

Consequences of excessive plasticity in the hippocampus induced by perinatal asphyxia

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Perinatal asphyxia (PA) is one of the most frequent risk factors for several neurodevelopmental disorders (NDDs) of presumed multifactorial etiology. Dysfunction of neuronal connectivity is thought to play a central role in the pathophysiology of NDDs. Because underlying causes of some NDDs begin before/during birth, we asked whether this clinical condition might affect accurate establishment of neural circuits in the hippocampus as a consequence of disturbed brain plasticity. We used a murine model that mimics the pathophysiological processes of perinatal asphyxia. Histological analyses of neurons (NeuN), dendrites (MAP-2), neurofilaments (NF-M/Hp) and correlative electron microscopy studies of dendritic spines were performed in Stratum radiatum of the hippocampal CA1 area after postnatal ontogenesis. Protein and mRNA analyses were achieved by Western blot and RT-qPCR. Behavioral tests were also carried out. NeuN abnormal staining and spine density were increased. RT-qPCR assays revealed a β -actin mRNA over-expression, while Western blot analysis showed higher β -actin protein levels in synaptosomal fractions in experimental group. M6a expression, protein involved in filopodium formation and synaptogenesis, was also increased. Furthermore, we found that PI3K/Akt/GSK3 pathway signaling, which is involved in synaptogenesis, was activated. Moreover, asphyctic animals showed habituation memory changes in the open field test. Our results suggest that abnormal synaptogenesis induced by PA as a

consequence of excessive brain plasticity during brain development may contribute to the etiology of the NDDs. Consequences of this altered synaptic maturation can underlie some of the later behavioral deficits observed in NDDs. © 2016

Habituation memory

M6a

Neurodevelopmental disorders

PI3K/Akt/GSK3 pathway

Synaptogenesis

?-Actin

beta actin

glycogen synthase kinase 3

messenger RNA

microtubule associated protein 2

neurofilament M protein

neuron specific nuclear protein

phosphatidylinositol 3 kinase

protein kinase B

messenger RNA

nerve protein

animal experiment

animal model

animal tissue

anxiety

Article

brain synaptosome

controlled study

dendrite

dendritic spine

female

habituation

hippocampal CA1 region

hippocampus

mouse

nerve cell

nerve cell plasticity

neurofilament

nonhuman

perinatal asphyxia

priority journal

protein expression

pyramidal nerve cell

rat

signal transduction

stratum radiatum

synaptogenesis

analysis of variance

animal

asphyxia

avoidance behavior

cell fractionation

electron microscopy

exploratory behavior

genetics

hippocampus

metabolism

nerve cell plasticity

pathology

pathophysiology

physiology

pregnancy

Sprague Dawley rat

ultrastructure

Analysis of Variance

Animals

Asphyxia

Avoidance Learning

Dendritic Spines

Exploratory Behavior

Female

Hippocampus

Microscopy, Electron

Nerve Tissue Proteins

Neuronal Plasticity

Pregnancy

Pyramidal Cells

Rats

Rats, Sprague-Dawley

RNA, Messenger

Signal Transduction

Subcellular Fractions