Neurometabolism in children with chronic liver disease or portosystemic shunting: a 1H-MRS/MRI study at 7T

Cristina Cudalbu, Lijing Xin, Giannopoulou Mikelidis, Tablel Kaller, Sarah Latchef, Marcella Herrmann, Florian Zieren-Fegert, and Valerie Milot

Center for Genomics in Medicine, University of Geneva Medical School, Geneva, Switzerland, LTS5, École Polytechnique Fédérale de Lausanne, Lausanne, Switzerland, Department of Pediatrics, Gynecology and Obstetrics, University Hospitals Geneva, University of Geneva Medical School, Geneva, Switzerland, Department of Radiology, University Hospital of Lausanne, Lausanne, Switzerland, 7T Solvay Nuclear Magnetic Resonance Center, Lausanne, Switzerland, Swiss Pediatric Liver Center, Department of Pediatrics, Gynecology and Obstetrics, University Hospitals Geneva, University of Geneva Medical School, Geneva, Switzerland.

SYNOPSIS

Children with chronic liver disease (CLD) or congenital portosystemic shunts (CPSS) present with neurometabolic deficits that are not entirely reversible following liver transplantation on the top of the underlying mechanisms of which are largely unknown. Understanding the molecular underpinnings by non-invasive means could inform disease management. Very few MRI studies have been performed in children with CLD, and those were limited by low magnetic fields (1.5 T). One study obtained only proton MRS data at 1.5T (1). This led to partial volume effects and reduced signal-to-noise ratio, and the signal from ethanol detected due to a laboratory water bottle being placed close to the RF coil. At 7T, patients with compensated CLD and CPSS showed an increased signal in the globus pallidus compatible with chronic HE as described in adults (2). The resolution of the 7T-MRS at 1.5T was insufficient to measure reliably NAA or to characterize meaningful. This led us to take advantage of the increased resolution provided by the 7T scanner to examine for the first time detailed the neurometabolic profile, brain volumes and T1 relaxometry at CLD and CPSS patients and correlate these findings with neurometabolic and neurological outcomes.

BACKGROUND

As many as 40-50% of children with chronic liver disease (CLD) or congenital portosystemic shunts (CPSS) present with neurometabolic deficits that are not entirely reversible following liver transplantation on the top of the underlying mechanisms of which are largely unknown. Understanding the molecular underpinnings by non-invasive means could inform disease management. Very few MRI studies have been performed in children with CLD, and those were limited by low magnetic fields (1.5 T). One study obtained only proton MRS data at 1.5T (1). This led to partial volume effects and reduced signal-to-noise ratio, and the signal from ethanol detected due to a laboratory water bottle being placed close to the RF coil. At 7T, patients with compensated CLD and CPSS showed an increased signal in the globus pallidus compatible with chronic HE as described in adults (2). The resolution of the 7T-MRS at 1.5T was insufficient to measure reliably NAA or to characterize meaningful. This led us to take advantage of the increased resolution provided by the 7T scanner to examine for the first time detailed the neurometabolic profile, brain volumes and T1 relaxometry 

METHODS

Children (8-16 years) presented with chronic liver disease (CLD) or porto-systemic shunting were enrolled. Exclusion criteria included antibiotic administration within 6 weeks of assessment, use of psychotropic treatment as well as the conventional MRI exclusion criteria. 1H-MRS data were acquired on an investigational 7T MR scanner (Siemens Healthcare, Germany) using a single-channel quadrature transmit and 24-channel receive radio-frequency (RF) coils (BioMedical Imaging AG, Lausanne, Switzerland). A 3D MPRAGE sequence (TR=2300ms, TE=2.58ms, T1=1100ms, flip angle=120°, 0.6 x 0.6 x 1.0mm3 resolution, 330 x 330 x 256 matrix size). T1-maps were obtained to correct for field inhomogeneity in the 7T-MRS experiments and subsequent partial volume corrections, and generate T1-maps for investigating the T1 signal hypointensity of the globus pallidus. Signal brain atrophy was recently shown in adults with CLD. Automated segmentation of deep brain structures were performed using the FreeSurfer pipeline (12) with an age-appropriate atlas that represents the average anatomy for the age range of 8–16 years. Absolute volume and T1-values were calculated for each segment and normalised to T1-values in healthy children (2) for each age range.

RESULTS

Eight patients (6-14 years) including five CLD (two girls) and one with CPSS (one girl) were enrolled; as seen in Table 1 (CTR: 13 years, girls: 10 years). Cause of CLD included congenital disorder of glycogenolysis, progressive familial intralenticular crystalline type-2, portal stellate derangement, autoimmune hepatitis, AASLD (4). All patients with CLD showed scores in range or above average on Total Intellectual Quotient measure (101±10). One scored below average on the working memory WISC-IV, while the others showed scores between 85-95. Most patients with CLD had decreased T1 relaxometry (-15%). No statistically significant differences were observed between the CLD patients and controls.

CONCLUSION

In conclusion with compensated CLD, there were no significant neurometabolic alterations as assessed by high resolution 1H-MRS, while small changes in hippocampus and amygdala volumes were measured. In CPSS, however, neurometabolic changes were pronounced, together with a marked decrease in measured brain volumes, and likely related to measurable impaired neurocognitive functioning.

ACKNOWLEDGMENTS

Supported by CIBM of the UNIL, LTS5, École Polytechnique Fédérale de Lausanne, and the SNF grant no 310030/173221.

REFERENCES