Review article

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BRAIN MAGNETIC RESONANCE SPECTROSCOPY IN MIGRAINE

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Migraine is a common neurological disorder that is characterized by episodes of moderate to severe headache. Magnetic resonance spectroscopy (MRS) is a noninvasive method that enables *in vivo* studying of tissue metabolism by utilizing the magnetic properties of certain atomic nuclei, mainly hydrogen (1H) and phosphorous (31P).

1H-MRS is most commonly used to measure the concentration of gamma aminobutyric acid (GABA), glutamate, phosphocreatine (PCr), creatine, choline, N-acetylaspartate (NAA), myo-inositol, aspartate and lactate.

31P-MRS enables noninvasive *in vivo* measuring of concentration of compounds containing phosphorus nuclei. This allows the measurement of metabolites involved in brain energy metabolism including concentrations of phosphocreatine (PCr), inorganic phosphate, creatine, adenosine diphosphate (ADP) and adenosine triphosphate (ATP).

1H-MRS studies reported significant differences in levels of GABA, glutamate, lactate and NAA between migraine patients and controls, measured in various brain regions, while most of the studies found no significant differences in levels of myo-inositol, choline and total creatine.

The main consistent findings using 31P-MRS are concomitantly decreased PCr and increased inorganic phosphate, that is, a decreased PCr/inorganic phosphate ratio, as well as decreased magnesium measured in cortical regions of migraine patients.

For identifying a biomarker in migraine it is necessary for future MRS studies to obtain additional information of the ictal state in migraine as well as before and after interventions. Severity of the disease (disease duration and migraine attack frequency) has to be taken into account to detect possible correlation with MRS findings which also needs further research.

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Introduction

Migraine is a common neurological disorder that is characterized by episodes of moderate to severe headache. It is associated with autonomic symptoms and sometimes is preceded by aura in the form of transient neurological symptoms (1). It is considered that migraine affects subjects with an inherited alteration of brain excitability and that it is a neurovascular disorder with recurrent sensitization and activation of the trigemino-vascular pathways, as well as diencephalic nuclei and brain stem (1-3).

Imaging and neurophysiological studies indicate that chronic migraine can be correlated with functional and structural alterations in some brain regions, especially brainstem dysfunction and cortical hyperexcitability (4-6). Technological advances in neuroimaging have enabled the exploration of different aspects of cerebral metabolism in migraine patients, and complementary animal research indicates that there are possible links between trigeminovascular activation and metabolic factors in migraine pathophysiology (7).

The implementation of advanced magnetic resonance imaging (MRI), including magnetic resonance spectroscopy (MRS), represents a significant step forward in the understanding of the underlying mechanisms in migraine, giving insight into structural and functional brain alterations in migraine patients (1). Magnetic resonance spectroscopy (MRS) is a noninvasive method that enables *in vivo* studying of tissue metabolism by utilizing the magnetic properties of certain atomic nuclei, mainly hydrogen (1H) and phosphorous (31P). This technique

has been used for the past three decades to study brain metabolism in a variety of diseases, including migraine (8).

1H-MRS

1H-MRS is a neuroimaging technique that allows the separation of neurometabolites according to their chemical structure. Differentiation of spectra is possible through observation of the radiofrequency signal detected from hydrogen nuclei spins and their chemical environment when placed in a magnetic field (9). Neurometabolites can be differentiated along an x-axis depending on their radiofrequency that is chemical-specific, also termed chemical shift. Signal strength represents the level of neurometabolite (10).

1H-MRS is most commonly used to measure the concentration of gamma aminobutyric acid (GABA), glutamate, phosphocreatine (PCr), creatine, choline, N-acetylaspartate (NAA), myo-inositol, aspartate and lactate, depending on field strength and the exact sequence (8). The concentration of the measured metabolite can be reported as absolute concentration, quantified from measured water peak and assumptions of water concentration or as the relative ratio to the measured total creatine concentration in the spectrum (11, 12).

