

THE EFFECTIVENESS OF RELAXATION TRAINING IN REDUCING TREATMENT-RELATED SYMPTOMS AND IMPROVING EMOTIONAL ADJUSTMENT IN ACUTE NON-SURGICAL CANCER TREATMENT: A META-ANALYTICAL REVIEW

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SUMMARY

Cancer patients often have to deal with severe side effects and psychological distress during cancer treatment, which have a substantial impact on their quality of life. Among psychosocial interventions for reducing treatment-related side effects, relaxation and imagery were most investigated in controlled trials. In this study, meta-analytic methods were used to synthesize published, randomized intervention–control studies aiming to improve patients' treatment-related symptoms and emotional adjustment by relaxation training. Mean weighted effect sizes were calculated for 12 categories, treatment-related symptoms (nausea, pain, blood pressure, pulse rate) and emotional adjustment (anxiety, depression, hostility, tension, fatigue, confusion, vigor, overall mood). Significant positive effects were found for the treatment-related symptoms. Relaxation training also proved to have a significant effect on the emotional adjustment variables depression, anxiety and hostility. Additionally, two studies point to a significant effect of relaxation on the reduction of tension and amelioration of the overall mood. Intervention features of the relaxation training, the time the professional spent with the patient overall (intervention intensity) and the schedule of the intervention (offered in conjunction with or independent of medical treatment to the cancer patient) were relevant to the effect of relaxation on anxiety. The interventions offered independently of medical treatment proved to be significantly more effective for the outcome variable anxiety. Relaxation seems to be equally effective for patients undergoing different medical procedures (chemotherapy, radiotherapy, bone marrow transplantation, hyperthermia). According to these results relaxation training should be implemented into clinical routine for cancer patients in acute medical treatment. Copyright © 2001 John Wiley & Sons, Ltd.

INTRODUCTION

Cancer patients have to deal with physically and emotionally distressing situations, e.g. diagnosis, side effects of medical treatment, problems arising in the context of the family and the threat of death. As survival rates have improved with ad-

vances in medical care, the importance of psychological interventions designed to assist cancer patients in dealing with diagnosis and treatment has increased (Fawzy *et al.*, 1995). Advances in medical care have increased the chance of survival but also increased toxicities. Actual cancer treatments involve higher doses of chemotherapy and different combinations of emetogenic drugs. The increased toxicities give the control of drug-induced side-effects, such as nausea, an important dimension in the treatment of cancer (Lazlo and Lucas, 1981; Morrow, 1984). Many side effects are not pharmacological but (classically)

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conditioned in nature, i.e. sights, smells, taste sensations and even thoughts come to elicit anxiety, nausea and vomiting (Nesse *et al.*, 1980; Redd and Andresen, 1981). Relaxation training is the most commonly investigated and clinically used intervention in this field. Advantages of relaxation training are that it is inexpensive and has few if any negative side effects (Lader and Mathews, 1970). It is generally easy to learn and readily accepted by the patient.

The effectiveness of relaxation training among cancer patients in acute treatment has been shown in various empirical studies (e.g. Burish and Lyles, 1981; Morrow, 1986; Cotanch and Strum, 1987; Bridge *et al.*, 1988). Qualitative reviews have been published focussing on the special use of relaxation training in reducing the side effects of cancer treatment (Redd and Andrykowski, 1982). Some reviews compare relaxation to other psychological intervention strategies (Burish *et al.*, 1983; Carey and Burish, 1988; Fawzy *et al.*, 1995). Despite the wide clinical use and positive experience, there has been no published meta-analysis about the effectiveness of relaxation training in the *acute* treatment setting to date. A first meta-analysis in this field was published by Meyer and Mark (1995), where the authors summarized studies analysing the effectiveness of different psychosocial intervention strategies (i.e. cognitive-behavioral interventions, informational and educational treatment, non-behavioral counseling or psychotherapy, social support by non-professionals and unusual treatments, such as music therapy) for adult cancer patients, either in the acute or the rehabilitation setting. The analysis clearly points to the positive effect of psychosocial interventions on emotional adjustment, functional adjustment and treatment- and disease-related symptoms. Redd (1995) concluded from this meta-analysis that it points to the further need to identify the effective *components* of psychosocial interventions in cancer patients. Meyer did not differentiate between different kinds of cognitive-behavioral intervention or between acute and rehabilitation settings. The effectiveness of relaxation training in the acute setting therefore cannot be extrapolated from the given calculated information.

This study aims to examine the effectiveness of relaxation training in helping cancer patients undergoing acute medical treatment. Medical treatment in this analysis is not limited to chemotherapy and radiotherapy but includes

modern medical treatments such as bone marrow transplant and hyperthermia. The meta-analysis focuses on results of treatment-control studies measuring intervention effects on treatment- or disease-related symptoms like nausea, vomiting, pain, and variables of emotional adjustment, such as depression and anxiety. This meta-analysis focuses also on the possible heterogeneity of effects. Resolving heterogeneity is a useful way to identify effective settings and conditions of a treatment, i.e. more narrow components of psychosocial interventions which Redd (1995) has already called for. Clinical use would benefit from a close definition of the effective settings and conditions of the relaxation intervention. Past research can be used to facilitate the development of an effective model of psychological intervention that could be readily integrated into comprehensive care of cancer patients.

RESEARCH QUESTIONS

The main question of this meta-analysis is how effective relaxation training has been in recent years for cancer patients undergoing medical treatment, and which particular intervention features most influence the effectiveness of relaxation training. For statistical reasons (Hedges, 1986: 'the chance that at least one of the statistical tests leads to erroneous rejection of the null hypothesis increases with the number of hypothesis tests'), only three potential moderator variables were chosen for further analysis: (1) Does the *intensity* of the intervention have an impact on the magnitude of the effects? In order to implement an intervention such as relaxation training in the medical context of cancer therapy, one has to find an adequate form and duration for this intervention. It is important to know the intensity of the intervention needed to reliably reduce side effects. This way one can prevent an implementation of an intervention that is useless because it may be too short to have any effect. (2) Does the *schedule* of the intervention influence its effectiveness? Some patients learn how to relax independently of the course of their medical treatment, e.g. before their first treatment, so that they may use the learned skill during the medical situation. Others get relaxation training in conjunction with medical procedures, e.g. the relaxation is induced a few minutes prior to the infusion of chemotherapy,

which itself is supplemented with guided imagery. It is important to know at what time the patients gain the most from the relaxation intervention. (3) Does the *intervention focus* (chemotherapy/radiotherapy/bone marrow transplantation/hyperthermia) influence the effectiveness of relaxation? Is there a difference in the effectiveness of relaxation training depending on the medical treatment setting? The underlying question is whether relaxation is, for example, more effective for patients coping with chemotherapy-related symptoms than for patients coping with radiotherapy-related symptoms. This subquestion should clarify whether a generalization of these different medical treatments is meaningful. Qualitative aspects make it necessary to rule out that something totally different in nature formed one single category within this meta-analysis.

