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Electromyogram-Biofeedback in Patients with Fibromyalgia
A Randomized Controlled Trial

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Men fear thought as they fear nothing else on earth - more than ruin - more even than death. Thought is subversive and revolutionary, destructive and terrible, thought is merciless to privilege, established institutions, and comfortable habit. Thought looks into the pit of hell and is not afraid. Thought is great and swift and free, the light of the world, and the chief glory of man.

Bertrand Russell (1872 – 1970)

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1. Table of Contents

2. Zusammenfassung

Electromyogram-Biofeedback bei Patienten mit Fibromyalgie: Eine randomisierte, kontrollierte Studie

Ziel: Untersuchung der Wirksamkeit von EMG-Biofeedback Training bei Fibromyalgiepatienten.

Design: Als Studiendesign wurde eine randomisierte kontrollierte Pilotstudie mit Verblindung des Untersuchers gewählt. Die Datensammlung erfolgte vor Therapiebeginn (T0), nach Therapieende (T1) und nach weiteren drei Monaten (T2).

Einrichtung: Ambulanz.

Patienten: Patientinnen auf der Warteliste der Tagesklinik für Fibromyalgia, welche die Einschlusskriterien erfüllen.

Intervention: Innerhalb von 8 Wochen 14 Sitzungen mit EMG-Biofeedback Training zusätzlich zur herkömmlichen Behandlung versus herkömmliche Behandlung.

Ergebnismessung und Analysen: Der Hauptzielparameter „krankheitsspezifischer Gesundheitszustand“ wurde mit dem Fibromyalgia Impact Questionnaire (FIQ) gemessen. Als Nebenzielparameter wurden Daten zu Schmerz (Tender Point Score), Tenderness (Tender Point Count = Anzahl der Tender Points, Druckschmerzschwelle), allgemeiner Gesundheit (SF-36), subjektiver Einschätzung der Veränderung aus Patientenperspektive (Patients’ Global Clinical Impression of Change) und psychischer Beeinträchtigung (Beck Depressionsinventar, Symptom Checklist 90-Revised) während des Untersuchungszeitraumes erhoben. Effekte wurden durch Sensitivitätsstatistiken (Effect size, ES) sowie parametrische und nicht-parametrische Signifikanz-Testung beurteilt.

Ergebnisse: Die Daten von 36 Patienten mit kompletten Verlaufsdaten konnten analysiert werden. Im Verlauf wurde keine Verbesserung des krankheitsspezifischen Gesundheitszustandes der Interventionsgruppe im Vergleich zur Kontrolle beobachtet (T1: ES = 0,02, p = 0,95, T2: ES = 0,26, p = 0,43). Mit Ausnahme der Druckschmerzschwelle (T1: ES = 0,26, p = 0,014) ergaben sich auch in den Nebenzielpararmetern keine signifikanten Unterschiede zwischen den Studiengruppen.

Schlussfolgerung: EMG-Biofeedback Training zusätzlich zur herkömmlichen Behandlung ist bei Fibromyalgiapatienten nicht effektiver als herkömmliche Behandlung alleine.

3. Abstract

Electromyogram-Biofeedback in Patients with Fibromyalgia: A Randomized Controlled Trial

Objective: To evaluate the effectiveness of EMG-biofeedback in patients with Fibromyalgia.
Design: The study design was a randomized controlled pilot trial with blinded assessors and three points of assessment: before intervention (baseline, T0), at the end of treatment (T1) and a 3-months follow-up (T2).
Setting: Outpatient clinic**.**
Patients: Patients from the waiting list of the Fibromyalgia day hospital program fulfilling the inclusion criteria.
Intervention: During eight weeks, 14 sessions of EMG-biofeedback training versus usual care only.
Outcome Measures and Analysis: For primary outcome, the disease specific health status was followed using the Fibromyalgia Impact Questionnaire (FIQ). Secondary outcome measures comprise assessment of pain (Tender Point Score), tenderness (Tender Point Count = number of Tender Points, Pain Pressure Threshold), generic health status (SF-36), Patients' Global Clinical Impression of Change and psychic impact (Beck depression Inventory, Symptom Checklist 90-Revised). Effects were analyzed with sensitivity statistics (effect size, ES), parametric and nonparametric tests.
Results: The data of 36 patients with complete follow-up data could be analyzed. EMG-EMG-biofeedback did not improve health status of patients with Fibromyalgia (FIQ, T1: ES = 0.02, p = 0.95, T2: ES = 0.26, p = 0.43). Also, the secondary outcome measures, with the exception of the pressure pain threshold (T1: ES = 0.26, p = 0.014), showed no superiority of EMG-biofeedback in addition to usual care compared to usual care alone.
Conclusion: In the treatment of patients with Fibromyalgia, EMG-biofeedback training in addition to usual medical care is not superior to usual medical care alone.

4. Abbreviations

ACR	American College of Rheumatology
AED	Anti-epileptic drug
AIMS	Arthritis Impact Measurement Scales
BDI	Beck Depression Inventory
CAM	Complementary alternative medecine
CBT	Cognitive behavioural therapy
EMG	Electromyogram
FIQ	Fibromyalgia Impact Questionnaire
FM	Fibromyalgia
FMS	Fibromyalgia Syndrome
CG	Control group
IC	Intervention group
MMPI	Minnesota Multiphasic Personality Inventory
RCT	Randomized controlled trial
SCL-90-R	Symptom Checklist 90 Revised
SCQ	Self-administered Comorbidity Questionnaire
SF-36	Short Form 36
T0	Baseline
T1	End of treatment
T2	3-months follow-up
TP	Tender Point
TPI	Tender Point Index
TPS	Tender Point Score
VAS	Visual analogue scale

5. Introduction

For the past 100 years a disorder characterized by chronic widespread pain, tenderness at specific anatomic sites, also known as Tender Points, mood disturbances and vegetative and functional symptoms like poor sleep and fatigue has been described.
In 1904, Sir William Gowers named this condition "Fibrositis" assuming that muscular rheumatism is the pathophysiological correlate. In the following decades, researchers in the Anglo Saxon and German speech area tried to develop more precise concepts of this syndrome. Accordingly, the aetiologically descriptive term "Fibrositis/Fibrositis Syndrome" was gradually dropped in favour of symptom-orientated descriptions, such as "Generalized Tendomyopathy" in 1970 and "Fibromyalgia Syndrome" in 1976 (Yunus, Masi et al. 1989; Muller and Lautenschlager 1990; Muller and Lautenschlager 1990; Inanici and Yunus 2004).

In 1990, Müller and Lautenschläger published extensive clinical criteria for the diagnosis of Fibromyalgia based on selected studies and a presentation at the 23rd congress of the German Society of Rheumatology. In the same year, Wolfe et al performed a multi-centre study that led to the development of the classification criteria of Fibromyalgia Syndrome, endorsed by the American College of Rheumatology. These criteria are also known as the ACR-criteria. Meanwhile, Fibromyalgia has become a well-established diagnosis and is included in the ICD-10 classification (M79.09) (Muller and Lautenschlager 1990; Muller and Lautenschlager 1990; Wolfe, Smythe et al. 1990).

Despite investigative efforts in the last 20 years, the aetiology remains enigmatic. Research groups of various disciplines have proposed different concepts. Some incorporate Fibromyalgia among affective disorders, others present arguments which support the idea that Fibromyalgia belongs to the field of developmental psychology. There are also groups that favour the adoption of a molecularbiological approach (See 5.3 Aetiology, p.14).

Since the pathology and pathophysiology remains unclear, it is not surprising that there is a variety of symptom-orientated treatment options. Up to now, a great number of different classes of medication, such as antidepressants, non-steroidal anti-inflammatory drugs, opiates, muscle relaxants and antiepileptic drugs have been used. There is also a wide range of non-pharmacological treatments like cognitive-behavioural therapy, exercise programs and physical modalities. Today, experts favour a multidisciplinary approach (Forseth and Gran

2002; Sprott 2003; Mease 2005; Burckhardt 2006; Arnold, Hauser et al. 2008).

5.1. Epidemiology and health costs

The prevalence of Fibromyalgia in the general population in industrialized countries has been estimated between 2% und 3% with a peak in the age group from 24 to 50 years. There is a gender specific imbalance; women are 6 to 8 times more likely to be affected than men. In total, about 6 % of patients in general practices and up to 20 % of patients in rheumatologic clinics meet the ACR-criteria for Fibromyalgia. Due to diagnostic uncertainty, it takes approximately 7 years from the onset of symptoms to diagnosis. Patients with Fibromyalgia often present an extensive health care utilization. In comparison to average medical users, they consult a greater number of doctors, undergo more pain-related operations and have more pain-related hospital and rehabilitation stays. Certain types of medication, e.g. non-steroidal anti-inflammatory drugs and antidepressants, are prescribed more frequently (Conrad 2003; Robinson, Birnbaum et al. 2003; Hauser 2005).

5.2. Symptoms and diagnosis

Due to symptom complexity, there is no gold standard for the diagnosis of Fibromyalgia. In clinical settings, diagnosis is mostly based on the criteria from Müller and Lautenschläger and the ACR-criteria developed by Wolfe et al. (Eich, Hauser et al. 2008).

According to Müller and Lautenschläger, patients with Fibromyalgia have to present chronic spontaneous pain in muscles, tendons and their insertions, further positive Tender Points, a number of autonomic and functional symptoms, as well as psychopathological findings and normal results in routine diagnostic tests (Muller and Lautenschlager 1990). Although the ACR-criteria have originally been developed for research purposes, they are frequently used as a simple and practical instrument to diagnose Fibromyalgia in the clinic. They have proven to have high sensitivity and specificity. The criteria require that patients report chronic widespread pain and have at least 11 of 18 typical Tender Points at examination. Pain is considered widespread, when it occurs spontaneously in several areas throughout the whole body at the same time. A tender point is considered positive, if the digital palpation with a force of 4 kg maximum is painful to the patient. Figure 1 displays the locations of the 18 Tender Points (Wolfe, Smythe et al. 1990).

Figure 1: Tender point locations (Wolfe, Smythe et al. 1990)

The mentioned criteria can shorten the diagnosis process to identify affected persons. However, the use of the ACR-criteria in the clinic has been criticised because Fibromyalgia comprises many more symptoms of varying occurrence which are not included in the classification criteria (Wolfe et al., 2003) (Hauser, Zimmer et al. 2008).

Characteristically, patients report musculoskeletal pain of changing intensity. The location of the painful regions may change daily or even within hours. Frequently, pain begins at one site of the body, e.g. at the lower back or cervical spine, and then generalizes. Accordingly, the patient may not be able to name the main site of pain. Cold and wet weather is often described as an aggravating, warm weather as a relieving factor. Pain is sometimes accompanied by morning stiffness, perceived muscle tenderness, non restorative sleep or day-time fatigue. Patients may also experience a subjective swelling of muscle-associated soft tissue and joints (Muller and Lautenschlager 1990; Conrad 2003). Physical performance and strength are often reduced (Panton, Kingsley et al. 2006). Some patients report a decline in memory, cognitive function and mental alertness (Dick, Verrier et al. 2008; Glass 2008). Consequently, patients may find it very difficult to face the tasks of everyday life, and often feel limited in their ability to work (Henriksson, Liedberg et al. 2005).

