EJP
European Journal of Pain

REVIEW ARTICLE

Efficacy, acceptability and safety of guided imagery/hypnosis in fibromyalgia – A systematic review and meta-analysis of randomized controlled trials

N. Zech[1], E. Hansen[1], K. Bernardy[2], W. Häuser[3,4]

1 Department of Anaesthesiology, Universitätsklinikum Regensburg, Germany
2 Department Pain Therapy, Berufsgenossenschaftliches Universitätsklinikum Bergmannsheil GmbH Bochum, Ruhr University Bochum, Germany
3 Department Internal Medicine I, Klinikum Saarbrücken, Germany
4 Department Psychosomatic Medicine and Psychotherapy, Technische Universität München, Germany

Correspondence
Winfried Häuser
E-mail: whaeuser@klinikum-saarbruecken.de

Funding sources
None.

Conflicts of interest
Ernil Hansen and Winfried Häuser are members of the scientific board of the German Milton Erickson Society of Clinical Hypnosis. Nina Zech and Kathrin Bernardy have no conflicts of interest to declare.

Protocol Number: PROSPERO 2016: CRD42016034115

Accepted for publication
19 July 2016

doi:10.1002/ejp.933

Abstract

This systematic review aimed at evaluating the efficacy, acceptability and safety of guided imagery/hypnosis (GI/H) in fibromyalgia. Cochrane Library, MEDLINE, PsycINFO and SCOPUS were screened through February 2016. Randomized controlled trials (RCTs) comparing GI/H with controls were analysed. Primary outcomes were ≥50% pain relief, ≥20% improvement of health-related quality of life, psychological distress, disability, acceptability and safety at end of therapy and 3-month follow-up. Effects were summarized by a random effects model using risk differences (RD) or standardized mean differences (SMD) with 95% confidence intervals (CI). Seven RCTs with 387 subjects were included into a comparison of GI/H versus controls. There was a clinically relevant benefit of GI/H compared to controls on ≥50% pain relief [RD 0.18 (95% CI 0.02, 0.35)] and psychological distress [SMD −0.40 (95% CI −0.70, −0.11)] at the end of therapy. Acceptability at the end of treatment for GI/H was not significantly different to the control. Two RCTs with 95 subjects were included in the comparison of hypnosis combined with cognitive behavioural therapy (CBT) versus CBT alone. Combined therapy was superior to CBT alone in reducing psychological distress at the end of therapy [SMD −0.50 (95% CI −0.91, −0.09)]. There were no statistically significant differences between combined therapy and CBT alone in other primary outcomes at the end of treatment and follow-up. No study reported on safety. GI/H hold promise in a multicomponent management of fibromyalgia.

Significance: We provide a systematic review with meta-analysis on guided imagery and hypnosis for fibromyalgia. Current analyses endorse the efficacy and tolerability of guided imagery/hypnosis and of the combination of hypnosis with cognitive–behavioural therapy in reducing key symptoms of fibromyalgia.

1. Introduction

Fibromyalgia (FM) is a clinically defined chronic condition of unknown aetiology characterized by chronic widespread pain that frequently co-exists with sleep disturbances, cognitive dysfunction and fatigue (Wolfe et al., 2011). Patients often report high disability levels and negative mood (Häuser et al., 2015a). Psychotherapies focus on reducing key symptoms, improving daily functioning, mood and sense of personal control over pain (Bernardy et al., 2013).

Recent evidence-based guidelines on the management of FM stress the importance of non-

pharmacological therapies such as aerobic exercise and psychological therapies (Ablin et al., 2013). The best studied and guideline recommended psychological treatment of FMS is cognitive behavioural therapies (CBTs) (Ablin et al., 2013; Bernardy et al., 2013).

Although hypnosis is among the oldest therapies for pain, interest in hypnosis for control of chronic pain rose only in the last decade (Jensen, 2009). A hypnotic induction is a procedure designed to induce hypnosis. Hypnosis is defined a state of consciousness involving focused attention and reduced peripheral awareness characterized by an enhanced capacity for response to suggestion (Elkins et al., 2015). The suggestions can be direct (traditional hypnosis) or permissive (Ericksonian hypnosis) (Peter, 2015). Imagery is defined as a dynamic, psychophysiologic process in which a person imagines and experiences an internal reality in the absence of external stimuli. These images can be initiated by the patient or guided by a therapist (guided imagery) (Menzies and Taylor, 2004). Both techniques aim to promote changes in subjective experience, alterations in perception, sensation, emotion, thought or behaviour by suggestion and/or imagination (Menzies and Taylor, 2004; Elkins et al., 2015). In an Internet survey, 3% of German (Häuser et al., 2012) and 3% of US (Bennett et al., 2007) respondents reported to use hypnosis to relieve FM-symptoms.

In 2011, we published a systematic review on guided imagery/hypnosis (GI/H) which included six randomized controlled trials (RCT) with 239 patients. We found that the significant effect on pain at final treatment was associated with low methodological and low treatment quality. We concluded that further studies with adequate methodological quality assessing all key domains of FM are necessary to clarify the efficacy of GI/H in FM (Bernardy et al., 2011).

In the meanwhile, the requirements of systematic reviews of chronic pain trials changed demanding responder analysis [e.g. pain, health-related quality of life (HRQOL)], analyses of acceptability and safety also for psychological therapies (Bernardy et al., 2013) and grading of the quality of evidence (Guyatt et al., 2011). Therefore, we saw the need to update that systematic review with meta-analysis (Bernardy et al., 2011) to reassess the efficacy, i.e. the reduction of key symptoms of FM, including analyses of responders, acceptability and safety of GI/H compared to control therapies in FM patients of any age.

2. Methods

The review was performed according to the PRISMA-statement (Preferred Reporting Items for Systematic Reviews and Meta-Analyses (Moher et al., 2009) and the recommendations of the Cochrane Collaboration (Higgins and Green, 2011).

