

# PSYCHOLOGY, PSYCHIATRY & BRAIN NEUROSCIENCE SECTION

## Original Research Articles

# The Effect of Deep and Slow Breathing on Pain Perception, Autonomic Activity, and Mood Processing—An Experimental Study

Volker Busch, MD,\* Walter Magerl, MD,<sup>†</sup> Uwe Kern, MD,<sup>‡</sup> Joachim Haas, MD,\* Göran Hajak, MD,\* and Peter Eichhammer, MD\*

\*Department of Psychiatry and Psychosomatic Medicine, University of Regensburg, Regensburg;

<sup>†</sup>Department of Neurophysiology, Centre of Biomedicine and Medical Technology Mannheim (CBTM), University of Heidelberg, Mannheim;

<sup>‡</sup>Centre for Pain Management & Palliative Care, Wiesbaden, Germany

*Reprint requests to:* Volker Busch, MD, Center for Pain and Affective Disorders, Department of Psychiatry, Psychotherapy and Psychosomatic Medicine, University of Regensburg, Universitätsstraße 84, 93059 Regensburg, Germany. Tel: 49-941-941-0; Fax: 49-941-941-2925; E-mail: volker.busch@medbo.de.

Authors Approval/Disclosure: All authors have personally reviewed and given final approval of the version submitted, and neither the manuscript nor its data have been previously published or are currently under consideration of publication.

## Abstract

**Objective.** Deep and slow breathing (DSB) techniques, as a component of various relaxation techniques, have been reported as complementary approaches in the treatment of chronic pain syndromes, but the relevance of relaxation for alleviating pain during a breathing intervention was not evaluated so far.

**Methods.** In order to disentangle the effects of relaxation and respiration, we investigated two different DSB techniques at the same respiration rates and depths on pain perception, autonomic activity, and mood in 16 healthy subjects. In the attentive

DSB intervention, subjects were asked to breathe guided by a respiratory feedback task requiring a high degree of concentration and constant attention. In the relaxing DSB intervention, the subjects relaxed during the breathing training. The skin conductance levels, indicating sympathetic tone, were measured during the breathing maneuvers. Thermal detection and pain thresholds for cold and hot stimuli and profile of mood states were examined before and after the breathing sessions.

**Results.** The mean detection and pain thresholds showed a significant increase resulting from the relaxing DSB, whereas no significant changes of these thresholds were found associated with the attentive DSB. The mean skin conductance levels indicating sympathetic activity decreased significantly during the relaxing DSB intervention but not during the attentive DSB. Both breathing interventions showed similar reductions in negative feelings (tension, anger, and depression).

**Conclusion.** Our results suggest that the way of breathing decisively influences autonomic and pain processing, thereby identifying DSB in concert with relaxation as the essential feature in the modulation of sympathetic arousal and pain perception.

**Key Words.** Breathing; Mood; Pain; Relaxation; Respiration; Skin Conductance Level

## Introduction

Deep and slow breathing (DSB) techniques are widely used in a variety of diseases encompassing somatic disorders such as hypertension and pulmonary diseases [1] as well as psychiatric disorders including anxious and depressive syndromes [2,3] or stress-related disorders [4–10]. With regard to chronic pain syndromes, DSB techniques being part of many physical, mental, and spiritual disciplines such as yoga [11], Qi-Gong [12], or Tai Chi [13] are integrated into multimodal treatment approaches. Chalaye and colleagues [14] found higher pain thresholds and tolerances in healthy adults after a DSB training.

However, despite these findings, inconsistent results about the therapeutical efficacy point to the fact that breathing interventions may be based on a complex interplay of distinct factors not entirely identified until now [15].

In this context, relaxation may play a pivotal role in transforming breathing techniques into an effective method in the therapy of pain and stress-related disorders. Furthermore, DSB in concert with relaxation has proven to efficiently reduce stress-related biological activity in healthy volunteers as mirrored by a reduction in the sympathetic tone [7]. In contrast, a DSB training associated with a concentration challenge and guided by respiratory feedback failed to reduce sympathetic arousal [16]. Moreover, sustained concentration on inhaling and exhaling during attentive breathing interventions has demonstrated an increase in sympathetic arousal [17].

For this reason, relaxation may constitute a biologically and clinically effective component of breathing techniques, additionally influencing mood processing [18]. This aspect seems of utmost importance, considering that breathing management is able to modulate emotional processing in the presence of pain, thereby pointing to the mutual relationship between pain and mood processing [19]. However, in analogy to the pain- and stress-related effects of DSB, recent studies do not provide any insight that would clarify the distinct impact of respiration and relaxation on emotional processing [20].

For this reason, our study aims at elucidating the relevance of relaxation as an independent factor which may mediate the effect of DSB on pain perception, sympathetic activity, and mood. In detail, we used two different DSB techniques characterized by identical respiration rates and depths and distinct from the presence of relaxation. To the best of our knowledge, this is the first human study estimating the impact of relaxation during a DSB technique on pain perception.

## Methods

### Subjects

Sixteen young and healthy undergraduate students (13 female, 3 male) at the local university (Regensburg, Germany) participated in the study. Exclusion criteria were the following: any psychiatric disorders or neurological syndromes, any cardiac or respiratory diseases, a history of migraines or other (chronic) pain syndromes, or the use of pain medication or psychotropic drugs. All participants underwent a neurological examination and were interviewed by a psychiatrist (first author), who additionally administered the SCID-1 screening instrument (Structured Clinical Interview for DSM-IV Axis I Disorders, Clinician Version [SCID-I<sub>CV</sub>]). Moreover, the participants completed the Beck Depression Inventory (BDI) and the "Trait anxiety" part of the State and Trait Anxiety Inventory (STAI-X2). Informed consent was obtained from all volunteers and the study was approved by the local ethics committee.

### SCID-I<sub>CV</sub>

The SCID-I<sub>CV</sub> is a diagnostic exam used to determine DSM-IV Axis I disorders including mood disorders, anxiety disorder, psychotic disorders, and substance-use disorders (original publication [21]; German version [22]; psychometric properties [23,24]).

### BDI

The level of depression was assessed using the "Beck Depression Inventory—BDI," covering emotional, behavioral, and somatic symptoms (original publication [25]; German version [26]; psychometric properties [27]). The BDI is a 21-question inventory, which is worldwide among the most used self-rating scales to assess the intensity of depression on the basis of the main symptoms discriminating between depressives and nondepressives [28]. Higher total BDI scores indicate more severe depressive symptoms, BDI scores  $\geq 18$  indicate a depressive disorder.

