MIGRAINE TRAINERS AS MODELS:
The effectiveness of lay trainers with migraine for behavioural attack prevention

Saskia Mérelle

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MIGRAINE TRAINERS AS MODELS: THE EFFECTIVENESS OF LAY TRAINERS WITH MIGRAINE FOR BEHAVIOURAL ATTACK PREVENTION

MIGRAINETRAINERS ALS ROLMODEL: DE EFFECTIVITEIT VAN LEKENTRAINERS MET MIGRAINE IN GEDRAGSMATIGE AANVALSPREVENTIE

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Voor Jeanne

`For all the benefits of belonging'

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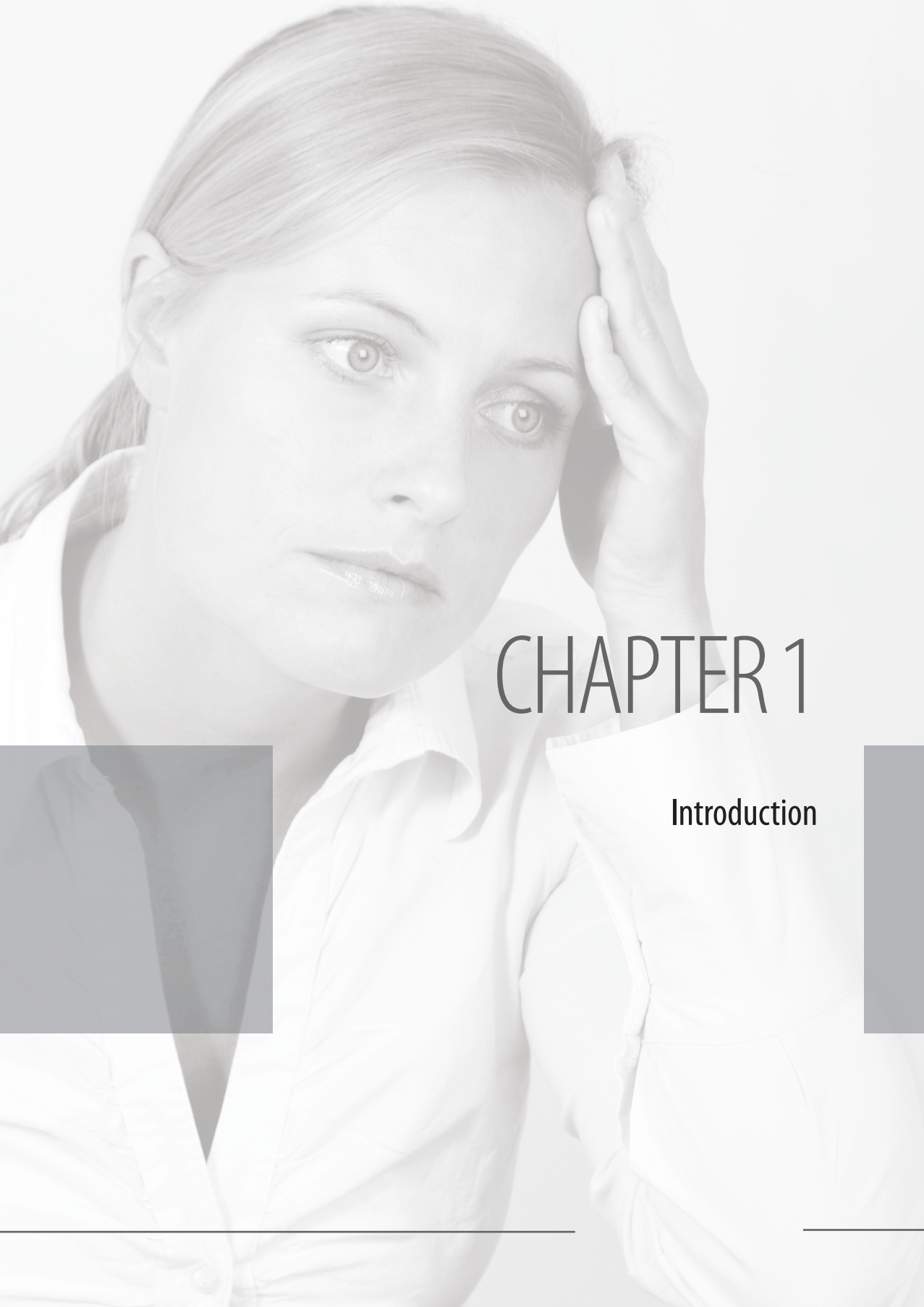


CHAPTER 1

Introduction

INTRODUCTION

Migraine is a chronic brain disorder, characterized by attacks of severe headache accompanied by nausea, vomiting and sensitivity to light, sound and smell.[1,2] Attacks can be preceded by premonitory symptoms such as fatigue, muscular stiffness or negative affect.[3] It has been shown that cortical spreading depression, the trigeminovascular system and central sensitization play an important role in the pathophysiology of migraine.[4-7] In addition, gene mutations appear to be responsible for lowering the threshold for stimuli in the hours before a migraine attack sets in.[8] Therefore, genetic factors may induce susceptibility for migraine triggers such as stress, female hormones and skipping meals.[8,9] Migraine is a common disorder affecting 12% of the general population in western societies (6% men, 17% women).[10,11] The burden of migraine is high and patients' well-being and ability to function are affected in several domains, such as work performance, mental health and social activities.[12,13]

The government and health insurance companies insist nowadays on application of evidence-based and cost-effective interventions.[14,15] The efficacy of pharmacological treatment for migraine is well established and the so-called 'triptans' are successful in aborting a migraine attack.[16,17] Prophylactic treatment is increasingly used for patients with severe and frequent migraine attacks and new preventive therapies are emerging.[2,18] New developments are also needed in the field of psychological interventions. Behavioural treatment (BT) has proven to be effective in reducing attack frequency by 30-55%.[17,19] Home-based BT is a relatively new treatment format and consists of minimal clinical contacts, and the training at home is supported by manuals and telephonic consultation.[20,21] Home-based BT was found to be as efficacious as clinic-based BT and five-fold more cost effective.[22] A parallel development is the rise of self-management programmes, which aim at an active involvement of patients by improving their knowledge about the disease together with their self-efficacy to take control.[23-25] There is increasing evidence that lay trainers with a chronic condition can deliver this type of intervention.[24,26] A recently developed method is online digital assistance (ODA), which provides mobile monitoring of symptoms and cognitive-behavioural coaching through a personal digital assistant.[27] This e-health method may support the self-regulation of chronic diseases that are applied with minimal professional guidance.

This thesis addresses the effectiveness of a behavioural training (BT) provided in a self-management format by lay trainers with migraine to small groups at home. The primary aims of BT are to reduce attack frequency, and to increase internal control over and self-confidence in attack prevention.

This chapter provides a general introduction to the major themes and presents the aim and outline of the thesis.

Migraine Classification

Table I presents the diagnostic criteria for migraine without aura according to the second edition of the International Classification of Headache Disorders (ICDH-2).[28] The duration of migraine attacks is 4 to 72 hours, with at least two of four pain features and at least one of two sets of associated symptoms. When migraine attacks occur on ≥15 days per month the classification is `chronic migraine´. [29] Migraine with aura concerns headache which fulfils the criteria of migraine without aura and, in addition to these criteria, consists of the following aura characteristics: focal neurological features that usually precede migraine headache but may also accompany it or occur in the absence of the headache. Aura symptoms develop over ≥5 minutes prior to a migraine attack and last no more than 60 minutes. Visual aura is the most common and is characterized by visual manifestations (e.g. a crescent with a bright ragged edge that scintillates). Somatosensory symptoms occur in about one third of patients, consisting of numbness and tingling (or paresthesia) and usually occur in a patient's face and hand.[29] Last, hemiplegic and basilar subtypes of migraine with aura exist and are associated with symptoms such as dysphasia, motor weakness and changes in level of consciousness.[29]

Table 1. ICDH-2 diagnostic criteria for Migraine without Aura

A. At least 5 attacks fulfilling criteria B to D below
B. Headache attacks lasting 4–72 hours (untreated or unsuccessfully treated)
C. Headache has at least two of the following characteristics:
1. unilateral location
2. pulsating quality
3. moderate or severe pain intensity
4. aggravation by or causing avoidance of routine physical activity (e.g., walking or climbing stairs)
D. During headache at least one of the following:
1. nausea and/or vomiting
2. photophobia and phonophobia
E. Not attributed to another disorder

Migraine often combines with tension-type headache (TTH), which is the most common type of primary headache, with a one-year prevalence ranging from 31-74%. [29] TTH episodes last from 30 minutes to 7 days and headache has at least two of the following characteristics: 1) bilateral location, 2) pressing/tightening (non-pulsating) quality, and 3) mild or moderate intensity.

Prevalence and Quality of life

Migraine has a 1-year prevalence of 10-12% in Western countries.[10,11] The life-time prevalence is approximately 8% for men and 25% for women.[12] The prevalence is about three times higher in females than in males, and is quantitatively related to the levels of female sex hormones.[30] A large epidemiological study (n=18,968, age >12 years) recently found a 1-year prevalence of 11.7% (5.6% men, 17.1% women).[11] Migraine prevalence was highest in those aged 30-

39 years for both men (7.4%) and women (24.4%), followed by 40-49 years, and 18-29 years. Statistics Netherlands reported that in 2006 12.1% of the Dutch population suffered from this chronic disease.[31] The female to male ratio in the Netherlands was 16.5% for women and 7.7% for men.[32] Finally, the incident rates showed a peak in males around 5 years of age (6.6/1000 person-years) for MA, and a peak for MO around 10-11 years (10/1000 person-years). In females the peak incidence rate is higher but also later at 12-13 years (14.1/1000 person-years) for MA, and at 14-17 years for MO (18.9/1000 person-years).[12]

Migraine affects several domains of patients' daily functioning. Compared to other chronic conditions (such as diabetes), migraine patients were more impaired in mental health, work performance and social activities.[12,33] Consequently, the direct costs of migraine are considerable in the Netherlands.[34] According to the report of the World Health Organization migraine is one of the leading causes of years of life lost to disability (19th position for both sexes, 12th position for females).[13] Between attacks, patients reported elevated levels of emotional distress, fatigue, and anxiety for a new attack.[35-37] Attack frequency can be an important disabling factor, whereby a higher migraine frequency leads to greater impairments in daily life.[38,39] Psychological consequences can further diminish a patient's quality of life. It has been shown that catastrophizing, characterized by rumination, magnification and helplessness, contributed independently to an impaired quality of life.[40] Another study showed that patients who reported more negative emotions during pain experienced more problems with physical mobility and social isolation.[41] Finally, the burden of migraine is also worsened by the association with a number of psychiatric disorders. According to a literature review, persons with migraine were from 2.2 to 4.0 times more likely to have depression.[42] Migraine was also associated with generalized anxiety disorder (odds ratio:3.5 to 5.3), panic disorder (OR: 3.7), and bipolar disorder (OR: 2.9 to 7.3). Besides psychiatric disorders migraine also coincides with epilepsy and stroke.[43]

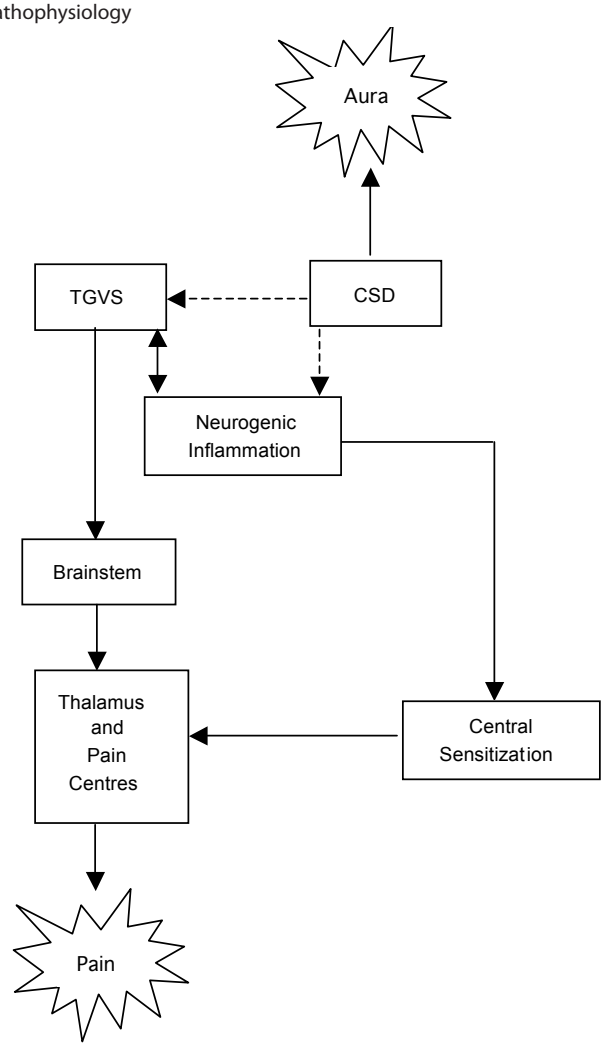
In conclusion: migraine is a common disease and patients' well-being and ability to function is affected in several domains.

Pathogenesis

Pain perception studies have indicated that sensitization of the central nervous system plays an important role in the pathophysiology of headaches.[6] In migraine, increased pain sensitivity has been demonstrated during the migraine attack.[6] Central sensitization may lead to an altered perception in which normally nonpainful stimuli are perceived as very painful.[7] Twin and family studies showed that genetic factors may play an important role by lowering the threshold for triggers of migraine attacks.[8] In common migraine, multiple genes and environmental factors appear to be involved.[4,5,8] However, gene mutations were only identified in a rare subtype of migraine with aura patients.[4] This monogenic subtype is called familial hemiplegic migraine (FHM) and is characterized by some degree of weakness (hemi paresis).[4] In FHM, gene mutations were related to a dysfunction in ion transport (calcium channels) and

increased the susceptibility to cortical spreading depression (CSD).[4,44] CSD is a short-lasting wave of depolarisation that moves across the cortex and leads to changes of cerebral blood flow during migraine attacks with aura.[45] This intense neuronal activity is followed by a period of overshoot to neuronal inactivity.[5] CSD is likely to be a self-defence mechanism of the brain to strong stimuli and can adequately explain the aura phase.[4] The relationship between CSD and the headache phase is not yet fully elucidated. However, most experts believe that the headache and associated symptoms are caused by activation of the trigeminovascular system (TGVS).[4,5]

Figure 1. Migraine Pathophysiology



TGVS; trigeminovascular system CSD; cortical spreading depression. Adapted from Genetic Models of Migraine. *Arch Neurol.* 2007;64:643-646. Copyright (c), American Medical Association. All Rights reserved.

The TGVS consists of the meningeal and superficial cortical blood vessels that are innervated by the trigeminal nerve, which projects into the trigeminal nucleus caudalis in the brainstem which, in turn, projects into higher-order pain centres.[5] As Figure 1 shows, CSD might activate the TGVS; however, up to now evidence is only available from animal experiments. According to this theory, during CSD potassium, protons, neurotransmitters and metabolites are released and can activate the TGVS, and subsequently the trigeminal nucleus caudalis in the brainstem. This leads to the activation of higher-order pain centres such as the thalamus via the modulatory periaqueductal gray. Activation of the TGVS (and possibly CDS) induces meningeal neurogenic inflammation, resulting in central sensitization. Autonomic symptoms (e.g. fatigue, appetite disturbances and malaise) are frequently observed during migraine attacks and may be mediated by the pathways between the TGVS and the higher-order pain centres.[46]

The throbbing nature of migraine pain and its worsening during movement may be caused by sensitization of central trigeminocervical neurons, which increase nociceptive inputs during arterial pulsation.[46] Last, calcitonin gene-related peptide (CGRP) is released from trigeminovascular axons and leads to vasodilatation, which in turn provokes neurogenic inflammation. Acute pharmacological treatment with triptans can inhibit CGRP release and successfully abort a migraine attack.[46]

In conclusion: basic research suggests a crucial role for central sensitization and the trigeminovascular system in the pathogenesis of migraine. Genetic factors and central sensitization may induce the susceptibility to trigger factors.

Triggers and premonitory symptoms

Behavioural treatments focus on the recognition, avoidance and management of headache triggers such as stress, missed meals, poor sleep, certain foods and visual disturbance.[9,47] Trigger factors have also been demonstrated in epidemiological studies among children.[48] A recent study evaluated trigger factors in 1207 patients, and 3 out of 4 patients reported triggers (40% infrequently, 27% frequently and 9% very frequently).[49] The most frequent triggers were: stress (80%), female hormones (65%), not eating (57%), weather (53%), sleep disturbance (50%), perfume or odour (44%), neck pain (38%), light(s) (38%), alcohol (38%), smoke (36%), sleeping late (32%), heat (30%), food (27%), exercise (22%), and sexual activity (5.2%). It is noteworthy that stress is most frequently reported by migraine patients; however, the studies investigating this topic suffer from methodological shortcomings, e.g. the use of a retrospective questionnaire.[50] A diary study showed that in the 24-60 hours before a migraine attack significantly more daily hassles were reported, psychological arousal increased (irritability, annoyance and tenseness), and fatigue also increased with a peak immediately before the attack.[51] Therefore, daily hassles can be an important trigger factor, which in combination with other trigger factors may augment the risk of a migraine attack.[52] Hormonal changes are also an important factor that can lower the migraine threshold. In a population sample of

1181 Dutch women (aged 13 to 55 years) attacks of menstrual migraine were more severe, of longer duration, and more resistant to treatment than migraine attacks at other times of the month.[53]

The presence of several trigger factors in a short timeframe may increase the risk of the occurrence of a migraine attack.[50] How migraine triggers actually acquire the capacity to precipitate a migraine attack remains a scientific challenge, and more experimental studies are needed.[54] One recent laboratory study failed to verify the biological relationship between mental stress as a trigger and the onset of migraine.[55] Furthermore, studies of the autonomic nervous system report both sympathetic hyper-function and hypo-function in migraine patients.[56] Therefore, the relationship between stress and migraine is complex and an ongoing topic of scientific debate. In conclusion: there is a great variability in migraine triggers of which stress is the most frequently reported.

A migraine attack consists of three multiple phases – premonitory, headache, resolution – and may include a separate aura phase before the headache sets in. The initial phase of the attack is characterized by the presence of `prodromes' or `premonitory symptoms'.[57] In the ICDH-2 classification premonitory symptoms are defined as `symptoms preceding and forewarning of a migraine attack by 2-48 hours, occurring before the aura in migraine without aura (MA) and before the onset of pain in migraine without aura (MO)'.[29] These premonitory symptoms include (combinations of) fatigue, difficulty in concentrating, neck stiffness, sensitivity to light or sound, blurred vision, yawning and pallor.[29,57] Compared to the migraine aura, premonitory symptoms develop more gradually, are more likely to arise from different areas of the central nervous system, are characterized by general/behavioural features, have a longer duration, and may not resolve prior to pain onset.[57]

An electronic diary study analysed the occurrence and predictive value of premonitory symptoms in 97 patients.[3] Seventy-two percent of the migraine headaches were correctly predicted by these symptoms (up to 72 hours before the attack). Patients who reported a lower health status more accurately predicted a migraine attack than those functioning well, probably reflecting an underlying biological mechanism. Tiredness and cognitive slowing (difficulty with concentration, thoughts, reading and speech) were the most frequently occurring symptoms. Stiff neck, light or noise sensitivity and negative affect were also frequent entries in the diaries. This predictive ability of premonitory symptoms may offer the opportunity for early treatment to prevent attack occurrence. In a clinic-based study, 87% of the 378 migraine patients who responded to a questionnaire reported at least one premonitory symptom, and 71% reported two or more.[58] Again, fatigue was most frequently reported (47%), followed by sensitivity to noise (36%) and yawning (36%). Age, education, MA or MO and attack frequency were not related to the number of premonitory symptoms.

In conclusion: premonitory symptoms are features of the initial phase of a migraine attack and early recognition of them can provide therapeutic chances for preventive treatment.

Behavioural treatment

Although migraine is highly prevalent and burdensome in daily life, many patients do not seek medical treatment.[59] A large-scale implementation of effective and broadly accessible evidence-based treatments seems therefore justified. In the past decades the clinical utility of behavioural treatments (BT) for migraine (and tension-type headache) has been proven in numerous studies.[19] BT has proven effective in reducing attack frequency by 30-55%, and to be significantly superior to waitlist control (5%) and to attention control conditions (9%).[17,19,60] Long-term studies showed that short-term improvements were well maintained or even improved after a follow-up period up to 12 months.[61,62] BT is focused on secondary prevention of migraine attacks and aims at: 1) reduction of attack frequency, 2) reduction of medication use, 3) improvement of internal control over migraine, and 4) decrease of impairments and emotional consequences due to migraine.[63] Active involvement of patients is crucial and patients should take control over their lifestyle (i.e. self-management).[64] Attack prevention is the main target of BT and two strategies are crucial to achieve this goal: 1) identification and modification of triggers and premonitory symptoms, and 2) use of physiological self-regulation skills.[19,65] BT can be categorized in three basic methods: relaxation, biofeedback and stress-management therapy. Relaxation methods are the most commonly applied approaches in research and clinical practice.[21] They consist of various procedures such as progressive muscle relaxation training, diaphragmatic breathing and autogenic training. The latter method is commonly used in migraine and, according to meta-analyses, produces medium effect sizes in headache improvement.[66]

Despite the broad application of relaxation methods, the mechanism in relation to migraine pathophysiology is still not clear. A well-founded theoretical model and scientific evidence are lacking. Relaxation methods are presumed to reduce physiological arousal and decrease sympathetic activity.[19] A reduction in general arousal is supposed to lead to a reduction in central processing of peripheral sensory inputs.[21] Furthermore, relaxation methods may increase patients' feelings of self-control by teaching patients to control their physiological stress responses, such as muscle tension.[63] Self-control is important for migraine patients, because migraine is an intermittent disease and patients often feel insecure and anxious about a subsequent migraine attack.[63] In line with the new insights on migraine pathophysiology, it is plausible that relaxation methods reduce arousal, sensory sensitivity and overexertion, and therefore could help to prevent attack occurrence.[67] Furthermore, these methods could also buffer the patients susceptibility to trigger factors, because evoked and event-related potential studies identified a lack of habituation to stimuli between attacks.[68]

Home-based behavioural treatments (HBT) or minimal contact BT are treatments in which contact time with a therapist is considerably reduced; patients practice more independently at home, supported by manuals, audiotapes with relaxation techniques, and/or telephonic support.[20] The frequency and duration of treatment varies, but HBT usually consists of 3 to 4 monthly clinical sessions and 45 to 60 minutes per session.[69,70] The advantages of HBT (besides

reduction of costs) are: 1) increased availability of psychological interventions for headache, 2) higher knowledge and active involvement of patients, and 3) the transfer of knowledge and skills to daily life after completion of therapy.[20,71-73]

In the 1990s, the effectiveness of a Dutch mass media BT was examined.[74] This programme consisted of 10 lessons broadcast by television, supported by the radio, a self-help textbook, an exercise book, and audiocassettes with relaxation exercises. Of the 164 participants who were analyzed (61% of the participants) 40-60% showed a clinically significant reduction of headache activity and medication intake at 4-month follow-up (>50% reduction). These results were in line with a meta-analysis of controlled studies, which concluded that home-based BT is as efficacious as clinic-based BT and five-fold more cost-effective.[22]

In conclusion: behavioural treatments have been proven effective in reducing attack frequency and can function as additional evidence-based treatment for migraine prevention. Home-based BT is a shortened treatment format that may increase the accessibility of BT.

Self-management and Lay trainers

Developed healthcare systems are shifting from paternalistic to partnership models of care.[26] Policymakers, clinicians and consumers are seeking ways to promote increased involvement of patients in their own management. This intention refers to the concept of `patient empowerment', which states that patients are experts of their chronic disease, share responsibility for the management of the disease, and therefore should be involved in achieving efficient and effective health care.[23,24,75] The earliest programmes included asthma self-management plans that encouraged people to alter their dosage of asthma medication in response to altered symptoms or peak expiratory flow measurements.[26] A widespread and successful example of self-management programmes is the Chronic Disease Self-Management Programme that was developed by Lorig et al.[76] This programme is based on Bandura's self-efficacy theory, a social cognitive theory which states that the key predictors of successful behaviour change are confidence (self-efficacy) in the ability to carry out an action, and expectation that a particular goal will be achieved (outcome expectancy).[26,77] Self-efficacy is a prerequisite for behaviour change which, through improved self-management, may influence health and health care use. According to meta-analyses, self-management programmes significantly reduce disease parameters in hypertension (blood pressure) and diabetes (blood glucose control) and increase self-efficacy, although pain in arthritis was not affected.[78-80]

There is increasing awareness that lay trainers with a chronic condition can adequately deliver this type of intervention. A recent review on lay-led interventions summarized the short-term results of 17 trials (n=7442) and found small but significant reductions in pain, disability and self-efficacy.[26] However, no significant effect was found for psychological well-being and health-related quality of life. A recent study on lay trainers with migraine, who were educating fellow patients in a clinic-based setting, also found positive effects on disability and headache days.[81]

In conclusion: self-management education programmes aim at active involvement of patients by improving their knowledge about the disease together with their self-efficacy to take control. There is increasing evidence that lay trainers with a chronic condition can also provide this intervention.

Online digital assistance

Online digital assistance (ODA) is a new method which was developed to monitor health and to coach health behaviour in daily life, independently of time or space, and as adjuvant to cognitive behavioural treatment.[27] The monitoring feature of ODA was based on experience sampling or ecological momentary assessment, which was applied to reliably measure symptoms, mood or other fluctuating states in real-time.[27] A personal digital assistant (PDA) produced randomized calls, which prompted participants to answer diary items. The coaching feature was based on the possibility of connecting PDAs wirelessly to the internet, which allowed participants to receive tailored feedback and behavioural directives based on the momentary diaries, on-the-spot and directly in daily life, when attack prevention is at stake.[27] ODA might have the potential to support home-based BT, provided with minimal professional guidance. In the case of migraine, ODA was tailored to support the timely detection of premonitory symptoms and to reinforce the taking of preventive action against attack occurrence. Doing this in `real' life is particularly relevant in migraine, because patients tend to neglect the elusive premonitory symptoms and focus on the agony of the attack. They also tend to increase efforts to `get things done' when they feel an attack developing (instead of calming nervous system activation) which generally aggravates excitation and is therefore counterproductive.

Home-based BT provided by lay trainers with migraine

The promising meta-analysis on HBT concerned individual treatments. Therefore, a subsequent step would be to offer home-based BT in a group setting and to employ lay trainers with migraine as providers, under the supervision of a therapist. Lay trainers' motivational assistance may also prevent the large dropout rates associated with self-help applications.[82] This approach is partly in line with a study in Sweden, where (Bachelor) psychology students were trained to provide relaxation training to adolescents with migraine and tension-type headache. Of the 108 trained adolescents 53% achieved a clinically significant reduction.[83] Despite the numerous self-management studies, lay trainers with migraine may have to deal with different types of challenges. First, they not only need social skills to encourage information exchange and manage group sessions, but also have to individually coach patients to detect migraine triggers and premonitory symptoms, and promote behavioural and lifestyle changes. Secondly, lay trainers have to cope with peaks of disabling attacks of which fatigue and exertion are well-known risk factors. The demand on their disease management is therefore high. A third challenge is that little is known about the qualities of lay trainers and their training procedure. It is reported that the lay trainer's capacity to deliver the training

is impressive, but that the training for lay trainers was experienced as intense and tiring.[84,85] Finally, few quantitative data are available to confirm whether or not the health status of lay trainers was positively or negatively affected by the training of fellow patients.[86] In view of these challenges, we developed a new home-based behavioural training which was adapted from a clinic-based protocol.[87-89] BT could be provided by lay trainers with migraine to small groups of fellow patients, and took place in the residence of the trainers. The components of the standardized training protocol are given in Appendix I.

THE CURRENT THESIS

The primary aim of this thesis is to evaluate the effectiveness of this new BT provided in a self-management format by lay trainers with migraine (n=13) to 30 groups at home (mean group size was 3.8 persons). Primary aims of BT were to reduce attack frequency and increase internal control over and self-confidence in attack prevention. Guidelines of the International Headache Society for controlled trials on prophylactic treatment were applied if possible, to set up a randomized control trial.[90] In addition, guidelines of the American Headache Society for trials of behavioural treatments were also adhered to in the design of this study.[91] Last, this thesis also aimed at exploring predictors of BT response, evaluating the qualities of lay trainers with migraine, and testing the clinical utility of ODA when applied in this home-based BT. A long-term goal of this project is national implementation of this method via the network of the Dutch Society of Headache Patients.

Design

The study design was a randomized controlled trial in which the eligible patients were randomly allocated to the BT condition or to a waitlist-control (WLC) condition, receiving usual care. Parallel measurements were made pre-BT (T1: months 0-1), post-BT (T2: months 5-6) and at 6-months follow-up (T3: months 12-13). The WLC group received BT after the waitlist period. Patients completed a prospective 4-week headache diary and valid questionnaires. The questionnaires employed included the HSLC (internal locus of control), HMSE (self-efficacy), SF-36 (health status), MSQOL (quality of life), and MIDAS (disability). BT was provided to three cohorts of the BT and three cohorts of the WLC condition. Data collection included a 6-month follow-up and took place from July 2003 to January 2007.

Outline of the thesis

Chapter 2 starts with the pilot study, which aimed at evaluating the preliminary results of the first lay trainers. Because lay trainers with migraine had to deal with demanding trainer tasks, we evaluated the qualities and pitfalls of the first group of lay trainers.

In *Chapter 3* the short-term effects of a randomized controlled trial in experimental BT patients and waitlist-control patients are evaluated, who completed the study protocol. The results of all patients who were randomized were also analyzed. Significant reductions in attack frequency of BT patients versus WLC patients were expected, as well as significant improvements of internal control over and self-confidence in migraine prevention.

Chapter 4 describes whether or not the changes were maintained six months after completion of BT. Since the patients in the control group were trained directly after the waitlist period, their results were added to those of the BT group. We expected that the short-term results might improve as patients had more time to deepen their BT skills and to apply these skills in daily life to prevent attack occurrence. Patient characteristics assessed at baseline were also explored for their possible relationship to training outcome after six months.

In *Chapter 5* the qualities of lay trainers with migraine are evaluated by a specially constructed questionnaire. This questionnaire was based on a literature review, experiences of previous lay trainers, and the qualities of professional trainers for psychotherapeutic interventions.[92,93] New in this research area was the exploration of the influence of the trainer qualities on the outcomes in their trainees, and the possible benefits for their own health.

In *Chapter 6* the clinical utility of online digital assistance (ODA is examined and its preliminary effectiveness is explored. Utility was defined as the feasibility and acceptability of ODA when employed while patients were in-training. Subsequently, the effectiveness of ODA was tested by comparing the group who received ODA during the training with a matched group who did not receive ODA over the three time points.

Chapter 7 constitutes a general discussion on the main findings of the current thesis. The implications for national implementation are addressed and recommendations are made for future research.

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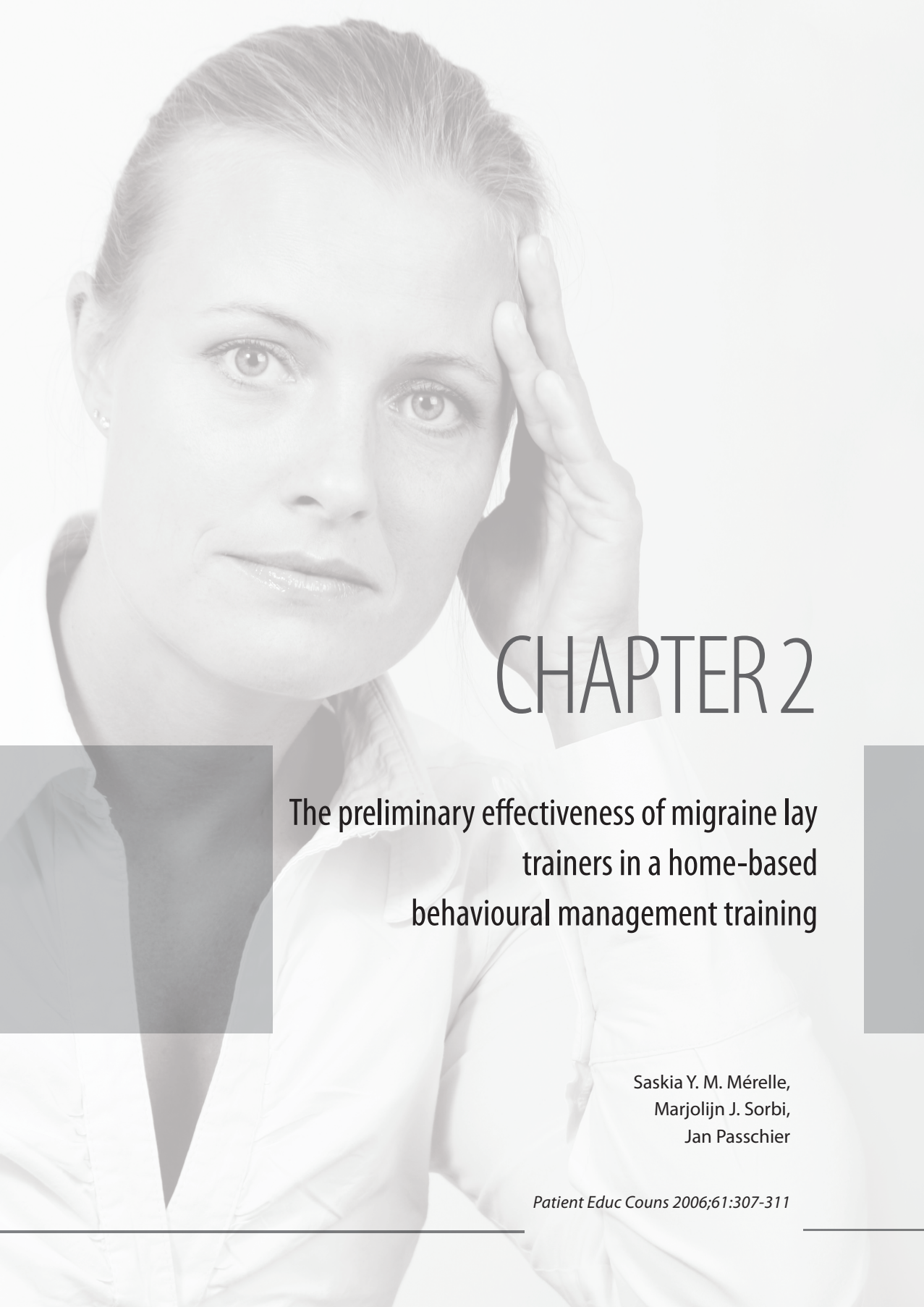

CHAPTER 2

The preliminary effectiveness of migraine lay trainers in a home-based behavioural management training

Saskia Y. M. Mérelle,
Marjolijn J. Sorbi,
Jan Passchier

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ABSTRACT

Objective This pilot study examined the effectiveness and trainer skills of the first lay trainers with migraine.

