Magnetic Resonance Imaging and Spectroscopy in Hepatic Encephalopathy

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Hepatic encephalopathy is a brain alteration associated to liver failure that produces cognitive impairments at long term. Neuroimaging are non-invasive methods for the study of the brain by means of spectroscopy and imaging techniques. These technologies give huge information about cerebral metabolism and water distribution to explore brain pathways involved in the pathogenesis of hepatic encephalopathy. Furthermore, new magnetic resonance implementations such as voxel-based morphometry or resting-state functional magnetic resonance imaging allow studying brain atrophy and neuronal connectivity of the cerebral network involved in the neurocognitive impairments observed in the patients. The development of magnetic resonance technology will generate handy tools for the brain study of liver failure to elucidate the time-course of the pathology and thus to obtain an early diagnosis of cerebral complications. (J Clin Exp Hepatol 2015;5:S69–S74)

Hepatic encephalopathy (HE), a liver failure complication, is a metabolic encephalopathy that covers a wide range of neurological manifestations, from subtle cognitive deficits (MHE: minimal HE) to deep coma (overt HE). The ammonia accumulation and/or inflammation seem to be involved in the pathogenesis of HE; however, the time-course of these events is not well established. Classically, HE is classified in three types according to the origin of liver injury, type A HE is related to acute liver failure; type B HE to porto-systemic shunts; and type C to cirrhosis that additionally could be minimal (MHE) or overt (in that case could be episodic or persistent).[1]

Patients with MHE have not an apparent cognitive impairment and it is only detectable by some psychometric tests such as critical flicker frequency (CFF) or psychometric hepatic encephalopathy score (PHES). However, it is difficult to distinguish those cirrhotic patients with MHE from those without HE because of the lack of a "gold" standard in the diagnostic criteria of MHE. In addition, it was estimated that in the future some of these patients with MHE develops an overt HE. For this reason, an early diagnostic of MHE is crucial to avoid future cognitive complications.

Patients with overt HE have brain alterations, from mild upsets (e.g. confusion, depression, somnolence) to deep coma. The grades of HE are well established by neurological assessment (West Haven). Recently, operational definition of the severity of HE according to West Haven have been proposed (HESA: HE Scoring Algorithm).[2] The HE grade, the number of episodes and the persistence of HE is important to minimize the long-term cognitive detriment of the patients, especially with chronic liver disease and these factors should be considered in the clinical management (e.g. treatment or transplant).[3]

MAGNETIC RESONANCE

The magnetic resonance (MR) is a non-invasive technique used for the assessment of HE degree by spectroscopic and imaging clinical studies. Almost all studies in patients are based on proton signals from metabolites or water content among tissues and organs, respectively. These evaluations allow studying metabolic composition, anatomical structures or functional brain connectivity, according to the processing and the complexity of the sample.

MR spectroscopy (MRS) provides information about the metabolic status of the tissues. MRS consists in evaluating the proton relaxation of a small volume of tissue to obtain a spectrum of signals depending on frequency in which each metabolite has a specific position along the spectrum. This allows the identification of a compound in a mixture of metabolites and the metabolite concentration through the area below the peak. Proton MRS in brain

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Abbreviations: ADC: apparent diffusion coefficient; CFF: critical flicker frequency; fMRI: functional magnetic resonance imaging; HE: hepatic encephalopathy; MR: magnetic resonance; MRI: magnetic resonance imaging; MRS: magnetic resonance spectroscopy; MT: magnetization transfer; MTR: magnetization transfer ratio; NAA: N-acetyl aspartate; PHES: psychometric hepatic encephalopathy score; VBM: voxel-based morphometry

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mainly detects lactate (an end-product of anaerobic glycolysis); N-acetyl aspartate (NAA) (considered as neuronal marker); glutamate and glutamine (substrate and precursor of the amino acid involved in the excitatory neurotransmission); creatine and phosphocreatine (metabolites of energetic reservoir); choline derivates (cell membrane components); and myo-inositol (putative glia marker with unknown function).[4]