### STAI-X2

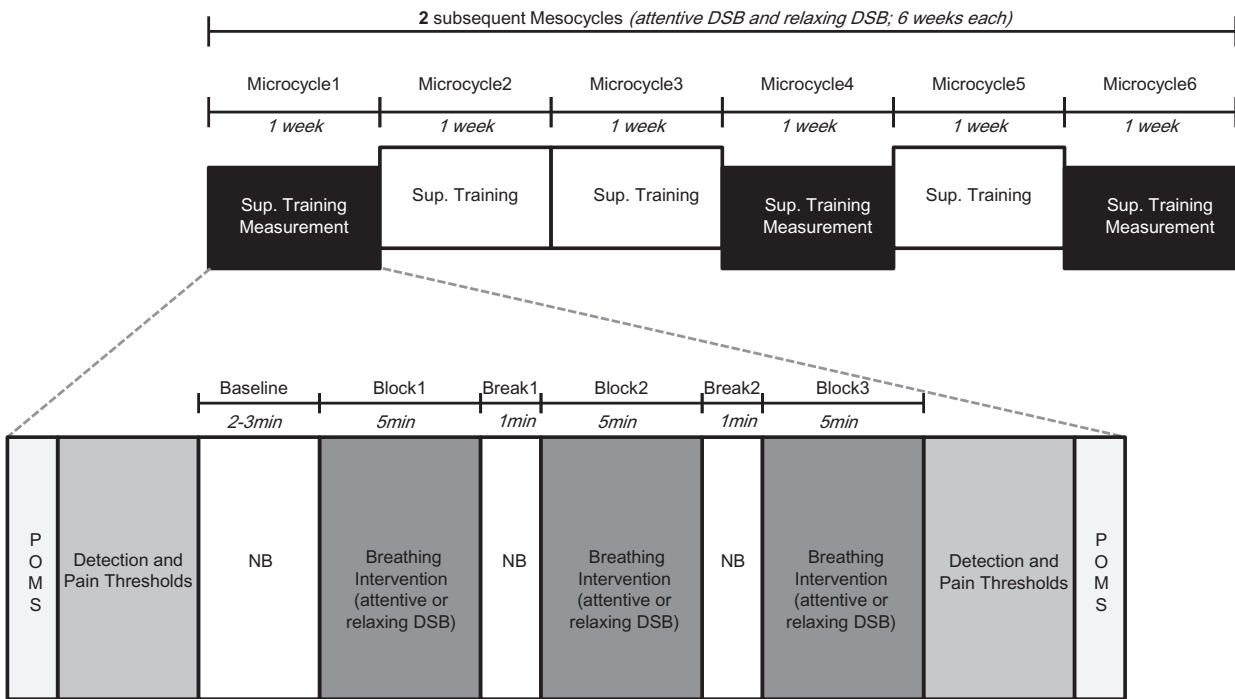
We further assessed anxiety with the "State and Trait Anxiety Inventory—STAI-," a psychological 20-question inventory based on a 4-point Likert scale (original publication [29]; German version [30]; psychometric properties [31]). Scores range from 20 to 80 with higher scores correlating with greater trait or state anxiety. There are no cutoffs, as normative values for trait or state anxiety depends on genus and age [29]. We only used the "Trait anxiety" part (STAI-X2) for our study.

### Study Design and General Information

The study (macrocycle) consisted of two succeeding breathing interventions, each lasting 6 weeks (mesocycles). Each of the two mesocycles consisted of 6 weeks (microcycles) (Figure 1). All measurements were taken from the same experimenter, who supervised the breathing trainings. A second experimenter, who was blinded for the type of intervention as well as for the microcycle, assessed all further analyses.

### Breathing Interventions

Both interventions were separated by a "wash-out" period of 6 months to avoid any carryover effects. All subjects were instructed not to practice at home and were furthermore not allowed to participate in any breathing trainings or meditation programs during the washout period. After inclusion, all subjects received written handouts explaining the course of the study and an instruction manual for DSB, according to the recommendations from breathing literature [32]. Furthermore, they received two experimental sessions of DSB guided by a biofeedback and breathing expert scheduled several days apart from the beginning of each of both interventions. The two different breathing interventions were:



**Figure 1** Course of the study. Sup. Training = training under supervision; min = minute; POMS = profile of mood states; DSB = deep and slow breathing; NB = natural breathing.

1. **Attentive DSB (aDSB):** The subjects were asked to breathe according to a respiratory feedback task [33], assuming an “externally paced” respiration with the help of a given ideal breathing curve representing respiration frequency and depth. The ideal breathing curve and the individual breathing curve were presented together on a monitor. The subjects had to try to fit their own respiration curve to the ideal curve, which required constant attention and concentration on the breathing task.
2. **Relaxing DSB (rDSB):** The subjects were told to direct their awareness on the experience of breathing. They had to look on a spot on a wall with their eyes kept open. They were “internally paced” by verbal instructions of the experimenter in order to provide similar respiration rates and depths compared with the aDSB intervention. The subjects did not get a visual control of their performance, as their breathing activities were not fed back on a monitor. These aspects provided a type of breathing that required very little cognitive processing and which has been reported to induce a more meditative state [7,34–36].

In both interventions, the subjects were instructed to keep a constant, slow, and deep diaphragmal breathing rhythm with a respiration rate of 7 cpm (cycles per minute), which is approximately half of the normal rate, that had been recommended in previous studies investigating the effects of DSB on arousal [37]. Furthermore, a respiration depth of 2 cm amplitude/cycle was required. Both interventions

were supervised and guided by a trained biofeedback expert. The subjects were instructed not to hold their breath, but to breathe slowly and deeply throughout the breathing cycle. In both interventions, expiratory/inspiratory time ratio of each breathing cycle was 60/30%, followed by a brief pause (10%), similar to the recommendation for DSB in literature [16,38]. To control for interaction effects between the experimenter and the participant and in order to get similar breathing depths and rates, the experimenter provided similar breathing instructions and supported the participants by giving the same number of directly addressed verbal suggestions in both groups. Structured sentences were based upon voice dialogue recommendations used in deep relaxing breathing therapy regimens [39]. Total duration of the breathing training in each microcycle was 20 minutes, consisting of one baseline period of 2–3 minutes, followed by three breathing blocks of 5 minutes (interrupted each by short breaks of 1 minute). The baseline period served as an adaptation phase to get accustomed to the laboratory situation and to allow the experimenter to calibrate the equipment. Values from baseline and breathing breaks were not used for further analyses.

**Measurement of Breathing Parameters**

Breathing techniques used in biofeedback and voluntary breathing training paradigms are often designed to control for thoracic or abdominal respiration movements [40]. In studies of voluntarily controlling of breathing activity, the

abdominal control of respiration—with and without visual control—accurately reproduced specified breathing frequencies and depths [41]. Therefore, we used an abdominal respiratory module fixed around the subject's upper abdomen using a strain gauge belt. To ensure the same and correct position, the device was mounted 5 cm above the umbilicus, directly on the skin. The module was a two-channel device (resolution 0.2 mm, measurement range 20 cm) producing a digitalized signal of the analogue respiration movements (amplitude in mm/cycle, frequency in cpm). The respiration rates and depths from all three blocks of one microcycle and then from the first, fourth, and sixth microcycles were averaged.

### *Measurement of Detection and Pain Thresholds*

Thermal detection thresholds and pain thresholds for cold and hot stimuli [42] were measured using a TSA 2001-II thermal sensory testing device (Medoc, Ramat Yishai, Israel) according to the quantitative sensory testing (QST) protocol developed by the German Research Network on Neuropathic Pain [43]. All QST measurements were obtained from the right-hand dorsum with a contact area of the thermode of  $3 \times 3$  cm ( $9 \text{ cm}^2$ ). A strap was affixed to maintain constant pressure between the hand and the thermode. Cold detection threshold (CDT) and warm detection threshold (WDT) were measured first, followed by cold pain threshold (CPT) and heat pain threshold (HPT). The baseline temperature was  $32^\circ\text{C}$  and all thermal stimuli were applied as ramps with a change of  $1^\circ\text{C}/\text{second}$  from baseline. Cutoff temperatures were 0 and  $50^\circ\text{C}$ . The respective thresholds were recorded and stimuli were terminated when the subject pressed a button to signal the detection of the respective sensation. The mean threshold temperature of three consecutive measurements before and after the first, fourth, and sixth microcycles was calculated, respectively. During the experiment, the subjects were not able to watch the computer screen. WDTs and CDTs along with CPTs and HPTs were z-transformed on the basis of the following calculation, ensuring that all parameters were scaled in units of the standard normal distributions ( $0 = \text{mean}$ ,  $1 = \text{standard deviation [SD]}$ ):  $z\text{-score} = (\text{X}_{\text{single value}} - \text{Mean}_{\text{group}}) / \text{SD}_{\text{group}}$  (group = 15; across all data points). We adjusted the algebraic sign of z-score values for WDT and HPT ( $*-1$ ) and subsequently pooled CDT together with WDT (= thermal detection), as well as CPT together with HPT (= thermal pain). The z-transformation had been carried out in order to be able to compare mean change of thresholds and to generate one value for detection and one value for pain perception, respectively. This transformation was done according to the recommendations of a recent QST reference article [44]. As a consequence, the transformed and pooled data reflected the participant's sensitivity for this parameter. Changes of z-scores above "0" indicate a gain of function (more sensitive), while changes of z-scores below "0" indicate a loss of function (less sensitive) [45]. In addition, the initial thresholds before the aDSB and rDSB were compared in order to determine if carryover effects were present, according to Wallenstein and colleagues [46]. Although

the breathing training was performed six times in each mesocycle under supervision of the trainer (once per week), the thermal detection and pain thresholds only from the first, fourth, and sixth microcycles were measured, each before and after the breathing intervention.

