

MR spectroscopy in metabolic disorders

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Magnetic resonance spectroscopy (MRS) allows noninvasive detection and measurement of normal and abnormal metabolites and plays an important role in the diagnostic workup of neurometabolic diseases. Technically, MRS is based on the differences in resonance frequencies of normal and abnormal molecules within the nervous tissue. This allows for identification of individual metabolites which are represented graphically in the spectrum in the form of deviations from the baseline, the so-called peaks.

Proton (^1H) MRS is presently available on clinical MRI units and can be performed automatically on most situations. Because of the narrow chemical shift range, however, only few metabolites are detectable. Available ^1H MRS techniques include single-voxel and multi-voxel (ie, chemical shift imaging -CSI) methods. Single-voxel ^1H MRS is more widespread and used routinely; it produces spectra from manually selected volumes-of-interest. Acquisition is possible at short (20-30 ms), intermediate (135-144 ms), and long (270-280 ms) echo times, techniques, yielding different possibilities for metabolite identification and peak analysis.

The metabolites normally detected in the brain, regardless of the adopted echo time, include N-acetyl aspartate (NAA), a neuronal marker, choline (Cho), a membrane marker, and creatine (Cr), an energy metabolism marker. Short echo-time techniques allow for additional metabolite identification, including myoinositol (mI), a glial marker. Absolute and relative concentrations of metabolites are age-dependent. In newborns, Cho is the most prominent peak, whereas NAA is rather inconspicuous. Progressive NAA peak increase occurs in the following months until an adult appearance is reached by approximately six months. Other metabolites, including lactate and glutamine-glutamate complexes, are undetectable in normal conditions. Thus, their identification indicates the presence of an abnormal process, although specificity is limited to a few disorders. Lactate indicates anaerobic glycolysis and cerebral lactic acidosis. Identification of lactate may suggest mitochondrial diseases and is effective in monitoring therapy of these disorders. Secondary lactic acidosis is also found in a host of other metabolic disorders, including propionic acidemia, maple syrup urine disease, nonketotic hyperglycinemia, urea cycle defects, and Zellweger disease. Albeit technically possible, absolute quantification of normal or abnormal metabolites is not routinely performed. Relative changes of concentrations in the form of metabolite ratios are frequently used instead. In most instances, an aspecifically pathological spectrum consisting of

increased Cho/Cr and decreased NAA/Cr ratios is detected, indicating loss of neuroaxonal integrity and increased myelin turnover, sometimes associated with presence of lactate, indicating impaired energy metabolism. Rarely, specific spectral patterns are found, including the pathological increase of NAA in Canavan disease and the absence of creatine in the group of creatine biosynthesis/transportation deficiencies.

Appropriate selection of the acquisition technique (short or long echo-time) and positioning and size of the sampling voxel are important technical aspects in clinical ^1H MRS of brain.

The ^1H MRS findings are strongly influenced by operator-dependent factors, including choice of the echo-time and volume-of-interest placement. Ideally, at least one short TE (20-30 ms) sequence and one either intermediate (135 ms) or long (270 ms) sequence should be obtained in the course of the MR evaluation of patients suspected of harboring metabolic diseases. Short-TE techniques are necessary to demonstrate mI and branched chain aminoacids, but the typically noisier background may impair efficient detection of small peaks. NAA, Cho, and Cr are efficiently recognized on both intermediate and long TE sequences as is lactate, which has the peculiarity of showing up as an inverted doublet at 135 ms. Voxel placement is a critical issue. Focal lesion areas are typically sampled, but the results may be contradictory in that sampling of necrotic areas may not reflect the metabolic status of the rest of the brain; furthermore, lactate often shows up as an indication of impaired energy metabolism, and should not be misinterpreted as an indicator of “mitochondrial disease”. In fact, spectra from apparently unaffected brain regions may be more indicative. Calcified, hemorrhagic or cystic-necrotic areas should not be sampled in order to avoid magnetic field inhomogeneity.

In summary, MR spectroscopy is an extremely useful integration to the MR imaging evaluation of patients harboring metabolic disorders. “Specific” spectral patterns that univocally indicate a particular disease are very rare. Thus, MR spectroscopy should not be expected to make a specific diagnosis but should, rather, be employed as an important part of a global examination that includes conventional MR imaging as well as clinical and laboratory correlations. A strong knowledge of technical issues and pitfall is necessary in order to manage operator-dependent factors that may critically alter the information obtained with this technique.