Methods In a stepwise training program eight lay trainers with migraine participated in a behavioural management training (BT) aimed at the prevention of migraine attacks by proactive relaxation and trigger management. After successful reduction of their migraine attacks, three lay trainers with migraine provided BT under supervision at home to one fellow patient and subsequently to a small group.

Results Migraine frequency was significantly reduced in five out of eight patients trained by lay trainers with migraine (mean 48%) and medication use decreased substantially in four patients (mean 41%). Qualities of lay trainers with migraine concerned their motivational assistance, knowledge of premonitory symptoms and exchange of disease specific problems. Pitfalls were that migraine symptoms hampered an active guidance of the sessions and providing tailored feedback was difficult.

Conclusion The first lay trainers with migraine were successful in training fellow patients in behavioural prevention of migraine attacks.

Practice Implication Continuous supervision of lay trainers' health and trainer skills is recommended but is likely to have implications for the cost-effectiveness.

Keywords: migraine, self-management, behavioural management, chronic disease, lay leaders, empowerment, cost-effectiveness

1. INTRODUCTION

Migraine is a chronic neurovascular disorder characterized by attacks of severe headache and accompanied by autonomic and neurological symptoms [1, 2]. It affects 6% of men and 15-18% of women in the general population [3, 4]. Migraine causes disability in all aspects of daily life, including employment and social activities, not only during but also between attacks [5, 6]. The effectiveness of behavioural management techniques, particularly relaxation training, aimed at reducing migraine attacks is well established. Controlled clinical trials showed that relaxation training reduced attack frequency with 30-50% [7-12]. Minimal contact applications have been found equally effective as intensive clinic-based treatments [13, 14]. The employment of migraine patients as lay trainers may increase the treatment availability in a cost-effective manner, while lay trainers' motivational assistance may also prevent large dropout rates found with self-help applications [15]. Lay-led trainings applied to various other chronic conditions such as heart disease, lung disease and arthritis demonstrated an increased self-efficacy, decreased health distress and reduced health care utilization [16-19]. These results did not, however, include direct effects in terms of symptom reduction, which is conceivable given the health education approach. In contrast, lay trainers with migraine may have to deal with more demanding trainer tasks. First, lay trainers with migraine have to individually coach patients to detect migraine triggers and premonitory signs and promote behavioural and lifestyle changes, in addition to social skills to encourage information exchange and manage group sessions [20]. Secondly, lay trainers with migraine have to cope with peaks of disabling attacks of which fatigue and exertion are well known risk factors. The demand on their disease management is therefore particularly high.

In previous studies lay leaders were often briefly trained, but pitfalls in their functioning were not mentioned nor have training procedures or required qualities been elucidated. For example, studies only reported that lay leaders' capacities to deliver the training were impressive [21]. However, it was also found that the lay leader training was intense and tiring [22]. We conducted a pilot study in collaboration with the Dutch Society of Headache Patients (DSHP) according to the current focus on patient empowerment in health care [23-25]. The following research issues were examined:

1) What are the changes in migraine frequency and medication use after a home-based behavioural management training led by lay trainers with migraine?
2) Does being a lay trainer with migraine involve particular qualities and pitfalls regarding the trainer skills to promote behavioural and lifestyle changes?

The home-based behavioural management training (BT) was based on an established clinical protocol [26] and tailored to a group training with 7 2-hour sessions. Three weekly sessions focused on the detection of migraine triggers and premonitory symptoms by daily monitoring and registration [27-30] and acquisition of relaxation skills. Three two-weekly sessions were then directed at the application of relaxation and other proactive strategies to

counteract migraine triggers and premonitory symptoms. Evaluation took place in session 7 and advices were given to maintain the skills.

2. METHODS

2.1. Sample

Lay trainers with migraine (n=8) were recruited by an announcement in 'Hoofdzaken', the periodical of the Dutch Society of Headache Patients. A second advertisement recruited migraine patients to be trained by lay trainers with migraine. Eight patients (30%) had migraine that fulfilled the classification criteria [31]; 1 to 6 migraine attacks during 4 weeks of diary keeping; no medication overuse (> 4 triptans, > 2 ergots a week); absence of psychopathology according to SCL-90's norm for the clinical pain population (total score < 178) [32]. The local Medical Ethical Committee approved the study.

Table 1 Patient characteristics

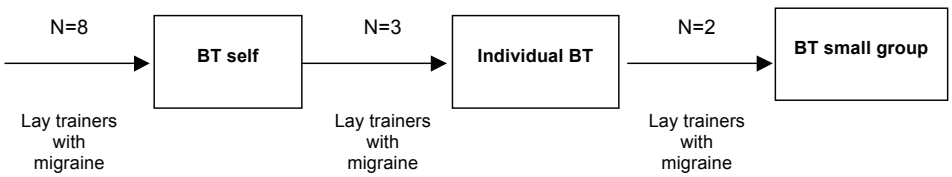
	Lay trainers with migraine (n=3)	**Patients (n=8)**
Age	46,3 (4,6)	45 (9,2)
Gender		
Female	3	7
Male	0	1
Education		
Low	0	2
Middle	1	2
High	2	4
Migraine duration (number of years)	32,7 (11,1)	22,8 (11,6)
Migraine frequency (during 1 month)		
1 attack	2	1
2-3 attacks	1	4
4 attacks	0	1
5-6 attacks	0	2

2.2. Training procedure for lay trainers with migraine

Eight lay trainers with migraine received BT in 2 groups from the first author. In the second half of BT couples of lay trainers with migraine coached each other to (1) test their preliminary trainer skills; (2) enhance their behavioural and lifestyle changes needed to act upon triggers and premonitory symptoms. Their coaching consisted of giving weekly feedback by e-mail to headache diaries and evaluation forms. The first author had access to all the materials exchanged. Five lay trainers with migraine (63%) were selected to train fellow patients based on the successful reduction of their own migraine attacks and previously shown trainer skills. Two

trainers dropped out due to unexpected life-events and health problems other than headaches. The remaining three trainers first applied BT at home to one fellow patient under supervision of the first author and continued practicing their own skills. They received a structured manual of the content and procedure per session and directives for basic trainer skills: instruction and evaluation of relaxation and registration assignments, provision of feedback, motivational and emotional assistance, time-management. They kept a brief evaluation form per session and received supervision by phone and e-mail. Subsequently, two trainers provided BT at home to respectively two and three patients. Supervision was tailored to individual needs and less frequent. Payment to each trainer was for individual training 150 euros (€14 per hour) and for a small group training 300 euros (€21 per hour). The costs of BT in a group format are considerably less (72%) than those of a professional trainer (€75 per hour). Furthermore, the home-based setting instead of a clinical setting also reduced the costs (Fig. 1).

Figure 1. Stepwise training procedure for lay trainers with migraine



2.3. Measures

The patients trained by a lay trainer with migraine (n=8) filled in a headache diary to assess attack frequency and medication use during baseline and post BT (4 weeks). A post BT semi-structured interview conducted by a research assistant evaluated in both trainers and their trained patients (n=11) the basic trainer skills (see 2.2).

2.3. Data analysis

Attack frequency and medication use per four weeks were calculated from the headache diaries. Wilcoxon Signed Ranks testing was used to analyse changes in migraine frequency after BT. The interviews were analysed by grouping qualities and pitfalls of lay trainers with migraine reported by the trainers and their patients.

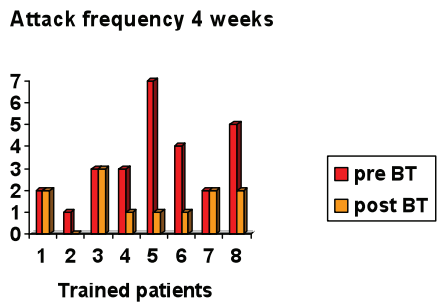
3. RESULTS

3.1. Changes in attack frequency and medication use

Five patients (63%) trained by a lay trainer with migraine showed a large (≥50%) decrease in migraine frequency, three patients' attack frequency didn't change and on average attack

frequency decreased 48%. On a group level, attack frequency decreased significantly (p=0.04) from 3.4 (SD 1.9) to 1.5 (SD 0.9) attacks.

Figure 2 Changes in attack frequency pre- and post-BT



Of the trained patients seven used abortive migraine medication, one took prophylactics. After BT medication use was reduced considerably (50-100%) in four patients, moderately in one and not reduced in two patients.

Table 2 Changes in medication use pre- and post-BT

Patient	Acute treatment (dosage (mg)	Pre-BT	Post-BT	Change
1	Imigran (100)	2	1	-50%
2	Imigran (100)	1	0	-100%
3	No acute treatment			
4	Naramig (2.5)	2	1	-50%
5	Cafergot (2)	6	0	-100%
6	Imigran (25)	7	5	-29%
7	Maxalt (10)	2	2	0%
8	Naramig (2.5)	3	3	0%

3.2. Trainer skills

Qualities reported by the trained patients were that lay trainers with migraine served as role models in coping with a shared health problem. Particular qualities were (1) the motivational assistance as their successful migraine management facilitated the credibility and acceptance of training techniques. It also motivated the patients to put extra effort into practicing, (2) exchange of migraine specific problems because patients felt well understood, and (3) their knowledge in recognizing migraine triggers and premonitory symptoms that facilitated this process in the patients. Among the pitfalls were three patients who reported insecurity of one trainer who was inexperienced in leading a group and had difficulties in setting boundaries to a demanding patient. Other pitfalls were (1) fatigue or migraine symptoms during the

session that caused concentration problems and errors in application of the training protocol (2) complexity of analysing headache diaries and providing individually tailored feedback (3) one trainer who gave too much pharmacological advice.

4. DISCUSSION AND CONCLUSION

4.1. Discussion

This pilot study indicated that lay trainers with migraine seem successful in training patients in behavioural prevention of migraine attacks, to an extent comparable to that achieved by professional trainers [8]. Limitations of the present pilot are a small sample size, relatively high dropout of trainers and the trainer skills were subjectively assessed. In the current RCT a follow-up measurement is held (time points 0-6-12 months) to strengthen the design. Strong points were the selection of lay trainers with migraine based on their successful reduction of migraine attacks and the intensive but stepwise training. This training resulted in credible and competent role models evidenced by positive patient evaluation. The pilot study confirmed our expectations that the trainer tasks were demanding for lay trainers with migraine. Their performance was hampered by migraine symptoms and fatigue, although absenteeism didn't obstruct the training. The most demanding trainer skills were to give individually tailored feedback and to manage a group while sticking to the training protocol. One study on the impact of peer educators' qualities also found that individualization and directive group-management was related to positive outcomes [33]. In the current study the trainer skills are systematically evaluated based on theoretical hypotheses of required qualities e.g. credibility, similarity and active guidance [33-35]. Headache internal locus of control and self-efficacy seem also core qualities to maintain successful migraine management [36, 37].

4.2. Conclusion

The first lay trainers with migraine in a home-based behavioural management training successfully reduced fellow patients' migraine frequency and medication use. The stepwise training was time consuming but appeared worth the effort.

4.3 Practice Implications

The preliminary findings indicated that lay trainers with migraine need continuous supervision to keep up their own migraine management and support their basic trainer skills. In the current RCT bi-annual master classes are held using vicarious learning, verbal persuasion and modelling. These investments seem essential but are likely to restrict the cost-effectiveness of lay-led BT.

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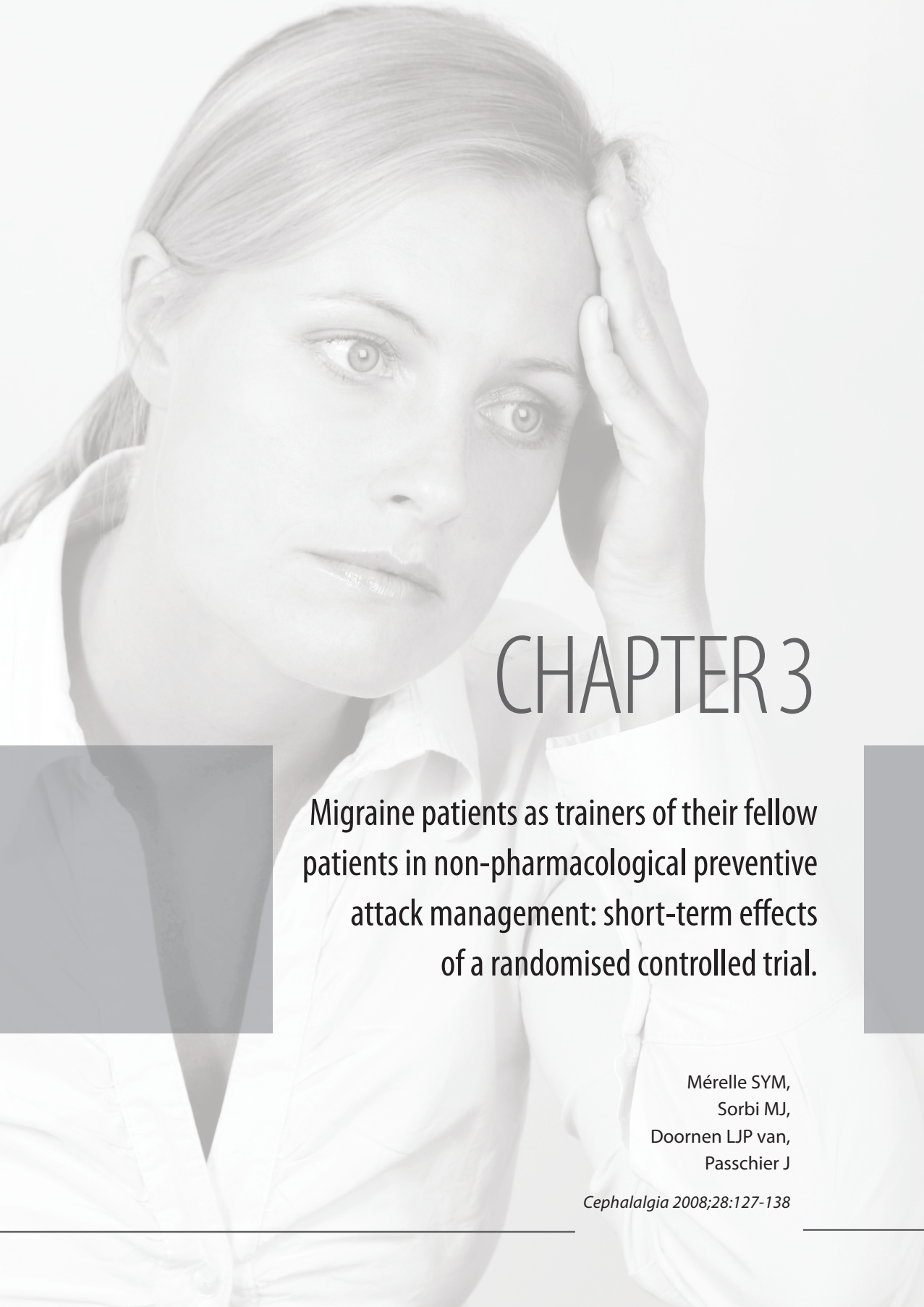

CHAPTER 3

Migraine patients as trainers of their fellow patients in non-pharmacological preventive attack management: short-term effects of a randomised controlled trial.

Mérelle SYM,
Sorbi MJ,
Doornen LJP van,
Passchier J

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ABSTRACT

In conformity with current views on patient empowerment, we designed and evaluated the effects of a home-based behavioural training (BT) provided by lay trainers with migraine to small groups of fellow patients. The primary aims of BT were to reduce attack frequency and increase perceived control over and self-confidence in attack prevention. In a randomised controlled trial the BT group (N=51) was compared with a waitlist-control group (WLC), receiving usual care (N=57). BT produced a minor (-21%) short-term effect on attack frequency and clinically significant improvement in 35% of the participants. Covariance analysis showed a non-significant trend (p=0.07) compared to WLC. However, patients' perceived control over migraine attacks and self-confidence in attack prevention increased significantly with large effect sizes. Patients with high baseline attack frequency might benefit more from BT than those with low attack frequency. In conclusion, lay trainers with migraine strengthened fellow patients' perceived control but did not induce a significant immediate improvement in attack frequency.

Keywords: attack prevention, behavioural treatment, lay trainer, migraine, patient empowerment, self-management.

1. INTRODUCTION

Although migraine is highly prevalent and burdensome in daily life, many patients do not seek medical treatment (1). Extending the reach of education and treatment is thus a pressing issue and should be realized cost efficiently, given the high prevalence. One method is to involve lay trainers with migraine, which has proved effective in educating patients with frequent episodic migraine from a clinic-based population (2). The present study extends the role of lay trainers with migraine from the clinic to the open population and from education to training of skills to prevent migraine attacks.

The pharmacological treatment of migraine is focussed on abortion and prevention of attacks and its efficacy is well established (3). Attack prevention can also be accomplished with behavioural treatment or training (BT). According to meta-analyses BT reduces attack frequency by 35 to 55% and is significantly superior to control conditions (4-6). BT is targeted at attack prevention through the following strategies: 1) detection and modification of migraine triggers; and 2) employment of physiological self-regulation skills, which may be supported with cognitive techniques (4, 7). Individual home-based were found to be as efficacious as clinic-based BT and five-fold more cost-effective (8, 9). These treatment formats were based on less than half of the usual clinical contacts (3-4 instead of 8-12) and supplemented with written manuals and telephone support. Home-based BT and the employment of lay trainers with migraine accord with the current focus in health care and society on 'patient empowerment'. This view holds that patients are experts of their chronic disease, share responsibility for the management of the disease and therefore should be involved in achieving efficient and effective health care (10-12). According to a meta-analysis such health educational programs significantly reduce disease parameters in hypertension (blood pressure) and diabetes (blood glucose control) (13) and increase self-efficacy, although pain in arthritis was not affected (14, 15). A recent study showed that intensive education provided by lay trainers with migraine to their fellow-sufferers supplementary to medical treatment, significantly decreased migraine disability and reduced headache days in the latter group (2). These results suggest that a home-based self-management approach might work in migraine and that patient trainers might be able to deliver such training to a group of fellow patients (9, 16-21).

This paper presents immediate pre-post training results of a home-based BT provided by lay trainers with migraine to a small group of fellow patients at home. The primary aims of BT were to reduce attack frequency and increase feelings of control and self-confidence in attack prevention. The secondary aims were to improve patients' quality of life and to reduce migraine-related disability. Finally, this study also explores factors that might explain the changes in outcomes after BT.

2. METHODS

2.1. Patients

According to the power analysis (22), 50 patients were required in each group since a minimal between-group difference in attack frequency of 30% was needed to exceed the placebo effect (23). To account for potential drop-out, more patients were recruited (24). Patients were included according to the scientific guidelines of the IHS subcommittee on clinical trials (25). Participants had to be aged 18 to 65 years, fulfil the IHS criteria for migraine with (G43.1) or without (G43.0) aura (26), have an attack frequency of 1-6 per month. Excluded were patients with headache occurring on 15 or more days per month, a migraine duration less than one year, migraine onset at an age above 50 years referring to underlying organic disease (25), and an above average score (>178) on the Symptom Checklist 90 (SCL-90) (27) indicative of psychopathology.

The study was carried out in cooperation with the Dutch Society of Headache Patients and profited from its support and website for recruitment. To reach a broad population, members of the patient organisation were invited, local headache specialists could refer patients, and newspapers, magazines and websites of the research centres were used. Migraine patients interested in BT provided by an experienced fellow patient were asked to respond if they did not suffer from daily headaches and were living in or around the research centres at Rotterdam (including Leiden) and Utrecht (including Amsterdam). The selection of participants was based on 1) a standard questionnaire covering the IHS classification criteria (26) which also inquired whether subjects had consulted a physician and had been diagnosed with migraine; 2) a 4-week headache diagnostic diary; 3) the SCL-90 psychopathology screening list. The presence of migraine with aura was derived from the IHS questionnaire and headache diaries. Two headache specialists were consulted for a second opinion on included patients and to verify the diagnoses in case of doubt, and to rule out headache due to medication overuse. The Ethics Committee of the Erasmus University Medical Centre approved the study.

2.2. Study design and procedure

The study design was a randomised controlled trial in which the eligible patients were randomly allocated to the BT condition or to a waitlist-control (WLC) condition. The WLC condition was chosen in view of the difficulty previous studies had in realising a placebo procedure that was plausible and also provided non-therapeutic control for attention (28, 29). Comparison with a professional therapist group was not an aim of this study; the focus was whether or not this innovative approach might work. Moreover, such an equivalence study would require a much larger sample size and considerable resources. Parallel measurements were conducted in both groups pre-BT (4 weeks) and post-BT (4 weeks). The WLC group received BT after the waitlist period.

Participants were randomised by a statistician within blocks of the four cities blinded to the investigators, and were centrally assigned to BT or WLC according to a random number table. Participants were notified about their allocation prior to baseline measurement, because information about the start of BT was considered ethical and also necessary since BT sessions had to be planned during baseline measurement. A research assistant assigned patients and trainers to BT training groups and scheduled the training sessions. He also blinded headache diaries to the researchers, to prevent assessment bias when they scored the diaries for the analyses.

BT was provided to 3 cohorts of the BT and WLC condition, respectively, and cohorts were separated by approximately 6 months to account for summer and winter vacations. Data collection took place from July 2003 to July 2006. The relatively low number of trained lay trainers with migraine produced a backlog of potential participants in the first year. In consultation with the patient organisation, we decided to allocate all enrolled but delayed patients to BT in the second year.

2.3. Home-based, group-delivered behavioural training (BT) and waitlist-control (WLC)

BT was based on an established clinical protocol for individual treatment (30-33) and tailored to the format of a home-based group intervention. Patients received a written manual, an organizer for homework assignments, diary ratings and self-evaluations, and a CD-Rom with auditory relaxation exercises. The intervention consisted of BT strategies that are central to attack prevention in migraine: 1) identification and modification of triggers and affective, cognitive and behavioural premonitory symptoms; 2) use of physiological self-regulation skills. The main relaxation technique was autogenic training, which is commonly used in migraine and according to meta-analyses produces medium effect sizes in headache improvement (5, 34, 35). In addition, breathing exercises and cue-controlled relaxation were learned, as well as additional strategies to proactively reduce physical or mental exertion (through time-out or taking breaks) or arousal (through self-assurance and positive thinking).

BT consisted of seven 2-hour sessions spread over 10 weeks. Sessions 1 to 3 were conducted weekly and focused on 1) detection of migraine triggers and premonitory symptoms (36, 37) by daily monitoring, and 2) acquisition of relaxation skills by stepped practice of autogenic and breathing exercises twice per day at home. Trigger and symptom detection was supported by personal feedback of the trainer and group members and resulted in a personalized map of triggers and premonitory symptoms, which was tailored to the individual case. Relaxation skills were trained progressively by stepwise inclusion of cue-controlled relaxation, while autogenic exercises were condensed over time. Sessions 4 to 6 took place every two weeks and focused on 1) application of relaxation skills and other proactive strategies under the condition that premonitory symptoms or triggers prevailed, while continuing the daily exercises at home, and 2) a personalized prescription for migraine and health. Each participant formulated individualized target conditions of being at risk for developing a migraine attack,

as well as individualized actions and lifestyle changes to reduce this risk and prevent attack occurrence. Evaluation took place in session 7, which included the specification of individual goals and actions to maintain training skills.

BT was delivered in smalls groups of 2-4 patients and its feasibility was established in a pilot study (16, 38). The WLC group continued their current treatment, i.e. care as usual. All participants were urged not to change their medication or start alternative migraine treatments while in the trial and to inform the researchers in case this was unavoidable. To keep participants informed and committed to the study they received a newsletter about the research project once per year.

2.4. Lay trainers with migraine

Five lay trainers with migraine were recruited as part of the pilot study (16, 38) and nine were recruited during the trial. They lived in the vicinity of Rotterdam/Leiden (N=8) or Utrecht/Amsterdam (N=6) and underwent a training consisting of three steps: 1) self-experience through receiving BT for their own migraine attacks; 2) application of individual BT to one new patient under supervision of the first author; 3) provision of BT to a small group of new patients under continued supervision. Potential lay trainers with migraine could participate in step 2, provided that they were motivated to become a lay trainer and were successful in managing their own migraine attacks.

Trainers received a structured manual of the content and procedure per BT session, which included directives for basic trainer skills regarding instructions and evaluations of registration assignments and relaxation exercises, time-management of the sessions, and the provision of feedback and motivational or emotional assistance to trainees. They kept a brief evaluation form per session with track records per trainee. This form served as the basis for supervision by e-mail and telephone provided by the first author after BT sessions 1, 3 and 6. In addition, trainers participated in three 3-hour workshops led by the second author, directed at the promotion of basic trainer skills while safeguarding their own migraine management. A fourth workshop focussed on advanced knowledge of relaxation training and was given by an expert in the field of relaxation. The lay trainers with migraine received a payment of 150 euros (14 euros per hour) for individual BT, and 300 euros (21 euros per hour) for a home-based group BT.

2.5. Measurements

The primary outcome variable, attack frequency per 4 weeks, was prospectively measured in a headache diagnostic diary according to the guidelines for clinical trials in prophylactic treatment (25). Pain intensity was rated by allocating the following score, every six hours: 1 is mild headache - I can do everything but with some difficulty; 2 is moderate headache - I cannot do all or most things; 3 is severe headache - I am unable to do things, bed rest is necessary. When migraine occurred, associated symptoms were registered per 24 hours, as were brief

descriptions of observed triggers or premonitory symptoms. Medication type and dosage unit for acute and preventive treatment were also registered in the diary.

The two additional primary outcome variables, feelings of control and self-confidence regarding attack prevention, were assessed with questionnaire measurements of headache-specific locus of control and self-efficacy. Locus of control refers to the belief that the factors that influence the occurrence and relief of headache are within the individual's control (internal control) or are under external control, which is exerted either by chance or by a medical professional (39). Because the training was not designed to influence healthcare use, patients' belief in control by professionals was not further analyzed. Self-efficacy refers to the confidence that one can take actions to prevent or manage headache episodes (40). We used a forward-backward method (41) to translate the 33-item Headache Specific Locus of Control Scale (HSLC) (39) and the 25-item Headache Management Self-Efficacy Scale (HMSE) (40) and tested their reliability in our sample. The (sub)scales of the HSLC and the HMSE yielded good to excellent internal consistency with a Chronbach α of, respectively, 0.91 (internal control,11-item subscale), 0.81 (external chance control, 11 items) and 0.90 (self-efficacy). The HMSE was translated during the first year of data acquisition and could therefore not be administered to about 25% of the total sample. The sum scores of the HSLC sub-scales were calculated separately to indicate the degree to which participants perceived self-control over migraine or attributed this control to chance. The sum score of the self-efficacy questionnaire was calculated (ranging from 25 to 175) whereby a higher score reflects a stronger self-confidence in the patients' own capacity to prevent and manage attacks of migraine.

The secondary outcome variables concerned health status, migraine-specific quality of life and migraine-related disability.. Health status was measured with the Dutch version of the Medical Outcomes Study 36-item Health Survey (SF-36) (42, 43), which is a validated instrument for the self-evaluation of physical and mental health and commonly used in migraine (44). The SF-36 comprises four scales for physical health (physical functioning, role-physical functioning, bodily pain and general physical health) and four for mental health (vitality, social functioning, role-emotional functioning and general mental health). Raw scores were linearly converted to a 0 to 100 scale and mean scores were calculated for physical and mental health status with a higher score indicating better health. Quality of life between attacks was established with the 20-item Dutch version of the Migraine-Specific Quality of Life Questionnaire (MSQOL) with a sum score ranging from 20 to 80 (45). This questionnaire is valid, highly reliable and related to psychological well-being, perceived severity of migraine, and disruption of life caused by migraine (46). Migraine-related disability was measured with the Migraine Disability Assessment Scale (MIDAS) that consists of five questions concerning the number of days lost to migraine in the past 3 months. Internal consistency, reliability and validity of the MIDAS were shown to be satisfactory (47). The sum score reflects the number of productive days lost in settings considered to be the most important in middle-aged patients, i.e. the

workplace and at home (48). The HSLC, HMSE, SF-36, MSQOL and MIDAS were administered pre and post BT and WLC.

2.6. Data analysis

Data from the headache diagnostic diary were prepared as follows. To count attack frequency, migraine episodes were identified according to the IHS criteria (26): headache had at least two migraine characteristics (unilateral location, pulsating quality, moderate or severe pain intensity and aggravation by physical activity) plus at least one associated symptom (nausea/vomiting; photo- or phonophobia). Since triptan use for acute treatment modifies clinical features (25), the diagnostic criteria for migraine were adapted as follows. If a triptan was used headache was qualified as a migraine attack if 1) at least two of the above-described characteristics were present, but associated symptoms were absent; or 2) one migraine characteristic was present, together with at least one associated symptom. A migraine attack that was interrupted by sleep or recurred within 48 hours was counted as one attack (25). Medication use for acute treatment was calculated by counting separately the dosage units of triptans and of analgesics over the 4-week diary period (25). Patients who had >25% of the items of a specific (sub)scale of a questionnaire missing were removed from the analysis on the sum score concerned.

The analyses were first carried out in the total sample that entered the baseline measurement according to the intention to treat (ITT) principle and repeated on subjects who completed the study protocol (CP) (49). The CP analysis is reported as primary analysis and ITT results are added when these differed from the CP results, e.g. significant in CP analysis and non-significant in ITT analysis. Results are presented as mean pre-post differences per group and mean between-group differences, both unadjusted and adjusted for baseline scores and accompanied by 95% confidence intervals, indicating the precision of the estimates. Wilcoxon's two-sample test (Mann-Whitney U-test) was used to test differences in dichotomous variables between the BT and WLC group. Independent t-tests were used for continuous variables. Analyses of co-variance (ANCOVA) were performed with the variables for attack frequency, locus of control, self-efficacy, headache-free days, quality of life and migraine disability as dependent variables, the group (BT vs. WLC) as independent variable, and the corresponding baseline measure as covariant. Cohen's d was calculated to indicate effect size (22) with $d<0.3$ indicating a negligible effect, $0.3 \leq d < 0.5$ a small, $0.5 \leq d < 0.8$ a medium and ≥ 0.8 a large effect.

In order to control for Type I error in the primary and secondary analyses we performed Bonferroni's correction: $1-(1-\alpha)^{1/m}$, with an alpha of 0.05 and m indicating the number of tests (50). According to this formula a significance level of 0.0125 is required for the results of the primary analyses, but also for those of the secondary analyses given that the present study involved four analyses. The model used was checked for violation of the assumptions of normality, and attack frequency, internal locus of control, self-efficacy, migraine-specific quality of life, migraine disability and mental quality of life were transformed (square root) because

of a non-normal distribution of the scores. Missing values of migraine frequency post training were estimated by using the maximum likelihood method (51). Explorative analyses were performed to explain the primary outcomes. The Bonferroni correction was not employed here given the tentative character of these analyses. Treatment responder rate was calculated for attack frequency, with a reduction greater than 50% indicating a clinically significant improvement (52). Differential attack reduction for those who entered BT with a high (4-6) versus a low (1-3) attack frequency at baseline was performed and tested by 2x2 (group*baseline frequency) ANOVA. Finally, changes in triptan use and use of analgesics were analysed with paired t-tests. Results for patients who did not use prophylactic medication were analysed by ANCOVA (53).