METHODS

Literature search and selection of studies

The following computer databases were searched for relevant studies: MEDLINE, PSYCINFO, PSYINDEX and CANCERLIT, including published empirical studies from 1980 to December 1995. The literature research was kept broad including keywords such as 'relaxation techniques', 'progressive muscle relaxation' (PMR), 'autogenic training', 'hypnosis', 'imagination', 'guided imagery' in combination with 'neoplasms', 'cancer treatment', 'chemotherapy', 'radiotherapy', 'drug therapy' and 'bone marrow transplantation'. Reference sections of located studies, review articles and informal sources were also screened for relevant studies. Through the informal pathway, i.e. by interviewing expert professionals information was sought on other relevant studies. In this way the main techniques proposed by Cooper (1989) were accomplished. The definition of relaxation training was kept broad, including induction techniques which *aim to induce a relaxed physical and mental state* in the patient: PMR with or without guided imagery, hypnosis and autogenic training. This definition was used because of joint supposed underlying modes of actions, i.e. muscular relaxation, distraction, perceived control/self-efficacy, counterconditioning and other non-specific factors (e.g. patients expectations, placebo effects), for further

explanations see e.g. Redd and Andrykowski (1982), Burish *et al.* (1983) and Carey and Burish (1988). The different modes of action of relaxation techniques should be viewed as cooperating and interacting rather than competing to produce an effect (Carey and Burish, 1988). Similarly, Redd and Andrykowski (1982) note that the different kinds of relaxation ('hypnosis-with-imagery technique' created by Redd *et al.* and the 'progressive-muscle-relaxation-with-imagery' created by Burish *et al.*) differ 'only in respect to the manner in which relaxation is initially induced'. Of interest is the adult (16 years and older) cancer population only, consisting of patients undergoing different medical cancer treatment methods.

In a broad literature search, 280 abstracts were found. Reviewing the abstracts resulted in 58 possibly relevant studies. Fifteen studies only qualified along the inclusion criteria for meta-analysis. The diagram in Figure 1 clarifies the selection of suitable studies for meta-analysis. The following criteria were used in the study selection: (1) Sample criteria included: all or most patients were not undergoing acute medical treatment. Cancer surgery was excluded from the possible medical cancer treatments because surgery differs in many aspects from chemotherapy, radiotherapy, hyperthermia and bone marrow transplant. The latter are all continuous treatments and not a single invasive medical procedure such as surgery, which is in most cases under anesthesia. (2) Intervention criteria included: intervention packages/programmes, psychological intervention combined

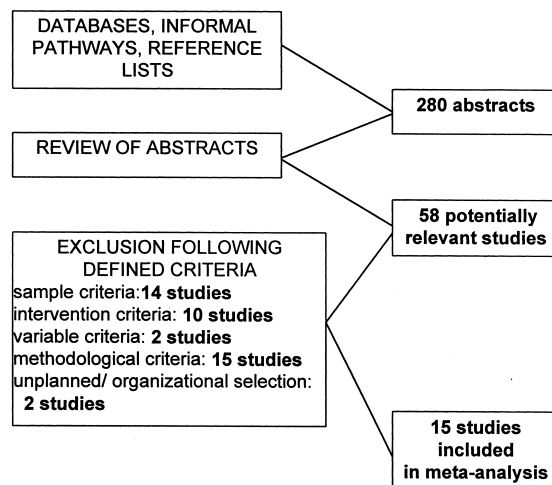


Figure 1. Process of selection of suitable studies for meta-analysis.

with different pharmacological treatments, general psychotherapy, relaxation as part of systematic desensitization and biofeedback without relaxation training. (3) Variables criteria included: very rarely analysed variables, e.g. weight change, sleep-onset latency, survival time. (4) Methodological criteria included missing of a control group, dependent studies using the same patients as other studies, study stop, missing information in order to calculate effect sizes. (5) Organizational criteria were related to availability of the studies within a defined time frame. One exclusion criterion was sufficient for a study to be excluded from meta-analytical calculations. Most of the studies had to be excluded because of several defined exclusion criteria.

Because of the specific focus on a close defined setting and psychological intervention methods, the selection resulted in 15 studies. A benefit of this meta-analysis is indeed to present these studies, which are very comparable along the defined criteria. It is less a comprehensive overview but more a thoughtful search for narrow defined comparable studies in order to analyse the effectiveness of relaxation in a special setting.

The following studies qualified for meta-analysis: Burish and Lyles (1981), Lyles *et al.* (1982), Reeves *et al.* (1982), Morrow (1986), Burish *et al.* (1987, 1991), Cotanch and Strum (1987), Bridge *et al.* (1988), Lerman *et al.* (1990), Burish and Jenkins (1992), Decker *et al.* (1992), Larsson and Starrin (1992), Syrjala *et al.* (1992, 1995) and Vasterling *et al.* (1993).

