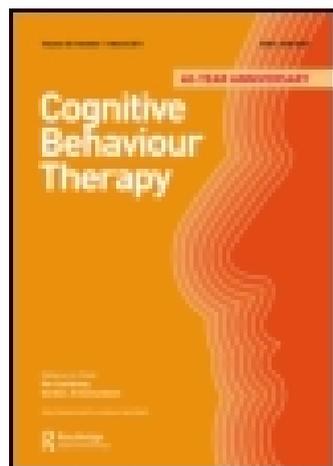


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# A Feasibility study on Combining Internet-Based Cognitive Behaviour Therapy with Physical Exercise as Treatment for Panic Disorder—Treatment Protocol and Preliminary Results

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**Abstract.** Internet-based cognitive behaviour therapy (ICBT) is a recommended, cost-effective and efficacious treatment for panic disorder (PD). However, treatment effects in psychiatric settings indicate that a substantial proportion fail to achieve remission. Physical exercise improves symptoms in patients with PD, and acts through mechanisms that can augment the effect of ICBT. The feasibility of combining these two interventions has not previously been investigated, and this was the aim of this study. The intervention comprised guided ICBT combined with one weekly session of supervised and two weekly sessions of unsupervised physical exercise for a total of 12 weeks. Treatment rationale, procedures and protocols are presented together with preliminary results for four patients with PD who have currently finished treatment. Quantitative and qualitative results are reported on the feasibility of adhering to the treatments, treatment outcome as assessed by clinician rating and estimation of reliable and clinically significant change for outcome measures, and participants' satisfactions with the combined treatment. The preliminary results indicate that the combined treatment is feasible to complete, and that the combination is perceived by the participants as beneficial. *Key words:* Internet-based CBT; panic disorder; physical exercise; feasibility; anxiety.

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## Introduction

Panic disorder (PD) is a severe and prevalent anxiety disorder, with lifetime prevalence rates estimated to range from 3.5% to 4.7% (Bijl, Ravelli, & van Zessen, 1998; Kessler, Berglund, et al., 2005), and 12-month prevalence ranging from 2.2% to 2.7% (Carlbring, Gustafsson, Ekselius, & Andersson, 2002; Kessler, Chiu, Demler, & Walters, 2005). PD is a highly

frequent comorbid disorder to depression, a co-occurrence that is associated with increased suicide risk, greater functional impairment and reduced treatment response (Roy-Byrne et al., 2000). PD is further characterised by altered cardiac regulation, as indexed by reduced heart rate variability (HRV; Cohen et al., 2000; Klein, Cnaani, Harel, Braun, & Ben-Haim, 1995). The increased risk of coronary heart disease (CHD) in patients with PD has been

attributed to this cardiovascular feature (Gomez-Camirero, Blumentals, Russo, Brown, & Castilla-Puentes, 2005; Weissman, Markowitz, Ouellette, Greenwald, & Kahn, 1990). HRV has been related to both the duration and the severity of PD (Hovland et al., 2012), emphasising the importance of available and effective treatment.

Cognitive behaviour therapy (CBT) is the treatment of choice for PD (McManus, Grey, & Shafran, 2008; National Institute for Health and Clinical Excellence, 2011), yielding remission rates of approximately 80% (Andrews et al., 2003; McManus et al., 2008). CBT is unfortunately not sufficiently available to those who need it, mainly due to shortage of therapists with adequate training (Cavanagh, 2014; Emmelkamp et al., 2014). Guided self-help treatment is suggested as a way to increase access to treatment for patients with PD (National Collaborating Centre for Mental Health, 2011). Guided self-help in the form of Internet-based cognitive behaviour therapy (ICBT) is particularly efficacious (Andersson, Cuijpers, Carlbring, Riper, & Hedman, 2014; Haug, Nordgreen, Öst, & Havik, 2012). Treatment response has, however, been reduced in psychiatric settings, with approximately 70% responding to treatment (Bergström et al., 2010), indicating that a substantial proportion of these patients fail to recover. In terms of dropout from ICBT, this seems to be equivalent to what has been found in face-to-face treatment with an average of 31% (Melville, Casey, & Kavanagh, 2010). Mechanisms behind dropout from ICBT are still largely unknown, but therapist contact has been suggested to be a possible mediator for preventing this (Melville et al., 2010).

