Journal of Advances in Science and Technology
Vol. 18, Issue No. 1, March-2021, ISSN 2230-9659

Magnetic Resonance Spectroscopy's Use in the Diagnosis of Congenital and Developmental Brain Disorders

Sanjay Singh*

Research Scholar, NIMS University, Jaipur

Abstract – In the study of brain development and in vivo metabolism, magnetic resonance spectroscopy (MRS) has shown to be a useful tool. Non-ionizing radiation is not used in MRS, which is a non-invasive method. White matter and metabolic issues, neurological ailments, and brain malignancies are just a few of the conditions that may be studied using MRS imaging to extract information about an infant's developing brain. Additionally, MRS provides quantitative information on particular metabolites, which can aid in illness diagnosis and therapy evaluation. This article focuses on the use of MRS in the diagnosis of congenital or developmental brain disorders. A brief explanation of the technical elements of MRS precedes the discussion of MRS diagnoses, which is followed by a review of normal brain spectroscopy in neonates & changes with normal brain development.

Keywords – Magnetic Resonance Spectroscopy, Development Brain Disorder, Physical Principles of MRS, Technical Aspects of MRS

----------X----------

INTRODUCTION

NMR spectroscopy, which has been used in chemistry and physics for more than 50 years, is nearly identical to MRS in terms of its sensitivity and precision. When used to biology or medicine, NMR spectroscopy is referred to as MRS. Biological and medical applications of NMR avoid using the phrase "nuclear" in order to avoid the connotation that nuclear radiation is related with therapeutic procedures. Magnetic resonance imaging and MRS have a lot in common (MRI). The identification of NMR signals created by chemical compounds other than water is common in MRS research, but the detection of NMR signals produced by tissue water is common in MRI studies to build pictures that reflect soft tissue macroscopic anatomy, such as the brain [Novotny EJ (2003)]. Science and technological advancements over the past several decades have made magnetic resonance imaging (MR) an essential tool for researchers in the neuroscience field.

PHYSICAL PRINCIPLES OF MRS

Atomic nuclei may act as spinning bar magnets, which is useful for MRS experiments. The nuclear magnetic fields of a sample under investigation are affected by the magnetic fields created by a powerful magnet [Lyoo IK (2002)]. The transfer of energy between nuclear and external magnetic fields is accomplished by magnetic interaction. Resonance is a word used in engineering and physics to characterise this type of energy exchange. In physics and chemistry, the technique of finding the precise frequency at which resonance occurs is referred to as "spectroscopy." Magnetic resonance has a temporal influence on the electromagnetic oscillation of radio waves used in television and radio. Principles of Physics, please, MRS. MRS takes advantage of the spinning bar magnetism of certain atomic nuclei. In the presence of nuclear magnetic fields and a magnetic field created by those fields, a powerful magnet is utilised to place the material being analysed. As a result of this interaction, the nuclear magnetic fields and the external magnetic field can exchange energy with each other. Resonance is the term used in engineering and science to describe this type of energy exchange. To give an example, the term "spectroscopy" is used in chemistry and physics to describe the study of the frequency or wavelength where resonance occurs. Using radio waves, electromagnetic oscillations have a time dependence comparable to atomic magnetic resonance. Hence, the term "MRS" is commonly used interchangeably with "RF spectroscopy.

Superconducting magnet technology is used to produce a 1.5 T magnetic field surrounding the material, organism, or organ being researched when conducting human research. For animal studies and in vitro MRS tests, significantly stronger magnetic fields are applied to improve sensitivity. Static

magnetic field strength affects the strength of the MRS signal, thus making your magnetic field as strong as possible is a good method. Of course, there are certain practical restrictions. Only research programmes employ magnets with a field strength of greater than 3.0 T because of their prohibitive cost.

In addition, a second, external magnetic field with a periodicity in its intensity is required for MRS. This time-varying magnetic field might be used to detect the precise resonance contact (i.e., the spectroscopy). It is common to refer to the second required magnetic field as "radio frequency" ('rf') since it has features with television and radio waves. It is necessary to place the RF coil near or on top of the sample or body part being studied in order for the RF field to be created.

An 'rf' coil must be attached to the object of interest in order to collect MRS data. Next, a "rf" field created by the "rf" coil pulse interactions is applied to the sample and interacts with several nuclei at once. Radiation-free (rf) coils produce a wide range of electromagnetic signals based on their ability to interact with nuclear magnetism and a static magnetic field. Samples or body parts must be put in close proximity to a "RF" field generator, a coil that generates a high-frequency electromagnetic field.

An 'rf' coil must be attached to the object of interest in order to collect MRS data. A "rf" field generated by the "rf" coil pulses then interacts with several nuclei in the sample. Radio-frequency (rf) coil signals are created depending on frequency by nuclear magnetism and static magnetic field interaction.