Variables

Dependent variables. The effect of relaxation training is measured on different variables. To be included in meta-analysis, a variable had to be measured in at least two studies. In view of the low number of included studies, categories of variables were established (e.g. anticipatory, during- and post-chemotherapy/transplantation nausea formed one category) to strengthen the evidence of meta-analysis by calculating effect sizes relying on more studies. Altogether, 13 categories of variables were incorporated into meta-analysis. The *treatment-related symptoms* categories consist of nausea, which was mostly measured by visual analogue scales and total time, vomiting/emesis, including measurements such as nurses' records and pain, mostly measured by

visual analogue scales. Pulse rate and blood pressure were measured by the usual techniques. The *emotional adjustment categories* include anxiety, depression, hostility/angry feelings facing medical treatment, tension, vigor/challenging feelings facing medical treatment, and fatigue. An illustrative measure for anxiety, depression and hostility is the Multiple Affect Adjective Check List, the Profile of Mood States for the variables tension, vigor, fatigue, confusion and overall mood.

Selection of treatment and control group. Effect sizes were calculated on the basis of treatment-control comparisons. In some studies more than one treatment-control comparison was realized, e.g. the effect of relaxation was not only compared to a control group but also compared to another intervention or the effectiveness of relaxation was compared to a therapist support group and a true control group. If more groups were analysed within a study, it was decided to select only one intervention group and one true control group from each study in order to keep effect sizes independent from each other. If more than one treatment/control group matched the criteria, the effect sizes had to be averaged. All the included effect sizes are based on the comparison of an intervention group and a true control group. In view of 15 included studies, 18 treatment-control comparisons are included in meta-analytic calculations.

Moderator variables and coding. The coding of study qualities mainly serves as a quantitative description of the features of all studies analysed. The coded study features can also be analysed as potential moderator variables influencing the effectiveness of relaxation. Some features of potential interest could not be included: whether PMR, autogenic training or hypnosis are of different effectiveness, whether therapists gave their patients a relaxation tape or not, whether guided imagery was included in relaxation, whether guided imagery was individually tailored to the patients' needs or not, whether relaxation had a different effect on patients in different stages of disease, of different ages, different sex or whether the profession of the relaxation trainer made a difference in the effectiveness could not be classified because of missing information. This problem that coding schemes using high degrees of detail, generally result in a greater degree of missing data, is also described by Hedges (1986). In view

of a low number of studies, a moderating variable is only meaningful if all of the studies included in meta-analysis contain information about the special feature.

The chosen moderator variables, trying to answer our subquestions are: (1) *Intervention intensity* (high/low), i.e. overall time spend with the professional. The classification in two classes was done in terms of the empirical distribution (see Table 2). Since three studies were located on the median of 112.5 min (for explanation see text below Table 2), the cut-off point was set at 120 min. The intensity below 120 min was classified *low intervention intensity* (eight studies). The other studies were classified as the *high intervention intensity* studies (seven studies). (2) *Intervention schedule* divides studies into those where the psychological intervention was administered *in conjunction with* medical procedures (seven studies) and those where the relaxation training was administered *independently of* the medical procedure (eight studies). (3) *Intervention focus* (chemotherapy/radiotherapy/bone marrow transplantation/hyperthermia) classifies studies across medical treatments, i.e. patients were receiving chemotherapy, radiotherapy, bone marrow transplantation and hyperthermia.

DATA ANALYSIS

Effect sizes were calculated following the method proposed by Hedges and Olkin (1985): the unit-free effect size g was converted to d which accounts for small samples, being an unbiased (corrected by sample size) effect size. For the 13 categories separate meta-analyses of effect sizes were conducted. The effect for the population results from a weighted mean D_w , following the precision of the single effect sizes depending on s_d^2 . The statistical analysis was done with the aid of D-STAT, software created by Johnson (1989). To avoid an overrepresentation of studies where multiple measures, different subgroups of variables, different measures of the same variable or different measure time points, etc., were analysed, only one averaged effect size per variable per study was included.

Overall, 246 single effect sizes were calculated. This number was reduced to 56 independent effect sizes, which were included in the final calculations of the meta-analysis. Effect sizes were only calcu-

lated for those variables in the studies where the necessary information was given (e.g. means and standard deviations, F -values, chi-squared values). Effect sizes were not set at zero for variables omitted from the result section in the studies, or just noted in the studies by the remark that they did not reach significance. Setting these at zero is a very conservative estimation and clearly underestimates the effects of the intervention. This method is further discussed in the 'Discussion'. Following Cooper (1981) the value and significance of the average effect size are of relevance for its interpretation. The reliability of the mean effect size is shown by the level of significance. The significance level was set at $p < 0.05$. The case of an effect size being significantly different from 0, the effect size was judged to be interpretable in terms of Cohen's (1988) index of effect magnitude. The implication of an effect size can also be shown by the *fail safe number* of studies necessary to reduce the *average effect size estimate* to the 'no effect level', according to Orwin (1983), in terms of Hedges and Olkin (1985). If the fail safe number indicates an effect hardly to be reduced by further more studies the effect size can be interpreted in terms of the noted classification of Cohen (1988). The resulting effect size for the population is only interpretable in the case of homogeneity. A homogeneous set of effect sizes can be considered as a sample from a single underlying effect size. In the analyses therefore a test of homogeneity is conducted. If the conducted test of homogeneity Q_B points to heterogeneity of the effect sizes of the different studies, the heterogeneity can be explained by the special features of the study.

RESULTS

Characteristics of the studies

Descriptors of the studies are limited to the studies done in the time frame of interest. The results are, strictly speaking, limited to the described population and special kind of relaxation intervention. Out of the included 15 studies, 13 were conducted in the USA, one in Sweden and one in the UK. The time frame of publication of these studies was from 1981 to 1995. Seven of the selected studies are published 1990 and after.

Description of study samples

Basic characteristics of the studies (sample size, mean age and sex of subjects) are summarized in Table 1. Altogether 742 subjects were included in this meta-analysis.

All subjects were undergoing acute medical treatment at the time of the study. Most (nine) studies concentrated on the effect of chemotherapy on patients. Three studies focused on radiotherapy. Two studies dealt with side effects of bone marrow transplantations. One study dealt with side effects during hyperthermia. Primary cancer sites were diverse. Most of the study samples included certain common primary cancer sites like breast, leukemia (hematological cancer and lymphomas) and lung. In all probability, these cancer sites also constitute the largest overall number of subjects in this meta-analysis.

In cases where antiemetic medication was dispensed, four studies specified that the dosage was kept constant throughout the study. Three studies equated the groups according to antiemetic medication. This means that 40% of the studies controlled in one way or another for antiemetic medication. Two additional studies noted that the subjects of both groups received the 'standard antiemetic therapy'.