Augmenting recommended treatments to improve remission rates has become increasingly popular. One way of increasing remission rates from ICBT is to reduce dropout from treatment by way of short telephone calls (Carlbring et al., 2006). Another way is to improve existing treatment. Most studies on treatment augmentation have addressed major depressive disorder, and physical exercise has been investigated as an augmentation strategy in combination with psychotherapy, antidepressive medication or both (Martinsen, Medhus, & Sandvik, 1985; Trivedi et al., 2011; Veale et al., 1992). There are several reasons for also considering augmenting psychother-

apeutic treatment for PD with physical exercise.

First, individual studies have demonstrated large reductions in key symptoms following 10–12 weeks of physical exercise compared with pill placebo (Broocks et al., 1998), though with smaller treatment effects than psychotropic medication or CBT (Broocks et al., 1998; Hovland et al., 2013). Studies have also found that an acute bout of physical exercise greatly reduces the risk of having a panic attack in patients with PD (Esquivel et al., 2008; Ströhle et al., 2009). Physical exercise also reduces anxiety sensitivity (Broman-Fulks & Storey, 2008; Smits et al., 2008), a change that was found to mediate the reductions in general anxiety following from physical exercise (Smits et al., 2008).

Second, physical exercise appears to impact mechanisms that are either different from, or could act in concert with those mechanisms that are manipulated by ICBT. The mechanisms behind the effects of both ICBT and physical exercise are still not fully understood, although we know that CBT for PD aims to reduce fear of bodily symptoms to break the vicious cycle of panic attacks (Clark, 1986). Physical exercise elicits physical symptoms similar to those experienced during panic attacks, and the study by Smits et al. (2008) suggests that exposure to bodily symptoms could be important in explaining the effect of physical exercise on anxiety. Delivered in combination with CBT, supervised exercise can provide guided *in situ* exposure, which has been demonstrated to improve treatment efficacy of CBT (Gloster et al., 2011). Ströhle et al. have demonstrated that acute physical exercise leads to increased plasma concentrations of atrial natriuretic peptide, which was found to be related to the anxiolytic effect of exercise (Andreas Ströhle, Feller, Strasburger, Heinz, & Dimeo, 2006; Ströhle, Kellner, Holsboer, & Wiedemann, 2001). A further potential mechanism is the modulation of brain-derived neurotrophic factor (BDNF), a protein in the family of neurotrophins known to be a key mediator in the extinction of conditioned fear (Peters, Dieppa-Perea, Melendez, & Quirk, 2010). Low serum concentrations of BDNF have been associated with impaired treatment response for CBT in patients with PD (Kobayashi et al., 2005). Physical exercise increases BDNF levels acutely in healthy and

anxious patients, and resting levels of BDNF for both healthy and psychiatric (i.e. depressed) subjects performing regular exercise (Szuhaný, Bugatti, & Otto, 2015).

Third, adding therapist contact through supervised exercise may increase the efficacy of the ICBT, as therapist support can improve outcome compared with self-guided Internet-based treatment (Haug et al., 2012). The effect of adding therapist contact through supervised exercise could thus improve efficacy and reduce dropout rates from ICBT.

Finally, combining recommended treatment for PD with physical exercise has been specifically advocated for patients with PD who suffer from comorbid CHD with reference to the cardioprotective properties of physical exercise for these patients (Sardinha, Araújo, Soares-Filho, & Nardi, 2011). Comorbid PD in patients referred to cardiac outpatient clinics has been estimated to be as high as 60% (American Psychiatric Association [APA], 2000; Chignon, Lepine, & Ades, 1993), and preliminary efforts to develop suitable manuals for this purpose have been recently published (Gomes, Sardinha, Araújo, Nardi, & Deslandes, 2014).