### *Measurement of Sympathetic Activity*

The skin conductance level (SCL) represents the electrical conductance of the skin, which varies with its moisture level. Any changes in eccrine sweating are related to changes of the SCLs [47]. Human sweat glands are controlled by the sympathetic nervous system [48], so skin conductance is used as an indication of psychological or physiological arousal [49] and has recently been shown to covary with the perception of pain stimuli [50,51]. The SCL was recorded using a constant-voltage device (Biofeedback Expert 2000, Schuhfried, Mödling, Austria; distributed by Schwa-Medico, Ehringshausen, Germany), according to Venables and colleagues [47]. SCL responses were recorded continuously throughout the microcycle (range:  $0\text{--}50 \mu\text{S}$ ; digital resolution:  $0.024 \mu\text{S}$ ). Before attaching the Ag/AgCl electrode to the nondominant hand (on the palmar surface of the middle phalanx of the ring finger), the skin was cleaned with a small disposable alcohol pad [52]. Time markers, separating breathing blocks and breaks, were synchronized with the recording of the physiological data on a common time line. The mean changes of the SCLs during the breathing maneuvers were calculated as the proportion of the SCL values of the first minute and the last minute of one breathing block. Mean changes of SCL were then averaged from all three blocks of one microcycle. Raw data (in  $\mu\text{S}$ ) were used to study the change of SCL in terms of percentage. The respiration depths and rates and the SCLs during the first, fourth, and sixth microcycles were recorded.

### *Measurement of Mood States*

The subjects were asked to complete the "Profile of Mood States" (POMS) before and after the first, fourth, and sixth microcycles. The POMS is a well-established, factor-analytically derived self-report measure of psychological distress characterized by high levels of reliability and validity (original publication [53]; German version [54]; psychometric properties [55,56]), which was used in several investigations studying anxiety, depression, or pain [57–60]. The POMS consists of 65 adjectives rated on a 0–4 scale, providing six different mood states and one total mood score: tension–anxiety (TA), depression–dejection (DD), anger–hostility (AH), fatigue (F), vigor (V), confusion–bewilderment (CB), and total mood disturbance (TMD). The POMS was assessed prior to and after the breathing training of the first, fourth, and sixth microcycles.

### *Laboratory Environment*

The experimental room was sound attenuated and provided with a diffuse light during the entire session. Music was omitted, because its exposure was found to influence



physiological response to stress [61,62]. Room temperature was kept stable at 20°C [63]. As many substances can affect the sympathetic activity measured by SCL, subjects were asked to refrain from drinking alcohol for at least 48 hours, from drinking more than two cups of coffee on the day of the measurement, and from smoking for at least 2 hours before the recording [64,65]. The subjects were encouraged to sit comfortably in a chair and rest their hands on their laps.

## Statistics

We used three-factorial analyses of variance for repeated measures (general linear model) to assess the effect of the breathing intervention on z-transformed detection and pain thresholds. Within-subject factors were “intervention” (aDSB vs rDSB), “course” (microcycle 1 vs microcycle 4 vs microcycle 6; = time across the microcycles), and “session” (before vs after a 20-minute breathing training; = time across one breathing session). Comparisons of initial pain thresholds were assessed with paired Student’s *t*-tests. Likewise, comparison of respiration parameters was assessed with paired Student’s *t*-tests. Correlations of mean SCL changes and thermal pain threshold changes were tested by using Pearson correlation analyses. Nonparametric Wilcoxon tests for comparison of the mood states were conducted. Effect sizes were calculated using Cohen’s *d* to examine the size of the *post hoc* differences [66] allowing for correlated design (due to the repeated measurements) [67]. Results were regarded as significant with  $P < 0.05$ .

The statistical analyses were performed using SPSS for Windows 17.0 (SPSS Inc., Chicago, IL, USA).

## Results

### Subjects

One male subject did not finish the second breathing intervention. His data were not used for further analyses (per protocol). The mean age of the final sample of 15 subjects was  $25.1 \pm 2.1$  years (range 23–30). The mean

score of the final sample for BDI was  $4.27 (\pm 3.24)$ , which is significantly below the cutoff of 18 points indicating a depressive disorder [25]. The mean score of the final sample for anxiety (trait) was  $38.70 (\pm 8.80)$ , well within the 95% confidence interval for male and female adolescents (age 15–29;  $34.49 \pm 5.5$  female adolescents,  $35.65 \pm 5.7$  male adolescents) [30]. All remaining subjects (13 female adolescents, 2 male adolescents) accomplished both mesocycles of the study. None of the subjects reported any undesirable side effects.

### Data Distribution

After the averaging process, mean respiration depths and rates, SCL and detection and pain thresholds in each of the three microcycles were normally distributed (Shapiro–Wilks Tests for small sample sizes; qq-Plots). The POMS marginally failed normal distribution. Further analyses of the mood states were done with nonparametric tests (s.statistics).

### Respiration

Mean values of respiration rates and depths were similar during both breathing interventions, with a significant return to baseline during the breaks (Table 1).

### Detection and Pain Thresholds

No significant differences of the initial detection thresholds (CDT:  $t = 0.36$ , ns [0.73], WDT:  $t = 1.02$ , ns [0.32]) and pain thresholds (CPT:  $t = 0.15$ , ns [0.88], HPT:  $t = -0.93$ , ns [0.37]) between both intervention could be found. Detection thresholds (CDT, WDT) and pain thresholds (CPT, HPT) before and after breathing interventions for the first, fourth, and sixth microcycles are shown in Table 2. For statistical analyses, the detection and pain thresholds were converted into a standard normal distribution (z-transformation, as pointed out in the Methods). CPTs/HPTs and CDTs/WDTs, respectively, were then pooled in order to build one compound variable for detection and one compound variable for pain perception. Analyses of variance for repeated measures for the z-transformed

**Table 1** Respiration parameters

		aDSB M $\pm$ SD	rDSB M $\pm$ SD	T	P
Respiration depths (cm)	Baseline	$0.95 \pm 0.50$	$1.01 \pm 0.37$	−0.45	ns (0.66)
	Breathing blocks	$2.25 \pm 0.70$	$2.02 \pm 0.77$	1.53	ns (0.15)
	Breaks	$0.98 \pm 0.43$	$0.95 \pm 0.40$	0.52	ns (0.61)
Respiration rates (min <sup>−1</sup> )	Baseline	$15.05 \pm 2.04$	$14.16 \pm 2.54$	1.29	ns (0.22)
	Breathing blocks	$7.04 \pm 0.52$	$7.65 \pm 1.26$	−1.10	ns (0.29)
	Breaks	$15.77 \pm 2.59$	$14.45 \pm 2.57$	1.85	ns (0.09)

Comparison of the mean ( $\pm$ SD) respiration depths and rates for the baseline period, all breathing blocks, and breaks of the first, fourth, and sixth microcycles in the aDSB and rDSB intervention.

aDSB = attentive deep and slow breathing; rDSB = relaxing deep and slow breathing; M = mean; SD = standard deviation; T = paired test statistic; P = Significance; ns = nonsignificant.