3. RESULTS

3.1. Patient flow through the study and participant characteristics

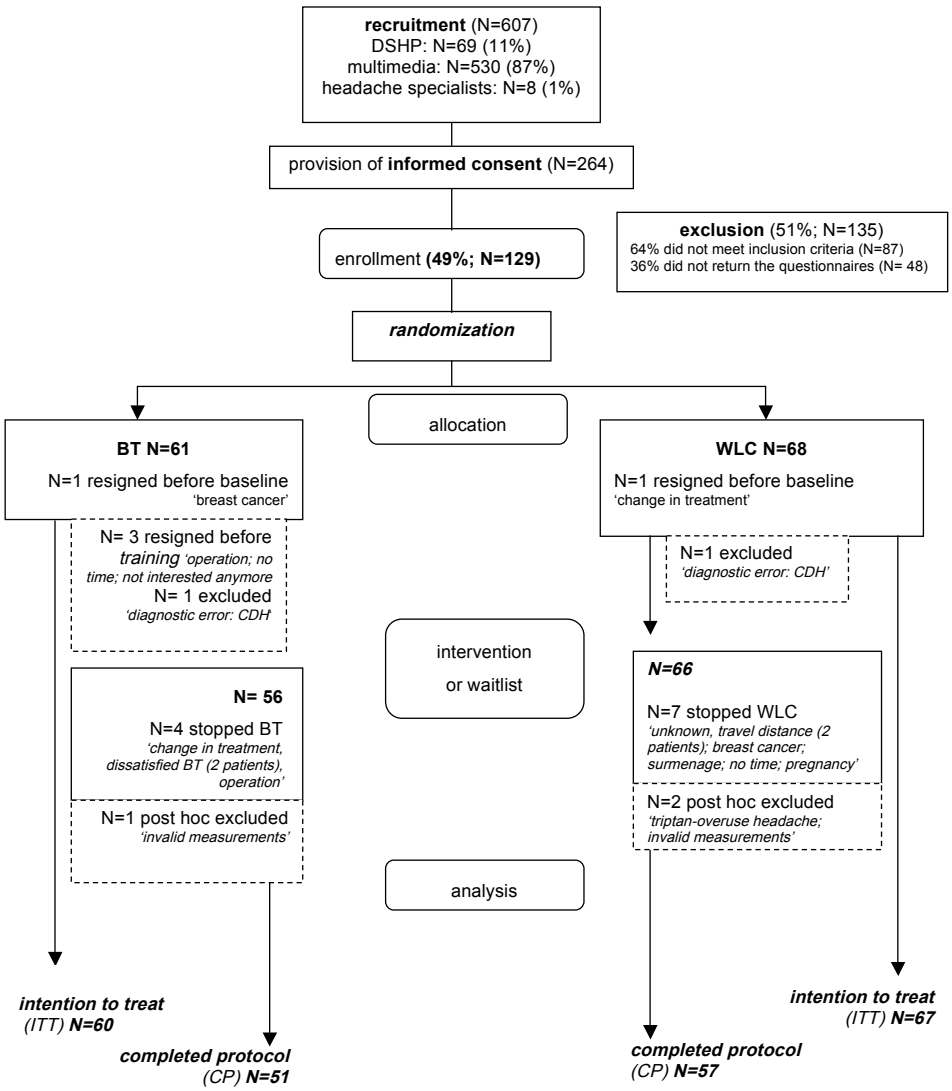
Participant flow through the study and reasons for attrition are shown in Figure 1. Of the 264 subjects who gave informed consent, 135 (51%) were excluded because they did not return the materials (N=48) or did not meet the inclusion criteria (N=87). Of the latter group 63% had a headache frequency that was either too low or too high, 21% were excluded for diagnostic reasons provided by the headache specialists, and 16% scored above the SCL cut-off score for psychopathology. After randomization of the 129 participants (BT: N=61, WLC: N=68), 21 resigned or stopped. Of these patients, one in each condition resigned before baseline. Therefore the ITT analyses included 60 subjects in the BT and 67 in the WLC group, while 108 patients were included in the CP analyses. Missing values due to missing headache diaries were 7% in the ITT analyses and 1% in the CP analysis.

Table 1 presents the characteristics of the 129 selected patients. At baseline, the BT and WLC groups were similar regarding demographics, migraine characteristics and medical history. The total MIDAS score (24.3) showed a relatively high disability compared to population studies from the USA (19.5) and the UK (12.8) (47). The number of patients that changed their medication during the trial was comparable between the BT (18%) and the WLC (18%) group. The number of life events during the training period also did not differ significantly (BT; 39%, WLC;30%).

3.2. BT effects on primary outcomes

The results of the subjects who adhered to the training protocol are reported. Attack frequency was reduced in the BT group from 3.1 at baseline to 2.4 after training (-21%) per 4-week period. In the WLC group attack frequency changed from 3.1 to 2.9 (-6%). The overall effect size was small (-0.29) and a non-significant trend was found (p=0.07) in the CP analysis In the ITT analysis the difference was not significant. Patients' self-confidence in own ability to

Figure 1 Patient flow chart



BT: behavioural training, WLC: waitlist-control, DSHP: Dutch Society of Headache Patients
ITT: intention to treat, CP: completed protocol

prevent migraine attacks, increased significantly and to a large extent (self-efficacy: effect size 0.79), which was also found regarding their belief that factors influencing the occurrence and relief of migraine attacks are under own control (internal control: effect size 0.97). Patients' belief that migraine is a matter of chance or bad fate weakened significantly and to a medium extent (external control: effect size -0.73).

Table 1 Characteristics of the BT and WLC group summarized for all patients and for subjects who completed the protocol

Characteristics	**ITT**			**CP**		
	BT n=60	WLC n=67	Total n=127	BT n=51	WLC n=57	Total n=108
Age mean	44 (25-59)	43 (18-65)	44 (18-65)	44 (25-59)	43 (23-63)	44 (23-63)
Gender (%)						
Female	85	90	87	82	91	87
Male	15	10	13	18	9	13
Education level (%)						
Low	5	6	6	4	5	4
Average	30	28	29	29	25	27
High	65	66	65	67	70	69
Migraine duration mean (range) in years	18 (3-45)	20 (2-50)	19 (2-50)	19 (4-45)	20 (3-50)	20 (3-50)
Migraine diagnosis (%)						
With Aura G43.1	32	35	33	28	33	31
Without Aura G43.0	68	65	67	72	67	69
Attack frequency (%)						
1-3 attacks	60	69	65	61	68	65
4-6 attacks	40	31	35	39	32	35
Pain intensity migraine mean (SD)	1.90 (0.69)	1.91 (0.69)	1.91 (0.69)	1.88 (0.73)	1.97 (0.59)	1.93 (0.66)
Consultations (%)						
General Practitioner	98	98	98	96	98	97
Neurologist	55	63	58	53	65	59
Psychologist	8	22	16	8	18	13
Physiotherapist	47	41	43	41	40	41
Medication use (%)						
Triptans	75	81	78	75	81	78
Analgesics	43	37	40	45	40	43
Prophylactics	23	16	20	20	18	19
MIDAS mean (sum score, SD)	25.6 (21.2)	23. (13.2)	24.3 (17.5)	23.2 (16.9)	23.9 (13.5)	23.6 (15.2)

BT: behavioural training, WLC: waitlist-control, ITT: intention to treat, CP: completed protocol
SD: standard deviation
MIDAS: migraine disability assessment scale, a higher score reflects a higher disability of migraine in daily life

Figure 2 shows that 35% of the BT patients improved to a clinically significant extent, but 47% did not change and 18% responded adversely. In the waitlist condition 19% of the patients were clinically changed, 60% did not change and 21% responded adversely. A non-significant trend was found when testing the clinically improved of the BT group versus the waitlist condition (p=0.07). In the ITT analysis the difference was not significant.

Table 2 Between-group comparisons of changes in primary and secondary outcomes of subjects who completed protocol

Characteristics	**BT** pre	**BT** post	**WLC** pre	**WLC** post						
Primary outcomes					Δ	Δ[a]	CI[a]	F[a]	p[a]	ES
	(n=51)	(n=51)	(n=57)	(N=57)						
Attack frequency (diary)[b]	3.08	2.43	3.09	2.89	-0.45	-0.42	-0.69 to -.15	3.45	0.07	-0.29
SD	1.61	1.73	1.67	1.71						
	(n=48)	(n=48)	(n=57)	(n=57)						
Internal locus of control	34.6	42.6	36.1	36.7	7.39	4.3	3.03 to 5.54	27.9	0.000*	0.97
(HSLC)[b] SD	10.6	8.3	9.9	9.3						
External control chance	35.4	29.1	35.5	34.4	-5.17	-3.8	-4.92 to –2.59	19.3	0.000*	-0.73
(HSCL)SD	8.7	7.1	8.6	8.6						
	(n=33)	(n=33)	(n=43)	(n=43)						
Self-efficacy (HMSE)[b]	88.4	104.8	90.1	93.5	13.0	8.67	8.48 to 8.86	14.6	0.000*	0.79
SD	23.2	24.7	18.6	20.4						
Secondary outcomes										
	(n=50)	(n=51)	(n=57)	(n=57)						
Physical health status	67.1	73.4	70.0	72.6	3.67	4.30	1.30 to 7.30	0.30	0.58	0.17
(SF-36) SD	21.1	18.5	18.2	16.4						
	(n=51)	(n=51)	(n=57)	(n=57)						
Mental health status	74.2	74.8	70.7	72.1	-0.72	0.99	-1.45 to 3.43	0.13	0.72	-0.05
(SF-36)[b] SD	16.0	15.4	21.8	18.4						
	(n=51)	(n=51)	(n=57)	(n=57)						
Migraine specific QOL	57.1	58.2	56.6	56.8	0.95	0.67	-.23 to 1.56	0.72	0.39	0.17
(MSQOL)[b] SD	8.74	7.24	8.76	8.94						
	(n=51)	(n=51)	(n=57)	(n=57)						
Migraine Disability	23.2	21.3	23.9	20.9	1.01	-2.49	-4.49 to -.50	0.23	0.63	0.06
(MIDAS)[b] SD	16.9	16.6	13.5	14.0						

Means pre and post, differences (Δ) in changes BT (behavioural training) versus WLC (waitlist-control), 95% Confidence Intervals (CI) of Δ and standardized effect size (ES).

* Considered significant at p<0.0125 after Bonferroni's correction

[a] Adjusted for baseline score (employed as covariate)

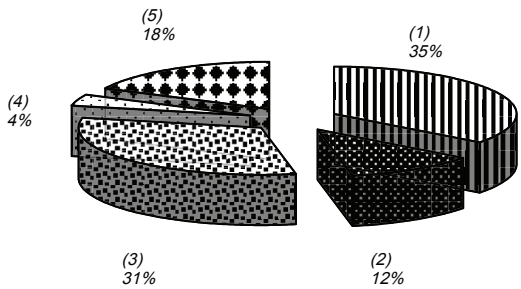
[b] Square root transformation of scores

Migraine specific QOL; a higher score reflects a higher quality of life between attacks

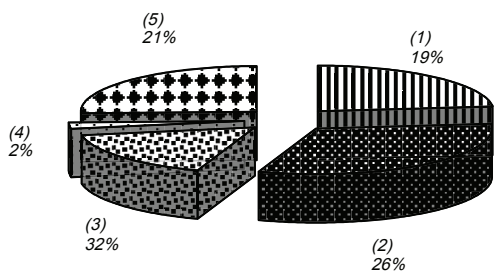
3.3. BT effects on secondary outcomes

Migraine-specific quality of life at baseline was similar in both groups and was not significantly changed post training (irrespective of the Bonferroni correction), indicating that BT did not affect patients' quality of life between attacks (Table 2). Immediate post-training differences in general physical and mental health status were unsubstantial, as were changes in migraine disability. Comparisons with the control condition yielded no between-group differences.

Figure 2 Treatment responder rate in BT (first figure) and WLC group (second figure)



(1) Clinically significant improvement (>- 50%)	**Responders (35%)**
(2) Modest improvement (-25 to -49%)	
(3) No change (-25 to 25%)	**Non-responders (47%)**
(4) Modest worsening (25 to 49%)	
(5) Clinically significant deterioration (>50%)	**Adverse responders (18%)**



(1) Clinically significant improvement (>- 50%)	**Responders (19%)**
(2) Modest improvement (-25 to -49%)	
(3) No change (-25 to 25%)	**Non-responders (60%)**
(4) Modest worsening (25 to 49%)	
(5) Clinically significant deterioration (>50%)	**Adverse responders (21%)**

3.4. Exploratory analyses

After the training the use of triptans decreased (from 3.8 to 3.5) and the use of analgesics increased (3.0 to 3.8). The waitlist condition also showed a decrease in triptan use (4.2 to 3.7) and an increase in analgesics use (3.7 to 4.1). Both these changes in acute medication use did not reach significance for the BT group. However, in the ITT analysis the increase in analgesic intake was significant (t=-2,12, p=0.04). Analysis of the change in attack frequency of patients without prophylactic treatment showed a similar result to that of all patients.

BT participants with high attack frequency showed a reduction from 4.8 attacks to 3.0 post training (-37%), whereas the WLC group showed a reduction of 5.2 to 4.6 attacks (-12%). Patients with high attack frequency had significantly more benefit from BT than those with low attack frequency, whose attack frequency changed from 1.9 attacks to 2.0 attacks post training (p=0.03).

4. DISCUSSION

In the present study patient trainers offered a home-based behavioural training to small groups of fellow patients that was aimed at the non-pharmacological prevention of migraine attacks. The study could not confirm that BT would reduce migraine attack frequency immediately after training. This effect was modest (-21% for BT participants and -6% for controls) and only a non-significant trend was found in the completed protocol analysis (p=0.07). This non-significant finding for the primary outcome variable is in line with a review of Larsson (2005) showing that self-help or school-nurse administered approaches were inferior to therapist-delivered relaxation in youngsters with chronic headache (54). However, the results confirmed the expectations that BT would increase patients' feelings of control over migraine attacks (effect size 0.97) and confidence in their own capacity to prevent or manage attacks (effect size 0.79). These effects remained significant after correction for multiple testing. No effects were found for quality of life and disability.

The exploratory analyses yielded indications that patients with a high frequency of attacks had significantly more benefit from BT than those with a low frequency. This finding must be considered with caution because the subgroups are rather small. Further, according to the ITT analysis the use of analgesics increased significantly after BT. The CP analysis also indicated that the use of analgesics increased, while the use of triptans decreased. This was observed in both conditions, but these findings remain inconclusive, as they were all non-significant. The use of prophylactics has been reported as a contra-indication for behavioural treatment (53). This was not confirmed by the present study, since restricting the analysis to patients who did not use prophylactics did not affect the effect of BT on attack frequency.

Below we discuss four aspects of the present study, regarding to the severity of the migraine problem in the present sample, the choice of the WLC condition, the employment of

patient trainers and the importance of follow-up results. First, it is evident that the present results are obtained in a patient group characterized by relatively severe migraine and relatively impaired quality of life. The participants were under medical care for migraine, 11% had joined the patient organization (45), and migraine-related disability was high compared to an international population study (47). Secondly, a waitlist-control group was used instead of a placebo-control group. While we had good reason to do so, a placebo-intervention could have produced improvement comparable to the present BT outcome (6, 28). Therefore, had we performed a placebo-controlled study the conclusions on attack frequency would have been the same.

Thirdly, with regard to the employment of patient trainers, our pilot study showed that the present trainers sometimes suffered from fatigue or migraine themselves during the session and thus had to struggle to manage their own migraine (16). Other problems included leading a group and balancing attention, and difficulties in providing individualized feedback. Individualization, the tailoring of attention and findings to the individual case, was shown to be an effective quality of peer educators in health education programs (55). It might be more difficult and demanding to realize individualization successfully within a behavioural training program than in a health educational program, and the present BT application drew heavily on this ability of the trainer. However, none of the patient trainers dropped-out from the present study and, despite the difficulty of the task, being a trainer was experienced as rewarding. Nevertheless, the question remains whether the task of training fellow patients is too demanding, given the complexity of BT and the presentation to a group. This issue is not yet resolved for two reasons. Since the effect of BT provided by healthcare professionals was established on the basis of individual treatment, future research needs to establish whether patient trainers might be successful with individual provision of BT (instead of a BT group application). Also, one could consider devoting more extensive care to the specific handling of individualization in preparing and supervising patient lay trainers who provide BT. This is a challenging question, especially given our present investment in training and supervision of patient trainers and the costs involved in increasing this investment.

Lastly, it might be too ambitious to aim for a significant decrease in attack frequency immediately after the present BT. The participants may still be in the process of learning to adapt their life-style at the end of BT. The significant increase in subjective control and confidence in attack prevention may reflect an increased ability in the participants to predict attack occurrence. This may also indicate that the anxiety of the migraine attack lessened, while its acceptance increased (56, 57). Longer-term effects of BT are therefore also of interest.

In conclusion, we found that a home-based behavioral training provided by lay trainers with migraine to small groups of fellow patients produced a minor (-21%) short term effect on attack frequency and clinically significant improvement in 35% of the participants. Covariance analysis showed a non-significant trend ($p=0.07$) compared to the waitlist control condition. In addition, BT convincingly strengthened perceived control over migraine and self-confidence

in attack prevention. Last, BT did not alter quality of life or migraine-related disability. Follow-up data can show whether these effects are maintained or may improve over time.

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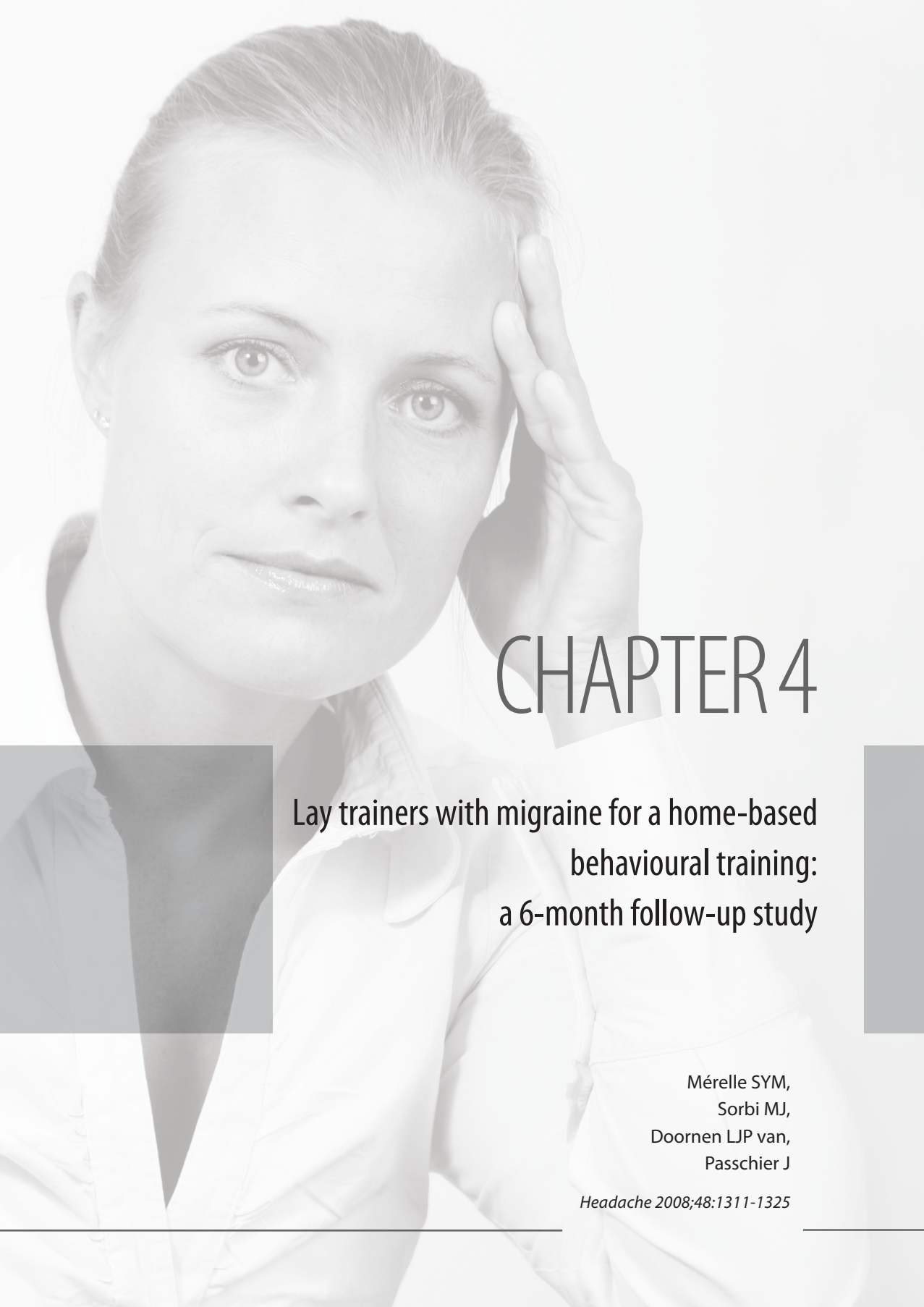

CHAPTER 4

Lay trainers with migraine for a home-based behavioural training: a 6-month follow-up study

Mérelle SYM,
Sorbi MJ,
Doornen LJP van,
Passchier J

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ABSTRACT

Objective To evaluate the changes after a home-based behavioral training (BT) provided by lay trainers with migraine to small groups of fellow patients at 6-months follow-up.

Background The need for self-management programs and cost-effective treatments gave rise to this study.

Methods In a previous randomized controlled trial we compared the BT group with a waitlist-control group, receiving usual care. For the present study, the control group was trained directly after their waitlist period and their results were added to those of the BT group. Measurements in both groups were held pre-BT, post-BT and at 6-months follow-up.

Results Six months after BT 42% was categorized as responders (>50% decrease in attack frequency), 42% did not change (-49 to 49%) and 16% responded adversely (>50% increase). In the group as a whole (n=95) attack frequency significantly decreased from 3.0 attacks at baseline to 2.5 post-BT and to 2.3 at 6-months follow-up (-23%, medium effect size 0.6). The strong improvements of perceived control over and self-confidence in attack prevention were maintained at follow-up. Disability and health status were not changed six months after completion of BT; however, quality of life significantly improved over time (p=0.007). BT was also more beneficial for patients who entered the training with a high attack frequency. Linear regression analysis demonstrated that a larger belief at baseline that migraine is due to chance (external control) significantly predicted a lower attack frequency at follow-up.

Conclusion Home-based lay trainers with migraine can train small groups of fellow patients in behavioral techniques. At 6-months follow-up attack frequency and quality of life were modestly improved, and feelings of control and self-confidence remained strongly improved.

Keywords: migraine, behavioral treatment, self-management, lay trainer, follow-up, predictors

1. INTRODUCTION

The need for a large-scale implementation of behavioral treatments challenges providers and researchers to develop and investigate cost-effective and broadly accessible treatments for headache disorders (1). Therefore, individual home-based applications of behavioral treatment (BT) were developed, in which the training was provided in 3-4 sessions and supplemented with manuals and telephone support (2). The cost-effectiveness of home-based BT was found to be five times higher than intensive clinic-based treatments (3). New developments in healthcare also led to the development of self-management programs for various chronic disorders. Such programs actively encourage patients to deal with their symptoms, treatment, and the emotional and physical consequences of living with a chronic disease (4-6). Health professionals are usually the providers of such programs but lay trainers with chronic conditions can also deliver the interventions (7).

In line with these developments our group was the first to examine a home-based BT that could be provided by migraine patients as lay trainers. In addition, BT was delivered to small groups of patients and at the home of the trainers to further increase the cost-effectiveness. A previous randomized controlled trial (n=108) showed that BT produced a minor (-21%) short-term reduction of attack frequency, which was a non-significant trend (p=0.07) compared with the waitlist-control group (8). In addition, 35% of the participants showed a clinically significant improvement (>50% decrease in attack frequency). Finally, patients' perceived control over migraine and self-confidence in attack prevention were significantly strengthened, but BT did not affect migraine-related quality of life and disability (8).

Follow-up studies on migraine patients as lay trainers of behavioral techniques have not been conducted so far. Follow-up effects are interesting because of the innovative character of using migraine patients as trainers for groups of fellow patients and the home-based setting. In a review on the maintenance of BT effects, Blanchard reported that short-term improvements (obtained by biofeedback, relaxation and stress-management) were well maintained or even improved after a follow-up period of 3 to 12 months (9). Furthermore, little is known about predictors of BT response. Some studies suggest that a higher headache severity at baseline, a shorter duration of headache history, less psychosomatic complaints, little external stress and a high self-motivation predict a positive outcome (10-12). However, these studies reported different outcome variables, e.g. headache severity and percentage improvement. In addition, knowledge on the predictors of our primary outcome, attack frequency, is scarce and mainly available from epidemiological studies (13-15). These prospective studies indicated that medication overuse, female gender, presence of other pain symptoms and depression increased the probability of having frequent attacks.

The present study aimed to determine the maintenance of changes after 6 months follow-up of a home-based BT provided by lay trainers with migraine. Primary aims of this training were to reduce attack frequency and increase perceived control and self-confidence in attack

prevention. This was investigated by a comparison of the follow-up results with baseline and post-training results. The secondary aims of the study were to test for an improvement of patients' quality of life and a reduction of migraine-related disability. Patient characteristics assessed at baseline were also explored for their possible relationship to training outcome after six months.

2. METHODS

2.1. Patients

Patients were included according to the scientific guidelines of the IHS subcommittee on clinical trials and the guidelines of the AHS for behavioral trials (16, 17). Participants were aged 18 to 65 years, fulfilled the IHS criteria for migraine without (G43.0) or with (G43.1) aura (18) and had an attack frequency of 1-6 per month. A broad range of 1-6 attacks was chosen to enhance the external validity of the study. Excluded were patients with headache occurring on 15 or more days per month, a migraine duration less than one year, migraine onset at an age above 50 years because this may refer to underlying organic disease (16), and an above average score (>178) on the Symptom Checklist 90 (SCL-90) indicative of psychopathology (19). The study was carried out in cooperation with the Dutch Society of Headache Patients and profited from its support and website for recruitment. Patients were recruited through the website of the patient organisation, newspapers magazines and referral by local headache specialists. The instruments for selection consisted of a standard questionnaire based on the IHS classification criteria, a prospective 4-week headache diary, and the SCL-90 psychopathology-screening list. Two headache specialists verified the diagnoses and ruled out medication-overuse headache in case of doubt. All patients who were selected for the clinical trial on the short-term effectiveness were invited to participate in the follow-up measurements (8). The Ethics Committee of the Erasmus University Medical Centre approved the study.

2.2. Study design and procedure

This was a clinical trial in which the eligible patients were randomly allocated to the training group (BT) or the waitlist-control group. This pragmatic design was chosen in view of the difficulties previous studies had in realizing a placebo procedure that was plausible and also provided non-therapeutic control for attention (20, 21) . In addition, comparison with a professional therapist group was not an aim of this study; the focus was whether or not this innovative approach might work. Moreover, such an equivalence study would require a much larger sample size and considerable resources. Measurements were made pre-BT (T1: months 0-1), post-BT (T2: months 5-6) and at 6-months follow-up (T3: months 12-13). There was not any contact with participants during the follow-up period. All participants were informed

about the burden and duration of the study during the selection procedure by the informed consent form.

The waitlist-control group (WLC) received BT directly after their waitlist period (T0: pre-waitlist, T1: post-waitlist/pre-BT). Consequently, the duration of the study was 19 months for the WLC group, six months longer than the BT group. The data of the waitlist group were added to those of the BT group to enlarge the power of this study. BT was provided to six cohorts over three consecutive years, with one BT and one waitlist group per year. Data collection took place from July 2003 until March 2007.

2.3. Home-based, group-delivered behavioral training (BT) and waitlist control

BT was based on an established protocol for individual behavioral treatment of migraine delivered by healthcare professionals (22, 23). For this study the protocol was adapted to the format of a self-management training for small groups to be delivered at home by lay trainers with migraine. Patients received a manual containing background information and diary ratings, an organizer containing homework assignments and self-evaluations, and a CD-Rom with relaxation exercises. BT was focused on two strategies that are central to attack prevention in migraine: 1) identification and modification of triggers and premonitory symptoms of migraine attacks, and 2) application of physiological and cognitive-behavioral self-regulation skills. Autogenic training was used for physiological self-regulation, supplemented by breathing exercises and cue-controlled relaxation. Autogenic training is commonly applied in migraine and produces medium effect sizes in headache improvement (24-26). Cognitive-behavioral self-regulation involved taking breaks or time-out, and employing self-assurance and positive thinking to reduce physical or mental exertion and arousal (22, 23, 27, 28).

BT consisted of seven 2-hour sessions spread over 10 weeks. The practice at home took 30 minutes per day for the relaxation exercises, 15 minutes for the registration assignments and one hour per week for reading the theoretical information of the training. Sessions 1 to 3 were conducted weekly and focused on 1) detection of migraine triggers and premonitory symptoms (29, 30) by daily monitoring, and 2) acquisition of relaxation skills by stepped practice of autogenic and breathing exercises twice per day at home. Trigger and symptom detection was supported by personal feedback of the trainer and group members, and for each participant resulted in a map of triggers and premonitory symptoms, which was tailored to his/her individual case. Relaxation skills were trained gradually by stepwise inclusion of cue-controlled relaxation, while autogenic exercises were shortened from 15 till 5 minutes. Sessions 4 to 6 took place every two weeks and focused on 1) the proactive application of physiological and cognitive-behavioral self-regulation skills under the condition that premonitory symptoms or triggers prevailed, while continuing the daily exercises at home, and 2) a personalized written prescription or recipe for behavioral attack prevention. In these prescriptions the participants formulated individualized target conditions of being at risk for developing a migraine attack, as well as individualized actions and lifestyle changes to reduce this risk and prevent attack

occurrence. Evaluation took place in session 7, which included the specification of individual goals and actions to maintain training skills. BT was delivered in smalls groups of 2-4 patients and its feasibility was established in a pilot study (31, 32). The WLC group continued their current treatment, i.e. care as usual. All participants were urged not to change their medication or start alternative migraine treatments while in the trial, and to inform the researchers in case this was unavoidable. To keep participants informed and committed to the study they received a newsletter about the research project once per year.

2.4. Lay trainers with migraine

Fourteen lay trainers with migraine underwent a training consisting of three steps: 1) self-experience through receiving BT for their own migraine attacks, 2) application of individual BT to one new patient under supervision of the first author, 3) provision of BT to small groups of 2-4 patients under continued supervision. Potential lay trainers could participate in step 2, provided that they were motivated to become a lay trainer and were successful in managing their own migraine attacks.

Trainers received a structured manual of the content and procedure per BT session, which included directives for basic trainer skills regarding instructions and evaluations of registration assignments and relaxation exercises, time-management, provision of feedback, and motivational or emotional assistance. They kept a brief evaluation form per session with track records per trainee for the purpose of supervision. Trainers were supported by three supervisions per training, provided individually through e-mail and telephone by the first author, as well as by 3-hour workshops offered twice per year. Three workshops were directed at the promotion of basic trainer skills while safeguarding the trainers' own migraine management; a fourth workshop offered advanced knowledge of self-relaxation techniques. The lay trainers received a payment of 150 euros (14 euros per hour) for individual BT, and 300 euros (21 euros per hour) for a home-based group BT.

2.5. Measurements

The primary outcome measure attack frequency was prospectively measured in a headache diary according to the guidelines for clinical trials in prophylactic treatment and the guidelines for behavioral trials (16, 17). Participants registered their headache for 4 weeks prior to BT, directly after BT and six months after completion of BT. Attack frequency was averaged per 4 weeks. It was not feasible to carry out a baseline measurement of 8 weeks in addition to 4 weeks of registration during the selection procedure. A longer assessment period may also have biased the measurement due to motivational problems to fill in the headache diary. Pain intensity was rated by allocating the following score, every six hours: 1 is mild headache - I can do everything but with some difficulty; 2 is moderate headache - I cannot do all or most things; 3 is severe headache - I am unable to do things, bed rest is necessary. When headache occurred patients registered once a day their migraine characteristics (unilateral location,

pulsating quality, moderate or severe pain intensity, aggravation by physical activity) and associated symptoms (nausea/vomiting; photo- or phonophobia). Furthermore, medication type and dosage unit for acute and preventive treatment were registered per 24 hours.

The two additional primary outcome measures, perceived control over migraine and self-confidence in attack prevention, were assessed with questionnaire measurements. Of the 33-item Headache Specific Locus of Control Scale (HSLC) (33) the subscales `internal control' and `external control – chance' were used to indicate the degree to which participants perceived control over migraine prevention. The score for `internal control' reflects the degree of perceived control over migraine (range 11-55), while the score for `external control' indicates the degree to which migraine is perceived as being due to chance (range 11-55). The sum score of the 25-item Headache Management Self-Efficacy questionnaire (HMSE) reflects the patients' self-confidence to take action that might prevent migraine attacks (34). A higher score indicates a larger confidence in own capacity (range 25-175). A forward-backward method (35) was used to translate the HSCL and HMSE, and both questionnaires had a very good reliability in our sample (8). The HMSE was translated during the first year of data acquisition and could therefore not be administered to about 25% of the total sample.

The secondary outcome measures concerned health status, migraine-specific quality of life and migraine-related disability. Health status was measured with the Dutch version of the Medical Outcomes Study 36-item Health Survey (SF-36) (36, 37), which is a validated instrument for the self-evaluation of physical and mental health and commonly used in migraine (38). The SF-36 comprises four scales for physical and four scales for mental health. Raw scores of the eight subscales were linearly converted to a 0-100 scale, and a mean score was calculated for physical and mental health, with higher scores on both dimensions indicating a better health status. The 20-item Dutch version of the Migraine Specific Quality of Life Questionnaire (MSQOL) is a valid and reliable instrument to assess migraine-specific quality of life (39), whereby a higher sum score reflects a better quality of life between attacks (range 20-80). The Migraine Disability Assessment Scale (MIDAS) consists of five questions concerning the number of days lost to migraine in the past 3 months. Internal consistency, reliability and validity of the MIDAS were satisfactory. The sum score reflects the number of productive days in the workplace and at home (40). The HSLC, HMSE, SF-36, MSQOL and MIDAS were administered pre-BT (T1), post-BT (T2) and at 6 months follow-up (T3).