2.1 Protocol

Methods of analysis and inclusion criteria were specified in advance (PROSPERO 2016:CRD42016034115).

2.1.1 Criteria for considering studies for this review

2.1.1.1 Types of participants. We included patients of any age with a clinical diagnosis of FM by any published, recognized and standardized criteria.

2.1.1.2 Types of interventions. Studies with GI/H as an active treatment of primary interest for FM were included. GI/H should use pain-related and/or pain-addressed suggestions and/or images. We post hoc decided to add a comparison of the combination of hypnosis with another psychological therapy (e.g. cognitive behavioural therapy) versus the other psychological therapy alone.

Studies on relaxation only (without trance induction or without the use of imagination) or on the combination of hypnosis with a defined pharmacological therapy as an active treatment of primary interest were excluded. Experimental studies (single session) with hypnosis/guided imagery were not included.

2.1.1.3 Type of controls. Any type of control was accepted. In case of multiple control groups, we predefined the following order for comparison: Psychological placebo (nonspecific elements of hypnosis/guided imagery such as education, emotional support, pure relaxation with the same amount of time as in the hypnosis/guided imagery group), treatment as usual, waiting list, active therapy (any defined pharmacological or nonpharmacological intervention other than hypnosis/guided imagery).

2.1.1.4 Types of studies. We selected randomized or quasi randomized controlled trials (RCTs) of hypnosis/guided imagery for treatment in FM. A trial was eligible, if (on the basis of the best available information) the individuals were definitely or

possibly assigned prospectively to one of two (or more) alternative forms of health care using random allocation or some quasi-random method of allocation (such as alternation, date of birth or case record number). We also considered cluster-randomized trials to be eligible. We included studies with a parallel and cross-over design. We included studies with a cross-over design if (1) separate data from the two periods were reported, or (2) data were presented that excluded a statistically significant carry-over effect, or (3) statistical adjustments were carried out in case of a significant carry-over effect. Trials should report at least one of the outcomes of efficacy, acceptability or safety as defined below. Inclusion criteria for RCTs were: full publication or a report of the RCT in a peer-reviewed journal or in a database (detailed below); a design that placed hypnosis/guided imagery as an active treatment of primary interest; a credible hypnosis/guided imagery content; 10 or more participants in each treatment arm for analysis at the end of therapy;

2.1.1.5 Types of outcomes measures.

Primary outcomes:

(1) Pain relief of ≥50%
(2) Improvement of disease-related quality of life in the Fibromyalgia Impact Questionnaire (FIQ) (Bennett, 2005) of ≥20%
(3) Psychological distress: If more than one psychological distress symptom was reported, we used the following order: depression, anxiety, other psychological symptoms.
(4) Disability (continuous variable)
(5) Acceptability: total dropout rate (patients who terminated the trial early for any reason during the treatment period (Cipriani et al., 2009). Reasons for dropout were analysed, whenever reported.
(6) Safety: Frequency of adverse psychological events, irrespectively regarded to be treatment-related or not by the authors.

Secondary outcomes

(1) Pain relief of 30% or greater
(2) Mean pain reduction
(3) Coping with pain
(4) Self efficacy (beliefs in one's capabilities to manage one's own pain)
(5) Fatigue
(6) Sleep problems

For all continuous variables, combined measures were preferred to single item measures. We assessed these outcomes at the end of treatment and at follow-up (at least 3 months after the completion of therapy).

2.2 Search methods for identification of studies

2.2.1 Electronic searches

We searched the Cochrane Central Register of Controlled Trials (CENTRAL) (The Cochrane Library 2016, Issue 1), MEDLINE (30 December 2010 to 29 February 2016), PsycINFO (30 December 2010 to 29 February 2016) and SCOPUS (30 December 2010 to 29 February 2013).

The search strategy for MEDLINE was as follows: {['Hypnosis' (Mesh) OR 'Imagery (Psychotherapy)' (Mesh)]} AND 'Fibromyalgia' (Mesh) AND {[clinical (Title/Abstract) AND trial (Title/Abstract)] OR clinical trials (MeSH Terms) OR clinical trial (Publication Type) OR random* (Title/Abstract) OR random allocation (MeSH Terms) OR therapeutic use (MeSH Subheading)}.

The search strategy was adapted for the other databases. No language restrictions were made. In addition, reference sections of original studies were screened manually.

2.2.2 Searching other resources

We searched http://www.clinicaltrials.gov (web site of the US National Institutes of Health) for ongoing trials (last search 29 February 2016), and the reference lists of reviewed articles.

2.3. Measures of treatment effect

The effect measures of choice were risk differences (RD) for dichotomous data and standardized mean difference (SMD) for continuous data (method inverse variance). We used a random-effect model because we assumed clinical heterogeneity was found. Uncertainty was expressed using 95% confidence intervals (CIs).

Number needed to treat for an additional benefit (NNTBs) was calculated as the reciprocal of the absolute risk reduction (ARR). For unwanted effects, the NNTB becomes the number needed to treat for an additional harm (NNTH) and is calculated in the same manner. For dichotomous data, we calculated risk differences (RDs). The threshold

for 'clinically relevant benefit' or 'clinically relevant harm' was set for categorical variables by an absolute risk reduction or increase ≥10% corresponding a NNTB or NNTH of <=10 (Moore et al., 2008).

Cohen's categories were used to evaluate the magnitude of the effect size of continuous data, calculated by SMD, with values for Hedges' g as follows: 0.2–0.5 equating to a small effect size, 0.5–0.8 equating to a medium effect size, and more than 0.8 equating to a large effect size (Cohen, 1988). We considered values of g less than 0.2 to equate to a 'not substantial' effect size (Häuser et al., 2015b). The threshold 'clinically relevant benefit' was set for continuous variables by an effect size of more than 0.2 (Fayers and Hays, 2014).