Concerning comorbidities, patients were found to have a higher lifetime prevalence of mood and anxiety disorders, e.g. major depression disorder and panic disorder (Walker, Keegan et al. 1997) Furthermore, they are more likely to be affected by headaches, systemic lupus erythematosus and rheumatoid arthritis (Weir, Harlan et al. 2006).
A high percentage of Fibromyalgia symptoms overlap with those of other so called central pain syndromes, for example Irritable Bowel Syndrome, Chronic Fatigue Syndrome and Temporomandibular Syndrome (Lund, Bengtsson et al. 1986; Aaron, Burke et al. 2000; Clauw and Crofford 2003; Dadabhoy and Clauw 2006).
Important differential diagnoses are rheumatic or other systemic diseases, e.g. colitis ulcerosa, endocrine disturbances or malignancies. These severe illnesses can mimic Fibromyalgia and have to be excluded carefully (Hwang and Barkhuizen 2006).

5.3. Aetiology

Up to now, specialists in pain treatment, psychosomatics, rheumatology, physical and rehabilitation medicine and neurobiologists have not found a clear answer to the question of the aetiology of Fibromyalgia.

A substantial number of Fibromyalgia patients meet the diagnostic criteria for psychiatric disorders, such as major depression disorder or bipolar disorder. Even those patients, who do not completely fulfil the criteria for major depression disorder, sometimes present the same clinical symptoms in lower intensity. Consequently, some psychiatric experts regard Fibromyalgia as an affective spectrum disorder (Raphael, Janal et al. 2004; Raphael, Janal et al. 2004).

Experts in the field of developmental psychology argue that patients with somatoform disorder and patients with Fibromyalgia share some striking ailments. On the one hand, both patient groups suffer from sleep disturbances and various vegetative, cardiovascular, neurological and gastrointestinal complaints of unknown origin. On the other hand, childhood adversities were found to a similar extent in both patient groups. In comparison to healthy controls, patients with Fibromyalgia report more negative life events during childhood/adolescence and adulthood in the form of physical and psychological abuse, neglect and death of a parent (McBeth, Macfarlane et al. 1999; Imbierowicz and Egle 2003). Within the meaning of the biopsychosocial model of illness, Egle et al. hypothesize that negative experiences in early childhood and adulthood can lead to chronic stress in form of life-long

victimization. The authors deduce that this kind of stress could play an important role in the origin and maintenance of Fibromyalgia (Van Houdenhove, Neerinckx et al. 2001; Egle and van Houdenhove 2006).

Neurobiologists, however, assume that alterations in central pain pathways are the reason for this syndrome. Beside demonstrating neuroanatomical changes (Kuchinad, Schweinhardt et al. 2007) neuroimaging studies support the idea that amplification of pain sensitivity plays an important role in the pathogenesis of Fibromyalgia. In functional magnetic resonance tomography, for instance, painful pressure leads to the same pattern of brain activation in patients with Fibromyalgia and healthy controls. But the pressure force that is needed to evoke this specific pattern has been significantly lower in the patient group. Additionally, examinations with single-photon emission computer tomography show reduced blood flow in pain-related regions, what could also point towards altered pain processing (Bradley, McKendree-Smith et al. 2000; Gracely, Petzke et al. 2002; Guedj, Cammilleri et al. 2008; Burgmer, Pogatzki-Zahn et al. 2009). Further arguments for changes in central pain processing have been delivered by studies investigating the reply to repetitive painful heat and mechanical stimulation. Following the stimuli, patients have after-sensations with greater magnitude, which last longer and are more often painful than in healthy controls. This enhanced temporal summation of second pain ("windup") indicates central pain amplification and so called central sensitization. Furthermore, Price et al. assumes that evoked or ongoing impulse input from deep tissue, e.g. minor pathological changes, might sensitize intramuscular nociceptors leading to long-term neuroplastic changes and, consequently, central sensitization (Price and Staud 2005). These pathological changes in deep tissues like muscles, for example, have been found as a low amount of intramuscular collagen, "rubber band" morphology and disturbed regulation of intramuscular microcirculation that causes hypoxia and pH changes (Lund, Bengtsson et al. 1986; Jacobsen, Bartels et al. 1991; Gronemann, Ribel-Madsen et al. 2004). Two other findings also indicate ongoing activity in afferent nociceptive nerves. First, Substance P, a neuropeptide in the central nervous system, has been found to be elevated in the Cerebrospinal Fluid in patients with Fibromyalgia. Second, skin biopsies have revealed neurogenic inflammation which is also caused by substance P, possibly released from the peripheral endings of primary afferent nociceptive nerves (Vaeroy, Helle et al. 1988; Russell, Orr et al. 1994; Kim 2007).

In addition to the approaches mentioned above, the neurotransmitter system in the central

nervous system is also a target of investigation, because the serotonin system is involved in pain processing and in mood regulation. Alterations of the specific serotonin transporter have been observed, which seem to be related to the severity of Fibromyalgia symptoms (Bazzichi, Giannaccini et al. 2006). Additionally, levels of 5-hydroxy indoleactic acid, a metabolite of serotonin, are lower than normal concentrations in the cerebrospinal fluid. Findings from tryptophan depletion tests, especially in regard to an augmented expression of Interleukin 6, indicate a dysregulation of tryptophan and serotonin metabolism. Interleukin 6 is considered to mediate the interaction between the neurotransmitter and the neuroendocrine system. This fact is remarkable, because available evidence already suggests that the hypothalamic-pituary-adrenal axis is disturbed in patients with Fibromyalgia (Russell, Vaeroy et al. 1992; Crofford, Pillemer et al. 1994; Barkhudaryan and Dunn 1999; Schwarz, Offenbaecher et al. 2002; Crofford, Young et al. 2004). Recent studies further indicate a disturbance of the dopamine response to pain (Wood, Schweinhardt et al. 2007).

Recently, there is a tendency towards a more holistic approach. Analogously to psychiatric research, molecularbiologists are trying to find a link between psychological factors and neuroendocrine dysregulation, because several neuroendocrine abnormalities occur as a result of chronic stress and are also observed in Fibromyalgia. Gupta et al hypothesize that Fibromyalgia develops subsequently to chronic stress (Gupta and Silman 2004). Weissbecker et al describe childhood physical and sexual abuse in women with Fibromyalgia as predictors of flattened diurnal cortisol rhythms. Consequently, they suggest that traumatic early life experiences may be a factor of adult neuroendocrine dysregulation among Fibromyalgia patients (Weissbecker, Floyd et al. 2006).

5.4. Treatment

Only recently, standardized guidelines for treating this patient group have been developed. (Hardinghaus 2008; Klement, Hauser et al. 2008). However, in this guideline, only very few interventions (cognitive-behavioural therapy, aerobic exercise training and medication with amitriptyline and multidisciplinary interventions) show the highest level of evidence. The uncertainty of the effectiveness of many other interventions may be the consequence of the variety of symptoms and the uncertainty about aetiology. Nevertheless, maximizing health, functioning and independence are the primary rehabilitation aims in all therapeutic approaches.

A large variety of medication such as antidepressants, antiepileptic drugs, non-steroidal anti-inflammatory drugs, opiates and sleeping aids are used in the treatment of patients with Fibromyalgia. Antidepressive substances are essential in the pharmacological treatment of Fibromyalgia (Littlejohn and Guymer 2006; Sommer, Hauser et al. 2008). The tricyclic agent Amitriptyline is generally the first choice for initial therapy. The dosage is normally prescribed lower than the dosage necessary for patients suffering from depression. Amitriptyline has been shown to be efficacious in improving sleep quality and decreasing moderate pain in 25 to 45 % of the patients. But it seems to have no effect on tenderness and stiffness. However, the exact mode of action is not known (Arnold, Keck et al. 2000; Nishishinya, Urrutia et al. 2008).

Beside the relatively old tricyclic substances, the newer specific reuptake inhibitors have been seen to be effective. Interestingly, the coupled serotonin and norepinephrine reuptake inhibitors like Milnacipran, Duloxetine or Venlafaxine appear to be more beneficial than single reuptake inhibitors. The intake of these substances reduces pain in 60% of the treated patients. This effect seems to be independent of the effect on mood, as it appears prior to improvement of mood disorder (Sayar, Aksu et al. 2003; Arnold, Lu et al. 2004; Gendreau, Thorn et al. 2005; Lawson 2006; Littlejohn and Guymer 2006; Uceyler, Offenbacher et al. 2008). Additionally, the selective serotonin reuptake inhibitor Fluoxetine and the selective norepinephrine reuptake inhibitor Reboxetine lead to alleviation of some Fibromyalgia specific symptoms (Arnold, Hess et al. 2002; Krell, Leuchter et al. 2005).

Recently, Antiepileptic Drugs have come up in the treatment of chronic pain conditions. Actually, there is evidence that Pregabalin and Gabapentine lead not only to clinically meaningful improvement concerning pain relief, but also to a decrease of fatigue and improvement of sleep and health-related quality of life in patients with Fibromyalgia (Crofford, Rowbotham et al. 2005; Mease 2005; Arnold, Goldenberg et al. 2007; Lyseng-Williamson and Siddiqui 2008).

The original assumption of Fibromyalgia having an inflammatory background was replaced by the opinion that there is no tissue inflammation involved in the pathogenesis. Consistent with this concept, clinical studies failed to prove the effectiveness of non-steroidal anti-inflammatory drugs and steroidal drugs like Prednisone (Goldenberg, Burckhardt et al. 2004). Nevertheless, patients report a modest benefit from these types of substances. This could be due to the reduction of painful comorbidities, e.g. tendonitis, or other peripheral tissue pathology that contribute to central sensitization (Dadabhoy and Clauw 2006).

Although Tramadol was found to reduce pain, narcotic analgesics are not generally recommended for the treatment of Fibromyalgia (Biasi, Manca et al. 1998; Bennett, Kamin et al. 2003; Goldenberg, Burckhardt et al. 2004; Bennett, Schein et al. 2005).
Additional sleep inducing substances are often prescribed for a short time in order to deal with disturbed sleep patterns and resulting fatigue, e.g. the atypical benzodiazepine Zolpidem (Moldofsky, Lue et al. 1996).
Apart from the more or less established medication concepts, there have been investigational approaches with interesting, though often limited, results for the use of the dopamine-3-receptor antagonist Pramipexole, the specific 5HT3 antagonist Tropisetron or the injections of Growth Hormone (Kohnen, Farber et al. 2004; Holman and Myers 2005; Jones, Deodhar et al. 2007).

Non-pharmacological treatment is mostly applied in order to deal with the psychosocial and functional consequences of Fibromyalgia. The idea is to prevent the decrease of activity, isolation and maladaptive illness behaviours and to manage poor sleep and distress (Dadabhoy and Clauw 2006).
General patient education about the nature and course of the illness has been shown to improve patients' self-efficacy for managing pain. They gain greater sense of controlling their condition and feel less anxious and helpless (Hammond and Freeman 2006). Further psychological interventions, especially cognitive-behavioural therapy, are meant to positively influence psychosocial factors that are connected to illness behaviour, health-care seeking and self-management for pain, pain perception and coping skills (Williams 2003; Kashikar-Zuck, Swain et al. 2005; Thieme, Hauser et al. 2008). Teaching and applying relaxation techniques, for example Progressive Muscle Relaxation or Biofeedback training, is considered to be useful for managing pain and insomnia and can lead to better functioning and concentration (JAMA 1996 [no authors listed]; Adams and Sim 2005). In order to treat physical impairment and prevent inactivity, aerobic exercise training and low-dose intensity sports, e.g. slow walking, cycling, swimming and easy gymnastical exercise (Mannerkorpi and Iversen 2003; Redondo, Justo et al. 2004) are recommended. Additional physical therapy modalities, such as physiotherapy, massage, cryotherapy and TENS (Transcutaneous Electrical Nerve Stimulator), are able to contribute to reducing impairment in functioning and disease consequences (Offenbacher and Stucki 2000).

