Journal of Integrative Medicine 20 (2022) 135–144

Contents lists available at ScienceDirect

Journal of Integrative Medicine

journal homepage: www.jcimjournal.com/jim
www.journals.elsevier.com/journal-of-integrative-medicine

Original Research Article

Stress reduction via neuro-emotional technique to achieve the simultaneous resolution of chronic low back pain with multiple inflammatory and biobehavioural indicators: A randomized, double-blinded, placebo-controlled trial

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ARTICLE INFO

Article history:
Received 22 February 2021
Accepted 27 October 2021
Available online 3 December 2021

Keywords:
Neuro-emotional technique
Biopsychosocial model
Emotion
Mind-body therapies
Inflammation
Biomarker

ABSTRACT

Background: Beginning with the concepts of stress developed by Selye, an approach to stress and pain management, known as neuro-emotional technique (NET), has been developed. It is a treatment approach based on the principle that the stressor effects of dormant and/or current unresolved issues or trauma are what determine one's bodily responses. These responses are relatively personalized to the conditioned, experiential and emotional reality of the individual.
Objective: To determine the effect of NET on patients with chronic low back pain (CLBP) over time.
Design, setting, participants, and interventions: In a randomized, double-blinded, placebo-controlled study conducted in a single clinic, NET or control treatments were given twice weekly for 4 weeks in a population of 112 patients.
Main outcome measures: Outcome measures, including Oswestry Disability Index, Quadruple Visual Analogue Scale, the psychoneuroimmunology markers of blood serum levels of C-reactive protein, tumour necrosis factor-α, interleukin-1 (IL-1), IL-6, and IL-10, and 10 dimensions of the Short Form Health Survey scale, were assessed at baseline and at 1, 3 and 6 months following the intervention period.
Results: Compared to placebo, NET produced clinical and statistical significance ($P < 0.001$) via declines of virtually all physiological, pain and disability markers, accompanied by gains in quality-of-life indicators at 0 (baseline), 1, 3 and 6 months. Reductions of the percentages of patients whose 5 biomarkers lay outside the normative range were achieved at 1, 3 and 6 months by NET but not control interventions.
Conclusion: A randomized, controlled trial of CLBP patients indicated that 8 NET interventions, compared to placebo, produced clinically and statistically significant reductions in pain, disability and inflammatory biomarkers, and improvements in quality-of-life measures.
Trial registration: The trial was registered with the Australian and New Zealand Clinical Trials Registry (No. ACTRN12608000002381).

Please cite this article as: Bablis P, Pollard H, Rosner AL. Stress reduction via neuro-emotional technique to achieve the simultaneous resolution of chronic low back pain with multiple inflammatory and biobehavioural indicators: A randomized, double-blinded, placebo-controlled trial. *J Integr Med.* 2022; 20(2): 135–144.

1. Introduction

Supported by the reports of Selye [1], stress has highlighted the mental component in health maintenance, which, in turn, has allowed an abundance of investigations to establish the comorbid-

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https://doi.org/10.1016/j.joim.2021.12.001

ity of mental and physical health problems [2]. Psychiatric and medical pathologies have converged most prominently in pain disorders [3]. Further elaboration of the interrelatedness of the body's systems in reaction to stress appeared with the biopsychosocial model developed by Engel [4], which considers illness to be a stressor that involves the complex interaction of biological, psychological, and social variables [3,5]. Thus, pain is an experience that results from both peripheral stimulation and inhibitory and facilitating messages descending from the brain, i.e., the brain was shown to play a key role in the generation of subjective pain responses [5].

Nowhere has such pain been more widely recognized and experienced than in low back pain (LBP). Experts have estimated that 80% of all individuals will experience back pain at some time in their lives [6]. Accordingly, Waddell et al. [7] concluded that the coexistence of chronic stress and chronic pain indicated that stress reduction needed to be included in the treatment of chronic nonspecific LBP.

It became clear that there needed to be an interdisciplinary approach to treating back pain. Emotions are associated with distorted cognitions or thought patterns that could arise from chronic pain, and that knowledge of the context of pain could restructure the cognition of that pain in terms of perception and propagation. Cognitive behavioural therapy (CBT) considers conditioned reactions to be largely self-activated on the basis of learned expectations, and systematically introduces coping skills to patients to help in times of distress [8].

Building upon these principles and incorporating several health disciplines, neuro-emotional technique (NET) was introduced by Walker [9], who based it on the principle that the stressor effects of dormant and/or unresolved-issues-trauma are what determines the body's responses. These responses are relatively personalized to the conditioned, experiential and emotional reality of the individual. NET is defined as a multimodal stress reduction mindfulness-based intervention and was founded upon 3 essential concepts [9]. (1) Cognitive behavioural psychology: sharing aspects in common with standard CBT for traumatic stress, in terms of exposure therapy, NET seeks the reversal or extinction of classically conditioned, distressing emotional responses to trauma-related stimuli, such as stress. (2) Traditional Chinese medicine: NET engages the energy system, in which a patient touches a pulse point that is determined to be involved in the body's stress reaction to a particular stimulus. The links between emotions and the meridian system have been expressed in acupuncture theory for 2000 years [10]. Current concepts hold that tightness in the fascial system might represent acupoints and meridians in the human body [11]. (3) Muscle testing: this feedback technique is believed to be an indicator of altered physiological function, in which a given muscle is less capable of resisting an outside force when there is some alteration in the function of the nervous system [12]. Specifically, Walker [13] proposed that the muscle test responds to cognitive and emotional stimuli.

Cytokines remain closely linked to emotions, as shown in a recent meta-analysis of 49 studies that found significant stress-related elevations of the inflammatory cytokines interleukin-1β (IL-1β), IL-6, and tumour necrosis factor-α (TNF-α) [14]. In addition, other studies have shown that C-reactive protein (CRP) levels can increase as the result of stress [15]. Elevated levels of IL-6, TNF-α, and CRP have been linked to symptoms of depression [16], while exposure to psychological trauma—known to increase the risk of developing certain chronic conditions—has been positively associated with CRP, IL-1β, IL-6, and TNF-α as shown in a transdiagnostic meta-analysis [17].

Previous limited investigations have provided evidence supporting the efficacy of NET. One trial was conducted with 60 participants with neck tenderness who received a short single NET treatment, while the control group received a control NET protocol [18]. Other case-based reports have demonstrated some scope of application for NET [19–22].