1H-MRS studies reported significant differences in levels of GABA, glutamate, lactate and NAA between migraine patients and controls, measured in various brain regions, while most of the studies found no significant differences in levels of myo-inositol, choline and total creatine.

Gamma aminobutyric acid (GABA)

Gamma aminobutyric acid (GABA) is a predominant inhibitory neurotransmitter in the central nervous system (13) and can serve as a potential biomarker for migraine (14). GABA has been implicated in neuronal disorders, such as pain, and the temporal modulation of neuronal excitability and it is widely distributed in the brain (15). Changes in GABA levels in the brain could result in pathophysiological events leading to migraine (16) as it is a crucial regulator of excitation and inhibition (17). In order to gain an understanding of migraine pathogenesis, it is essential to study migraine GABA levels (14).

Some studies of migraine with and without aura showed decreased GABA levels in the occipital lobe measured interictally (18, 19) which could be explained as increased susceptibility to excitatory inputs and/or reduction in the inhibitory mechanisms (8). However, one meta-analysis showed that the level of GABA in migraine was significantly increased compared with controls (10) which is more difficult to explain (19, 20). It is hypothesized that increased GABA levels reflect a homeostatic response to the increased glutamate through the GABA metabolic pathway (21) or that GABA has a protective role in suppressing headaches (19). Increased GABA levels may represent a pathophysiological migraine mechanism that has yet to be fully explained (10). For example, GABA may have a role in neurogenic inflammation in migraine (22) or control of vasodilation (23). GABA is generally thought to reflect "inhibitory tone" (24) but increased GABA may be a response to increased excitation (10). Studies have implicated polymorphisms in genes encoding for GABA receptor subunits in migraine (25). Reduced GABA-receptor activity may lead to hyperexcitability of both inhibitory and excitatory neurons and hence increased levels of neurotransmitters (10). Some studies indicate that drugs targeting GABAA or GABAB-receptor activity (26) could be used as a treatment for pain disorders, including migraine.

Glutamate

There is no consensus on the best way to test glutamate levels. Glutamate is present at higher concentrations (27) than GABA, but difficulties in distinguishing it from glutamine and glutathione (24) have been highlighted. Although some studies assess glutamate alone (28), others choose to estimate Glx, the combined measure of glutamate and glutamine, even though the signal also contains glutathione (10).

1H-MRS studies in migraine with and without aura reported increased levels of glutamate in the anterior paracingulate (29) and visual cortex (30), and during visual stimulation in migraine with aura in the visual cortex (18). Glutamate is the main excitatory neurotransmitter in the brain and is thought to be a central factor in the migraine brain hyperexcitability theory, which entails an imbalance in excitatory and/or inhibitory activity (16). This possibly enhances the excitability of the migraine brain, both by leading to the mechanism of cortical spreading depression in the migraine aura and the activation of trigeminovascular pain pathways (16, 31-33).

Cortical spreading depression is a process that is uniquely associated with transient neurological conditions such as epilepsy and migraine (34). Cortical spreading depression is characterized as a wave of excitation accompanied by inhibition that spreads through the brain. High levels of glutamate have been thought to trigger this process (34, 35). As the recorded increases in glutamate are measured interictally, migraine patients may exert persistently altered brain excitability and increased sensitivity to excitatory stimulation (8). The glutamate abnormalities are consistent with previous genetic findings of glutamate regulation and homeostasis abnormalities, likely involving the glutamate transporter-1 receptor (36, 37). Also, some studies reported increased glutamate levels in plasma and cerebrospinal fluid interictally (38).

Lactate

The inconsistency in patient selection criteria and methodologies in brain lactate level studies in migraine patients means that a firm conclusion cannot be drawn (39, 40). Brain lactate levels were elevated in patients with migraine with aura (41, 42) but not in those with migraine without aura (43-45). Occipital baseline lactate levels were increased in patients with a purely visual aura relative to healthy

controls but not in those with complex neurological auras (41). Lactate levels increased significantly during photic stimulation in patients with complex neurological auras but not in patients with a purely visual aura (41).

