Subcortical brain volumes in social anxiety disorder: an enigma-anxiety international mega-analysis of 37 samples

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Results: Participants who received active tFUS showed decreased left amygdala (F(1,24)=5.44, p=0.03), hippocampal (F(1,28)=4.27, p=0.05), insular (F(1,28)=3.05, p=0.04), and dorsal anterior cingulate (F(1,28)=5.85, p=0.02) BOLD activation during the fear-inducing trials, compared to the sham tFUS group. The decrease in left amygdala BOLD activation was correlated with a decrease in anxiety ratings (r(23)=0.414, p=0.05).

Conclusions: These results suggest that tFUS can be used to change BOLD activation in subcortical regions such as the amygdala, as well as its associated emotional correlates. Future studies can investigate the use of tFUS in individuals with clinical levels of fear and anxiety.

Funding Source: Tiny Blue Dot Foundation

Keywords: Low Intensity Focused Ultrasound, Amygdala, Fear Extinction, Anxiety

39. Subcortical Brain Volumes in Social Anxiety Disorder: An Enigma-Anxiety International Mega-Analysis of 37 Samples

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Background: Multiple studies have investigated subcortical brain volumes in patients with social anxiety disorder (SAD). Their results are often inconsistent, probably due to variations in methodological approaches, such as study-specific sample selections based on age and clinical characteristics.

Methods: Within the framework of the ENIGMA-Anxiety Working Group, we performed a mega-analysis to investigate subcortical volumes in adults and adolescents with SAD relative to healthy controls (HC). Individual participant data from 37 international samples (n=1115 SAD, 2775 HC) were obtained using ENIGMA-standardized protocols for image segmentation and quality control. Linear mixed-effects analyses were adjusted for comparisons across seven bilateral subcortical regions using family-wise error (FWE) correction. Mixed-effects d effect sizes were calculated.

Results: Patients with SAD showed smaller bilateral putamen volume than controls (left: d=-0.077, pFWE=0.037; right: d=-0.104, pFWE=0.001), and a significant interaction between SAD and age was found for the left putamen (r=-0.034, pFWE=0.045). Smaller bilateral putamen volumes (left: d=-0.141, pFWE<0.001; right: d=-0.158, pFWE<0.001) and larger bilateral pallidum volumes (left: d=0.129, pFWE=0.006; right: d=0.099, pFWE=0.046) were present in adult patients with SAD, but no volumetric differences were apparent in adolescents with SAD. Comorbid anxiety disorders and age of SAD onset were additional determinants of SAD-related volumetric differences in subcortical regions.

Conclusions: Subtle alterations in subcortical brain volumes in SAD were identified. Heterogeneity in age and clinical characteristics might partly explain inconsistent previous results. Future longitudinal studies are needed to further explore the association between alterations in subcortical volumes and SAD illness progression from adolescence into adulthood.

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Keywords: Social Anxiety Disorder, Volumetric Neuroimaging, ENIGMA consortium

40. Early Life Stress Predicts Adolescent Trajectories of Emotional Problems and Hippocampal Volume

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Background: As the percentage of the population that experiences early life stress (ELS) continues to rise, it is crucial to identify trajectories of both neural and emotional development across adolescence that may contribute to the onset of psychopathology. The development of subcortical structures such as the hippocampus, which plays a significant role in stress and emotion regulation, may be particularly salient.

Methods: We used longitudinal k-means clustering to identify different trajectories of hippocampal volume and emotional problems across three assessments conducted approximately two years apart (mean age at baseline = 11.33 years). Participants with data from at least two assessments were included in analyses (N=152).

Results: We identified three clusters of participants: Cluster A, with low hippocampal volume and emotional problems; Cluster B, with high hippocampal volume and low emotional problems; and Cluster C, with mid-level hippocampal volume and the highest levels of emotional problems. All trajectories were relatively stable across time. Importantly, ELS severity was associated with a two-fold greater likelihood of belonging to Cluster C than to Clusters A (OR=0.49, 95% CI=0.31, 0.79) or B (OR=0.48, 95% CI=0.30, 0.78).

Conclusions: Relative to the clusters of participants with lower levels of problems, the participant cluster with mid-level hippocampal volume was associated with the highest level of emotional problems. Importantly, ELS severity predicted membership in this cluster. These findings underscore the importance of considering simultaneously the development of adolescent emotional problems and neural structure in studying the adverse effects of exposure to ELS.

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Keywords: Adolescent Development, Early Life Stress, Hippocampal Volume

41. Cerebellar Structure and Cognitive Ability in Psychosis and Psychosis Phenotypes

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Background: Dysconnectivity theories and advances in cognitive neuroscience have increased interest in cerebellar abnormalities in psychosis. Recent work highlights the unique contributions of cerebellum to motor and cognitive psychological processes. While globally smaller cerebellar volume is most consistently reported, region-specific effects and relationships to psychosis phenotypes remain unclear.

Methods: The current study evaluated cerebellar structure in 357 patients (249 schizophrenia-spectrum, 108 bipolar with psychotic features) and 217 non-psychiatric controls. The psychosis sample was also divided into neuropsychologically intact, deteriorated, and compromised groups using estimated premorbid cognitive functioning and current cognitive functioning. Additionally, we used a mediation analysis to evaluate the relationship between cerebellar grey matter volume in the sensorimotor network and psychomotor disturbance via processing speed. Statistical analyses included total intracranial volume, age, sex, and chlorpromazine equivalents as covariates.