

Behavioral Therapy for Chronic Migraine

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Abstract Chronic migraine is a disabling condition which affects a considerable proportion of patients. Several risk factors and lifestyle habits contribute to the transformation of migraine into a chronic form. Behavioral treatments, including relaxation, biofeedback, and cognitive behavioral therapy reduce the risk of episodic into chronic migraine transformation, thus restraining the headache-related disability. The rationale of behavioral therapies is that a medical problem should be recognized and thoroughly examined by the patient to be successfully managed. Being aware of factors which precipitate or aggravate migraine allows patients to progressively modulate the frequency and duration of their attacks. Similarly, the acquisition of healthy habits improves the quality of life and the subjective well-being of patients and contributes to breaking the vicious cycle that leads to migraine chronification. The highest level of care is achieved when behavioral therapies are integrated with other treatments, including physical and pharmacological interventions.

Keywords Pain · Chronic migraine · Behavioral therapy · Quality of life · Disability

Introduction

Pain is defined as *an unpleasant sensory and emotional experience associated with actual or potential tissue damage*. It is classified as chronic when persisting beyond the normal time of healing whose upper limit is traditionally

fixed at 3 months [1]. Although a temporal criterion is generally adopted, growing evidence suggests that defining chronic pain only on the basis of its duration may be reductive [2•]. In fact, a chronic pain profile should be defined not only on the basis of how long pain lasts but also in light of prognostic indicators, denoting the likelihood that pain will continue or recur in the future. Such prognostic indicators include psychological and behavioral components, that play a central role in the pathophysiological process leading to chronification [2•]. The presence of risk factors which predict the transformation of pain from episodic to chronic has to be carefully traced, in order to promptly start behavioral therapies and improve the quality of life of the patients.

Chronic migraine belongs to chronic pain syndromes. It affects 1 % to 3 % of the population with a relevant burden on quality of life of patients and their productivity [3–5]. Chronic migraine is classified by the second edition of the International Classification of Headache Disorders (ICHD-II) as a complication of basic migraine [6]. To diagnose chronic migraine specific features must be present. Such features include unilateral and pulsating pain of moderate or severe intensity, which is aggravated or precipitated by routine physical activities and is combined with nausea and/or vomiting, photophobia, and phonophobia. Besides, the term *chronic migraine* implies that the migraine headache is present on ≥ 15 days per month and that any other medical condition, which may cause headache, has been excluded. A revision of diagnostic criteria for chronic migraine has been recently proposed [6]. The need for a revision is raised from the consideration that the above reported criteria are too restrictive and fail to include a large proportion of patients who experience attacks with a high frequency. In fact, migraine without aura may be sometimes misdiagnosed as tension-type headache, especially when an efficient early treatment hinders the recognition of a migraine attack [7••]. For this reason, some migraine patients are at risk of

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not entirely fulfilling diagnostic criteria, if the attack is aborted before the typical characteristics of migraine develop. To avoid misdiagnoses, revised criteria for chronic migraine have been introduced (Table 1). Such criteria take into account the influence of early treatments on the natural course of headache and exclude attacks resulting from medication overuse which are classified apart as medication overuse headache [7••]. Revised criteria for chronic migraine are able to capture >90 % of patients with frequent migraine attacks [8••].

From Episodic to Chronic Migraine. The Role of Risk Factors

Several risk factors contribute to the transformation of episodic headache into chronic migraine. Non modifiable risk factors include female gender, age, low education/socioeconomic status, first-generation immigrant, a history of head injury, and genetic predisposition [9]. Modifiable risk factors include stressful life events, sleep disturbances, obesity, baseline headache frequency, acute medication overuse, coffee abuse, other pain syndromes, allodynia, proinflammatory, and prothrombotic states [9]. The excess rates of chronic migraine in women may be attributed to the effect of female sex steroids on the modulation of nociceptive signalling [10, 11]. Recent evidence suggests that estrogens may increase the excitability of trigeminal nociceptors, thus influencing the process of sensitization leading to migraine [11]. Prevalence of chronic migraine is higher in young adults and decreases slightly with advancing age. This confirms that specific behavioral profiles, whose