A significant consideration is that stimulus-induced rises in cortical lactate levels are physiological (46) and are explained by the astrocyte-to-neuron lactate shuttle (47), the process by which astrocytes supply neurons with energy when they become activated. The lack of a stimulus-induced increase in lactate levels in migraine patients may therefore be considered pathological, as it could make them vulnerable to an energy crisis, particularly because neuronal activation is likely to have a higher energy demand in migraine patients than in healthy individuals because their sensory information processing is abnormal (48). Research incorporating the quantification of lactate in the cortex and the electrophysiological monitoring of brain-evoked responses would be able to explain this relationship between function and metabolism (7).

N-acetylaspartate

N-acetylaspartate (NAA) is widely distributed in the central nervous system in both neurons and glia (49). It has a variety of functions, and it can be a potential marker for neuronal health as measured using MRS techniques (50). In the healthy brain, NAA is one of the highest peaks of the acquired MRS spectrum (51). The ratio between NAA and total creatine (NAA/Cre) was found to be clinically useful, as total creatine usually remains constant (52).

Studies reported decreased levels of NAA in the occipital lobe (53) and thalamus (45, 54) in migraine with and without aura and in the cerebellum of sporadic and familiar hemiplegic migraine (55, 56). Low NAA levels have been reported in the serum of migraine patients (57). No studies reported ictal findings using 1H-MRS.

Decreased NAA level is generally believed to indicate a neuronal loss (58) and impairments of energy metabolism decrease NAA levels in the brain (51). Migraine brain has been suggested to be hyperexcitable or to have alterations in migraine energetics due to possible mitochondrial dysfunction (51) and it has been proposed that the NAA decrease might indicate a subsided mitochondrial dysfunction if accepted that the synthesis is mitochondrial, thus contributing to the abnormal energy metabolism (58). In addition, one genetic study documented a higher prevalence of mitochondrial DNA mutations in migraine patients relative to controls, indicating a link between mitochondrial dysfunction and susceptibility to migraine (59).

31P-MRS

31P-MRS enables noninvasive *in vivo* measuring of concentration of compounds containing phosphorus nuclei. This allows for measurement of metabolites involved in brain energy metabolism including concentrations of phosphocreatine (PCr), inorganic phosphate, creatine, adenosine diphosphate (ADP) and adenosine triphosphate (ATP). Energy in the form of ATP is formed by oxidative phosphorylation under aerobic conditions. ATP is also generated with a higher synthesis rate by glycolysis under anaerobic conditions, resulting in concomitant lactate production and decreased intracellular pH. Intracellular pH is estimated from the chemical shift between PCr and inorganic phosphate in the 31P-MRS spectrum (60). Transfer of inorganic phosphate from PCr to ADP, by the creatine kinase, produces ATP and creatine (8).

The main consistent findings using 31P-MRS are concomitantly decreased PCr and increased inorganic phosphate, that is, a decreased PCr/inorganic phosphate ratio, measured in cortical regions of migraine patients with and without aura in both ictal and interictal conditions (61-64). In addition, four studies recorded decreased phosphorylation potential (61, 62, 65, 66), three of which additionally reported increased ADP and V/Vmax in migraine with (61, 62) and without aura (65). Overall, the results suggest that there is insufficient availability of free energy in the cell (67-69).

The use of 31P-MRS has shown that mitochondrial oxidative phosphorylation is impaired in the brain of migraine patients between (39, 61-63, 65, 70, 71) and during migraine attacks (64). This impairment is seen as decreased levels of organic phosphate, decreased phosphorylation potential and increased levels of ADP (7). Modified 31P-MRS technique was used to specifically measure the brain ATP, which was found to be decreased by 16% between attacks in patients with migraine without aura compared with healthy controls (66). Most severely affected patients had the lowest ATP concentrations, a result that coincides with other studies showing moderate associations between brain hypometabolism and attack frequency (66, 71, 72).

