

Heavy alcohol exposure activates astroglial hemichannels and pannexons in the hippocampus of adolescent rats: Effects on neuroinflammation and astrocyte arborization

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A mounting body of evidence indicates that adolescents are specially more susceptible to alcohol influence than adults. However, the mechanisms underlying this phenomenon remain poorly understood. Astrocyte-mediated gliotransmission is crucial for hippocampal plasticity and recently, the opening of hemichannels and pannexons has been found to participate in both processes. Here, we evaluated whether adolescent rats exposed to ethanol exhibit changes in the activity of astrocyte hemichannels and pannexons in the hippocampus, as well as alterations in astrocyte arborization and cytokine levels. Adolescent rats were subjected to ethanol (3.0 g/kg) for two successive days at 48-h periods over 14 days. The opening of hemichannels and pannexons was examined in hippocampal slices by dye uptake, whereas hippocampal cytokine levels and astroglial arborization were determined by ELISA and Sholl analysis, respectively. We found that adolescent ethanol exposure increased the opening of connexin 43 (Cx43) hemichannels and pannexin-1 (Panx1) channels in astrocytes. Blockade of p38 mitogen-activated protein kinase (MAPK), inducible nitric oxide synthase (iNOS) and cyclooxygenases (COXs), as well as chelation of intracellular Ca²⁺,

drastically reduced the ethanol-induced channel opening in astrocytes. Importantly, ethanol-induced Cx43 hemichannel and Panx1 channel activity was correlated with increased levels of interleukin-1 β (IL-1 β), tumor necrosis factor- α (TNF- α), IL-6 in the hippocampus, as well as with profound alterations in astrocyte arbor complexity. Thus, we propose that uncontrolled opening of astrocyte hemichannels and pannexons may contribute not only to the glial dysfunction and neurotoxicity caused by adolescent alcohol consumption, but also to the pathogenesis of alcohol use disorders in the adulthood. © 2018 Gómez, Falcon, Maturana, Labra, Salgado, Rojas, Oyarzun, Cerpa, Quintanilla and Orellana.

Alcoholism

Astrocyte

Connexins

Cytokines

Glia

Hippocampus

Pannexins

4-(4-fluorophenyl)-2-(4-hydroxyphenyl)-5-(4-pyridyl)imidazole

connexin 43

cyclooxygenase 1

cyclooxygenase 2

cytokine

gamma interferon

gap junction protein

glial fibrillary acidic protein

inducible nitric oxide synthase

interleukin 1 β

interleukin 6

mitogen activated protein kinase p38

pannexin 1

pannexon

prostaglandin E2

prostaglandin synthase

tumor necrosis factor

unclassified drug

adolescent

alcohol consumption

alcoholism

animal cell

animal experiment

animal model

animal tissue

antibody detection

Article

astrocyte

brain dysfunction

calcium cell level

cell structure

cell survival

confocal microscopy

controlled study

enzyme linked immunosorbent assay

glia cell

hippocampus

image analysis

image processing

male

membrane channel

nerve cell plasticity

nerve fiber

nervous system inflammation

nonhuman

pathogenesis

rat

signal transduction

synaptic transmission

toxicity and intoxication