2.6. Data analysis

Migraine episodes in the headache diary were identified according to the IHS criteria (17). Since triptan use for acute treatment modifies clinical features (16), the following criteria were adopted to establish the occurrence of migraine: if a triptan was used then headache was qualified as a migraine attack if either 1) at least two migraine characteristics were present, but associated symptoms were absent, or if 2) one migraine characteristic was present, together with at least one associated symptom. A migraine attack that was interrupted by sleep or

recurred within 48 hours was counted as one attack (16). Medication use for acute treatment was calculated by counting separately the dosage units of triptans and of analgesics over the 4-week diary period (16).

The analyses were first carried out in the total sample that entered the baseline measurement according to the intention-to-treat (ITT) principle and were repeated on subjects who completed the study protocol (CP). The CP analysis is reported as primary analysis and ITT results are added when these differed from the CP results, e.g. significant in CP analysis, or a non-significant trend ($p<0.10$), and non-significant in ITT analysis or vice versa. Results are presented as mean scores of the group as a whole and were calculated separately for the original BT and waitlist-control group regarding the measurements pre-BT, post BT and at 6-months follow-up. Independent t-tests were performed to detect any differences between both conditions. Mean within-group differences are presented, including 95% confidence intervals indicating the imprecision of the differences. Cohen's d was calculated to indicate the effect size according to the formula $d= (\text{Mean T1-Mean T2})/s_{T1}*\sqrt{(1-r)}$ with $d<0.2$ indicating a negligible effect, $0.2<d<0.5$ a small, $0.5<d<0.8$ a medium and $d>0.8$ a large effect (41). Multivariate analysis of variance (MANOVA) was performed on the primary outcome measures (attack frequency, internal control, external control, self-efficacy) as dependent variables over the three time points. MANOVA was also used to test the changes in secondary outcomes (physical and mental health status, migraine-specific quality of life, migraine-related disability). When the overall time effect was significant then the nature of the time trend was examined and tested whether this trend was linear and or quadratic. A linear time trend is called the first order comparisons measure (X, linear relationships) and implies that the mean values of the measurements are located on a straight line (within fluctuation of error). The quadratic trend is called the second order comparisons measure (X^2, quadratic relationships) and implies that the mean value of the second measurement could not be statistically located on a straight line (i.e. curvature in the line).

The models used for MANOVA were checked for violation of the assumptions of normality and homoscedasticity. Because of non-normal distributions the scores for attack frequency, internal control, self-efficacy, mental health status and medication use were transformed (square root, except for analgesics which was log transformed). Missing values of the primary outcome migraine frequency were estimated by using the expectation maximization likelihood method. The confidence intervals were adjusted after the EM likelihood method was applied. Adjustments were not made for missing data from questionnaires. Patients who had >25% of the items of a specific (sub)scale of a questionnaire missing were removed from the analysis on the sum score concerned. A dropout analysis tested whether non-completers significantly differed from completers regarding headache, medical consumption and demographic characteristics.

In order to control for Type I error we performed Bonferroni's correction: $1-(1-\alpha)^{1/m}$, with an alpha of 0.05 and m indicating the number of tests (42). According to this formula a significance

level of 0.0125 is required for the results of the primary and for the secondary analyses. If a significant change over time was found by MANOVA, paired t-tests were applied to detect in which period a significant change took place (T1→T2, T2→T3 or T1→T3).

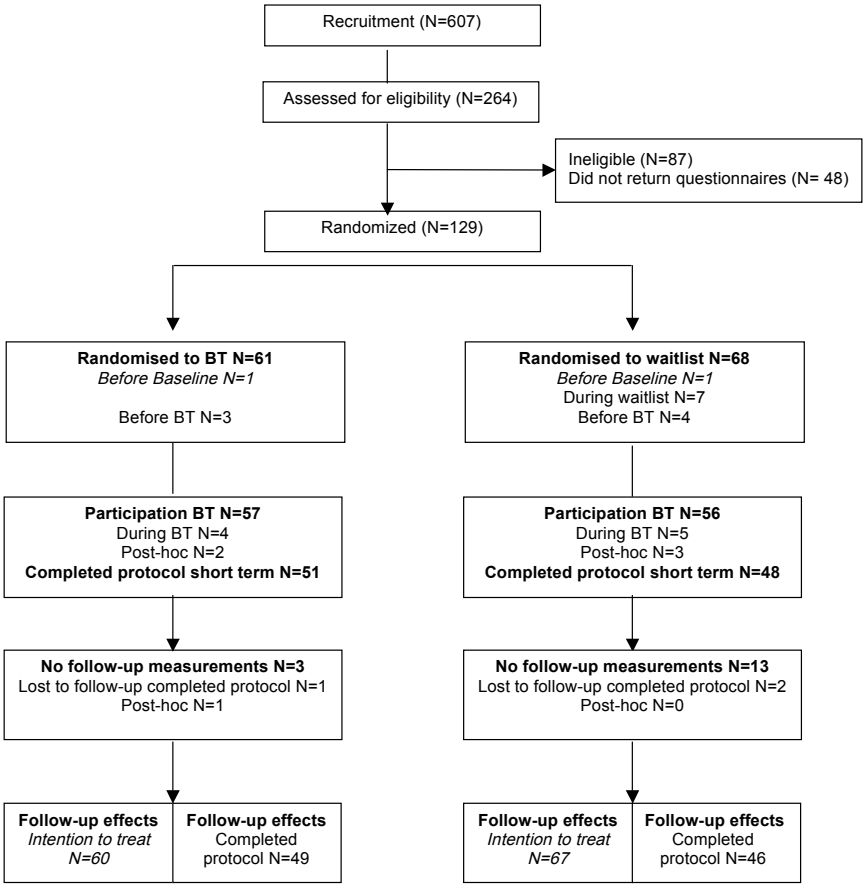
In addition, explorative analyses were performed to explain the primary outcomes. First, treatment responder rate was calculated for attack frequency. Responders were defined as patients with >50% improvement in migraine frequency from baseline compared to follow-up. Secondly, we explored patient baseline characteristics that may be related to training outcome at follow-up. The method of backward elimination in the stepwise linear regression analysis was applied with R^2 as measure of performance of the model. The following baseline variables entered the equation to test their predictive value: migraine duration (years), migraine aura, use of triptans and analgesics, internal control, external control, self-efficacy, physical and mental health status, migraine-specific quality of life, migraine-related disability. Because of the exploratory function of this prognostic analysis a p-value<0.20 was allowed (43). In our previous study on the short-term effects of BT with the present sample, attack frequency was significantly more reduced for those who entered BT with a high frequency (4-6 attacks) versus low frequency (1-3) (8). To see if this could be replicated in a large sample size, including the waitlist-control group, the outcomes of both groups (high versus low) were explored separately. Last, MANOVA was employed to test changes in medication use (triptans, analgesics) and to find out whether results improved when patients who used prophylactics were excluded from analysis, according to recommendations for behavioral research (17). SPSS for Windows, version 11.0 was used to conduct the statistical analyses.

3. RESULTS

3.1. Patient flow through the study

Participant flow through the study and reasons for attrition are reported in Figure 1. After randomization of the 129 participants (BT: N=61, waitlist: N=68), 16 patients stopped before the training, of whom two before baseline. In the BT group 57 patients participated in the training (93%) and 4 of these patients stopped (7%). In the waitlist-control group 56 patients (82%) participated in BT after the waitlist period and 5 stopped (9%). At follow-up 16 patients (12%) did not provide data and a satisfying drop-out rate <20% was achieved (39). Of these patients, three belonged to the patient group who had fully adhered to the short-term study protocol. Six patients were post-hoc excluded from the analysis due to invalid measurements and diagnostic errors (Figure 1, Reasons for attrition). Therefore the completed protocol group of the follow-up study consisted of 95 patients, while the intention-to- treat group included 127 patients for the primary outcome, attack frequency. Missing values due to missing headache diaries were 6% post-BT and 12% at follow-up in the ITT analysis. The characteristics of the patients are presented in Table 1. The dropout analysis yielded two significant differences

Figure 1 Participant flow for behavioral training (BT)



Reasons for attrition per phase of the study

Study phase		Immediate BT		BT after waitlist
Before baseline	N=1	Breast cancer	N=1	Change in treatment
During waitlist period	_		N=7	Unknown; Travel distance (2 patients); Breast cancer; Surmenage; No time; Pregnancy
Before BT	N=3	Operation; No time; No longer interested	N=4	Travel distance (3 patients); Change in treatment
During BT	N=4	Change in treatment; Dissatisfied BT (2 patients); Operation	N=5	Change in treatment; Dissatisfied BT; No time (2 patients); Breast cancer
Post-hoc	N=1	Diagnostic error; Invalid measurement	N=3	Diagnostic error; Triptan-overuse headache; Invalid measurement
Follow-up period	N=3	No longer interested; Unknown; Breast cancer	N=13	Not interested anymore (6 patients); Unknown (3 patients); Pregnancy, birth of child (2 patients); Cancer (2 patients)
Post-hoc	N=1	Invalid measurement	-	

between completers (n=95) and non-completers (n=32). At baseline, the use of triptans was significantly higher among non-completers (5.6 per 4-week period) than among completers (3.6). Non-completers were also less often highly educated (42% versus 74%). The primary outcome attack frequency did not differ significantly at baseline (2.9 attacks versus 3.2) between the groups. The number of patients who changed their medication or started with alternative migraine treatments was 19% post-BT and 35% at follow-up.

Table 1. Characteristics of all analyzed patients (intention-to-treat; ITT) and patients who completed the protocol (CP)

Characteristics	**ITT** (n=127)	**CP** (n=95)
Age mean (range) in years	44 (18-65)	44 (24-63)
Gender (%)		
Female	87	86
Male	13	14
Education level (%)		
Low	6	4
Average	29	22
High	65	74
Migraine duration mean (range) in years	19 (2-50)	20 (3-50)
Migraine diagnosis (%)		
With Aura G43.1	33	35
Without Aura G43.0	67	65
Attack frequency (%)		
1-3 attacks	65	68
4-6 attacks	35	32
Pain intensity migraine mean (1-3 scale, SD)	1.91 (0.69)	1.75 (0.79)
Consultations (%)		
General Practitioner	98	98
Neurologist	58	58
Psychologist	16	14
Physiotherapist	43	42
Acute medication use mean (per 4 weeks, SD)		
Triptans	4.0 (4.0)	3.6 (3.5)
Analgesics	3.3 (6.5)	3.6 (6.7)
Prophylactics (%)	20	22
MIDAS mean (sum score, SD)	24.3 (17.5)	21.9 (15.8)

3.2. Changes in primary outcomes

The results of the patients who adhered to the training protocol are presented in Table 2. The only significant difference between the original BT group and WLC group was self-efficacy post-BT, which was significantly higher in the WLC group. Attack frequency was reduced in the group as a whole (n=95) from 2.95 at baseline to 2.48 post BT, and to 2.27 attacks per 4-week

period at follow-up (-23%, medium effect size 0.6). Multivariate analysis yielded a significant improvement over time (see Table 2) and a linear trend was found (F(1,94)=17.7, p=0.000).

Table 2 Changes in primary outcomes over time of subjects who completed the protocol

Primary outcomes		**BT group**	**WLC group**	**Total group**	**Total group T1 - T2 T1 - T3**			**Total group T1, T2, T3**	
		Mean (SD)	Mean (SD)	Mean (SD)	Mean Δ	95% CI Δ	ES	F	p
Attack Frequency		(n=49)	(n=46)	(n=95)					
	T1	3.00 (1.69)	2.89 (1.69)	2.95 (1.6)					
	T2	2.35 (1.45)	2.62 (1.77)	2.48 (1.6)	0.47	0.12 to 0.82	0.38		
	T3	2.12 (1.52)	2.42 (1.83)	2.27 (1.7)	0.68	0.33 to 1.03	0.57	8.93[a, b]	0.000*
Internal Control		(n=46)	(n=45)	(n=91)					
	T1	34.3 (10.7)	37.2 (8.54)	35.7 (9.7)					
	T2	42.2 (8.20)	42.6 (8.27)	42.4 (8.2)	-6.6	-8.26 to -4.94	-1.08		
	T3	40.3 (9.52)	41.2 (9.28)	40.7 (9.4)	-5.2	-7.0 to -3.46	-0.81	36.5[a, b, c]	0.000*
External control		(n=46)	(n=45)	(n=91)					
	T1	35.7 (8.71)	33.7 (8.63)	34.7 (8.7)					
	T2	29.2 (7.19)	27.4 (9.44)	28.3 (8.4)	6.3	4.62 to 7.98	1.11		
	T3	27.9 (7.76)	28.2 (9.61)	28.1 (8.7)	6.8	4.95 to 8.60	1.06	35.7[b, c]	0.000*
Self-efficacy		(n=31)	(n=34)	(n=65)					
	T1	86.9 (22.9)	95.5 (19.4)	91.5 (21.3)					
	T2	103.9 (24.9)	117.9 (17.9)	111.3 (22.4)	-19.9	-24.7 to -15.0	-1.47		
	T3	107.0 (22.4)	106.3 (23.4)	106.9 (22.7)	-17.9	-22.4 to -13.3	-1.14	45.9[a, b, c]	0.000*

* Significance level was fixed at p<0.0125 to account for multiple testing

[a] Square root transformation of scores [b] Linear trend, [c] Quadratic trend (see text)

T1 (baseline), T2 (post-BT) and T3 (follow-up), F- and p-value represent main effects of MANOVA

BT (original behavioral training group), WLC (waitlist-control group who received BT after the waitlist period), Total group (all trained patients)

T-tests showed that the changes from baseline to post BT and from baseline to follow-up were significant (p=0.01, p=0.000, respectively). Attack frequency post BT did not differ significantly from follow-up (p=0.16), indicating no further improvement but also maintenance of training results. Patients' belief that factors influencing the occurrence and relief of migraine attacks are under own control significantly increased over time (see Table 2) and a linear and quadratic trend were found (internal control: F(1,89)=40.5, p=0.000 and F(1,89)=29.5, p=0.000 respectively). This finding indicates that patients' perceived control strongly improved over time, but also that the improvement post-BT declined at follow-up. Their belief that migraine is a matter of chance or bad fate significantly changed in the opposite direction and a linear and quadratic trend were identified (external control: F(1,89)=55.5, p=0.000 and F(1,89)= 18.7, p=0.000). In both cases significant changes took place from T1àT2 (p=0.000) and from T1→T3 (p=0.000), but not from T2→T3. An even stronger improvement was found in self-confidence in own ability to prevent migraine attacks and a linear and quadratic trend were found (self-efficacy: F(1,64)=61.3, p=0.000 and F(1,64)=34.2, p=0.000). The same pattern in significant changes over T1, T2 and T3 was found for self-efficacy.

3.3. Changes in secondary outcomes

Table 3 shows that migraine-specific quality of life significantly improved over time. A linear trend was detected (F(1,92)=10.7, p=0.002), with the largest change from T1àT3 (p=0.002), followed by T1àT2 (p=0.02). Migraine-related disability and physical and mental health status did not change over time.

3.4. Exploratory analyses

Directly after BT 34% of the participants was categorized as responders (≥50% decrease in attack frequency), 46% did not change (-49 to 49%) and 20% responded adversely (≥50% increase). At 6- months follow-up the responder group increased to 42% and the adverse responder group decreased to 16%. The results of the linear regression analysis demonstrated that only external control significantly predicted attack frequency at follow-up (β=-0.29, p=0.02), adjusted for attack frequency at baseline, age, gender and education. This finding implies that a larger belief at baseline that migraine is due to chance increased the probability of a lower attack frequency at follow-up. The variance in attack frequency explained by this model was 37%.

Figure 2a shows that in the high frequency group (n=30), mean attack frequency was significantly reduced from 4.8 attacks pre BT to 3.0 post BT (T1→T2, -37%, p=0.000) and remained 3.0 at follow-up (T2→T3, -1%, p=0.89). In contrast, the low frequency group (n=65) showed no significant change at post-BT (T1→T2, +10%, p=0.31) or at 6-months follow-up (T2→T3, -3%, p=0.10). Figure 2b shows the absence of a regression to the mean effect from baseline within the group that started with a waitlist period. In the high frequency group no changes occurred before and after the waitlist period, whereas after the training migraine

Table 3 Changes in secondary outcomes over time of subjects who completed the protocol

Secondary outcomes		BT group	WLC group	Total group	Total group			Total group T1, T2, T3	
		Mean (SD)	Mean (SD)	Mean (SD)	T1 - T2/T3 Mean Δ	95% CI Δ	ES	F	p
Physical health status		(n=48)	(n=45)	(n=93)					
	T1	66.9 (21.2)	71.5 (16.5)	69.1 (19.1)					
	T2	72.9 (18.5)	71.5 (18.4)	72.2 (18.4)	-2.9	-7.0 to 1.19	-0.22		
	T3	73.8 (18.3)	72.5 (18.1)	73.1 (18.1)	-3.7	-8.53 to 1.06	-0.24	1.50	0.23
Mental health status		(n=49)	(n=45)	(n=94)					
	T1	73.9 (16.2)	71.1 (17.9)	72.6 (17.0)					
	T2	74.4 (15.6)	75.5 (17.2)	74.9 (16.3)	-2.4	-6.08 to 1.31	-0.18		
	T3	76.1 (15.6)	74.7 (17.3)	75.5 (16.3)	-2.8	-5.86 to 0.24	-0.28	2.17[a]	0.12
Migraine-specific QOL		(n=49)	(n=46)	(n=95)					
	T1	57.0 (8.8)	56.7 (9.2)	56.9 (9.0)					
	T2	58.1 (7.3)	58.7 (8.1)	58.4 (7.6)	-1.5	-2.88 to -0.19	-0.31		
	T3	59.8 (8.1)	58.4 (8.6)	59.1 (8.3)	-2.3	-3.69 to -0.89	-0.46	5.28[b]	0.007*
Migraine Disability		(n=49)	(n=46)	(n=95)					
	T1	23.5 (17.2)	20.2 (14.1)	21.9 (15.8)					
	T2	21.7 (16.7)	20.0 (11.6)	20.9 (14.4)	1.0	-1.43 to 3.51	0.12		
	T3	16.2 (15.7)	20.6 (17.0)	18.3 (16.4)	3.5	0.73 to 6.36	0.37	0.36[a]	0.55

* Significance level was fixed at p<0.0125 to account for multiple testing

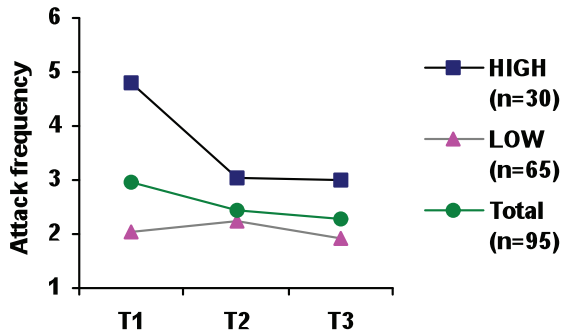
[a] Square root transformation of scores [b] Linear trend

T1 (baseline), T2 (post-BT) and T3 (follow-up), F- and p-value represent main effects of MANOVA

BT (original behavioral training group), WLC (waitlist-control group who received BT after the waitlist period), Total group (all trained patients)

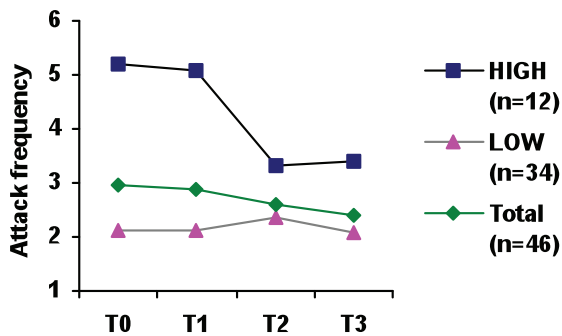
frequency significantly decreased (-34%, p=0.004). The high and low frequency groups did not differ regarding their level of perceived control, self-confidence, or quality of life over the three time points. However, the high frequency group was significantly more disabled at baseline as measured by the MIDAS, i.e. 27.4 impaired days per 3 months versus 19.4 for

Figure 2a Changes in attack frequency over time and as a function of high migraine occurrence (4-6) and low occurrence (1-3) at baseline (T1) in total group (n=95)



T1 is pre-BT, T2 is post-BT, T3 is follow-up

Figure 2b Changes in attack frequency over time in the waitlist group (n=46)



T0 is pre-waitlist, T1 is post-waitlist/pre-BT, T2 is post-BT, T3 is follow-up

the low frequency group. More important, this group showed a significant improvement in disability from baseline to follow-up (27.4→22.6, p=0.04).

Triptan use significantly decreased from 3.60 to 3.32 post BT and to 2.68 at follow-up, i.e. mean difference of 1.0 dosage unit per 4-week period. Use of analgesics did not change significantly in the group completing the protocol (from 3.62 dosage units to 3.80 post BT and to 3.37 at follow-up), but in the intention-to-treat analysis a quadratic trend was found ($F(1,100)=7.40$, $p=0.008$). The latter finding indicates that patients used more analgesics post-BT but this change declined at follow-up. The analysis of patients without prophylactic treatment did not lead to better results than those achieved by the total group.

4. DISCUSSION AND CONCLUSION

4.1. Discussion

This study examined the changes after 6 months follow-up of a home-based behavioral training (BT) provided by migraine patients as lay trainers to small groups of fellow patients. Six months after BT 42% was categorized as responders (>50% decrease in attack frequency), 42% did not change (-49 to 49%) and 16% responded adversely (>50% increase), while directly after BT the number of responders was 34%, 46% did not change and 20% responded adversely. In the group as a whole (n=95) attack frequency significantly decreased from 3.0 attacks at baseline to 2.5 post-BT and to 2.3 at 6-months follow-up (-23%, medium effect size 0.6). The strong improvements in perceived control over and self-confidence in attack prevention were maintained at 6 months follow-up. The modest results of attack frequency at follow-up did not exceed the expected 20-30% of medical placebo studies (44) and were below the 35-55% achieved by healthcare professionals (45). However, a mean change of 23% was larger than the 9-12% found in placebo-controlled BT (20, 46).

The modest change is in line with our previously reported RCT, in which 51 BT patients were tested against 57 patients during their waitlist period (8). A review of Larsson et al. (2005) also showed that self-help or school-nurse administered approaches were inferior to therapist-delivered relaxation in youngsters with chronic headache (47). It is intriguing that BT participants maintained their feelings of control at follow-up but this did not translate into a large headache relief. In social cognitive theory self-efficacy is considered fundamental to behavior change (48, 49), and is also regarded as an important mediating factor of headache outcome in behavioral studies (50). In our study internal control and self-efficacy were not significantly associated with attack frequency at follow up (r=0.13 and r=0.11, respectively). However, a post-hoc analysis showed that the individual change score of attack frequency (T1-T3) was significantly though modestly correlated with the change of self-efficacy (r=-0.27, p=0.03), and significantly related to the change of external control (r=0.34, p=0.001). Rothrock et al. recently found positive effects on disability and headache days of lay trainers with migraine educating fellow patients in a clinic-based setting; however, psychological effects were not reported (4).

In our sample, the lack of change in migraine-related disability may be explained by the modest changes in attack frequency and, therefore, the number of unproductive days did not change. Nevertheless, in the high frequency group, which showed the largest improvement in attack frequency after BT, disability diminished significantly from baseline to follow-up. In contrast to the findings of our short-term RCT, migraine-specific quality of life significantly improved over time (8). The absolute difference of 2.4 points in migraine specific quality of life seems small, but this number corresponds with the findings of Patrick et al. on the effects of zolmitriptan on the MSQOL (51).

Exploratory analyses showed that BT was more beneficial for patients who entered BT with a high attack frequency. This group significantly improved after BT but did not change towards follow-up measurement, and the proportion with clinically meaningful changes was two times higher (50% versus 26% in the low frequency group). A regression to the mean effect seemed unlikely to explain this finding, as the waitlist-control patients with a high attack frequency did not change before and after the waitlist period, but did change after having received BT. The present study also explored factors other than migraine severity that might predict attack frequency at follow-up. The linear regression analysis revealed that a larger belief that migraine is due to chance at the start of BT (external control) significantly predicted a lower attack frequency at 6-months follow-up. External believers may benefit more from the training as they can learn how to influence themselves the occurrence of migraine attacks by modification of triggers and premonitory symptoms and by relaxation and other lifestyle changes. Participants who already were successful in behavioral prevention of migraine attacks may gain less from the training. This finding finding also corresponds with data on `maladaptive versus adaptive coping´ in chronic pain patients, which show that maladaptive coping is positively related to treatment outcomes (52). A post-hoc analysis showed that 22% of BT participants achieved clinically meaningful changes both post BT and at follow-up, while 46% did not improve. These groups did not differ in external control at the start of BT; however, the decrease in external control at follow-up was significantly larger for the first group (-12 points versus -4.0, p=0.000). The change in internal control at follow-up was similar for both groups (6.9 versus 4.6 points, p=0.32). These findings suggest that external control might act as an important mediating factor for headache improvement. In chronic pain patients perceived control was recently found to be the mediator that explained the greatest proportion of the effect of a cognitive behavioral program (53).

Cost-effectiveness was a major reason to set up this study and can be calculated with the formula of Haddock et al (3), i.e. "%improvement (headache index)/ contact time (minutes)". This comparison must be taken with caution as the primary outcome in this study is attack frequency. The group average in this study was 3.8 participants and therefore, the contact time was (840/3.8=) 221 minutes (7*2 h sessions). All together, the cost-effectiveness of lay trainers was (23/221=) 0.10 versus 0.37 for professionals and professional trainers are likely to be more cost-effective than lay trainers with migraine. However, this lower cost-effectiveness is partly compensated by the lower fee for lay trainers (20 € per hour for lay trainers, versus 80 € for professionals) and the location at home of the trainers also reduces the costs.

The clinical strength of the present study is the development of a feasible home-based behavioral training that could be provided by lay trainers with migraine to a group of fellow patients. We also established a stepwise training program for patient trainers that was based on continuous and individualized supervision and workshops to increase trainers' skills. Moreover, many migraine patients responded to our call for participation in this study. Strong methodological points of the current study were the careful selection and diagnostic

procedure, the valid measurements and its statistical power (17). The dropout rate at follow-up (12%) was also acceptable, which might be explained by personal contact with their trainer and peers.

Strong limitations of the study are the use of a waitlist-control condition and an uncontrolled follow-up period. As a consequence, the role of non-specific factors (e.g. attention) cannot be ruled out beforehand and conclusions about causality, i.e. improvements due to BT, can not be drawn. Another limitation is that selection bias might have played a role. The majority of the participants were high medical consumers, female, and relatively highly educated. Dropouts during BT were relatively low educated and their triptan use was significantly higher than completers, however, they were not different regarding attack frequency. Both the absence of a placebo control and the selection bias was a consequence of implementing evidence-based BT methods from the clinical science into headache practice (54). Other study limitations are that 35% of the participants changed their treatment during the follow-up period and this might have influenced the training results. Furthermore, patients with low migraine frequency, i.e. once per month, were included in the trial while the assessments periods were one month in duration. However, when the analysis was restricted to a sample (n=76) without this group, the same conclusions can be drawn, with somewhat better test results. Treatment responder would also not have been better if we had excluded this low frequency group (43% responders, 44% non-responders and 12% adverse responders). Last, MIDAS is recommended as secondary outcome measure in behavioral headache research (55), but this scale employs a retrospective 3-month assessment interval. Consequently, the results of disability directly after the training should be taken with caution.

4.2. Conclusion

Home-based lay trainers with migraine can train small groups of fellow patients in behavioral techniques. At 6-months follow-up attack frequency and quality of life were modestly improved, and feelings of control and self-confidence remained strongly improved. Migraine severity, use of triptans, level of education and changes in perceived control may influence training outcome.

4.3. Future recommendations

The trainer tasks were demanding for migraine trainers as they had to deal with their own migraine management, while leading a group and providing individualized feedback. However, their commitment during the study remained high and being a trainer was experienced as rewarding (8). Yet, the effects of healthcare professionals are based on individual training formats and to use a group format for lay trainers may be a bridge too far. Therefore, a next step would be to replicate the study with BT provided to one individual patient instead of a group. BT may still be provided in a group format if pairs of lay leaders and healthcare professionals are used. If new RCTs would find more favorable results, then a large-scale implementation

would be justified. Future RCTs should also more accurately assess participants' compliance in daily life, which may also explain the large variability in headache improvement. In this respect, palmtop computers (PDA's) can provide more valid and reliable measurements than paper & pencil registrations (50). Finally, more knowledge about the psychological mechanisms in behavioral treatments is also warranted.

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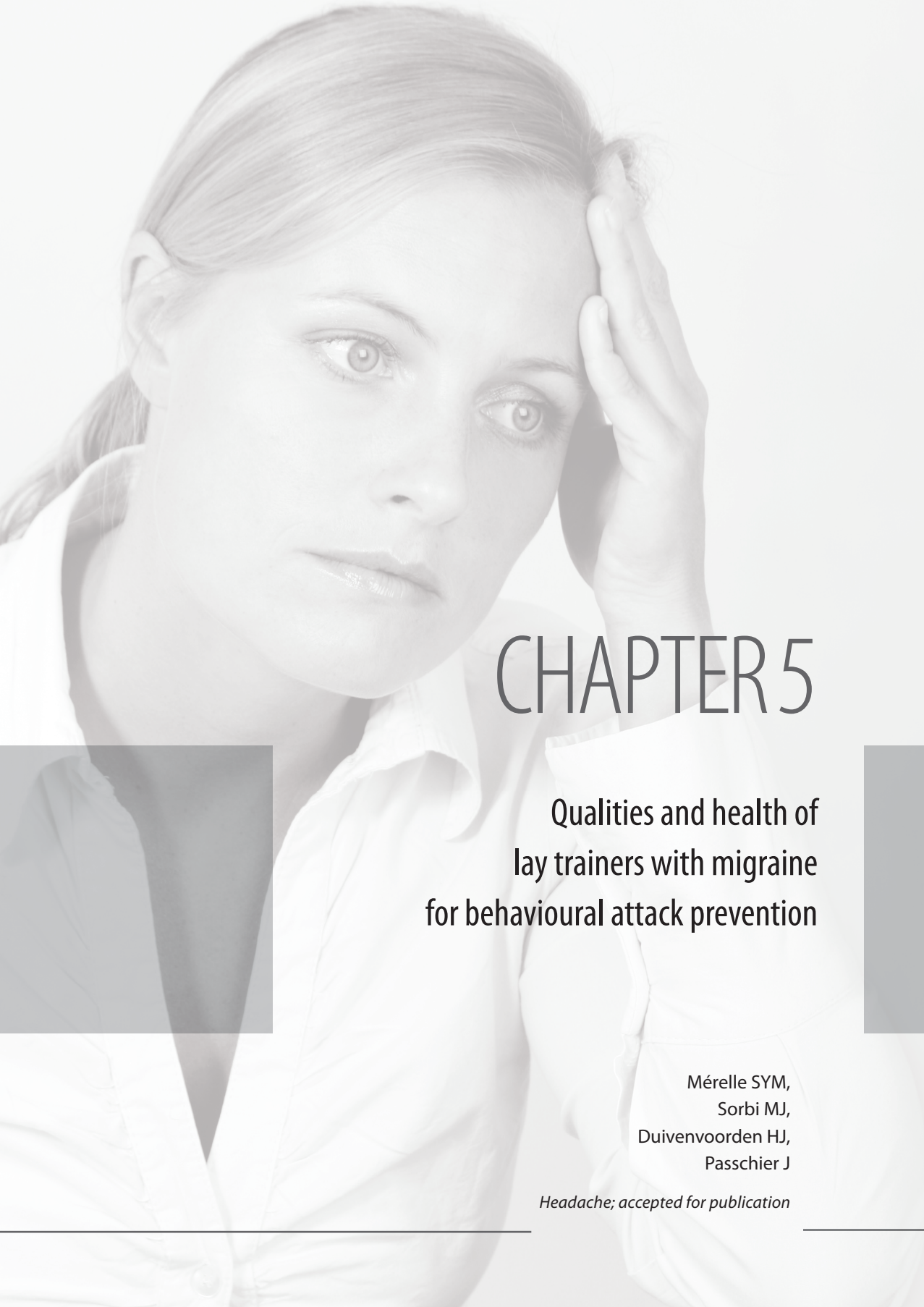

CHAPTER 5

Qualities and health of lay trainers with migraine for behavioural attack prevention

Mérelle SYM,
Sorbi MJ,
Duivenvoorden HJ,
Passchier J

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ABSTRACT

Objectives To evaluate the qualities of lay trainers with migraine and to quantify their self-management results.

Background Little is known about the qualities of lay trainers with chronic diseases and the benefits for their own health.

Methods Thirteen lay trainers (12 F, 1 M) completed a 3-step program that consisted of self-experience of a behavioral training (BT), providing BT to one fellow patient, and subsequently to a small group at home. Successful mastery of own migraine attacks was required for participation, and lay trainers received intensive guidance. Evaluation of the qualities of trainers took place post-BT by means of a specially constructed questionnaire. Their self-management was measured before self-experience of BT, post-BT and at 6-month follow-up by a headache diary and questionnaires.