In four of the nine studies using chemotherapy, the emetogenic potential of the chemotherapeutic drugs was described as being high. They stated that the chemotherapeutic protocol 'was likely to produce post-chemotherapy nausea and vomiting' or that 'the emetogenic potential was greater than 60%'. Two of the studies used the emetogenic potential of the chemotherapy as an entry criterion for the study. An emetogenic rating from 1-5 to 1-6 for a chemotherapy protocol had to have a rating of at least 3.

Table 1. Basic characteristics of study sample

	Mean	Median	Range	N_{study}
Sample size per study	49	46	16-128	15
Mean age (years)	50	51	32.7-61	9
Sex (% women)	64.4	64.86	42.22-100	14

N_{study} represents the number of studies actually describing their sample by these characteristics. The whole meta-analytic sample has to be inferred from this information.

Characteristics of study intervention

A specification of the intervention features was done in all studies (Table 2). The median of the duration was located at 37.5 min, this number presents the mean of the described duration of the single session as '30-45 min'. It was hypothesized that across all intervention sessions and across all subjects, this range would result in the mean time. The single session and the intervention intensity only reflect the time a professional spent with the patient during one single session/overall. The exact duration of the relaxation training during a single session/overall is unclear. Often in the first relaxation session a brief explanation of the procedure, the rationale, etc., was included. It is also assumed that the relaxation trainer spent some of the time during the following sessions in general conversation. This means that the actual time of relaxation training in the individual sessions and the overall intervention intensity of relaxation is shorter than noted. This is especially noteworthy in view of the rather short mean session time of 40 min.

Following the definition of the intervention as inclusion criterion all included intervention groups used relaxation as a psychological method. The most common relaxation technique used was Jacobsen's PMR or its abbreviated form developed by Bernstein and Borkovec (1973). PMR was used in 87.5% of interventions. The additional two studies used hypnosis as the intervention method. Most of the interventions included additional intervention methods to the proper relaxation induction. In 11 (73%) of the interventions, PMR was combined with guided imagery. In 81.82% of these studies the guided imagery was tailored to the patients individual needs. The individual preference was assessed in an interview either before or after the intervention. In two intervention groups, PMR was supplemented by autogenic training. Other intervention

Table 2. Basic intervention features

	Mean	Median	Range
Number of sessions	3.6	3	1-7
Duration of single session (min)	40	37.5	15-90
Intervention intensity (duration overall) (min)	149.1	112.5	15-360

Basis: 15 studies.

supplements were diaphragmatic/deep breathing or giving a cue-word for cue-controlled relaxation. In 86.66% of studies, patients were instructed or suggested to practice relaxation at home. The remaining studies did not mention such an instruction. The concrete instructions were diverse, from a defined number of minutes per day (e.g. 15 min per day), number of times daily (five studies proposed at least daily), number of times per week (e.g. four times a week) to general suggestions to practice at home (four studies). If a tape was given to patients, they were instructed to listen to it at certain times per day. Overall, in 80% of studies, either an audio cassette or written instructions were handed to patients. In 62.5% of the intervention groups, patients were provided only or additionally with an audio cassette. In 43.75% this 'give away'/hand-out consisted only or additionally in written instructions. The tape was either a standard relaxation tape or the first relaxation training session was recorded and the tape was given to the patients. Patients had different kinds of instructions for the use of this tape. In one study, the patients should listen to it while receiving chemotherapy. The tapes of the other studies should be used for home practice. In one study, a wallet card to cue the patients to practice relaxation was given.

The intervention schedule differed in the studies. A total of 46.66% of studies used relaxation training in conjunction with sequential chemotherapy sessions. The relaxed state was induced prior to the administration of chemotherapy, directly measuring the outcome variables after each chemotherapy. In the other studies, relaxation training was provided independently of medical procedure. The schedule of this intervention differed. Four of the studies (26.67%) scheduled the psychological intervention before the acute medical treatment. They noted a defined time when the intervention took place, e.g. 2 weeks before the first treatment, or noted that the patients were

'scheduled' for medical treatment. Another four (26.67%) studies provided relaxation training during the course of medical treatment, but not in conjunction with the medical procedure, e.g. two sessions between the 4th and 5th course of chemotherapy.

Average effect sizes

The effects of relaxation on the 13 variables are presented in terms of effect sizes. Variables related to the medical cancer treatment were nausea, vomiting, pain, higher pulse rate and blood pressure. Emotional adjustment variables were anxiety, depression, hostility, tension, vigor, fatigue, confusion and overall mood.

Treatment-related symptoms

Significant beneficial effects of relaxation on cancer patients were found in the treatment-related symptoms nausea, pain, pulse rate, blood pressure ranging from 0.45 to 0.55. The effect sizes were homogenous across all studies for all variables (Table 3). The fail safe values indicate that from 129 to 440 studies are necessary to reduce the average effect size estimate to a negligible level ($D_C = 0.01$) according to Orwin (1983) in terms of Hedges and Olkin (1985, p. 306). For the variable pain it has to be said that the number of studies and subjects is very low and the confidence interval quite large (from no effect to a large effect), although the effect reached significance at the 0.05 level. Another variable was initially tried to analyse within this meta-analysis, the vomiting response. To our regret the effect size cannot be interpreted for several reasons. First of all, the single effect sizes of the studies are very heterogeneous, the g -values varied from -0.0488 to 1.4332 . Another problem concerning this variable was very rare incidences over all

Table 3. Treatment-related symptoms

	N_{studies}	N_{ES}	N_{subjects}	D_w	95% CI	Homogeneity	Fail safe N
Blood pressure	5	23	144	+0.5518*	+0.21/+0.89	Yes	270
Pulse rate	4	26	103	+0.5382*	+0.14/+0.94	Yes	212
Nausea	10	56	399	+0.4545*	+0.25/+0.65	Yes	440
Pain	3	8	96	+0.4383*	+0.03/+0.84	Yes	129

* $p < 0.05$.

groups and sessions. Five studies, which could not be included into the calculation of the composite effect size for vomiting because of missing data, noted that the mean incidence rate was in all groups per session below 1.0, that only two patients in each condition vomited during one or both sessions or that 78% of the patients did not vomit at all during treatment. One of the included studies noted that 'the vomiting levels of patients in all groups showed considerable volatility over sessions'. It was decided not to interpret or further analyse the effect size ($+0.5451^*$, confidence interval (CI): $+0.12/+0.97$, no homogeneity) of vomiting because of this high number of noted statements, six studies out of eight studies measuring vomiting. Because of a possible floor effect any comparison between groups was judged not to be reasonable.