A challenge when seeking to improve treatment by adding elements to existing paradigms is reduced cost-effectiveness and increased demand for scarce therapist resources. In this study, we aim to combine ICBT, a cost-effective treatment that demands few therapist resources, with supervised physical exercise once a week, combined with two weekly sessions of unsupervised exercise performed at the participants' convenience. This format allows for the augmentation of CBT through physical exercise, while utilising only limited therapist resources, and aiming to provide a treatment paradigm that is feasible for patients to complete.

The aim of this study is to assess the feasibility of combining ICBT for PD with manualised physical exercise, in accordance with the recommendations for the development of new interventions (Craig et al., 2008). It has previously been demonstrated that the Internet can be used to deliver physical activity in depressed samples (Ström et al., 2013), and that a combination of physical exercise and group CBT can be acceptable for patients with PD (Merom et al., 2008), but this

study is to the best of our knowledge the first to investigate the feasibility of augmenting individual guided self-help (i.e. ICBT) with physical exercise. This paper presents study procedures and treatment protocol together with preliminary findings.

## Methods

### Participants

Referrals for 23 patients were screened for possible eligibility according to the inclusion and exclusion criteria. From these, 14 patients were scheduled for an onsite screening interview with the principal investigator (AH) and the therapist (HJ). The presence of PD was at this stage determined through an unstructured clinical interview based on the criteria for PD in the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV-TR; APA, 2000). For included participants, the presence of PD was later confirmed through structured clinical interview by a second, independent clinical psychologist. Lack of inclusion at this stage, pertained to one of the following reasons: no PD ( $n = 4$ ), could not engage in physical exercise due to scheduling difficulties ( $n = 2$ ) and improved condition ( $n = 1$ ). The remaining seven patients were all included and treatment was initiated. Three of these participants were still in treatment at the present time. A total of four participants have thus far completed the treatment protocol, and all assessments and have been included in the study.

The four participants were all women ranging from 38 to 49 years in age, with a mean age of 41.5 years ( $SD = 5.2$ ). All met diagnostic criteria for PD with agoraphobia, with an average duration of illness of 11.0 years ( $SD = 6.9$ ). One participant also met the diagnostic criteria for comorbid social anxiety disorder. One participant had previously received recommended treatment (i.e. CBT) for her PD. All were employed at the time of inclusion. Average BMI was 22.3 ( $SD = 1.2$ ), and two participants used psychotropic medication (i.e. a selective serotonin reuptake inhibitor) for their condition. Participants' aerobic capacity ranged from a  $VO_{2max}$  of 32.1 (*below average*) to 49.8 (*excellent*) for women according to their age.

## Assessment

*Clinician assessments.* Prior to treatment, participants were routinely scheduled for a structured clinical interview with a clinical psychologist to determine overall clinical status and to confirm diagnosis of PD with or without agoraphobia by the use of the MINI International Neuropsychiatric Interview (MINI; Lecrubier et al., 1997). Following treatment, the same clinical psychologist determined the presence of PD with or without agoraphobia according to the DSM-IV-TR criteria, using the panic module of the Structured Clinical Interview for DSM-IV axis I Disorders (SCID-I; First, Spitzer, Gibbon, & Williams, 1995).

*Primary outcome measures.* Body Sensations Questionnaire (BSQ; Chambless, Caputo, Bright, & Gallagher, 1984) was used to measure fear of bodily sensations related to anxiety. The 17 items are rated on a scale ranging from 1 (*not at all frightened by this sensation*) to 5 (*extremely frightened by this sensation*). Chambless et al. (1984) reported Cronbach's  $\alpha$  in outpatients with agoraphobia to be .87.

Agoraphobia Cognitions Questionnaire (ACQ; Chambless et al., 1984) assesses the frequency of thoughts common in agoraphobia, and is considered to be a measure of fear of fear. The 14 items are rated on a scale ranging from 1 (*thought never occurs when I am nervous*) to 5 (*thought always occurs when I am nervous*). Chambless et al. (1984) reported Cronbach's  $\alpha$  for ACQ in outpatients with agoraphobia to be .80.

