Abstract

Background: Early diagnosis of schizophrenia could improve the outcomes and limit the negative effects of untreated illness. Although participants with schizophrenia show structural/functional alterations on the group level, these findings have a limited diagnostic utility. Novel methods of MRI analyses, such as machine learning (ML), may help bring neuroimaging from bench to the bedside. Here, we used ML to differentiate participants with a first episode of schizophrenia-spectrum disorder (FES) from healthy controls (HC) based on neuroimaging data and compared the diagnostic utility of such approach with the utility of between group comparisons using classical statistical methods.

Method: Firstly, we performed a classical fMRI experiment in FES using a self/other-agency task (SA/OA) and compared FES (N=35) versus controls (N=35) using conventional statistics. We than classified FES and healthy controls (HC) using linear kernel support vector machine (SVM) from the resting-state functional connectivity (rsFC) and fractional anisotropy (FA) in 63/63 and 77/77 age- and sex-matched FES and HC participants. We also investigated the between-group differences in rsFC and FA using classical between-group comparisons.

Results: FES group exhibited a decreased activation during the emergent SA experience within the central medial structures (CMS), which reflects a biological correlate of FES. The SVM applied to the rsFC and FA distinguished the FES from the control participants with an accuracy of 73.0% (p=0.001) and 62.3 % (p=0.005), respectively. In the case of rsFC, the classification was significant when the anterior insula/salience network was used. The classification accuracy was not significantly affected by medication dose or by the presence of psychotic symptoms. The between-group differences in rsFC and FA overlapped with the regions contributing to the SVM classification.

Conclusions: Unlike classical between-group comparisons, ML in combination with rsFC and FA can be utilised for diagnostic classification, even early in the course of schizophrenia. The classification was likely based on trait rather than state markers, as symptoms or medications were not significantly associated with classification accuracy. Our results also support the role of anterior insula/salience network and CMS in the pathophysiology of FES.