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Abstract

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Novel Implications of Lingo-1 Signaling in the Prefrontal Cortex of Perinatal Phencyclidine Treated Rats in a Neurodevelopmental Model of Schizophrenia

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Background and Aims: 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. We aimed to investigate the developmental profile of Lingo-1 signaling proteins in a phencyclidine (PCP) neurodevelopmental rat model of schizophrenia.

Methods: Male Sprague Dawley rats received *s.c.* injections of PCP (10mg/kg) or saline at postnatal days (PN)7, 9 and 11. Rats (n=6) were sacrificed at three time points, PN12, 5 weeks or 14 weeks. We examined the relative protein expression levels of Lingo-1, NgR, p75, TROY, WNK1 and Myt1, as well as Myelin Basic Protein (MBP) and Myelin Oligodendrocyte Glycoprotein (MOG) as markers of myelination within the prefrontal cortex of the treated rats.

Results: At PN12, Myt1 was decreased in the PCP treated rats, (10; p=0.044). There were no significant changes in the expression of any of the tested proteins at PN 5 weeks ($0.129 \leq p \leq 0.909$). At PN 14 weeks, Lingo-1, NgR, TROY and WNK1 were increased in the PCP treated rats (7%-18.5%; $0.002 \leq p \leq 0.036$). No alterations in myelination markers were found in any group ($0.208 \leq p \leq 0.986$).

Conclusions: This is the first study to have shown an alteration of Lingo-1 signaling pathways in the PFC in a neurodevelopmental schizophrenia animal model. This will allow us to gain a better understanding of the mechanisms implicated in schizophrenia.