3. Results

3.1 Search

The updated search produced 26 hits. Finally, we included six new studies (Castel et al., 2009, 2012; Picard et al., 2013; Menzies et al., 2014; Verkaik et al., 2014; Onieva-Zafra et al., 2015). These studies add 274 new participants.

Two studies with 59 participants from the previous review were removed because of the modified exclusion criteria: These studies included <10 participants per treatment arm into analysis (Alvarez-Nemegyei et al., 2007; Grøndahl and Rosvold, 2008). In sum, nine studies were included into the qualitative and quantitative analysis (see Fig. 1) with a total of 457 patients.

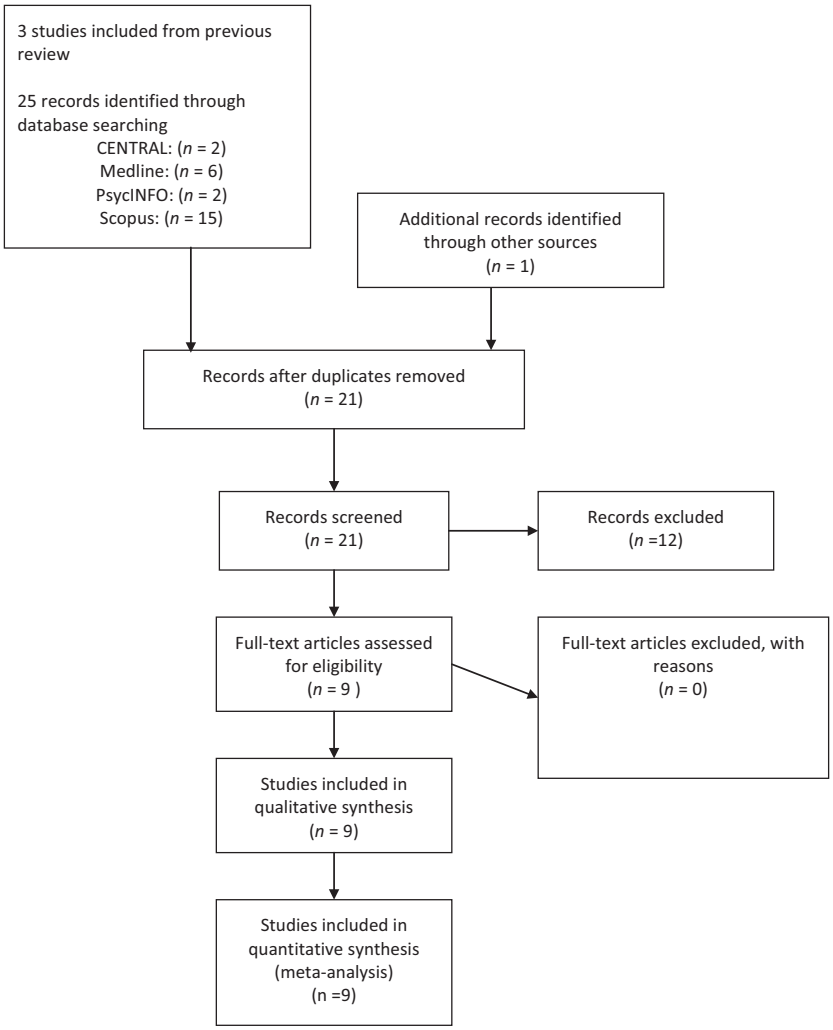

Figure 1 PRISMA flow diagram.

3.2 Included studies

The main characteristics of the studies are summarized in Table 1, for details see Table S1.

3.2.1 Settings

Five studies were conducted in Europe, of which two were conducted in the Netherlands (Haanen et al., 1991; Verkaik et al., 2014) and one each in France (Picard et al., 2013), Italy (Rucco et al., 1995) and Spain (Onieva-Zafra et al., 2015). All studies were outpatient-based and single-centre studies. Only one study reported the setting in which therapy was delivered, namely in a centre for complementary medicine (Verkaik et al., 2014).

3.2.2 Types of therapies

Four studies provided guided imagery with home exercises of the patient by audio media without further personal contact (Menzies et al., 2006, 2014; Verkaik et al., 2014; Onieva-Zafra et al., 2015). Two studies offered two additional group sessions (Verkaik et al., 2014; Onieva-Zafra et al., 2015). The content of guided imagery was relaxation in all studies, pleasant images in three studies (Menzies et al., 2006, 2014; Verkaik et al., 2014) and modification of pain experience in two studies (Verkaik et al., 2014; Onieva-Zafra et al., 2015).

Three studies offered hypnosis in individual sessions. Two studies offered individually tailored (Ericksonian) (Rucco et al., 1995; Picard et al., 2013) and one study used a standardized (traditional) approach (Haanen et al., 1991). Two studies used non-pain-related (e.g. relaxation, ego-strengthening, feelings of security, improvement of sleep, stress management) and pain-related (e.g. pain control, pain acceptance) suggestions (Haanen et al., 1991; Picard et al., 2013). One study focussed on the

Table 1 Main characteristics of included studies.

