

Long-term deficits to memory and motor coordination ability are sustained in a murine model of pediatric Type C HE after liver injury resolution.

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Introduction: Chronic liver disease (CLD) in the pediatric population is a growing problem worldwide with an estimated 3-5% of all CLD cases globally occurring in children under 18. Stemming from both lifestyle and genetic causes, CLD complications such as hepatic encephalopathy (HE) in children pose a greater risk to quality of life due to the vulnerable state of development the body, and most importantly the brain, is at. Case studies have identified a potential association between experiencing an HE event during neurodevelopment and long-term deficits to learning and memory, cognitive, and neuromuscular abilities. Little is understood of the unique pathology of HE in pediatric cases and the current study aimed to investigate these long-term neurologic changes in a novel murine model of Type C HE in juveniles. **Methods:** Mice were given 0.2 mL/kg CCl₄ via intraperitoneal injection for 8 weeks beginning at PND14. Neuromuscular and motor coordination, learning and memory, and neuropsychiatric assessments were performed prior to tissue collection and biochemical assessments. A second cohort was allowed 8 weeks to recover from CCl₄ treatment, then followed the same behavioral assessment paradigm. Liver function was assessed via serum chemistries, Sirius Red and H&E staining, and blood ammonia levels. Neuroinflammation was assessed via immunohistochemistry for markers of glial cell activation. Morphological assessments to determine glial cell immune subtype were performed in ImageJ. **Results:** Neuromuscular ability and motor coordination in mice in recovery from CCl₄-induced Type C HE improved significantly but still showed a significant delay in ability compared to peers receiving only vehicle. This same trend was observed when assessing long-term memory ability, but interestingly no long-term changes in anxiety or depression-like behaviors were observed. **Conclusions:** Despite allowing the liver to make a full recovery from CLD, the consequences of experiencing HE during crucial points in neurodevelopment are long-lasting and potentially irreversible. Key pathways such as synaptogenesis, myelination, and synaptic pruning may be impacted during HE pathology and could be responsible for the long-term cognitive changes observed.