The Mobility Inventory of Agoraphobia (MIA; Chambless, Caputo, Jasin, Gracely, & Williams, 1985) comprises 27 items assessing frequency of avoidance for situations relevant to everyday life. The questionnaire consists of two subscales that assess avoidance when alone or when accompanied (henceforth referred to MIA-alone and MIA-accompanied, respectively). Items are rated on a scale ranging from 1 (*never avoid*) to 5 (*always avoid*). Chambless et al. (1985) reported Cronbach's  $\alpha$ s for MIA-alone and MIA-accompanied in outpatients with agoraphobia to be .96 and .97, respectively.

*Panic frequency and panic-related distress* was measured by the Panic Attack Scale, where participants rated panic frequency and

panic-related distress and disability on a five-point scale ranging from 0 (*no panic attacks*) to 4 (*one or more panic attacks per day*) and on a nine-point scale running from 0 (*not at all disturbing*) to 8 (*very disturbing*), respectively. This measure is described by Clark et al. (1994).

*Secondary outcome measures.* Beck Anxiety Inventory (BAI; Beck & Steer, 1993) was used to assess general anxiety. Cronbach's  $\alpha$  for BAI in mixed sample of psychiatric outpatients is reported to be .92.

Beck Depression Inventory II (BDI-II; Beck, Steer, & Brown, 1996) assessed level of depression. Cronbach's  $\alpha$  for BDI-II in psychiatric outpatients is reported to be .92.

*Qualitative interview.* Qualitative data of the participants' experiences were obtained by semi-structured interviews that aimed to facilitate an explorative dialogue of participants' experience of outcome after the intervention. An interview schedule with three general questions invited participants to talk about (1) what made them sign up for the treatment, (2) their experience of participating in the treatment and (3) changes that might have occurred during or after the treatment. More narrow probe questions were used for elaboration on specific themes when necessary.

*Treatment satisfaction.* Participants also rated their satisfaction with the treatment, treatment procedures and the change they had experienced following treatment (for wording, please refer to "Treatment satisfaction" under Results). Items were rated on scales ranging from 6 (*very satisfied/changed very much/only had positive impact/altogether correct treatment/demanded minimal*) to 1 (*not satisfied at all/not changed at all/substantial negative impact/altogether wrong treatment/demanded much too much*).

*Physical fitness test.* Estimates of  $VO_{2max}$  was obtained with the Aastrand and Ryhming's submaximal bicycle ergometer test as an index of physical fitness (Noonan & Dean, 2000; Swain, 2014) during the second and last week of treatment. All outcome measures were completed by paper and pencil.

## Study procedure

The study was approved by the Regional Committee for Medical and Health Research Ethics and by the Norwegian Social Science

Data Services. All participants provided written informed consent prior to inclusion in the study. The study was conducted at a community mental health clinic (DPS) in Norway, and participants were recruited through ordinary procedures for referral to the clinic. To be included, subjects had to be between 18 and 50 years old, and meet the DSM-IV-TR (APA, 2000) criteria for PD with or without agoraphobia. Criteria for exclusion were brain-organic disorders, psychotic disorders, substance-abuse including habitual use of benzodiazepines, medical conditions that precluded participation in physical exercise, more than two sessions per week of habitual physical exercise of moderate or higher intensity, ongoing severe major depressive episode, pregnancy, or difficulties with reading and writing. Once eligibility was established, patients were presented with four treatment options: Manualised CBT for PD delivered in groups, guided ICBT for PD, inclusion to this treatment study, or referral to outpatient individual face-to-face treatment. Participants were informed about the nature and rationale of the different treatments. Participants were specifically informed that their preferences regarding treatment would not have any impact on further help and services.

