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Hippocampus Proteomic of Major Depression and Antidepressant Treatment: Involvement of Cell Proliferation, Differentiation, and Connectivity

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Abstract : Memory and emotion require hippocampal cell viability and connectivity and are disrupted in major depressive disorder (MDD). Applying shotgun proteomics and stereological quantification of neural progenitor cells (NPCs), intermediate neural progenitors (INPs), and mature granule neurons (GNs), to postmortem human hippocampus, identified differentially expressed proteins (DEPs), and fewer NPCs, INPs and GNs, in untreated MDD (uMDD) compared with non-psychiatric controls (CTRL) and antidepressant-treated MDD (MDDT). DEPs lower in uMDD vs. CTRL promote mitosis, differentiation, and prevent apoptosis. DEPs higher in uMDD vs. CTRL inhibit the cell cycle, and regulate cell adhesion, neurite outgrowth, and DNA repair. DEPs lower in MDDT vs. uMDD block cell proliferation. We observe group-specific correlations between numbers of NPCs, INPs, and GNs and an abundance of proteins regulating mitosis, differentiation, and apoptosis. Altered protein expression underlies hippocampus cellular and volume loss in uMDD, supports a trophic effect of antidepressants, and offers new treatment targets.

Keywords : proteomics, hippocampus, depression, mitosis, migration, differentiation, mitochondria, apoptosis, antidepressants, human brain
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