S24-03 - **GLYCOGEN SYNTHASE KINASE-3ß AND ASSOCIATED PROTEINS IN THE PHOSPHOINOSITIDE 3- KINASE/AKT SIGNALING AXIS: ROLE IN MAJOR DEPRESSION**

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Objectives: Major depression disorder (MDD) is still a major public health problem and the understading of its neurobiology is still poor. We are interested in the impairment of the neuroplasticity, as hypothesis. Evidence suggest that Akt/GSK3ß axis plays a role mediating hormones actions in neuronal survival. The objective of our study was to assess, in MDD, the regulation of protein and lipid kinases involved in the signaling pathway: PI3K-Akt/PKB-GSK3α/ß-ß-catenin and a phosphatase, PTEN.

Methods: Drug-free *postmortem* brain cortices (VPFC) from *antemortem* diagnosed depressed subjects, and in few cases, neuroblastoma cells, were used. Applying the methods of western blot, enzymatic activity, we measured the activities, the levels of several proteins and their expression: Akt1 ; GSK3ß ; pGSK3ß ; PI3K ; PTEN ; ß-catenin. Statistical significance was set at $p< 0.05$.

Results: With respect to control subjects, the main changes observed in MDD can be summarized as follow : The PI3K enzymatic activity was decreased without changes in protein levels. The GSK3ß activity was increased, but the total activity (α+ß isoforms) was not changed, nor were the total GSKαβ protein levels. The Akt1 activity was decreased, The PTEN protein levels were decreased. The ß catenin levels and the tGSK3ß-to-pGSK3 ratio were altered.

Conclusions: The data show a major depression-associated blunting of the PI3K-Akt-GSK3 signaling pathway. The study of protein and lipid kinases and phosphatases is particularly relevant because of crucial roles played by these proteins in neuron survival, proliferation and apoptosis. It adds further support to the neuroplastic hypothesis of affective disorder.

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