SECTION XXII.
SCIENCES MÉDICALES ET SANTÉ PUBLIQUE

DOI 10.36074/logos-01.10.2021.v2.15

ASTROGLIAL REACTIVITY IN THE EXPERIMENTAL ACUTE HEPATIC ENCEPHALOPATHY

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Liver pathologies associated with severe functional failure in most cases are complicated by potentially reversible but still dangerous neurocognitive disorder termed acute hepatic encephalopathy (AHE) [1]. It is believed that AHE underlying mechanisms are generally focused on the ammonia neurotoxicity. Hyperammonemia mostly target brain astrocytes as they are the only cell population that contain glutamine synthetase and metabolize ammonia along the brain [2]. Increased ammonia induces glutamine overload of astrocytes, followed by their cytotoxic edema and generalized edema of the brain. Considering region- and context-dependent constituent heterogeneity of astroglia through the brain, its response to various pathological actions is also supposed to be highly diverse. In response to triggering factors astroglia become reactive, while earlier studies have reported downregulation of GFAP in astroglia in condition of hyperammonemia [3]. The purpose of the study was analyzing immunohistochemical (IHC) features of the astroglial reactivity in different brain regions in the conditions of experimental AHE. The study was performed in Wistar rats, which were subjected to acetaminophen induced liver failure (AILF) [4]. Astroglial reactivity was determined by IHC evaluation of the GFAP expression in the sensorimotor cortex and subcortical white matter as the relative area (S rel., %) of $GFAP^+$ labels from 16 up to 24 hours after AILF-procedure. At 12 hours after injection, non-survived animals showed slight, statistically unreliable increase in GFAP values in the cortex and white matter compared to control ($p > 0.05$). In further time-points both survived and non-survived animals displayed substantial and dynamic decrease in the GFAP immunolabeling in two studied regions compared to control values in the same areas. Thus, in the subcortical white matter of the non-survived rats up to 24 h after AILF-procedure, the indicators of GFAP expression was equal to 4.21 (3.21; 5.76) %, that mean reduction by 125.65% compared to control values at 9.50 (6.31; 10.69), ($p < 0.05$). Starting from 18th hour there was observed the dramatic decrease of the indicators in the cortex compared to control: 0.40 (0.11; 1.82) % and 2.59 (2.48; 3.33) %, $p < 0.05$, meaning loss of immunolabeling by 537.5% (6.47 times). Overall, in the conditions of experimental acute hepatic encephalopathy, there is early dynamic attenuation of the astroglial reactivity in the cortical and white matter rat brain regions. The more significant decrease of GFAP level in the cortex indicates this area as more vulnerable and susceptible to incoming systemic detrimental factors in the conditions of acute liver

failure as well as emphasizes the special kind of sensitivity or reactivity of local astroglial population to the action of toxic molecules. The reduction of the level of GFAP in the rat brain, positively associated with dynamic deterioration of the anima state, reflects the role of the abnormal astroglial reactivity in the mechanisms of AHE.

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