For patients with more severe limitations of functioning, multidisciplinary programs that include patient education, exercise, psychological interventions and physical medicine are recommended. This combination is likely to be able to face the symptom complexity and the various problems patients have to deal with (Goldenberg, Burckhardt et al. 2004; Adams and Sim 2005; Burckhardt 2006). Recently, due to emerging pharmacological opportunities, there is also a call for further trials that study the standardized use of drugs, embedded in multidisciplinary programs. (Forseth and Gran 2002; Arnold 2006; Arnold, Hauser et al. 2008).

However, the existing conventional treatment approaches haven't yet brought satisfying results. As a consequence, complementary and alternative medicine has gained increasing popularity among individuals with Fibromyalgia (Pioro-Boisset, Esdaile et al. 1996; Astin, Berman et al. 2003; Holdcraft, Assefi et al. 2003; Gard 2005; Langhorst, Hauser et al. 2008).

5.5. Electromyogram – Biofeedback (EMG-biofeedback)

Since 1987, a few studies have explored the effectiveness of EMG-biofeedback in patients with Fibromyalgia.

The idea of biofeedback in general is to make body parameters, of which one is normally unaware, observable for the client. These parameters are, for example, heart rate, blood pressure, skin temperature or muscle tension. The client receives the information about the parameter in form of sound or visualization on a screen. By help of this feedback, he or she can learn to gain operant control over the respective parameter.

The target system of Electromyogram-Biofeedback is the muscle – specifically the muscle tension. This kind of Biofeedback training is a scientifically established technique to reduce stress and tenseness and can be combined with relaxation techniques. Normally, surface electromyogram is used. The electrodes are placed on distinct formerly chosen muscles to measure their activity. The results are displayed visually on a screen and/or are indicated by a tone. This permits the patient to see and/or hear the level of muscle tension and learn how to influence it consciously. EMG-biofeedback training is successfully employed in the treatment of migraine, chronic tension headache or chronic whiplash associated disorder. Moreover, the method was shown to be beneficial without having inconvenient side-effects (Bogaards and ter Kuile 1994; Voerman, Vollenbroek-Hutten et al. 2006; Nestoriuc and Martin 2007) .

Since there are parallels in the pathology of the above-mentioned diseases and Fibromyalgia,

there were several attempts to transfer the beneficial effect of EMG-biofeedback to patients suffering from Fibromyalgia. In this context, four publications from Ferraccioli (1987), Buckelew (1998), Van Santen (2002) and Drexler (2002) have to be mentioned (see table 1).

In a controlled clinical trial, the group around Ferraccioli showed that EMG-biofeedback had a positive effect on the Tender Point Count, morning stiffness and pain intensity. Post-hoc analyses indicated that patients with depression in the Minnesota Multiphasic Personality Inventory or with a "psychosomatic background" apparently didn't have that benefit. (Ferraccioli, Ghirelli et al. 1987).

In 1998, Buckelew et al. compared Biofeedback/Relaxation training to exercise only, the combination of exercise and biofeedback/relaxation and to education/attention that served as control. They found enhanced "self-efficacy" in all 3 treatments groups. The authors concluded that EMG-biofeedback training had some beneficial effect. Yet, they only found a statistically significant improvement in the Tender Point Index in relation to the education/attention group. So, it remained unclear, if EMG-biofeedback was more effective than the control (Buckelew, Conway et al. 1998).

Van Santen et al. conducted a randomized controlled trial to compare EMG-biofeedback training to fitness training and control. The authors ascertained that they could not detect a greater benefit from biofeedback and fitness training than usual medical care. As possible reasons, they mentioned the restricted biofeedback protocol, the selected outcome measures and the high variability of outcome results between and within the groups (van Santen, Bolwijn et al. 2002).

In the study published by Drexler et al, the 24 patients were first classed into a "psychologically abnormal" and a "psychologically normal" group according to their results in the Minnesota Multiphasic Personality Inventory. Both groups then underwent the same biofeedback training program. The baseline values of Pressure Point Sensitivity, Sensory and Affective Pain dimension and the SF-36 showed greater impairment in the "Abnormal group". After treatment, both groups improved in Pressure Point Sensitivity – the "normal" more than the "abnormal" group - and secondary symptoms. The "abnormal group" showed more positive changes in generic health status and decreased Sensory and Affective Pain. The authors assumed that both groups benefited from EMG-biofeedback training. The findings raise the question as to what degree and in which way psychological background factors interfere with responsiveness to treatment (Drexler, Mur et al. 2002).

The comparison of these four studies shows that the studies are heterogeneous, the study

designs and outcome measures have some weaknesses and the conclusions of the authors are different. Accordingly, this randomised controlled trial with the objective to evaluate the effectiveness of EMG-biofeedback in patients with Fibromyalgia was designed. The specific aim was to examine the effectiveness of EMG-biofeedback training in patients with Fibromyalgia by measurement of health status assessed in the Fibromyalgia Impact Questionnaire Total Score. Weaknesses of previous studies were addressed by performing an RCT with blinded assessors. Valid, reliable and international measures of outcomes relevant to the patient were used (Mease 2005; Mease, Arnold et al. 2007). The intervention group received EMG-biofeedback in addition to usual medical care, but no additional instructions of relaxation techniques that could mask the effect of EMG-biofeedback.

Table 1 (Part 1): Clinical studies in the field of Fibromyalgia and EMG-biofeedback

Author	Interventions	Control	Fibromyalgia specific measures	Pain	Tenderness
Ferraccioli et al.	EMG-biofeedback on M. frontalis with Progressive Muscle Relaxation (N = 6)	"false EMG-biofeedback" (N = 6)	• Morning stiffness *	• VAS *	• Tender Point Count *
Buckelew et al.	EMG-biofeedback on M. trapezius with not specified relaxation techniques (N = 29), exercise (N = 30) and Combination of EMG-biofeedback and exercise (N = 30)	Education/attention (N = 30)	• Sleep measure * • Arthritis Impact measurement scales (AIMS): Physical activity scale **	• VAS * • Pain behaviour measure *	• Tender Point Index * • Total Myalgic Score **
Van Santen et al.	EMG-biofeedback on M.frontalis with Progressive Muscle Relaxation(N=56) and fitness program (N = 58)	Usual care (N=29)	• General fatigue ** • Physical fitness ** • Arthritis Impact Measurement Scales – Total Score **	• VAS **	• Tender Point Count ** • Total Myalgic Score **
Drexler et al.	EMG-biofeedback on M.frontalis with Progressive Muscle Relaxation(N=56) and fitness program (N = 58)	No control group	No measures	• Pressure Point sensitivity * • Pain Perception Scale (*/**)	No measures

Table 1: Clinical studies in the field of Fibromyalgia and EMG-biofeedback, * = significant improvement, ** = no significant improvement

Table 1 (Part 2): Clinical studies in the field of Fibromyalgia and EMG-biofeedback

Author	General Health	Mental Health	Additional measures	Outcome	Comment
Ferraccioli et al.	No measures	• Minnesota Multiphasic Personality Inventory	No measures	EMG-biofeedback is effective in reducing pain and the number of Tender Points and in improving the symptomatology	ACR-criteria not available at point of inclusion; small sample size
Buckelew et al.	No measures	• Symptom Checklist 90 Revised * • Center for Epidemiologic studies – Depression Scale *	• Physician's rating of disease severity * • Self – efficacy *	EMG-biofeedback is effective (within-group comparison) in reducing pain, pain behaviour and psychological distress and in improving sleep. Yet, improvement in between-group comparison was only observed in Self-efficacy. There was no effect on physical activity.	Use of Yunus and ACR-criteria;
Van Santen et al.	No measures	• Symptom Checklist 90 Revised **	No measures	EMG-biofeedback is not superior to usual care (between-group comparison). There were no effects on pain, psychological distress, physical fitness, functional ability and patients' subjective well being.	Four study arms; between-group comparison by ANOVA
Drexler et al.	• Short Form 36	• Minnesota Multiphasic Personality Inventory	No Measures	EMG-biofeedback improves health related quality of life, importance of patients' psychological status	No RCT

Table 1: Clinical studies in the field of Fibromyalgia and EMG-biofeedback, * = significant improvement, ** = no significant improvement

6. Methods

6.1. Study Design

This project was conceptualized as a one-centre randomized, assessor-blinded controlled trial with an intervention and a control group. There were three points of assessment: before intervention (baseline, T0), at the end of treatment (T1) and at follow-up after 3 months (T2) (figure 2, p).

The study was approved by the ethical committee of the Ludwig-Maximilians-University Munich, Germany.

The study design is shown in figure 2 (p.26).

6.2. Setting

The study was conducted in the outpatient clinic of the department of Physical Medicine and rehabilitation at the Ludwig-Maximilians-University Munich, Germany.

6.3. Patient recruitment and data collection procedure

Patients were recruited from the waiting list of the Fibromyalgia day hospital program of the department of Physical Medicine and Rehabilitation. In this context, the diagnosis was confirmed in accordance to the ACR-criteria and the criteria of Müller and Lautenschläger (Muller and Lautenschlager 1990; Wolfe, Smythe et al. 1990).

The recruitment process of our study started with the invitation of patients to the baseline visit (T0) of the study. A specialist in Physical Medicine and Rehabilitation asked for the medical history of the patient and performed a general examination including body height, weight, blood pressure and heart rate. Then, the Tender Points defined by the ACR-criteria and control points were palpated (Okifuji, Turk et al. 1997). The 3 pairs of control points were located at the humeral-radial joint, in the dorsal soft tissue between ulna and radius in the transition zone between medial and distal forearm and in the soft tissue between first and second beam of the hypothenar.

Patients were finally included in the EMG-biofeedback study, if they were female, between 18 and 65 years old, had the cognitive ability and sufficient German language skills to fill in the questionnaires and signed the provided informed consent. Exclusion criteria were major medical disorders, i.e. cancer, chronic heart failure NYHA IV or asthma requiring cortisone medication, suffering from psychosis or major affective disorders, substance abuse, co-

medication with opiates or benzodiazepine, transmeridian flight in the last weeks or shift-work or gravity.

Patients who fulfilled the inclusion criteria and who had no exclusion criteria were asked to fill in the informed consent. The patient then received the first set of questionnaires and was randomized to the treatment or control group.

Patients were randomized by a block randomization of two or four to the treatment or control group. Block sizes were determined by a random fashion. Random numbers were generated by the Microsoft EXCEL program. A person who was neither involved in the intervention nor in the assessments provided sealed envelopes with the group assignments.

Within three days after inclusion, the patient was presented to a specialist in psychosomatic medicine for additional evaluation. After that the first meeting with the Biofeedback therapist took place. To avoid bias in the psychosomatic evaluation, patients were not informed about their group allocation prior to the first visit.

Intervention patients proceeded to perform 14 sessions of EMG-biofeedback training according to the study protocol (see 6.4). During the first three weeks, they had three appointments per week and one appointment per week during the following five weeks.