**Table 2** Detection and pain thresholds

(In °C)		CDT		WDT		CPT		HPT	
		Pre M (±SD)	Post M (±SD)	Pre M (±SD)	Post M (±SD)	Pre M (±SD)	Post M (±SD)	Pre M (±SD)	Post M (±SD)
aDSB	M1	31.03 (±0.44)	30.96 (±0.39)	33.51 (±0.48)	33.45 (±0.52)	24.85 (±3.88)	25.16 (±3.89)	38.16 (±2.97)	37.86 (±2.87)
	M4	30.74 (±0.60)	30.74 (±0.58)	33.22 (±0.73)	33.39 (±0.95)	23.27 (±5.11)	23.98 (±4.98)	39.71 (±3.41)	39.67 (±3.35)
	M6	30.40 (±0.91)	30.18 (±0.95)	33.64 (±0.53)	33.79 (±0.54)	21.44 (±5.67)	21.79 (±5.59)	39.59 (±4.13)	40.19 (±3.22)
rDSB	M1	30.97 (±0.49)	30.43 (±0.69)	33.35 (±0.50)	33.69 (±0.60)	24.67 (±2.99)	24.24 (±3.26)	39.01 (±3.71)	39.76 (±4.04)
	M4	30.70 (±0.71)	30.08 (±0.90)	33.41 (±0.30)	33.56 (±0.53)	23.40 (±4.62)	21.98 (±4.77)	38.96 (±3.79)	40.23 (±3.39)
	M6	30.69 (±0.90)	30.01 (±0.87)	33.55 (±0.41)	33.76 (±0.54)	22.71 (±3.89)	20.90 (±4.21)	40.54 (±4.12)	41.36 (±3.72)

Detection and pain thresholds of the first, fourth, and sixth microcycles before (pre) and after (post) the breathing maneuvers in the aDSB and rDSB intervention (in °C).

aDSB = attentive deep and slow breathing; rDSB = relaxing deep and slow breathing; CDT = cold detection threshold; WDT = warm detection threshold; CPT = cold pain threshold; HPT = heat pain threshold; SD = standard deviation; M = mean; SD = standard deviation; M1 = microcycle 1; M4 = microcycle 4, M6 = microcycle 6.

thermal thresholds showed significant effects for the factor "session" and the interaction of "intervention\* session" for both detection and pain thresholds. The factor "course" and its interactions did not explain a significant portion of variance in this model (Table 3). *Post hoc* analyses allocated the overall increase of pain ( $-0.27$ ,  $P < 0.001$ , Cohen's  $d = 1.01$ ) as well as detection ( $0.73$ ,  $P < 0.001$ ; Cohen's  $d = 0.88$ ) thresholds under the condition of the rDSB, whereas no change of the overall pain ( $0.04$ ,  $P = \text{ns}$  [0.62]; Cohen's  $d = -0.09$ ) and detection ( $-0.12$ ,  $P = \text{ns}$  [0.20]; Cohen's  $d = 0.23$ ) thresholds occurred in the aDSB (Figure 2).

## SCL

The SCL decreased significantly during the rDSB intervention in the first, fourth, and sixth microcycles. In contrast, there was no significant change of SCL in the aDSB intervention in any of the microcycles, rather tending toward an increase of sympathetic arousal. The mean overall change of SCL ( $\Delta\%$ ) revealed a highly significant decrease by 18% in the rDSB intervention ( $T = 3.88$ ,  $P = 0.002$ ; Cohen's  $d = 1.35$ ) and a mean overall nonsignificant increase of 1% in the attentive breathing intervention ( $T = 0.85$ ,  $P = \text{ns}$  [0.41]; Cohen's  $d = -0.23$ ) (Figure 2).

## Correlation Analyses

The overall changes of the z-transformed pain thresholds and the overall changes of SCL were inversely correlated with regard to the rDSB ( $r = -0.40$ ;  $P < 0.05$ ) but not to the aDSB ( $r = -0.30$ ;  $P = \text{ns}$  [0.11]). The overall changes of z-transformed detection thresholds and the overall changes of SCL were not significantly correlated with regard to the rDSB ( $r = -0.14$ ;  $P = \text{ns}$  [0.48]) or to the aDSB ( $r = -0.18$ ;  $P = \text{ns}$  [0.35]).

## Profile of Mood States

Feelings of tension, depression, and anger were significantly reduced after attentive and relaxed breathing exercises, but without any significant differences between the types of breathing intervention. Feelings of vigor, fatigue, and confusion did not change significantly, neither after the aDSB, nor after the rDSB. Total mood disturbances decreased significantly after both interventions, but again without a significant difference between the types of breathing intervention (Table 4).

## Discussion

Despite their frequent clinical use, the specific symptom-related effects of DSB techniques have been barely elucidated so far. We focused on the impact of two distinct DSB techniques on mood, sympathetic arousal, and especially pain perception in 15 healthy subjects. More precisely, both breathing interventions were characterized by similar breathing instructions, verbal suggestions, as well as similar breathing depths and rates. However, in one of these interventions, the subjects performed an

**Table 3** ANOVA for repeated measurements for detection and pain thresholds

Main Factors and Interactions	df <sub>hypothesis</sub>	df <sub>error</sub>	Detection Thresholds		Pain Thresholds	
			F	P	F	P
Intervention	1	29	3.55	ns (0.07)	0.68	ns (0.41)
Course	2	28	0.15	ns (0.98)	0.54	ns (0.59)
Session	1	29	16.08	<b>&lt;0.001</b>	8.72	<b>&lt;0.01</b>
Intervention * course	2	28	0.46	ns (0.63)	0.17	ns (0.84)
Intervention * session	1	29	19.02	<b>&lt;0.001</b>	6.75	<b>0.01</b>
Course * session	2	28	0.04	ns (0.96)	2.35	ns (0.11)
Intervention * course * session	2	28	0.90	ns (0.42)	1.92	ns (0.17)

Analyses of variance for repeated measurements for z-transformed detection and pain thresholds. Main effects and interactions are shown for a three-factorial model with “intervention” (attentive deep and slow breathing vs relaxing deep and slow breathing), “course” (microcycle 1 vs microcycle 4 vs microcycle 6), and “session” (before vs after a breathing training) as within subject factors. ANOVA = analysis of variance; F = ANOVA test statistic; P = significance; df = degrees of freedom of hypothesis and error; ns = nonsignificant. Bold denotes significant results.

aDSB associated with a concentration task requiring persistent attentional focusing, whereas in the other intervention, a DSB mode particularly aiming at pure relaxation without mental effort was chosen.

The most striking finding in the present study was a significant increase of pain thresholds in our subjects only after the rDSB condition in all of the three microcycles, thereby indicating an attenuation of pain perception (becoming less sensitive). In contrast, the aDSB mode did not alter pain and detection thresholds.

In keeping with our findings of increased pain thresholds after the rDSB, recent work underscores the potential utility of a DSB training in reducing pain intensity ratings as compared with a natural or rapid breathing mode [14,18,68]. Intriguingly, due to the study design, the aforementioned investigations could not differentiate between the effect of relaxation and the effect of respiration on pain perception. In detail, a control group was missing, which had to breathe at similar respiration depths and rates, however without the possibility of relaxation. For this reason, our study suggests relaxation as an essential prerequisite of a DSB technique in efficiently modulating pain perception.