Emotional adjustment

The variable hostility was put together with other variables measuring, in general, angry feelings facing medical treatment. Besides hostility before and after chemotherapy these were anger during radiotherapy courses and appraisal threat and/or harm-loss during radiotherapy. The variable vigor represents another category of variables, including vigor during the courses of radiotherapy and appraisal challenge during radiotherapy. Overall, the average effect sizes for emotional adjustment variables varied from 0.08 to 0.54. The effect sizes for the variables depression, hostility, tension, anxiety and mood reached significance at the 5% level. Of these variables tension and mood represent the results of only two studies and therefore must be interpreted very carefully. For all variables, with the exception of

anxiety, homogeneity was found (Table 4). The fail safe N indicates 21–352 studies are necessary to reduce the average effect size estimate to a negligible level ($D_C = 0.01$), according to Orwin (1983) in terms of Hedges and Olkin (1985, p. 306).

Explanation of heterogeneity

For 11 of 13 categories of dependent measures, the set of effect sizes proved to be homogenous. The exception was for vomiting, which was not further analysed, and the measures of anxiety. In order to interpret the calculated effect sizes, heterogeneity must be resolved following Hedges and Olkin (1985). Neither the removal of an outlier nor the splitting of the variables into subgroups could resolve the heterogeneity of anxiety. All subgroups reached the significance level, but the effect size for the pretreatment anxiety was also heterogeneous, only during treatment and post-treatment anxiety were they homogenous (pretreatment anxiety: $N_{\text{studies}} = 3$, $N_{\text{ES}} = 11$, $N_{\text{subjects}} = 132$, $D_w = +0.7292^*$, 95% CI = $+0.36/+1.10$, no homogeneity; during treatment anxiety: 5, 32, 197, $+0.3888^*$, $+0.10/+0.67$, homogenous; post-treatment anxiety: 5, 15, 162, $+0.5588^*$, $+0.24/+0.87$, homogenous).

Whether one of the potential moderator variables *intervention intensity*, *intervention schedule* and the *intervention focus* could explain the heterogeneity of anxiety, was analysed by a categorical classification into two or more classes. It was verified whether the mean effect sizes of the classes did differ significantly from each other. In meta-analytic terms: the possible moderator variables were tested following the fixed effects categorical model of homogeneity versus class

Table 4. Emotional adjustment

	N_{studies}	N_{ES}	N_{subjects}	D_w	95% CI	Homogeneity	Fail safe N
Depression	6	24	274	$+0.5422^*$	$+0.30/+0.78$	Yes	318
Tension	2	5	150	$+0.5156^*$	$+0.19/+0.84$	Yes	102
Anxiety	8	61	351	$+0.4511^*$	$+0.23/+0.67$	No	352
Mood	2	5	151	$+0.4421^*$	$+0.12/+0.77$	Yes	86
Hostility	6	27	284	$+0.3438^*$	$+0.11/+0.58$	Yes	198
Fatigue	2	5	150	$+0.2366$	$-0.09/+0.56$	Yes	46
Confusion	2	5	150	$+0.2266$	$-0.10/+0.55$	Yes	44
Vigor	3	7	214	$+0.0849$	$-0.18/+0.35$	Yes	21

* $p < 0.05$.

differences of effects sizes (Hedges and Olkin, 1985). A highly significant difference between the categories relaxation training offered independent versus in conjunction with medical treatment $Q_B(1) = 7.0515$, $p = 0.0079$. Furthermore a tendency toward a significant differences between low versus high intervention intensity $Q_B(1) = 3.73$, $p = 0.05$ was found. The significant difference of the intervention schedule subgroups points to a greater efficacy of relaxation training offered independently from medical treatment concerning the reduction of anxiety. Interestingly, the difference of intervention intensity subgroups pointed to a benefit of the low intervention intensity (compared to high intervention intensity), i.e. relaxation training intensities below 2 h tending to have a higher average effect on anxiety. For the moderator variable intervention focus a comparison between classes could not be made since all studies measuring anxiety belonged to the same category (chemotherapy).

DISCUSSION

Interpretation of effect sizes

In the following, the magnitudes of effect sizes are interpreted in terms of the Cohen index, i.e. $D(w)$, 0.20 small effect, 0.50 medium effect, 0.80 large effect (Cohen, 1988). The relaxation intervention proved to have a small but significant effect on the *treatment-related symptoms* of the medical treatment of cancer: nausea and pain. Patients who received relaxation training experienced significantly less nausea and pain. Relaxation training also significantly reduced pulse rate and blood pressure in these patients (medium effect). The reduction of blood pressure and pulse rate seems to confirm the supposed effectiveness of relaxation through muscular relaxation. A deep somatic restfulness reduces anxiety and physiological arousal, thereby reducing side effects such as gastrointestinal upsets that are caused or exacerbated by high levels of anxiety and arousal. The muscular relaxation may also directly inhibit the characteristic sequence of muscular activity that generally precedes nausea and vomiting (Burish *et al.*, 1983). Concerning *emotional adjustment*, relaxation training has a significant (medium) effect on depression and a significant (small) effect in the reduction of anxiety and hostility. Patients receiv-

ing relaxation training were found to be less depressive, anxious and hostile in the context of the acute medical setting. The analysis of two studies only, pointed to an additional effect of relaxation on the reduction of tension and amelioration of the overall mood state. Patients were shown to be less tense and in a better mood or to have fewer mood disturbances. Apparently relaxation has no effect on patients' levels of vigor, fatigue and confusion.