With an interval of 8 weeks, the control group had only two encounters with the therapist. During the observation period, all patients in both groups received the usual medical care. This included the temporary intake of acetaminophen for acute pain, which patients were asked to record in a diary. Additionally, they were asked not to begin any other treatment for Fibromyalgia during the study.

The intervention group was given the second set of questionnaires at the end of the 14th training session, the control group at the second appointment with the therapist.

Before undergoing the second clinical examination at the end of treatment (T1), all patients were instructed not to mention to which group they belonged in presence of the examiner.

After 12 weeks (T2), the third set of questionnaires was sent to all patients.

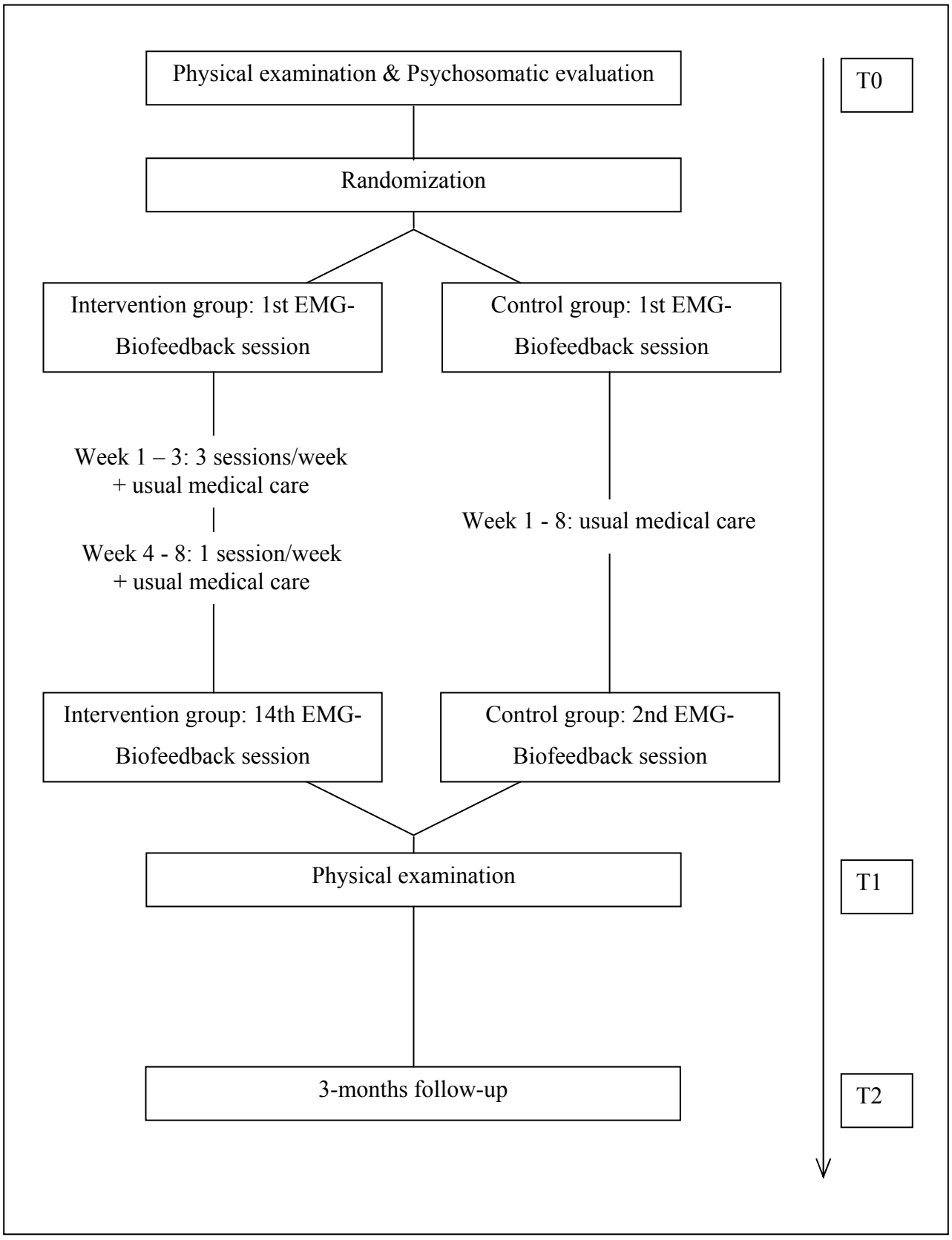

Figure 2: Study design, T0 = baseline, T1 = end of treatment, T2 = 3-months follow-up

6.4. Technical aspects and Biofeedback training protocol

The biofeedback training was performed with the Schuhfried Biofeedback apparatus and software "Biofeedback 2000 x-pert", all provided by Schwa-medico, Ehringshausen, Germany.

At the beginning of each treatment session, patients were asked to assess pain, nervousness, depressive mood, fatigue, and stiffness on a visual analogue scale. Then, the Biofeedback apparatus' electrodes were placed on both the upper and lower trapezius muscle; the grounded electrode was placed on the medial part of the upper trapezius muscle. The apparatus displayed one EMG curve for each side on a computer screen, which visualized the muscle tension. First, the EMG activity of the trapezius muscle was measured for 5 minutes in order to get a solid baseline. The intervention patients were instructed that an ascending curve corresponded to increasing and a descending curve to decreasing muscle tension. There was no instruction about specific relaxation techniques. After that, the task of the patient was to consciously strain the trapezius muscles for 3 minutes. In the following 10 minutes the patients were asked to relax these muscles. During the entire duration of muscle straining and relaxation, they received visual feedback of muscle tension in form of EMG curves. The procedure of conscious muscle straining and relaxation was done twice. After each cycle, the self-assessment with visual analogue scales was repeated as in the beginning. At the end of the training session, these results and the patients' feeling of muscle tension were discussed in relation to the EMG-biofeedback curves. Finally, patients were encouraged to do a home exercise program, in which they consciously relaxed the muscle by using "their" relaxation technique analogously to the biofeedback session for about 15 minutes per day. Additionally, they should try to apply the techniques in stressful situations, for example appointments at the dentist's.

The patients in the control group, however, had two encounters with the therapist, where they assessed visual analogue scales and their trapezius muscle activity was measured during 5 minutes, just as in the intervention group. But afterwards, they did not continue with muscle straining and relaxation.

6.5. Measures

In this study, data was collected at three time-points. Table 2 displays the measures and their application at each assessment.

Measure	Baseline (T0)	End of treatment (T1)	3 – months – follow-up	Outcome domaines
Sociodemography	**X**	--	--	Sociodemographic data
SCQ	**X**	--	--	Comorbidities
FIQ	**X**	**X**	**X**	Disease specific
Tender Point Score	**X**	**X**	**X**	Self-reported pain
Dolorimetry	**X**	**X**	--	Tenderness, Pain Pressure Threshold
Tender Point Count (number of Tender Points)	**X**	**X**	--	Tenderness, widespread pain
SF - 36	**X**	**X**	**X**	Generic health status
Patients' Global Clinical Impression of Change	--	**X**	**X**	Change of health
BDI	**X**	**X**	**X**	Depression
SCL90-R	**X**	--	**X**	Psychological distress

Table 2: Measures

Legend to table 2: SCQ = Self–administered Comorbidity Questionnaire, FIQ = Fibromyalgia Impact Questionnaire, SF – 36 = Short Form 36, BDI = Beck Depression Inventory, SCL90-R = Symptom Checklist 90 Revised

6.5.1. Measures of sociodemography and comorbidities

Sociodemographic characteristics were assessed by a questionnaire asking for first language, education, status of employment, working hours per week, smoking, alcohol consumption and physical activity.

Further, patients were asked for the date of onset of Fibromyalgia symptoms.

Comorbidities were evaluated using the Self-administered Comorbidity Questionnaire. It asks for the presence of a number of health problems, for example heart disease or back pain. For each problem the questionnaire has the option to ask "Do you receive treatment for it?" and "Does it limit your activities?" as proxies for disease severity and the burden of disease. In the present German version, there are 13 medical problems and three optional conditions. The maximum score is 3 points for each problem/condition. The total maximum score is 39 points, if only the defined items are included, or 48 points, if the optional items are included. (Sangha, Stucki et al. 2003).

6.5.2. Primary outcome measure

The Fibromyalgia Impact Questionnaire is a disease specific multidimensional measure of patient status, progress and outcomes. It is considered to capture the global effect of Fibromyalgia symptomatology, and covers the dimensions physical functioning (11 items), well-being (1 item), work situation (2 items), pain (1 item), fatigue /sleep (2 items), stiffness (2 items) and psychological symptoms (2 items). It is extensively used and has shown good responsiveness to change in clinical studies. Scoring ranges from 0 to 80 with the latter number being the worst case. Specifically, the Fibromyalgia Impact Questionnaire Total Score gives a summary of patients' impairment and is recommended as a highly sensitive measure of change in Fibromyalgia treatment programs and clinical studies (Burckhardt, Clark et al. 1991; Dunkl, Taylor et al. 2000; Maura Daly 2003; Bennett 2005). There are translations in different languages available. In this study the German validated version was used (Offenbaecher, Waltz et al. 2000).

6.5.3. Secondary outcome measures

Pain measures comprise instruments for self-report pain and tenderness.

The Tender Point Score consists of a body diagram, where patients can rate the pain intensity at 24 locations of the front and the back side of the body that are commonly indicated as painful by Fibromyalgia patients. It allows calculating a total score for the whole body, as well as specific local scores (Lautenschlager, Seglias et al. 1991).

According to the Tender point manual survey, the Tender Point Count was assessed by thumb palpation. The examiner applied discrete pressure of 4 kg/cm² to each of the 18 Fibromyalgia typical Tender Points. When the patients expressed pain, the tender point was considered positive.

For measuring the Pressure Pain Threshold, the assessor first searched for an induration with pressure pain in the M trapezius pars descendens on each side of the muscle. The palpated part of the muscle was always located above or on a line between the acromioclavicular joint and the spinous process of vertebrae C 7. These two structures also served as coordinates to write down the exact place of the palpated taut band. Second, using a Fischer dolorimeter (figure 3) with a stamp of 1 cm², the examiner applied vertical pressure to the selected point and successively augmented the pressure until the patient signalled pain. In this way, the pressure pain threshold was measured in kg/cm² (Fischer 1987; Nussbaum and Downes 1998).

Figure 3: Fischer dolorimeter

The generic health status was measured by the German version of the Short-Form 36 (SF-36), a generic, multi-purpose, short-form health survey containing 36 questions to assess different

aspects of health status. It yields an eight-scale profile of scores which are Physical Functioning, Role-Physical, Bodily Pain, General Health, Vitality, Social Functioning, Role-Emotional and Mental Health. This questionnaire has been proven to be useful in comparing general and specific populations, estimating the relative burden of different diseases, differentiating the health benefits resulting from a wide range of different treatments, and screening individual patients. (Ware and Sherbourne 1992; Bullinger 1995; Ware and Gandek 1998).

The self rated Patients' Global Clinical Impression of Change Score was applied, which is a validated measure of overall change compared with study onset, including six possible scores from "very much worse" (score 1) to "very much better" (score 6) (Guy 1976).

Depression was assessed by the Beck Depression Inventory (BDI). This is a questionnaire developed and validated for patients with depression and has been applied in clinical trials of patients with Fibromyalgia. It contains 21 items that assess the cognitive, affective and neurovegetative factors associated with depression (Beck, Ward et al. 1961; Hautzinger 1991).