A nonspecific psychomotor effect following the DSB intervention may have been associated with relaxation, thus providing a nonspecific increase in detection and pain thresholds, as fatigue and a reduction in alertness both were found to slightly increase mean reaction times [69]. However, in our study, fatigue was equivalent in both groups and did not change significantly during the DSB interventions. In addition, it has been shown recently that mental fatigue did not affect the temporal preparation time in a choice reaction time task [70]. Moreover, such changes, if any, are unlikely to explain a threshold difference of approximately 1°C in our study, as this would afford reduced reaction times of almost 1 second. Interestingly, following two yoga-based relaxation techniques,

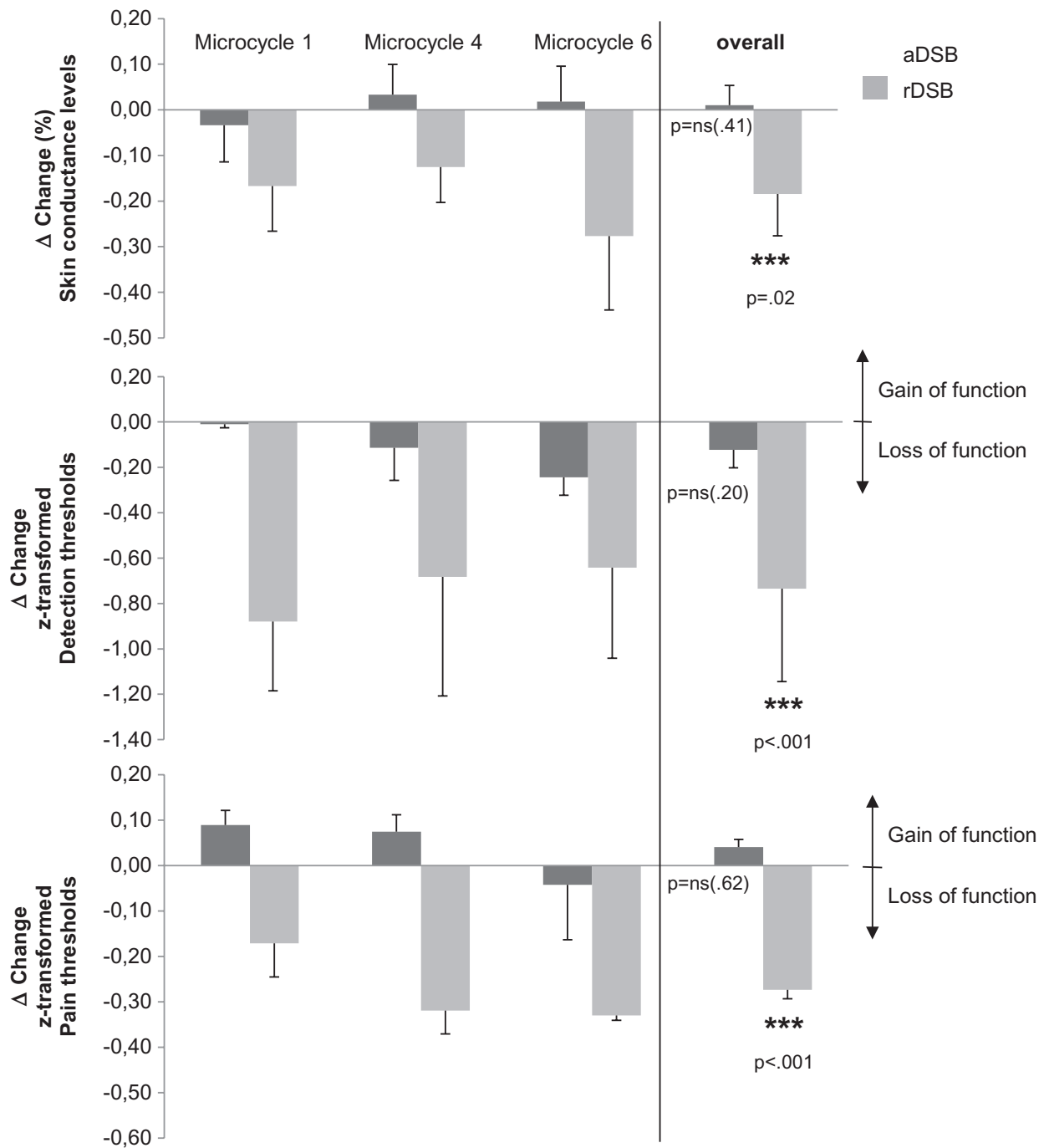
in a psychomotor task motor speed [71] and psychomotor vigilance was even improved, even in novice meditators [72].

One could argue that the subjects may not be distracted equally during both interventions and that a different amount of distraction between both groups may have additionally contributed to the effects of the breathing trainings on detection and pain thresholds. However, we take the view that distraction may not significantly separate both interventions, as some of the subjects may be more distracted by fitting their respiration curve onto an ideal curve during the first intervention; some others may be similarly distracted by dwelling on thoughts during the second intervention.

Interestingly, detection as well as pain thresholds increased following the rDSB, suggesting that this type of breathing intervention may have induced a general loss of somatosensory perception. In support of our observation, a multitude of studies report significant decreases in late somatosensory event-related potentials (SERP) in response to nociceptive stimulation during hypnotic analgesia [73,74]. De Pascalis et al. found increases in sensory and pain thresholds mirrored by a reduction of certain components of the cortical SERP across different hypnosis conditions [75]. In this context, it is tempting to speculate that relaxation may exert its effect on somatosensory perception by inhibiting thalamocortical activity via a frontal cortex feedback loop [73].

Moreover, our study revealed a significant decrease of SCLs in all of the three microcycles indicating a slowing down of sympathetic activity clearly restricted to the rDSB condition. The changes of pain thresholds and SCLs were inversely correlated in the rDSB condition.

As the changes of SCL and detection and pain thresholds were only weakly correlated, we would strongly suggest discussing any potential (causal or not causal)



**Figure 2** Mean changes of skin conductance level and detection and pain thresholds. Mean changes ( $\pm$  standard deviation) and *post hoc* analyses of skin conductance levels and of the z-transformed detection and pain thresholds from the first, fourth, and sixth microcycles and overall for both breathing interventions. aDSB = attentive deep and slow breathing; rDSB = relaxing deep and slow breathing; \*\*\* $P < 0.001$ ; ns = nonsignificant.



**Table 4** Profile of mood states

	aDSB				rDSB				Comparison			
	Pre		Post		Pre		Post		aDSB vs rDSB		Z	
	M (±SD)		M (±SD)		M (±SD)		M (±SD)					P
Tension	6.62 (±3.66)		2.40 (±2.50)	-3.41	6.53 (±2.82)		2.22 (±1.60)	-3.41	<0.001		-0.21	ns (0.83)
Depression	5.42 (±5.86)		1.82 (±2.09)	-3.13	6.13 (±6.12)		2.93 (±3.13)	-2.94	<0.01		-0.41	ns (0.68)
Anger	3.62 (±3.34)		1.67 (±1.40)	-2.67	4.42 (±1.19)		1.80 (±1.42)	-2.93	<0.01		-0.98	ns (0.33)
Vigor	16.42 (±4.54)		15.56 (±4.79)	-1.29	15.96 (±3.99)		14.91 (±5.25)	-0.63	ns (0.53)		-0.22	ns (0.83)
Fatigue	6.24 (±4.21)		6.40 (±3.85)	+0.01	7.69 (±3.41)		6.49 (±3.07)	-1.32	ns (0.19)		-1.36	ns (0.17)
Confusion	4.71 (±2.98)		4.44 (±2.04)	-0.77	5.04 (±2.59)		4.47 (±2.51)	-1.88	ns (0.06)		-0.66	ns (0.51)
Total mood disturbances	9.87 (±21.44)		0.90 (±10.54)	-1.99	13.98 (±19.91)		3.04 (±12.42)	-2.73	<0.01		-0.59	ns (0.55)

Nonparametric comparisons (Wilcoxon tests) of the profile of mood states and the total mood disturbances before (pre) and after (post) the aDSB and rDSB intervention. Values are means of the first, fourth, and sixth microcycles (overall).

aDSB = attentive deep and slow breathing; rDSB = relaxing deep and slow breathing; M = mean; SD = standard deviation; Z = test statistic; P = significance; ns = nonsignificant.

relationships carefully. However, our results are in agreement with other studies investigating the effects of deep relaxation techniques on the autonomic nerve system. As has already been demonstrated, the basal electrodermal activity was significantly reduced during meditation [76], mindfulness-based stress reduction [77], or an integrative body–mind training [78]. In contrast, the aDSB mode along with a concentration task did not reduce, but rather tended to increase the sympathetic arousal in our sample. As a potential mechanism underlying this phenomenon, the attentional demands during the aDSB may have maintained vegetative arousal (finally resulting in maintenance or even increase of SCLs). This hypothesis is in agreement with a study conducted by Cappel and Holmes, demonstrating that the effort involved in accomplishing a challenging attentive breathing exercise did not reduce, but even heightened subjects' sympathetic arousal during the practice period [16]. In support of this finding, control of respiration combined with an attention tracing condition did not reduce the subjects' stress responses [79]. Moreover, in a clinical population characterized by high trait anxiety scores, rDSB without concentration on a pacing tone resulted in a greater reduction of skin conductance responses than conventional aDSB, providing greater effort on the breathing challenge [80].

