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Brain Volume Alterations in Patients with Panic Disorder and Social Anxiety Disorder

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ABSTRACT

Recent studies have investigated structural brain changes in gray matter from biomarker and further endophenotype among Panic Disorder (PD) and Social Anxiety Disorder (SAD) patients and controls. Further research in this field promises to clarify the trajectory of heritable brain changes and their contribution to anxiety disorders.

Keywords: Panic disorder, Social anxiety disorder, Endophenotypes, Grey matter.

ABOUT THE STUDY

Among anxiety disorder subtypes, Panic Disorder (PD) and Social Anxiety Disorder (SAD) present unexpected and expected panic attacks, respectively, besides common manifestations of the threat-relevant responses. In this line, it is plausible that PD and SAD may have incompletely similar etiology and pathophysiology based on genetic susceptibility shared across anxiety disorders [1,2] but no familial aggregation between anxiety disorder subtypes in probands and relatives [3]. Recently two meta-analyses on structural MRI studies investigated the unique and shared neuroanatomical characteristics of Grey Matter (GM) volumes in PD and SAD by comparisons both between the two patient groups and with Healthy Controls (HC) [4,5]. Meanwhile, by a case-control design other individual studies compared GM structural alterations between one anxiety type and HC, i.e. biomarkers associated with a particular condition [6].

Using meta-analysis approach smaller cortical and subcortical Gray Matter (GM) volumes in PD patients compared to HC, as well as inconsistent GM volumetric alterations in SAD patients compared to HC, while no common regions of GM volumetric alterations [5]. Similarly, in PD patients compared to HC, recent research mainly reported smaller GM volumes in the left middle temporal gyrus [7] and lower Cortical Thickness (CT) in bilateral insula and right pars triangular is by whole-brain analysis, as well as smaller volumes in the right amygdala, hippocampal sub region and the bilateral nucleus accumbens [8-10] and lower CT in the right Fusiform Gyrus (FG) [11], despite larger right hippocampal tail [12] by Region Of Interest (ROI) analysis. In SAD patients compared to HC, recent research reported lower CT in the bilateral Pre Frontal Cortex (PFC) and right lateral Orbito Frontal Cortex (OFC), but increased Cortical Surface Area (CSA) in the bilateral PFC, right lateral OFC and left Superior Temporal Gyrus (STG) by whole-brain analysis [13], as well as smaller ROI volumes in the bilateral STG, Heschl's gyrus and planum temporal, and anterior and posterior insula [14,15], together with larger GM volumes in the bilateral OFC, left insula and right thalamus [16,17].

Notably, most studies have often compared regional brain structures in one anxiety diagnosis to that of a non-clinical control group to produce convergent, although not always consistent, evidence of abnormal brain structures relating to that disorder. Thereby, a different approach is needed for delineating structural alterations common across anxiety disorders or unique to a specific subtype of anxiety. Given the comorbidity among anxiety disorders and the lack of disorder-specific developmental predictive validity, it may be useful to conceptualize specific diagnoses as reflecting common core neural abnormalities augmented by higher-order phenotypes that orient individuals to a specific focus of anxiety. Individual and meta-analytical research focusing on anxiety disorders have been done to further promote this work [18,19].

In addition to highlighting these neuroimaging biomarker studies, endophenotypes are by definition heritable and reflective of the genetic vulnerability to development of psychopathology and this important characteristic distinguishes endophenotypes from biomarkers [20]. Endophenotypes can be used to identify individuals at risk and provide clues for improvement of treatments for psychiatric disorders, but research on endophenotypes for anxiety disorder is still in its infancy [21]. By using a multiplex multigenerational family design, the first reported morphological changes in the volume of the globus pallidus, the CT of the frontal and temporal regions, and the CSA of the fusiform gyrus, have been suggested to be candidate endophenotypes for SAD [22]. The potential of anatomical brain alterations as candidate endophenotypes has also been mentioned in two reviews [23,24]. However, the stability over time and the potential genetic variants of the abovementioned and available candidate endophenotypes need to be explored in the future research to gain insight into the genetic susceptibility to PD and SAD.

Besides, predictive brain imaging markers promise important scientific, clinical, and societal applications. Currently, the developments and optimization of innovative strategies such as online psychotherapy, virtual reality exposure, wearable devices, and pharmacological augmentation of psychotherapy are promising as augmentative measures of accelerating and enhancing the long-term effectiveness of clinical outcomes of PD and SAD [25,26]. In addition to traditional pharmacotherapy, psychotherapy, and a combination of both [27,28]. Several lines of evidence suggest that neuroimaging markers are valuable for predicting the treatment outcomes across time in anxiety disorders, even the long-term course of them, outperforming prediction based on genetic, demographic, and clinical variables, and supporting the use of neuroimaging in precision psychiatry [29-34]. Collecting a wide range of individual and neuroimaging features/biomarkers in large-scale, multicenter long-term naturalistic studies, and implementing recent technological innovations (e.g., “Big data” platforms and machine learning techniques) may help to identify reliable predictive models in anxiety disorders.

Taken together, some attempts have been made to perform multi-diagnostic comparisons in delineating structural brain abnormalities from biomarker and further endophenotype that are shared, distinct and "Semi-distinct" (i.e. shared by some but not all disorders) within an anxiety diagnostic "Family" using mono-modality. However, the inconsistencies existed in the reported findings which may be due to heterogeneity in diagnoses, paradigms, study designs, image acquisition methods, or analysis, in addition to various confounding factors such as small sample size, comorbidity and medication. Thereby, from the perspective of neurogenesis and development, a longitudinal family design with a large sample size recruiting homogeneous (non-comorbid versus comorbid, and drug-naïve versus drug) probands and their relatives, will be required to elucidate the neurobiological mechanisms and genetic susceptibility underlying PD and SAD outcomes [19,24,35].

CONCLUSION

The development and validation of trans diagnostic characterizations of anxiety disorder subtypes as described in the neuroimaging collaboration focusing on anxiety disorders have being on the way to promise to clarify the trajectory of heritable brain changes and their contribution to anxiety disorders and the relation to other established risk factors. As the field evolves, future research may enable us to utilize more effective strategies for the prevention and individualized treatment of anxiety disorders including PD and SAD derived from neurobiological perspectives.

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