A pilot randomized controlled trial of NET for chronic low back pain (CLBP) reported that NET treatment resulted in significant improvements in pain and disability, compared to a placebo [23]. Our current approach, therefore, sought to assess the effects of an NET regimen on CLBP compared to a placebo control. We evaluated NET's effects on a broad array of measures, including pain, disability, neurotransmitters and an inflammatory protein product, and quality-of-life indices, in a population of CLBP patients. The aim was to assess the relationships among the components of each of these 4 classes of outcome measures in response to NET intervention.

2. Methods

2.1. Patient recruitment and randomization procedure

Individuals aged 18 or over, with CLBP constantly or frequently for at least 3 months, who responded to advertisements in print media, were invited to participate in the trial. They were also required to be positive for ileocecal valve point tenderness [24,25]. Exclusion criteria included the following: (i) currently undergoing manual therapy or psychological intervention for depression or suicidal ideation; (ii) the presence of any red flag conditions, such as bowel, bladder, sexual or other dysfunction; (iii) current involvement with medico-legal proceedings, such as worker's compensation claims; and (iv) pregnancy. The study setting was a private chiropractic practice located in the eastern suburbs of Sydney, Australia.

Using data from our previous inter-examiner reliability trial on an NET diagnostic procedure [26], we projected a 10% attrition rate. Planning for an 80% power, an α of 0.05, and an effect size of six points in the Oswestry Disability Index (ODI) as being clinically significant [27,28], we calculated that recruitment of 60 participants in each of the treatment and control groups was sufficient. A random number generator in the GenStat statistical package used a form of block randomization design [29]. A research assistant allocated each study entrant to a treatment group according to this randomization schedule. A clinic file was generated for each participant, the cover of which included a code number that secretly identified the group allocation status to the treating practitioners, allowing them to deliver the appropriate intervention. The inclusion criteria were assessed by the administrative staff, and the practitioners were unaware of any background details of the study participants. The participants, having had no prior experience with NET treatment, were blinded to the intervention that they received. The clinician who administered the outcome measure surveys and the nurse who took blood samples were each blinded to the participants' group membership.

2.2. Treatment interventions

Two practitioners were certified in the application of the technique by the international NET coordinating body based in the USA. They completed training sessions to ensure that they handled participants in exactly the same manner. The trial was registered with the Australian and New Zealand Clinical Trials Registry (No. ACTRN12608000002381) and awarded ethics clearance by the Macquarie University Human Research Ethics Committee (HE26SEP2003-R02600).

The NET intervention, following the basic protocol outlined by Walker [9], was described previously [30]. The placebo procedure involved all of the NET steps described, substituting semantic test-

ing that was designed to avoid any specific faculty or emotional scenario. Challenge statements were bland and referred to non-controversial subjects such as the weather, colour preferences, or food tastes. Instead of percussive spinal stimulation, therapy involved a physical stimulus, removed from the lower back (such as tapping the shoulder blades), with absence of any visualization of the participant's LBP or reflection on any emotions. In this manner, both the hypothesized diagnostic and therapeutic portions of the regular NET protocol were completely removed in the control treatment [31].

2.3. Allocation and treatment frequency

After patients were allocated to treatment groups, NET and control interventions were delivered twice weekly for a total of 4 weeks.

2.4. Outcome measures

Outcome measures were assessed at 0 (baseline) and at 1, 3 and 6 months after the commencement of interventions.

2.4.1. Primary outcome measures

The reliability [32] and sensitivity [33] of the ODI have been confirmed. The minimum clinically important difference for the ODI has been reported to be 6 points (corresponding to 12 percentage points) [27,28].

2.4.2. Secondary outcome measures

The Quadruple Visual Analog Scale (QVAS) measures current, maximum, minimum, and average pain on a 10-point scale [34]. A VAS change in the order of 2 units (20 mm) or greater is considered to be of clinical significance in a population of LBP sufferers [35,36].

The Short Form Health Survey (SF-36) is a 36-question generic health status measure that facilitates comparison with normative data, becoming one of the most widely used patient-assessed health outcome measures [37]. The SF-36 essentially measures functional health and well-being from the participant's perspective [38]. Ten components were selected.

Four cytokines and the inflammatory protein product (TNF-α, IL-1, IL-6, IL-10 and CRP) were chosen as blood-based markers in this investigation. Blood samples were collected by a registered nurse, with the pathology service Pathlab (now owned by Symbion Health Ltd/Dorevitch Pathology), located in Melbourne, Australia, contracted to analyze all blood samples. Pathlab is accredited by Australia's National Association of Testing Authorities.

2.5. Statistical procedures

The SF-36, QVAS, ODI scores, and blood markers were all treated as continuous measures, analyzed using a linear mixed-effects and repeated measures statistical analysis, with a power model to determine correlation over time, using the GenStat software program [29]. *P* values from *F* tests were reported from the repeated measures analysis rather than from Chi^2-based Wald tests, as the latter *P* values are known to underestimate the probabilities in small sample designs. These *F* tests allow the comparison of any change in LBP of the NET treatment group with that of the control group at the first, third, and sixth months after the commencement of treatment. *P* values < 0.05 were considered statistically significant. The repeated measures model used a restricted maximum likelihood (REML) algorithm to provide effect estimates. Use of a REML-based analysis produces unbiased treatment means in the presence of data missing at random. Such an analysis is considered an intention-to-treat analysis.

3. Results

A total of 138 individuals were excluded from the 311 study recruits. An additional 61 recruits withdrew prior to receiving the initial intervention, leaving 112 participants who were randomized into control (placebo) and treatment groups. Reasons for exclusions and withdrawals are shown in Fig. 1 and are presented in the discussion.

Table 1 summarizes the demographic and baseline characteristics of the trial participants. There were no significant differences in the ages ($P > 0.99$) or overall percentages for control and treatment groups ($P > 0.22$) who had sought health services, reporting activities affected by symptoms.

Table 2 indicates that at the first, third and sixth months following the commencement of the NET or control interventions, all benchmarks total of current (Q1), mean (Q2), best (Q3) and worst (Q4) scores for ODI, QVAS, CRP, TNF-α, IL-1, IL-6, and IL-10 responded to the NET intervention with statistically significant differences ($P < 0.001$ to $P < 0.05$), compared to the placebo group. Clinically significant differences were also obtained for the ODI and QVAS composite markers (the between-group comparisons at 0, 1, 3, and 6 months are presented in Tables 2 and 3).

Table 3 shows that at the first, third and sixth months following the commencement of the NET or control interventions, participants who received the NET intervention had statistically significant improvements ($P < 0.001$) in all four components of the QVAS, and all ten dimensions of the SF-36 scores, compared to the placebo group.

