Resting state functional connectivity in patients with periodic hypersomnia

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Introduction

The Kleine–Levin Syndrome (KLS) is a rare but relatively well-defined disorder characterised by excessive sleep periods (periodic hypersomnia) associated with behavioural disturbances such as binge eating (hyperphagia), irritability, and increased sexual interest (hypersexuality) [1]. The etiology of KLS is still unknown. Several neuroimaging methods have been applied to investigate the neural correlates to KLS. A recent functional Magnetic Resonance Imaging (fMRI) study by us implicated thalamic hyperactivity in working memory [2]. Our team has also shown fronto-temporal hypoperfusion on Single Photon Emission Tomography (SPECT) [3]. In the current study, functional connectivity of intrinsic fluctuations in the ‘resting brain’ was investigated in order to further scrutinize the neuropathology in this patient group.

Methods

Nine patients with KLS (6 females, 3 males, mean age = 23 years) and nine healthy controls (4 females, 5 males, mean age = 28 years) were recruited to the study. The subjects were instructed to rest with their eyes closed during image acquisition. Following image parameters were used: TR=2.7 s, TE=40 ms, Voxel size = 3X3X3 mm³, No. Slices = 32, Slice acquisition = axial, No. Dynamics = 80, Acq. Time = 216 s = 3 min 36 s, Slice order = interleaved. Images were pre-processed with movement correction, normalising to MNI template, and smoothing with 8 mm Gaussian kernel using SPM5 (Wellcome Department of Imaging Neuroscience, University College London). Afterwards, the images were analysed with group Independent Component Analysis (ICA) implemented in the GIFT toolbox (http://icatb.sourceforge.net) applying the InfoMax algorithm. Twenty components were extracted from all data. Visual inspection and correlation to network templates [4] resulted in 8 components representing the default mode, attention, and executive networks. Statistical analysis (two sample t-test) was performed in SPM5 to make comparisons between KLS patients and healthy controls.

Results

Results from the second level analysis revealed two components with differences in functional connectivity between KLS patients and healthy controls. One component has its main peaks in left fronto-temporal regions (Fig. 1a). KLS patients showed increased coupling within this network in the middle frontal gyrus (BA 9) and the inferior frontal gyrus (BA 44) (fig 1c). The other component with significant differences represents the dorsal attention network (Fig 1b). Within this network, the patients elicited decreased coupling in the superior temporal gyrus (Wernicke’s area).

Discussion

The main findings of this study were that the KLS patients exhibited increased coupling in the middle and inferior frontal gyri (Broca’s area) and decreased coupling in the left superior temporal gyrus (Wernicke’s area). These areas are traditionally attributed to language function. In a previous study we showed that KLS patients have decreased verbal working memory ability compared to healthy controls [2]. The working memory dysfunction is accompanied by hyperactivity in the left thalamus and the inferior frontal gyrus as well hypoactivity in dorsomedial prefrontal cortex as assessed by fMRI. These findings suggest aberrant function in the thalamo-cortical networks, which might explain the patients’ symptoms. We will further investigate this topic in future studies.

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References


Fig. 1: a) ICA component in left fronto-temporal regions, b) ICA component representing the dorsal attention network, c) Increased coupling for KLS patients in the middle and inferior frontal gyri (Broca’s area), d) Decreased coupling in the superior temporal gyrus (Wernicke’s area).