trended and band-pass filtered (0.01-0.08Hz). ReHo was calculated based on a cluster size of 27 voxels and standardized by the global mean within the whole brain. The statistical analysis contained both of one-sample T test within the PLS and NC groups respectively and two-sample T test to reveal the group difference. For multiple comparison correction, the AlphaSim program implemented in AFNI (http://afni.nih.gov/afni/docpdf/AlphaSim.pdf) was used to control the false positive rate (corrected p<0.05).

Results: For one-sample T test, both of the NC and PSL groups showed increased ReHo in the bilateral posterior cingulate/precuneus cortex as compared to the global mean across the brain (Fig. 1 and 2), indicating the typical default mode network at rest. The RLS group showed the largely reduced cluster size as compared to the NC group. For two-sample T test, the RLS group showed increased ReHo in bilateral middle frontal gyrus, anterior cingulate cortex, caudate nucleus, insula, left putamen, thalamus and right posterior cingulate cortex as compared to the NC group (Fig. 3).

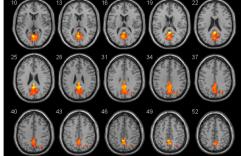


Fig. 1. Increased ReHo region against the global mean for NC subjects (corrected p<0.05)

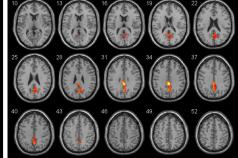


Fig. 2. Increased ReHo region against the global mean for RLS patients (corrected p<0.05)

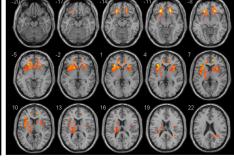


Fig. 3. Increased ReHo regions for RLS patients vs. NC subjects (corrected p<0.05)

<u>Discussion and Conclusion:</u> In this preliminary study, we found increased ReHo regions in bilateral middle frontal gyrus, anterior cingulate cortex, caudate nucleus, insula, left putamen and thalamus for the RLS group as compared to the NC group. To our knowledge, this may be the first resting-state fMRI study applied to RLS. Further study requires more subjects and needs to correlate the changes of local brain activity with other clinical and biological indicators.

References:

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