In terms of normative values, Table 4 [39] illustrates how all but the social function component of the SF-36 achieved normative status after 1 month of the NET, but not the control intervention. By 3 and 6 months, the social function component achieved normative status (Tables 2 and 3). With regard to the standard ranges of the 5 blood markers shown in Table 5, a noteworthy reduction in the percentages of values that lay outside of that range was achieved at 1 month by the NET, but not the control treatment (Fig. 2).

Adverse events were extremely rare, involving only 5 of the 112 participants, with mild symptoms that were resolved within 2 weeks of the study intervention, without recurrence. The symptoms reported included a mild headache, back stiffness, neck stiffness, and a mild level of anxiety.

4. Discussion

The NET intervention in this trial produced clinically and statistically significant improvements in the primary outcome (ODI), the secondary outcome (QVAS) and 9 of the 10 SF-36 indices we used. For all 5 blood markers (CRP, TNF-α, IL-1, IL-6, and IL-10), our interpretation is cautious. We report that all markers showed statistical improvement with the NET treatment, but that clinical improvement was lacking—except for TNF-α at the first month. Thus, we looked more carefully at the percentages of patients whose blood marker values lay outside of the normal threshold range with or without NET intervention. Significant reductions of those percentages appeared in patients who underwent NET therapy, as shown in Fig. 2. The same pattern can be seen in the SF-36 components (Figs. 3 and 4).

NET was designed to assist in the natural healing process by discharging unresolved emotional issues and their harmful effects.

Key components of the NET protocol have been scrutinized within several diagnostic reliability studies [24,41–44]. With regards to muscle testing, (i) good interexaminer reliability was demonstrated for the deltoid and psoas muscles [26,45]; (ii) the ileocecal valve test (involving stimulation of a point on the abdo-

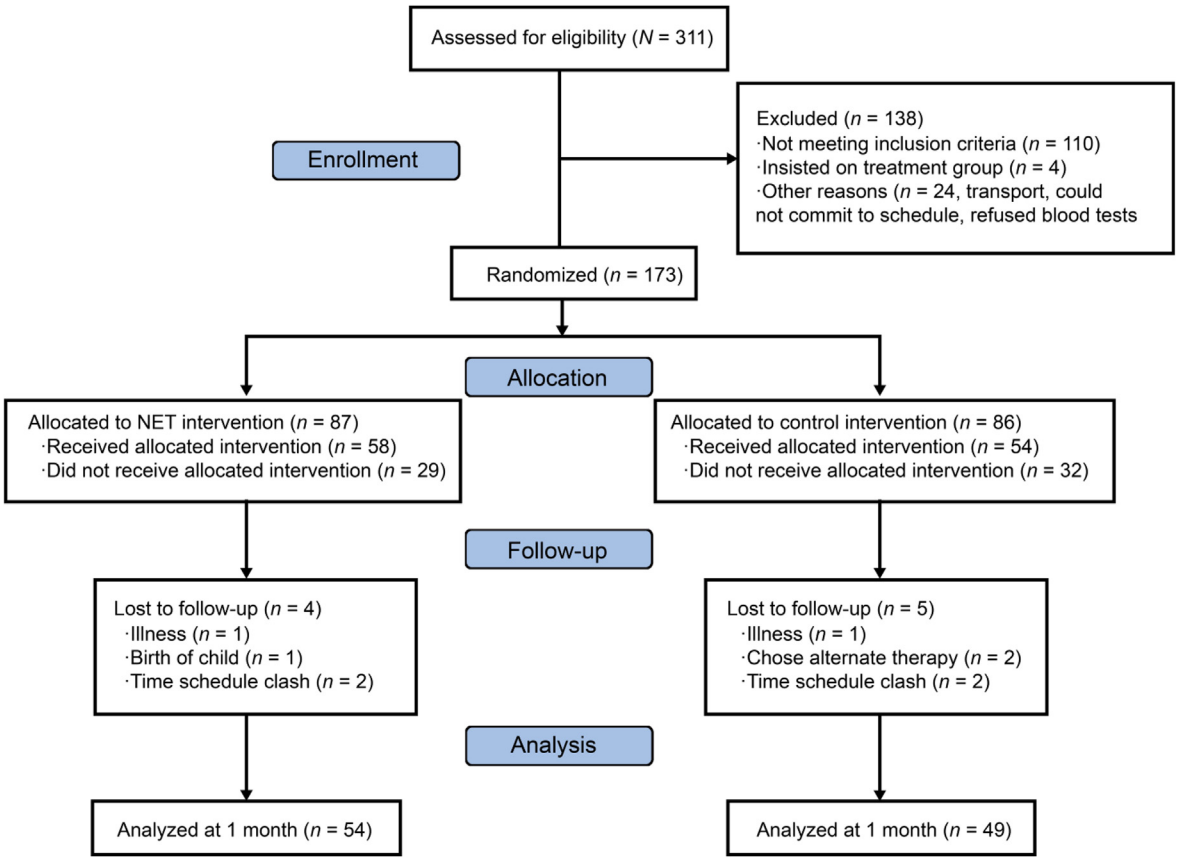

Fig. 1. Flow chart for participant progress through the randomized controlled trial. NET: neuro-emotional technique.

Table 1
Demographic and baseline data on participants.

Variable	Intervention group (*n* = 58)	Control group (*n* = 54)	*P* value
Age (mean ± standard deviation, year)	43.6 ± 11.9	48.0 ± 15.2	
Prior health services utilisation (*n*, %)			
General practitioner	15 (50.0%)	15 (50.0%)	1.000
Medical specialist	15 (62.5%)	9 (37.5%)	0.221
Physiotherapist	25 (52.1%)	23 (47.9%)	0.773
Chiropractic	29 (52.7%)	26 (47.3%)	0.686
Pain variable: duration of pain (*n*, %)			
> 3 and ≤ 6 months	3 (5.2%)	1 (1.8%)	
> 6 and ≤ 12 months	5 (8.6%)	5 (9.3%)	
> 12 and ≤ 36 months	12 (20.7%)	12 (22.2%)	
> 36 and ≤ 120 months	22 (37.9%)	19 (35.2%)	
> 120 months	16 (27.6%)	17 (31.5%)	0.957
Reporting physical stress (*n*, %)	22 (37.9%)	20 (37.0%)	0.758
Reporting mental stress (*n*, %)	30 (51.7%)	25 (46.3%)	0.500
Symptoms affecting work (*n*, %)	25 (44.8%)	22 (40.1%)	0.564
Symptoms affecting sleep (*n*, %)	21 (36.2%)	20 (37.0%)	0.876
Symptoms affecting routine activities (*n*, %)	37 (63.8%)	36 (66.7%)	0.907
Symptoms affecting other activities (*n*, %)	6 (10.3%)	5 (9.3%)	0.763

men) was validated and correlated with the presence of CLBP [24]; and (iii) manual muscle testing was validated as a diagnostic procedure for distinguishing phobic and asymptomatic patients [46].

