„Reshaping" the Brain – Longitudinal Assessment of Changes in Functional and Structural Connectivity During Weight Gain in Anorexia Nervosa

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Extended abstract for website

Introduction

In acute anorexia nervosa (AN), brain function and structure are reduced. Severe AN is often treated in an inpatient setting. Inpatient treatment commonly comprises multimodal therapy and aims at counteracting the intense fear of gaining weight and at developing and strengthening healthy attitudes towards eating. Core aim of such a multimodal therapy is a structured and step-wise weight gain. The neurobiological underpinnings of weight gain have been scarcely investigated. First, little is known about the dynamic interplay between regions over the course of the therapy. Investigation of resting-state functional connectivity accounts for fundamental and constitutive processes in the brain (van den Heuvel & Hulshoff Pol 2010). Second, it is not clear at which time in therapy neurobiological changes occur that "re-shape" the brain towards normal. Of the few longitudinal neuroimaging studies in AN, all comprised one time point of underweight and one time point of restored weight. What is completely lacking is a "neurobiological status" in between.

Aims

The primary aim of this study was to elucidate changes of functional connectivity in AN over the course of a standardized multimodal inpatient treatment. Moreover, we investigated potential associations with changes in eating disorder pathology such as excessive weight concerns. A secondary aim was to differentiate the neurobiological changes with regard to an intermediate and a late stage of therapy.

Methods

Using a 3-Tesla scanner, we applied functional magnetic resonance imaging in the restingstate in 16 women with AN and 20 closely age-and intelligence-matched healthy women (HW). The longitudinal study design comprised three time points, each reflecting a distinct stage of the therapeutic process: T1 (stage of severe underweight) with a BMI under 15.5; T2 with a BMI in between of 15.5 and 17.5; T3 with a BMI over 17.5. We analysed resting-state functional connectivity (rsFC) using network-based statistics (Zalesky et al. 2010). Network-based statistics is sensitive for detecting effects in spatially extended conglomerates of altered connectivity, and thus accounts for mutual and dynamic interactions between many brain regions. We determined which networks showed altered rsFC in AN at T1 and examined their development over the course of weight gain. Moreover, correlations between functional connectivity and the weight concern subscale of the widely-used Eating Disorders Examination Questionnaire were assessed.

Results
Compared to HW, AN patients showed reduced rsFC at T1 in frontal cortex, temporal cortex, basal ganglia, and anterior insula. This network of reduced rsFC recovered with weight normalization. Interestingly, this normalization took place relatively early in therapy, that is, between T1 and T2. Conversely, rsFC remained largely unchanged between T2 and T3. Network changes significantly correlated with changes in clinical variables: The larger the difference in rsFC was between T1 and T2, the more profound was the amelioration in patients' weight concerns.

Conclusions
This study demonstrates disturbances in the communication between brain regions in acute, severe AN. These regions have also been implicated in the pathophysiology of AN by previous neuroimaging studies (Frank 2015). They are well known for processes associated with cognitive-emotional integration, learning, and reward. The present results suggest that the identified disturbances in the abovementioned brain regions widely turn toward normal connectivity across the course of weight gain. Neurobiologically, with regard to "re-shaping" the brain towards normal, the early phase of the therapy seems to be pivotal. The identified correlations between neurobiological changes and clinical variables (weight concern) warrant future investigation of the exact brain-behaviour relationship in the treatment of AN. Additionally, since many courses of AN are chronic, the long-term development of the identified brain normalization deserves further attention.

Note: Here, only analysis of resting-state functional connectivity are reported. Analysis of structural connectivity will follow and contribute to a more complete pattern of disrupted and potentially recovering brain network. Impact of the results will also be increased by an enlarged sample size (n = 30).

References
Frank GKW: Advances from neuroimaging studies in eating disorders. CNS Spectr 2015, 20:391–400. van den Heuvel MP, Hulshoff Pol HE: Exploring the brain network: a review on resting-state fMRI functional connectivity. Eur Neuropsychopharmacol 2010, 20(8):519-534. Zalesky A, Fornito A, Bullmore ET: Network-based statistic: identifying differences in brain networks. Neuroimage 2010, 53(4):1197-1207.

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