adoption is more diffuse in the young, mainly contribute to the process of conversion from episodic to chronic migraine. Low socioeconomic status also plays a central role in the progression of migraine. The highest prevalence is recognizable in Georgia, Moldova, and Brazil [9, 12, 13]. Conversely, the prevalence in Europe and in the United States is significantly lower [9]. Possible explanations for this discrepancy include the absence of headache services in low-income countries and a pattern of drug intake mainly characterized by self-management and indiscriminate analgesic use [14]. A history of head injury also contributes to a change in the characteristics of headache. The prevalence of chronic headache in soldiers after a deployment-related concussion is 5-fold higher than that recognized in the general population [15]. However, the nature and severity of the trauma does not correlate with the headache profile, thus suggesting that a post-traumatic stress disorder rather than the trauma itself mediates the chronification of previous migraine [15]. On the contrary, when a causal relationship between the injury and the headache onset is clearly identified, the headache is classified as secondary post-traumatic headache [16]. A genetic predisposition may also favor the process of chronification. It has been estimated that about 30,000 genes might be involved in pain expression and that specific polymorphisms are responsible for interindividual differences in pain perception [17, 18]. Among modifiable risk factors, stress is considered one of the greater contributors to chronification. The association between stressors and migraine has been found in all age groups including the adolescents who may particularly benefit from behavioral therapies aimed at improving coping strategies for stress [19]. The emotional stress is one of the

Table 1 Revised International Headache Society criteria for chronic migraine

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- A. Headache (tension-type and/or migraine) on ≥ 15 days per month for at least 3 months
 - B. Occurring in a patient who has had at least 5 attacks fulfilling criteria for 1.1 migraine without aura
 - C. On ≥ 8 days per month for at least 3 months headache has fulfilled C1 and/or C2 below, that is, has fulfilled criteria for pain and associated symptoms of migraine without aura
 - 1. Has at least 2 of a–d
 - (a) unilateral location
 - (b) pulsating quality
 - (c) moderate or severe pain intensity
 - (d) aggravation by or causing avoidance of routine physical activity (eg, walking or climbing stairs) and at least one of a or b
 - 2. Treated and relieved by triptan(s) or ergot before the expected development of C1 above
 - D. No medication overuse^a and not attributed to another causative disorder^b
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^aMedication overuse as defined under 8.2 medication-overuse headache.

^bHistory and physical and neurological examinations do not suggest any of the disorders listed in groups 5–12, or history, and/or physical, and/or neurological examinations do suggest such a disorder but it is ruled out by appropriate investigations, or such disorder is present but headache does not develop in close temporal relation to the disorder.

migraine triggers most frequently reported by patients [20]. Indeed, how stressful events may favor the development of chronic migraine is still debated. Neurochemical changes which are induced by different physiological responses to stress may be involved [21]. The conversion from episodic to chronic migraine may rely on conditions of increased cortical excitability which is favored by stress through an adrenergic overflow. Behavioral strategies and β -blockers may reduce the frequency of migraine attacks by modulating adrenergic effects [21]. Sleep disorders also increase the frequency of migraine attacks. Too much or too little sleep is commonly reported by patients with chronic migraine as a precipitating factor for headache [20]. Insomnia, which is characterized by difficulties in initiating or maintaining sleep leading to daytime fatigue and distress, is frequently associated with chronic medical disorders including migraine [22]. Obstructive sleep apnea and habitual snoring were also identified as risk factors for the development of chronic daily headache [22]. Patients with migraine have a higher sleep latency than patients without [23] and show an improvement in migraine severity and frequency after continuous administration of melatonin is started [24, 25]. This suggests that disturbances in melatonin secretion may be somehow involved in the pathogenesis of chronic migraine [26]. However, the relationship between sleep disorders and chronic migraine is bidirectional, as migraine may interfere with a restorative sleep and sleep disorders may contribute to initiating and maintaining chronic migraine. Among modifiable risk factors, obesity has also been associated with an increased risk of chronic migraine especially in reproductive-aged women [27]. Obesity may favor the progression from the episodic toward chronic migraine by inducing a status of systemic inflammation and insulin resistance [27]. This is in line with several observations suggesting an association between chronic migraine and inflammation-related conditions of various natures [28–30]. Finally, some comorbidities are more common in patients with chronic migraine compared with patients with episodic migraine (Fig. 1), [30–33, 34•]. These comorbidities include arthritis, other chronic pain disorders, anxiety, depression, bipolar disorder, obesity, circulation problems, heart disease, hypertension, stroke, allergies, asthma, acute and chronic bronchitis, emphysema or chronic obstructive pulmonary disease, and sinusitis [30]. It is difficult to establish the pathophysiological substrate linking chronic migraine to the above comorbidities. Nevertheless, the greater disability, which is experienced by patients with chronic rather than episodic migraine, may also result from the association of persisting pain with such comorbidities. Therefore, a combined treatment, aimed at containing both migraine and comorbidities, is mandatory to improve the quality of life of patients. The need of reducing disability is even more evident if we consider that the disability itself, as