Another component of NET underlies these interventions and offers further insight into its mechanisms; it details how the recollection of a past stress-related event is sufficient to stimulate the body to recreate the same chemical conditions present when the original event occurred [47]. It suggests that the neurochemical change that occurs during periods of stress has a lasting effect and has the potential to hinder a patient's ability to resolve health issues; it indicates the potential for a widespread reaction to pain that extends beyond the location of the pain [9]. These elements play roles in the concept of psychoneuroimmunology (PNI), a school of thought that maintains that the recalled memories of past stressful events induce similar chemical conditions, even though the stressor may no longer be present [47]. NET posits that this neurochemical change has a lasting or recurrent effect on patients, while PNI addresses the interaction between psychological processes and the nervous and immune systems of the body [48]. Areas of the body responsible for emotional modulation contain significant concentrations of neuropeptide and cytokine receptors and are called nodal points. Recognized as informational molecules, neuropeptides and cytokines carry complex messages to their receptors throughout the body. What brings this entire discussion of chemical messengers and the connection between the brain, spinal cord, and immune systems into the context of LBP is that significant concentrations of the nodal points of these informational molecules have been found in these particular locations [49].

The decrease in 4 of the 5 proinflammatory blood biomarkers (CRP, TNF-α, IL-1, and IL-6) [50–53], in the NET intervention group but not in the placebo group suggests a physiological, systemic effect that appears to be stimulated by this approach. Its practical value may lie in the fact that a wide range of chronic diseases,

Table 2
Changes in primary and secondary outcomes resulting from NET and control interventions.

Variable	Intervention group (n = 58)	Control group (n = 54)	Change from baseline score (95% CI)	P value
ODI score				
Baseline	14.53 ± 5.23	14.69 ± 5.69	−0.16 [−1.89, 2.21]	0.877
1 month	7.54 ± 4.88*	14.39 ± 6.70	6.85 [4.53, 9.16]	≤ 0.001
3 months	7.25 ± 5.47*	14.09 ± 7.65	6.84 [4.29, 9.39]	≤ 0.001
6 months	6.83 ± 4.83*	14.19 ± 7.85	7.36 [4.79, 9.93]	≤ 0.001
QVAS score (sum of the mean)				
Baseline	22.31 ± 4.40	22.02 ± 4.86	−0.29 [−2.05, 1.47]	0.741
1 month	12.39 ± 5.22*	21.14 ± 7.74	8.75 [6.87, 10.62]	≤ 0.001
3 months	12.96 ± 7.08*	22.16 ± 9.02	9.20 [6.94, 11.48]	≤ 0.001
6 months	12.00 ± 7.16*	21.86 ± 10.39	9.86 [7.30, 12.42]	≤ 0.001
CRP value (mg/mL)				
Baseline	4.74 ± 5.10	4.83 ± 5.86	0.10 [−1.22, 1.41]	0.884
1 month	2.35 ± 1.68	4.53 ± 5.82	2.18 [0.84, 3.51]	≤ 0.001
3 months	2.20 ± 1.64	5.25 ± 6.92	2.91 [0.56, 5.26]	0.013
6 months	2.06 ± 1.61	5.49 ± 7.63	2.99 [0.59, 5.39]	0.013
TNF-α value (pg/mL)				
Baseline	1.54 ± 1.73	1.55 ± 1.54	0.00 [−0.43, 0.43]	0.989
1 month	0.90 ± 0.79*	1.77 ± 1.58	0.87 [0.68, 1.06]	≤ 0.001
3 months	0.92 ± 0.80	1.23 ± 1.06	0.31 [0.07, 0.75]	0.015
6 months	0.80 ± 0.46	1.11 ± 0.98	0.31 [−0.04, 0.65]	0.050
IL-1 value (pg/mL)				
Baseline	4.58 ± 3.65	4.57 ± 3.85	−0.01 [−0.90, 0.88]	0.980
1 month	3.51 ± 1.59	4.83 ± 4.14	1.32 [0.84, 1.79]	≤ 0.001
3 months	3.75 ± 1.46	4.64 ± 3.04	0.89 [0.22, 1.89]	0.011
6 months	3.84 ± 0.86	4.60 ± 2.15	0.76 [−0.19, 1.56]	0.116
IL-6 value (pg/mL)				
Baseline	7.40 ± 5.44	7.45 ± 5.41	0.05 [−1.24, 1.34]	0.939
1 month	5.35 ± 3.34	7.59 ± 5.72	2.25 [1.32, 3.18]	≤ 0.001
3 months	5.35 ± 3.11	6.75 ± 4.74	1.44 [−0.13, 3.13]	0.050
6 months	5.27 ± 2.64	7.53 ± 8.61	2.26 [−0.77, 5.29]	0.116
IL-10 value (pg/mL)				
Baseline	6.05 ± 2.94	6.24 ± 3.26	0.19 [−0.48, 0.85]	0.580
1 month	4.83 ± 2.06	6.08 ± 3.03	1.25 [0.56, 1.93]	≤ 0.001
3 months	4.68 ± 1.92	6.42 ± 2.71	1.82 [0.61, 3.03]	0.003
6 months	4.98 ± 1.61	6.30 ± 2.29	1.74 [0.50, 2.99]	0.005
SF-36 physical function score				
Baseline	59.05 ± 20.75	59.72 ± 23.90	0.67 [−7.82, 9.16]	0.875
1 month	82.99 ± 14.65*	60.82 ± 23.60	−22.17 [−30.01, −14.34]	≤ 0.001
3 months	86.94 ± 12.96*	59.83 ± 22.05	−27.11 [−34.69, −19.53]	≤ 0.001
6 months	90.55 ± 13.40*	59.86 ± 20.16	−30.69 [−38.27, −23.11]	≤ 0.001

*Clinically significant change: ODI scores baseline 6 [32,33] and QVAS scores baseline 2.0 [40]. ODI: Oswestry Disability Index; QVAS: Quadruple Visual Analog Scale; NET: neuro-emotional technique; CRP: C-reactive protein; TNF-α: tumor necrosis factor-α; IL: interleukin; SF-36: Short Form Health Survey; CI: confidence interval. Data are presented as mean ± standard error of the mean.

including diabetes [54], osteoarthritis [55], atherosclerosis [56], cardiomyopathy [57], and asthma [58], have an inflammatory component. Indeed, the role of inflammation, particularly the role of cytokines in plaque development, has previously been described in detail [59].