Further, the Symptom Checklist 90 Revised (SCL-90-R) was used, which generates 9 specific scales, one additional unspecific scale and three general scores. The 9 dimensions of the scale are as follows: SCL 1 = somatization; SCL 2 = obsessive-compulsive symptoms; SCL 3 = interpersonal sensitivity; SCL 4 = depression; SCL 5 = anxiety; SCL 6 = hostility; SCL 7 = phobic anxiety; SCL 8 = paranoid ideation; SCL 9 = psychoticism. The Global Severity Index serves as a measure of psychological distress (Derogatis, Lipman et al. 1973; Franke 1995).

6.6. Analyses

6.6.1. Sample size calculation

The sample size calculation was based on the hypothesis that EMG-biofeedback may have a similar effect as a cognitive behavioural approach, shown in a randomized clinical trail (Redondo, Justo et al. 2004). The analysis to determine the sample size was performed with the formula $2N = 4(Z\alpha + Z\beta)^2 \sigma^2 / \delta^2$.

From the assumption of a power (1-ß) of 0.9, a level of significance (α) of 0.05, a reduction of the Fibromyalgia Impact Questionnaire by 12.8 points (SD 11.4), a sample size of 17 patients per treatment arm was necessary in order to detect a statistically significant difference. If the dropout rate up to T1 had been 10 %, a total sample size of 38 patients would have been necessary (Redondo, Justo et al. 2004).

6.6.2. Scoring of questionnaires

The Fibromyalgia Impact Questionnaire Total Score was obtained according to the validation of the German 8-item version. The physical function items are rated on a 4-point Likert type scale; the well being and the first work related question ask the patient to mark the number of days they felt well and the number of days they were unable to work (including housework) in the last week .The other items are rated on visual analogue scales. Each item has a maximum possible score of 10. The Total score was calculated by adding the physical functioning score, numbers of days felt well, pain, fatigue, morning tiredness, stiffness, anxiety and depression. The highest possible score is 80 what indicates maximum impact of disease (Offenbaecher, Waltz et al. 2000).

In the body diagram of the Tender Point Score, patients rated pain with 6-point Likert scales from 0 = no pain to 5 = maximal pain. All ratings of the 24 locations were added leading to a total score for general pain, which is maximum 120. In addition, local pain in the M. Trapezius region was assessed (Lautenschlager, Seglias et al. 1991).
Concerning tenderness measures, the Tender Point Count was performed according to ACR-criteria (Wolfe, Smythe et al. 1990). Further, we calculated the mean of the Pain Pressure Threshold of both sides of the M. Trapezius in order to compare the change over time.

Following the SF-36 Health Survey Manual and Interpretation Guide, patients' questionnaires were only included for calculation, if each scale of the SF-36 had at least 50% of the corresponding items answered. Each scale ranges from 0 indicating 'maximal symptoms/maximal limitations/poor health' to 100 indicating no 'symptoms/no limitations/excellent health' (Bullinger 1998).

The mean of the patient ratings was calculated for the Patients' Global Clinical Impression of Change (Guy 1976).

The sum score of the Beck Depression Inventory was obtained as recommended in the handbook for the German version. The range of score is from 0 to 63, where values above 11 indicate presence of mild to moderate depressive symptoms, and values above 18 indicate clinically relevant depression (Hautzinger 1995).

The items of the Symptom Checklist 90 Revised scales are rated on a 5–point Likert scale (O = not at all – 4 = very strong). In concordance with SCL-90-R manual the GSI is calculable in all questionnaires in the following fashion:

$$GSI = GS/ (90 – \text{number of missing items})$$

GS = sum score of all answered items.

The resulting scores are transformed to "t-values" by help of standard lists in the manual. "T-values" between 60 and 70 indicate a distinct, 70 and above a high burden of psychological distress. The maximum score is 80 (Franke 1995).

6.6.3. Group comparison

The null hypothesis (H0) for the primary outcome was that there is no difference of the changes of the FIQ Total Score between treatment and control group at T2 (Change score: T2-T0). Analogously, H0 for secondary outcome measures were no differences of the changes at T1 (T1-T0) and T2 (T2-T0).

In order to examine the statistical significance between the score changes, the data were tested on normality with the help of histograms and the comparison of means and medians. In case of normal distribution the t-test for independent samples was used, otherwise, the Mann-Whitney U test for significance was performed.

The group comparisons for secondary outcome measures were performed analogously.

Additionally, effect sizes (ES) were calculated by Cohen's d at the end of treatment and at the 3-months follow-up.

d is defined as the difference of two means divided through the pooled standard deviation (Rosenthal 1994).

$$d = M1 - M2 / \sigma pooled$$

$$\sigma pooled = \sqrt{[(\sigma 1^2 + \sigma_2^2) / 2]}$$

M1 = change of mean intervention group (IC), M2 = change of mean control group (CG), $\sigma 1$ = standard deviation intervention group, $\sigma 2$ = standard deviation control group

Cohen considered an effect size of 0.2 as a small, of 0.5 as a medium and 0.8 as a large positive effect of therapy. Positive effect sizes indicate an advance for the treatment groups (Cohen 1988).

All data analyses were performed by using SPSS for windows, version 14.0. Outcome scores are illustrated by simple graphs.

7. Results

7.1. Patients

Between April 2005 and April 2006, 40 female patients were enrolled in the study.

In the intervention group as well as in the control group, one patient withdrew for private reasons before end of treatment. Also in the follow-up (T2), there were two drop-outs, one person in each group. Both patients did not return the set of questionnaires and could not be contacted despite several attempts.

Finally, 36 out of 40 patients completed the study (90%).

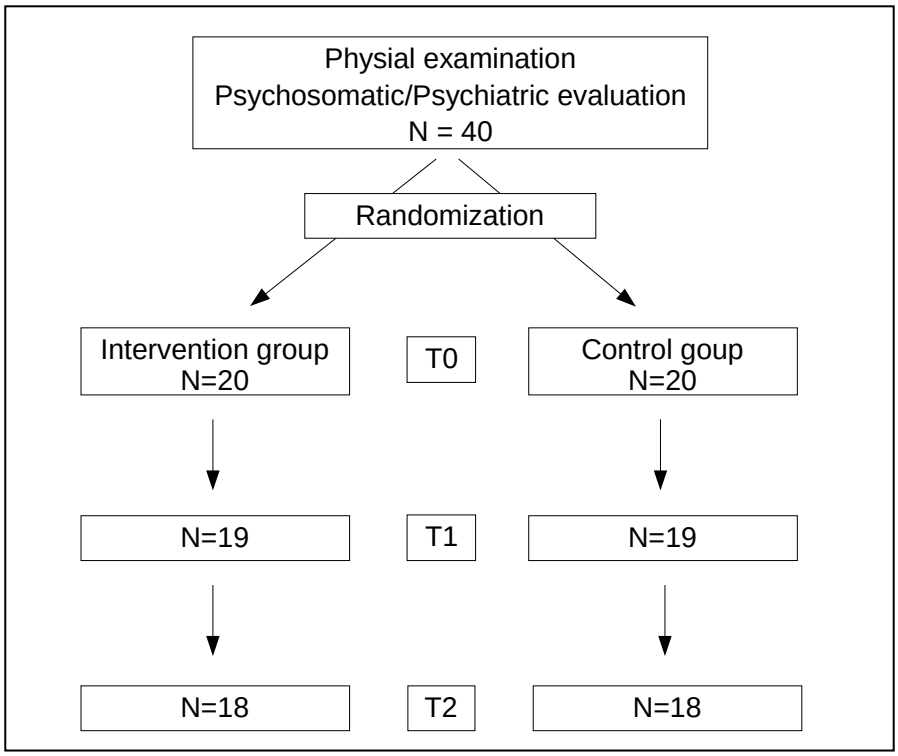

Figure 4: Patients, T0 = Baseline, T1 = end of intervention, T2 = 3-months follow-up

7.2. Patients characteristics

7.2.1. Sociodemography

Sociodemographic characteristics are presented in table 3. Regarding age, marital status and alcohol consummation there were no differences between the intervention and the control group. Further, the groups did not differ statistically significant in education status, smoking habits and physical activity (p–values not presented).

	Intervention group N=18	Control group N=18
Age, mean yrs (SD)	55.4 (6.07)	55.97 (6.14)
Mother tongue German	94.4%	100.0%
School Education level		
Basic level (9 yrs)	38.9%	16.7%
Middle level (10 yrs)	33.3%	61.1%
Higher level (10-13 yrs)	27.8%	22.2%
Marital Status		
Unmarried	22.2%	11.1%
Married	55.6%	61.1%
Divorced	22.2%	16.7%
Widowed	0.0%	11.1%
Smoking	5.6%	22.2%
Alcohol consommation		
None	22.2%	22.2%
Occasionally	55.6%	55.6%
1x/d	22.2%	16.7%
Several times/d	0.0%	11.1%
Daily physical activity		
None	5.6%	5.6%
< 30 min/d	44.4%	22.2%
30 to 60 min/d	38.9%	50.0%
> 60 min/d	11.1%	22.2%
Weekly sporting activity		
> 2 hours/w	27.8%	50.0%
1 to 2 hours/w	50.0%	38.9%
< 1 hour/w	5.6%	11.1%
None	16.7%	0.0%

Table 3: Sociodemography

7.2.2. Clinical data at baseline

Table 4 summarizes the results of the outcome measures at baseline. In the Fibromyalgia Impact Questionnaire Total Score and most other measures there was no statistical group difference. Only the Vitality and the Role-Emotional scale of the Short-Form 36 were significantly better in the control group.

	Intervention group (N=18) Mean (SD)	**Control group (N=18)** Mean (SD)	**p-value**
Years of complaints, mean yrs (SD)	12.44 (12.24) [range 1-43]	16.39 (9.06) [range 2-38]	0.28
Comorbidities, mean (SD)	5.5 (4.03)	5.83 (2.6)	0.46
FIQ Total Score	42.59 (9.71)	40.44 (14.21)	0.60
Tender Point Score			
Total Score	55.97 (18.62)	58.82 (20.34)	0.66
Trapezius Score	3.08 (1.10)	3.56 (0.92)	0.17
Tender Point Count, mean (SD)	15.95 (1.51)	16.32 (1.67)	0.33
Dolorimetry (kg/cm²)	1.55 (0.70)[3]	1.63 (0.65)[3]	0.71
SF-36			
Physical functioning	47.62 (13.42)[1]	54.17 (19.19)	0.25
Role-Physical	26.56 (34.72)[2]	38.89 (39.50)	0.36
Bodily Pain	38.59 (10.65)[1]	36.94 (12.49)	0.68
General Health	37.94 (18.88)[1]	41.83 (14.35)	0.50
Vitality	26.76 (17.32)[1]	37.22 (12.86)	0.05*
Social functioning	53.68 (24.91)[1]	60.42 (23.58)	0.40
Role-Emotional	25.00 (35.49)[2]	57.41 (43.99)	0.04*
Mental Health	50.82 (15.48)[1]	57.28 (16.77)	0.25
BDI, mean (SD)	17.55 (8.16)	12.77 (6.36)	0.06
SCL90-R			
Global Severity Index, mean (SD)	66.89 (11.29)	60.83 (13.60)	0.16

Table 4: Baseline characteristics of Fibromyalgia patients (N=36)

Legend to table 4:

SD = standard deviation (written in parenthesis), [1] N = 17, [2] N = 16, [3] N = 19

FIQ (= Fibromyalgia Impact Questionnaire) Total Score scale: 0 = best health status, 80 = worst health status, Tender Point Score Total Score Scale 0 = no pain, 100 = maximal pain, Trapezius Score scale 0 = no pain, 5 = maximal pain, Dolorimetry = applied pressure in kg/cm², SF-36 scale 0 = worst health, 100 = best health, BDI (= Beck Depression Inventory) scale 0 – 11 = no depression, 12 – 18 = depressive symptoms, 19 – 63 = clinical meaningful depression, SCL90-R (Symptom Checklist 90 Revised) Global Severity Index scale: 60 - 70 = moderate psychological distress, > 70 = high burden of psychological distress.