measured by the MIDAS score, is one of the best predictors of a further chronification [3, 35].

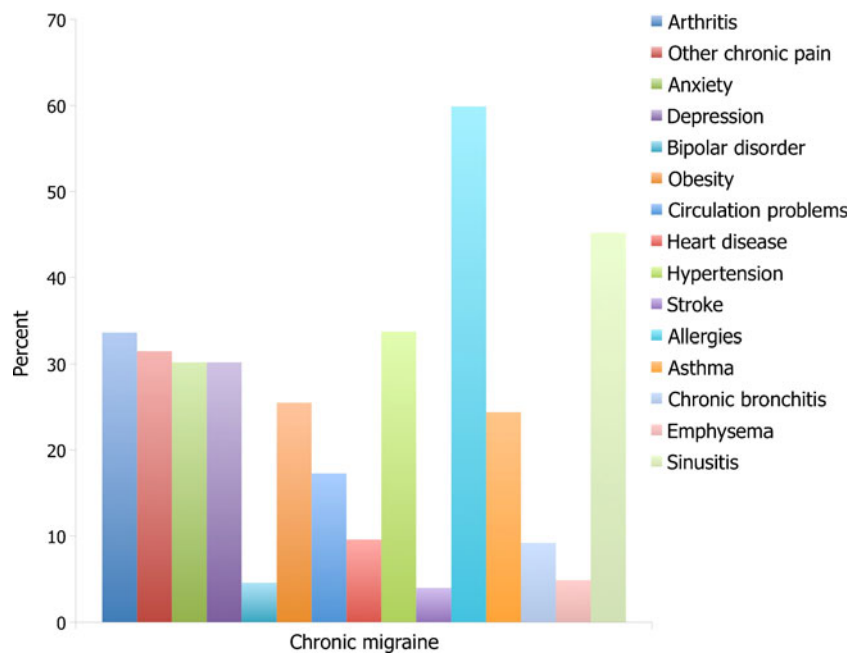
Behavioral Management of Chronic Migraine

Interindividual differences in the risk and psychological profiles leading to chronic migraine suggest that its management should be necessarily tailored to the single patient. Lifestyle factors which contribute to the transformation of episodic migraine into a chronic syndrome should be promptly recognized and managed to break the vicious cycle fostering the recurrence of headaches. This is even more mandatory if we consider that analgesics and prophylactic treatments are often ineffective in patients with chronic daily headache, due either to low adherence to prescribed treatments or previous medication overuse. Cognitive and behavioral interventions may improve the quality of life of patients by enhancing their coping strategies for psychosocial stressors and encouraging treatment adherence. Behavioral therapies can be grouped into 3 categories including relaxation, biofeedback, and cognitive behavioral therapy. All these therapies require the motivation of the patients and look to enhancing their responsibility, thus reducing the dependence on physicians. Self-management treatments imply that while physicians are expert on diseases, patients are expert on their own lives.