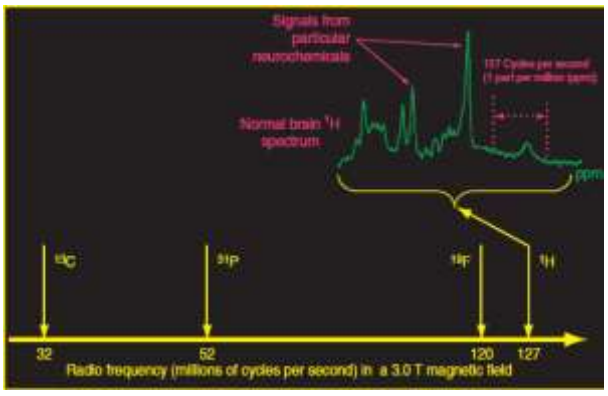


Figure 1 Signal frequency measurements in magnetic resonance spectroscopy (MRST). The frequency of MRS signals from distinct atomic nuclei (e.g., 13C, 31P, 19F, & 1H) vary at different field strengths. The intrinsic frequencies for some of the most regularly utilised isotopes in brain MRS are displayed.

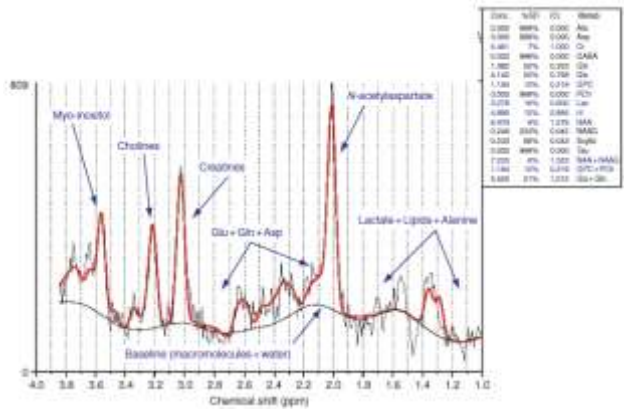


Figure 2: A normal brain magnetic resonance spectroscopy (MRS) is demonstrated, as well as 1H-MRS with fitting and quantitation. The black line depicts localisedsinglevolume 1H-MRS of a typical human brain.

However, MRS signals tend to be weaker than those from other forms of spectroscopy used in biology and medicine, therefore their conclusions are less reliable. To identify MRS signals, a variety of detection methods must be combined, requiring a large number of re-examinations of the process. An averaging process works because the noise is unexpected, and it fluctuates from time to time.

In Vitro & In Vivo MRS

In vitro MRS investigations frequently make use of sample preparation. Acid extraction can be used to remove chemicals with low molecular weight from tissue samples. It is done in a manner similar to the analytical chemistry NMR facility's NMR spectroscopy approach to process the tissue extract. Extraction can produce high-quality spectra at magnetic field intensities that are many orders of magnitude larger than those needed to perform the extraction procedure.. The extraction spectrum displayed in Figure 3 offers a considerably more sensitive and exact MRS fingerprint of all compounds present when compared to in vivo MRS experiments.

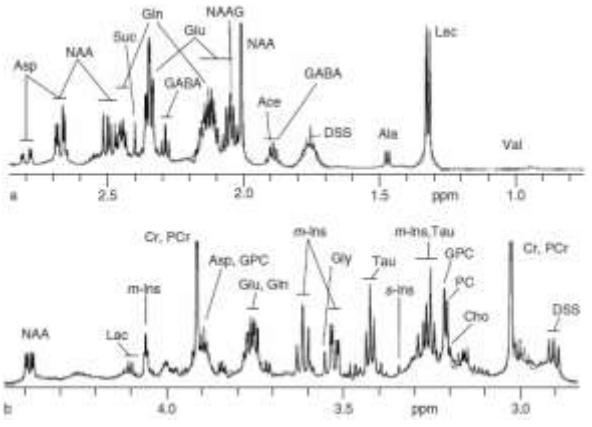


Figure 3: Magnetic resonance spectroscopy (MRS) of the brain, showing a 1H-MRS brain extract. The

spectrum's 0.5–3.0ppm region (a) 2.8–4.5 ppm portion (b) are shown in two frames of 1H-MRS of an acid extract of rat brain tissue (b). When compared this spectrum to those in Figures 1 & 2, it's clear that extract spectra have more information than in vivo spectra. With improved sensitivity, plenty more signals may be uniquely detected. Abbreviations in the diagram identify the tissue molecules that created many of the signals.

When using in vivo MRS, just a tiny and well-defined area of the brain has to be studied. If particular localization processes are employed, signals from the whole brain and surrounding tissue are more likely to be gathered. Because the MRS approach is so sensitive, the volume of tissue that can generate enough MRS signal intensity in a short period of time is theoretically limited. Approximately 1 cm3 of volume is considered the realistic minimum in human brain research. An MRS area of interest in a human brain may be seen in Figure 4. Animal research may benefit from quantities as small as 10–50mm3 if the appropriate technologies were available. There are two main ways to localise MRS. For example, these techniques are known as MRS (magnetic resonance imaging) and SV-MRS. This technique makes use of a series of magnetic resonance scans to locate the tissue under examination precisely. Only MRS signals have been recorded at this location (Figure 4). By utilising MRI, MRSI is able to focus the scope of the research (Figure 5). In MRSI, all volume elements in the research area are used to build a spectral array. These data may be used to create visual representations of how individual signals move across the array, or to evaluate the spectra created by different locations.

The amount of time it takes to collect data in in vivo MRS studies is a major concern. The person must remain practically immobile for the 10 or more minutes it takes to collect MRS data. Many adults can deal with this, but certain ill people and small children may have difficulty. These folks require anaesthesia or sedation. To prevent animals from moving while MRS data is collected, sedation, anaesthesia, or paralysis is frequently necessary.

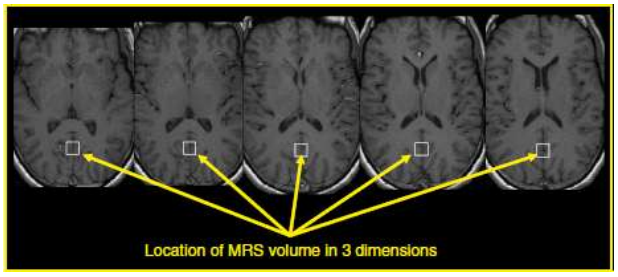
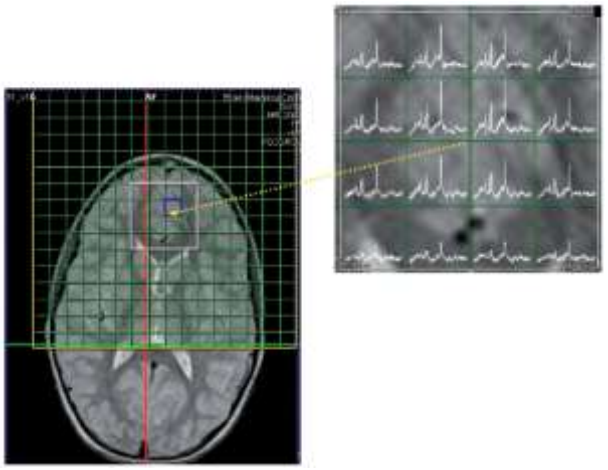


Figure 4 Localized magnetic resonance spectroscopy (MRS) volume selection. A magnetic resonance imaging (MRI) study is done initially in localised MRS examinations of the brain. The anatomy visualisation offered by MRI is then used to determine which single volume of brain tissue should be examined with MRS.



To learn more about magnetic resonance spectroscopy, visit MRSI (Figure 5). After determining the slice of interest, Each of the volume elements depicted in the green grid is utilised to generate an MRS spectrum.

TECHNICAL ASPECTS OF MRS

Rapid, low-cost, and automated methods that may be used in conjunction with MRI scans have made clinical MRS a reality. In 1995, the Food and Drug Administration authorised MRS as a clinical method. According to Rubaek Danielsen (1999), As far as MRS is concerned, the only nuclei that may be employed are phosphorus (31P) and hydrogen (1H), both of which are abundant in the human body. Increasingly, metabolic pathways without phosphorylated metabolites are being studied using proton (1H) MRS. Using magnets to manipulate protons provides both a high degree of sensitivity and a high degree of spatial resolution due to the abundance of protons in nature. Aside from a few steps before data collection that are not visible to patients, the MRS process is nearly identical to an MRI [Rubaek Danielsen (1999)].

The first step in getting diagnostic data is to verify that the magnetic field is uniform. As a workaround, "shimming," an automated method that may need manual intervention from the user, can be used Metabolites have concentrations that are 10,000 times lower than the water concentrations. According to this, protons from water molecules would dominate the hydrogen spectrum's significant resonance (resonance peak), outpacing millimolar amounts of other metabolites, according to Burtscher IM (2001). This has resulted in the need of water suppression, which is accomplished by introducing water suppressing pulses into MRS. SVS and MRSI are two extensively used spectroscopic technologies that may provide metabolite maps. What we call a "voxel" is the amount of tissue being studied. Researchers can acquire quantitative data, even though the SVS can only analyse a small amount of tissue. By using CSI's many smaller voxels inside the observed volume, larger amounts of tissue may be probed.

The two-dimensional CSI method necessitates more time for data gathering and post-processing. employing 3D MRSI, a wide range of brain regions may be mapped and metabolite images can be produced..

Measurements like as repetition time (TR) and echo time (ET) are used to establish if MRS methods are appropriate in the context of a certain clinical inquiry (TE). There are specific amino acids and metabolites that require just brief TE assessments, such as glutamine, glutamate, myo-inositol, etc. (20 to 35 ms) in order to identify them. In order to identify metabolites such N-acetyl aspartate, choline, creatine and lactate/lipids, long TE investigations are needed. (135 to 270 msec) The following are references: Zimmerman RA. An MRS research must first be designed to answer a clinical question.

MRS has a slew of flaws, regardless of the technique employed. The magnetic susceptibility of bone, air, fat, and blood is significantly different from that of brain tissue, making MRS in or near these materials challenging. Because of the artefacts created by these structures, as well as the difficulty in creating a uniform magnetic field, this has occurred. TE studies lasting between 135 and 270 milliseconds are needed to identify major metabolic metabolites such as N-acetyl aspartate (NAA), choline (Cho), creatine (Cr), and lactate/lipids (LL). Before the design of an MRS study can begin, the clinical problem must be established.

The restrictions of MRS are the same regardless of the approach used. Bone, air, fat, or blood should be avoided when doing MRS because of their high magnetic susceptibility variations. Inconsistent magnetic fields and the artefacts produced by these structures are to blame. 2D-CSI MRS was used in this study. It may be possible to solve this issue by employing outside volume suppression slices and in-field-of-view saturation bands.

According to the TE, TR, and localization sequence, the metabolite resonances (or peaks) have varying amplitudes. Some of the metabolite resonances have signal intensity values that SVS automatically delivers. When using 2D-CSI MRS, post-processing is necessary to get signal intensity values, measure metabolite concentrations, and determine the metabolite ratios. Automated computing techniques like the linear combination model methodology (LC-model) can be used to perform these computations. Magnetic Resonance User Interface (MRUI).

MRS AND NORMAL BRAIN DEVELOPMENT

Encephalopathy and MRS in neonatal hypoxic-ischemia It is possible that the anomalies or the hypoxic-ischemic damage in neurometabolic illnesses might lead to neurological issues. Thus, MRS in hypoxic-ischemic injury is up for dispute. MRS can detect acute damage until both diffusion imaging and conventional MRI are negative. Energy metabolism changes to anaerobic glycolysis, which produces lactic acid, because hypoxic-ischemic injury inhibits oxidative phosphorylation. Lactate levels that aren't linked to acidosis linger for up to two weeks after the acute phase of lactic acidosis. Both in the acute and late phases of hypoxic ischemia, this biphasic pattern of energy failure may be seen on MRS. (Figure. 6).

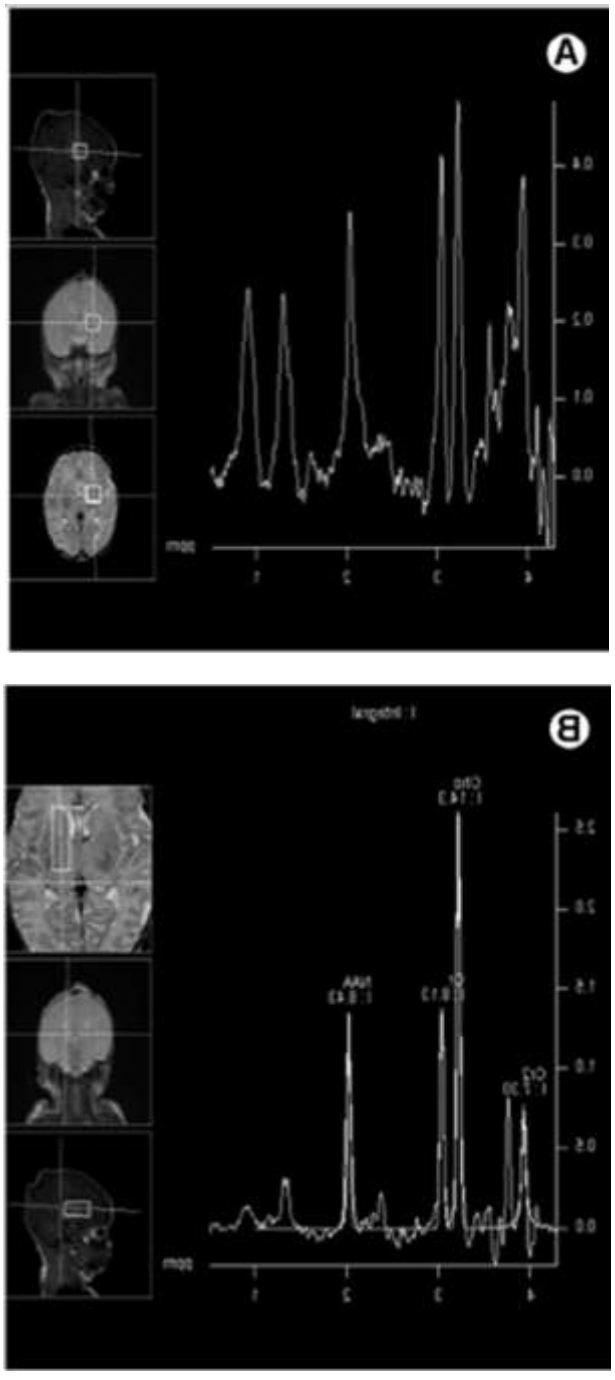


Figure 6 Severe hypoxic-ischemic injury at birth. 3T indicates increased lactate in a one-month-old kid who had severe hypoxic damage at birth. Lactate levels can be very high in the acute phase, although they should decrease as time. Lactate level has an inverse relationship with prognosis. CSI se270 (B) indicates 1.33 ppm of lipid lactate.

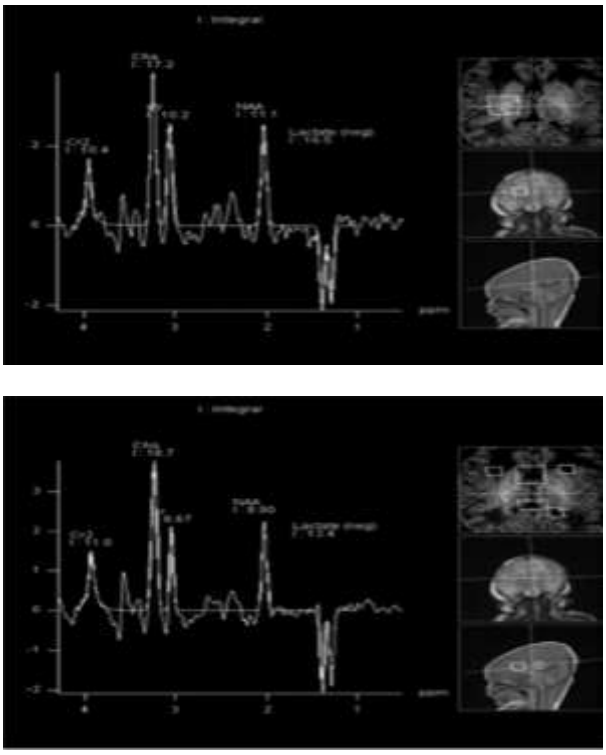


Figure 7 Severe hypoxic damage in a 6 day old patient. Lactate levels are quite high. The intensity of brainstem involvement might indicate an underlying metabolic imbalance with acute hypotensive damage. The severity of the damage increases as the lactate level rises.

These hypoxic-ischemic patients had higher lactate levels in their basal ganglia than in their occipital parietal cerebrum, according to single-voxel MRS. Following an episode of hypoxic ischemia, abnormalities in diffusion-weighted imaging are common. On the proton MRS scan, additional metabolites help determine the severity of hypoxic-ischemic encephalopathy and its prognosis. In chronic hypoxic-ischemic foetal brain injury, absolute quantification studies in MRS have shown a decrease in cerebral NAA. According to 1H MRS, glutamine and glutamate levels increased after hypoxic-ischemic injury. When a foetus suffers brain injury, myo-inositol concentrations increase. Preterm newborns with chronic perinatal white matter damage have higher levels of myo-inositol. Glial cell marker myo-inositol explains why preterm newborns have a higher density of astroglial cells. Macromolecules and lipids may be detected at 0.9 and 1.3 ppm, respectively, using short TE MRS. NAA/choline and NAA/creatine metabolite ratios have been used to evaluate the metabolic integrity of brain injury in newborns. At least 1-2 weeks after the occurrence, lower NAA levels were shown to be associated with worse neurodevelopmental outcomes. While NAA ratios at the early stages show a moderate correlation with the final result, later stage NAA ratios show a strong correlation. The lactate/NAA peak ratio in the deep grey matter of the brain is thought to reliably predict NHE (Figure. 7).

DIAGNOSES OF MRS IN DEVELOPMENTAL BRAIN DISORDER

Physical and technological fundamentals that underlie both spectroscopy and imaging of magnetic resonance are identical (MRI). Both systems rely on the magnetic properties of protons (hydrogen nuclei) exposed to a strong magnetic field for their signal. For an MRI to work, all of the water molecule's protons must have the same magnetic properties. Because protons in various molecules have slightly varied magnetic properties, MR spectroscopy may be used to find small compounds in the body. In order for an MR spectrum to be useful, the compounds must be mobile and present in concentrations greater than 1 mmol/l. An x-axis frequency variation may be used to identify molecules, with the peak area matching to their concentration (Figure 8). According to Ross B (2001), Oz G (2014), and Alger JR (2014), Chemical substances that are not found in healthy tissue, or where the relative amounts of metabolites differ from those found in healthy tissue, are linked to a multitude of disorders. Creatine, choline, and N-acetylaspartate make up the majority of the peaks in the brain's magnetic resonance spectrum (MRS). Myo-inositol and glutamine/glutamate, two naturally occurring compounds in brain tissue, were also identified under the test circumstances. Most of the time, magnetic resonance spectroscopy cannot detect lactate levels in normal brain tissue (MRI). Because lipids are bonded in stationary forms, this approach is generally ineffective in detecting them.

Pre-pathological anatomical changes in brain tissue may be detectable by MR spectroscopy. As early as the mid-1980s, doctors felt that MR spectroscopy might be utilised to help diagnose patients with MRI. particularly in the field of cancer, would follow suit. The reality, on the other hand, fell well short of these ambitious goals. Use of this method is now widely accepted in combination with MRI to identify central nervous system abnormalities. The results of MR spectroscopy can have an immediate impact on a patient's treatment and follow-up in some conditions. Neurometabolic diseases and brain tumours are good candidates for this approach. MR spectroscopy is used often in St. Olavs hospital to diagnose and monitor patients with these conditions. We provide MR spectrum data for a number of conditions based on personal experience and a literature review.

Neurometabolic disorders

As far as congenital diseases go, neurometabolic disorders fall into a broad spectrum. According to Applegarth and Sanderson, one in 800–2500 newborns will be affected by one of these diseases, despite the fact that each of these diseases has an extremely low prevalence. Developmental delays or neurological symptoms in children are common in patients with neurometabolic diseases. The opposite is true for people who suffer from neurometabolic

diseases. Neurometabolic diseases may be difficult to diagnose based only on MRI because of the lack of distinct anatomical abnormalities in the central nervous system. Neurometabolic disorders can benefit from MR spectroscopy since it is able to identify the metabolite composition of brain tissue. A small number of illnesses have an MR spectroscopy profile that is completely disease-specific, whereas others have a distinctive MR spectroscopy characteristic for the condition. N-acetylaspartate levels, choline concentrations, myo-inositol concentrations, and lactate can all be seen in pathological MR spectra. Diseases of the nervous and metabolic systems, such as mitochondrial disease and enzyme deficiencies, can be detected using MR spectroscopy (Figures 8a and 8b).

ENZYME DEFECTS

Biological processes can be disrupted if an enzyme is deficient or malfunctioning. Because the severity of an illness is based on the enzyme that is malfunctioning, there is a wide range of clinical manifestations for these diseases. Canavan disease, a leukodystrophy, is linked with oedematous white matter and fluid-filled cavities (Figure 8d). Canavan disease is caused by mutations in aspartoacylase, a gene that converts N-acetylaspartate to aspartate and acetate. As a result of the enzyme deficiency, N-acetylaspartate builds up in the brain and inhibits myelin synthesis. It is particularly common in infants under 6 months old and causes serious brain damage. Symptoms include irritation, hypotonia, and a loss of upper-body control as the illness worsens. An enlarged circumference of the head, as well as stiffness in the eyes and muscles, can all be symptoms of the condition, which can have a significant impact on the child's growth. There is a 10-year life expectancy. People with Canavan disease have an elevated MR spectroscopy signal for the N-acetylaspartate molecule (Figure 8b). There is just one known metabolic disorder that raises N-acetylaspartate levels: canavan illness.

MITOCHONDRIAL DISEASES

There are a number of mitochondrial illnesses that cause random or progressive brain injury. On MRI, oedema and tissue loss can be seen, however bilateral basal ganglia inclusion is typical. Mitochondrial abnormalities can be more easily detected and studied with the use of MR spectroscopy in conjunction with MRI and clinical data. N-acetylaspartate levels fall as a result of changes in intracellular energy synthesis, which leads to lactate formation. There is a mitochondriopathy called Leigh syndrome, which can cause developmental delays and stiffness in children and young adults, as well as brainstem dysfunction in certain cases. On MRI, symmetrical signal changes can be seen in the basal ganglia, thalamus, and brain stem. The presence of lactate in the MR spectra from these sites suggests the presence of Leigh syndrome (Figure 8a).

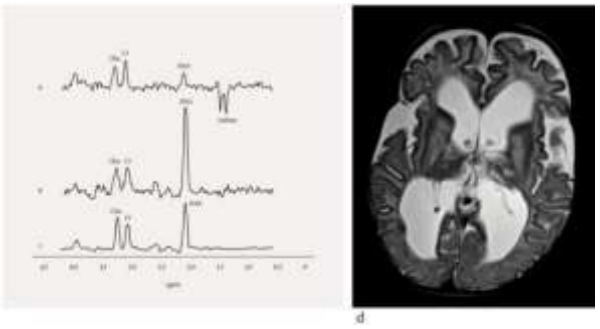


Figure 8: MR spectra of (a) a patient with Leigh syndrome, (b) a patient with Canavan disease, (c) a healthy individual, (d) a patient with Canavan disease's T2-weighted MRI. All of the spectra were captured with a lengthy echo time (135 ms). Changes in these signals can frequently be connected to disease. Choline (Cho), creatine (Cr), and N-acetylaspartate (NAA) present in all spectra. Leigh syndrome is characterised by the presence of lactate (a). The signal from N-acetylaspartate is significantly more prevalent in the spectrum of Canavan illness (b) than in the spectrum of a healthy control (c). At 4.7 ppm (parts per million), water produces a strong signal that is muted and outside the range displayed. The creatine signal is used to scale the spectra.

Brain Tumour

As many as 300 persons in Norway each year are diagnosed with a primary malignant brain tumour, with around 250 of these cases being high-grade gliomas. MR spectroscopy [Brando LA (2013)] can distinguish between tumours and other forms of lesions in the brain, such as abscesses and subacute infarcts, with high accuracy. N-acetylaspartate and creatine were lower in brain tumours than in normal tissue, whereas choline, lactate, and mobile lipids were greater. Chromolysaccharides (choline and creatine) are higher in high-grade tumours, as are N-acetylaspartate and choline to creatine ratios (Figure 9). In the year 2016 [Usinskiene J]. Glioblastomas frequently have lactate and mobile lipids, although they can also be seen in metastases.

For the most part, high-grade gliomas are treated surgically or with radiochemotherapy. Radiation therapy-induced oedema and contrast uptake at the surgical site is known as pseudoprogression. However, the use of MR spectroscopy can help distinguish between tumour development and radiation response and pseudoprogression, which is difficult to discern on an MRI. Choline is frequently seen in high concentrations in the MR spectrum, lactate, and mobile lipids as a marker of necrosis in regions with pseudo-advancement in cases of tumour progression. MR. Adding MR spectroscopy

to diffusion MRI enhances the accuracy of determining if a tumour is genuine or fake, according to a study published in Radiology. In the year 2007, [Zeng QS] MR spectroscopy has a limited ability to diagnose tumours on its own, but when paired with MRI methods, it can be effective. It is [Brando LA (2013)]

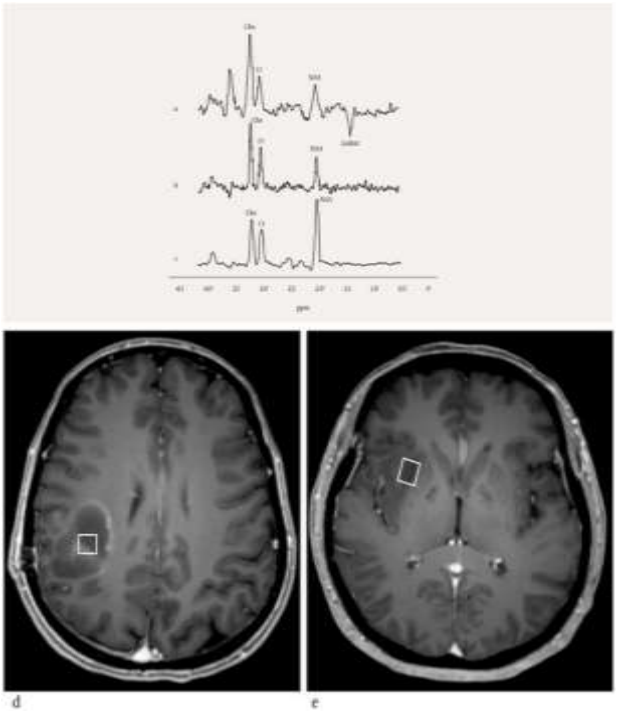


Figure 9: Images illustrating volume localization for the MR spectroscopy for T1 MRI (d) a high-grade glioma (a) with peripheral contrast uptake,(e) a low-grade glioma (b) with no contrast uptake, and MR spectra of (a) high-grade glioma, (b) low-grade glioma, (c) a healthy individual, and T1-weighted With a long echo time, all of the spectra were caught (135 ms). The N-acetylaspartate (NAA) peak in the spectrum from a healthy control (c) is greater than the peaks for choline (Cho) and creatine (Cr), whereas choline (3.2 ppm) is the main peak in both the high grade (a) and low grade (b) glioma spectra (b). In the high-grade glioma, a negative peak from lactate can also be seen at 1.3 ppm (a). The spectra are scaled using the creatine signal.

CONCLUSION

Magnetic resonance spectroscopy (MRS) is a noninvasive technique for tissue characterisation that complements magnetic resonance imaging (MRI). MRS has been the most commonly utilised clinical application in the assessment of central nervous system diseases. In chemistry, the method of spectroscopy has been frequently used to analyse substances in solution. Although MRS may potentially be done in practically every tissue in the human body, clinical MRS research have mostly focused on the brain. The approach simply needs magnetic field exposure. MRS is increasingly being utilised in clinical settings to assess a variety of brain disorders. It could also be beneficial in fundamental neuroscientific research.

REFERENCES

Applegarth DA, Toone JR, Lowry RB (2000). Incidence of inborn errors of metabolism in British Columbia, 1969-1996. Pediatrics; 105: e10. [PubMed][CrossRef]

Barker PB (2005). Fundamentals of MR Spectroscopy. In: Gillard JH,Waldman AD, Parker PB, eds. Clinical MR neuroimaging: diffusion,perfusion, and spectroscopy. Capetown: Cambridge University Press: pp. 1–17.

Brandão LA, Castillo M. (2013). Adult brain tumors: clinical applications of magnetic resonance spectroscopy. Neuroimaging Clin. N. Am.; 23: pp. 527–55. [PubMed][CrossRef]

Burtscher IM, Holtas S. (2001). Proton magnetic resonance spectroscopy inbrain tumors: clinical applications. Neuroradiology; 43: pp. 345–52.

Castillo M, Kwock L, Mukherji SK (1996). Clinical applications of protonMR spectroscopy. AJNR Am J Neuroradiol.; 17: pp. 1–15.

Cecil KM, Lindquist DM (2013). Metabolic disorders. I: Blüml S, Panigrahy A, red. MR spectroscopy of pediatric brain disorders. New York, NY: Springer: pp. 401.

Else R, Danielson BR (eds): (1998). Magnetic Resonance Spectroscopy Diagnosisof Neurological Diseases. New York, Marcel Dekker, Inc.

Frahm J, Bruhn H, Gyngell ML, et al. Localized Proton NMR spectroscopyin different regions of the human brain in vivo: relaxationtimes and concentrations of cerebral metabolites. MagnReson Med1989; 11: pp. 47–63.

Galanaud D, Le Fur Y, Nicoli F, et al. (2001). Regional metabolite levels ofthe normal posterior fossa studied by proton chemical shift imaging.MAGMA;13: pp. 127–33.

Helsedirektoratet. Pakkeforløp for hjernekreft. https://helsedirektoratet.no/retningslinjer/pakkeforlop-for-hjernekreft (1.12.2017).

Hoshino H, Kubota M. (2014). Canavan disease: clinical features and recent advances in research. Pediatr. Int.; 56: pp. 477–83. [PubMed][CrossRef]

Kreis R, Ernst T, Ross BD (1993). Development of the human brain: in vivoquantification of metabolite and water content by proton magnetic resonance spectroscopy. MagnReson Med.; 30: pp. 424–37.

Lenkinski RE, Schnall MD (1991). MR Spectroscopy and the biochemicalbasis of neurological disease. In: Atlas SW, ed. Magnetic ResonanceImaging of the Head and Spine. New York: Raven: pp. 1099–1121.

Lyoo IK and Renshaw PF (2002). Magnetic resonance spectroscopy: Current and future applications in psychiatric research. Biological Psychiatry 51: pp. 195–207

Maheshwari SR, Fatterpekar GM, Castillo M, Mukherji SK (2000). ProtonMR spectroscopy of the brain. Semin Ultrasound CT MR;21: pp. 434–51.

Mescher M, Merkle H, Kirsch J, et al (1998). Simultaneous in vivo spectralediting and water suppression. NMR Biomed 11: pp. 266 –272.

Novotny EJ, Jr., Fulbright RK, Pearl PL, et al. (2003). Magnetic resonancespectroscopy of neurotransmitters in human brain. Ann Neurol.; 54: pp. S25–31

Oz G, Alger JR, Barker PB et al. (2014). Clinical proton MR spectroscopy in central nervous system disorders. Radiology; 270: pp. 658–79. [PubMed][CrossRef]

Pfefferbaum A, Adalsteinsson E, Spielman D, et al (1999). In vivo spectroscopicquantification of the N-acetyl moiety, creatine, and choline fromlarge volumes of brain gray and white matter: Effects of normal aging.MagnReson Med 41: pp. 276-284.

Provencher SW (1993). Estimation of metabolite concentrations from localizedin vivo proton NMR spectra. Mag Reson Med; 30: pp. 672–9.

Ross B, Bluml S. (2001). Magnetic resonance spectroscopy of the human brain. Anat Rec.; 265: pp. 54–84. [PubMed][CrossRef]

Rubaek Danielsen E, Ross B (eds.). (1999). Magnetic resonance spectroscopydiagnosis of neurological disease. New York. Marcel Dekker, Inc.

Sanderson S, Green A, Preece MA et al. The incidence of inherited metabolic disorders in the West Midlands, UK. Arch Dis Child 2006; 91: pp. 896–9. [PubMed][CrossRef]

Saneto RP, Friedman SD, Shaw DW (2008).. Neuroimaging of mitochondrial disease. Mitochondrion; 8: pp. 396–413. [PubMed][CrossRef]

Usinskiene J, Ulyte A, Bjørnerud A et al. (2016). Optimal differentiation of high- and low-grade glioma and metastasis: a meta-analysis of perfusion, diffusion, and spectroscopy metrics. Neuroradiology; 58: pp. 339–50. [PubMed][CrossRef]

Valk J, Barkhof F, Scheltens P. (2002). Magnetic resonance in dementia.Berlin Heidelberg, Springer-Verlag.

Vigneron DB, Barkovich AJ, Noworolski SM, et al. (2001). Threedimensionalproton MR spectroscopic imaging of premature andterm neonates. AJNR Am J Neuroradiol; 22: pp. 1424–33.

Wang ZJ, Zimmerman RA (1998). Proton MR spectroscopy of pediatricmetabolic disorders. NeuroImagClin N Am; 8: pp. 781–807.

Weybright P, Maly P, Gomez-Hassan D, Blaesing C, Sundgren PC (2004). MR spectroscopy in the evaluation of recurrent contrast enhancinglesions in the posterior fossa after tumor treatment. Neuroradiol; 46: pp. 541–9.

Zeng QS, Li CF, Liu H et al. (2007). Distinction between recurrent glioma and radiation injury using magnetic resonance spectroscopy in combination with diffusion-weighted imaging. Int. J. Radiat. Oncol. Biol. Phys; 68: pp. 151–8. [PubMed][CrossRef

Zimmerman RA, Wang ZJ (1997). The value of proton MR spectroscopyin pediatric metabolic brain disorders. AJNR Am J Neuroradiol; 18: pp. 1872–9.

Corresponding Author

Sanjay Singh*

Research Scholar, NIMS University, Jaipur