S20-04

EFFECTS OF GENETIC VARIANTS ON NEURAL CIRCUITS IN MAJOR DEPRESSION

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Introduction: The underlying neurobiology of major depressive disorder (MDD) is likely to represent an interaction between genetic susceptibility and environmental factors like stress. There is growing evidence that epigenetic processes might mediate the effects of the social environment during childhood on gene expression.

Objectives: We investigated in multimodal high-resolution MRI-genetic studies whether microstructural and functional brain changes are the result of gene-environment interactions.

Methods: Patients with major depressive disorder (MDD), high-risk subjects for developing MDD and healthy participants were investigated using high-resolution magnetic resonance imaging (MRI), high angular resolution diffusion imaging (HARDI) and functional MRI. Furthermore, we assessed early life adversity and measured the serotonin transporter polymorphisms (5-HTTLPR).

Results: We demonstrated that patients with MDD have smaller hippocampal and frontal cortex volumes associated with gen-environment interactions. Healthy Subjects at risk for developing depression, who manage to stay healthy, show better activation of the frontal cognitive control system. Those who had stronger fibre connections between frontal and temporal brain regions also better managed incidences of adversity in early life.

Conclusions: Stress x gene interactions seem to account for at least some of the structural brain changes. Resilience against environmental stressors might be associated with stronger neural fibre connections and more effective cognitive control networks.

https://doi.org/10.1016/S0924-9338(11)73788-9 Published online by Cambridge University Press