MR imaging (MRI) is based on proton signals from water content among tissues and organs. The conventional images in MRI are proton density in which the contrast is proportional to the amount of hydrogen, T1-weighted images that provide information of the T1 relaxation time of the tissues (fat tissue is bright while water is dark) and T2-weighted images give transverse relaxation of tissue trough T2 relaxation time (fluids are more brilliant than fat tissue).[5]

Techniques that are more sophisticated allow quantifying brain alterations of different pathologies such as water content, atrophy or connectivity. Magnetic transfer ratio (MTR) images offers contrast from the interactions between the protons in free fluid and those protons bound in macromolecules and both type of protons are in constant exchange. Low MTRs indicate reductions in brain structures in which exchange magnetization with the surrounding water molecules and could reflect myelin damage, cell destruction, or changes in water content.[5] Diffusion imaging shows local water diffusion by the apparent diffusion coefficient (ADC) and a variant of this imaging, diffusion tensor imaging, gets different anisotropic parameters to study the structural integrity, additionally.[6] Furthermore, the amount of brain water has also absolutely quantified using a complex method of MR.[7]

The volumetric measurements provide tools to determine brain atrophy by different strategies. Classically, these studies consisted in drawing regions of interest of whole brain or subparts (e.g. ventricles) on the brain images and calculating the volume enclosed.[3] In recent years, voxel-based morphometry (VBM) has developed to analyze differences in brain anatomy using diverse statistical approaches.[8]

Currently, a huge MR area has been developed to explore brain activity by functional MRI (fMRI).[9] These techniques are based in the assessment of local blood flow and hemoglobin oxygenation changes due to the metabolic changes because of brain activity. A subdivision is the resting-state fMRI that consists in studying the brain when the subject is not performing an explicit task due to cerebral activity.[10] These studies are useful to explore the brain's functional connectivity as well as to examine alterations in neurological or psychiatric diseases.

MAGNETIC RESONANCE STUDIES IN HEPATIC ENCEPHALOPATHY

Magnetic resonance (MR) is a non-invasive technique used for the assessment of HE degree by spectroscopic and imaging clinical studies. However, almost all clinical MR studies have performed in patients whose at the moment

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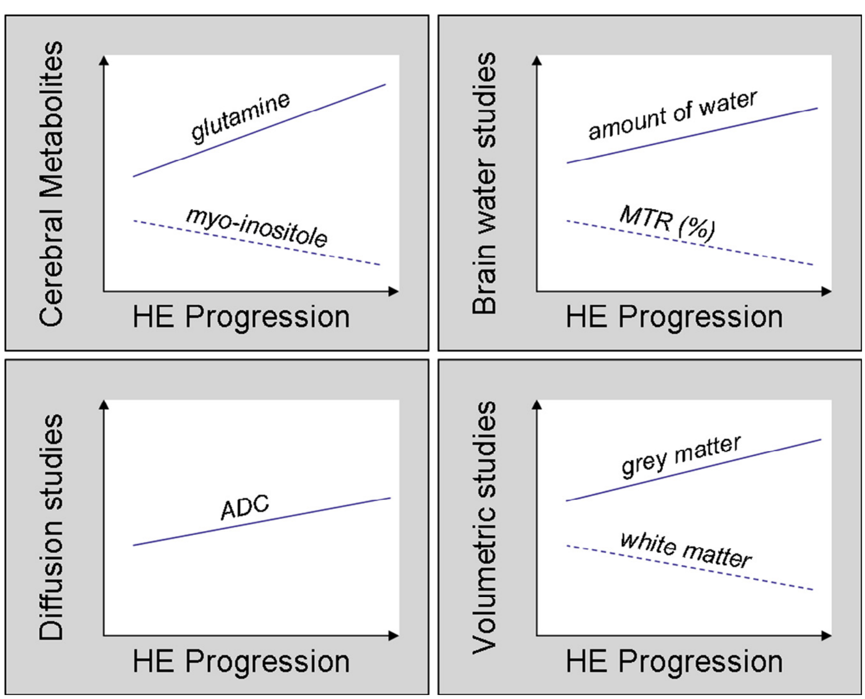

Figure 1 Schema of the general results found in MR studies according to the progression of HE.