The fact that levels of the anti-inflammatory IL-10 showed a decrease in response to NET, rather than the expected increase, may initially seem counterintuitive. In our study of chronic rather than acute LBP, the anticipated increase in IL-10 may have occurred much earlier in the back-pain episode and was now returning to normal levels, with the passage of time characteristic of a chronic condition. As such, a variety of factors capable of reducing IL-10 production, as part of an exquisite intracellular control mechanism, have been identified and described elsewhere [60].

Nevertheless, the unique combination of accessing the emotions, physical intervention, and traditional Chinese medicine, known as NET, has produced improvements in multiple indicators of systemic inflammation as well as CLBP. This has been measured across a broad spectrum of both subjective and objective outcome measures, and these measures have responded to the NET intervention in a lockstep fashion, lending further support to the notions that mind and body are intimately connected and that emotions can trigger measurable physiological changes [49]. This echoes a substantial body of literature that has found marked increases in the levels of inflammatory cytokines in cases of post-traumatic stress disorder [61–63]. Finally, this study's reduction in inflammatory risk factors, which are associated with common life-threatening conditions, including cardiovascular disease and stroke, provides a blueprint for future epidemiological research into the application of NET protocol to treat and prevent these potentially fatal conditions. The proposed interrelatedness of mindfulness interventions, as depicted by NET, includes the brain, psychology, physiology, and behaviour (Fig. 5) [64].

Robust support for this hypothesis was provided by a team of researchers at Thomas Jefferson University headed by Monti [65], who demonstrated in a randomized, controlled trial that an NET intervention, compared to a waitlist control, reduced the emotional and autonomic reactivity associated with memories of a cancer diagnosis in patients. They further found that there was a correlation between receiving the NET intervention and changes in connectivity among the cerebellum, limbic structures and brain

Table 3
Changes in subcategories of secondary outcomes resulting from NET and control interventions.

Variable	Intervention group (n = 58)	Control group (n = 54)	95% CI	P value
VAS Q1 current level of pain				
Baseline	5.78 ± 1.06	5.54 ± 1.13	−0.24 [−0.65, 0.18]	0.258
1 month	2.38 ± 1.63*	5.20 ± 1.14	2.81 [2.24, 3.39]	≤ 0.001
3 months	2.51 ± 1.52*	5.78 ± 1.04	3.27 [2.56, 3.99]	≤ 0.001
6 months	1.43 ± 1.19*	5.58 ± 1.22	4.15 [3.45, 4.82]	≤ 0.001
VAS Q2 average level of pain				
Baseline	5.63 ± 1.47	5.61 ± 1.63	−0.01 [−0.60, 0.57]	0.964
1 month	2.65 ± 1.26*	5.20 ± 1.25	2.55 [2.06, 3.05]	≤ 0.001
3 months	2.52 ± 1.13*	5.62 ± 1.70	3.10 [2.30, 3.89]	≤ 0.001
6 months	2.86 ± 1.45*	5.66 ± 1.65	2.80 [1.53, 3.99]	≤ 0.001
VAS Q3 pain level at its best				
Baseline	2.75 ± 1.90	2.78 ± 1.33	0.03 [−0.73, 0.67]	0.931
1 month	1.21 ± 1.33	2.65 ± 1.68	1.44 [0.84, 2.04]	≤ 0.001
3 months	1.28 ± 0.76	2.75 ± 1.58	1.47 [0.90, 2.04]	≤ 0.001
6 months	1.23 ± 1.07	2.67 ± 1.62	1.44 [0.70, 2.16]	≤ 0.001
VAS Q4 pain level at its worst				
Baseline	8.15 ± 1.22	8.14 ± 1.53	−0.01 [−0.54, 0.51]	0.963
1 month	6.17 ± 2.24	8.06 ± 1.48	1.89 [1.14, 2.63]	≤ 0.001
3 months	6.60 ± 2.25	8.03 ± 1.60	1.43 [0.36, 2.50]	≤ 0.001
6 months	6.46 ± 2.86	7.96 ± 1.69	1.50 [0.01, 2.98]	≤ 0.001
SF-36 physical mean score				
Baseline	42.01 ± 36.94	43.52 ± 40.97	1.50 [−13.35, 16.36]	0.839
1 month	84.69 ± 29.20*	48.00 ± 40.17	−36.39 [−50.61, −22.78]	≤ 0.001
3 months	86.93 ± 22.82*	44.58 ± 41.71	−42.35 [−59.42, −25.28]	≤ 0.001
6 months	92.50 ± 15.16*	42.41 ± 40.43	−50.09 [−66.30, −33.88]	≤ 0.001
SF-36 bodily pain score				
Baseline	41.90 ± 18.11	39.83 ± 16.18	−2.06 [−8.60, 4.48]	0.528
1 month	68.88 ± 14.05*	43.61 ± 16.22	−25.27 [−31.21, −19.34]	≤ 0.001
3 months	77.75 ± 10.59*	37.71 ± 16.34	−40.04 [−46.46, −33.62]	≤ 0.001
6 months	83.80 ± 11.05*	36.58 ± 15.30	−47.22 [−53.86, −40.59]	≤ 0.001
SF-36 general health score				
Baseline	55.16 ± 16.78	55.87 ± 19.18	0.71 [−5.59, 7.00]	0.822
1 month	79.71 ± 11.62*	54.93 ± 16.50	−24.78 [−30.40, −19.15]	≤ 0.001
3 months	86.39 ± 11.67*	49.52 ± 16.98	−36.87 [−43.33, −30.41]	≤ 0.001
6 months	89.61 ± 9.61*	49.21 ± 14.44	−40.40 [−46.38, −34.42]	≤ 0.001
SF-36 vitality score				
Baseline	48.39 ± 19.38	49.07 ± 18.17	0.68 [−6.44, 7.78]	0.848
1 month	68.59 ± 10.41*	46.37 ± 18.52	−22.22 [−28.23, −16.21]	≤ 0.001
3 months	75.69 ± 8.99*	41.39 ± 16.25	−34.30 [−40.06, −28.54]	≤ 0.001
6 months	81.08 ± 8.39*	38.83 ± 14.96	−42.25 [−47.97, −36.53]	≤ 0.001
SF-36 social functional score				
Baseline	60.61 ± 26.43	62.27 ± 23.48	1.66 [−7.73, 11.04]	0.724
1 month	83.98 ± 16.22	62.77 ± 24.80	−21.21 [−29.57, 12.84]	≤ 0.001
3 months	91.18 ± 10.66*	56.25 ± 26.05	−34.93 [−43.79, −26.07]	≤ 0.001
6 months	96.38 ± 5.47*	53.26 ± 22.07	−43.12 [−51.39, −34.85]	≤ 0.001
SF-36 role emotional score				
Baseline	53.17 ± 41.86	53.09 ± 42.22	−0.09 [−15.94, 15.76]	0.991
1 month	88.41 ± 21.76*	50.79 ± 45.67	−37.61 [−51.96, −23.27]	≤ 0.001
3 months	98.76 ± 7.11*	45.31 ± 45.74	−53.45 [−68.66, −38.24]	≤ 0.001
6 months	100.00 ± 0.00*	45.53 ± 43.98	−54.47 [−69.71, −39.95]	≤ 0.001
SF-36 mental health score				
Baseline	67.24 ± 16.21	68.15 ± 16.15	0.91 [−5.21, 7.02]	0.767
1 month	80.26 ± 9.39*	63.48 ± 18.22	−16.78 [−22.60, −10.96]	≤ 0.001
3 months	87.05 ± 7.97*	59.89 ± 19.02	−27.16 [−33.50, −20.82]	≤ 0.001
6 months	90.02 ± 6.21*	56.92 ± 18.40	−33.10 [−39.52, −26.68]	≤ 0.001
SF-36 physical component				
Baseline	39.35 ± 6.82	39.32 ± 8.54	−0.03 [−2.98, 2.92]	0.982
1 month	50.82 ± 6.32*	41.02 ± 9.13	−9.80 [−12.92, −6.68]	≤ 0.001
3 months	52.29 ± 5.15*	39.83 ± 8.16	−12.46 [−15.51, −9.41]	≤ 0.001
6 months	54.29 ± 4.50*	39.67 ± 6.67	−14.62 [−17.38, −11.86]	≤ 0.001
SF-36 mental component				
Baseline	44.91 ± 11.33	45.38 ± 10.75	0.47 [−3.66, 4.60]	0.819
1 month	53.21 ± 5.82*	43.12 ± 12.87	−10.09 [−14.10, −6.08]	≤ 0.001
3 months	57.27 ± 3.09*	40.58 ± 12.33	−16.69 [−20.57, −12.81]	≤ 0.001
6 months	58.65 ± 2.22*	39.15 ± 11.74	−19.50 [−23.39, −15.61]	≤ 0.001