Author (Reference)	Country	Type of therapy Type of control	Duration study (weeks) Follow-up (months)	Number of sessions with a therapist Total treatment duration with therapist (hours)	Number of patients in guided imagery / hypnosis group % women	Number of patients in control group % women Total treatment duration with therapist (hours)
Castel et al. (2009)	Spain	Traditional hypnosis with CBT	12	12	16	16
		CBT	None	18	100	94 18
Castel et al. (2012)	Spain	Traditional hypnosis with CBT	14	14	29	34
		CBT	3 and 6	28	98	94 28
Haanen et al. (1991)	Netherlands	Traditional hypnosis	12	8	20	20
		Physiotherapy	3	8	95	95 12–24
Menzies et al. (2006)	USA	Guided imagery	10	O	24	24
		Treatment as usual	None	Not calculable	100	100 Not calculable
Menzies et al. (2014)	USA	Guided imagery	10	O	36	36
		Treatment as usual	None	Not calculable	100	100 Not calculable
Onieva-Zafra et al. (2015)	Spain	Guided imagery	4	2	28	27
		Waiting List	1	3	97	96 3
Picard et al. (2013)	France	Tailored hypnosis	6	5	30	29
		Waiting List	3	5	100	100 0
Rucco et al. (1995)	Italy	Ericksonian hypnosis	26	Flexible	24	11
		Autogenic training	None	Not calculable	100	100 4
Verkaik et al. (2014)	Netherlands	Guided imagery	5	5	32	33
		Attention control	None	5	100	95 5

solution of intrapsychic (emotional) conflicts (Rucco et al., 1995). Two trials recommended homework with hypnosis based on audiotapes of the hypnosis sessions (Haanen et al., 1991; Picard et al., 2013).

Two studies compared CBT plus hypnosis with CBT alone. These studies used pain-related and non-pain-related suggestions in a group setting. Homework with hypnosis based on audiotapes of the hypnosis sessions was recommended (Castel et al., 2009, 2012).

3.2.3 Study design

All studies had a parallel design. All studies with guided imagery recommended the daily use of audiotapes, but only one study (Menzies et al., 2006) assessed the frequency of use. Study duration was 4 weeks (Verkaik et al., 2014; Onieva-Zafra et al., 2015) and 10 weeks in two studies each (Menzies et al., 2006, 2014).

One of the studies with hypnosis tested the hypnotizability of the participants (Castel et al., 2009). The treatment duration of the studies with hypnosis was 18 h in 12 sessions (Castel et al., 2009), 28 h in 14 sessions (Castel et al., 2012), 8 h in eight sessions (Haanen et al., 1991), 5 h in five sessions (Picard et al., 2013 and individually fixed number of sessions (Rucco et al., 1995). Study duration ranged between 8 (Picard et al., 2013), 12 (Haanen et al., 1991; Castel et al., 2009), 14 (Castel et al., 2012) and 26 (Rucco et al., 1995) weeks.

Two studies with hypnosis performed a follow-up after 12 weeks (Haanen et al., 1991; Picard et al., 2013) and one after 3 and 6 months (Castel et al., 2012), one study with guided imagery did a follow-up after 4 weeks (Onieva-Zafra et al., 2015).

3.2.4 Controls

For comparisons of this review, the following control groups were used: Three studies compared with treatment as usual (Menzies et al., 2006, 2014; Onieva-Zafra et al., 2015), four studies each with other active treatment (physiotherapy: Haanen et al., 1991; autogenic training: Rucco et al., 1995; CBT: Castel et al., 2009, 2012) and one each with attention control (Verkaik et al., 2014) and waiting list (Picard et al., 2013).

3.2.5 Patients

The guided imagery studies included 232 and the hypnosis studies 252 persons. Participants were referred and recruited from self-help organizations (Picard et al., 2013; Verkaik et al., 2014; Onieva-Zafra et al., 2015), by media advertisement in practices affiliated with the study centre (Menzies et al., 2006, 2014), and by a pain clinic (Rucco et al., 1995 and Castel et al., 2009, 2012). The mean age of the participants ranged between 40 and 50 years. Four studies included only women (Rucco et al., 1995; Menzies et al., 2006, 2014; Picard et al., 2013), the percentage of women was >90% in the remaining studies. More than 90% of participants were Caucasians. The studies used different criteria of disease duration. Therefore, we did not calculate median values. Overall, the studies included patients with a long history of disease (more than 5 years), except in one study which requested a FM-diagnosis <6 years (Verkaik et al., 2014).

3.2.6 Diagnosis of FM

FMS was diagnosed in all studies by the American College of Rheumatology (ACR) 1990 classification criteria (Wolfe et al., 1990), except one which used Smythe criteria (Smythe and Moldofsky, 1977) (Haanen et al., 1991).

3.2.7 Exclusion of anxiety or depressive disorder

All studies excluded patients with 'major' mental disorders or 'severe psychopathology'. It remains unclear if patients with anxiety or depressive disorders were excluded or not, e.g. patients with major depression.

3.2.8 Reported treatment quality

Two studies had a low (Rucco et al., 1995; Picard et al., 2013), four studies a moderate (Castel et al., 2009, 2012; Haanen et al., 1991; Verkaik et al., 2014) and three studies had a high reported treatment quality (Menzies et al., 2006, 2014 Onieva-Zafra et al., 2015) (see Table S2).

3.2.9 Funding and conflicts of interest

Five studies reported public funding (Menzies et al., 2006, 2014; Picard et al., 2013; Verkaik et al., 2014). Only two studies reported that the authors have no conflict of interest (Castel et al., 2012; Onieva-Zafra et al., 2015).

3.3 Risk of bias in included studies

Risk of bias could not be properly assessed in all studies due to incomplete method reporting. According to the predefined categories, five studies were low-quality studies (Haanen et al., 1991; Rucco

et al., 1995; Castel et al., 2009; Menzies et al., 2014; Onieva-Zafra et al., 2015) and four were moderate quality studies (Menzies et al., 2006; Castel et al., 2012; Picard et al., 2013; Verkaik et al., 2014) (see Fig. 2 for risk of bias summary and graph).

3.4 Effects of interventions

3.4.1 Guided imagery/hypnosis versus controls at end of treatment

The quality of evidence of this comparison was downgraded by three levels because of limitations of study design, indirectness and imprecision. There was low-quality evidence that GI/H were superior to controls in ≥30% and ≥50% pain relief, in reducing psychological distress, fatigue, sleep problems and in improving coping with pain at the end of therapy (see Table 2; see Fig. S1).

