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Dysregulation of insulin signaling pathways in schizophrenia

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Background: Schizophrenia (SCZ) is a neuropsychiatric disorder characterized by symptoms such as hallucinations, delusions, and altered cognition. Dysregulation of insulin signaling pathways may contribute to SCZ pathogenesis. Serum-glucocorticoid kinase 1 (SGK1), a regulator of insulin signaling and neurite formation, may play a role in SCZ, but its specific contribution remains poorly understood.

Objectives: This study aimed to investigate SGK1 activity in two models of SCZ: Human induced pluripotent stem cell (hiPSC)-derived neural precursor cells (NPCs) and postmortem dorsolateral prefrontal cortex tissue. Additionally, SGK1 activity and changes in morphology of differentiated SH-SY5Y cells under stress conditions were examined.

Methods: NPCs were generated from seven SCZ subjects and four healthy controls from the Central Valley of Costa Rica. Additionally, dorsolateral prefrontal cortex (DLPFC) from 40 SCZ subjects and 40 healthy matched controls were used to study SGK1 activity. SH-SY5Y cells were differentiated and subsequently stressed under various models. Western blot analysis was used to normalize to VCP levels. Changes in morphology of SH-SY5Y cells were tracked using IncuCyte NeuroTrack software.

Results: Differences between SCZ and control groups were analyzed through GraphPad's Welch's t-test. We found statistically significant differences between SCZ and control groups in pSGK1 expression ($p < 0.05$); however no significant difference was found between SCZ and controls group in total SGK1 expression ($p > 0.05$).

Conclusion: Perturbations of established insulin signaling pathways could contribute to an increased risk of SCZ. We examined the potential role of SGK1 in SCZ in two separate models, hiPSC and postmortem, through western blot analysis. With increased SGK1 activity evident in SCZ, our findings suggest an abnormality in canonical insulin signaling pathways.

Keywords: Schizophrenia,Cognitive Disorders

