Presentation Abstract

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Presentation Title:	Postnatal mGluR5 receptor ablation from parvalbumin-positive interneurons induced select impairments of relevance to schizophrenia pathophysiology
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Abstract:

Along with cognitive impairments and social dysfunction, alterations in parvalbumin (PV) inhibitory neurons are core to schizophrenia, and the metabotropic glutamate receptor 5 (mGluR5) is involved in the maturation of these neurons. Moreover, N-methyl-D-aspartate (NMDA) receptor antagonists, such as phencyclidine (PCP), are often used to model various aspects of schizophrenia, further implicating an aberrant glutamatergic system in the disorder. Thus, the assessment of sociability, learning, memory (spatial and recognition) and PCP sensitivity in mice with postnatal ablation of the mGluR5 on PV-interneurons (PV-mGlu5-/-) was performed. Social preference was assessed in a 3-chambered box. After an inter-trial interval (1, 5 or 10 min), social recognition was then assessed. Novel object/place recognition was conducted in an identical manner, except new objects/locations instead of mice were used. The Barnes maze was used to assess learning and spatial memory. Mice were treated with PCP (0-10mg/kg i.p.) and locomotor activity or prepulse inhibition (PPI) were assessed. PV-mGlu5-/- mice displayed intact social preference yet reduced social recognition. Novel object recognition was also impaired in PV-mGlu5-/- mice suggesting global recognition memory deficits in these mice. PV-mGlu5-/- mice showed an early performance deficit in the Barnes Maze, mediated by increased perseverative errors, yet Barnes maze reversal learning was unaffected. In addition, performance in both the Barnes maze probe and retention trials and the

novel place recognition test were unaffected, suggesting that spatial memory was not impaired. Increased grooming was evident in PV-mGlu5-/- mice. Reduced sensitivity to the PCP-induced disruptions in both the open-field and PPI were observed in PV-mGlu5-/- mice. In summary, postnatal ablation of the mGluR5 from PV-interneurons, previously shown to reduce GAD67 levels and GABAergic synaptic contacts, had no effect on sociability, spatial memory or reversal learning. However, impairments in social and object recognition were evident suggesting dissociable deficits in select forms of memory and social function. Further, increased grooming and perseverative behavior was evident, perhaps indicative of compulsive-like behavior. In addition, the reduced sensitivity to PCP-induced behavioral alterations may indicate reduced NMDA receptor function in these mice, suggestive of potential links with the NMDA receptor hypofunction hypothesis of schizophrenia. Therefore, the neurobiological dysfunctions characterizing these mice may contribute to similar impairments to those seen in schizophrenia.

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