Impact of the moderator variables

The effect of relaxation on the anxiety level of patients depends on two *intervention features*. First, if relaxation techniques have been learned prior to the acute medical treatment, they reduce anxiety significantly better. Second, relaxation interventions below 2 h overall intensity (time spent with the professional) have a tendency towards a higher effect on the reduction of anxiety. Regarding the impact of these moderating variables, we can speculate about possible explanations:

(1) Medical cancer treatment may especially provoke anxiety about something that cannot be influenced. The infusion of drugs seen by the patient as 'poison' has to be accepted, and nothing can be done against this. The patient may feel helpless, hopeless and anxious. In this situation, relaxation affords an active coping strategy for the patient, the feeling of greater self-efficacy (see Bandura, 1977) may be extremely relevant (Carey and Burish, 1988; Lyles *et al.*, 1982; Redd and Andrykowski, 1982). If the patients feel they are gaining control over at least the side effects of this drug, they suffer less anxiety in this stressful situation. Unlike the intervention given in conjunction with medical treatment, where the patients 'go through' like the medical treatment itself, the intervention offered independently can be used *voluntary* and may also have a more general effect. The *intervention intensity* may be related to the motivation, a 'short explanation and demonstration' of the procedure could motivate the patients to practice on their own a lot more than in the case of getting training on a more regular basis. The fact that the patients have 'worked this method out mostly on their own' could directly influence their feeling of self-efficacy. Past research analysing the form of presentation of relaxation nevertheless points to a more effective relaxation intervention

administered by a professional therapist than by a trained volunteer therapist (Carey and Burish, 1987) and to a more effective live presentation instead of tape presentation only (Morrow, 1984). The formerly helpless confrontation with the medical treatment becomes something that can be influenced by the patient, treatment-related symptoms seem to be manageable. The patient has learned a method to prevent or lessen side-effects, thereby reducing anxiety. This result contradicts the hypothesized mechanism of action of relaxation being simply a distracter. It could be assumed that interventions focusing on the patient's own capacity for learning to relax are more effective than those trying to offer as much training with an expert as possible. The ability of the expert to motivate the patients to practice on their own may be of special importance. This aspect is often neglected but is worthy of becoming ameliorated perhaps by adding special components, e.g. integrating family members of the patient in the relaxation intervention. Nevertheless it is reasonable to assume limitations of this probably most effective form of relaxation training, because very ill patients (e.g. low Karnofsky Index) or high anxiety patients may not be able to practice as much on their own and may especially need the individual therapist's support and aid with the training process.

(2) A different hypothesis in accordance with learning theories is that learning of the relaxation intervention proves to be more effective if it is not learned within the stressful anxiety provoking environment of the medical treatment but in a harmless and calm surrounding. Therefore, any relaxation intervention offered independently from medical treatment can reduce direct treatment-related symptoms and emotional adjustment, especially anxiety, much better.

(3) An alternative explanation of the result found, intervention offered independently from medical treatment being more effective has to be taken into account. The sample of study interventions offered independently is probably biased in the way that the patients taking part in the intervention group offered independently are more highly motivated than those taking part in intervention groups offered in conjunction with medical treatment. Looking at the schedule of the intervention offered independently we assume that in some of the studies the relaxation training represented an extra visit to the hospital for the patients. This practical aspect of the study design

was not explicitly noted in any of the studies. Patients who came exclusively for the psychological intervention, are presumed to be more highly motivated about the relaxation intervention and are believed to be training much more often on their own.

Nevertheless heterogeneity of effects on anxiety could not be completely explained since not only Q_B proved to be significant but also Q_W . This illustrates a significant difference between classes, but the classes are heterogeneous within. The moderator variable therefore could not completely explain the difference found. There seem to be additional variables to the ones discussed above, which are having an influence on the effect of relaxation on anxiety. In view of the number of included studies, any further subclassification or supposing of different moderator variables was not carried out. To discover these other moderating variables would be extremely useful since, as noted earlier, the effective reduction of anxiety may also reduce nausea and vomiting by lowering the general physiological arousal. The hypothesized comparability of different medical cancer procedures, including modern procedures like bone marrow transplant or hyperthermia, proved to be correct. Patients under different acute medical treatments do benefit equally from relaxation training. This points to the favorable extension of the routine clinical use of relaxation training into newer medical settings, like BMT. The question of effectiveness of relaxation in the BMT setting is addressed in an ongoing study of Hasenbring *et al.* (1998), where it is compared to music therapy. BMT results in more severe forms of the same side effects seen in other cancer populations (see Chapman *et al.*, 1987; Chapko *et al.*, 1989 noted in Syrjala *et al.*, 1992).

External validity

Some caution is necessary in assuming that the results apply equally to different populations (Meyer and Mark, 1995). Meta-analysis is limited to the presentation of the mean population, it does not take into account the individual effectiveness depending on individual factors. For example, for women below 55 years (Bridge *et al.*, 1988), patients with low hypnotic susceptibility (Reeves *et al.*, 1982), high-anxiety patients (Carey and Burish, 1985), ethnic minorities or patients not interested in the intervention, relaxation training may not be equally effective. Describing the

average population (see means in 'characteristics of the studies') represented by the meta-analysis results, leads to breast, hematological, lymphoma and lung cancer patients at the age of 50, mostly women. The patients are treated in an outpatient setting receiving highly emetogenic chemotherapy. They are trained in PMR with individually tailored guided imagery which consists of three sessions at 40 min each, the mean overall intervention intensity is about 2.5 h. The patients are given a relaxation audiocassette or written instructions to practice relaxation at home. Extending the results of meta-analysis by analysing the variance of effectiveness depending on individual factors surely is a worthwhile target for future research.

