Exploring the Mechanisms of Major Depression and Antidepressant Response Using Gene and miRNA Expression

Dunsworth, Ethan (School: Wentzville Holt High School)

Major depressive disorder (MDD) is a debilitating illness, and antidepressant treatment often yields inadequate response rates. It is not currently understood why antidepressant response rates remain so low, partially due to the incomplete knowledge of how MDD itself functions in the brain. This study attempts to further elucidate the biological mechanisms that define MDD and antidepressant response. To do this, the miRNA expression of MDD patients who did and did not respond to treatment were compared to uncover patterns in differential expression. Analysis showed that miRNAs 146a-5p, 146b-5p, miR-24-3p, and 425-3p all are significantly down-regulated in responders following treatment, have stronger down-regulation in responders, and are all likely involved in biological processes which reduce depressive symptoms—findings corroborated by one of the studies whose data this project uses. Cross-referencing multiple databases that predict the target genes of miRNA suggests that antidepressant response correlates with a disruption in axon guidance, MAPK signalling, and TCR-signalling pathways. To explore the presence of these miRNA in external validation sets, the gene expression of postmortem brain tissues were analyzed to find differential gene expression between control subjects and subjects diagnosed with MDD. The results of the genetic analysis supported the miRNA findings and suggest that the biological processes of MDD are sexually dimorphic—again consistent with the findings of the original study's authors.

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