* Clinically significant change: VAS Q1 current level of pain baseline 2.0 [40], VAS Q2 average level of pain baseline 2.0 [40], VAS Q3 pain level at its best baseline 2.0 [40], and VAS Q4 pain level at its worst baseline 2.0 [40]. NET: neuro-emotional technique; SF-36: Short Form Health Survey; CI: confidence interval. Data are presented as mean ± standard error of the mean.

Table 4
Comparison of SF-36 component outcomes at 1 month following NET *vs.* control interventions: attainment of mean age and sex standardized normative values for an Australian population [39].

Variable	Intervention group (n = 58)	Control group (n = 54)	Mean	Achieved normative status
Physical function	82.99	60.82	83.60	Yes
Role physical	84.69	48.00	79.70	Yes
Bodily pain	68.88	43.61	76.90	Yes
General health	79.71	54.93	71.50	Yes
Vitality	68.59	46.37	63.90	Yes
Social function	83.98	62.77	84.60	Yes
Role emotional	88.41	50.79	83.70	Yes
Mental Health	80.26	63.48	75.70	Yes
Physical component	50.82	41.02	50.0	Yes
Mental component	53.21	43.12	50.0	Yes

NET: neuro-emotional technique; SF-36: Short Form Health Survey.

Table 5
Normal range thresholds of blood serum levels of biomarkers in the control and NET groups [39].

Blood marker	Normal range threshold
CRP	0.0–5.0 mg/mL
TNF-α	0.0–1.0 pg/mL
IL-1	0.0–5.0 pg/mL
IL-6	0.0–8.0 pg/mL
IL-10	0.0–8.0 pg/mL

NET: neuro-emotional technique; CRP: C-reactive protein; TNF-α: tumor necrosis factor-α; IL: interleukin.

stem. Essentially, this study established a neurological signature of the effect of an NET intervention treatment and linked emotion to the regulation of the autonomic nervous system [65].

Finally, the marked and sustained elevation of all 10 quality-of-life markers into the normative range speaks to the overall well-being of the CLBP patients who received the NET intervention in this study. This is in keeping with a systematic review that demonstrated a reduction of cytokines and other inflammatory markers in response to meditation and mindfulness [66].

With regard to the higher than anticipated dropout rate in this study (after allocation but before receiving treatment), a pragmatic decision was made at the start of the project that the control and treatment interventions would commence simultaneously once the required participant numbers (n = 120) had been reached. This took longer than anticipated. Consequently, some participants withdrew from the study because the study did not begin as quickly as they wanted (group A = 21 and group B = 19). Another reported reason for withdrawing from the study was that participants discovered that the time commitment would be too great (group A = 5 and group B = 6). There were additional withdrawals due to the issue of timely access to the clinic (group A = 6 and group B = 4), and difficulties finding open treatment time slots at the clinic hosting the study. As noted in Fig. 1, withdrawals were 32 in group A and 29 in group B, which were equally distributed between the groups. Accordingly, one would anticipate that the results of this distribution in terms of outcomes would be negligible. This is further mitigated by our use of the REML-based statistical analysis, as it is considered an intention-to-treat analysis.