Consistently reported finding was also decreased magnesium in the ictal and interictal state in cortical regions in migraine with and without aura in cortical regions (62, 71, 73, 74). 31P-MRS studies of neural metabolism often measure magnesium because it is an essential cofactor for ATP production (7). These studies have shown that cytosolic free magnesium is reduced in the occipital lobes of patients with migraine, consistent with alterations in oxidative phosphorylation (62, 71, 74). Decreased serum magnesium levels have been shown to raise the chances of a migraine attack (75). Since magnesium is a cofactor in oxidative phosphorylation and stabilizes the mitochondrial membrane, magnesium level abnormalities can suggest a mitochondrial factor in migraine pathophysiology (76). These results, therefore, indicate reduced availability of neuronal energy and mitochondrial dysfunction in the migraine brain (8).

The possible mitochondrial dysfunction in migraine can be explained by a decrease in the number or efficiency of the mitochondria (66) or a decrease of mitochondrial enzymes (77). Q10 (78) and riboflavin (79) have shown efficacy as preventive migraine treatment, possibly by increasing the mitochondrial activity (8).

Table 1. 31P-magnetic resonance spectroscopy and 1H-magnetic resonance spectroscopy studies in migraine

Study	Participants	Type of MRS	Brain region	Scanner Strength (model, brand)	TR/TE (ms)	Results
Barbiroli et al. (82)	MpA (4) MS (4) C (15)	31P-MRS	Occipital	1.5 T (Signa, GE)	5000/NS	+ PCr/Pi + PCr/ATP = PME/ATP = PDE/ATP = pH
Barbiroli et al. (61)	MA (12) C (12)	31P-MRS	Occipital	1.5 T (Signa, GE)	5000/NS	- PCr + Pi - PP + ADP + V/Vmax - pHi = Magnesium
Lodi et al. (62)	MA (7) MpA (3) MbA (5) C (12)	31P-MRS	Occipital	1.5 T (Signa, GE)	5000/NS	- PCr + Pi - PP + ADP + V/Vmax - Magnesium + pHi
Lodi et al. (71)	MO (21) MA (37) MpA (13) C (36)	31P-MRS	Occipital	1.5 T (Signa, GE)	5000/NS	- Magnesium - DGATPhyd
Montagna et al. (65)	MO (22) C (18)	31P-MRS	Occipital	1.5 T (Signa, GE)	5000/NS	- PCr - PP + ADP + V/Vmax = Pi
Reyngoudt et al. (66)	MO (19) C (25)	31P-MRS	Occipital	3.0 T (Siemens)	4000/2.3	- PCr - PP - ATP = Pi = Magnesium = pHi
Uncini et al. (83)	FHM (2) MO (1) Family members (2) C (30)	31P-MRS	Occipital	1.5 T (Signa, GE)	5000/NS	- PCr + Pi - PP + ADP + V/Vmax = pH
Arngrim et al. (84)	MA (15) C (14)	1H-MRS	Occipital	3.0 T (Achieva, Philips) PRESS	5000/36.5	= Glutamate = Lactate = NAA = tCr
Bigal et al. (19)	MO (10) MA (9) C (9)	NS	Occipital	4.0 T (Inova, Varian)	NS	- GABA
Bridge et al. (18)	MA (13) C (13)	-MRS (MRS type not specified in paper, assumed 1H-MRS)	Occipital	3.0 T (Verio, Siemens)	4000/8.5	No visual stimulation: - GABA = Glutamate —————————— Visual stimulation: = GABA + Glutamate
Reyngoudt et al. (85)	MO (25) C (25)	1H-MRS	Occipital	3.0 T (TIM Trio, Siemens) PRESS	2000/30	= NAA = tCr = Choline = Myo-inositol
Reyngoudt et al. (43)	MO (20) C (20)	1H-MRS	Occipital	3.0 T (TIM Trio, Siemens)	2000/288	= Lactate/ tCr = Lactate/NAA = NAA/ tCr = Choline/ tCr
Sarchielli et al., 2005 (53)	MA (22) MO (22) C (10)	1H-MRS	Occipital	1.5 T (GEMS LX system)	2000/144	No visual stimulation: - NAA/Choline - NAA/ tCr = Choline = tCr —————————— Visual stimulation: - NAA/Choline - NAA/ tCr = Choline = tCr

