

6th Pharmacovigilance Congress

September 28-30, 2016 Toronto, Canada

Prenatal exposure to alcohol impairs the long term integration of GABA interneurons and the proteolytic endothelial activity in mouse neonates

Léger C¹, Hauchecorne M¹, Dupré N¹, Aligny C¹, Leroux P¹, Marret S^{1,2} and Gonzalez B J¹

¹Normandy University, « NeoVasc » Laboratory, Inserm, IRIB, Rouen University, France

²Department of Neonatal Pediatrics and Intensive Care, Rouen Hospital, France

During brain development, the NMDA receptor exerts trophic activities and is required for a correct integration of GABAergic interneurons. The literature informs us that a prenatal alcohol exposure impacts the glutamatergic transmission. It is now established that brain vessels are involved in the migration of GABAergic neurons and we recently showed that endothelial cells express NMDA receptors. In the present study, we hypothesized that in utero alcohol exposure might impact the cortical integration of GABAergic neurons via an alteration of the endothelial cell activity. Using Gad67-GFP mice, we investigated the effects of a prenatal alcohol exposure on the survival of GABAergic precursors, the activation of endothelial MMPs and tPA and the long term integration of GABAergic neurons in the neocortex. Treatment of cortical slices from E15 fetuses with ethanol revealed no significant modification of the apoptotic death. In contrast, both in situ and gel zymographies showed that alcohol markedly reduced the proteolytic activities of MMP9 and tPA in cortical microvessels. These effects were mimicked by the NMDA antagonist MK801. A long term follow-up of the GABAergic interneuron population revealed that a prenatal alcohol exposure increased the density of cortical GABAergic neurons and GFP expression levels but decreased the density of primary dendrites per neuron. Altogether, these findings support that a prenatal alcohol exposition disturbs the activity of vascular matrix proteases and the long term integration of GAD67-GFP interneurons. They raised the question of long term effects of molecules with NMDA antagonist properties such as anesthetics.

Biography

Cécile Leger works at Normandy University, « NeoVasc » Laboratory, Inserm, IRIB, Rouen University, France.

cecile.leger3@gmail.com

Notes: