



Presentation Abstract

Program#/Poster#: 632.30/X6

Presentation Title: Early ablation of mGluR5 receptor affects the maturation of parvalbumin interneurons: Consequences for synaptic transmission and plasticity in the hippocampus

Location: Halls B-H

Presentation time: Tuesday, Nov 12, 2013, 2:00 PM - 3:00 PM

Topic: ++C.16.d. Animal models

Authors: ***A. PINTO-DUARTE**^{1,2,3}, M. BEHRENS¹, T. J. SEJNOWSKI¹;
¹The Salk Inst. For Biol. Studies and Howard Hughes Med. Inst., LA JOLLA, CA;
²Inst. of Pharmacology and Neurosciences, Fac. of Medicine, Univ. of Lisbon, Lisbon, Portugal; ³Unit of Neurosciences, Inst. of Mol. Med., Lisbon, Portugal

Abstract: Fast spiking (FS) interneurons play an important role in controlling the activity of pyramidal cells by providing them with strong perisomatic inhibitory inputs. The dysfunction of FS cells has been implicated in several brain illnesses, including schizophrenia. It is known that glutamatergic hypofunction induced by NMDA receptors blockade around the perinatal period affects the maturation of FS interneurons, leading to the downregulation of their calcium buffer, parvalbumin (PV). It was also shown that this effect can be counteracted by the activation of the glutamate receptor mGluR5. It is not known, however, whether glutamatergic hypofunction due to the impairment of mGluR5 activity can also lead to a deficient maturation of FS cells, with associated losses in PV expression. To investigate this, we produced a mouse model in which mGluR5 is deleted postnatally exclusively in PV neurons, by crossing a mouse line expressing mGluR5 flanked by LoxP sites (floxed) with a mouse line carrying Cre-recombinase in PV neurons. We found that mice with a deletion of mGluR5 in PV neurons developed normally and had no major alterations in their brains, but showed a pronounced reduction in the number of PV synaptic contacts in several brain regions, including the hippocampus. Preliminary patch-clamp recordings in CA1 pyramidal cells of hippocampal slices indicated that this downregulation was accompanied by a reduction in the frequency of miniature postsynaptic inhibitory currents. Moreover,

input-output curves of fEPSPs were different in PV-mGluR5 KOs, as compared to wildtype mice, suggesting an impairment in basal synaptic transmission. On the other hand, short-term potentiation induced by a paired-pulse stimulation protocol and long-term potentiation evoked by high-frequency stimulation or a theta burst were not significantly different between wildtype and PV-mGluR5 KO mice. These results suggest that the early ablation of mGluR5 in PV neurons affects their maturation, with important consequences for basal neuronal communication.

Disclosures: **A. Pinto-Duarte:** None. **M. Behrens:** None. **T.J. Sejnowski:** None.

Keyword(s): SCHIZOPHRENIA

HIPPOCAMPUS

PARVALBUMIN

Support: Calouste Gulbenkian Foundation Fellowship to APD

HHMI to TJS

NARSAD to MMB

NIH Grant MH091407 to MMB