Siniatchkin et al. (30)	MA (10) C (10)	1H-MRS	Occipital	3.0 T (Achieva, Philips) PRESS	2000/37	+ Glx = NAA
Watanabe et al. (42)	MA (3) MbA (1) MI (1) MpA/MI (1) C (6)	1H-MRS	Occipital	1.5 T (Signa, GE)	1500/270	+ Lactate/NAA = NAA/Choline = NAA/(Choline+ tCr)
Ramadan et al. (74)	MO (11) MA (8) C (25)	31P-MRS	Frontal Temporal Occipital	1.89 T (Bruker)	NS	- Magnesium = pHi
Welch et al. (86)	MO (12) MA (8) C (27)	31P-MRS	Frontal Occipital	1.89 T (Bruker)	NS	= pHi
Welch et al. (64)	MO (12) MA (8) C (27)	31P-MRS	Frontal Occipital	1.89 T (Bruker)	NS	Ictal: - PCr/Pi - PCr/TP + Pi/ TP = pHi ———————— Interictal: +Pi/TP = PCr/Pi = PCr/ TP = Pi/ TP = pH
Dichgans et al. (40, 55)	FHM1 (15) C (17)	1H-MRS	Parietal Occipital Cerebellum	1.5 T (Signa, GE)	2000/35	- Glutamate - NAA + Myo-inositol = tCr = Choline
González de la Aleja et al. (87)	MO (19) MA (8) C (19)	1H-MRS	Anterior paracingulate cortex Occipital	3.0 T (Signa, GE)	2000/28	Anterior paracingulate cortex: + Glutamate = Glutamine = Glutamate/Glutamine = tNAA = Choline ———————— Occipital lobe: + Glutamate/Glutamine = Glutamate = Glutamine = tNAA = Choline
Grimaldi et al. (88)	FHM2 (4) C (10)	1H-MRS	Parietooccipital Ventricles	1.5 T (Signa, GE)	4000/35 1500/288	= Lactate = NAA = Choline = Myo-inositol
Sándor et al. (41)	MA (5) FHM/SHM (5) C (11)	1H-MRS	Occipital + Tempoparietal	1.5 T (Gyroscan ACS-NT, Philips)	1500/288	+ Lactate = tCr = Choline
Zielman et al. (56)	SHM (10) FHM1 (5) FHM2 (3) C (19)	1H-MRS	Cerebellum Pons Occipital Hypothalamus	7.0 T (Achieva, Philips)	2000/21	- tNAA/ tCr = Glx/ tCr = Myo-inositol/ tCr = Choline/tCr
Becerra et al. (89)	MO (17) MA (15) C (33)	1H-MRS	Anterior cingulate cortex	3.0 T (TIM Trio, Siemens)	2000/31-229	= Glutamine = Glutamate = GABA = NAA = Aspartate = NAAG = Lactate = Myo-inositol
Prescot et al. (90)	MX (10) C (8)	1H-MRS	Anterior cingulate cortex Insula	4.0 T (Inova, Varian)	2000/30-260	= Glutamate = NAAG = Glutamine = Lactate = NAA = Choline
Aguila et al. (20)	MX (19) C (19)	1H-MRS	Posterior cingulate cortex	3.0 T (Discovery MR750, GE)	1800/68	+ GABAþ = Glx
Fayed et al. (91)	MX (33) C (183)	1H-MRS	Posterior cingulate gyrus	1.5 T (Signa, GE)	2000/35	= NAA = Glutamate = Glx = Myo-inositol = Choline