Implication of meta-analytical methodology

The magnitude of effects of the psychological intervention on treatment and disease-related symptoms and emotional adjustment are comparable with the results found by Meyer and Mark (1995). The effects of relaxation on treatment-related symptoms are slightly higher than on emotional adjustment. Compared with Meyers study, our results seem to be higher in their magnitude which is explainable with our slightly different categories and included studies and less conservative calculations. Since the meta-analysis calculates effects of a psychological intervention on severe side effects it was decided to calculate less conservatively in the form of keeping the β -error low. Instead of withholding the patient an effective intervention to lessen his/her side effects of the acute medical treatment, the offer of an unprofitable intervention (probably only unprofitable for the reduction of side effects) was judged as being more reasonable. Because of these reasons we decided not to risk a clear underestimation of effects by setting results simply stated as non-significant or not further mentioned in the result section of the studies at zero in our calculations. The fail safe N , pointing depending on the categories from 21 to 440 studies necessary to reduce the average effect size estimated to a critical effect size of 0.01, ruled out the possibility of an overestimation of the effect of relaxation. For the effect sizes which reached significance the fail safe number is at least 86. Following Rosenthal (1984) cited after Fricke and Treinies (1985) there is no agreed standard concerning the magnitude

of a fail safe number necessary to reject the null hypothesis of no effect. For the use of the fail safe as a decision criterion, a rule of thumb is proposed: the underlying true effect of the calculated effect size (taking the publication bias into account) is different from zero if the fail safe value exceeds five times plus 10 the number of studies included in the effect size calculations. In all variables it exceeds this defined number with the exception of vigor. Only 15 studies were found within the defined criteria, it seems improbable that 86 unpublished studies found no effect of relaxation training on the variables analysed. Only one study published in 1997 (Yoo *et al.*, 1997) is known to fulfill the defined criteria for entry in analysis but was omitted from analyses because of the defined time frame. The study did not have contradictory outcomes. The study outcomes mainly confirm our results.

The number of included studies (15) poses several problems: First, it leads to less power in the model testing, probably categories did not reach significance or not as high as in reality, because of high degrees of freedom. Because of the small number of treatment-control comparisons β -errors are possible. Second, theoretical driven hypotheses were not possible to check, since many studies would be lost because of missing information about specific features. The subquestions were decided *post hoc* in order to keep all studies in further calculations. Third, resolving the heterogeneity within classes by further subclassifications of the moderator variables was impossible in view of the number of effect sizes.

Clinical and practical implication of study results

The consistency of the positive results obtained in the group of studies of the meta-analysis is remarkable: clinical significant reductions in nausea, pain, anxiety, depression, hostility and physiological arousal (blood pressure and pulse rate) were achieved despite wide variations in type of cancer, stage of disease, chemotherapy protocol, etc. This fact is especially noteworthy if one considers that the research was conducted by separate groups of investigators using different research methods. Overall it can be assumed that relaxation during the courses of cancer treatment makes the experience less stressful in effectively reducing side effects. It is a skill which patients can learn easily, giving them a personal sense of

mastery and control over their problems rather than an increased sense of helplessness resulting from further dependency on drugs (Redd *et al.*, 1982–1983). It does not need to be cost-intensive, since the short intensities of the intervention below 2 h overall proved to be very effective, probably even more effective. Of potential relevance may be the ability of the therapist to motivate the patient to practice on his/her own. Relaxation does not only enable the patient to alleviate his or her experience of treatment-related symptoms such as nausea, but also potentially benefits the patients in other areas, long after the treatment is completed. Its benefits may extend beyond the control of side effects in even helping family members (Burish *et al.*, 1988, 1991).

Other modalities in combination with relaxation (e.g. antiemetic medication, counseling/therapy, educational intervention regarding chemotherapy (Burish *et al.*, 1991), positive suggestions of improved appetite (Cotanch and Strum, 1987), nutritional advice (Fürst *et al.*, 1992), may contribute a *potentiating* effect to the traditional relaxation training, thus producing a more complete outcome. Therefore, an implementation of relaxation training into clinical routine for diverse kinds of medical treatment proved to be effective by the research of the past 15 years. It surely should be used as standard adjunctive treatment in the care of cancer patients.

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REFERENCES

- Bandura A. 1977. Self-efficacy: toward a unifying theory of behavioral change. *Psychol Rev* **85**: 447–454.
- Bernstein DA, Borkovec TD. 1973. *Progressive Relaxation Training: A Manual for the Helping Professions*. Research Press: Champaign, Ill.
- Bridge LR, Benson P, Pietroni PC, Priest RG. 1988. Relaxation and imagery in the treatment of breast cancer. *Br Med J* **5**: 1167–1172.
- Burish TG, Lyles JN. 1981. Effectiveness of relaxation training in reducing adverse reactions to cancer chemotherapy. *J Behav Med* **4**(1): 65–78.
- Burish TG, Jenkins RA. 1992. Effectiveness of biofeedback and relaxation training in reducing the side effects of cancer chemotherapy. *Health Psychol* **11**(1): 17–23.
- Burish TG, Carey MP, Redd WH, Krozely MG. 1983. Behavioral relaxation techniques in reducing the distress of cancer chemotherapy patients. *Oncol Nurs Forum* **10**(3): 32–35.
- Burish TG, Carey MP, Kozely MG, Greco FA. 1987. Conditioned side effects induced by cancer chemotherapy: prevention through behavioral treatment. *J Consult Clin Psychol* **55**(1): 42–48.
- Burish TG, Vasterling JJ, Carey MP, Matt D, Krozely MG. 1988. Post treatment use of relaxation training by cancer patients. *Hospice J* **4**: 1–8.
- Burish TG, Snyder SL, Jenkins RA. 1991. Preparing patients for cancer chemotherapy: effects of coping preparation and relaxation interventions. *J Consult Clin Psychol* **59**(4): 518–525.
- Carey MP, Burish TG. 1985. Anxiety as a predictor of behavior therapy outcome for cancer chemotherapy patients. *J Consult Clin Psychol* **53**: 860–865.
- Carey MP, Burish TG. 1987. Providing relaxation training to cancer chemotherapy patients: a comparison of three delivery techniques. *J Consult Clin Psychol* **55**(5): 732–737.
- Carey MP, Burish TG. 1988. Etiology and treatment of the psychological side effects associated with cancer chemotherapy: a critical review and discussion. *Psychol Bull* **104**(3): 307–325.
- Chapko MK, Syrjala KL, Schilter I, Cummings C, Sullivan KM. 1989. Chemotherapy toxicity during bone marrow transplantation: time course and variation in pain and nausea. *Bone Marrow Transplant* **4**: 181–186.
- Chapman CR, Kornell JA, Syrjala KL. 1987. Painful complications of cancer diagnosis and therapy. In *Cancer Pain Management*, Yarbo CH, McGuire D (eds). Grune and Statton: Orlando, FL; 47–67.
- Cohen J. 1988. *Statistical Power Analysis for the Behavioral Sciences* (revised edn). Lawrence Erlbaum Associates Publishers: Hillsdale, NJ.
- Cooper HM. 1981. On the significance of the effects and the effects of significance. *J Person Soc Psychol* **41**: 1013–1018.
- Cooper HM. 1989. *Integrating Research. A Guide for Literature Reviews* (2nd edn). Sage: Newbury Park, CA.
- Cotanch PH, Strum S. 1987. Progressive muscle relaxation as antiemetic therapy for cancer patients. *Oncol Nurs Forum* **14**(1): 33–37.
- Decker TW, Cline EJ, Gallagher M. 1992. Relaxation therapy as an adjunct in radiation oncology. *J Clin Psychol* **48**(3): 388–393.