Most significantly, these data do not indicate whether the improvements to pain and disability outcome measures in response to NET treatment correlated with significant changes in one or more blood markers in individual patients. However, it is likely that these parallel improvements were experienced in some patients, with the understanding that individual participants remain unidentified. Secondly, our interpretation of clinically significant changes in the blood markers is relative to the normative ranges. These ranges were drawn from a representative Australian population matching the demographics of the subjects recruited in this investigation. It is true, however, that normative ranges vary considerably from laboratory to laboratory [50,67–69]. Finally,

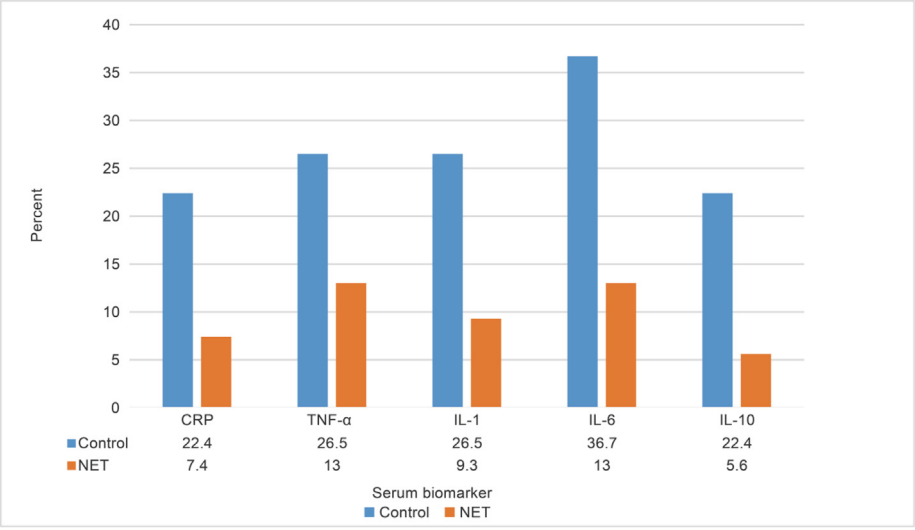

Fig. 2. Blood serum levels of inflammatory markers outside of normal ranges. NET: neuro-emotional technique; CRP: C-reactive protein; TNF-α: tumor necrosis factor-α; IL: interleukin.

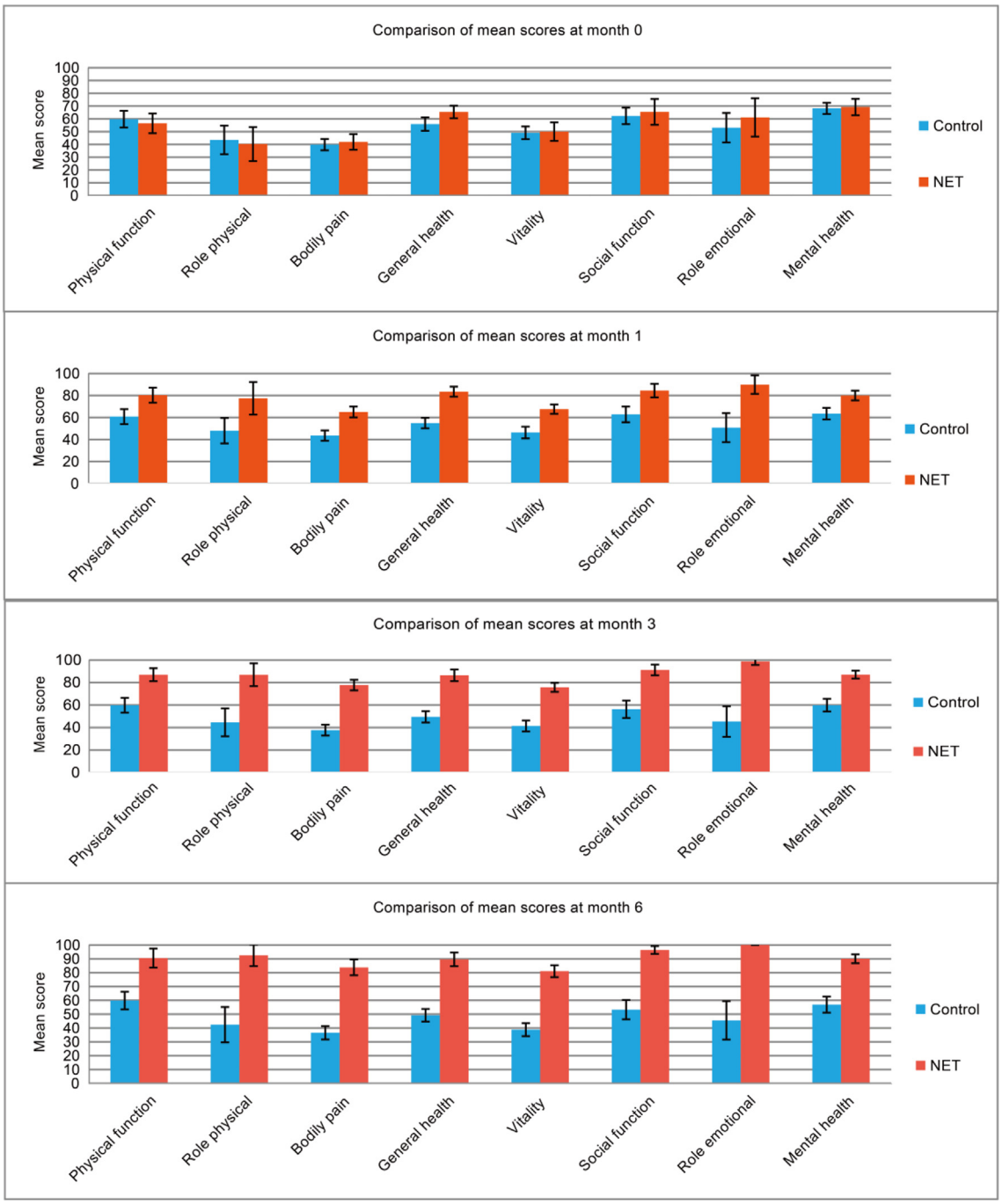

Fig. 3. SF-36 mean scores. The change in SF-36 mean scores across months 1 to 6 is significant ($P < 0.001$) for the 2 groups. Symbols and error bars denote mean ± standard error of the mean of data analyzed. NET: neuro-emotional technique; SF-36: Short Form Health Survey.

confirmation of blinding success was not conducted by querying participants after the conclusion of the trial.

5. Conclusion

A unique combination of muscle testing, psychological principles, and traditional Chinese medicine, known as NET, produced clinically and statistically significant ($P < 0.001$) improvements across a broad spectrum of both subjective and objective health outcome measures in participants with CLBP, compared to a placebo procedure. These included pain (QVAS), disability (ODI), qualify of life and function capacity (10 components of the SF-36 scale) as subjective markers, and possibly of even greater significance, a suite of indicators of inflammation sampled from the blood (CRP, TNF-α, IL-1, IL-6, and IL-10). The improvements were observed at the first month after eight treatments. Overall, the results from this study are encouraging, although future large-scale studies that follow patients for a longer period will help to better understand the utility of the NET intervention for patients with CLBP.