Based on these data, it is tempting to conclude that the required concentration component in our aDSB group may have attenuated the sympathetic decrease. Therefore, a DSB pattern does not decrease stress responses inevitably, but may strongly be dependent on the magnitude of relaxation. In general, biological evidence points to a strong interplay between autonomic functioning and pain perception. In this context, painful cold pressor tests have been shown to elicit sympathetic activity [81]. Moreover, either the elevation [82] or the hyperreactivity [83,84] of the basal sympathetic tone was a finding frequently replicated in patients suffering from chronic pain syndromes such as fibromyalgia. Elevated SCL was associated with increased anxiety and muscle pain in these patients [85]. Reduced autonomic responsiveness and pain perception after DSB exercises in patients suffering from fibromyalgia may result from a complex modulation of sympathetic arousal and pain perception [86] as defined by a downregulation in stress activity [87].

With regard to the mood states, we found a significant reduction of tension, anger, and depressive feelings after both breathing interventions, indicating a more general reduction of the stress level. As has been shown, several studies parallel to our findings have demonstrated a reduction of negative feelings due to breathing exercises both in patients with chronic pain and healthy controls [2–4,18,35,88–92]. In contrast to our findings that only rDSB is able to selectively modify autonomic response and pain perception, mood processing was affected in a similar manner irrespective of the breathing maneuver. As a matter of fact, self-reports of mood or stress levels do not necessarily conform to autonomic responses in stress reduction tasks [77]. Moreover, mood in itself was not sufficient to explain the changes of pain and nociceptive

processing in patients with chronic back pain [93] or major depression [94], indicating that affective and sensory pain processing may follow different courses. Interestingly, DSB without a relaxation component was shown to be ineffective in reducing pain levels, although most of the subjects felt it was useful and increased the patient's feeling of rapport [95]. Therefore, different factors apart from relaxation may drive mood improvement in breathing techniques. One possible explanation may be based on psychological reasons, grounded in the subject's expectation, that a breathing intervention, commonly known as an effective stress reduction strategy, is able to attenuate the feelings of tension and anger. Alternatively, considering the close structural connection between respiratory regions and neurons within the amygdala complex [96,97], breathing may more directly modulate mood via biological mechanisms. Irrespective of the mode of action, our data lend further support to the notion that breathing interventions are effective in influencing affective processing.

Both interventions were executed successively and not counterbalanced. We are aware of the fact that this may be a limiting factor for the interpretation of our results. However, neither during the first nor during the second intervention we found an effect of breathing trainings on detection and pain thresholds, SCL, or mood states over the course of the study (= time across the microcycles). Therefore, we assume that all the more after the end of one mesocycle no relevant long-term effects had an impact on the following mesocycle a half year later. Moreover, although the experimenter provided similar respiration rates and depths during both interventions in our subjects, the attentive vs the relaxing breathing technique was quite different in the way of performance. Hence, we do not think that our subjects were essentially capable to use their experience from the aDSB for the rDSB. Anyway, hypothesizing subtle training effects, we think that a period of a half year between both interventions is long enough to "wash-out" these small carryover effects. Finally, we ascertained that there was no breathing training the weeks prior to the second intervention, as the participants were instructed not to practice at home (which was not possible due to the absence of adequate sophisticated technical equipment) and it was not allowed to participate in breathing trainings or meditation programs.

Some of the issues of our present design were chosen, because they are geared toward patients with chronic pain. For example, we used a breathing training of 20 minutes (separated into single 5-minute blocks) over the course of several weeks in our study, because this duration refers to a conventional breathing session in the scope of a therapeutical application [16,38]. We think that our result may provide an encouraging rationale for the investigation of the effect on DSB techniques in patients with pain syndromes with a similar breathing regimen. The effect sizes of detection (1.01) and pain (0.88) threshold changes due to the relaxed DSB were high suggesting a profound clinical relevance of our find-

ings. However, we are aware that a potential decrease in experimental pain perception due to DSB interventions in pain patients does not inevitably mean a significant alleviation of their clinical pain. Further studies should be provided focusing on the effects of DSB techniques on patients with different pain syndromes and including different pain modalities.

## Conclusions

Taken together, our results suggest that the way of breathing decisively influences autonomic and pain processing. Based on an experimental study design, we could extend most recent work identifying DSB together with relaxation as the essential feature in the modulation of sympathetic arousal and pain perception. Our finding of a similar decrease of sympathetic activity together with an attenuation of pain perception in all three microcycles may suggest that a rDSB intervention is easy to learn and may facilitate an inhibitory influence on pain processing. In contrast, changes in affect processing seem to depend on different biological factors as both breathing modes as used in our study lead to similar effects in mood improvement. Consequently, our findings point to a more individualized use of DSB guided by clinical core features especially with regard to pain-related diseases. Disentangling the symptom specific relevance of distinct DSB components may pave the way to a further increase in its use and optimize the therapeutic value of breathing techniques representing a broadly used approach in a variety of diseases such as chronic pain, which are characterized by obvious limitations in drug treatment.

## Acknowledgments

The authors thank Ms. Mariya Kozhuharova for her assistance carrying out the study.

## Conflicts of Interest/Grants or Supports

None of the authors declares a financial or other conflict of interest. No grants or any other forms of support were given for this study.

## References

- 1 Gilbert C. Clinical applications of breathing regulation. Beyond anxiety management. *Behav Modif* 2003;27: 692–709.
- 2 Brown RP, Gerbarg PL. Sudarshan Kriya Yogic breathing in the treatment of stress, anxiety, and depression. Part II—Clinical applications and guidelines. *J Altern Complement Med* 2005;11:711–7.
- 3 Kim SD, Kim HS. Effects of a relaxation breathing exercise on anxiety, depression, and leukocyte in hemopoietic stem cell transplantation patients. *Cancer Nurs* 2005;28:79–83.
- 4 Han JN, Stegen K, De Valck C, Clement J, Van de Woestijne KP. Influence of breathing therapy on com-

