

Extracellular Matrix Abnormalities in Schizophrenia

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Research question and background

Schizophrenia is a major debilitating psychiatric disorder characterized by a heterogeneous constellation of positive, negative, and cognitive symptoms. Although several theories have been proposed over the decennia, its underlying neurobiology has remained elusive. Here, we employ novel approaches to study the role of the extracellular matrix in this disease.

Methods and tissues used

We perform lectin-based immunoprecipitations followed by quantitative mass spectrometry-based proteomics on postmortem entorhinal cortex from patients diagnosed with schizophrenia and healthy controls. Proteomics findings were confirmed by dual immunofluorescent microscopy, quantitative PCR, and Western blot. Finally, we employed in silico genetic analyses to examine genetic links to these extracellular matrix proteins

Results and conclusion

Proteomics results showed extensive dysregulations in extracellular matrix proteins in the patient cohort versus controls. Specifically, these abnormalities seemed to be restricted to singular families of proteins. Dual immunofluorescence showed an interesting vascular origin for these abnormalities, and genetic analysis showed de novo mutations identified in the same genes. Quantitative PCR, however, showed an absence of upregulation of these proteins. Together, these converging postmortem and genetic findings point to the extracellular matrix as an interesting novel hub in the pathophysiology of schizophrenia.