Funding

This work was supported by the Foot Levelers, Inc, Roanoke, VA. The funding sponsor had no involvement in the study design, data collection, analysis and interpretation, writing of the manuscript, or decision to submit for publication.

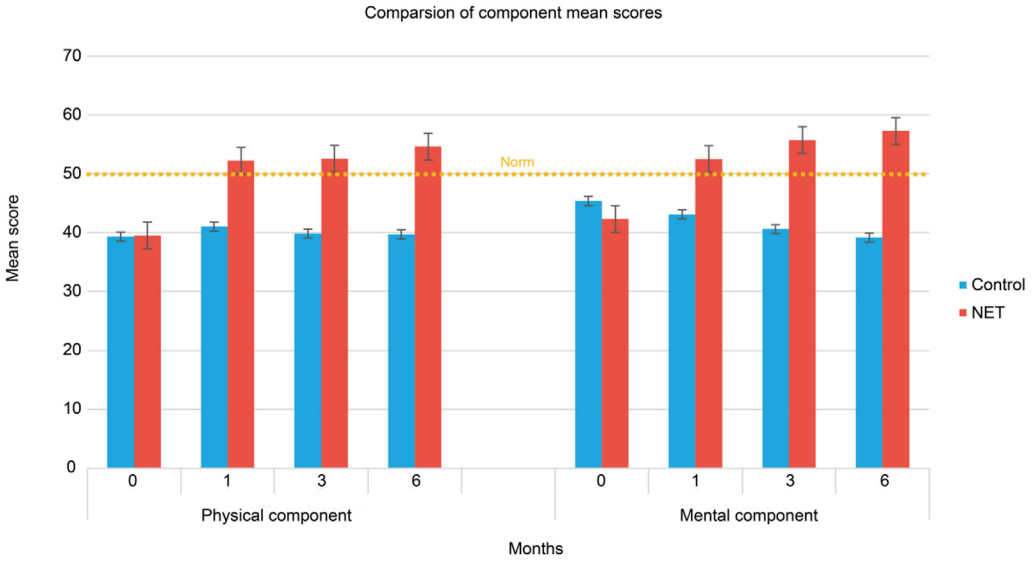

Fig. 4. SF-36 physical and mental component mean scores. The change in these scores across months 1–6 is significant ($P < 0.001$) for the 2 groups. Symbols and error bars denote mean ± standard error of the mean of data analyzed. Norm: normative value [39]. NET: neuro-emotional technique; SF-36: Short Form Health Survey.

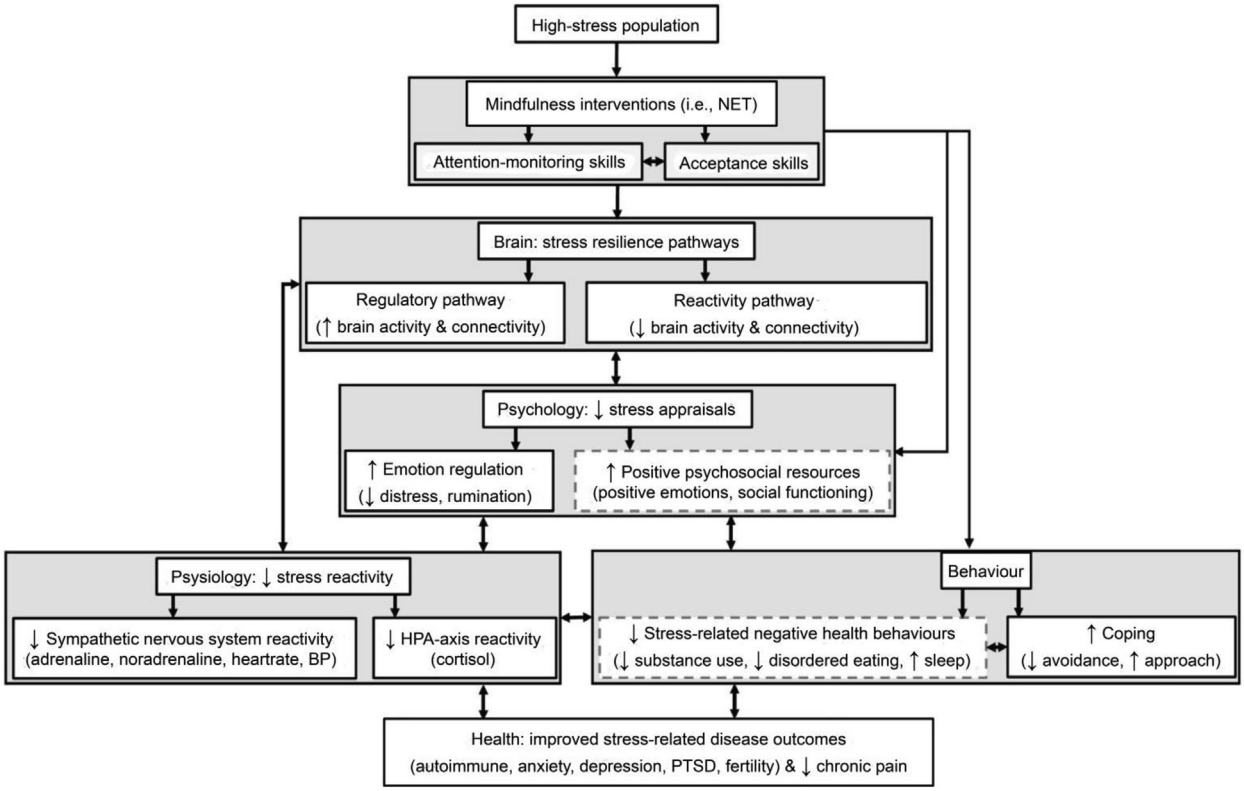

Fig. 5. The interrelatedness of mindfulness interventions. The interrelations of NET, brain, psychology, physiology, and behaviour and their effects upon health-related outcomes are proposed. NET: neuro-emotional technique; BP: blood pressure; HPA: hypothalamic–pituitaryadrenal; PTSD: post-traumatic stress disorder.

Authors' contribution

PB and HP designed the hypotheses and the experiments, performed the experiments and their analysis. PB was responsible for data collection. PB and HP participated in data analysis. All authors participated in data interpretation and manuscript writing and review. All authors were responsible for preparation of the tables and figures. All authors contributed to the scientific discussion of the data and of the manuscript.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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