Tests for significance: Number of Tender Points, Role-Physical, Social Functioning, Role-Emotional: Mann – Whitney U – test; All other scales: t - test for independent samples.

* = statistically significant difference

7.2.3. Primary and secondary outcome measures

The primary outcome, the Fibromyalgia Impact Questionnaire Total Score, and all secondary outcome measures, including the Tender Point Score, the Tender Point Count and the Pressure Pain Threshold, the SF-36 and Patients' Global Clinical Impression of Change, the Beck Depression Inventory and the Global Severity Index of the SCL-90-R are shown in table 5. Figure 5 shows the course of the Fibromyalgia Impact Questionnaire Total Score for both groups.

There was no difference in the changes of the FIQ Total Score between the intervention and the control group at the end of treatment (ES = 0.02, p = 0.95). Their scores improved by the same degree. Also at the follow-up there were no group differences, even though the intervention group maintained approximately the same level and the controls´ score increased (ES = 0.26, p = 0.43).

With only one exception, there were also no statistically significant differences in the changes of the secondary outcome measures between the groups. Only the Pain Pressure Threshold at the end of treatment was significantly higher in the intervention group (ES = 0.26, p = 0.014).

Table 5: Outcome of Fibromyalgia patients from baseline to 3-months follow–up (N = 36)

	Baseline (T0)		T1			T2		
	Intervention group (N18)	Control group (N18)	Intervention group (N18)	Control group (N18)	Comparison of changes	Intervention group (N18)	Control group (N18)	Comparison of changes
	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	(p-value /ES[4])	Mean (SD)	Mean (SD)	(p-value /ES[4])
FIQ								
Total Score	42.59 (9.71)	40.44 (14.21)	37.11 (14.89)	35.23 (17.16)	0.95/0.02	37.87 (9.65)	38.28 (15.58)	0.43/0.26
Tender Point Score								
Total Score	55.97 (18.62)	58.82 (20.34)	54.56 (19.13)	63.44 (21.76)	0.37/0.45	53.00 (20.69)	58.94 (16.54)	0.44/0.22
Trapezius Score	3.08 (1.10)	3.56 (0.92)	2.94 (1.20)	3.31 (0.88)	0.73/-0.12	3.08 (1.27)	3.17 (1.06)	0.25/-0.39
Tender Point Count	15.95 (1.51)	16.32 (1.67)	14.74 (1.91)	15.68 (2.29)	0.402/0.3			
Dolorimetry	1.55 (0.70)[3]	1.63 (0.65)[3]	2.08 (0.94)[3]	1.72 (0. 74)[3]	0.014*/0.84			
SF-36								
Physical functioning	47.62 (13.42)[1]	54.17 (19.19)	49.31(19.41)[1]	54.23 (24.34)	0.67/0.14	51.64 (21.01)[1]	51.64 (21.01)	0.21/0.43
Role-Physical	26.56 (34.72)[2]	38.89 (39.50)	14.06 (27.34)[2]	33.33 (38.35)	0.47/-0.21	15.62 (25.62)[2]	20.83 (32.37)	0.57/0.25
Bodily Pain	38.59 (10.65)[1]	36.94 (12.49)	36.71(16.00)[1]	30.44 (16.92)	0.43/0.27	36.88 (11.52)[1]	36.17 (15.34)	0.84/-0.07
General Health	37.94 (18.88)[1]	41.83 (14.35)	36.53 (19.21)[1]	44.67 (18.53)	0.14/-0.52	43.50 (16.50)[1]	44.44 (18.33)	0.47/0.24
Vitality	26.76 (17.32)[1]	37.22 (12.86)	28.24 (17.58)[1]	41.67 (14.85)	0.52/-0.22	28.63 (16.35)[1]	38.80 (15.49)	0.94/0.03
Social functioning	53.68 (24.91)[1]	60.42 (23.58)	50.00 (22.10)[1]	60.42 (27.20)	0.61/-0.14	53.68 (25.68)[1]	61.11 (25.69)	0.86/-0.03
Role-Emotional	25.00 (35.49)[2]	57.41 (43.99)	47.92 (47.09)[2]	57.41 (43.99)	0.16/0.54	35.42 (42.98)[2]	59.26 (47.90)	0.77/0.2
Mental Health	50.82 (15.48)[1]	57.28 (16.77)	51.35 (20.14)[1]	60.67 (21.49)	0.53/-0.21	51.06 (17. 86)[1]	57.50 (18.36)	1.00/0
Global clinical impression			3.37(0 60)	3.00 (0. 67)	0.08/0.58	3.17 (0.62)	2.78 (1.00)	0.17/0.47
BDI	17.55 (8.16)	12.77 (6.36)	16.11 (8.78)	12.89 (7.3)	0.44/0.26	16.91 (8.33)	12.30 (6.31)	0.93/-0.03
SCL90-R								
Global Severity Index	66.89 (11.29)	60.83 (13.60)				66.11 (11.28)	63.22 (12.75)	0.12/0.53

Legend to table 5:

SD = standard deviation (written in parenthesis), [1] N = 17, [2] N = 16, [3] N = 19

FIQ (= Fibromyalgia Impact Questionnaire) Total Score scale: 0 = best health status, 80 = worst health status, Tender Point Score Total Score Scale 0 = no pain, 100 = maximal pain, Trapezius Score scale 0 = no pain, 5 = maximal pain, Dolorimetry = applied pressure in kg/cm², SF-36 scale 0 = worst health, 100 = best health, Clinical global impression scale 1 = "very much worse", 5 = "very much better", BDI (= Beck Depression Inventory) scale 0 – 11 = no depression, 12 – 18 = depressive symptoms, 19 – 63 = clinical meaningful depression, SCL90-R (Symptom Checklist 90 Revised) Global Severity Index scale: 60 -70 = moderate psychological distress, > 70 = high burden of psychological distress.

ES = effect size = [4](score at end of treatment – score at baseline) / standard deviation at baseline and [5](score at 3-months follow-up – score at baseline) / standard deviation at baseline.

Tests for significance: Number of Tender Points, Tender Point Score Total Score, Role-Physical, Social Functioning, Role-Emotional: Mann – Whitney U – test; All other scales: t - test for independent samples.

Null hypotheses: difference (mean at end of treatment - mean at baseline) = zero and difference (mean at 3-months follow-up - mean at baseline) = zero; $p > 0.05$: we accept the null hypothesis at type I error = 5%.

* = statistically significant difference

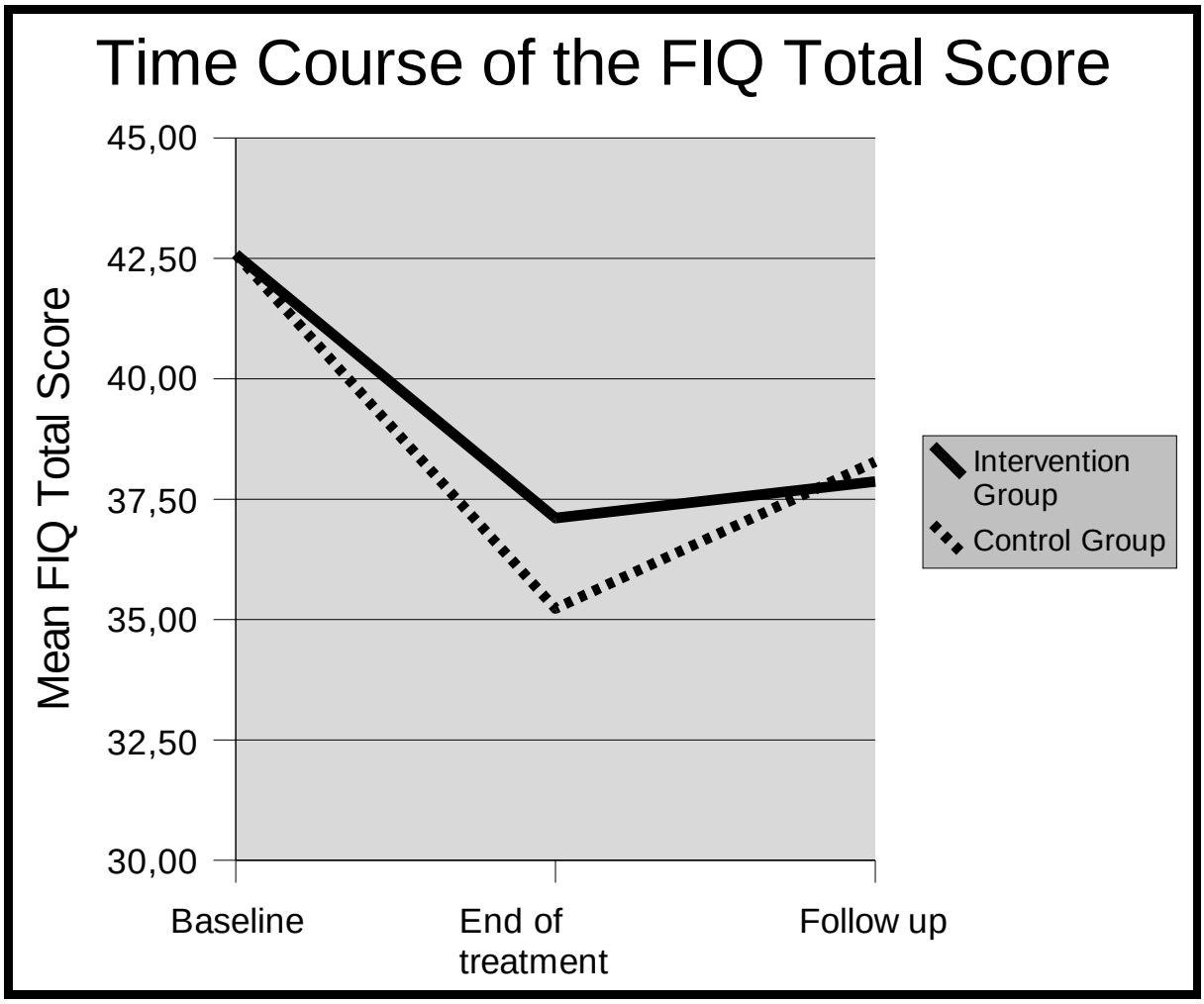

Figure 5: Time course of the FIQ Total Score. 0 = best health status, 80 = worst health status

8. Discussion

In this randomized controlled trial EMG-biofeedback did not improve health status of patients with Fibromyalgia. The primary outcome measure (FIQ) and all secondary outcome measures, with the exception of the pressure pain threshold in the trapezius muscle, showed no superiority of EMG-biofeedback in addition to usual care compared to usual care alone.