Relaxation Techniques

The aim of relaxation-based approaches is to reduce sympathetic arousal and muscle tone and to encourage a state of bodily relaxation. This approach moves from the assumption that a restricted arousal, together with the modulation of attention through distraction, may help to reduce the central processing of peripheral sensory inputs [36••]. Indeed, relaxation helps to contain anxiety feelings which commonly contribute to the development and maintenance of chronic migraine. Relaxation techniques include progressive muscle relaxation training, diaphragmatic breathing, autogenic training, guided imagery, and meditation [36••]. During progressive muscle relaxation training, patients are instructed to maintain their eyes closed and to repeatedly tense and relax specific muscle groups proceeding from forehead to toes and then in reverse order. Tension and relaxed periods last 10 and 20 seconds respectively. In the meanwhile patients are invited to concentrate on sensations arising from tension and relaxation. Video and audio programs are commonly used as relaxation facilitators [36••]. During diaphragmatic breathing, patients are in a supine position with the hands along the sides of the body and palms upward. They are encouraged to take deep breaths through the diaphragm, minimize chest movements, and

Fig. 1 Percent frequency of comorbidities in chronic migraine (data from [30])



reduce the pauses between breaths [37]. During autogenic training patients perform specific conditioning exercises resulting in relaxation and auto-suggestion. The aim of such procedures, including limb heaviness exercise, cardiac exercise, respiration exercise, solar plexus warmth exercise, and forehead cooling exercise, is to induce a consciously directed altered state of awareness, similar to self-hypnosis [38, 39]. Guided imagery is aimed at distracting the head pain attention of the sufferer away from the painful condition [40]. Patients may be guided to imagine themselves in a pleasant place, to recall a peaceful time, to concentrate first on a color they associate with tension, and then mentally replace it with one they find soothing. Finally, meditation, a self-regulatory mind-body practice, includes focused attention meditation, which entails voluntary and sustained attention on a chosen object, and open monitoring meditation, which involves non-reactive monitoring of the moment-to-moment content of experience [41].

Biofeedback

In biofeedback-based approaches patients use specific instruments to measure, amplify, and feedback physiological information which enable them to gain control over the target response and regulate it as they desire [36•]. Besides, biofeedback techniques affect the bioavailability of nitric oxide and oxygen free radicals, which are involved in the central sensitization of pain [42•, 43]. Biofeedback approaches may be general or specific. General approaches, also known as biofeedback-assisted relaxation, help patients to get a complete state of relaxation through the monitoring of physiological responses which are reactive to stress. Fluctuations of the above responses, including muscle

tension, electrodermal activity, and peripheral temperature, are considered as signs of sympathetic recruitment and arousal. Through biofeedback signals patients improve their strategies to decrease arousal and to enhance relaxation [36•]. A limit of biofeedback-assisted relaxation is that it requires a therapist assistance to be performed while isolated relaxation may be carried out even without additional support. On the other hand, specific biofeedback approaches are based on the evaluation of more specific signals such as blood volume pulse from the superficial temporal artery, Color Doppler blood flow, and electroencephalographic fluctuations which are used as markers of the physiological dysfunction underlying the pain condition [36•]. Patients with recurrent migraine may learn to recognize and manage those responses in the attempt to modify their pain condition through a trained control of vasoconstriction [44], cortical excitability [45], and hemodynamics [46]. To date, the above reported biofeedback techniques are considered experimental and need to be further investigated to check their efficacy and effectiveness [36•].

Cognitive Behavioral Therapy

Maladaptive thinking and behaviors may negatively affect the course of several medical disorders, including migraine. Cognitive-based approaches are based on the assumption that *much of how we feel is determined by what we think*. It follows that a more informed status about the natural course of diseases, precipitating factors, and underlying mechanisms may enable patients to develop more effective coping strategies to manage the disease itself. In fact, patients who are familiar with their headache are more likely to prevent risky behaviors, to make better therapeutic

