

Headaches, Magnesium Depletion and Biological Clock Dysrhythmia

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Introduction

Migraine is a complex neurological condition which is classified by the World Health Organisation as the 7th most disabling disease worldwide, the 4th for women [1]. The majority of headaches are idiopathic in origin. A clinical approach shows a continuum ranging from mild to moderate then severe headache, with clinical symptoms, pathophysiological mechanisms and therapies similar in tension type headache and migraine [2-4]. Migraine may be accompanied by nausea, vomiting, diarrhoea, confusion. Sensitivity to light with photophobia—a clinical marker, noise and strong smells is also frequently reported during and between the algic attacks [3,4]. The concept of hyperexcitability of the brain has arisen in the 15 last years, involving low cerebral magnesium levels, mitochondrial abnormalities, increased NO (nitric oxide) and calcium channelopathy [5-8]. In this regard, we showed two decades ago that the magnesium status and the Biological Clock (BC) function were strongly correlated and interacted between them [2,4,9]. One must distinguish between two types of magnesium deficit: Deficiency (a simple insufficient intake) and depletion (corresponding to a dysregulation of the magnesium status, due to the association of a reduced magnesium intake with various types of stress including BC dysrhythmias). Different common pathologies are clearly related to the chronopathological forms of magnesium depletion and these data would have consequences in terms of treatments [10-12].

The hyperexcitability would result from BC hypofunction (hBC) with decreased melatonin levels—the elective marker of the BC—and reactive photophobia [2-4] or to a secondary response to light hypersensitivity, with aggravation of the symptoms when light is important. In those patients, appear a dishabituation i.e., the disappearance of habituation, a physiological phenomenon considered to be a protective mechanism of the brain, by decreasing responses to repetitive stimuli (light, smell, noise) [4]. We used this characteristic to propose a murine test of photic sensitization in a murine photosensitive magnesium depletion model [13].

By contrast, since other cephalalgia are predominantly nocturnal (cluster headaches, cephalalgia with obstructive sleep apnea periods) we suggested that those clinical forms of migraines would be rather linked to BC hyperfunction (HBC) with a hyposensitivity to inducing light, increased melatonin levels and aggravation of the pathology when light is low or absent [2-4].

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Both dysrhythmias are characterized by clinical and biological markers summarized in **Table 1**.

The pharmacological treatment of migraine may be acute or preventive [8]. Traditional and emerging treatments are important but out of the scope of the present paper [14]. The following treatments only concern only the chronopathological aspects of magnesium depletion.

The hBC would benefit from darkness therapy per se (either dark goggles, or better by placing the patient in a dark room) which reverse the action of bright light, by increasing the melatonin levels. Melatonin, Magnesium, L-tryptophan and Taurine are darkness mimicking agents. Exogenous melatonin (3 mg/day) replaces the missing physiologic melatonin. Magnesium at nutritional dose may stimulate the BC, but many studies are still needed to precise the better salt, route of administration and indications). L tryptophan may stimulate the tryptophan pathway but may induce toxicity. Supplementation with Taurine may act as a protective inhibitory neuromodulator which improve brain function, notably its melatonin production [2,4]. Chromatotherapy is an energetic medicine deriving from the Chinese tradition which takes into account the nocturnal or diurnal prevalence of clinical signs. It distinguishes the night which is “yin” and the day which is “yang”. The diurnal pathologies are linked to excessive “yang” energies, heat and wetness, characteristic of both daylight and movement. Heat corresponds to any type of inflammation, aggravated by movement. Wetness corresponds to hyper hydration. For diurnal pathologies, the colours used are orange which induces cold organic answer consequently anti-heat and green which induces a dryness

Table 1: Chronopathological forms of Mg depletion in migraines.

	BC Hypofunction (hBC)	BC Hyperfunction (HBC)
Feature	Hypersensitivity to inducing light, leading to a decreased homeostatic response and to a reactive protective photophobia	Hyposensitivity to inducing light, leading to an Increased homeostatic response
Consequence	Nervous hyper excitability	Nervous hypo-excitability
Patients	Photophobic photosensitive migraine	Photophiles <ul style="list-style-type: none"> • Cluster headaches • Obstructive sleep apnea
Characteristics		
Period at risk	When light is maximum day light spring and summer	When light is low night autumn and winter
Major biological characteristic	Decreased melatonin levels (or its metabolite)	Increased melatonin levels (the elective marker of the BC)
Clinical form central forms associating manifestations		
Psychic	Neural hyperexcitability (ranging from anxiety to panic attack) Photogenic epilepsy	Asthenia, depressive state
Algic	Diurnal cephalalgia (migraine with photophobia, characterized by occipital cortex hyperexcitability)	Cephalalgia without photophobia
Hypnic	Delayed sleep phase syndrome	Advanced sleep phase syndrome
Peripheral signs neuromuscular	Myalgia	Fibromyalgia and muscular asthenia
Treatment	Darkness therapy per se, melatonin, Mg, L-tryptophan, Taurine	Bright light therapy
	Chromatotherapy/orange or green	Chromatotherapy/red or blue
	Pharmacotherapy/anxiolytic and/or anticonvulsant drugs	Pharmacotherapy/psychostimulating and/or anti-depressive drugs

organic answer consequently anti-wetness [14]. Even though not validated to date, Chromatotherapy gives excellent results in practice if different conditions are respected (appropriate colour filters, duration of exposure (4 Mn) followed by 20 Mn of darkness, only one treatment per week) [15]. Pharmacologic treatment is mainly symptomatic.

The HBC may be improved by bright light therapy (>2000 lux for 2-6 h or 10000 lux for 30 min) early in the morning to lengthen the photoperiod. It improves mood (anti-depressive effect), sleep anomalies, and non-migraine headaches, without photophobia [10]. The “yin” energies characteristic of both night and immobility are coldness (which correspond to any type of degenerative processes) and dryness (which correspond to any

type of dehydration). For night pathologies, the colours used are red which provokes a heat, consequently anti-cold organic answer and blue which induces a wet, consequently anti-dryness answer. Pharmacologic treatment is mainly symptomatic.

Conclusion

Magnesium status (mainly depletion) and Biological Clock (BC) are strongly correlated. Different pathologies including migraines may be linked to primary BC dysrhythmia or to a secondary abnormal sensitivity to light. Hyper-and hypo-functions of BC are characterized by common clinical and biological markers which could be of interest in a therapeutic purpose.

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