The four previous clinical studies that investigated EMG-biofeedback in the treatment of Fibromyalgia used very different outcome measures and EMG-biofeedback protocols (see table 1, p.19/20). In the following the comparison of this study to the previous ones is structured by the measured outcomes.

In this RCT, the primary outcome was measured by the disease specific health status measure Fibromyalgia Impact Questionnaire Total Score. Ferraccioli at al. (1987), Buckelew et al. (1998) and Van Santen et al. (2002), used also disease specific patient-orientated measures (see table 1). In the study of Buckelew et al. "physical activity" was measured by the Arthritis Impact Questionnaire measurement scales (AIMS). The AIMS had served as a model to develop the Fibromyalgia Impact Questionnaire. In consistence with this trial Buckelew did not detect improvements in the disease specific health status measured by the AIMS. Likewise, Van Santen found no improvement in the AIMS. In contrast, Ferraccioli found significant improvements in "Morning stiffness" and "day-time fatigue", domains that are included in the corresponding FIQ subscales. However, the positive effect cannot be clearly related to biofeedback, because patients in that study were taught Progressive Muscle Relaxation for use during the biofeedback sessions.

In this study, self-reported pain – throughout the body and locally – did not decrease significantly. Consequently, the assumption that it might be possible to achieve local and general pain relief by reduction of muscle tension was not confirmed. However, we found a positive effect in the clinical test of tenderness. The Pressure Pain Threshold increased significantly in the target area (ES = 0.84). In contrast, there was no significant change in the number of Tender Points (ES = 0.30).

The disconnection of self-reported pain and tenderness is consistent with results from Buckelew et al. (1998). But in contrast to our study, Buckelew et al. found a significant improvement, but not in the pressure pain threshold measured by dolorimetry (Total Myalgic Score). However, the pain relief in that study was only significant in within-group, but not in between-group comparison. In the study of Van Santen et al. (2002), there was no change,

neither in self reported pain (Hassett, Radvanski et al.) nor in tenderness (Total Myalgic Score), whereas Ferraccioli et al. observed important pain relief (Hassett, Radvanski et al.). Drexler et al. assessed the pain quality and could not detect significant changes in the sensory and affective dimensions of pain (Ferraccioli, Ghirelli et al. 1987; Buckelew, Conway et al. 1998; Drexler, Mur et al. 2002; van Santen, Bolwijn et al. 2002).

Generic health status was assessed by the SF-36. At baseline, the study sample differed significantly in the SF-36 subscales for "Vitality" and "Role-Emotional". Whereas the difference in "Vitality" was maintained at the end of treatment, the intervention group showed fewer restrictions in facing daily tasks due to emotional problems (ES = 0.54). However, the total of the changes of the SF-36 subscales showed no clear tendency for a benefit of EMG biofeedback. This is in contrast with the results of Drexler et al. who had found beneficial effects in health status after biofeedback training. The authors emphasized that the degree of benefit depended on the Minnesota Multiphasic Personality Inventory profile of their clients. The "psychologically normal" group showed statistically significant improvements only in "Vitality" and "Mental Health"; in contrast, the "abnormal" group improved in all subscales, except "Role Emotional". The study is limited, because a comparison with a control group was not performed. But it points out that patients' psychological profiles may influence response to treatment and self-perception of health status. This supports the opinion that subgroups of Fibromyalgia exist and that these require different kinds of treatments adapted to their needs (Turk, Okifuji et al. 1998; Drexler, Mur et al. 2002; Giesecke, Williams et al. 2003; Muller, Schneider et al. 2007).

The possible improvement in mental condition due to treatment was a topic in the present study and in the studies of Buckelew and Van Santen. The assessment instruments were similar.

The Beck Depression Inventory showed no statistically significant improvement in the intergroup comparison, neither at the end of treatment nor in the follow-up. Also, the effect sizes were small. This corresponds with the findings of Buckelew et al., who had employed the Center for epidemiologic studies – Depression scale, which covers 20 items to measure depressive symptoms. In that study only the within-group comparison showed significant improvement. With respect to the Global Severity Index of the SCL-90R, that reflects the burden of symptomatology, our control group scored higher at the end of the observation period, which suggests more psychological distress, whereas the intervention group remained stable. The effect size reflected a moderate benefit (ES = 0.56), but the result was not

significant. This finding is consistent with the study of Van Santen et al. and the between-group comparison of Buckelew et al.. The latter study group found an improvement in the Global Severity Index only in the pre-post comparison within the treatment group.
Due to the inconsistent outcome of the BDI and the SCL-90-R Global Severity Index, one cannot conclude that the intervention may lead to a certain stabilization of mood regarding the burden of psychological distress. Drexler et al. treated the aspect of mental health in a different way. They followed the idea of Ferraccioli who postulated that patients respond different to treatment depending on their profile in the Minnesota Multiphasic Personality Inventory. So, rather than investigating if EMG-biofeedback improved patients' mental condition, Drexler's group examined the association between patients' mental condition and the outcome of EMG-biofeedback training.

When asked for their Global Clinical Impression of Change, patients undergoing EMG-biofeedback training reported that they felt a tendency toward improvement of their condition. In contrast, the controls announced slight worsening. The statistics revealed a moderate clinical effect (T1: ES = 0.58, p = 0.081, T2: ES = 0.47, p = 0.171), but this was not significant. The patients' expectation in the intervention group that they underwent a potential beneficial treatment may have influenced the result of the global impression scale.

One important question in the comparison of EMG-biofeedback studies is whether differences in the combinations of EMG-biofeedback and instructions to relaxation strategies may result in different outcomes. In the last decades it has been found that relaxation training alone has a beneficial effect in the treatment of chronic pain. Different relaxation techniques have been studied and are recommended for the treatment of Fibromyalgia (JAMA 1996 [no authors listed]; Holdcraft, Assefi et al. 2003; Williams 2003; Castel, Perez et al. 2007).
In this study, EMG-biofeedback was purposely not combined with techniques, such as Progressive muscle relaxation of Jacobsen, autogenic training or breathing relaxation. The goal was to mediate relaxation solely through visual feedback of muscle tension and not with a specific technique supported by EMG-biofeedback. That means that we differentiated between biofeedback relaxation training and biofeedback-assisted relaxation. Contrarily, Van Santen et al. taught Progressive muscle relaxation in order to use it during EMG-biofeedback training. In the same fashion, Buckelew et al. proceeded with instruction of "cognitive and muscular relaxation strategies". In the end, the two groups came to opposite conclusions of the effectiveness of EMG-biofeedback training what could be due to the different relaxation

strategies. Similar to the present study, Drexler et al. do not mention having employed a special relaxation strategy during the EMG-biofeedback training. However, that study showed positive effects of EMG-biofeedback. The reason might be found in the realisation of EMG-biofeedback training itself. Unlike us, for example, Drexler et al. used acoustic feedback in addition to visual feedback of muscle tension. This may have lead to a more pronounced feedback and finally to a more beneficial effect.

In this RCT we selected outcome measures that cover symptoms, problems in body functions and limitations in activities that are most relevant from the patients' perspective and that were appropriate for the aims of the project. Specifically, the Fibromyalgia Impact Questionnaire Total Score was selected as primary outcome measure, because it covers impairments of high relevance for patients with Fibromyalgia, and it has been found to be sensitive to changes in the health status of patients in Fibromyalgia treatment programs and in clinical trials. The questionnaire was exclusively developed for Fibromyalgia and measures the components of health status that are believed to be mostly affected in Fibromyalgia. (Dunkl, Taylor et al. 2000; Maura Daly 2003; Bennett 2005). The Fibromyalgia Impact Questionnaire is criticized, because it was primarily validated for women and tends not to detect changes in patients with low levels of disability. In this study, participants were all female and had FIQ baseline values as high as in other trials (Offenbaecher, Waltz et al. 2000; Bennett 2005; Mease 2005). This confirms the selection of the FIQ as primary outcome measure.

Self-reported clinical pain and tenderness are both characteristic and necessary in diagnosing Fibromyalgia. Yet, their functional association and how they are related to one another is not clear (Jacobs, Rasker et al. 1996). It has been shown that these entities do not equally respond to treatment interventions (Gracely, Grant et al. 2003). In this study, clinical pain was evaluated with the body diagram of Lautenschläger. The body diagram allows calculating a sum score for overall pain intensity that measures generalized pain similar to a visual analogue scale (Hassett, Radvanski et al.) that asks for general pain. Tenderness was assessed by Pressure Pain Threshold in the M. trapezius region where the EMG-biofeedback electrodes were placed. The Total Myalgic Score and the Tender Point Index for all Tender Points were not measured. Fibromyalgia patients had not only been found to be more sensitive to pressure at Tender Points than healthy controls, but throughout the whole body, for example, at the M. trapezius and M. frontalis (Tunks, Crook et al. 1988; Bendtsen, Norregaard et al. 1997; Petzke, Clauw et al. 2003). A recent study has noticed that "sham points" had

higher pain thresholds than Tender Points, but can be used as an equivalent of the total myalgic score that consists in measuring the pain threshold at all Tender Points with dolorimeters (Harden, Revivo et al. 2007).

Although the Short From–36 (SF-36) has not yet been evaluated for responsiveness in Fibromyalgia, it can be expected to be sensitive to change such as in studies for somatic and psychiatric diseases (Bullinger 1995; Bullinger 1998; Igl, Zwingmann et al. 2006). As already mentioned, Fibromyalgia patients frequently suffer from depressive symptoms or unspecific psychological distress. Their influence on aetiology, onset and maintenance is widely discussed. It has been found that chronic pain patients are more likely to become depressive than healthy controls, and that depressed mood correlated with ongoing pain and physical impairment in Fibromyalgia (Fishbain, Cutler et al. 1997; Epstein, Kay et al. 1999; Finset, Wigers et al. 2004). As EMG-biofeedback was able to reduce depression in patients with migraine, this study employed the Beck Depression Inventory and the Global Severity Index of the Symptom Checklist 90 Revised (Nestoriuc and Martin 2007). The Beck Depression Inventory and the Symptom checklist 90-Revised are widely used to assess depressive symptoms and have also been recommended for Fibromyalgia trials (Mease 2005). In total, the selected measures in this study covered the most relevant outcome domains of patients with Fibromyalgia and have shown sensitivity to change in similar populations.

The generalizability of this study may be limited by the method of recruitment of patients. As patients were recruited from the waiting list of the Fibromyalgia day hospital, a tertiary care centre, the patients may not be representative for the whole population of patients with Fibromyalgia. Patients who apply for the day hospital are usually highly motivated to begin a multidisciplinary therapy program. They had several unsuccessful treatments in primary care. In addition, patients with Fibromyalgia who are restricted by their disease or by comorbidities from participating in the day hospital program may not even have applied for this program. Another selection criteria that has become obvious during recruitment was the fact that (full-time) working women, in particular those with school children, refused participation because they found it to difficult to come to the study centre three times a week for three weeks This is may be the reason for the mean age of both groups (IC = 55. 4; CG = 55. 97) that is higher than in some other studies. Clearly, the study sample did not include the whole diversity of patients with Fibromyalgia. However, there is no obvious reason that the selection of patients introduced biased to the results.

Another limitation of the study is the low number of patients. A sample size calculation was performed a priory, but it may have been too optimistic. Due to the small sample size it is possible that we have missed effects that are relevant, but too small to become statistically significant. However, the set of outcome measures did not even show a trend for a better outcome in the treatment group. Some effect sizes for the treatment were positive and others were negative. Accordingly, it is unlikely that we missed a relevant beneficial effect on the main outcome domains.