choices and to avoid chronic pain. In addition, the implementation of stress management strategies reduces the development of stress-related reactions including increased muscular tension, sympathetic hyper-arousal, and increased activity of the hypothalamic anterior-pituitary adrenocortical axis. This is particularly relevant for patients with chronic migraine who commonly show anxiety-related personality traits and poor coping strategies for the management of chronic pain. Besides, pharmacologic treatments are usually not tolerated by those patients, who often show medical contraindications or insufficient response to treatments. Through cognitive behavioral strategies, patients learn to recognize and avoid risky behaviors for recurrent headaches and to contain psychiatric disorders and comorbidities which further influence the progression from episodic to chronic migraine [47]. They are recommended to keep headache diaries and to record sleep disorders, bad eating habits, caffeine or alcohol overuse, smoking, frequency of physical exercise, prodromal symptoms, and headache triggers. Moreover, patients need to be informed about the main characteristics of headache, its clinical course, pathophysiology, and treatment options to avoid the structuring of a catastrophizing thinking pattern. Once patients are instructed about their risk profile and headache characteristics, they need to be taught about lifestyle choices and appropriate use of analgesic and prophylactic medications, to avoid adverse effects and drug interactions [47]. Indeed, lifestyle interventions include behavioral therapy for sleep regulation to optimize duration, quality, and regularity of sleep and behavioral management of high risk conditions such as obesity and alcohol or caffeine overuse. With respect to sleep, patients are recommended to use specific schedules to avoid sleep/wake changes on weekends, to choose a dark environment for the sleep time, to avoid daytime naps, and to cope with snoring and insomnia which may further contribute to avoid a restorative sleep [48]. Besides, caffeine, nicotine, and alcohol, which may alter the sleep quality, should be minimized [48]. With respect to eating habits, patients need to be instructed to keep a regular diet schedule, without missing or postponing meals [48]. A regular physical activity, such as aerobic exercises for 30 minutes, 5 days a week, is also recommended. Physical activity should be of average level, as both high and low level exercises may increase the risk of migraine development and transformation [48].

Effectiveness of Behavioral Therapies

Several studies investigated the effectiveness of behavioral therapies in patients with migraine but data specifically driven to patients with chronic migraine are not available [36••, 49–56]. Such studies focused on different age groups

and compared behavioral treatments with placebo or other active treatments. Primary outcomes included the frequency, severity, and duration of headache and the response to pharmacological treatments. Secondary outcomes included pain-related disability, lost work/school time, anxiety and depression, and acute medication intake. Relaxation and biofeedback treatments, as well as cognitive behavioral therapy, resulted in improvements in primary and secondary outcomes [36••, 49–52]. Indeed, a comprehensive meta-analysis recently confirmed the effectiveness of relaxation and cognitive behavioral therapy, also in the management of recurrent childhood headaches [53–56]. However, the research design of the reported studies is too heterogeneous and too weak to draw definitive conclusions on the effectiveness of behavioral therapies. Only a few studies met the criteria for randomized controlled trials and most of them investigated the role of behavioral therapies in the prevention of episodic migraine, without focusing on the risk for chronification. Further studies are necessary to confirm the effectiveness of behavioral approaches both for episodic and chronic migraine. Indeed, there is a general consensus that cognitive behavioral approaches are not equally suitable for all subjects. Patients who are more likely to benefit from behavioral therapy include those with chronic or refractory migraine, poor coping strategies, and psychiatric comorbidities such as anxiety and mood disorders [57]. Strong candidates for behavioral therapy also include children and adolescents, due to the adverse effects of pharmacological treatments which may be particularly deleterious during growth [36••, 57].

Coping Is Better Than Avoiding. An Integrated Model of Headache Care

As already mentioned, good management of chronic migraine entails the identification of precipitating and behavioral factors for the development of pain, the best available pharmacological treatment, and the adoption of behavioral strategies. However, some triggers are hardly identifiable and, among the identifiable ones, there are triggers which cannot be avoided (ie, menstruation) [58]. Besides, an avoidance-based lifestyle may be extremely stressful and the stress itself may trigger a vicious cycle leading to chronic migraine and disability. In this respect, coping interventions, which enable patients to adaptively manage their pain condition, may be better than avoiding strategies, which may ultimately enhance anxiety feelings and negatively affect the modulation of pain. Thus, preventing chronic migraine does not merely mean avoiding triggering stimuli. On the contrary, recent evidences suggest that the long-lasting exposure to common triggers such as noise, visual disturbances, or hunger, while patients are relaxed, induces a