Results The qualities of the 13 trainers were positively evaluated by 95 trainees; particularly their warmth, expertise, organization, explanation of BT, active control, and advice and guidance. Higher active control of lay trainers during the group sessions was significantly related to improvements on migraine frequency and internal locus of control in their trainees post-BT. Advice and guidance increased the likelihood of less attacks at follow-up and supportive encouragement promoted a higher internal locus of control. However, humor slightly increased the likelihood of more attacks post-BT, while fellowship and individualization negatively influenced internal locus of control. Lay trainers showed significantly more improvement in migraine frequency than their trainees at follow-up, as well as enhanced internal locus of control and quality of life.

Conclusions Participation in a stepwise training program can produce capable trainers and may positively influence their own health. Lay trainers may be more motivated to enhance their self-management skills as they have to present the benefits to their trainees.

Keywords: migraine, behavioral treatment, self-management, patient education, professional training

1. INTRODUCTION

There is an extensive body of research on self-management programs delivered by healthcare professionals, which aim at improving disease outcomes together with patients' self-efficacy to take control over their chronic disease (1-3). There is also increasing awareness that lay trainers with a chronic condition can adequately deliver this type of intervention (2, 4). Advantages are that lay trainers can function as a positive role model and provide credible information, they cost relatively less and, last but not least, may achieve beneficial effects for their own health (5-7). A recent review on lay-led interventions summarized the short-term results of 17 trials (n=7442) and found small but significant reductions in pain and disability and improved self-efficacy (4). Psychological well-being and health-related quality of life, however, were not significantly affected. These results were partly in line with those of our earlier randomized controlled trial (RCT) that showed a small short-term effect on attack frequency (8). Nevertheless, strong improvements were found in internal locus of control over migraine prevention and self-efficacy.

The present study concerns a further exploratory analysis of the RCT data and focuses on the qualities of lay trainers with migraine and the influence of these qualities on training outcomes. Despite the growing attention for lay trainers with chronic conditions, little is known about their qualities as trainers. Our previous pilot study suggested that the qualities of lay trainers mainly concerned their motivation of trainees, knowledge of premonitory symptoms, and sharing of disease-specific problems (9). They did experience difficulty, however, in providing feedback on the basis of the headache diaries of the trainees and in leading a group. Furthermore, during the sessions the lay trainers suffered from fatigue or migraine themselves. In their review on professional and lay trainers of cancer peer-support groups, Price et al. identified eight studies, but there was insufficient data to detect any differences between professionals and lay trainers (10). In general, trainers who actively intervened and provided a meaningful framework induced improved outcomes. Ozer et al. examined the impact of lay educators' qualities on the effectiveness of an AIDS prevention program among adolescents (11). Highly individuated lay educators were viewed positively, which was associated with a low risk for AIDS among the participants. These educators personalized the prevention program, e.g. by using personal stories and eye contact. A highly organized training environment was also related to greater improvements (11).

The third focus of this study concerns the impact of training fellow patients on the lay trainers' own health. Few quantitative data are available concerning whether lay trainers themselves benefit from providing the intervention (12). According to qualitative research, lay trainers' self-confidence and disease acceptance increased and their disease management improved (13). In addition, they appreciated the social contacts and comparisons with fellow patients, the altruistic act, and the feeling of being valued (12, 13). Considering the focus nowadays in healthcare on 'patient empowerment' (i.e. on shared responsibilities and active

disease management) it is worthwhile to examine the health changes in the providers (1, 2, 14).

This article concerns an explorative study that aims to: 1) evaluate the qualities of lay trainers with migraine, 2) examine the influence of these qualities on training outcomes in their trainees, and 3) to quantify the potential benefits for lay trainers' own self-management. Consequently, the research questions of this study were: 1) how did trainees evaluate the qualities of lay trainers post training, 2) did the qualities of trainers reduce attack frequency and enhance internal locus of control over migraine prevention in trainees post-training and at 6-month follow-up, and 3) which self-management results did lay trainers personally achieve regarding attack frequency, internal locus of control, quality of life, health status, and mastery of BT skills.

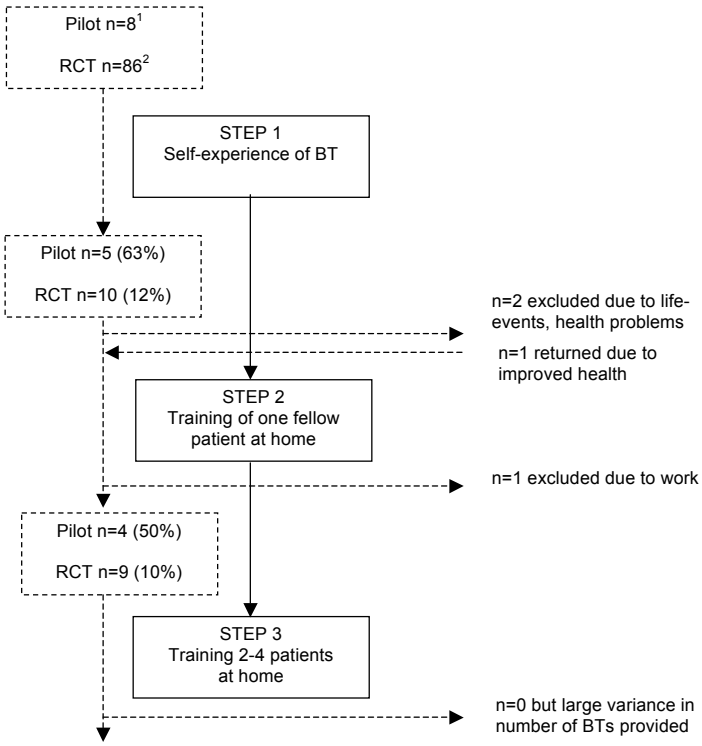
2. METHODS

2.1. Lay trainers with migraine

Figure I presents the flowchart of lay trainers with migraine during the training program. Nine patients (12%) were selected after self-experience of BT during the RCT, in addition to the five lay trainers from the pilot study. The selection instruments for participation in the RCT consisted of a standard questionnaire to establish the migraine diagnosis according to the International Classification of Headache Disorders, a prospective 4-week headache diary, and the SCL-90 psychopathology-screening list (15-18). Two headache specialists verified the diagnoses of migraine with or without aura and ruled out medication-overuse headache in case of doubt. There were about twice as many potential trainer candidates, but the majority gave priority to their own self-management rather than to following a training program. Two pilot trainers were excluded before step 2 due to life-events and health problems, one of them returned later because of an improved health status. A busy work schedule necessitated one lay trainer to stop after step 2 (individual training), but none of the other trainers dropped out or was excluded before step 3 (group training). Each trainer provided at least one group training, which included leading 7 BT sessions. However, some trainers only provided one training while others trained six groups of fellow patients. The mental load of providing BT in addition to work or family life was a reason for some trainers to deliver BT less frequently. Logistical problems were also a barrier, e.g. some trainers lived outside the city, and some trainees refused to travel too far. Finally, four out of nine trainers (44%) completed step 2 by assisting an experienced lay trainer during the group sessions. The main reason for this protocol deviation was the lack of appropriate candidates who were suitable to receive individual BT.

Similar to their trainees, lay trainers (n=13) were middle aged (mean age 45, range 24-58 years), predominantly female (1 man, 12 women) and highly educated (23% average, 77% high education level). At baseline the trainers did not significantly differ from the trainees

Figure 1 Flow chart of the stepwise training program for lay trainers with migraine



[1]In the pilot study, the first eight patients were trained by the first author
[2]In the third year of the RCT investigating trainees, no new patients entered the training program
BT (behavioral training), RCT (randomized controlled trial)

regarding migraine frequency, internal locus of control, quality of life, health status and medication use.

2.2. Design

Data collection took place from July 2003 until March 2007. The Ethics Committee of the University Medical Center approved the RCT. The lay trainers with migraine provided their behavioral training (BT) to six cohorts of patients over three consecutive years, who were randomly allocated to either BT or to the waitlist control group (8). The three experimental groups received BT during the fall and the three waitlist groups received BT directly after their waitlist period during the spring. As all patients received BT, they were all used for the analysis of this study. The qualities of lay trainers were evaluated by the trainees post-BT. Their self-management of migraine was measured before self-experience of BT (T1: months 0-1), directly after BT (T2: months 5-6) and at 6-month follow-up (T3: months 12-13). The selected

lay trainers started to train one new fellow patient during the follow-up period. There was no contact with the other participants during the follow-up period.

2.3. Behavioral training

The behavioral training (BT) was based on a clinical protocol for individual training, and tailored to the format of a self-management program (16, 17, 19, 20). Manuals supported BT and contained theoretical information, headache diaries with instructions, homework assignments and self-evaluations, and a CD-Rom with auditory relaxation exercises. Aim of BT was to prevent migraine attacks by: 1) identification and modification of triggers and premonitory symptoms, and 2) application of physiological and cognitive-behavioral self-regulation skills. BT consisted of seven 2-hour sessions spread over 10 weeks. Sessions 1 to 3 were conducted weekly and focused on 1) detection of triggers and premonitory symptoms by daily monitoring and 2) acquisition of relaxation skills by autogenic and breathing exercises twice per day at home (21-25). Sessions 4 to 6 took place every two weeks and focused on 1) the proactive application of physiological and cognitive-behavioral self-regulation skills under the condition that premonitory symptoms or triggers prevailed, and 2) a personalized prescription for behavioral attack prevention with specified conditions of being at risk, as well as actions and lifestyle changes to reduce this risk. Evaluation took place in session 7, which included the specification of individual goals and actions to maintain training skills.

2.4. Training program of the lay trainers

The development of the training program for lay trainers was based on Bandura's social cognitive theory stating that patients' ability to change increases with knowledge of their disease and with perceived self-efficacy in controlling their health behavior (26, 27). In our study, knowledge of migraine was provided as part of BT, which aimed to promote self-efficacy in the participants. The next task involved the ability to coach fellow patients while maintaining own migraine self-management and, in this respect, serving as a role model for new patients. Other self-management programs have emphasized the relevance of self-experience of lay leaders, and our pilot study underscored the importance of a graded and guided training program (summarized in Table I) (9, 13).

We employed a 3-step program. For step 1 it was mandatory that a lay trainer underwent BT and completed it successfully (self-experience). Successful performance was defined by: 1) a decrease of migraine frequency registered in the headache diaries throughout the training, 2) a positive self-report of BT skills measured by a questionnaire at the end of the training (mean score 3 or higher on a 5-point Likert scale, see 'Measures'), and 3) a good mastery of the relaxation exercises and registration assignments observed by the trainer during the group sessions. On the basis of these measures we invited suitable and motivated trainer candidates for an interview (see Table I). In step 2 and step 3 difficulty increased from providing individual BT to coaching a small group, while guidance decreased from 6 supervisions (step 2)

Table 1 Stepwise training program for lay trainers with migraine

Phase	Targets	Guidance	Evaluation (tool)	Selection
Step 1: Self-experience	**Behavioral prevention of migraine attacks by**:	**Manual** containing theoretical information, training program per session and headache diary with instructions. **Organizer** containing homework assignments and evaluation forms.	**Successful reduction of migraine attacks** (established with the headache diary).	**Interview** to assess the motivation and capacities of trainer candidates in the context of positive training results.
	1. Identification and modification of triggers and premonitory symptoms	**Lay trainer with migraine** providing individual feedback and motivational and emotional assistance.	**Good mastery of BT skills** (according to self-report questionnaire and self-observation of lay trainer).	With positive training results, trainer capacity and motivation → **entry to step 2**.
	2. Application of physiological and cognitive-behavioral self-regulation skills.	**Group member** (`migraine buddy') offering bilateral assistance in completing assignments and exercises.		
Step 2: individual BT	1. **Self-awareness of BT skills** and planned **actions** for future migraine self-management	**Manuals** containing topics per session, a time scheme, instructions for assignments and exercises and take home messages per session, with tips of experienced lay trainers.	**Results trainee and coaching** (open questions **Trainers` qualities and pitfalls** (with a semi-structured interview of the trainee)	**Review** of training results of trainee, of trainers' qualities and pitfalls and of the status of trainers' own self-management
	2. **Development of basic trainer skills** by practicing instructions, tailored feedback, emotional assistance and motivation, time management and evaluations of progress, and by adapting personal expertise to the process of change in the trainee.	**Supervision (6x)** by telephonic contact and e-mail, based on track records of progress per training session, in order to support the learning process, to check trainers' needs and to promote trainers' adherence to the protocol.	**Knowledge of BT content** and **acquisition of trainers' skills** to coach their trainee in attack prevention (as assessed in the supervision).	With maintenance of trainers' own migraine self-management and positive results of trainee → **entry to step 3**.

	3. **Reflection on personal attitude** concerning the degree to which it was neutral, empathic, encouraging, supportive and respectful.	**Website** for downloads of manuals and handouts per session, with examples of difficult training situations and their solutions, as well as the material of the workshops for trainers.		
Step 3: BT small groups	Extension of the skills of trainers with those related to **group management**	**Supervision (3x)** focusing on (1) group composition and diversity in headache history and self-management experience (2) individual progress of trainees, and (3) directives for the maintenance of BT skills.	**Knowledge of BT content**, **maintenance of trainers' skills** and **group management** (as assessed in the supervision).	Additional evaluation concerned the monitoring of health problems or life-events that could obstruct the trainers' tasks.

BT: Behavioral Training

to 3 supervisions (step 3). BT instructions and assignments were taken from clinical protocols, while directives for communication skills and personal attitude were derived from didactic material for medical (Bachelor) students (16, 17, 28-30). Lay trainers received a payment of 150 euros for individual BT and 300 euros per group.

Lay trainers received an extensive manual, which included information and instructions, and evaluation forms per BT session. The supervision aimed to check the trainers' needs, to support the development of the skills of trainers, and to promote adherence to the protocol. The supervision was based on the track records per trainee and was conducted via telephone contact and by e-mail. Supervision in step 2 took place after each BT session. It was personalized to support self-awareness and evaluation of BT skills, and to the maintenance of migraine self-management, the development of basic trainer skills, the provision of feedback, reflection on personal attitude, time management of the sessions, and to motivate the trainees in their process of change. Supervision in step 3 was less frequent and (in addition to the above-mentioned targets) was directed at managing the group process, paying attention to different self-management processes, and at promoting the sharing of problems and solutions between group members.

All trainers were invited to participate in four 3-hour workshops, offered bi-annually by a senior clinical psychologist with expertise in migraine management and a physical therapist with expertise in self-regulation by relaxation methods. These workshops aimed at advancement of trainers' self-efficacy by modeling, guided practice, vicarious learning and goal setting (31).

As mentioned earlier, step 1 was evaluated by headache diaries, a self-report questionnaire of BT skills, and observations by the trainer. In step 2 the individual provision of BT was reviewed by a written evaluation provided by the trainer, while the functioning of the lay trainer as experienced by the trainee was assessed in a semi-structured interview conducted by the first author. Progress to step 3 depended on the appraisal of the qualities of trainers. In step 3 no further selection took place, except for health problems or other life-events that might obstruct the trainer tasks.

2.5. Measures

There were no psychometrics tools available for assessing the qualities of lay trainers. Since `patient empowerment' was the major issue of this study we wanted to evaluate the qualities from the perspective of their trainees. In addition, consensus on how to adequately measure patient satisfaction is limited and many different instruments exist (32). There is also a need for disease- and care-specific items (33). Therefore, we constructed a novel questionnaire to evaluate the qualities of lay trainers after their group training. First, the literature review of Ozer et al. provided a theoretical foundation based on the social cognitive theory, social comparison processes, and research on the influence of training or `classroom' environments on the effectiveness of peer educators (11). Constructs as `individualization', `organization', `similarity', `perceived expertise' and `humor' were selected from this literature review. The quality of `fellowship' was derived from the study of Hainsworth and Barlow, expressing the ability of sharing disease-specific problems and learning from each others disease management (13). Last, skills of professional trainers that may be relevant for lay trainers were derived from the study of psychotherapeutic interventions, conducted by Trijsburg et al, and concerned `warmth', `supportive encouragement', `training rationale', `active control', `advice and guidance' and `expertise' (34).

In the present study the first, second and fourth author formulated two items per theoretical trainer quality, based on the above-described theoretical constructs. Table II lists the 22 items of the Questionnaire on the Qualities of Lay Trainers. Trainees assessed the qualities of trainers on a 4-point Likert scale. The reliability of the pair-wise qualities was good (Cronbach's α 0.68 to 0.88). After performing an exploratory factor analysis we did a confirmatory factor analysis. The best fitting model was identified by five performance measures (see Table III). The factor loadings of the items were estimated (loading $\geq \left|0.60\right|$ indicating high relevance). The statistical program Mplus for Windows (version 4.0) was used. The model based on the theoretical constructs with 11 qualities turned out to be more plausible than a model covering one general factor, with factor loadings ranging from 0.82 to 0.98. The χ^2 test divided by the number of degrees of freedom was better, WRMR was very good, and CFI and TLI were excellent. The performance based on RMSEA was inconclusive though sufficient.

The self-management of lay trainers and their trainees was assessed by self-reported measures, i.e. a prospective headache diary and questionnaires. Primary outcome attack frequency

Table 2 Questionnaire on the qualities of lay trainers

Qualities of Lay Trainers/ items	CFA Standardized Loadings
Warmth	
1. My trainer was sympathetic with my situation	0.98
2. I felt I was supported by my trainer	0.98
Expertise	
3. My trainer was an expert	0.85
4. My trainer knew what was involved with migraine	0.85
Individualization	
5. My trainer made the training interesting by using personal examples	0.92
6. My trainer made a clearly personal contribution	0.92
Similarity	
7. My trainer had a lot in common with me	0.96
8. I recognized a lot in the situation of my trainer	0.96
Humor	
9. My trainer had a sense of humor	0.89
10. During the training we could also have a laugh	0.89
Fellowship	
11. It helped that the trainer is also a migraine patient	0.82
12. My trainer was a good example of how you can cope with migraine	0.82
Organization	
13. My trainer organized the sessions very well	0.92
14. My trainer kept a good eye on the time	0.92
Supportive encouragement	
15. My trainer encouraged me to keep on practicing	0.88
16. My trainer kept an eye on my personal progress	0.88
Training rationale	
17. My trainer could explain the training well	0.92
18. My trainer could clearly explain why the training was useful for migraine	0.92
Active control	
19. My trainer could stay focused on a topic when necessary	0.93
20. My trainer intervened if we wandered off the topic	0.93
Advice and guidance	
21. My trainer gave advice that was useful to me	0.87
22. My trainer showed me various ways how I can practice the training	0.87

CFA: confirmatory factor analysis

was assessed as follows: patients registered headache intensity and migraine characteristics in a 4-week diary, including associated symptoms and their medication use (16, 17). The second primary outcome, internal locus of control, was assessed with the 33-item Headache Specific Locus of Control Scale (HSLC) (35). The subscale internal locus of control indicates the degree

to which participants perceived control over migraine prevention (range 11-55). The 25-item Headache Management Self-Efficacy questionnaire (HMSE) was translated into Dutch during

Table 3 Performance of the exploratory factor analysis (EFA) versus the confirmatory factor analysis (CFA)

Performance indicators	EFA	CFA
χ^2/df (score <2.0 = good fit)	(788.75/209) 3.77	(322.72/165) 1.96
CFI (0.0 to 1.0; 1.0 = perfect fit)	0.96	0.99
TLI (0.0 to 1.0; 1.0 = good fit)	0.95	0.98
RMSEA (0.05 = close fit)	0.17	0.10
WRMR (0.90 to 1.0 = perfect fit)	1.33	0.80

CFI: Comparative Fit Index, TLI: Tucker-Lewis index
RMSEA: Root Mean Square Error of Approximation, WRMR: Weighted Root Mean Square Residual

the first year of data acquisition and therefore could not be administered to 10 of the 13 trainers (36). As a consequence, self-efficacy was not analyzed for the present study.

Secondary outcomes, quality of life and health status, were measured by the 20-item Migraine-Specific Quality of Life Questionnaire (MSQOL) and the Dutch version of the Medical Outcomes Study 36-item Health Survey (SF-36) (37-39). A higher sum score on the MSQOL reflects a better quality of life between attacks (range 20-80) (37). Raw scores of the eight subscales of the SF-36 were linearly converted to a 0-100 scale, and a mean score was calculated for physical and mental health, with higher scores indicating a better health status. Mastery of BT skills was evaluated with a self-report questionnaire that was derived from the clinical protocol (20). Ten items evaluated the mastery of relaxation skills and seven items measured the mastery of trigger-management on a 5-point Likert scale.

2.6. Data analysis

For research question 1 the evaluation of the qualities of trainers was established by calculating the mean percentage of trainee responses for each pair of items. For research question 2 the sum score of the two items per quality was calculated. The method of backward elimination in the stepwise linear regression analysis was applied, with attack frequency and internal locus of control at T2 and T3 as dependent variables, adjusted for their baseline values. To test their predictive value the 11 qualities of trainers were included at once to the equation. The percentage of variance (R^2) explained by the regression model was used as model performance and the standardized regression coefficient (β) as a measure of relative importance of the individual predictor variables. Because of the exploratory function of this analysis a p-value<0.20 was allowed (40). A sensitivity analysis was applied to test the robustness of the standardized regression coefficients (41). Regression analyses were performed on all trainers except one (each time one trainer was left out) for the relevant (significant) qualities of trainers (13 analyses because of 13 trainers). Subsequently, the mean of the βs was calculated and

the standard deviation, and this mean β was compared with the overall standardized regression coefficients. Last, because of non-normal distributions the scores for attack frequency and internal locus of control were transformed (square root). For research question 3 paired t-tests were applied to analyze the changes in lay trainers' attack frequency, internal locus of control, quality of life, health status and mastery of BT skills after self-experience (T1→T2), and the training of fellow patients (T1→T3). All significance testing took place at the 0.05 level of significance (two-sided). Because of the small sample size and explorative character of this study Bonferroni's correction was not performed to control for Type I error. SPSS for Windows version 11.0 was used to conduct the statistical analyses.

3. RESULTS

3.1. Evaluation of lay trainers' qualities

The qualit ies of lay trainers were very positively evaluated (see Table IV). `Warmth', `expertise', `organization', `training rationale', `active control' and `advice and guidance' of the lay trainers with migraine were positively evaluated by more than 90% of the trainees. `Individualization', i.e. personalizing the content of the training program, was reported by 81%. Only `similarity' differed as almost 50% of the trainees did not recognize his/her situation in that of their trainer.

3.2. Influence of the qualities of lay trainers on BT results in the trainees

The results of the linear regression analyses are presented in Table V. This table shows that only `active control' of the lay trainers over the group sessions was significantly related to attack

Table 4 Evaluation of the qualities of lay trainers by the trainees[1]

Qualities of Lay Trainers	Strongly disagree	Disagree	Agree	Strongly agree
Warmth	0	1	68	31
Expertise	0	4	54	42
Individualization	0	19	62	19
Similarity	1	47	48	5
Humor	0	12	67	21
Fellowship	0	14	55	31
Organization	0	5	62	33
Supportive encouragement	0	10	70	20
Training rationale	1	5	67	28
Active control	0	8	69	23
Advice and guidance	0	9	72	19

[1]The figures represent mean percentages (2 items per category)

frequency post-BT in the trainees (β=-0.33, p=0.002). `Humor' of trainers somewhat increased the probability of more migraine attacks post-BT (β=0.17, p=0.1). An `active control' of lay trainers over the training process was also positively related to perceived migraine control in the trainees post-BT (β=0.33, p=0.001). However, the quality of fellowship was significantly and negatively associated with internal locus of control (β =-0.22, p=0.02); similarly, the quality of individualization was negatively related (β=-0.16, p=0.13). Useful `advice and guidance' during BT slightly increased the possibility of less migraine attacks in the trainees at follow-up (β=-0.16, p=0.09). Supportive encouragement by trainers was significantly and positively associated with a higher internal locus of control at follow-up (β=0.21, p=0.04). Again, fellowship was somewhat negatively related to patients' internal locus of control (β=-0.14, p=0.16). The sensitivity analysis shows that overall the mean of the βs (fourth column) was in line with the standardized regression coefficients (second column). Furthermore, the standard deviations of these mean βs were within acceptable limits.

Table 5 Relevant qualities of trainers in relation to attack frequency and internal locus of control post-BT and at follow-up

Primary outcomes	Relevant qualities of trainers[a]	βs[a]	R^2	βs[b] Mean (SD)
Attack Frequency T2	Active control	-0.33	33%	-0.34 (0.04)
	Humor	0.17		0.17 (0.03)
Internal locus of control T2	Active control	0.33	52%	0.36 (0.03)
	Fellowship	-0.22		-0.21 (0.04)
	Individualization	-0.16		-0.18 (0.03)
Attack frequency T3	Advice and guidance	-0.16	26%	-0.16 (0.02)
Internal locus of control T3	Supportive encouragement	0.21	44%	0.16 (0.04)
	Fellowship	-0.14		-0.13 (0.02)

T2 is post-BT, T3 is at 6-month follow-up, BT is behavioral training

[a]Standardized regression coefficients of the backward elimination in the stepwise linear regression analysis in which qualities of trainers with a p-value >0.20 were excluded.

[b]Mean βs of the sensitivity analysis in which regression analyses of all trainers except one were performed and the robustness of the standardized regression coefficients were tested.

3.3. Changes in self-management of lay trainers

The average attack frequency was reduced in all lay trainers with migraine (n=13) from 3.2 at baseline to 2.3 attacks per 4-week period post-BT (29%), and significantly improved from baseline to 1.6 attacks at follow-up (52%, p=0.02). Trainers' beliefs that factors influencing the occurrence and relief of migraine attacks are under one's own control increased over time. Again, the change from baseline to follow-up was significant (p=0.04). Migraine-specific quality of life and health status also improved over time, although only quality of life was significantly increased at follow-up. Last, lay trainers' mastery of BT skills significantly improved from post-BT towards follow-up, i.e. from 3.3 to 4.0 on a 5-point scale (relaxation skills), and from 3.2 to 3.6 (detection and modification of triggers and premonitory symptoms) (Tabel VI).

Table 6 Lay trainers' change in self-management over time

Measure/time	Lay trainers (n=13) Mean (SD)	T2 – T1 T3 – T1 Mean Δ	95% CI Δ	t	p
Attack Frequency[a]/ T1	3.18 (1.7)				
T2	2.27 (1.9)	-0.91	-2.23 to 0.42	-1.53	0.16
T3	1.64 (1.4)	-1.55	-2.76 to -0.33	-2.83	0.02*
Internal locus of control/T1	34.4 (13.8)				
T2	41.4 (10.8)	7.00	-6.22 to 20.2	1.30	0.24
T3	46.1 (7.4)	11.7	0.71 to 22.7	2.61	0.04*
Migraine-specific QOL/T1	59.6 (7.2)				
T2	60.9 (5.9)	1.3	- 3.0 to 5.51	0.69	0.51
T3	63.3 (6.5)	3.63	0.17 to 7.08	2.48	0.04*
Physical health status/T1	71.9 (18.0)				
T2	64.1 (18.2)	-7.8	- 31.4 to 15.8	-0.78	0.46
T3	85.7 (8.1)	13.8	-1.62 to 29.2	2.12	0.07
Mental health status/ T1	71.1 (17.6)				
T2	80.3 (9.20)	9.2	-6.25 to 24.5	1.40	0.20
T3	78.1 (13.5)	6.9	-5.46 to 19.3	1.32	0.23
Relaxation skills[a]/T2	3.35 (0.37)				
T3	4.00 (0.60)	0.65	0.22 to 1.08	3.57	0.009*
Trigger-management[a]/T2	3.23 (0.45)				
T3	3.64 (0.49)	0.41	0.17 to 0.65	4.00	0.005*

* Significance level was set at $p<0.05$

[a] Figures of trainers who were selected during the pilot (n=4) concern attack frequency and mastery of relaxation skills and trigger-management, as HSCL, MSQOL and SF-36 were not administered during the pilot study

BT (behavioral training)

T1 (baseline), T2 (post-BT) and T3 (follow-up)

4. DISCUSSION AND CONCLUSION

4.1. Discussion

This study explores the qualities of lay trainers with migraine, the influence of these qualities on training outcomes, and the changes in their own self-management results. Thirteen lay trainers (12 F, 1 M, middle-aged) completed a 3-step program that consisted of self-experience of a behavioral training (BT), providing BT to one fellow patient, and subsequently offering BT to a small group at home. Successful self-management of migraine attacks was a requirement

to enter the training program of lay trainers. Since psychometric tools to evaluate the qualities of lay trainers were lacking, we developed a 22-item questionnaire. This questionnaire was based on a literature study, and its psychometric properties in this sample proved to be satisfactory (11, 13, 34). The qualities of trainers were positively evaluated; in particular their warmth, expertise, organization, training rationale, active control and advice and guidance were positively rated by more than 90% of the trainees. This finding, however, must be considered with caution as a very high number of satisfied patients is common in patient satisfaction research (32). In addition, the highly positive evaluation might have been an overestimation of the actual qualities as trainees may have wanted to please their lay trainers or reward their efforts. Similar to other lay-led interventions, none of the trainers produced any adverse events (4).

Higher active control of trainers during the group sessions was significantly associated with a lower attack frequency and a higher internal locus of control post-BT in their trainees. Supportive encouragement was positively associated with internal locus of control over attack prevention at follow-up. Actively leading a group and balancing attention may indeed be a successful strategy, considering the condensed content of BT and the numerous exercises and assignments. In addition, trainers who stimulated patients to keep on practicing and kept an eye on the personal progress may have facilitated the internalization of BT. In contrast to our expectations, the trainer as a role model and the possibility of sharing experiences was negatively related to internal locus of control (13). This opportunity of sharing may increase patients' knowledge about the disease, but too much conversation could hamper the performance of the exercises as well. In line with the social cognitive theory of Bandura, successful self-experiences are important for controlling one's health behavior (26). The lack of influence of individualization may be explained by the fact that the unique and effective contribution of trainers may not have been identified by the questionnaire. In the study of Ozer et al. observations of the peer-led sessions were used to specify the characteristics of successful educators (11). In conclusion, the present study confirms the relevance of active control and highlights the quality of supportive encouragement (10). The contribution of other qualities of trainers, despite their positive evaluation, remains questionable.

The lay trainers (n=13) showed significant improvements in migraine frequency, internal locus of control and quality of life towards the follow-up measurement. The improvement in migraine frequency of lay trainers was considerably larger than that of their trainees (52% versus 23% for trainees) (42). As trainers were selected on the basis of positive outcomes, confounding by indication could have explained these results. However, in contrast to the major difference at follow-up, the difference between lay trainers and trainees was not substantial post-BT (29% versus 21% for trainees). Therefore, selection bias seems less likely to explain the positive findings. During the follow-up period lay trainers provided BT to one new patient under supervision and also participated in one workshop. This part of their training program was aimed at increasing their self-awareness of BT skills and planning actions for future self-

management, and developing basic trainer skills. This continuation may explain why modest headache improvements directly after BT increased to substantial improvements at 6-month follow-up. Previous qualitative research also suggested beneficial outcomes for lay trainers (12, 13). Lay trainers might be more motivated to deepen their training skills, as they have to present the benefits of self-management to their trainees. We also compared post-hoc the results of lay trainers with their true peers, who underwent BT contemporaneously. Because of the small number per cohort of trainers these comparisons could not be tested. The lay trainers achieved overall better results than their peers on headache improvement, with the exception of one trainer who showed an increase of attack frequency post-BT. The results on internal locus of control, however, were inconclusive. Regarding the mastery of BT skills there were minor differences between lay trainers and their peers post-BT. However, lay trainers reported an increase of BT skills at follow-up measurement, whereas their peers assessed their BT skills as the same or somewhat lower level. In conclusion, the limited evidence suggests that participation in a stepwise training program promotes trainers' own self-management.

A strong point of this study is the clarification of a disease-specific protocol for trainers whereas most self-management studies make use of a generic approach. Furthermore, a novel and reliable questionnaire was constructed to evaluate lay trainers' qualities. Research on this topic is scarce and the present study might fill the gap between practice and research. Another strong point is that changes in lay trainers' own self-management were quantified by relevant clinical instruments, i.e. a headache diary (4). Limitations of this study are the small sample size and the low generalizability as almost all trainers were female, middle-aged, Caucasian and highly educated. Furthermore, chance findings may have played a role in exploring the associations found between the qualities of trainers and improvements of trainees. Also, because we did not control for the effects of attention or regression to the mean, the improvements among lay trainers cannot be attributed solely to the training program. Another limitation is that both trainers and trainees knew their condition and this may have induced information bias when filling in the questionnaires. Finally, self-reported measures (with possible bias) were used, and the questionnaire to evaluate the qualities of lay trainers was only validated for this particular study.

4.2. Conclusions and practice implications

This study shows that participation in a stepwise training program can produce capable trainers and can positively influence their own health. Despite the demanding tasks placed on the trainers, their qualities were positively evaluated. Higher active control of lay trainers and supportive encouragement were related to improvements in attack frequency and internal locus of control. External validation of our novel questionnaire for lay trainers in other samples is needed. The intensive training program could be simplified if lay trainers would only provide an individual BT rather than for a group. In our follow-up study we also suggested that a group format may be a bridge too far (42). Another recommendation is to develop lay trainer's skills

more systematically, e.g. teach them to actively control the sessions on the basis of analyzing videotapes. More qualitative research on the qualities of trainers is also recommended, e.g. to characterize the subgroup of lay trainers with good training results. Further development of the training program for lay trainers would be more justified if more evidence becomes available regarding longer-term outcomes of self-management programs by lay leaders (4).