Due to the small sample size, no analyses sample characteristics that may affect the response to treatment were performed. In other studies emotional, social and cognitive determinants of treatment outcomes were explored (Turk, Okifuji et al. 1998; Giesecke, Williams et al. 2003; Muller, Schneider et al. 2007). Psychological distress, for example, was found to have more influence on the Tender Point Count than on the pressure pain threshold measured by dolorimetry (Petzke, Gracely et al. 2003). Further, high scores of self-reported depression seem to impede response to pain treatment (Finset, Wigers et al. 2004). In this context, it has been proposed to differentiate between subgroups of Fibromyalgia patients and adapt treatment to their characteristics. However, standardized methods for the subgrouping of Fibromyalgia patients do not yet exist.

In this randomized controlled trial (RCT) we aimed to follow the Consort statement for randomized controlled trials in both the development of the study design and in the reporting of the results (Altmann, Schulz et al. 2007). Besides other criteria of the quality of RCT, primary and secondary outcome measures were clearly defined, methods of assessor blinding, randomization procedures and sample size calculation were described and effect sizes were calculated. Effect sizes ease comparisons with other studies and provide additional information of relevant effects besides the p-values of statistical significance. However, patients were not blinded to the intervention, because it did not seem feasible to maintain the blinding throughout the study

9. Conclusion

In conclusion, in this study EMG-biofeedback training as a single treatment was not effective in improving the health status of patients with Fibromyalgia. However, it was not designed to answer the question if EMG-biofeedback may amplify the benefits of specific relaxation strategies in a more comprehensive intervention. Another question for future research is the potentially different outcome of subgroups of patients with certain characteristics. For example, poor coping strategies such as catastrophizing have been associated with less favourable outcomes and may also predict the effects of EMG-biofeedback either alone or in combination with other relaxation strategies. (Hassett, Cone et al. 2000; Edwards, Bingham et al. 2006). Analyses of critical sample characteristics that might impede response could help to create a basis for more comprehensive individualized treatment modalities.

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11. Attachement

11.1. ACR-criteria (Wolfe, Smythe et al. 1990)

11.1.1. History of widespread pain (presence for at least 3 months)

Definition: Pain is considered widespread when all of the following are present: pain in the left side of the body, pain in the right side of the body, pain above the waist, and pain below the waist. In addition, axial skeletal pain (cervical spine or anterior chest or thoracic spine or low back) must be present. In this definition, shoulder and buttock pain is considered as pain for each involved side. “Low back” pain is considered lower segment pain.

11.1.2. Pain in 11 of 18 Tender Point sites on digital palpation.

Occiput: bilateral, at the suboccipital muscle insertions.

Low cervical: bilateral, at the anterior aspects of the intertransverse spaces at C5 – C7.

Trapezius: bilateral, at the mid point of the upper border.

Supraspinatus: bilateral, at origins, above the scapula spine near the medial border.

Second rib: bilateral, at the second costochondral junctions, just lateral to the junctions on upper surfaces.

Lateral epicondyle: bilateral, 2 cm distal to the epicondyles

Gluteal: bilateral, in upper outer quadrants of buttocks in anterior fold of muscle.

Greater trochanter: bilateral, posterior to the trochanteric prominence

Knee: bilateral, at the medial fat pad proximal to the joint line

11.2. Criteria for the diagnosis of Fibromyalgia according to Müller and Lautenschläger (Muller and Lautenschlager 1990)

- Spontaneous pain in the muscles, the tendons, their insertions (typically close to the trunk), present for at least three months in 3 different regions
- Pain on pressure at least at the half of the typical Tender Points (visible pain reaction at digital palpation with about 4 kg/cm²)
- Additional autonomic and functional symptoms, incl. sleep disturbances
- Psychopathological findings (mental features)
- Normal finding in routine diagnostic tests

For diagnosis of Fibromyalgia at least 3 of the following autonomic and functional symptoms have to be present.

Autonomic symptoms

- Cold hands
- Sicca complaints (mouth)
- Hyperhidrosis (hands)
- Dermographism
- Orthostatic dysregulation
- Respiratory arrhythmia
- Tremor (hands)

Functional symptoms

- Sleep disturbance
- Irritable bowel syndrome
- Globus feeling
- Respiratory distress without exertion
- Paresthesias
- Cardiac complaints
- Dysuria and/or dymenorrhoe

11.3. Sociodemographic questionnaire

Bitte beantworten Sie die folgenden Fragen durch Ankreuzen oder geschätzte Zeitangaben.

1. Welches ist Ihre Muttersprache (hauptsächliche Umgangssprache)?

❑ Deutsch ❑ Andere: _____

2. Welches ist Ihr höchster Schulabschluss:

- ❑ kein Abschluss
- ❑ Grund- und Hauptschule, Volksschule (Hauptschulabschluss, qualifizierender Hauptschulabschluss)
- ❑ Berufs, Handelsschule, Mittelschule, Realschule, Techniker-Schule (mittlere Reife)
- ❑ Gymnasium, Oberschule (Abitur/Fachabitur)
- ❑ Fachhochschule, Polytechnicum
- ❑ Universität, Hochschule

3. Wie sind Sie zur Zeit beschäftigt, bzw. woher beziehen Sie Ihre Einkünfte?

- ❑ in Ausbildung
- ❑ als Selbständige/r
- ❑ als Arbeiter/in
- ❑ als Beamte/r
- ❑ Invaliden-, Unfallrente

Ruhestandeinkommen:

- ❑ Rente
- ❑ Pension
- ❑ Vorruhestand

anderen Einkommens- oder Unterstützungsarten

- ❑ Arbeitslosengeld
- ❑ Arbeitslosenhilfe
- ❑ Sozialhilfe
- ❑ Hausfrau/-mann
- ❑ Anderes

4. Wie viele Wochenstunden sind Sie durchschnittlich in Ihrem Beruf tätig?
(auch Hausfrau/-mann) _____ Stunden pro Woche

5. Wie hoch ist das monatliche Nettoeinkommen, d.h. das verfügbare Haushaltseinkommen, das alle Haushaltsmitglieder zusammen nach Abzug von Steuern, Sozialabgaben, Miete Abzahlungsverpflichtungen und Versicherungen noch übrig haben:

- ❑ unter 500 €
- ❑ zwischen 500 und 1 000 €
- ❑ zwischen 1 000 und 1 500 €
- ❑ zwischen 1 500 und 2 000 €
- ❑ zwischen 2 000 und 3 000 €
- ❑ über 3 000 €

6. Wie groß ist der Ort in dem Sie wohnen?

- ❑ weniger als 5 000 Einwohner
- ❑ zwischen 5 000 und 50 000 Einwohner
- ❑ zwischen 50 000 und 100 000 Einwohner
- ❑ zwischen 100 000 und 500 000 Einwohner
- ❑ über 500 000 Einwohner

7. Wie viele Personen leben ständig in Ihrem Haushalt, Sie selbst mitgerechnet?

Insgesamt ____ Personen, davon

Unter 6 Jahre alt ____

Zwischen 6 und 15 Jahre ____

Von 15 bis 18 Jahre ____

Über 18 Jahre ____

Bei ____ Personen liegen besondere Betreuungsanforderungen (z.B. Behinderungen, chronische Erkrankungen) vor.

8. Wie häufig verbringen Sie Ihre Freizeit in folgenden Vereinigungen/Gesellschaften?

	häufig	**manchmal**	**nie**
Mit karitativer Zielsetzung (z.B. Kirchenvorstand)	❑	❑	❑
Mit künstlerischer Zielsetzung (z.B. Blaskapelle, Tanzgruppe)	❑	❑	❑
Mit politischer Zielsetzung (z.B. Bürgerinitiative, Partei)	❑	❑	❑
Mit sportlicher Zielsetzung (z.B. Tennisclub)	❑	❑	❑
Mit sonstiger Zielsetzung (z.B. Bridge-Club, Gartenverein, Elternbeirat)	❑	❑	❑

9. Rauchen Sie zurzeit?

❑ Nein ❑ Ja Wenn ja, ____ Zig./Tag seit ____ Jahren

10. Trinken Sie alkoholische Getränke?

❑ Nein

❑ Ja Wenn ja: ❑ gelegentlich ❑ 1x täglich ❑ mehrmals täglich

11. Wieviel Zeit verbringen Sie üblicherweise täglich mit Gehen, Fahrradfahren oder ähnlichen Tätigkeiten im Freien?

❑ keine

❑ etwas, aber weniger als 30 Minuten

❑ 30 bis 60 Minuten

❑ über eine Stunde

12. Wie lange treiben Sie gewöhnlich in der Woche Sport (oder irgendeine körperliche Aktivität), so dass Sie ins Schwitzen und außer Atem kommen?

❑ mehr als 2 Stunden in der Woche

❑ 1 bis 2 Stunden in der Woche

❑ weniger als 1 Stunde in der Woche

❑ keine sportliche Betätigung

13. Gab es in den letzten 12 Monaten ein/mehrere Ereignis/se, welche/s Ihr Leben nachhaltig beeinflusst haben, z.B. Tod einer vertrauten Person, Scheidung, Umzug, Verlust des Arbeitsplatzes, Hochzeit, Geburt eines Kindes/Enkelkindes, Urlaub?

❑ Nein

❑ Ja wenn ja: ❑ positiv ❑ negativ

11.4. German version of the Self-administered Comorbidity Questionnaire (SCQ)

For copyright reasons, this questionnaire cannot be displayed here.

11.5. German version of the Fibromyalgia Impact Questionnaire (FIQ)

For copyright reasons, this questionnaire cannot be displayed here.

11.6. German version of the generic health questionnaire Short-Form 36

For copyright reasons, this questionnaire cannot be displayed here.

11.7. Tender Point Score

For copyright reasons, this questionnaire cannot be displayed here.

11.8. German version of the Beck Depression Inventory

For copyright reasons, this questionnaire cannot be displayed here.

11.9. German version of the Symptom Checklist 90 Revised

For copyright reasons, this questionnaire cannot be displayed here.

12. Curriculum vitae

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Schullaufbahn:

1987 – 2000	Grundschule und Christoph-Jacob-Treu-Gymnasium in Lauf a.d. Peg.
06/2000	Allgemeine Hochschulreife

Berufsausbildung:

2000 – 2007	Studium der Humanmedizin an der LMU München
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Praktisches Jahr:	Erstes Tertial: Innere Medizin am Hôpital Riviera in Vevey/ Schweiz
	Zweites Tertial: Psychiatrie in der Psychiatrischen Klinik Nussbaumstrasse der LMU München
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Famulaturen:	Innere Medizin (Missionsärztliche Klinik Würzburg)
	Ambulante Anästhesie (Praxis Dr. Müller, München)
	Tropenmedizin (Instituto „Alexander v. Humboldt“, Hospital Cayetano Heredía, Lima/Peru)
	Physikalische Medizin und Rehabilitation (LMU München)
	Psychiatrie (Max-Planck-Institut für Psychiatrie, München)

Zusatzqualifikationen:

WiSe 2004/05	Propädeutik der Akupunktur I
SoSe 2003	Tropenmedizin II
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2003 - 2007	Assistentin in Hyperbarer Sauerstofftherapie (HBO) und ambulanter Anästhesie
seit September 2007	Assistenzärztin in der Klinik für Anästhesiologie am Klinikum München rechts der Isar der Technischen Universität München