- plaints, anxiety and breathing pattern in patients with hyperventilation syndrome and anxiety disorders. *J Psychosom Res* 1996;41:481–93.
- 5 Jerath R, Edry JW, Barnes VA, Jerath V. Physiology of long pranayamic breathing: Neural respiratory elements may provide a mechanism that explains how slow deep breathing shifts the autonomic nervous system. *Med Hypotheses* 2006;67:566–71.
- 6 Mourya M, Mahajan AS, Singh NP, Jain AK. Effect of slow- and fast-breathing exercises on autonomic functions in patients with essential hypertension. *J Altern Complement Med* 2009;15:711–7.
- 7 Pal GK, Velkumary S, Madanmohan M. Effect of short-term practice of breathing exercises on autonomic functions in normal human volunteers. *Indian J Med Res* 2004;120:115–21.
- 8 Raghuraj P, Telles S. Effect of yoga-based and forced uninostril breathing on the autonomic nervous system. *Percept Mot Skills* 2003;96:79–80.
- 9 Sydoruk LP, Tryniak MH. Effect of the special breathing exercises on the autonomic regulation of the functional state of respiration and muscular systems. *Lik Sprava* 2005;3:44–7.
- 10 Nardi AE, Freire RC, Zin WA. Panic disorder and control of breathing. *Respir Physiol Neurobiol* 2009;167:133–43.
- 11 Sovik R. The science of breathing—The yogic view. *Prog Brain Res* 2000;122:491–505.
- 12 Li TY, Yeh ML. The application of qi-gong therapy to health care. *Hu Li Za Zhi* 2005;52:65–70.
- 13 Li JX, Hong Y, Chan KM. Tai chi: Physiological characteristics and beneficial effects on health. *Br J Sports Med* 2001;35:148–56.
- 14 Chalaye P, Goffaux P, Lafrenaye S, Marchand S. Respiratory effects on experimental heat pain and cardiac activity. *Pain Med* 2009;10:1334–40.
- 15 Cahalin LP, Hernandez ED, Matsuo Y. Diaphragmatic breathing training: Further investigation needed. *Phys Ther* 2005;85:369–70, author reply 70–3.
- 16 Cappel BM, Holmes DS. The utility of prolonged respiratory exhalation for reducing physiological and psychological arousal in non-threatening and threatening situations. *J Psychosom Res* 1984;28:265–73.
- 17 Beary JF, Benson H. A simple psychophysiological technique which elicits the hypometabolic changes of the relaxation response. *Psychosom Med* 1974;36:115–20.
- 18 Zautra AJ, Fasman R, Davis MC, Craig AD. The effects of slow breathing on affective responses to pain stimuli: An experimental study. *Pain* 2010;149:12–8.
- 19 McDonnell L, Bowden ML. Breathing management: A simple stress and pain reduction strategy for use on a pediatric service. *Issues Compr Pediatr Nurs* 1989;12:339–44.
- 20 Arch JJ, Craske MG. Mechanisms of mindfulness: Emotion regulation following a focused breathing induction. *Behav Res Ther* 2006;44:1849–58.
- 21 First M, Spitzer R, Gibbon M, Williams J. Structured Clinical Interview for DSM-IV Axis I Disorders, Clinician Version (SCID-CV). Washington, DC: American Psychiatric Press, Inc.; 1996.
- 22 Wittchen HU, Zaudig M, Fydrich T. SKID—Strukturiertes Klinisches Interview Für DSM-IV. Göttingen: Hogrefe-Verlag; 1997.
- 23 Lobbstaël J, Leurgans M, Arntz A. Inter-rater reliability of the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID I) and Axis II Disorders (SCID II). *Clin Psychol Psychother* 2011;18:75–9.
- 24 Shear MK, Greeno C, Kang J, et al. Diagnosis of nonpsychotic patients in community clinics. *Am J Psychiatry* 2000;157:581–7.
- 25 Beck AT, Ward CH, Mendelson M, Mock J, Erbaugh J. An inventory for measuring depression. *Arch Gen Psychiatry* 1961;4:561–71.
- 26 Hautzinger M. The Beck Depression Inventory in clinical practice. *Nervenarzt* 1991;62:689–96.
- 27 Beck AT, Steer RA, Garbin MG. Psychometric properties of the Beck Depression Inventory: Twenty-five years of evaluation. *Clin Psychol Rev* 1988;8:77–100.
- 28 Richter P, Werner J, Heerlein A, Kraus A, Sauer H. On the validity of the Beck Depression Inventory. A review. *Psychopathology* 1998;31:160–8.
- 29 Spielberger CD, Gorsuch RL, Lushene RE. Manual for the State-Trait Anxiety Inventory. Palo Alto, CA: Consulting Psychologists Press; 1970.
- 30 Laux L, Glanzmann P, Schaffner P, Spielberger C. STAI—State Trait Angst Inventar. Göttingen: Hogrefe-Verlag; 1981.
- 31 Tilton SR. Review of the State-Trait Anxiety Inventory (STAI). *News Notes* 2008;48:1–3.
- 32 Scheibenbogen O, Prieler J. Biofeedback Aided Psychotherapy (BAP). New York: Kluwer Academic/Plenum Publishers; 2002.

**Busch et al.**

- 33 Marx R, Scheibenbogen O. Visualisierung der Respiration als verhaltenstherapeutische Intervention bei Angsterkrankungen. Foto-Medico—Internationaler Arbeitskreis für Medizinische Bilddokumentation 1999;9:7–9.
- 34 Brown RP, Gerbarg PL. Yoga breathing, meditation, and longevity. *Ann N Y Acad Sci* 2009;1172:54–62.
- 35 Paul G, Elam B, Verhulst SJ. A longitudinal study of students' perceptions of using deep breathing meditation to reduce testing stresses. *Teach Learn Med* 2007;19:287–92.
- 36 Wolkove N, Kreisman H, Darragh D, Cohen C, Frank H. Effect of transcendental meditation on breathing and respiratory control. *J Appl Physiol* 1984;56:607–12.
- 37 Harris VA, Katkin ES, Lick JR, Habberfield T. Paced respiration as a technique for the modification of autonomic response to stress. *Psychophysiology* 1976;13:386–91.
- 38 Strauss-Blasche G, Moser M, Voica M, et al. Relative timing of inspiration and expiration affects respiratory sinus arrhythmia. *Clin Exp Pharmacol Physiol* 2000;27:601–6.
- 39 Ehrmann W. Handbuch der Atemtherapie. Ahlerstedt: Param-Verlag; 2004.
- 40 Wang SZ, Li S, Xu XY, et al. Effect of slow abdominal breathing combined with biofeedback on blood pressure and heart rate variability in prehypertension. *J Altern Complement Med* 2010;16:1039–45.
- 41 Minyaev V, Petushkov M. Voluntary control of thoracic and abdominal respiratory movements. *Hum Physiol* 2005;31:44–8.
- 42 Fruhstorfer H, Lindblom U, Schmidt WC. Method for quantitative estimation of thermal thresholds in patients. *J Neurol Neurosurg Psychiatry* 1976;39:1071–5.
- 43 Rolke R, Baron R, Maier C, et al. Quantitative sensory testing in the German Research Network on Neuropathic Pain (DFNS): Standardized protocol and reference values. *Pain* 2006;123:231–43.
- 44 Magerl W, Krumova EK, Baron R, et al. Reference data for quantitative sensory testing (QST): Refined stratification for age and a novel method for statistical comparison of group data. *Pain* 2010;151:598–605.
- 45 Glass GV, Stanley JC. *Statistical Methods in Education and Psychology*. Boston, MA: Allyn & Bacon; 1970.
- 46 Wallenstein S, Fisher AC. The analysis of the two-period repeated measurements crossover design with application to clinical trials. *Biometrics* 1977;33:261–9.
- 47 Venables PH, Martin I. The relation of palmar sweat gland activity to level of skin potential and conductance. *Psychophysiology* 1967;3:302–11.
- 48 Fuhrer MJ. Stimulus site effects on skin conductance responses from the volar surfaces. *Psychophysiology* 1974;11:365–71.
- 49 Germana J. Effects on behavioral responding on skin conductance level. *Psychol Rep* 1969;24:599–605.
- 50 Breimhorst M, Sandrock S, Fechir M, et al. Do intensity ratings and skin conductance responses reliably discriminate between different stimulus intensities in experimentally induced pain? *J Pain* 2011;12:61–70.
- 51 Storm H. Changes in skin conductance as a tool to monitor nociceptive stimulation and pain. *Curr Opin Anaesthesiol* 2008;21:796–804.
- 52 Venables PH, Christie I. Electrodermal activity. In: Martin I, Venables PH, eds. *Techniques in Psychophysiology*. Chichester: Wiley; 1973:3–67.
- 53 McNair PM, Lorr M, Droppleman LF. *POMS Manual: Profile of Mood States*. San Diego, CA: Educational and Industrial Testing Service; 1992.
- 54 McNair D, Lorr M, Droppleman L. Profile of Mood States POMS—Ein Verfahren zur Messung von Stimmungszuständen. In: CIPS, ed. *Internationale Skalen für Psychiatrie*. Weinheim: Beltz Test Gesellschaft; 1981:1–5.
- 55 Lira FT, Fagan TJ. The profile of mood states: Normative data on a delinquent population. *Psychol Rep* 1978;42:640–2.
- 56 Pollock V, Cho DW, Reker D, Volavka J. Profile of Mood States: The factors and their physiological correlates. *J Nerv Ment Dis* 1979;167:612–4.
- 57 Cui J, Matsushima E, Aso K, Masuda A, Makita K. Psychological features and coping styles in patients with chronic pain. *Psychiatry Clin Neurosci* 2009;63:147–52.
- 58 Jungquist CR, O'Brien C, Matteson-Rusby S, et al. The efficacy of cognitive-behavioral therapy for insomnia in patients with chronic pain. *Sleep Med* 2010;11:302–9.
- 59 Malouff JM, Schutte NS, Ramerth W. Evaluation of a short form of the POMS-Depression scale. *J Clin Psychol* 1985;41:389–91.



