

Genome-wide DNA methylation analysis of depression in human brain samples

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Research question and background

Current perspectives on the molecular underpinnings of major depressive disorder (MDD) posit a mechanistic role of epigenetic DNA modifications in mediating the interaction between environmental risk factors and a genetic predisposition. However, conclusive evidence for differential methylation signatures in the brain's epigenome of MDD patients as compared to controls is still lacking.

Methods and tissue used

To address this issue, we conducted a pilot study including an epigenome-wide methylation analysis in six individuals diagnosed with recurrent MDD and six control subjects matched for age and gender, with a priori focus on the hippocampus and prefrontal cortex as pathophysiologically relevant candidate regions.

Results and conclusion

Our analysis revealed differential methylation profiles of 11 genes in hippocampus and 20 genes in prefrontal cortex, five of which were selected for replication of the methylation status using pyrosequencing. Among these replicated targets, GRIN2A was found to be hypermethylated in both prefrontal cortex and hippocampus. This finding may be of particular functional relevance as GRIN2A encodes the glutamatergic N-methyl-D-aspartate (NMDA) receptor subunit epsilon-1 (NR2A) and is known to be involved in a plethora of synaptic plasticity-related regulatory processes probably disturbed in MDD.