According to the predefined categories, there was a clinically relevant benefit of GI/H for 30% and 50% and more pain relief with an NNTB of 4 (95% CI 2–16) and NNTB 6 (95% CI 3–50), respectively. The effect sizes on reducing psychological distress, fatigue and in improving coping with pain were small and the ones on mean pain intensity and sleep problems were large indicating a clinically relevant benefit of GI/H.

Low-quality evidence indicates that there were no statistically significant differences between GI/H and controls in acceptability.

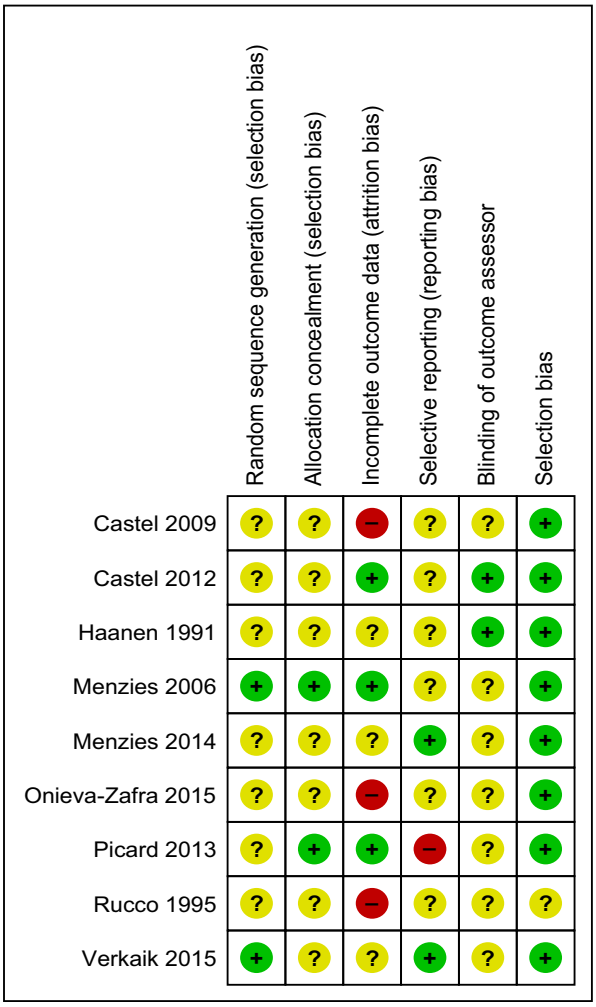

Figure 2 Risk of bias assessment of individual studies.

3.4.2 Hypnosis versus controls at 3-month follow-up

The quality of evidence of this comparison was downgraded by three levels because of limitations of study design, indirectness and imprecision. Low-quality evidence indicates that hypnosis was superior to controls in ≥30% pain relief, reduction of mean pain and sleep problems but not in other outcomes of efficacy. NNTB for ≥30% pain relief was 5 (95% CI 3–50) indicating a clinically relevant benefit of hypnosis. The effect size on mean pain intensity was small and on sleep problems was large indicating a clinically relevant benefit of hypnosis (see Table S3; see Fig. S2).

3.4.3 Hypnosis plus CBT versus CBT at end of treatment

The quality of evidence of this comparison was downgraded by three levels because of limitations of study design, indirectness and imprecision. Low-quality evidence indicates that hypnosis combined with CBT was superior to CBT alone in reducing psychological distress, but not in other outcomes of efficacy or in acceptability alone at the end of treatment (see Table 3; see Fig. S3). The effect size on depression was small indicating a clinically relevant benefit of hypnosis combined with CBT.

3.4.4 Hypnosis plus CBT versus CBT at 3-month follow-up

The quality of evidence of this comparison was downgraded by three levels because of limitations of study design, indirectness and imprecision. Low-quality evidence indicates that hypnosis combined with CBT was not superior to CBT alone in any outcome of efficacy (see Table S4; see Fig. S4).

Table 2 Effect sizes of guided imagery/hypnosis on selected outcome variables at end of treatment.

Outcome title	Number of studies	Number of patients	Effect size (95% CI)	Test for overall effect p-value	Heterogeneity I^2 (%)
50% and more pain relief	6	299	RD 0.24 (0.06, 0.42)	0.008	80
20% and more improvement of HRQOL	3	164	RD 0.06 (−0.15, 0.26)	0.57	54
Psychological distress	3	178	SMD −0.40 (−0.70, −0.11)	0.008	0
Disability	1	64	SMD −0.40 (−0.70, −0.11)	0.32	Not applicable
Acceptability	7	387	RD −0.03 (−0.13, 0.07)	0.36	80
30% and more pain relief	3	92	RD 0.25 (0.01, 0.50)	0.02	80
Mean pain intensity	6	299	SMD −1.12 (−1.97, −0.28)	0.009	91
Coping with pain	4	228	SMD −0.32 (−0.59, −0.05)	0.02	5
Fatigue	3	255	SMD −0.46 (−0.91, 0.00)	0.05	58
Sleep problems	3	134	SMD −0.91 (−1.51, −0.11)	0.02	72
Mean HRQOL	3	164	SMD −0.19 (−0.62, 0.24 9)	0.66	47

HRQOL, Health-related quality of life; RD, Risk difference; SMD, Standardized mean difference; CI, Confidence interval.

3.5 Heterogeneity

There was considerable heterogeneity (I^2> 75%) in the comparisons ≥30% and ≥50% pain relief, mean pain intensity and acceptability in the comparison GI/H at the end of therapy. Heterogeneity was mainly due to the hypnosis studies (see Fig. S1).

3.6 Publication bias

Studies including 415 participants with a null effect on ≥50% pain relief would have been required to make the result clinically irrelevant (NNTB of 10 or higher).

