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Topic: S524 - Exploring the molecular, functional and structural brain changes in Mood Disorders and their relevance for illness outcome

Stress-Gene Interactions on brain structure and function in major depression

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Introduction: Major depressive disorder (MDD) is a complex disorder and recent research suggests that muliple genetic and environmental factors seem to underly MDD criteria as well as seem to influence brain structure and function.
Objective and Aims: Aim of the study was to investigate whether epigenetic regulation and mRNA expression of glucocorticoid inducible genes (SGK-1, GILZ) are associated with structural alterations in hippocampal subfields and functional brain changes. Moreover, we investigated whether there are interactive effects between the genetic variant of the *BICC1* gene and ELA.

Methods: Patients with MDD and healthy controls were investigated using structural magnetic resonance imaging (MRI) and functional MRI with an emotion inhibition task. Analysis of a single nucleotide polymorphism in the *BICC1-1* (rs999845) gene as well as mRNA expression and methylation of DNA was performed.
Results: Hippocampal subfield volumes of dendate gyrus and CA2 were reduced in patients with MDD. These were associated with reduced mRNA expression of glucocorticoid inducible genes and with DNA methylation. Moreover, MDD patients with a history of ELA, who carry the protective T-allele, had smaller hippocampal head volumes compared to MDD patients without ELA. FMRI showed that patients and controls carrying the protective T-allele of *BICC1* activate the emotion regulation system significantly more compared to those participants homozygous for the major C-allele ($p<0.05$, family wise error corrected).

Conclusion: These results are suggestive for environment x gene interactions in MDD and for the impact of epigenetic regulation on brain structure and function.

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