Cerebral oedema is not responsible for motor or cognitive deficits in rats with hepatic encephalopathy

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Low-grade cytotoxic oedema is considered a main contributor to the neurological (motor and cognitive) alterations in patients with hepatic encephalopathy (HE). This assumption is mainly based on studies with cultured astrocytes treated with very large ammonia concentrations or with animal models of acute liver failure with strong HE. However, the possible contribution of cerebral oedema (vasogenic or cytotoxic) to cognitive or motor alterations in chronic mild HE has not been demonstrated. The aim of this work was to assess whether cerebral oedema contributes to cognitive and/or motor alterations in rats with chronic mild HE.

Methods: Motor activity and coordination and different types of learning and memory were assessed in rats with porta-caval shunts (PCS). Brain oedema was assessed by gravimetry in cerebellum and cortex and apparent diffusion coefficient (ADC) by magnetic resonance in 16 areas.

Four weeks after surgery, PCS rats show reduced motor activity and coordination, impaired ability to learn a conditional discrimination task in the Y maze and reduced spatial memory in the Morris water maze.

PCS rats did not show increased brain water content at 4 or 10 weeks or changes in ADC at 4 weeks. At 10 weeks, increased ADC in some areas is compatible with vasogenic but not cytotoxic oedema.

Conclusion: Cerebral oedema is not involved in motor and cognitive alterations in rats (and likely in humans) with mild HE. Proper understanding of the mechanisms responsible for the neurological alterations in HE is necessary to design efficient treatments.