3.7 Subgroup analyses

There were no statistically significant differences between guided imagery and hypnosis versus controls at the end of treatment, except that hypnosis was superior to guided imagery in the rates of ≥50% pain reduction with statistical significance (Fig. S1). The results of the subgroup analysis 'type of control' (active control vs. other types of control) are identical with the one of guided imagery and hypnosis for primary outcomes. The remaining prespecified subgroup analyses were not conducted due to lack of data.

3.8 Sensitivity analyses

Removing studies with physician-assessed outcomes led to a loss of statistical significance of ≥30% pain relief rates ($p = 0.27$), mean pain intensity ($p = 0.13$), fatigue ($p = 0.12$) and sleep problems ($p = 0.37$), but not for ≥50% pain relief rates ($p = 0.04$) in the comparison of GI/H versus controls at the end of treatment.

Removing studies with imputed and modified SDs did not change the statistically significant effect sizes on ≥50% pain relief ($p = 0.02$), psychological distress ($p = 0.01$), mean pain intensity ($p = .0.03$) and sleep problems ($p = 0.02$), but on ≥30% pain relief ($p = 0.15$) and coping with pain ($p = 0.16$).

4. Discussion

4.1 Summary of main findings

This meta-analysis found low-quality evidence of a clinically relevant benefit of GI/H compared to controls on ≥50% pain relief and psychological distress at the end of therapy, and of a clinically relevant benefit by hypnosis compared to controls in ≥30% pain relief, reduction of mean pain and sleep problems at 3-month follow-up. There was low-quality evidence that there were no statistically significant differences between GI/H and controls in acceptability at the end of treatment. There was low-quality evidence that hypnosis combined with CBT was clinically relevant superior to CBT alone in reducing psychological distress at the end of therapy.

Table 3 Effect sizes of hypnosis combined with cognitive behavioural therapy versus cognitive behavioural therapy alone on selected outcome variables at end of treatment.

Outcome title	Number of studies	Number of patients	Effect size (95% CI)	Test for overall effect *p*-value	Heterogeneity I^2 (%)
50% and more pain relief	2	95	RD 0.08 (−0.05, 0.21)	0.45	0
20% and more improvement of HRQOL	2	95	RD 0.18 (−0.01, 0.38)	0.07	0
Psychological distress	2	95	SMD −0.50 (−0.91, −0.09)	0.02	0
Disability	2	95	SMD 0.04 (−0.36, 0.44)	0.85	0
Acceptability	2	95	RD −0.01 (−0.09, 0.08)	0.85	0
30% and more pain relief	2	95	RD 0.04 (−0.12, 0.19)	0.64	0
Mean pain intensity	2	95	SMD −0.16 (−0.57, 0.24)	0.43	0
Coping with pain	1	53	SMD −0.26 (−0.80, 0.28)	0.35	Not applicable
Fatigue	2	95	SMD −0.05 (−0.46, 0.35)	0.80	0
Sleep problems	1	95	SMD −0.12 (−0.61, 0.38)	0.64	Not applicable
Mean HRQOL	2	95	SMD −0.31 (−0.71, 0.10)	0.14	0

HRQOL, Health-related quality of life; RD, Risk difference; SMD, Standardized mean difference; CI, Confidence interval.

4.2 Overall completeness and applicability of evidence

The possibility that negative study results with GI/H had not been published or had been missed by our search strategy cannot be ruled out.

The applicability of evidence is limited for the following reasons. It remains unclear, if patients with anxiety or depressive disorder, or both, which are frequently associated with FM, were included in most studies. The studies were limited to adults. The majority of the patients were middle-aged Caucasian women, making it difficult to apply the results to the total FM population, especially to male, adolescents and non-Caucasian patients.

4.3 Quality of the evidence

The quality of evidence of this review was based on the data presented in peer-reviewed journals and some additional details which were provided on request by the study authors in the first version of the review. We had no access to individual participant data.

4.4 Potential biases in the review process

The methodological and treatment quality of some studies might be underestimated, when some details required for calculation of the risk of bias and treatment quality scores were not reported. Efficacy outcomes were analysed by some studies using last observation carried forward to impute for missing data. This procedure may lead to an overestimation of efficacy (Moore et al., 2013). We had to calculate missing SDs by established imputation methods and to correct for incredibly reported low SDs for two studies each. We had to calculate ≥50% pain relief rates and ≥20% improvement rates of HRQOL by established imputation methods for all studies (Furukawa et al., 2005).

4.5 Agreements and disagreements with other studies or reviews

By including new studies with larger sample sizes and positive results into this review, positive effects of guided imagery/hypnosis on psychological distress, fatigue and sleep could be demonstrated that were not detectable in our previous review (Bernardy et al., 2011).

Hypnosis is the oldest psychological treatment which underwent assessment of its credibility and safety by medical associations already in the 19th century (Häuser et al., 2016). However, the US National Center for Complementary and Integrative

Health summarizes guided imagery/hypnosis under complementary and alternative treatments in the category 'mind-body therapies' (National Center for Complementary and Integrative Health, 2015). A Cochrane review on 'mind-body therapies' in FM (Theadom et al., 2015) searched the literature until October 2013 and included only two of the studies of this review (Picard et al., 2013; Onieva-Zafra et al., 2015). The results of the two studies were meshed into 'psychological therapies'. A Cochrane review on psychological therapies in chronic pain syndromes, except headache, in adults searched the literature until September 2011. No study with GI/H was included (Williams et al., 2012). We conclude that studies with GI/H were mainly neglected by most reviews on psychological therapies for FM.

Our analysis only partially confirms the results of a meta-analysis with 18 studies in which a cognitive–behavioural therapy was compared with the same therapy supplemented by hypnosis (Kirsch et al., 1995). That review indicated that the addition of hypnosis substantially enhanced treatment outcome, so that the average client receiving cognitive–behavioural hypnotherapy showed greater improvement than at least 70% of clients receiving non-hypnotic treatment. However, the review did not include studies with fibromyalgia patients.

