REDUCED CEREBRAL BLOOD FLOW IN THIOACETAMIDE-INDUCED HEPATIC ENCEPHALOPATHY IN RATS: AN ARTERIAL SPIN LABELING MRI STUDY

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Background: Hepatic encephalopathy (HE) is a complex neuropsychiatric disorder associated with acute or chronic liver failure in which ammonia is a major neurotoxin which eventually enter the brain. Cerebral blood flow (CBF) reflects brain energy demand and as such is able to provide a potential measure of an early decrease of brain activity. A global decrease of brain energy metabolism is one of the primary events associated with the pathogenesis of HE. Reduced cerebral oxygen consumption and CBF was observed in cirrhotic patients with an acute episode of overt HE, but not in cirrhotic patients without HE (Iversen et al., 2009). Other data indicate, that decreased post-TIPS (transjugular intrahepatic portosystemic shunt) CBF measured using Arterial Spin Labeling MRI method has a potential to predict the development of overt HE in patients with TIPS insertion (Zheng et al., 2012). Collectively, changes of CBF are to be considered as a causative and a predictive factor of overt HE.

However, the exact mechanism by which metabolic effects of ammonia in the brain metabolism are translated into CBF changes during thioacetamide (TAA)-induced HE have not been elucidated in detail.

Purpose: The aim of the study was to investigate the effect of TAA-induced HE in rats on the cerebral blood flow in the region of prefrontal cortex.

Methods: Male Sprague Dawley rats weighing 250–270 g at the beginning of the experiments were kept under standard lighting conditions and given food and water ad libitum. Liver failure was induced by three intraperitoneal injections of TAA (300 mg/kg) at 24 h intervals. MRI study was conducted 24 h after the last injection at the Department of Magnetic Resonance Imaging, Institute of Nuclear Physics, Polish Academy of Sciences, Kraków. MRI experiments were performed using a 9.4 T (BioSpec 94/20 USR , Bruker, Germany) scanner. High resolution anatomic images from prefrontal cortex were acquired with spin echo RARE (Rapid Acquisition with Relaxation Enhancement) sequence. For T1 relaxation time and tissue perfusion measurement FAIR-RARE (Flow-sensitive Alternating Inversion Recovery) sequence was used. Quantitative calculations were performed with in house written Matlab (MathWorks, U.S.A.) script. A statistical analysis of CBF was carried out by the Mann-Whitney U test. The Pearson correlation between body weight and CBF was performed for each animal.

Results and discussion: Statistical analysis of obtained data revealed that acute liver failure caused by TAA resulted in reduced CBF (by 40 %) in the region of prefrontal cortex compared to the control rats (P<0.05). Our results are consistent with the previous findings where CBF was measured in the whole brain by 133Xe clearance method (Pluta and Albrecht, 1986). The presented results also suggest that CBF changes observed in brain prefrontal cortex in TAA model may more likely reflect some alterations noticed during the chronic state of cirrhotic patients than the acute one (Iversen et al., 2009). Moreover, the decrease in CBF showed tendency to correlate with the loss of weight and deterioration in the condition of TAA-treated animals.

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