Boska et al. (92)	MO (19) MA (19) SHM (4) FHM (4) C (40)	31P-MRS	Anterior Posterior	3.0 T (Magnex)	1000/NS	Posterior region: - Magnesium (FHM+SHM) + PDE (MO) ———————— Anterior and posterior regions: = PCr = Magnesium = Pi = PME = pH
Schulz et al. (63)	MA (10) SHM+FHM (11) C (16)	31P-MRS	Temporoparietal	2.0 T (Bruker)	2500/NS	- PCr/P + Pi/ATP = PCr/ATP = pH
Lirng et al. (93)	MX (14) MX with depression (16)	1H-MRS	Dorsolateral prefrontal cortex	1.5 T (Signa, GE)	1500/35	+ Myo-inositol = NAA = Choline
Gu et al. (54)	MO (20) C (14)	1H-MRS	Thalamus, bilaterally	3.0 T (Signa, GE)	1000/144	- NAA/Choline = NAA/ tCr = Choline/ tCr
Mohamed et al. (45)	MO (22) C (10)	1H-MRS	Thalamus, bilaterally	1.5 T (Signa, GE)	1000/144 1000/35	- NAA/Choline - NAA/Cr + Myo-inositol /NAA + Lactate/NAA = Choline/Cr
Wang et al. (94)	CM (16) C (21)	1H-MRS	Hypothalamus, bilaterally	1.5 T (Signa, GE)	1500/144	= NAA = Choline
Schulz et al. (63)	MA (10) SHM+FHM (11) C (16)	1H-MRS	Basal ganglia	2.0 T (Bruker)	1500/135	= Lactate = NAA = Choline/Cr
Lai et al. (95)	EM (19) CM (53) C (16)	1H-MRS	Pons, dorsal rostral bilaterally PAG	1.5 T (Signa, GE)	1000/144	+ NAA = Choline
Macrì et al. (96)	MA (8) C (7)	1H-MRS	Cerebellum	1.5 T (Signa, GE)	1500/30	- Choline/NAA - Choline/ tCr = Choline/ tCr = tCr/NAA = Myo-inositol/NAA = Myo-inositol/ tCr = Myo-inositol/Choline
Stærmose et al. (97)	MA (14) C (16)	1H-MRS	Occipital, Somatosensory cortex	3.0 T (Magnetom Trio System, Siemens)	4000/8.50	= GABA = GABA/Cr+PCr (Total Creatinine) = GABA/NAA +NAAG(N-acetylaspartate + N-acetylaspartylglutamate)
Bell et al. (98)	PM (29) C (27)	1H-MRS	Thalamus, Sensorimotor cortex, Visual cortex	3.0 T (GE)	1800/80; 1800/35	= Glx = Glu = GABA
Bathel et al. (99)	M (15) C (15)	1H-MRS	Thalamus, Occipital	3.0 T (Achieva, Philips)	2000/30; 2000/68	+ Glx = GABA
Niddam et al. (100)	CM (25) EM (24) C (25)	1H-MRS	Anterior cingulate cortex, Occipital cortex, Thalamus	3.0 T (Trio, Siemens)	NS	- NAA

+: Significant increase when compared to controls; -: Significant decrease when compared to controls;
=: No significant difference when compared to controls; ADP, adenosine diphosphate; ATP, adenosine triphosphate;
C, controls; CM, chronic migraine; Cr, Creatine;
EM, episodic migraine; FHM, familiar hemiplegic migraine; FHM1, familiar hemiplegic migraine Type 1;
FHM2, familiar hemiplegic migraine Type 2;
GABA, g-aminobutyric acid; Glx, glutamate and glutamine;
MA, migraine with aura patients; MbA, basilar type migraine; MI, migraineous infarction; MO, Migraine without aura;
MpA, migraine with prolonged aura; MS, migraineous stroke;
PM pediatric migraine; MX, migraine type not reported; N, number; NAA, N-acetylaspartarte;
NAAG, N-acetyl aspartarylglutamate A; NS, not specified; PCr, phosphocreatine; PDE, phosphosdiesterase;
pHi, intracellular pH; Pi, inorganic phosphate; PME, phosphomonoesterase; PP, phosphorylation potential;
SHM, sporadic hemiplegic; tCr, creatine and phosphocreatine; TE, echo time;
tNAA, N-acetylaspartarte and N-acetyl aspartarylglutamate A;
TP, total phosphorous signal; TR, repetition time; V/Vmax, ATP-synthesis rate.