- 60 Casten RJ, Parmelee PA, Kleban MH, Lawton MP, Katz IR. The relationships among anxiety, depression, and pain in a geriatric institutionalized sample. *Pain* 1995;61:271–6.
- 61 Knight WE, Rickard Ph DN. Relaxing music prevents stress-induced increases in subjective anxiety, systolic blood pressure, and heart rate in healthy males and females. *J Music Ther* 2001;38:254–72.
- 62 Iwanaga M, Moroki Y. Subjective and physiological responses to music stimuli controlled over activity and preference. *J Music Ther* 1999;36:26–38.
- 63 Boucsein W. *Elektrodermal Activity*. Berlin: Springer; 1980.
- 64 Lyvers M, Miyata Y. Effects of cigarette smoking on electrodermal orienting reflexes to stimulus change and stimulus significance. *Psychophysiology* 1993;30:231–6.
- 65 Zahn TP, Rapoport JL. Autonomic nervous system effects of acute doses of caffeine in caffeine users and abstainers. *Int J Psychophysiol* 1987;5:33–41.
- 66 Cohen J. *Statistical Power Analysis for the Behavioral Sciences*. Hillsdale, NJ: Lawrence Earlbaum Associates; 1988.
- 67 Morris SB, DeShon RP. Combining effect size estimates in meta-analysis with repeated measures and independent-groups designs. *Psychol Methods* 2002;7:105–25.
- 68 Grant JA, Rainville P. Pain sensitivity and analgesic effects of mindful states in Zen meditators: A cross-sectional study. *Psychosom Med* 2009;71:106–14.
- 69 Appelle S, Oswald LE. Simple reaction time as a function of alertness and prior mental activity. *Percept Mot Skills* 1974;38:1263–8.
- 70 Langner R, Steinborn MB, Chatterjee A, Sturm W, Willmes K. Mental fatigue and temporal preparation in simple reaction-time performance. *Acta Psychol (Amst)* 2010;133:64–72.
- 71 Subramanya P, Telles S. Performance on psychomotor tasks following two yoga-based relaxation techniques. *Percept Mot Skills* 2009;109:563–76.
- 72 Kaul P, Passafiume J, Sargent CR, O'Hara BF. Meditation acutely improves psychomotor vigilance, and may decrease sleep need. *Behav Brain Funct* 2010;6:1–9.
- 73 Crawford HJ, Knebel T, Kaplan L, et al. Hypnotic analgesia: 1. Somatosensory event-related potential changes to noxious stimuli and 2. Transfer learning to reduce chronic low back pain. *Int J Clin Exp Hypn* 1998;46:92–132.
- 74 Zachariae R, Bjerring P. Laser-induced pain-related brain potentials and sensory pain ratings in high and low hypnotizable subjects during hypnotic suggestions of relaxation, dissociated imagery, focused analgesia, and placebo. *Int J Clin Exp Hypn* 1994;42:56–80.
- 75 De Pascalis V, Magurano MR, Bellusci A. Pain perception, somatosensory event-related potentials and skin conductance responses to painful stimuli in high, mid, and low hypnotizable subjects: Effects of differential pain reduction strategies. *Pain* 1999;83:499–508.
- 76 Travis F. Autonomic and EEG patterns distinguish transcending from other experiences during Transcendental Meditation practice. *Int J Psychophysiol* 2001;42:1–9.
- 77 Lush E, Salmon P, Floyd A, et al. Mindfulness meditation for symptom reduction in fibromyalgia: Psychophysiological correlates. *J Clin Psychol Med Settings* 2009;16:200–7.
- 78 Tang YY, Ma Y, Fan Y, et al. Central and autonomic nervous system interaction is altered by short-term meditation. *Proc Natl Acad Sci U S A* 2009;106:8865–70.
- 79 Holmes DS, McCaul KD, Solomon S. Control of respiration as a means of controlling responses to threat. *J Pers Soc Psychol* 1978;36:198–204.
- 80 Clark ME, Hirschman R. Effects of paced respiration on anxiety reduction in a clinical population. *Biofeedback Self Regul* 1990;15:273–84.
- 81 Victor RG, Leimbach WN Jr, Seals DR, Wallin BG, Mark AL. Effects of the cold pressor test on muscle sympathetic nerve activity in humans. *Hypertension* 1987;9:429–36.
- 82 Martinez-Lavin M, Hermosillo AG. Autonomic nervous system dysfunction may explain the multisystem features of fibromyalgia. *Semin Arthritis Rheum* 2000;29:197–9.
- 83 Qiao ZG, Vaeroy H, Morkrid L. Electrodermal and microcirculatory activity in patients with fibromyalgia during baseline, acoustic stimulation and cold pressor tests. *J Rheumatol* 1991;18:1383–9.
- 84 Cohen H, Neumann L, Shore M, et al. Autonomic dysfunction in patients with fibromyalgia: Application of power spectral analysis of heart rate variability. *Semin Arthritis Rheum* 2000;29:217–27.



- 85 Ozgocmen S, Ozyurt H, Sogut S, Akyol O. Current concepts in the pathophysiology of fibromyalgia: The potential role of oxidative stress and nitric oxide. *Rheumatol Int* 2006;26:585–97.
- 86 Hassett AL, Radvanski DC, Vaschillo EG, et al. A pilot study of the efficacy of heart rate variability (HRV) biofeedback in patients with fibromyalgia. *Appl Psychophysiol Biofeedback* 2007;32:1–10.
- 87 Craig AD. A new view of pain as a homeostatic emotion. *Trends Neurosci* 2003;26:303–7.
- 88 Harvey JR. The effect of yogic breathing exercises on mood. *J Am Soc Psychosom Dent Med* 1983;30:39–48.
- 89 Kim KS, Lee SW, Choe MA, et al. Effects of abdominal breathing training using biofeedback on stress, immune response and quality of life in patients with a mastectomy for breast cancer. *Taehan Kanho Hakhoe Chi* 2005;35:1295–303.
- 90 Tweeddale PM, Rowbottom I, McHardy GJ. Breathing retraining: Effect on anxiety and depression scores in behavioural breathlessness. *J Psychosom Res* 1994;38:11–21.
- 91 Gaines T, Barry LM. The effect of a self-monitored relaxation breathing exercise on male adolescent aggressive behavior. *Adolescence* 2008;43:291–302.
- 92 Kubzansky LD, Wright RJ, Cohen S, et al. Breathing easy: A prospective study of optimism and pulmonary function in the normative aging study. *Ann Behav Med* 2002;24:345–53.
- 93 Dickens C, Jayson M, Sutton C, Creed F. The relationship between pain and depression in a trial using paroxetine in sufferers of chronic low back pain. *Psychosomatics* 2000;41:490–9.
- 94 Kundermann B, Hemmeter-Spernal J, Huber MT, Krieg JC, Lautenbacher S. Effects of total sleep deprivation in major depression: Overnight improvement of mood is accompanied by increased pain sensitivity and augmented pain complaints. *Psychosom Med* 2008;70:92–101.
- 95 Downey LV, Zun LS. The effects of deep breathing training on pain management in the emergency department. *South Med J* 2009;102:688–92.
- 96 Fulwiler CE, Saper CB. Subnuclear organization of the efferent connections of the parabrachial nucleus in the rat. *Brain Res* 1984;319:229–59.
- 97 Yasui Y, Tsumori T, Oka T, Yokota S. Amygdaloid axon terminals are in contact with trigeminal premotor neurons in the parvocellular reticular formation of the rat medulla oblongata. *Brain Res* 2004;1016:129–34.