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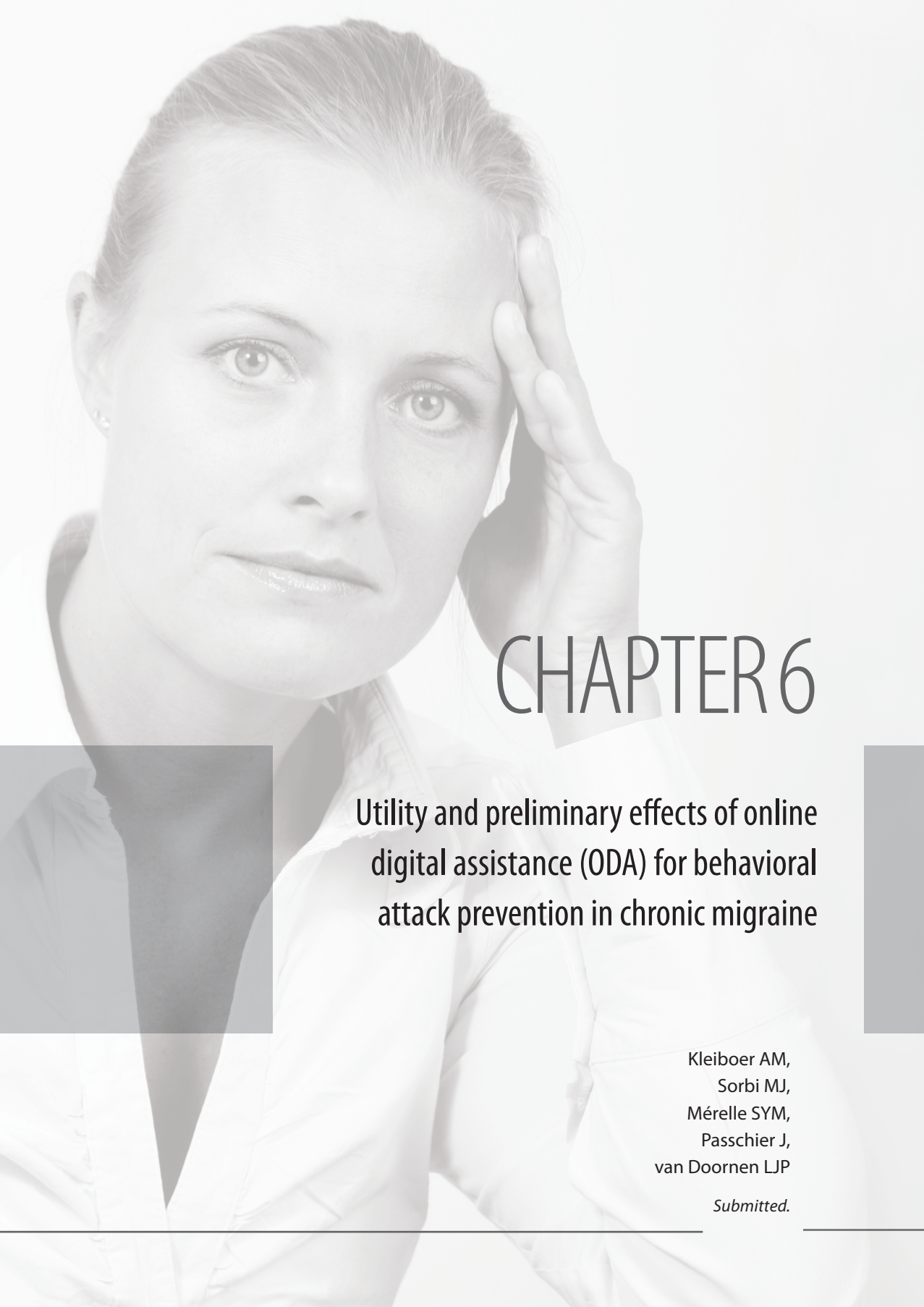


CHAPTER 6

Utility and preliminary effects of online digital assistance (ODA) for behavioral attack prevention in chronic migraine

Kleiboer AM,
Sorbi MJ,
Mérelle SYM,
Passchier J,
van Doornen LJP

Submitted.

ABSTRACT

Objectives 1) Establish the utility of `online digital assistance' (ODA), a generic software-based method designed to support behavioral training (BT) in migraine. 2) Test whether ODA can produce surplus effects in BT.

Methods Utility -feasibility and acceptability- was based on 44 migraine patients who received ODA as an adjuvant to BT. ODA tracking files were used to determine ODA feasibility. Acceptability was assessed by a structured interview. To examine ODA effects, 31 migraine patients who received ODA during BT and at 6 months follow-up were compared with a matched group of 31 participants who received BT only.

Results Feasibility was established based on minimal technical problems, good compliance and successful execution of ODA. Acceptability was confirmed by positive participant responses concerning usefulness, supportiveness and low burden. Finally, ODA participants did not mark better improvements considering migraine attack frequency, internal control and migraine-specific quality of life compared to those that underwent BT only.

Conclusion ODA is feasible and highly accepted by participants. Whether ODA can induce higher gains remains to be established.

Practice implications ODA has the ability to capture and influence critical moments as they happen in the patient's everyday life and is perceived to support self-care in migraine patients.

Key words: Migraine, Behavioral training, PDA, Online Digital Assistance, *e*Health

1. INTRODUCTION

A prominent mission report of the Dutch government on ICT and health care put early detection, prevention and self-management in chronic disease on the agenda [1]. The report emphasized the need for intelligent tools for 1) feedback on health status and health behavioral training, 2) mobile distance-monitoring of symptoms and medication use, and 3) home-based support of self-care. In accordance with these recommendations we developed `online digital assistance' (ODA). ODA is a generic software-supported method, which combines mobile real-time monitoring of actual state with direct and personalized coaching of health behavior in real life [2]. A current ODA application was designed to support self-management training for behavioral attack prevention in chronic migraine.

Migraine is a common neurological disorder, affecting 6% of men and 15-18% of women in the general population [3,4]. The disorder is characterized by attacks of severe headache accompanied by nausea, vomiting and sensitivity to light, sound and smell, and is precipitated by a visual aura in part of the patients [5]. Migraine symptomatology reflects a genetically primed hypersensitive brain [6], responding to internal and external changes in the patient's environment in the hours before a migraine attack sets in [7]. This sensitivity reflects a susceptibility to trigger factors (e.g. stress, weather conditions, hormonal changes or skipping meals) and the occurrence of premonitory symptoms (e.g. negative affect, yawning, or irritability) [8].

Pharmacological treatment of migraine is focused on the abortion and prevention of attacks [4,9]. In addition, the utility of behavioral training (BT) as a preventive treatment option in migraine is firmly established and recommended in neurological guidelines for headache [10,11]. BT has two goals: 1) early identification of migraine triggers and premonitory symptoms and 2) use of physiological and cognitive-behavioral self-regulation skills to prevent attack occurrence [12]. Meta-analytic review showed an average improvement of 35-55% in migraine frequency when BT is provided individually by health care professionals [12]. Currently the focus in health care on both patient empowerment and cost-effectiveness promotes self-management programs for chronic disorders [13] that are delivered by patient trainers [14]. We therefore developed a self-management BT program to be delivered to small groups by lay trainers with migraine at home, and investigated its effectiveness in a randomized controlled trial [15], with a 6-month follow-up [16].

The BT program consisted of seven 2-hour sessions, spread over 10 weeks [15,16]. Sessions 1 to 3 focused on detection of migraine triggers and premonitory symptoms by means of a paper headache diary, and learning of voluntary self-relaxation skills through daily practice of autogenic training at home. While daily exercise continued, sessions 4 to 6 focused on proactive application of physiological and cognitive-behavioral self-regulation skills when premonitory symptoms or triggers prevailed. This was concluded with the writing of a personalized prescription for behavioral attack prevention. Evaluation took place in session 7. The

issue was whether the pursuit of both BT goals would profit from mobile real-time monitoring and direct personalized coaching through the Internet.

ODA was employed through a personal digital assistant (PDA) with integrated Internet facility [2] and thus permits direct interaction independently of time or space when attack prevention in migraine is at stake. The ODA monitoring feature builds on previous experience with electronic diaries in migraine and chronic pain and is used to support the timely detection of attack precursors (the first goal of BT) [17-19]. The ODA coaching feature is grafted on the possibility to collect electronic diaries wirelessly and safely directly upon completion, and return advice through the Internet that is tailored to the patient's momentary state. The latter is employed to reinforce preventive actions against attack occurrence (the second BT goal).

ODA was tested in five patients who had previously completed BT and was well received and showed to work [2]. This set the stage to investigate the utility of ODA in a larger patient group, in an effort to directly reinforce migraine self-management while patients were still in training. In addition, we wanted to explore whether ODA could strengthen the effectiveness of the present BT, which was offered with minimal professional guidance. This might show directly after the training, and/or ODA might promote relapse prevention after patients were left to their own self-care. Therefore ODA was offered *in-training* during the last three weeks of BT in a subgroup of patients participating in the randomized controlled BT trial, and ODA was offered again to the same patients as a *fresh-up* in the three weeks preceding the 6-month follow-up measurement of this trial [15,16].

The first research issue was to establish the utility of ODA in 44 migraine patients. Utility depends on the feasibility and acceptability of ODA when employed while patients are in training. *Feasibility* will be confirmed when (1) technical problems in using ODA are minimal, (2) execution of monitoring and coaching is successful, and (3) participants comply with online monitoring to the extent that ≥80% of the diaries are completed [20-22]. *Acceptability* depends on whether participants (1) rate ODA as being useful, supportive and not burdening and (2) experience ODA as helpful in reinforcing the two BT goals. Given the novelty of ODA, positive and negative experiences with the method were also explored by a structured evaluative interview.

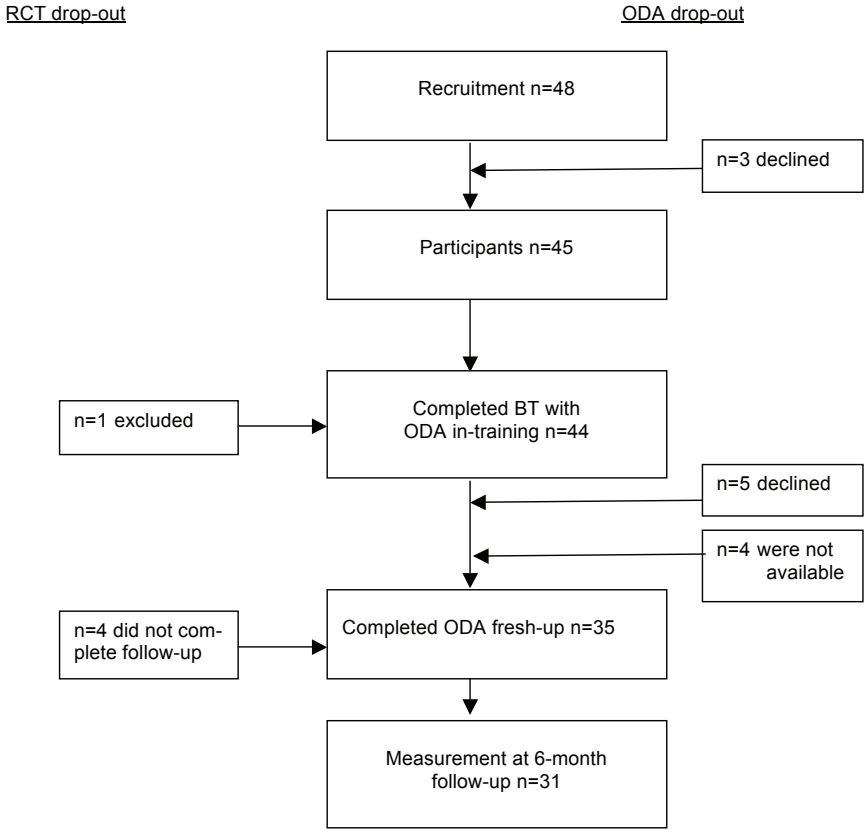
The second research issue was to test whether ODA produced surplus benefits of BT, primarily regarding improvement of attack frequency (prevention), and secondarily regarding an increase in internal locus of control and migraine specific quality of life. For this purpose, 31 patients who received ODA in-training and as a fresh-up, and who had completed all measurements (ODA+), were compared post-training and at 6-month follow-up with a matched group of 31 patients who completed BT without ODA (ODA-). Regarding this aim, we underscore that the present study was conducted within a randomized controlled trial of the effectiveness of BT, which limited the opportunity for a controlled testing of the ODA effect as such.

2. METHOD

2.1. Participants

A sub-sample of the participants in the BT randomized controlled trial (n=48: 13 training groups) was invited to receive ODA (see Figure 1 Flow Chart) [15,16]. BT participants were

Figure 1 Flow chart of ODA participants



Reasons for attrition per phase of study:

Study phase		Reason
Before start of ODA in-training	N=3	declined because of time constraint / work
During BT	N=1	excluded due to severe mental problems
Before start of ODA fresh-up	N=4	inconvenient time: being abroad (2), testing a new medication (2)
	N=5	declined because of time constraint /work (3), objections against ODA (2)
During 6-months follow-up	N=4	did not complete the follow-up measurements

recruited through the websites of the Dutch Society of Headache Patients and university departments, newspaper advertisement and referral by local headache specialists. Inclusion criteria for BT were, that migraine fulfilled the IHS classification criteria [5] and involved 1-6 attacks during 4 weeks, no overuse of abortive medications (>4 triptans, >2 ergots a week), and of psychopathology according to SCL-90-R norms for the clinical population (total score >178) [23]. Exclusion criteria were headache occurring on 15 or more days per month, migraine duration <1 year, and migraine onset at age >50 referring to underlying organic disease [24].

2.2. Design

The randomized controlled trial compared an intervention group receiving BT (N=51) with a waiting list control group (WLC; N=57) who underwent BT after their waitlist period of 3 months. Outcome measures were assessed immediately after BT [15] and at 6-month follow-up [16]. Participants in the ODA+ group were divided over the BT and WLC condition, and were matched with participants in the ODA- group on condition (BT or WLC), gender, age, education, and migraine attack frequency at 4-week baseline.

2.3. Online Digital Assistance

ODA runs on advanced and protected clinical software [2]. *Online monitoring* is grafted on the Experience Sampling Method (ESM) [19,20] or Ecological Momentary Assessment (EMA) [22,25], which is used to measure fluctuating states, behaviors and cognitions reliably in real life [26,27]. In ESM/EMA, participants are prompted at random moments to complete an electronic diary. This generates valid real time assessments unbiased by retrospection [22]. In the current study, online monitoring is used to assess 1) migraine attacks, 2) precursors of migraine and 3) actions taken by the participant to prevent attack occurrence. *Online coaching* involves direct and personal feedback concerning 1) the participant's actual state regarding attack precursors and attack risk: this is displayed by a traffic light and clarified by brief information

Figure 2 the template for ODA coaching on the PDA screen

Table 1 Examples of the three parts of ODA coaching in the case of, respectively, high, medium or no attack risk

	actual state (first BT goal)	**tips/advice** (second BT goal)	**Positive reinforcement**
red light high attack risk	How bad: you are in an attack just now. Good for you that you are at home – disconnect the phone (and your PDA if you want). Lay down.	Just let go. Close your eyes, close your mind. Consider your plans and all the rest later.	I wish you a speedy recovery: this is all that counts now. Talk to you later – we stay in touch.
	You are close to an attack: light headache, stiffness in neck & shoulders, eye strain. You feel worn out; you eat a lot of sweets.	Your body is over sensitive & needs rest. Loosen neck/ shoulders, stop working, drink water. No worry: your productivity will profit later.	Choose for yourself now: you can still do things to avert or amend a heavy attack. Good luck!
	Attention! You are in the `danger zone': light headache, lots of body tension. Take extra care because of your period!	Let your shoulders drop, practice differential relaxation while choosing light activities. Get some fresh air (bright light! - so take your sunglasses).	Allow yourself some repose. Do not be too harsh on yourself. You can catch up later. Take care!
orange light medium attack risk	You had a bad night, missed lunch & are very busy. Your neck/shoulders are tight and painful. You don't feel up to much	Practice cue-relaxation & neck/shoulder exercises; eat & drink (light); make choices & skip tasks/ activities.	You can do this without anybody noticing. Your health comes first!
	You don't have a headache yet – good! – but lots of warning signals: down, tired, difficulty concentrating; dry mouth, paleness etc.	Close your work for the day (it's 5 PM!), take a stroll / time-out with fresh air. Have a healthy, light meal. Can somebody cook for you?? Try and ask!	You will feel better if you slow down. Success with this – you will manage.
	You feel stirred up, angry, sad and weary. You just received bad news – so sorry. Give it some time; don't overpower this.	You took a break - good! Use belly breathing. Try positive thinking & be gentle with yourself. You can't change things now: try to divert attention.	Solutions will come in time. Let it not ruin your day. I'll be back & hope you are better then.
green light no attack risk	You are fine: fit, satisfied, composed. You did well this morning with your regular exercises & paid attention to your neck and shoulders.	Go on like this: you are doing very well & much better than last week. Well done! But keep a steady pace, OK?	You are well on track – I am glad for you & see the progress. Enjoy the party tonight!
	Yes! All is well: you are concentrated, energetic and content. You tune in well with things and there is no strain at the moment.	Keep this up. Remember the belly breathing and the cue-relaxation in the next hours. Plan an enjoyable & healthy meal for this evening.	It is good to see that you are doing well: this is rewarding for me too! Have a nice day.
	You are at ease, you do things you enjoy, there are no warning signals - that's good.	Attend to body posture; continue interruptions of computer work: very good! Role your shoulders; watch for tenseness neck in business meeting.	Go on like this. I wish you a successful and pleasant meeting!

from the present diary; 2) advice or tips for preventive action, and 3) positive reinforcement supported by an emoticon. Figure 2 provides an example of the feedback template on the PDA screen. Table 1 provides examples of the personal feedback. In this study, online monitoring aims primarily at the first BT goal by supporting the timely detection of attack precursors [7-9] and online coaching pertains primarily to the second BT goal by stimulating preventive action.

2.4. Procedure

The present study was approved by the Ethics Committee at Utrecht University Medical Center. The ODA+ group was approached through a letter from the university and then contacted by telephone to explain the research procedure and ask for their willingness to participate. ODA briefing took place after the fifth training session (week 7 of the BT program). The briefing consisted of an ODA demonstration, followed by instructions and signing of an informed consent form by the participants. Together with the PDA (PalmOne Treo 600™) they received an instruction booklet and a phone number to contact researchers in case of questions or technical problems. The PDA was activated immediately after the briefing and kept during the 3-week *ODA in-training* period.

The PDA beeped at random moments twice a day between 10 AM and 6 PM to prompt the participant to fill in a diary. The software was programmed in such a way that the alarm interval was 4 hours with a variation time of 2 hours and a minimum interval of 30 minutes. In addition to the `beep' or `time' diaries, a morning and evening diary had to be initiated by the participants. Feedback was tailored to the individual patient and diary and provided by clinically trained research assistants, two times per day on working days, within one hour after completion of the two time diaries. Debriefing took place after the last BT session. Participants received an evaluative interview, returned the PDA and were rewarded with € 25 for their participation.

ODA fresh-up was offered again for three weeks preceding the BT measurement at 6-month follow-up. Participants were contacted by telephone 4-5 months after completion of BT. Patients who agreed participation received the PDA at home, and additional instruction if required, shortly before the start of the fresh-up period. After the three weeks one of the researchers collected the PDA's from the patients' homes and participants were again rewarded with € 25.

2.5. Instruments

To answer research issue 1, patient ratings of ODA acceptability were obtained as part of a structured interview conducted after ODA in-training. Responses to standardized questions were collected on ODA usefulness (1 item), burden (1 item), supportiveness (1 item) and the extent to which ODA monitoring and coaching each helped to attain the two BT goals (4 items). All items were scored on a 4-point scale ranging from 1 (not at all) to 4 (very much).

In addition, participant's positive and negative experiences with ODA were assessed by two open answer questions. Satisfactory compliance with ODA monitoring was defined as obtaining ≥80% of the completed diaries [20-22].

For research issue 2, migraine attack frequency, the primary outcome measure, was assessed prospectively with a 4-week paper & pencil headache diagnostic diary conform the guidelines for clinical trials in prophylactic treatment and behavioral trials [24, 28]. The internal control subscale of the Headache Specific Locus of Control Scale (HSLC) was used to assess internal control [29,30]. The scale consists of 11 items scored on a 5 point scale, with higher scores indicating better internal control. The scale has good psychometric properties [29,30]. The 20-item Dutch version of the Migraine Specific Quality of Life Questionnaire (MSQOL) is a valid and reliable instrument to assess migraine-specific quality of life [31]. A higher sum score reflects a better quality of life between attacks (range 20-80). The headache diary and questionnaires were administered pre- and post-BT and six months after completion of BT [15,16].

2.6. Analyses

For research issue 1, the data of the ODA tracking files that were stored on a server, were analyzed to establish ODA feasibility by computing mean percentage scores (range) for technical problems, and mean scores (range) for the numbers of executed diary prompts and feedback deliveries. Participant's compliance was computed by: ((number of missed beeps) / (number of expected beeps based on the number of days that participants completed ODA - number of technical problems))*100. To establish ODA acceptability, mean scores (range) were calculated per item of the evaluative interview. Patient comments on positive and negative experience with ODA as registered during this interview were counted post-hoc according to content, and quantified by computing percentages per category.

For research issue 2, repeated measures analysis was conducted to test differences between ODA+ and ODA- with attack frequency, internal locus of control and migraine specific quality of life as the dependent variables. A significance level of $p<.05$ was used in all analysis. The models were checked for violation of the assumptions of normality and homoscedasticity. Because of non-normal distributions the scores for attack frequency and internal control were transformed. In addition, differences between ODA+ and ODA- were explored regarding treatment responder rate and dose response ratio. Treatment responders were defined as patients with a significant improvement in migraine frequency, both after BT and at follow-up of >50%, and the dose response ratio was tested for subjects who in-training had received ODA feedback <20 and >20 times.

3. RESULTS

3.1. Patient characteristics

Table 2 shows descriptive statistics of the participants who completed ODA in-training (research issue 1), and of the ODA+ and ODA- groups who completed the 6-month follow-up measurement (research issue 2). Participants who completed the study protocol (n=31) did not significantly differ from those who did not (n=13) on any of the variables summarized in Table 2. Additionally, the ODA+ and the ODA- group were highly comparable regarding all variables (p=ns in all analyses).

Table 2 Characteristics of patients who completed ODA in-training (research issue 1), and of the ODA+ and ODA- groups who completed the 6-month follow-up measurement (research issue 2)

	ODA in-training (n=44)	**ODA+** (n=31)	**ODA-** (n=31)
Gender (%)			
Female	82	84	90
Male	18	16	10
Age, mean (range) in years	43 (25-63)	44 (25-59)	44 (26-58)
Education level (%)			
Low	0	0	0
Average	23	26	23
High	77	74	77
Condition (%)			
BT	41	39	49
WLC	59	61	52
Attack frequency at 4-week baseline	3.2 (1-8)	3.0 (1-8)	2.8 (0-8)
Migraine duration, mean (range) in years	18 (3-40)	19 (3-40)	19 (4-45)
Aura (%)			
With aura	36	36	23
Without aura	57	61	68

3.2. Research issue 1: Utility of ODA

Feasibility. As shown in Table 3, participants completed 21 days of prompted diary monitoring on average. For some this period was extended because the final training session was delayed for one week. Others completed less than three weeks of monitoring, because they had a short holiday during the ODA in-training period. The average compliance with the time diaries was 85%. Additionally, participants completed 19 evening diaries and 20 morning diaries on average.

Acceptability of ODA. Table 4 shows that ODA was well accepted: it was rated as highly useful and supportive and the burden experienced was relatively low. According to subjective

Table 3 Feasibility of ODA in-training (n=44)

Number of days of ODA provision during BT	21.2 (13-28)
Technical problems	
Internet transmission problems[a], mean % (range)	4.1 (0-9)
Obstructions due to server problems, mean % (range)	0.2 (0-3)
PDA failures, mean % (range)	2.5 (0-36)
Electronic monitoring	
Total of diary prompts, mean (range)	42 (26-56)
Total of evening diaries, mean (range)	19 (12-27)
Total of morning diaries, mean (range)	20 (12-28)
Online coaching	
Total of feedback[b], mean (range)	23 (13-35)
Total of feedback relative to number of diary prompts[b], mean (range) %	92 (70-100)
Participants' compliance %	85 (61-100)

[a]Http:// connection problems due to for example tunnels or concrete buildings.
[b]ODA monitoring continued during weekends, while ODA coaching was executed on working days but not during weekends.

experience ODA helped in achieving the two BT goals: ODA monitoring and ODA coaching both instigated the detection of attack precursors as well as the taking of preventive action.

Positive experiences with ODA exceeded negative experiences (see Table 4). Most participants stated that ODA instilled awareness of own functioning, instigated a moment of self-reflection and stimulated them to take preventive action. Interestingly, one third of the participants spontaneously remarked that they felt 'watched over and not left alone'. The most prevalent negative aspect was that monitoring takes time and is sometimes inconvenient (the feedback never was). Some participants mentioned annoyance with not hearing the beep and other minor technical problems. Not being able to review previous questions or answers was also mentioned (but the PDA is deliberately set to prevent this, because going through the diary affects the sampling of actual state).

3.3 Research issue 2: Preliminary effects of ODA

Table 5 shows the descriptive statistics of migraine attack frequency, internal locus of control and migraine-specific quality of life at baseline, post-training and 6-month follow-up for participants who did and did not receive ODA. Both groups improved in attack frequency immediately after BT and this was maintained at follow-up ($F=4.30$, $p=.02$) with no between group differences ($F=0.41$, $p=.67$). There were no significant differences between the ODA+ en ODA- conditions in treatment responder rate or dose response ratio.

All participants reported higher internal locus of control after BT and this effect was preserved at follow-up ($F=26.3$, $p<.001$), regardless of whether they had received ODA ($F= 0.08$, $p=.93$). Last, the results showed that migraine specific quality of life remained stable in ODA+

Table 4 Acceptability of ODA in-training, and experiences with ODA derived from a structured evaluative interview (n=44)

Patient ratings of ODA acceptability during BT	**Mean (Range)**
Usefulness of ODA	3.7 (2-4)
Supportiveness of ODA	3.6 (2-4)
Burden of ODA	2.0 (1-4)
Patient ratings of ODA helpfulness during BT	**Mean (Range)**
Electronic monitoring helped detect attack precursors (goal 1)	3.4 (1-4)
Electronic monitoring helped taking preventive action (goal 2)	3.3 (1-4)
Online coaching helped detect attack precursors (goal 1)	2.9 (1-4)
Online coaching helped taking preventive action (goal 2)	3.0 (1-4)
Positive experiences with ODA	**%**
Increased self-reflection and awareness of own functioning	84
Beings instigated to take action	73
Being watched over and not standing alone	34
Negative experiences with ODA	**%**
No negative remarks	12
Diary monitoring takes time and is sometimes inconvenient	52
Minor technical problems such as not hearing the beep	20
Being reminded of migraine	12

participants, while in ODA- participants it improved significantly (F=4.10, p=.02) but to a small extent.

Table 5 Means (SD) of attack frequency, internal locus of control and quality of life for ODA+ (n=31) and ODA- (n=31) at baseline (BL), post BT and at six-month follow-up (FU)

Training outcomes	**ODA+**			**ODA-**				
	BL mean (SD)	Post BT mean (SD)	FU mean (SD)	BL mean (SD)	Post BT mean (SD)	FU mean (SD)	F[b]	P[b]
Attack frequency[a]	3.0 (1.8)	2.4 (1.5)	2.4 (1.9)	2.8 (1.7)	2.6 (1.6)	2.2 (1.4)	0.42	0.67
Internal locus of control[a]	37.3 (10.9)	43.6 (9.4)	42.0 (8.8)	35.4 (9.0)	42.5 (7.7)	40.5 (10.2)	0.08	0.93
Quality of life	58.6 (8.9)	59.1 (7.9)	58.3 (9.1)	56.3 (10.0)	59.3 (7.3)	60.8 (7.0)	4.10	0.02

[a] Square root transformation of scores

[b] Between ODA+ and ODA- condition

4. DISCUSSION & CONCLUSION

4.1. Discussion

The primary aim of the current study was to establish the utility of ODA, a new software based generic method presently used to support behavioral attack prevention in chronic migraine. The secondary aim was to explore whether ODA produced surplus effects in self-management training, offered with minimal professional guidance.

The present study confirmed the outcomes of the pilot study [2] regarding the feasibility and patient acceptability of ODA for a larger sample, and extended the evidence to patients who are in training while receiving ODA. The total number of technical problems resulting in data loss was acceptable (6**.**8%) and comparable to the percentages of technical problems in the pilot study [2]. Participant's compliance rate (85%) was in accordance with guidelines for good compliance [20-22]. Feedback was provided on 92% of all time diaries on working days, which approximates delivery as it was intended beforehand.

ODA was found useful and supportive, while burden was low, which is important as burdening participants through ODA could hamper instead of support the progress of training. Further, ODA was perceived as supporting the two target goals of attack prevention through self-management (detection of warnings in the earliest possible stage & behavioral action to avert deterioration). The predominantly positive experience with ODA underscored that participants encountered increased self-reflection and awareness of own functioning and that they felt primed to take action against attack occurrence. The feeling of being watched over also emerged, which may have been beneficial in neutralizing resistance against, or promoting the acceptance of, the guidance offered by ODA.

The results concerning the utility of ODA are in accordance with the outcomes of other studies of mobile online support in chronic disease [32-34]. Like the present study, these studies underscore the potential of this type of support as an interface between patient and disease [32], which captures real-time symptoms and behavior unobtrusively, while patients can go about with their own everyday life [33]. Offering applications that engage patients seems crucial to avoid attrition [33], and is promoted by interactivity [34], customization and personalization [35] and web-based personal exchange [34]. Compared to other applications in chronic disease [32-34], ODA stands out in terms of interactivity and personalization.

An important difference between ODA and other applications is that most applications are not used to extend a training program but are employed independently. This raises the issue whether ODA, with minor modifications, also could be used in its own right without BT. At the patient side, having a sense of control is the backbone of disease self-management, and internet-delivered (mobile) support is particularly capable of promoting this [32]. Previous research showed that a subjective sense of control over a chronic somatic disease corresponds with feeling less ill and experiencing more freedom [32]. This suggests that the acquisition of

subjective control may be as important as actual control reflected by recurrence or flare-ups of core symptoms.

Our study on BT effectiveness produced strong results on subjective control over attack prevention, which was more prominent than the improvements in actual attack occurrence [15,16]. The effect of BT on attack frequency was quite moderate (≤23%) and considerably below that of training offered with full professional guidance, but in accordance with other self-management programs offered by lay trainers with chronic conditions [36]**.** Subjective control might start to develop as a response to positive but smaller changes, for example by lowering the severity of the migraine headache or the duration of the attack. This process remains unnoticed when the focus is on prevention of the attack as such. These more subtle benefits could reinforce the sense of subjective control and self-efficacy, which could then spur skills to tackle the more difficult task of fully preventing a complete attack. This would imply that subjective control is a crucial endpoint in migraine self-management, which must be encouraged to attain actual attack prevention. This also underscores the need for further research on this issue and the potential role of mobile applications such as ODA (either stand alone or as an adjuvant to treatment).

The present results regarding the effectiveness of ODA showed that ODA did not make a difference in improving the benefits of BT. A between-group difference in migraine-specific quality of life (MSQOL) was found: the ODA+ group remained unaffected, while the ODA- group improved significantly, albeit to a minor extent. Unexpected results in MSQOL have been discussed in our research group. BT might induce changes in health-related values by making patients more conscious of their symptoms. This could translate into *lower* scores for MSQOL, a phenomenon known as `response shift' [37]. Thus, research should clarify the rationale for a BT-induced response shift in migraine and accurately test its implication for MSQOL assessment. In addition, such research would contribute to understanding the essentials of migraine self-management.

The present study has important limitations concerning the investigation of the second research issue. First, the study was bound to the protocol of the randomized BT trial, which restricted the sample size of the ODA+ and ODA- groups. Effects of a second intervention (ODA) up and above the effect of a primary intervention that served the same purpose (BT) are hard to detect when small groups hamper the power to detect effects between the groups. Second, we do not know who benefits from BT, but results suggest large differences between patients [15]. This variability in BT effect might further have threatened the probability of discerning surplus effects due to ODA. Third, it happened that the RCT hampered the execution of ODA due to time constraints resulting from the RCT design, which was a minor point, however. Although we were aware of these limitations, we decided to use the opportunity of the current RCT to extend the present study with a first test of ODA effectiveness. A last point is that three weeks of ODA might have been insufficient, because participants often needed a few days to adjust and thus probably benefited from ODA only during the last two weeks. A recent

study reported beneficial effects of feedback via text messages to support self-care in adolescent diabetes patients when feedback was provided throughout a year, which is considerably longer than in our study [38].

