Insular dysfunction within the salience network is associated with severity of symptoms and aberrant inter-network connectivity in major depressive disorder.

Abstract:

Major depressive disorder (MDD) is characterized by altered intrinsic functional connectivity within (intra-iFC) intrinsic connectivity networks (ICNs), such as the Default Mode- (DMN), Salience- (SN) and Central Executive Network (CEN). It has been proposed that aberrant switching between DMN-mediated self-referential and CEN-mediated goal-directed cognitive processes might contribute to MDD, possibly explaining patients' difficulties to disengage the processing of self-focused, often negatively biased thoughts. Recently, it has been shown that the right anterior insula (rAI) within the SN is modulating DMN/CEN interactions. Since structural and functional alterations within the AI have been frequently reported in MDD, we hypothesized that aberrant intra-iFC in the SN's rAI is associated with both aberrant iFC between DMN and CEN (inter-iFC) and severity of symptoms in MDD. Twenty-five patients with MDD and 25 healthy controls were assessed using resting-state fMRI (rs-fMRI) and psychometric examination. High-model-order independent component analysis (ICA) of rs-fMRI data was performed to identify ICNs including DMN, SN, and CEN.
Intra-iFC within and inter-iFC between distinct subsystems of the DMN, SN, and CEN were calculated, compared between groups and correlated with the severity of symptoms. Patients with MDD showed (1) decreased intra-iFC within the SN's rAI, (2) decreased inter-iFC between the DMN and CEN, and (3) increased inter-iFC between the SN and DMN. Moreover, decreased intra-iFC in the SN's rAI was associated with severity of symptoms and aberrant DMN/CEN interactions, with the latter losing significance after correction for multiple comparisons. Our results provide evidence for a relationship between aberrant intra-iFC in the salience network's rAI, aberrant DMN/CEN interactions and severity of symptoms, suggesting a link between aberrant salience mapping, abnormal coordination of DMN/CEN based cognitive processes and psychopathology in MDD.