In a state of reduced available energy and mitochondrial dysfunction, it is expected that ATP would be synthesized at an increased rate under anaerobic conditions to meet the increased energy needs (8). This process is followed by an increase in lactate concentration and a decrease in intracellular pH (68, 80). Lactate increase may be caused by glutamate increase to protect against glutamate excitotoxicity (81). However, these findings were not consistently reproducible in either the 1H-MRS or the 31P-MRS studies (8). It remains to be determined if the mitochondrial migraine deficiency is primary or secondary. (1). The defect of oxidative energy metabolism represents the rationale for the use of metabolic enhancers (riboflavin, coenzyme Q10, magnesium and ketogenic diet) in migraine prevention (40).

Conclusion

The limited reproducible findings are partly explained by the different techniques used in the studies, often conducted below the magnetic field strength of 3.0 T, inhomogeneity of migraine cohorts and variation in studied brain areas. Despite of the variation between the MRS migraine studies over time, some results were reproducible and consistent. 1H-MRS studies reported significant differences in levels of GABA, glutamate, lactate and NAA between migraine patients and controls measured in various brain regions. The main consistent findings using 31P-MRS are concomitantly decreased PCr and increased inorganic phosphate as well as decreased magnesium measured in cortical regions of migraine patients. Most of the MRS studies investigated the interictal state of migraine patients. For identifying a biomarker in migraine it is necessary for future MRS studies to obtain additional information of the ictal state in migraine as well as before and after interventions. Also, there are no studies that have taken the severity of the disease (disease duration and migraine attack frequency) into account to detect possible correlation with MRS findings which also needs further research (8).

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MAGNETNO REZONATNA SPEKTROSKOPIJA MOZGA U MIGRENI

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Migrena je čest neurološki poremećaj, koji se karakteriše epizodama umerene do teške glavobolje. Magnetno rezonatna spektroskopija (MRS) je neinvazivna metoda, koja omogućuva *in vivo* proučavanje metabolizma tkiva korišćenjem magnetnih karakteristika određenih anatomskih jezgara, pre svega vodonika (1H) i fosfora (31P).

1H-MRS najčešće se koristi za merenje koncentracije gama aminobuterne kiseline (GABA), glutamata, fosfokreatina (PCr), kreatina, holina, N-acetilaspartata (NAA), mioinozitola, aspartata i laktata.

31P-MRS omogućava neinvazivno *in-vivo* merenje koncentracije jedinjenja koja sadrže jezgra fosfora. Ovo omogućava merenje metabolita uključenih u moždani energetski metabolizam, uključujući koncentracije fosfokreatina (PCr), neorganskog fosfata, kreatina, adenozin-difosfata (ADP) i adenozin-trifosfata (ATP).

1H-MRS studije pokazale su signifikantne razlike u nivoima GABA, glutamata, laktata i NAA između bolesnika sa migrenom i bolesnika iz kontrolnih grupa, merenih u različitim regionima mozga, dok u većini studija nije pronađena signifikantna razlika u nivoima mioinozitola, holina i ukupnog kreatina.

Glavni konzistentni nalaz u 31P-MRS studijama je konkomitantno smanjenje PCr i povećanje nivoa neorganskog fosfata, odnosno povećanje PCr / neorganski fosfat odnosa, kao i smanjenje nivoa magnezijuma merenih u kortikalnim regionima mozga bolesnika sa migrenom.

Za identifikaciju biomarkera u migreni nephodno je da u budućim studijama budu pribavljene dodatne informacije o iktalnom stanju u migreni, kao i o stanju pre i posle terapije. Težina bolesti (trajanje bolesti i frekvencija migrenoznih napada) mora biti uzeta u obzir da bi se detektovala moguća korelacija sa MRS nalazima, što takođe zahteva dalje istraživanje.

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Ključne reči: *migrena, glavobolja, magnetno rezonatna spektroskopija*