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Childhood Trauma / Gene (BDNF, 5HTTLPR) Interactions in Psychosis: Impact On Cognition

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Objective: Brain derived neurotrophic factor (BDNF) is important for brain development and plasticity, and here we tested if the functional BDNF val66met variant modulates the association between high levels of childhood trauma, cognitive function, and brain abnormalities in psychoses. Serotonin transporter gene (5-HTTLPR) variants and childhood trauma were also investigated together with cognitive function in psychosis.

Method: A total of 323 patients with a broad DSM-IV schizophrenia spectrum disorder or bipolar disorder were consecutively recruited. A history of childhood trauma was obtained using the Childhood Trauma Questionnaire. BDNF val66met, 5-HTTLPR, and BDNF RNA were analyzed using standardized procedures. A subsample of n=108 underwent MRI scanning, and the FreeSurfer was used to obtain measures of hippocampal subfield. Cognitive function was assessed through a comprehensive, standardized neuropsychological test battery.

Results: Additive effects were observed between a history of childhood trauma and BDNF val66met, in the direction of met carriers with high levels of childhood trauma having the lowest BDNF mRNA levels. Moreover, met carriers reporting high levels of childhood trauma had significantly reduced hippocampal subfield volumes of CA2/3 and CA4 dentate gyrus, as well as reduced cognitive function. Lastly, we observed a significant interaction between homozygotic s-carriers of the serotonin transporter gene 5-HTTLPR variants exposed to high levels of childhood trauma and poorer cognitive functioning, compared to patients with low trauma and II- or sI- carriers.

Conclusion: Our results need replication but underline the importance of investigating childhood trauma and its interaction with genetic markers when studying cognitive abnormalities in psychotic disorders.