4.2. Conclusion

The current study corroborated the utility of ODA. ODA feasibility and acceptability was established convincingly for the employment of ODA as an adjuvant of self-management training in chronic migraine. ODA was perceived as supporting the two target goals of attack prevention and the predominantly positive experience of patients underscored that increased self-reflection and awareness of own functioning occurred. This means that the primary goals of ODA were fulfilled. Whether mobile support in real life through ODA is prolific in its own right, or can induce higher gains while patients undergo behavioral training, remains to be established.

4.3. Practice Implications

ODA is a new generic and software-based method developed for online monitoring and coaching through the internet and presently employed as an adjuvant to cognitive behavioral training in migraine attack prevention. ODA allows for contact with patients outside the professional setting, and has the ability to capture and influence critical moments as they happen in the patient's everyday life [39]. The current study showed convincingly that ODA is feasible, well accepted and perceived to support self-care in 44 patients with chronic migraine. Although the method is currently designed for patients with chronic migraine, it can be easily adapted for other health settings.

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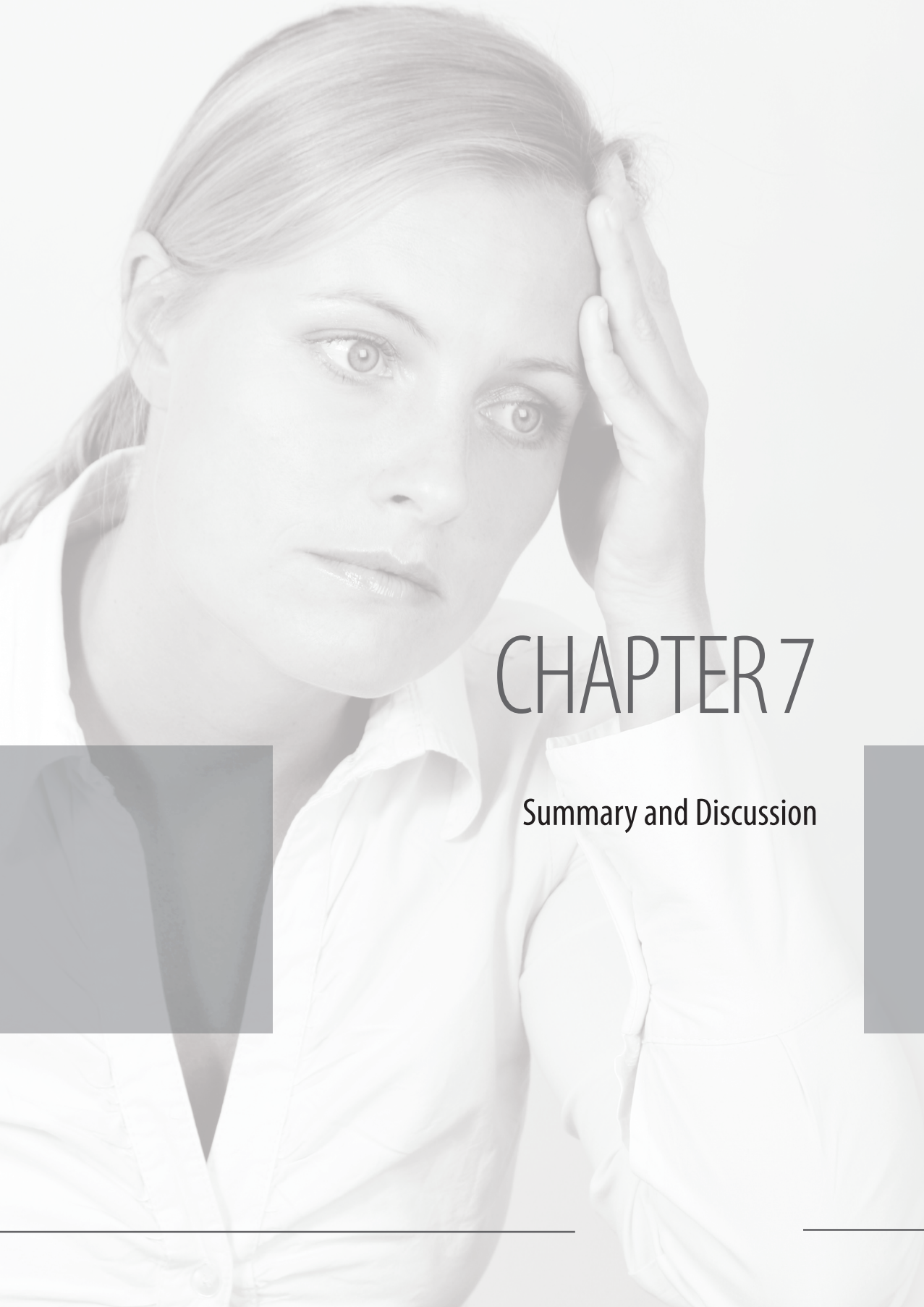

CHAPTER 7

Summary and Discussion

INTRODUCTION

Migraine is a chronic brain disorder and characterized by attacks of severe headache.[1] The availability of triptans since the early 1990s has been a significant advance for the patients and their efficacy for aborting a migraine attack has been proven.[2] Prophylactic treatment is increasingly used for patients with severe and frequent migraine attacks.[3,4] Medical headache treatment in the Netherlands is based on a stepped-care approach: general practitioners provide primary care, headache specialists (neurologists) deliver secondary care, and tertiary care (clinical treatment) is limited provided in multidisciplinary headache centers.[5] Although migraine is highly prevalent and burdensome in daily life, many patients do not seek medical treatment.[6]

This thesis concerns a self-care approach for the general population, which can be seen as a first step to treat migraine systematically in the echelon of primary care. The primary aim of this thesis was to examine the effectiveness of a new behavioural training, when provided in a self-management format by lay trainers with migraine to small groups at home. This behavioural training (BT) was evaluated among migraine patients, aged 18-65 years, who fulfilled the diagnostic criteria of the International Headache Society (IHS) and suffered from one to six attacks per month.[7,8] Targets of BT were to reduce attack frequency, and to increase internal control over and self-confidence in attack prevention. Secondary aims were to improve migraine-specific quality of life and to reduce migraine-related disability. This dissertation also aimed to detect predictors of successful training response, gain more insight in the qualities of migraine patients as lay trainers, assess the benefits for lay trainers' own health, and determine the clinical utility of online digital assistance (ODA) when applied in-training and at follow-up. This chapter will summarize and discuss the main findings, beginning with the feasibility and experiences of lay trainers with migraine. Additionally, the main outcomes of the randomized controlled trial will be reviewed and discussed from a methodological point of view. Last, we will suggest directions for national implementation and future research.

SUMMARY OF MAIN FINDINGS

The scientific challenge of this thesis was the fact that migraine patients coached fellow patients, the so-called `lay trainers with migraine´, in behavioural attack prevention at home. BT was based on an established clinical protocol,[9] which was adapted to the format of a self-management training. The seven group sessions focused on two strategies: 1) identification and modification of triggers and premonitory symptoms of migraine attacks, and 2) application of physiological and cognitive-behavioural self-regulation skills to prevent attack occurrence (chapter 3). The stepwise training of lay trainers consisted of three steps: self-experience, pro-

viding BT to one new patient and subsequently to small groups. Potential lay trainers were selected provided that they were successful in managing their own migraine attacks.

This thesis described whether this new BT approach could induce substantial improvements in migraine sufferers and addressed the following research questions:

1. What is the feasibility of lay trainers with migraine who train small groups of fellow patients in behavioural attack prevention at home (chapter 2)?
2. What are the short term effects of BT on attack frequency, perceived control over and self-confidence in attack prevention (chapter 3)?
3. What are the changes six months after completion of BT and which characteristics of patients at baseline predict successful BT response at follow-up (chapter 4)?
4. What are the qualities of lay trainers with migraine, what is their influence on the training outcomes in their trainees, and what are the potential benefits for their own health (chapter 5)?
5. What is the clinical utility of Online Digital Assistance (ODA) when applied in-training and at follow-up and does ODA produce surplus benefits in BT (chapter 6)?

Chapter 2 describes the development of the stepwise training programme for lay trainers with migraine. This pilot study indicated that our lay trainers with migraine were perceived as competent and credible role models, but also that the tasks of the trainers made significant demands on them. The results of the first three lay trainers were promising and 5/8 of their trainees (63%) achieved a clinically significant improvement (≥50% reduction in migraine frequency). Positive aspects of lay trainers with migraine concerned their ability to motivate the trainees, as well as their knowledge of premonitory symptoms, and sharing of disease-specific problems. Pitfalls were fatigue and migraine symptoms, which could obstruct an active guidance of the group sessions. Providing personalized feedback to headache diaries also appeared to be a complex task for them.

Chapter 3 presents the short term effects of the randomised controlled trial (RCT). The interest for our clinical trial was large, and more than 600 headache patients requested information. Consequently, the required number of participants was relatively easily accomplished. In total, 127 patients participated (87% women, the average age was 44 years, 65% had followed a higher education). Of these patients 108 completed the study protocol; 51 of the experimental group and 57 of the waitlist-control group (WLC), who received usual care. The effect of BT was small, i.e. 21% reduction in attack frequency in the experimental group in comparison with 6% in the WLC group (non-significant trend, $p<0.10$, effect size -0.29). Thirty-five percent of the participants showed a clinically significant improvement of ≥50% reduction in attack frequency, while this occurred in 19% of the WLC group (non-significant trend). The effects on self-efficacy and internal locus of control were strong and large in comparison with the controls ($p<0.001$, effect size 0.79 and 0.97, respectively). The effects on migraine-specific quality of life, perceived health status and migraine-related disability were not significant.

Chapter 4 describes whether the changes directly after BT were maintained six months after completion of BT. The results of the control group, who were trained directly after their waitlist period, were added to those of the experimental group. In the total group (n=95), attack frequency significantly decreased (-23%, effect size 0.6) and the strong improvements of internal control over and self-efficacy in behavioural attack prevention were maintained at follow-up. Moreover, 42% of the participants showed a clinically significant improvement (≥50% reduction), and migraine-specific quality of life significantly improved over time (p=0.007). A higher migraine severity and a higher external control at baseline were positively related to training outcome at 6-months follow-up.

Chapter 5 reports that the qualities of the lay trainers (n=13) were very positively evaluated; these qualities concerned `warmth', `expertise', `organization', `training rationale', `active control' and `advice & guidance'. Higher `active control' of lay trainers during the group sessions was significantly related to improvements of migraine frequency and internal control in their trainees, post-BT. At follow-up `personal advice & guidance' increased the chance of less attacks and `supportive encouragement' increased the chance of a higher internal control. However, `humour' slightly increased the possibility of more attacks post-BT, while `fellowship' and `individualization' negatively influenced internal control. Fellowship expressed the ability of sharing disease-specific problems and learning from each others disease-management. Individualization expressed the ability to personalize the training programme, e.g. by using personal stories. At follow-up lay trainers showed larger gains in migraine frequency, internal control over attack prevention, and quality of life than their trainees.

In *Chapter 6* the utility of Online Digital Assistance (ODA) is examined based on 44 migraine patients who received ODA as an adjuvant to BT in-training, and 31 migraine patients who received ODA as fresh-up prior to follow-up measurement. Minimal technical problems, good compliance and successful execution confirmed the feasibility of ODA. The predominantly positive experience with ODA underscored its acceptability. However, participant's who received ODA in-training and at follow-up did not show better improvements with respect to attack frequency, internal locus of control and migraine-specific quality of life compared to those that underwent BT only.

CONCLUSIONS

There is a large interest for a group-based behavioural training (BT) provided at home by lay trainers with migraine. The effectiveness of this new BT format on headache improvement is modest when compared with licensed clinical psychologists, but is in line with other lay-led self-management interventions. Furthermore, large effects for self-efficacy and perceived control over attack prevention are achieved. This intervention seems more successful for the more severe migraine sufferers (4-6 attacks per month) and those patients who are more externally

oriented at baseline. The stepwise training programme of lay trainers with migraine, in which they first learn to successfully reduce their own migraine attacks, is intensive and time consuming. However, the satisfaction among trainers and trainees is high and the trainer ship can positively influence their own health. `Active control', `personal advice & guidance' and `supportive encouragement' seem relevant qualities of trainers, whereas `humour', `fellowship' and `individualization' were less favourable than expected. ODA is a new software-based method applied online through the Internet, which has the advantage of detecting real-time symptoms and behaviour and providing direct feedback in an interactive manner. ODA was well received but did not make a difference in improving the benefits of BT. In view of the large interest for this self-care approach and the utility of preventive methods in primary care, future research on cost-effectiveness is recommended.

DISCUSSION

Feasibility of migraine trainers as models for behavioural attack prevention

Lay trainers in the pilot study were selected by means of in-depth interviews that were conducted by the main researcher and a senior clinical psychologist. We found that some trainer candidates were particularly motivated to fill the absence of a paid job, caused by disability through migraine.[10,11] Other trainer candidates stated that they wanted to share their knowledge about migraine with peers or would like to become a trainer of a University-based intervention. Although these reasons were plausible, exclusion was decided upon when the candidate's interest in BT per se was limited, or when migraine severity threatened the appropriate execution of the BT programme. To indicate the importance of affinity with behavioural methods (chapter 2) the following metaphor was used by the researcher who selected potential trainer candidates during the RCT: "A driving instructor must be a good driver himself and enjoy driving".

The selection procedure resulted in fewer candidates than we had expected. In general, after self-experience of BT one out of ten trainees was suitable for the training programme for lay trainers. There were about twice as many potential trainer candidates, but the majority gave priority to their own self-management rather than to following a training programme. This lower availability of lay trainers caused some logistical problems. The majority of the trainees did not want to travel too far, also caused by their vulnerability for migraine triggers (e.g. exertion). A long travel distance to the trainers (> 15 miles) led to withdrawal of participants in a number of cases. Another logistical problem was that in some regions more trainers were needed than could be provided. Two factors contributed to this shortage of trainer candidates. First, in some regions trainers provided less trainer candidates after their group training than in other regions. Secondly, the mental load of providing BT in addition to work or family life was a reason for some trainers to deliver BT infrequently. Therefore, the

employment of lay trainers differed considerably and logistical problems may threaten the feasibility of this approach.

Despite the above-mentioned obstacles, the commitment of lay trainers during the study remained high and being a trainer was experienced as rewarding. In addition, adverse events were not reported and only one trainer (7%) dropped out due to personal circumstances (chapter 3).

Experiences of migraine trainers as models for behavioural attack prevention

Previous qualitative studies showed that being a lay leader was an enjoyable and valuable experience. Lay leaders valued the act of altruism, the social interaction and involvement with similar others, and witnessing improvements in their trainees. Lay trainers also benefited from increased self-confidence and own improvement of self-management skills.[12,13] Negative aspects concerned their time commitment, administrative tasks, having to rigidly adhere to the course protocol, and keeping participants focused on the sessions.[14] The materials from the pilot study and continuous supervision during the RCT allow for a global evaluation of these issues in our lay trainers:

1) *Altruism* in our trainer sample was often a result of having experienced the disabling consequences of migraine in their youth, and later on in their family life and professional career. This training offered the opportunity to do something positive about this for other patients.
2) *The need for social interaction* was not mentioned by our lay trainers as a reason to participate. This might be explained by the younger age of our volunteers in comparison with the experiences of arthritis leaders (> 50 years)[13], where loneliness due to retirement or grown-up children might explain the need for companionship. In lay trainers with migraine, involvement with similar others was particularly appreciated to better carry out the exercises during their own training (`buddy system'; see chapter 5).
3) We agree with Barlow et al that *improvement of trainees and their positive feedback* are important factors to reinforce the altruistic act of training fellow patients for a small fee.[14] The RCT showed that there was a large variance in BT effects on migraine frequency. One third of the patients showed considerable headache improvements (≥50% decrease in attack frequency), while two third of the patients did not change in attack frequency (chapter 3). Therefore, lay trainers had to deal with disappointing training results of some of the trainees and seek for other reinforcement of their training efforts. In our view, the issue of non-responders did not seem to negatively influence the trainers' motivation. Because of the selected group we cannot generalize our findings to a broader population.
4) *Being reminded of behavioural strategies and improve their own mastery* were also mentioned as positive factors by our lay trainers. As reported earlier, participation in the training programme seemed to positively influence their own migraine frequency, quality of life and maintenance of self-management skills (chapter 5). However, in the case of

migraine, one should always take into account that flare-ups of the trainer's condition and co-morbidities can reduce the initial positive BT effects.

5) Another positive experience was *the credibility that lay trainers perceived* regarding the usefulness of behavioural methods for migraine. A lay trainer could relatively easily initiate relaxation techniques by telling participants about his/her successful experiences. This mechanism is described by Barlow et al. as `*upward social comparison'*, which explains that patients with chronic diseases can derive hope and inspiration from those whom they perceive to be coping well with their problems.[14] Several trainers reported their functioning as a role model to be the most valuable tool for providing BT. Their participants had often tried several (alternative) therapies and felt inspired by a trainer who had benefited him/herself from the intervention.
6) *Time commitment* was also an obstacle for our lay trainers. As reported earlier, lack of time sometimes caused a shortage of trainers, and in a few cases trainers did not have enough time to adequately prepare the group sessions.
7) *The stress of administrative tasks* in our sample was kept to a minimum. The recruitment of participants and scheduling of group sessions was done by the research team. Despite this precaution the registration tasks of the trainers (e.g. writing feedback to headache diaries, filling in evaluation forms for the supervision) may have caused strain when too many trainer tasks resulted in overuse of trainers' capacities. It is a very important point of attention to minimize such strain, while assuring support of the trainers and controlling thequality of their training at the same time.
8) *Adherence to the training protocol* was sometimes an issue when trainers tended to provide medical information or recommend certain medication. However, the biggest challenge was to manage the tension between the scheduled topics per sessions and the individual needs. This tension was caused by the large variance in headache history, self-management experiences, personal awareness and capacities for behavioural methods. Some BT topics also provoked disparity between general content and individual needs. For example, some trainees found it very difficult to detect premonitory symptoms of migraine and needed more time and instruction. Therefore, the supervisor paid attention to both instruction and evaluation of BT topics, and to the individual progress of trainees. In a few cases the supervisor became involved when the trainer could not solve the problems within the group setting.
9) *Keeping the attention of participants and staying focused* also played a role in our sample. Active control over the group sessions seemed to be positively related to training outcomes (chapter 5). Therefore, group management is an important tool for a successful delivery and may require additional attention during the training programme for lay trainers.
10) *The role of the supervisor* has not been elucidated in previous studies investigating lay trainers. In this study the patients appreciated the backing of the supervisor, particularly the clarity of her answers and respectful attitude (e.g. not being too pedantic). They also

valued the support of the trainer at times when their migraine worsened, and strategies were explored together with the supervisor to deal with this difficult period. Last, paying attention to the actual capacities of the trainers was also appreciated. Negative comments mainly concerned the fact that the lay trainers missed personal experience with the disorder in the supervisor who did not suffer from migraine herself.

Effectiveness of migraine trainers as models for behavioural attack prevention

This part of the discussion focuses on the main outcomes of the RCT, starting with the primary and secondary outcomes and followed by the explorative findings.

Primary outcomes: attack frequency, perceived control and self-efficacy

Chapter 3 showed that the improvement in attack frequency was relatively small. As such this thesis indicates that the effectiveness of lay-led BT on attack frequency of 23% was below the 30-55% achieved by healthcare professionals in an individual setting. The present outcome did not exceed that of medical placebo studies (20-30%),[15,16] but was well above levels established in placebo-controlled BT (9-12%),[17,18] and in line with the effectiveness of lay-led self-management interventions on pain.[19] Several factors may explain the difference between the present outcome and that of BT provided by healthcare professionals.

First, lay trainers without psychological education provided the training, which was a large contrast to the licensed academic clinical psychologists, who had been intensively trained. Further, the intervention of this thesis concerned a group based setting whereas previous behavioural studies mainly reported on individual interventions. In addition, the trainers had to deal with the complex tasks of group-management and this might have been a problem for the less qualified lay trainers. Last but not least, BT took place at home of the trainers where less control was available. The influence of situational factors might also have been less favourable, for example a living room in contrast to the status of an university centre.[20]

Secondly, our sample had a high record of healthcare use and medical consumption. Triptans, launched in the 1990s, have improved patients' quality of life considerably because of their rapid relief of pain and diminished side effects,[21] but nowadays also are prescribed more than in the 1990s.[22] Considering that the majority of BT studies that contributed to the effect of 30-55% were conducted before the triptans were (widely) available, it is reasonable to assume that significant improvements in migraine in those days were more easily achieved. Thirdly, the relationship between triggers and premonitory symptoms on the one hand and actual attack occurrence on the other is complex. Although premonitory symptoms were shown to predict attacks to a considerable extent,[23] there is no linear association between attack risk and distinct symptoms or triggers, and it is often the accumulation that counts. This was recently underscored by the editor of a prominent international journal `Headache': 'no single trigger – however potent – is common for all migraineurs and an established trigger rarely triggers a migraine attack each and every time in the affected individual' (p. 499).[24]

This complexity is a major issue, which may have induced differences between the trainers (and trainees). Other such issues pertain to the capacity to increase the awareness of bodily sensations in the trainees by the way of instructing the relaxation exercises, and the ability to motivate the trainees, while resisting to be distracted by the group discussions. Chapter 5 showed that control over the group sessions was an important quality of lay trainers and seemed more important than the companionship of peers.

We now turn to the short term improvements of internal locus of control and self-efficacy, which were large and significant in both the intention to treat and completed protocol analyses. In our opinion, more RCTs should include these outcomes. A recent meta-analysis on the efficacy of biofeedback for migraine found medium to large effect sizes for self-efficacy.[25] However, biofeedback is not frequently applied in the Netherlands, and the application of biofeedback is more difficult and relatively expensive due to the equipment. Overall, our thesis is one of the first to reveal strong short-term effects on psychological outcomes in migraine patients. This is an important finding for several reasons.

First, because chronic pain has multiple dimensions and affects the mental health of patients.[26] Secondly, subjective control might start to develop as a response to positive but smaller changes, e.g. pain intensity. These more subtle benefits could reinforce the sense of subjective control, which in turn could encourage skills to tackle the more difficult task of fully preventing a complete attack (chapter 6). This would imply that subjective control is a crucial endpoint in migraine self-management. Thirdly, if patients are more able to predict attack occurrence they may feel less insecure and anxious about new attacks. Although their headache pattern has not considerably changed in the short run, their acceptance of migraine might have been improved due to this higher self-control. In other chronic pain patients acceptance was found to be adaptive and predictive of adjustment.[27] Last, if patients feel more in control about their disease they might use more problem-focused strategies, which may also promote the ongoing adaptive process.[28] These problem-focused preventive actions might positively influence their health in the long run.

Secondary outcomes: migraine-specific quality of life, health status and migraine-related disability

The short term results showed that BT did not affect patients' quality of life between attacks. Changes in patients' general physical and mental health status were insubstantial, as were changes in migraine disability (chapter 3). Regarding disability, a 3-month retrospective assessment interval of the widely used MIDAS was not adequate to assess attack frequency post-BT (chapter 4).[29] In case of the follow-up measurement this was less of a problem, but we must admit that other indicators of disablements might have been more appropriate; not least because many patients found it difficult to recollect the headache days in the past 90 days and answer the productivity questions. Regarding the lack of change in quality of life and perceived health status several comments can be made.

First of all, a small effect size for migraine-specific quality of life was also found in a group of responders to triptan (0.25).[30] Also, there are few data available on RCTs measuring the relationship between pharmacological treatments and health status outcomes. One review of symptomatic treatment of migraine in children also advised to more frequently measure health-related quality of life in future research.[31] Third, response shift may explain the findings.[32] BT might induce changes in health-related values by making patients more conscious of their symptoms and their influence on their daily life. Usually patients are more aware of the agony of the attack itself and they do not want to worry about migraine in their headache-free period. Due to the monitoring, in particular in case of ODA, they may be more aware of how much their life is affected by migraine. This could translate into lower scores for MSQOL after BT.

Regarding the lack of change in health status, the group mean was selected to represent the BT response, but there was a large variability on the different subscales. Further, we agree with Terwindt et al. that the SF-36 was not designed to measure limitations specifically associated with migraine.[33] Therefore this measure might be less sensitive in evaluating health-related quality of life in these patients. In addition, personal values and subjective standards are also considered important indicators of quality of life. The SF-36 emphasizes the role of patients' ability to function, but functioning may not be a causal component of quality of life. Alternative approaches, such as the degree to which patients' expectations and needs are fulfilled, may also reflect their complete state of physical, mental and social well-being.[34] Last, due to the lack of norm scores for quality of life and health status it is difficult to describe how severely impaired our patient group was; this is important because lay trainers, who also suffered from migraine, had to coach this patient group. The average score on disability (>20) indicates that our group can be categorised as MIDAS grade IV, reflecting a great likelihood of severe disability.[35] The average scores on migraine-specific quality of life were in line with the age group 20-49 years (n=1012) of a clinic-based sample of Patrick et al, indicating that our sample might be more severe than the general population.[30] The health status scores were also in accordance with a sample of a large Dutch validation study of the SF-36 (n=423).[36] These patients, who suffered from a migraine attack in the past two weeks, scored significantly lower on all domains in comparison with healthy controls.

It can be concluded that the quality of life of our patient group was impaired and this underscores the accomplishment of the lay trainers.

Explorative findings: predictors of BT response and maintenance of training results

Chapter 4 reported that little information is currently available about the patient characteristics that predict treatment response and different outcome variables have been used. We found that a larger belief that migraine is due to chance at the start of BT (external control) significantly predicted a lower attack frequency at 6-months follow-up. In contrast to our expectations internal control was not a significant predictor of treatment response. External

believers may benefit more from the training because they learned how to influence themselves the occurrence of migraine attacks, while internal believers might have already been successful in behavioural prevention and gain less from the training. Chapter 3 also indicated that BT was more beneficial for patients who entered BT with a high attack frequency, which could not be explained by regression to the mean since it was not present in the control group. We consider this as highly relevant, because this suggests that our lay trainer approach may have the capacity to help the more impaired patients. In conclusion, this thesis adds some evidence to the scarce information about treatment responders. External believers and patients with regular migraine attacks (4-6 per month) may benefit in particular from BT. This conclusion is based on a largely white, female, middle-aged and higher educated population with high medical consumption. A more heterogeneous population might have led to different predictors.

Chapter 4 showed that at 6-months follow-up attack frequency and quality of life were modestly improved, and feelings of control and self-confidence remained strongly improved. This finding confirmed our hypthesis that results may improve over time because of an extended period of practicing and application of BT skills in daily life to prevent attack occurrence. Nonetheless, the motivation and supportive aspects of BT were no longer readily available, which could also have led to a relapse. However, the value of booster sessions in the context of self-management courses has not yet been proven.[13] Rothrock et al. examined the effectiveness of lay leaders in a university-based clinical sample (n=100), who provided intensive patient education in addition to routine medical management.[37] They found that mean MIDAS scores were significantly improved at 6-month follow-up compared to the control group, who received medical management only. These findings confirmed our hypothesis that results may improve over time. A long-term study would contribute to verification of this improvement as patients in our study were only measured six months after BT.

The finding that internal control and self-efficacy remained strongly and significantly improved over time provides further proof for the robust effects on psychological outcomes. In social cognitive theory self-efficacy is considered fundamental to behaviour change.[38] In headache research, both concepts are seen as independent determinants of preventive behaviours that lessen the likelihood of a migraine attack.[39] Our secondary analyses showed that individual change scores of attack frequency (T1-T3) were significantly though modestly correlated with the change of self-efficacy, and significantly related to the change of external control, but not to the change in internal control (chapter 4). In conclusion, self-efficacy and external locus of control may act as mediating factors for headache improvement, but their magnitude might be less than expected.

Explorative findings: qualities and health of lay trainers with migraine

We chose to evaluate the qualities of lay trainers from the perspective of their trainees since 'patient empowerment' was a major issue of this thesis. Chapter 5 indicated that the qualities

of trainers were very positively evaluated. This might have been an overestimation of the actual qualities caused by information bias, when trainees wanted to please their trainers or reward their efforts.[40] Nevertheless, a tentative impression about (in)adequate qualities of lay trainers can be given. Lay trainers who seem more capable of controlling the group sessions, giving useful advice, and encouraging their trainees in a supportive manner may achieve better training outcomes in their trainees. A trainer should not over-emphasize his/her own experiences or the sharing of experiences among trainees, since this seemed to lower the internal control of trainees. This unexpected finding might be explained by the fact that too much sharing distracts the attention from the exercises, while successful self-experiences are crucial for controlling one's own health behaviour[38,39]. The lack of influence of individualization may be explained by the fact that parts of the unique and effective contribution of trainers may not have been identified by our questionnaire. Observations during the training and rating of specific behaviours might have improved the validity of the measurements.[41,42]

Participation in the stepwise training for lay trainers appeared to improve their migraine frequency, and their internal control and quality of life; the changes found in trainers were larger than in their trainees. Selection bias can not explain this finding because the differences between trainers and trainees were larger at follow-up than post-BT. During the follow-up period lay trainers continued with BT, they taught their BT skills to one new patient under supervision and participated in a workshop with other trainers, which all might have contributed to better self-management results. A post-hoc comparison of lay trainers with their peers, who underwent BT at the same time, confirmed that the follow-up results of trainers of trainees were better than those of their trainees (chapter 5).

In conclusion, participation in a stepwise training programme can produce capable trainers and may positively influence their own health. Because of the paucity in research on this subject the results may be important for its potential to expand self-management and behavioural headache interventions to a broader patient population.

Cost-effectiveness

Cost-effectiveness was a major reason to set up this study, but the RCT was designed to establish the effectiveness of the innovative combination of lay trainers, group training and a home-based setting. This thesis can be seen as a first step to indicate the cost-effectiveness of this lay trainer approach. In chapter 4 we used the frequently cited meta-analysis of Haddock et al. to give a preliminary answer to the question of cost-effectiveness.[43] On this basis the present lay trainer approach seemed three times less cost-effective than BT provided by healthcare professionals (chapter 4). However, the results of Haddock et al. were based on changes in headache index, a composite score that was calculated from headache intensity, frequency and/or duration. Headache index is no longer recognized as a primary outcome measure,[2] probably due to the fact that researchers used different methods to calculate this index. In addition, this index obscures the effect on attack frequency, which is most relevant

to prevention. Furthermore, the lower cost-effectiveness of our approach was partly compensated by the actual costs of lay trainers, and the lower costs due to the location at the home of the trainers.

Online digital assistance

The additional value of ODA to BT is: 1) the possibility of detecting real-time symptoms and behaviour in an unobtrusive manner, and 2) providing direct feedback 'on the spot' in an interactive manner. Chapter 6 demonstrated that the results concerning the clinical utility of ODA were satisfying and in accordance with the outcomes of other studies on mobile online support in chronic diseases.[44-46] However, ODA did not make a difference in improving the benefits of BT. This falsification might be caused by methodological flaws, such as a small sample size. Further, ODA participants also received personal feedback of the trainer and group members, which might have provided sufficient support during BT. This would mean that ODA should be tested as a means to improve relapse prevention only. Last, three weeks of ODA might have been a relatively short period of time compared to other studies, which reported beneficial effects for the mobile support of self-care.[47] Therefore, a better option might be to deliver ODA alone with minor modifications. Applying ODA on its own has the advantage of direct feedback and support during daily activities and may lower the training load as patients do not have to participate in the group sessions.

Methodological considerations

In this part of the discussion we review the strengths and weaknesses of the randomized controlled trial.

Strong methodological aspects

A broad recruitment procedure was used to enhance the external validity of the study. The diagnostic criteria of the IHS were strictly adhered to by assessment of a 4-weeks diagnostic headache diary, and a second opinion by neurologists specialised in headache. The eligibility criteria were clearly defined and all criteria were in accordance with the scientific guidelines. In addition, patients were screened for psychiatric co-morbidities by the SCL-90 that were likely to interfere with the ability of patients to fully participate.[48] Severe mental complaints would also be too difficult to handle for the lay trainers. The cut-off value of 178 of chronic pain patients (total score) seemed adequate, since psychiatric complaints only occurred in a few cases. Furthermore, a neurologist was consulted in case of presumed medication overuse and issues concerning concomitant use of several medications. This second opinion appeared an adequate tool to verify the diagnosis as only 2 out of 127 patients had to be excluded post-hoc (chronic daily headache).