- Fawzy IF, Fawzy NW, Arndt LA, Pasnau RO. 1995. Critical review of psychosocial interventions in cancer care. *Arch Gen Psychiatry* **52**: 100–113.
- Fricke R, Treinies G. 1985. *Einführung in die Meta-analyse*. Huber: Bern.
- Fürst CJ, Johansson S, Frederikson M, Hursti T, Steineck G, Peterson C. 1992. Control of cisplatin induced emesis—a multidisciplinary intervention strategy. *Med Oncol and Tumor Pharmacother* **9**(2): 81–86.
- Hasenbring M, Schulz-Kindermann F, Hennings U, Florian M, Linhart D, Ramm G, Zander AR. 1998. The efficacy of psychosocial interventions for improving quality of life in BMT patients: first results from two randomized intervention studies. *Psycho-Oncology* **7**(4): Abstract no. 7.
- Hedges LV. 1986. Issues in meta-analysis. *Rev Res Educ* **13**: 353–398.
- Hedges LV, Olkin I. 1985. *Statistical Methods for Meta-analysis*. Academic Press: Orlando.
- Johnson BT. 1989. *DSTAT: Software for the Meta-Analytic Review of Research Literatures Manual*. Lawrence Erlbaum Associates Publishers: Hillsdale, NJ.
- Lader MH, Mathews AM. 1970. Comparison of methods of relaxation using physiological measures. *Behav Res Ther* **8**: 331–337.
- Larsson G, Starrin B. 1992. Relaxation training as an integral part of caring activities for cancer patients: effects on well-being. *Scand J Caring Sci* **6**(3): 179–185.
- Lazlo J, Lucas VS. 1981. Emesis as a critical problem in chemotherapy. *New Engl Med* **305**: 948–949.
- Lerman C, Rimer B, Blumberg B, Cristinzio S, Engstrom PF. 1990. Effects of coping style and relaxation on cancer chemotherapy side effects and emotional responses. *Cancer Nurs* **13**(5): 308–315.
- Lyles JN, Burish TG, Krozely MG, Oldham RK. 1982. Efficacy of relaxation training and guided imagery in reducing the aversiveness of cancer chemotherapy. *J Consult Clin Psychol* **50**(4): 509–524.
- Meyer TI, Mark MM. 1995. Effects of psychosocial interventions with adult cancer patients: a meta-analysis of randomized experiments. *Health Psychol* **14**(2): 101–108.
- Morrow GR. 1984. Appropriateness of taped versus live relaxation in the systematic desensitization of anticipatory nausea and vomiting in cancer patients. *J Consult Clin Psychol* **52**(6): 1098–1099.
- Morrow GR. 1986. Effect of cognitive hierarchy in the systematic desensitization treatment of anticipatory nausea in cancer patients: a component comparison with relaxation only, counseling, and no treatment. *Cognitive Ther Res* **10**(4): 421–446.
- Nesse RM, Carli T, Curtis GC, Kleinman PD. 1980. Pretreatment nausea in cancer chemotherapy: a conditioned response? *Psychosomatic Medicine* **42**: 33–36.
- Orwin RG. 1983. A fail-safe *N* for effect size. *J Educ Stat* **8**: 147–159.
- Redd WH. 1995. Behavioral research in cancer as a model for health psychology. *Health Psychol* **14**(2): 99–100.
- Redd WH, Andresen GV. 1981. Conditioned aversion in cancer patients. *Behav Ther* **4**: 3–4.
- Redd WH, Andrykowski MA. 1982. Behavioral interventions in cancer treatment: controlling aversion reactions to chemotherapy. *J Consult Clin Psychol* **50**(6): 1018–1029.
- Redd WH, Rosenberger PH, Hendler CS. 1982–1983. Controlling chemotherapy side effects. *Am J Clin Hypnosis* **25**(2–3): 161–172.
- Reeves JL, Redd WH, Storm FK, Minagawa RY. 1982. Hypnosis in the control of pain during hyperthermia treatment of cancer. *Adv Pain Res Ther* **5**: 857–861.
- Rosenthal R. 1979. The 'file drawer problem' and tolerance for null results. *Psychological Bulletin* **86**: 638–641.
- Rosenthal R. 1984. *Meta-analytic Procedures for Social Research*. Sage Publications: Beverly Hills.
- Syrjala KL, Cummings C, Donaldson GW. 1992. Hypnosis or cognitive behavioral training for the reduction of pain and nausea during cancer treatment: a controlled clinical trial. *Pain* **48**: 137–146.
- Syrjala KL, Donaldson GW, Davis MW, Kippes ME, Carr JE. 1995. Relaxation and imagery and cognitive-behavioral training reduce pain during cancer treatment: a controlled clinical trial. *Pain* **63**(2): 189–198.
- Vasterling J, Jenkins RA, Tope DM, Burish TG. 1993. Cognitive distraction and relaxation training for the control of side effects due to cancer chemotherapy. *J Behav Med* **16**(1): 65–80.
- Yoo HJ, Kim SH, Kim CY, Hong TY, Lee C, Han OS. 1997. Efficacy of relaxation training (RT) and guided imagery (GI) in reducing the side effects of cancer chemotherapy. *Proc ASCO* **16**: 86a.