4.6 Implications for practice

4.6.1 For people with fibromyalgia and physicians and mental health specialists

GI/H can reduce some key symptoms in some patients with FM. Trained hypnotherapists are rare and costs will not be covered by health insurance companies in many countries. But it is possible for patients to use these techniques at home by audio files provided by psychotherapists. Regular or on-demand use of these techniques might increase the self efficacy of patients. Free hypnosis sessions for FM are available in the Internet. The efficacy of their use has not been tested.

4.6.2 For Funders

Fully powered randomized and controlled trials exploring the open questions as outlined in 'Implications for research' should be funded.

Author contributions

WH performed the search of literature. WH and KB selected the studies. All authors extracted data or checked the extractions. WH entered the data into Revman. EH and NZ checked the data entry. WH wrote the manuscript. All authors discussed the results and commented on the manuscript.

Acknowledgements

None.

References

Ablin, J., Fitzcharles, M.A., Buskila, D., Shir, Y., Sommer, C., Häuser, W. (2013). Treatment of fibromyalgia syndrome: recommendations of recent evidence-based interdisciplinary guidelines with special emphasis on complementary and alternative therapies. *Evid Based Complement Alternat Med* 2013, 485272.

Alvarez-Nemegyei, J., Negreros-Castillo, A., Nuño-Gutiérrez, B.L., Alvarez-Berzunza, J., Alcocer-Martínez, L.M. (2007). Ericksonian hypnosis in women with fibromyalgia syndrome. *Rev Med Inst Mex Seguro Soc* 2007, 395–401. (Spanish).

Bennett, R. (2005). The Fibromyalgia Impact Questionnaire (FIQ): a review of its development, current version, operating characteristics and uses. *Clin Exp Rheumatol* 23, S154–S162.

Bennett, R.M., Jones, J., Turk, D.C., Russell, I.J., Matallana, L. (2007). An internet survey of 2,596 people with fibromyalgia. *BMC Musculoskelet Disord* 8, 27.

Bernardy, K., Füber, N., Klose, P., Häuser, W. (2011). Efficacy of hypnosis/guided imagery in fibromyalgia syndrome–a systematic review and meta-analysis of controlled trials. *BMC Musculoskeletal Disord* 15, 12.

Bernardy, K., Klose, P., Busch, A.J., Choy, E.H. and Häuser, W. (2013). Cognitive behavioural therapies for fibromyalgia. *Cochrane Database Rev* 9, CD009796.

Castel, A., Salvat, M., Sala, J., Rul, M. (2009). Cognitive-behavioural group treatment with hypnosis: a randomized pilot trail in fibromyalgia. *Contemp Hypnosis* 26, 48–59.

Castel, A., Cascón, R., Padrol, A., Sala, J., Rul, M. (2012). Multicomponent cognitive-behavioral group therapy with hypnosis for the treatment of fibromyalgia: long-term outcome. *J Pain* 13, 255–265.

Cipriani, A., Furukawa, T.A., Salanti, G., Geddes, J.R., Higgins, J.P., Churchil, R. (2009). Comparative efficacy and acceptability of 12 new-generation antidepressants: a multiple-treatments meta-analysis. *Lancet* 373, 746–758.

Cohen, J. (1988). *Statistical Power Analysis for the Behavioral Sciences*. (Hillsdale: Lawrence Erlbaum Associates).

Elkins, G.R., Barabasz, A.F., Council, J.R., Spiegel, D. (2015). Advancing research and practice: the revised APA Division 30 definition of hypnosis. *Int J Clin Exp Hypn* 63, 1–9.

Fayers, P.M., Hays, R.D. (2014). Don't middle your MIDs: regression to the mean shrinks estimates of minimally important differences. *Qual Life Res* 23, 1–4.

Furukawa, T.A., Cipriani, A., Barbui, C., Brambilla, P., Watanabe, N. (2005). Imputing response rates from means and standard deviations in meta-analyses. *Int Clin Psychopharmacol* 20, 49–52.

Grøndahl, J.R., Rosvold, E.O. (2008). Hypnosis as a treatment of chronic widespread pain in general practice: a randomised controlled pilot trial. *BMC Musculoskelet Disord* 9, 124.

Guyatt, G., Oxman, A.D., Akl, E.A., Kunz, R., Vist, G., Brozek, J. (2011). GRADE guidelines: 1. Introduction-GRADE evidence profiles and summary of findings tables. *J Clin Epidemiol* 64, 383–394.

Haanen, H.C., Hoenderdos, H.T., van Romunde, L.K., Hop, W.C., Mallee, C., Terwiel, J.P., Hekster, G.B. (1991). Controlled trial of hypnotherapy in the treatment of refractory fibromyalgia. *J Rheumatol* 18, 72–75.

Häuser, W., Jung, E., Erbslöh-Möller, B., Gesmann, M., Kühn-Becker, H., Petermann, F., Langhorst, J., Thoma, R., Weiss, T., Wolfe, F., Winkelmann, A. (2012). The German fibromyalgia consumer reports - a cross-sectional survey. *BMC Musculoskelet Disord* 13, 74.

Häuser, W., Ablin, J., Fitzcharles, M.A., Littlejohn, J., Luciano, J.V., Usui, H. and Walitt, B. (2015a). Fibromyalgia. *Nat Rev Dis Prim* 1:15022.

Häuser, W., Klose, P., Welsch, P., Petzke, F., Nothacker, M. (2015b). Methodology of the development of the updated LONTS guidelines for long-term administration of opioids in noncancer pain. *Schmerz* 29, 8–34.

Häuser, W., Hagl, M., Schmierer, A., Hansen, E. (2016). Medical hypnosis: a systematic review of meta-analyses of efficacy and safety in clinical practice. *Dtsch Aerztebl Int* 113, 289–296.

