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Novel implications of lingo-1 signaling in the post-mortem schizophrenia brain

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Abstract
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Abstract: Background: Myelination and neurite outgrowth are both processes occurring during brain development that have been previously implicated in the pathophysiology of schizophrenia. Leucine-rich repeat and immunoglobulin domain-containing protein, Lingo-1, is a potent negative regulator of both axonal myelination and neurite extension. The Nogo receptor (NgR)/TNF receptor orphan Y (TROY) and/or p75 complex, With No Lysine (K) (WNK1) and Myelin transcription factor 1 (Myt1), have been reported as co-receptors or co-factors in Lingo-1 signaling in the brain. However the roles of these proteins have never been explored in the pathogenesis of schizophrenia.

Methods: We examined the relative protein expression levels of Lingo-1, NgR, TROY, p75, WNK1, and Myt1 within the post-mortem dorsolateral prefrontal cortex (DLPFC) and hippocampus (both CA1 and CA3 regions) in a matched case-control population for schizophrenia (n=37 and n=20 for DLPFC and hippocampus respectively).

Results: There were significant increases in Lingo-1 (20%; p<0.001) and Myt1 (14.5%; p=0.029) levels in the DLPFC in schizophrenia compared to controls. There were also increases in both TROY (18%; p=0.002) and WNK1 (30%; p=0.021) levels in the CA1 in schizophrenia compared to controls. Finally there was an increase in the NgR levels (25%; p=0.019) in the CA3 of schizophrenia subjects compared to the controls. In contrast, a significant reduction in NgR levels (18%, p<0.001) was found in the DLPFC in schizophrenia.

Conclusions: This is the first time that a study has shown the involvement of altered Lingo-1 signaling pathways in schizophrenia. This novel finding may present a direct application for future schizophrenia therapy.

Disclosures: J.L. Andrews: None.