Resting-state networks and dissociation in psychogenic non-epileptic seizures studied using ICA

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Target audience

Clinical neuroscientists

Purpose

Psychogenic non-epileptic seizures (PNES) are paroxysmal episodes that lack epileptiform brain activity as seen on EEG. Instead, the episodes are of psychogenic origin [1]. In PNES, during rest, an emotional state can influence executive control, resulting in altered motor function. The process of dissociation has been suggested to explain this behavior [1]. To gain insight in the underlying mechanisms, we investigated the processing of information and emotion in the brain, using probabilistic independent component analyses (PICA) of resting-state fMRI. We focused on networks associated with *executive functioning, fronto-parietal activation, sensorimotor functioning,* and *default mode activation* [2]. Also, associations with dissociation tendency were investigated.

Methods

Patients Twenty-one PNES patients without psychiatric comorbidity (13F, age 34±12 y, number of seizures in previous month 12.3±34) and twenty-seven healthy controls (21F, age 36±12 y) underwent MR imaging at 3.0T (Philips Achieva). Global cognitive function was tested using the Raven's Matrices test and all participants completed questionnaires evaluating their dissociation tendency (Dissociation Questionnaire [DISQ], Dissociative Experiences Scale [DES], and Somatoform Dissociation Questionnaire [SDQ]). *MRI* Imaging was performed at 3.0-Tesla (Philips Achieva). For anatomic reference, first T1-weigthed three-dimensional (3D) turbo field echo (TFE) images were acquired with the following parameters: repetition time (TR) 8.2 ms, echo time (TE) 3.7 ms, flip angle 8°, matrix 240x240, field of view (FOV) 256x256x180 mm3, 1 mm adjacent coronal slices. Functional MRI data were acquired using a whole-cerebrum single-shot multi-slice BOLD EPI sequence, with TR 2 s, TE 35 ms, flip angle 90°, voxel size 2×2×4 mm3, matrix 128×128, 32 contiguous slices per volume, 195 volumes per acquisition. Two resting-state fMRI sessions were performed, in which subjects were instructed to think of nothing in particular. *Analysis* Probabilistic group ICA [3] (gICA) was applied to the concatenated resting-state fMRI data using MELODIC (FSL). The identified components were visually compared and cross-correlated with the 4 resting-state networks as reported in the literature (executive functioning, (right) fronto-parietal, sensorimotor and default mode) [2]. The components were mapped to the individual subject level using FSL's dual regression [4]. Permutation testing (N=5000) was performed to identify regions of aberrant functional connectivity for these networks in patients compared to controls. Results are corrected for multiple comparisons (controlling the local false discovery rate at p<0.05). Also, associations of network weights in these regions with dissociation tendency were investigated using the non-parametric Spearman correlation coefficient.

Results

Patients displayed significantly higher dissociation scores ((DES: 1.7±1.27 vs 0.6±0.58 [ctrl], p<0.001), (DISQ: 1.6±0.38 vs 1.4±0.22, p=0.007), and (SDQ: 28.0±6.80 vs 21.5±4.74, p<0.001)) and lower cognitive performance (Raven # correct: 46±7 vs 51±5, p=0.017). Automatic model-order estimation in MELODIC yielded 33 independent spatial components. Compared with healthy controls, patients with PNES demonstrated increased co-activation (network weights) in several regions for the four networks: the orbitofrontal, insular and subcallosal cortex in the resting-state network associated with fronto-parietal activation; the cingulate and insular cortex in the resting-state network associated with executive control; the cingulate gyrus, superior parietal lobe, pre- and postcentral gyri and supplemental motor cortex in the resting-state network associated with sensorimotor functioning; and the precuneus and (para-) cingulate gyri in the default-mode network. The network weights within these regions of interest were significantly and positively correlated with dissociation scores (rho>0.3, p<0.01). For illustrative purposes, the results of the right fronto-parietal network are shown (figure 1).

Discussion

Patients with PNES displayed a higher tendency to dissociate, which may be negatively related to their intelligence [5]. The alterations identified in the diverse resting-state networks could all contribute to the process of dissociation in patients with PNES in various ways: alterations in perception, somesthesis, and pain could originate from the frontoparietal and sensorimotor networks, deviant action-inhibition and emotion from the executive function network, and altered control and monitoring of actions from the default mode network [6]. Importantly, the dissociation tendency is significantly associated with the level of network integration. This is fully in line with previous findings in a smaller population [7].

Conclusion

Abnormalities in resting-state networks provide correlates for the underlying dissociation mechanism in psychogenic non-epileptic seizures.

References

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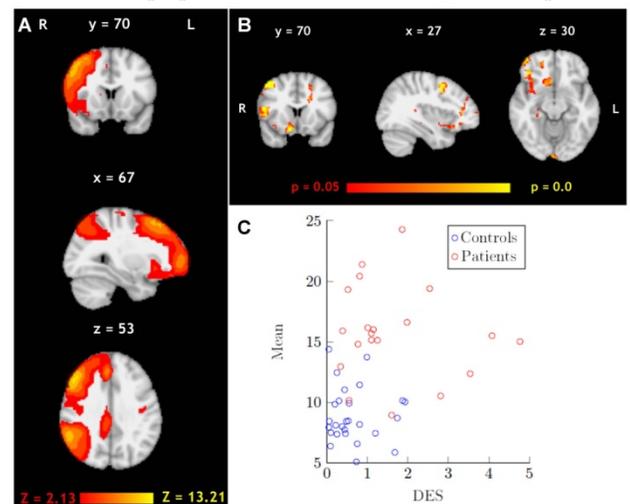
Figure 1. A) The primary (right) fronto-parietal network (group average), B) significant increased weights in PNES vs ctrl, and C) correlation of network weight and DES score (Spearman's rho=0.4084, p=0.0044).