Jensen, M.P. (2009). Hypnosis for chronic pain management: a new hope. *Pain* 146, 235–237.

Kirsch, I., Montgomery, G., Sapirstein, G. (1995). Hypnosis as an adjunct to cognitive-behavioral psychotherapy: a meta-analysis. *J Consult Clin Psychol* 63, 214–220.

Menzies, V. and Taylor, A.G. (2004). The idea of imagination: a concept analysis of imagery. *ADV: J Mind-Body Med* 20:4–10.

Menzies, V., Taylor, A.G., Bourguignon, C. (2006). Effects of guided imagery on outcomes of pain, functional status, and self-efficacy in persons diagnosed with fibromyalgia. *J Altern Complement Med* 12, 23–30.

Menzies, V., Lyon, D.E., Elswick, R.K. Jr, McCain, N.L., Gray, D.P. (2014). Effects of guided imagery on biobehavioral factors in women with fibromyalgia. *J Behav Med* 37, 70–80.

Moher, D., Liberati, A., Teztlaff, J. and Altman, G. and The PRISMA Group. (2009). Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *Ann Int Med* 51:1–7.

Moore, R.A., Barden, J., Derry, S. and McQuay, H.J. (2008). *Systematic Reviews in Pain Research: Methodology Refine*. (IASP Press).

Moore, R.A., Derry, S., Wiffen, P.J. (2013). Challenges in design and interpretation of chronic pain trials. *Br J Anaesthesiol* 111, 38–45.

Onieva-Zafra, M.D., García, L.H., Del Valle, M.G. (2015). Effectiveness of guided imagery relaxation on levels of pain and depression in patients diagnosed with fibromyalgia. *Holist Nurs Pract* 29, 13–21.

Peter, B. (2015). Hypnosis. In *International Encyclopedia of the Social and Behavioral Sciences*, 2nd edn, Vol 11, D.E. Wright, ed. (Oxford: Elsevier) pp. 458–464.

Picard, P., Jusseaume, C., Boutet, M., Dualé, C., Mulliez, A., Aublet-Cuvellier, B. (2013). Hypnosis for management of fibromyalgia. *Int J Clin Exp Hypn* 61, 111–123.

Rucco, V., Feruglio, C., Genco, F. and Mosanghini, R. (1995). Autogenic training versus Erickson's analogical technique in treatment of fibromyalgia syndrome. *Riv Eur Sci Med Farmacol* 17:41–50. (Italian).

Smythe, H.A., Moldofsky, H. (1977). Two contributions to understanding of the "fibrositis" syndrome. *Bull Rheum Dis* 28, 928–931.

Theadom, A., Cropley, M., Smith, H.E., Feigin, V.L. and McPherson, K. (2015). Mind and body therapy for fibromyalgia. *Cochrane Database Syst Rev* 4, CD001980.

Verkaik, R., Busch, M., Koeneman, T., van den Berg, R., Spreeuwenberg, P., Francke, A.L. (2014). Guided imagery in people with fibromyalgia: a randomized controlled trial of effects on pain, functional status and self-efficacy. *J Health Psychol* 19, 678–688.

Williams, A.C., Eccleston, C. and Morley, S. (2012). Psychological therapies for the management of chronic pain (excluding headache) in adults. *Cochrane Database Syst Rev* 11, CD007407.

Wolfe, F., Smythe, H.A., Yunus, M.B., Bennett, R.M., Bombardier, C., Goldenberg, D.L., Tugwell, P., Campbell, S.M., Abeles, M., Clark, P. (1990). The American College of Rheumatology 1990 criteria for the classification of fibromyalgia. Report of the multicenter criteria committee. *Arthritis Rheum* 33, 160–172.

Wolfe, F., Clauw, D.J., Fitzcharles, M.A., Goldenberg, D.L., Häuser, W., Katz, R.S. (2011). Fibromyalgia criteria and severity scales for clinical and epidemiological studies: a modification of the ACR preliminary diagnostic criteria for fibromyalgia. *J Rheumatol* 38, 1113–1122.

Web References

Higgins, J.P.T., Green, S. (eds). (2011). Cochrane Handbook for Systematic Reviews of Interventions *Version 5.1.0*. The Cochrane Collaboration. Available from www.cochrane-handbook.org. Accessed March 2011.

National Center for Complementary and Integrative Health. (2015). Complementary, alternative or integrative health? What's in a name? Available from https://nccih.nih.gov/health/integrative-health. Accessed January 2, 2016

Supporting Information

Additional Supporting Information may be found online in the supporting information tab for this article:

Methods S1. Data collection and analysis: Study selection, data extraction and management, assessment of risk of bias in included studies, grading the quality of evidence.

Methods S2. Unit of analysis issues, dealing with missing data, assessment of heterogeneity, assessment of publication bias, data synthesis, additional analyses.

Result S1. Primary and secondary outcomes.

Discussion S1. Implications for research.

Figure S1. Forest plots of outcomes of outcomes of guided imagery/hypnosis versus controls at end of treatment.

Figure S2. Forest plots of outcomes of hypnosis versus controls at 3-month follow-up.

Figure S3. Forest plots of outcomes of hypnosis combined with cognitive behavioural therapy versus cognitive behavioural therapy alone at end of treatment.

Figure S4. Forest plots of outcomes of hypnosis combined with cognitive behavioural therapy versus cognitive behavioural therapy alone at 3-month follow-up.

Table S1. Detailed characteristics of included studies with risk of bias assessment.

Table S2. Reported treatment quality of studies with guided imagery/hypnosis in fibromyalgia.

Table S3. Effect sizes of hypnosis versus controls on selected outcome variables at 3-month follow-up.

Table S4. Effect sizes of hypnosis combined with cognitive behavioural therapy versus cognitive behavioural therapy alone on selected outcome variables at 3-month follow-up.

References S1
References S2