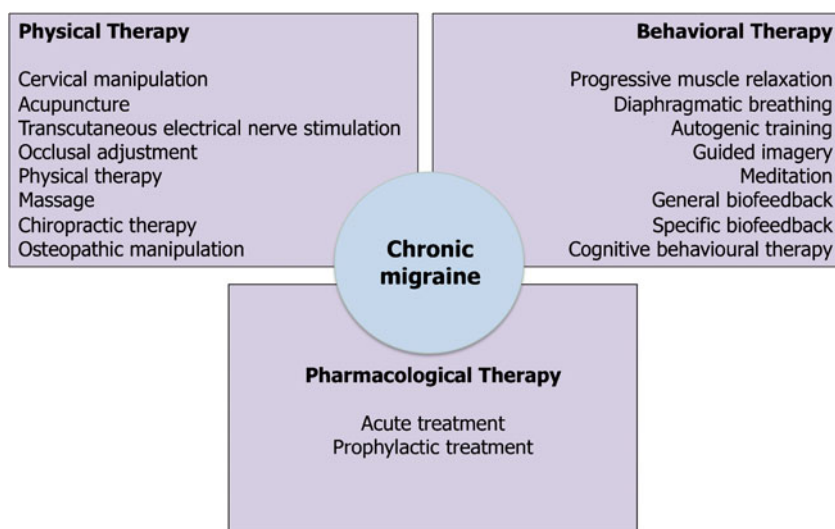
condition of toleration, while the strict avoidance of triggers enhances intolerance and pain sensitization [59–61]. Thus, the management of recurrent headaches is more likely to be successful if prompted to encourage adaptive behaviors. The maximum medical improvement is achieved when coping skills are achieved through complementary techniques. The combination of cognitive behavioral and relaxation techniques seems to be more effective than relaxation alone in reducing recurrent attacks of migraine [62]. Besides, a combination of pharmacologic and non pharmacologic approaches is considered the gold standard in the prevention and treatment of chronic migraine, in terms of long-term outcomes and improved adherence to treatments [36••]. An integrated model of health care, which has been conceptualized as a 3-legged stool, offers the best management for patients with chronic disorders including chronic migraine. The 3 legs identify pharmacologic, physical, and behavioral treatments, respectively [63]. A comprehensive headache management through the combination of the above reported treatments may successfully reverse the process of chronification, due to the synergic action of different treatments whose combined effect is greater than the sum of their individual effects (Fig. 2). Current guidelines suggest that tracing patients who show a high risk for migraine transformation, followed by the identification of risk factors associated with frequent headache, may help to prevent the progression from episodic to chronic migraine especially when integrated models of care are provided [64]. Once chronic migraine has developed, interdisciplinary programs including pharmacological and behavioral approaches, represent the best option to manage patients [65]. Among pharmacological agents, topiramate and local injection of botulinum toxin are considered the most effective treatments [66]. However, adherence to pharmacological treatments is usually lower in patients with chronic migraine, due to

increased side effects, increased costs, and psychiatric attitudes [47, 67]. Thus, the combination of pharmacological and behavioral approaches is usually more effective than pharmacological treatments alone. An integrated model of care may be profitably suggested also for patients with a medication overuse headache. They are patients who are particularly afraid of the increasing frequency of their attacks and tend to overuse acute medications. This overuse perpetuates headaches, as it represents an additional risk factor for the escalation from the episodic to the chronic form and for the maintaining of chronic migraine. The analgesic withdrawal, together with the use of migraine preventive medications, may not suffice to break the vicious cycle leading to medication overuse headache. Besides, patients are often not aware that analgesics overuse may lead to a worsening of headache frequency and severity [68]. Most of them show psychiatric comorbidities and dependent behaviors which interfere with a successful withdrawal from overused medications [69]. Several studies suggest that proper information about the correct use of acute medications, together with the starting of behavioral therapies, including psychoeducational interventions, biofeedback and relaxation strategies, may facilitate the management of such patients and improve their quality of life [70–73].

Conclusion

Further evidences are necessary to definitively establish the effectiveness of behavioral therapies in avoiding the transformation from episodic to chronic migraine. Available data suggest that the best improvement is achieved when behavioral therapies are integrated with other treatments, including physical and pharmacological interventions.

Fig. 2 An integrated model of chronic migraine care



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- Of major importance

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