Attack frequency per four weeks was the primary endpoint and a wide range of secondary outcomes was chosen to analyse the effectiveness of BT.[8,26] Migraine was of sufficient

frequency to demonstrate a change in frequency in response to BT. The broad range of 1-6 attacks enabled us to generalize the findings of our study to the general population. The inclusion of patients with one attack per month carried the risk of finding no changes or disproportional positive changes (of 100% in case of no attack post-BT in these participants). However, this low frequency group did not influence training outcomes (chapter 4). Further, a parallel-group design was applied to measure the effectiveness and take the influence of time into account. A pragmatic trial was used that was suitable for the aim of this thesis, i.e. to examine the utility of lay leaders for behavioural attack prevention. A waitlist-control condition, who continued their usual care, was considered appropriate for an effectiveness study.6 This thesis does not concern an efficacy study, which searches for possible mechanisms whereby interventions produce improvement, and requires a more controlled approach.[49]

The large interest for this study resulted in sufficient statistical power to detect a clinically relevant difference of 30% between the experimental and control condition.[50] In addition, the attrition rate was relatively low: of the 113 patients who participated in BT only 9 patients withdrew (8%), and the drop-out rate at follow-up (12%) was reasonable and much lower than the maximum of 20% required for Cochrane reviews.[51] These findings are noteworthy, because the intervention was evaluated in a real-world setting, at the home of the trainers, where less control was available. This naturalistic setting increased the clinical meaningfulness of the study, which is an important feature of effectiveness studies.[49] Finally, according to the CONSORT statement, intention-to-treat and completed protocol analyses were conducted to support the findings.[52]

Limitations

A waitlist-control condition seemed reasonable for the aim of our study. Nonetheless, a placebo-controlled study would have been a stronger design to control for the influence of non-specific factors (e.g. attention). We did not choose for a placebo design for various reasons: 1) it was very difficult to realise a placebo procedure that was plausible and provided non-therapeutic control for attention,[53] and 2) a trial in which a lay-led BT is compared with a professional-therapist group would require many resources. A major limitation of the study design, however, was the fact that the follow-up study was uncontrolled. Due to the gradual selection of lay trainers it was not possible to carry out the RCT in one year. We considered it unethical to further postpone the training for waitlist participants. Withholding the training for waitlist participants might also have been an option, since the intervention was new and its effectiveness had not yet been proven. In our view, withholding the training may have led to considerable drop-out among the waitlist participants. In conclusion, the lack of placebo and an uncontrolled follow-up period weakened the strengths of the findings, but was inevitable in the context of implementing clinical science into headache practice.[54]

Despite the broad recruitment procedure, our sample was not completely representative for the general population and this decreased the generalisability of our findings. Most of the

participants were high medical consumers and relatively high educated. Drop-outs during BT were relatively low educated and their triptan use was significantly higher than completers. However, they were not different regarding attack frequency. This selection bias may be a consequence of the self-volunteer approach. Other self-management studies were also biased by a white, female, middle-aged and highly educated sample.[55] Last, the findings cannot be generalized to migraine patients who are more medically or psychologically complicated (those who have co-morbidities). We do not consider this a problem because health professionals are better able to treat these patients.

The RCT was not double-blinded and the headache diaries and questionnaires were only blinded for the researchers to avoid assessment bias. The special attention that trainees received (the 'Hawthorne effect') might have caused a higher self-motivation in producing favourable results.[37] However, we agree with Rains et al. that administration of BT involves complex patient-trainer interactions.[53] Trainers explain, evaluate and reinforce the patients' acquisition of behavioural skills and cannot be blinded in the same manner as physicians providing pills.[11] Blinding of patients to BT is inherently difficult as awareness of psychological and physiological reactions is one of the key features of BT. Therefore, both trainers and participants knew their condition and this may have caused some information bias;[56] for example, when participants were too eager to demonstrate positive training results or wanted to please their trainer. However, a bias downwards could also have occurred in the waitlist-control condition, where patients seemed less motivated to fill in their headache diary after their waitlist period. There might also have been an effect in the opposite direction in case of secondary gain. Last, data were collected from self-report measures. Social desirability and recall bias may have played a role, where positive experiences were overrated. However, pain and the role of cognitions and beliefs in one's own capacities are only accessible by self-report.[57]

Prophylactic medication was allowed in this 'real-world' effectiveness study. These patients might have less of a margin for clinical improvement. Chapters 3 and 4 demonstrated that the analysis without this medication group did not lead to improved outcomes, indicating that this was not a limitation of the study. Furthermore, 35% of the participants changed their (non-) pharmacological treatment during the follow-up period and this might have influenced the training results (chapter 4). In addition, a measurement of one month was not optimal to show changes for the low frequency group. Due to the careful selection procedure it was not feasible to carry out a baseline measurement of 8 weeks in addition to 4 weeks of registration during the selection.

National implementation

In our view successful self-experience should be given priority in the recruitment procedure of lay trainers with migraine. Our view is stricter than the widely applied Chronic Disease Self-Management Course (CDSMC), in which self-experience prior to lay leader training is not a necessary condition.[12] Disadvantages of our approach are a smaller number of trainers and

a more vulnerable trainer pool. Solutions to promote sustainability of trainers might be the agreement to deliver group-based BT twice at least. This commitment was also made in the training of lay leaders for the CDSMC.[12] This solution will not work in the case of health problems or life-events, but will stimulate these trainers to return in a later phase.

Individual training formats may improve the feasibility and effectiveness of lay trainers with migraine for behavioural attack prevention. However, leaving out the possibility of sharing experiences with other group members may reduce patients' satisfaction. According to Barlow's qualitative study, sharing experiences in a supportive, reassuring environment was the key feature that was most appreciated.[14] Participants not only felt reassured that they were understood but also appreciated the emotional and practical support provided by other members of the group. This support helped when making changes to their self-management.[14] A simple solution would be to deliver BT in pairs of lay leaders and double the group size. The CDSMC also works with pairs of lay tutors and deals with larger groups.[12] However, a larger group size would require more equipment and space at home of the trainers and, above all, more advanced skills to manage this larger group. Therefore, the procedure of small groups could be maintained, provided that adequate supervision is available. In this respect a 'strip card' would be useful and provides the opportunity to ask for help for a certain amount of time.

Our disease-specific, long-term and gradual approach differed from the generic and brief training approach of the widely applied CDSMC.[12] In this training programme lay leaders with various diseases followed a course of 3 days, including CDSMC content, presentation skills, dealing with challenging participants, and the administrative and managerial tasks. Why can we not apply this successful training model to our lay trainers? In our view, a disease-specific approach is more suitable and offers the highest chance to improve trainers' knowledge and mastery of skills. In fact, the tension between generic topics and disease-specific needs was one of the pitfalls of the CDSMC.[14] Nonetheless, adaptations may be necessary to lower the time expenditure and costs of our intensive training programme for trainers. First, the workshops could be condensed to a brief course of 2 days (e.g. 8 hours). Second, employing master psychology students as supervisors might lower the costs, preferably those with migraine and having experienced BT themselves. Disadvantage of this approach is the fact that the master psychology student will also need supervision, which will eventually raise the costs. Another option might be to employ experienced lay trainers as master trainers, who could support and supervise the inexperienced lay trainers. However, this approach will dilute the professional input in the supervision. In case of an individual training this might be less of a problem than in the case of group management. In our view, a professional layer above lay trainers would still be the most optimal condition.

The study was carried out in cooperation with the Dutch Society of Headache Patients. This organisation supported the research by providing critical comments on the training and research protocol, and use of their website and journal for patient recruitment. The fact that some important members of this organisation participated in the training facilitated their

cooperation, since they were first doubtful about the usefulness of behavioural therapies for headache disorders. Most members of this society are severe migraine sufferers, which instigates frequent medication use but also carries the risk of medication overuse. Therefore, BT can offer them alternative and healthy strategies for attack prevention. An active role of this patient organisation is highly recommended with respect to their possible assistance in the implementation process. The patient organisation is represented in all regions of the Netherlands and new trainer candidates could fulfil the need of migraine patients who live outside the western urban area.

The following issues should be explicitly addressed during the training programme for lay trainers: 1) how to deal with non-responders to prevent demoralization of the trainers, 2) group management to increase the effectiveness of BT and lower the tension between scheduled topics and individual needs, 3) realistic expectancies about training outcomes considering the large variability in effects on attack frequency and attention to the relevance of and potential gain in internal control and self-efficacy, 4) trigger-management (`no simple solutions') and instructing relaxation skills (`relaxation takes time and bodily awareness').

Clinical implications

In an ideal situation the embedding of lay-led BT would be in primary care. The supervision of lay trainers with migraine could be done by health psychologists, preferably working in a health care centre, with general practitioners as medical back-up. In case of complex cases, headache specialists of the `Nederlandse Vereniging van Hoofdpijn' or psychologists with great expertise in headache could be consulted and referred to. The coordination tasks of the research team, e.g. selection of patients and scheduling of group sessions, could be taken over by medical assistants in the health care centres. It is estimated that in 2020 500.000 additional employees will be needed in health care in the Netherlands, and the socio-economic consequences of this number will be enormous.[58] A large investment in preventive treatments such as self-care approaches by lay leaders certainly seems worth the effort.

Future research

Notwithstanding the considerable resources required, we strongly recommend the execution of a more sophisticated clinical trial with a parallel-group design in which several applications of BT are investigated. This trial could examine the effectiveness of individual and group-based lay-led BT in comparison with home-based treatments by professionals (psychologists); the latter containing two in-person sessions and a few telephone sessions with a psychologist.[59] More efforts can also be made to create a plausible control condition. For example, an unstructured peer support group who discusses migraine-related themes. In addition, a clinical trial on mobile support in real life through ODA employed independently is recommended. This raises the issue of cost-effectiveness, which could be adequately examined by a real cost-

effectiveness design, e.g. a prospective, controlled study that compares the time expenditure, direct and indirect costs and also quantifies the burden of disease.[60]

A long-term study is currently being carried out, which follows the participants for 2-4 years after completion of BT. At the moment an internet-based application of BT is also being developed and tested. This application may reach a more representative population since logistical problems do not occur. Internet may also attract more males and young adults, or patients who prefer to remain anonymous and do not wish to share their health-related problems with peers. This electronic application can also be used to facilitate the training by lay trainers. Headache diaries and evaluation forms can be digitalized and the supervisor can have the right to look into the registration forms of trainees. The administrative tasks of trainers will also be reduced by the digital measurements. An internet application can also be used to develop a post-training buddy system that may assist some patients in maintaining hard-won changes.

Finally, this thesis concerned a pragmatic clinical trial in a real-life setting. Fundamental research is necessary to provide new theories to further substantiate the development of behavioural interventions. In this respect more basic studies on clarifying the role of triggers and premonitory symptoms and the relationship between relaxation and the hypersensitive brain of migraine patients are recommended. Further, the mediating role of self-efficacy and external control could be examined by assessing these variables multiple times when patients are in training.[57,61]

In conclusion, the effects of `migraine trainers as models' on migraine and quality of life were limited in the short run, but the results improved at follow-up. In view of the large interest for this self-care approach and the utility of preventive methods in primary care, future research seems certainly justified.

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CHAPTER 8

Nederlandse samenvatting

INLEIDING

De medische behandeling van migraine is gebaseerd op de `stepped care' benadering: huisartsen behandelen hoofdpijn in de eerste lijn van de gezondheidszorg, hoofdpijnspecialisten (neurologen) behandelen de meer complexe gevallen in de tweede lijn, en klinische multidisciplinaire behandeling vindt plaats in gespecialiseerde hoofdpijncentra in de derde lijn. Ondanks het feit dat migraine een hoge prevalentie heeft en het dagelijks leven ondermijnt, zijn er toch veel patiënten die geen medische behandeling krijgen. De in dit proefschrift beschreven studie richt zich op een zelfhulpbenadering voor de algemene bevolking, wat gezien kan worden als een eerste stap om migraine systematisch te behandelen op het niveau van de eerstelijnszorg. Het primaire doel van de studie was om de effectiviteit van deze zelf-management training (ZMT) van migraine te onderzoeken. Het hoofddoel van ZMT was het verminderen van de aanvalsfrequentie, het vergroten van de interne controle over en zelfvertrouwen in preventie van migraineaanvallen.

De zelf-management training en de training voor lekentrainers met migraine

Het wetenschappelijk vernieuwende aan de studie was dat migrainepatiënten getraind werden door andere migrainepatiënten (ook wel lekentrainers genoemd) in de gedragsmatige preventie van migraineaanvallen. De training bestond uit 7 groepssessies en is gebaseerd op een beproefd klinisch protocol. ZMT was gericht op twee strategieën: 1) het ontdekken en beïnvloeden van uitlokkers en vroege symptomen van een migraineaanval, 2) het aanwenden van fysiologische en cognitief-gedragsmatige zelfregulatievaardigheden om een migraineaanval te voorkomen (hoofdstuk 3). De stapsgewijze training van lekentrainers bestond uit zelfervaring van ZMT, het overbrengen van deze training aan één andere patiënt en vervolgens het leren trainen van kleine groepen (hoofdstuk 5). Potentiële trainerskandidaten werden geselecteerd op de voorwaarde dat zij zelf succesvol waren in de zelfregulatie van migraine.

De onderzoeksopzet

Om de effectiviteit van ZMT te onderzoeken werd een gerandomiseerde gecontrolleerde studie uitgevoerd. De geïncludeerde patiënten werden aselect toegewezen aan een experimentele conditie (ZMT) of een wachtlijst-controle conditie, waarin hun standaardbehandeling gecontinueerd werd. Parallel metingen werden verricht vlak voor ZMT, direct na afloop van ZMT en na 6 maanden. De wachtlijstgroep ontving ZMT na afloop van de wachtlijstperiode. Voor alle meetmomenten geldt dat patiënten 4 weken lang een prospectief hoofdpijndagboek bijhielden en gevalideerde vragenlijsten invulden.

Het perspectief van lekentrainers met migraine

Uit de pilotstudie (hoofdstuk 2) blijkt dat affiniteit met gedragsmatige behandeling van migraine belangrijker was voor het trainerschap dan een externe motivatie, bijvoorbeeld op zoek zijn naar vervangend werk vanwege arbeidsongeschiktheid. Na zelfervaring werd 1 op de 10 deelnemers geselecteerd voor het trainingsprogramma voor trainers, wat beneden de verwachtingen was. Er waren meer geschikte kandidaten, maar die gaven de voorkeur aan hun eigen zelf-management. Hierdoor ontstonden logistieke problemen en een tekort aan trainers in bepaalde regio's. Ook verschilden trainers in hoe vaak ze ZMT gaven, doordat voor sommige trainers de mentale belasting van de training te zwaar was in combinatie met hun werk en/of gezinsleven. Desalniettemin was er een grote betrokkenheid van de overgebleven trainers en voelden zij zich gewaardeerd. Er waren geen negatieve effecten van het trainerschap en er viel maar één trainer uit door persoonlijke omstandigheden.

De motivatie om trainer te worden werd vaak ingegeven door altruïsme, in de zin van zelf erg geleden hebben door migraine en er nu wat positiefs mee willen doen. Een ander voordeel was dat trainers de kans kregen hun eigen zelf-management vaardigheden te verbeteren. Geloofwaardigheid was een sterke troef van de trainers: zij konden deelnemers makkelijk overtuigen van het nut van ZMT, daar ze er zelf profijt van hadden. Dit verschijnsel wordt 'opwaartse sociale vergelijking' genoemd: patiënten met chronische aandoeningen kunnen hoop en inspiratie ontlenen aan degenen die in hun ogen goed omgaan met de aandoening. Lastige aspecten van het trainerschap waren de grote variatie in trainings-resultaten van deelnemers, de tijd die het trainerschap vergde en de registratietaken. Verder werd er soms afgeweken van het protocol, bijvoorbeeld door het geven van medicamenteuze adviezen, of wanneer de deelnemers erg verschilden in hoofdpijngeschiedenis en capaciteiten.

De effectiviteit van ZMT op korte termijn

Hoofdstuk 3 beschrijft de korte termijn effecten van de RCT. Meer dan 600 hoofdpijnpatiënten vroegen informatie aan en het vereiste aantal deelnemers werd relatief eenvoudig behaald. In totaal namen 127 patiënten deel, van wie 108 patiënten het studieprotocol volbrachten. Het merendeel van de deelnemers was vrouw, van middelbare leeftijd en hoger opgeleid. Het effect van ZMT was klein; 21% vermindering in aanvalsfrequentie in de experimentele groep versus 6% in de controle groep. Een klinisch relevante verbetering (≥ 50% vermindering in aanvalsfrequentie) werd bereikt in 35% van de ZMT groep, terwijl dit effect bij 19% van de controlegroep optrad. De effecten op interne controle en zelfvertrouwen waren sterk en groot in vergelijking met de controlepersonen. De effecten op migrainespecifieke kwaliteit van leven en beperkingen waren niet significant.

Verklaringen voor de relatief kleine effecten op de aanvalsfrequentie zijn in eerste instantie gelegen in de vernieuwende elementen van de training: lekentrainers die zonder universitaire scholing in de klinische psychologie de training gaven. Bovendien werd de werking van een groepstraining onderzocht, terwijl eerdere studies de effecten van individuele behandeling

betroffen. Verder zijn de complexe taken van het leiding geven aan een groep veelgevraagd. Eveneens speelt de setting van een thuistraining een rol, waar minder controle aanwezig is. Tenslotte kunnen contextfactoren een minder gunstig effect hebben; een woonkamer in tegenstelling tot de status van een academisch ziekenhuis.

In tweede instantie kenmerkte onze steekproef zich door een hoge medische consumptie. De doorgaans gerapporteerde 30-55% in hoofdpijnverbetering werd aangetoond in studies, die voor de komst van de zeer effectieve triptanen plaatsvonden. Verder kunnen verschillen tussen trainers een verklaring bieden. Alhoewel de voorspellende waarde van vroege symptomen is aangetoond, bestaat er geen lineaire relatie tussen specifieke uitlokkers enerzijds en het risico op een aanval anderzijds. Deze complexe materie kan variatie tussen trainers in de hand gewerkt hebben. Daarnaast verschillen trainers in vaardigheden om de ontspanningsoefeningen te instrueren, deelnemers te motiveren en weerstand te bieden aan groepsdiscussies. Hoofdstuk 5 impliceert ook dat actieve controle van de trainers over de groepssessies belangrijker lijkt te zijn dan het stimuleren van lotgenotencontact.

De sterke effecten op psychologische uitkomsten zijn uitermate belangrijk en verdienen ruime aandacht. Op de eerste plaats omdat chronische pijn multidimensioneel van aard is en de mentale gezondheid nadelig beïnvloedt. Verder zullen deelnemers die menen dat zij hun aanvallen beter kunnen voorspellen, minder angstig en onzeker zijn voor een volgende aanval. Dit kan de acceptatie en aanpassing aan de chronische pijn bevorderen. Tenslotte, kan een toename in ervaren zelfcontrole ook leiden tot een groter gebruik van probleemgerichte strategieën, wat de adaptatie aan pijn en gezondheid op de lange termijn ten goede kan komen.

ZMT had geen invloed op de kwaliteit van leven tussen de aanvallen in en de algehele gezondheidstoestand. Daarnaast veranderde de beperkingen in het werk, sociale of gezinsleven niet significant. Er zijn verschillende (methodologische) verklaringen voor deze falsificatie te geven. Beperkingen in het dagelijks leven werden gemeten door de retrospectieve vragenlijst MIDAS, die hoofdpijndagen en verminderde productiviteit in de afgelopen 3 maanden uitvraagt. Verder werd er bij het valideren van de MSQOL (kwaliteit van leven) eveneens een kleine effectsize gevonden voor triptanen. Tenslotte kan response shift een rol spelen, doordat deelnemers hun gezondheidssituatie in hoofdpijnvrije perioden anders zijn gaan waarderen na het volgen van de training.

Behoud van resultaten en voorspellers van ZMT

De studie in Hoofdstuk 4 toont aan dat in de totale groep die ZMT had volbracht (n=95), de aanvalsfrequentie en kwaliteit van leven 6 maanden na afloop van de training significant en in bescheiden mate waren verbeterd. Daarnaast waren de sterke verbeteringen in interne controle en zelfvertrouwen behouden bij follow-up. Bovendien liet 42% van de deelnemers een klinisch relevante verbetering ten opzichte van de voormeting zien. Wat betreft de voorspel-

lers van een gunstig trainingsresultaat waren een hogere aanvalsfrequentie en een grotere externe oriëntatie bij baseline positief gerelateerd aan hoofdpijnverbetering bij follow-up.

In tegenstelling tot onze verwachting was interne controle geen significante voorspeller van een gunstig trainingsresultaat. Dit kan verklaard worden doordat bij extern gerichte patiënten meer winst te behalen valt in vergelijking met de meer intern gerichte deelnemers, die al bekwaam waren in gedragsmatige beïnvloeding van migraine. Verder kon het gunstige effect voor mensen met een hoge aanvalsfrequentie niet verklaard worden door regresssie naar het gemiddelde, omdat dit effect niet in de controlegroep optrad. Tenslotte waren veranderingen in zelfvertrouwen en externe controle significant doch bescheiden gecorreleerd met veranderingen in aanvalsfrequentie. Dit impliceert dat deze variabelen als mediator kunnen fungeren voor hoofdpijnverbetering, maar dat hun invloed minder sterk is dan verwacht.

De kwaliteiten van trainers en hun gezondheid

Hoofdstuk 5 behandelt de kwaliteiten van de lekentrainers met migraine (n=13), die erg positief werden beoordeeld door deelnemers. Een grotere `actieve controle' van lekentrainers over de groepssessies was significant geassocieerd met een daling in aanvalsfrequentie en een stijging in interne controle in de deelnemers post-ZMT. Bij follow-up hadden `gericht adviseren & begeleiden' en `steun & bemoediging & bekrachtiging' een gunstige werking. In tegenstelling tot onze verwachting vergrootte `humor' de kans op meer aanvallen bij deelnemers post-BT, terwijl `lotgenotencontact' en `individualisatie' de interne controle leken te verminderen. Individualisatie geeft het vermogen van de trainer aan om het trainingsprogramma persoonlijk te maken, bijvoorbeeld door persoonlijke ervaringen in te brengen. Deze studie toonde verder aan dat bij de trainers zelf, de aanvalsfrequentie, interne controle en kwaliteit van leven bij follow-up in sterke mate waren verbeterd. Deze hoofdpijnverbetering bleek veel groter dan bij hun deelnemers was aangetoond. Het trainerschap lijkt de gezondheid dus in positieve mate te beïnvloeden.

Een grote mate van tevredenheid van deelnemers over hun zorgverleners komt vaker voor in satisfactie onderzoek. De werkelijke kwaliteiten van de lekentrainers kunnen dan ook overschat zijn door informatie bias, daar de beoordeling niet geblindeerd was. Dat lotgenotencontact ook averechts kan werken, zou verklaard kunnen worden door een te grote nadruk op het delen van ervaringen, waardoor de aandacht van de werkelijke oefeningen wordt afgeleid. Tenslotte kan de voorbeeldfunctie die trainers hebben, mogelijk de positieve gezondheidsgevolgen verklaren. Hierdoor zijn zij eerder geneigd om hun zelf-management vaardigheden te verdiepen.

De klinische relevantie en effectiviteit van interactieve digitale ondersteuning (ODA)

Hoofdstuk 6 beschrijft de klinische relevantie van interactieve digitale ondersteuning (ODA) gebaseerd op 44 migrainepatiënten, die ODA kregen als extra hulpmiddel tijdens ZMT, en 31 patiënten die ODA ontvingen als `opfrisser' voor de follow-up meting. De haalbaarheid van

ODA werd bevestigd door minimale technische problemen, goede compliance en succesvolle uitvoering. De gebruiksvriendelijkheid werd aangetoond door de voornamelijk positieve ervaringen die deelnemers in interviews aangaven. Deelnemers die ODA ontvingen lieten echter niet meer verbetering zien in aanvalsfrequentie, interne controle en migrainespecifieke kwaliteit van leven, vergeleken met degenen die alleen ZMT ontvingen.

Dit gebrek aan extra verbetering kan te maken hebben met de volgende factoren: de kleine steekproef, de feedback van trainers en medepatiënten die mogelijk al voldoende was tijdens de training en de relatief korte opfrisperiode van drie weken bij follow-up in vergelijking met andere studies. Een betere optie zou kunnen zijn om ODA zelfstandig aan te bieden met kleine aanpassingen. Dit heeft enerzijds als voordeel dat patiënten directe feedback en steun ontvangen tijdens dagelijkse activiteiten, anderzijds dat de belasting voor hen lager wordt, doordat ze niet aan de groepssessies hoeven deel te nemen.

Nationale implementatie en toekomstig onderzoek

De volgende aanbevelingen zijn gedaan voor nationale implementatie: succesvolle zelfervaring heeft de prioriteit in de selectie van lekentrainers met migraine, ZMT in de vorm van een individuele training kan de haalbaarheid van deze zelfhulpmethode vergroten en samenwerking met de Nederlandse Vereniging van Hoofdpijnpatiënten is van groot belang. In een ideale situatie wordt ZMT in de eerstelijnszorg aangeboden, met een gezondheidspsycholoog als supervisor van trainers en een huisarts als medische achterwacht. Hoofdpijnspecialisten zouden geconsulteerd kunnen worden bij complexe casuïstiek. Toekomstig onderzoek zou zich kunnen zich richten op: een grootschalige kosten-effectiviteitsstudie, een internetcursus waarmee mogelijk meer mannen en jong-volwassenen bereikt worden of deelnemers die anoniem willen blijven. Tenslotte is fundamenteel onderzoek hard nodig om de werking van gedragsmatige interventies te onderbouwen.

CONCLUSIE

Er is een grote belangstelling voor een groepsgewijze gedragsmatige training die gegeven wordt door lekentrainers met migraine. De effectiviteit van deze zelf-management training (ZMT) op de aanvalsfrequentie is bescheiden vergeleken met klinisch psychologen die individuele behandeling geven, maar komt overeen met ZMT's gegeven door lekentrainers met andere chronische aandoeningen. Tevens kunnen grote effecten op het gebied van interne controle over en zelfvertrouwen in gedragsmatige preventie van aanvallen bereikt worden. Deze interventie lijkt het meest geschikt voor de zwaardere migrainelijders (4-6 aanvallen per maand) en de patiënten die meer extern georiënteerd zijn bij de start van de training. De stapsgewijze training van lekentrainers, waarin ze eerst leren om hun eigen migraineaanvallen te verminderen, is intensief en tijdrovend. Desalniettemin, de tevredenheid van patiënten

is groot en deelname aan dit trainingsprogramma kan de gezondheid van trainers positief beïnvloeden. `Actieve controle', `gericht adviseren & begeleiden', `steun & bemoediging & bekrachtiging' lijken relevante kwaliteiten van trainers te zijn, terwijl `humor', `lotgenotencontact' en `individualisatie' minder gunstig lijken te werken. ODA is een nieuwe online software methode met als voordeel dat symptomen en gedrag in het dagelijks leven direct gedetecteerd worden en er feedback gegeven wordt op een interactieve manier. Alhoewel de haalbaarheid en gebruiksvriendelijkheid goed bevonden werden, kon deze studie niet aantonen dat ODA meer winst opleverde voor de trainingsresultaten. Gezien de grote belanstelling voor ZMT en de urgentie van preventieve methoden in de eerstelijnszorg wordt onderzoek naar de kosten-effectiviteit aanbevolen.

Appendix I. Programme content of Behavioural Training

Phase	Relaxation	Triggers and premonitory symptoms	Content
Block 1 Practice	**Stretched out phase 1** Autogenic: heaviness		**How does the training work?** 1. Introduction 2. Procedure training 3. Autogenic training phase 1 4. Feedback headache diary
	Stretched out phase 2 Autogenic: warmth Cue controlled relaxation Breathing exercises	**Migraine triggers**	**Why relaxation for migraine?** 1. Feedback diary, relaxation 2. Demand control model, relaxation cues, autogenic training phase 2 and breathing 3. New: migraine triggers
	Stretched out phase 3 Autogenic: heaviness + warmth	**Premonitory symptoms**	**Identification of signals and stress reactions** 1. Feedback diary, relaxation 2. Retrospective: triggers 3. Autogenic training phase 3 4. New: signals and stress reactions 5. Reinforcement of training efforts
Block 2 Application in daily life	**Stretched out and seated phase 3** Differential relaxation (seated) Application under the condition that signals and stressful situations occur	**Scheme of warning signals**	**Application of relaxation when signals occur** 1. Feedback diary, relaxation 2. Retrospective: signals and stress reactions 3. Autogenic training phase 4 4. New: positive relaxing thoughts and differential relaxation
	Favourite posture phase 3 and 4 Autogenic: extended and shortened Differential relaxation (standing) Application under the condition that signals and triggers of migraine occur	**Lifestyle measures** **Migraine recipe**	**Application of relaxation when triggers occur** 1. Feedback diary, relaxation 2. Retrospective: relaxing thoughts, differential relaxation, scheme of warning signals 3. Free choice of relaxation method 4. New: lifestyle measures and migraine recipe
	Favourite posture phase 3 and 4 Autogenic: extended and shortened Differential relaxation (action) Application under the condition that signals and triggers of migraine occur	**Rules of thumb** **Health recipe**	**Lifestyle measures to prevent migraine attacks** 1. Feedback diary, relaxation 2. Retrospective: lifestyle measures and migraine recipe 3. Free choice of relaxation 4. New: rules of thumb and health recipe

Phase	Relaxation	Triggers and premonitory symptoms	Content
Evaluation	**Favourite relaxation methods**	**Favourite lifestyle measures**	**How to maintain the training skills** 1. Feedback diary, relaxation 2. Retrospective: rules of thumb and health recipe 3. Free choice of relaxation 4. Evaluation: written (questionnaire) and verbal 5. Take home messages

Appendix I I. Stepwise training programme for lay trainers with migraine

Phase	Targets	Guidance	Evaluation (tool)	Selection
Step 1: Self-experience	**Behavioral prevention of migraine attacks by**:	**Manual** containing theoretical information, training program per session and headache diary with instructions. **Organizer** containing homework assignments and evaluation forms.	**Successful reduction of migraine attacks** (established with the headache diary).	**Interview** to assess the motivation and capacities of trainer candidates in the context of positive training results
	1. Identification and modification of triggers and premonitory symptoms	**Lay trainer with migraine** providing individual feedback and motivational and emotional assistance.	**Good mastery of BT skills** (according to self-report questionnaire and self-observation of lay trainer).	With positive training results, trainer capacity and motivation → **entry to step 2**.
	2. Application of physiological and cognitive-behavioral self-regulation skills.	**Group member** (`migraine buddy') offering bilateral assistance in completing assignments and exercises.		
Step 2: individual BT	1. **Self-awareness of BT skills** and planned **actions** for future migraine self-management	**Manuals** containing topics per session, a time scheme, instructions for assignments and exercises and take home messages per session, with tips of experienced lay trainers.	**Results trainee and coaching** (open questions **Trainers' qualities and pitfalls** (with a semi-structured interview of the trainee)	**Review** of training results of trainee, of trainers' qualities and pitfalls and of the status of trainers' own self-management
	2. **Development of basic trainer skills** by practicing instructions, tailored feedback, emotional assistance and motivation, time management and evaluations of progress, and by adapting personal expertise to the process of change in the trainee.	**Supervision (6x)** by telephonic contact and e-mail, based on track records of progress per training session, in order to support the learning process, to check trainers' needs and to promote trainers' adherence to the protocol.	**Knowledge of BT content** and **acquisition of trainers' skills** to coach their trainee in attack prevention (as assessed in the supervision).	With maintenance of trainers' own migraine self-management and positive results of trainee → **entry to step 3**.
	3. **Reflection on personal attitude** concerning the degree to which it was neutral, empathic, encouraging, supportive and respectful.	**Website** for downloads of manuals and handouts per session, with examples of difficult training situations and their solutions, as well as the material of the workshops for trainers.		

Phase	Targets	Guidance	**Evaluation** (tool)	Selection
Step 3: BT small groups	Extension of the skills of trainers with those related to **group management**	**Supervision (3x)** focusing on (1) group composition and diversity in headache history and self-management experience (2) individual progress of trainees, and (3) directives for the maintenance of BT skills.	**Knowledge of BT content**, **maintenance of trainers' skills** and **group management** (as assessed in the supervision).	Additional evaluation concerned the monitoring of health problems or life-events that could obstruct the trainers' tasks.

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Saskia Mérelle,
Zomer 2008.

CURRICULUM VITAE

Saskia Mérelle was born on the 17th of May 1973 in Alkmaar, the Netherlands. She graduated from high school (VWO, Petrus Canisius College, Alkmaar) in 1991. After that she studied Human Movement Sciences at the VU University, in Amsterdam. Her main subject was psychomotor therapy, with health sciences and clinical psychology as additional courses. Her internship took place at the rehabilitation centre Heliomare, in Wijk aan Zee, where she investigated a diagnostic method for chronic back pain. Her clinical internship took place at the Rivierduinen, GGZ Zuid-Holland. She was also a trainee at the Hogeschool van Amsterdam, department of Occupational Therapy, and received a didactic certificate for higher professional health education. In 1997 she graduated from the VU University. After her graduation she had several jobs as 'busy bee': she worked for four years as a psychomotor therapist at the Waterland Hospital in Purmerend, was a teacher at the Hogeschool van Amsterdam, and a research assistant at the EMGO Institute (VU University MC).

In 2001, she started to work as a teacher at the department of Medical Psychology and Psychotherapy of the Erasmus University Medical Centre under supervision of dr. Bonke. From 2002-2007 she carried out a PhD study on self-management for migraine, thanks to a grant of ZonMW/NWO, under supervision of prof. Passchier of Erasmus MC and prof. Sorbi from the department of Clinical and Health Psychology of Utrecht University. From 2004 to 2007 she also worked in the research team of prof. van Busschbach & dr. Couturier, where she examined the effectiveness of large scale screening at the work floor and subsequent treatment in headache clinics of the `Nederlandse Vereniging van Hoofdpijncentra'. In 2007, she continued with chronic pain research at the rehabilitation centre Rijndam in Rotterdam. During her PhD study she also participated in the Master Clinical Epidemiology at the NIHES in Rotterdam and graduated in 2008. She is currently working as an epidemiologist at the GGD Kennemerland (Dutch Health Association) in Hoofddorp and is involved in the internet course for migraine of Utrecht University.

Saskia Mérelle is married to Edward van Koningsbruggen, they live with their daughter named Jasmijn in Amsterdam.

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