Following obtained consent, participants were screened for risk factors related to heart disease (e.g. a family history of cardiac disease, hypercholesterolemia, diabetes, hypertension or smoking). Letters were routinely sent to participants' general practitioner (GP) with information regarding the nature of this study, and participants were instructed to schedule an appointment with their GP and return confirmation that their participation was safe and recommendable before initiating treatment. Participants were instructed to stabilise the use of psychotropic medication from four weeks prior to treatment and until final assessment of symptoms was conducted, approximately two weeks following treatment termination. Use of medication was not subsequently monitored.

Participants were then scheduled for a first session that included introduction to the therapist in the study, introduction to the Internet portal for ICBT, introduction to the exercise facility and introduction to an exercise diary. Baseline assessment of outcome measures was also obtained at this

point. Participants then followed the treatment for the designated period of 12 weeks. At the end of treatment, assessment of outcome measures was repeated and clinical rating was obtained. The qualitative interview was conducted in a separate session with a clinical psychologist (JV).

### **Physical exercise manual**

The exercise manual was based on the general recommendations for increasing physical fitness by the American College of Sports Medicine (Garber et al., 2011; Swain, 2014). The exercise was tailored for the current population, with initial sessions progressing carefully to allow participants to adjust to the exercise, in accordance with findings by Stein et al. (1992) and recommendations by Meyer and Brooks (2000). The physical exercise program consisted of one session of supervised exercise and two sessions of unsupervised exercise per week for 12 weeks. The exercise was supervised by an occupational therapist (HJ) who was experienced in coaching and supervising psychiatric outpatients.

The supervised exercise sessions lasted for a total of 45–60 minutes, and were conducted at fitness centre adjacent to the clinic. Each session consisted of a six-minute warm-up exercise followed by five minutes of stretching, before 20–45 minutes of endurance training between 65% and 85% of the maximal heart rate ( $HR_{max}$ ) was conducted.  $HR_{max}$  was stipulated using the formula:  $211 - (0.64 \times \text{age})$  (Nes, Janszky, Wisløff, Støylen, & Karlsen, 2013), and HR was registered during the exercise using the Polar RS800CXtm Heart Rate Monitor (Polar Electro Oy, Kempele, Finland). The endurance training consisted of brisk walking or running for 2.5 km on a treadmill (Technogym Run 900, Cesena, Italy), with pace to fit the HR-zone above. From the third week onwards, the 2.5 km was followed by interval training, starting with three intervals and peaking at 10 intervals from the 10th week of exercise. The intervals consisted of a 20-second high-intensity period where HR increased to approximately 80% of  $HR_{max}$ , followed by a period of low intensity consisting of walking at 3.5 km/h. The time between intervals was adjusted according to HR, so that the next interval started when the individual's HR had decrease below 65% of  $HR_{max}$ . On average, the period of low intensity lasted

from 45 to 90 seconds depending on the individual's fitness.

During the unsupervised sessions, participants were instructed to become at least slightly out of breath and sweaty, and were further encouraged to use the supervised exercise as a standard for the intensity during the unsupervised session. These sessions were all recorded in an exercise diary that was reviewed during the weekly supervised sessions.

The sum of the three sessions of exercise was calculated to equal approximately 560 metabolic equivalents of task (MET)  $\times$  minutes per week at the start of the program, and increased to approximately 1000 MET minutes per week at the end of the program. This is well within the recommended dose of exercise presented by the ACSM based on MET  $\times$  minutes per week deemed necessary to increase physical fitness (Garber et al., 2011).

### ICBT manual

The guided ICBT treatment for PD is developed by Carlbring et al. and has been evaluated in several randomised controlled trials (Bergström et al., 2010; Carlbring, Westling, Ljungstrand, Ekselius, & Andersson, 2001). The program has been translated and adapted to Norwegian in a separate project (Nordgreen et al., 2010) and is based on the cognitive model for PD (Clark, 1986). The program consists of 9 modules comprising 5–20 pages of text and pictures. Patients access a new module when the former is completed. The treatment starts with psycho-education, development of an idiosyncratic model and setting goals for treatment. The next step is to identify and challenge automatic thoughts through a number of exercises. Exposure and behavioural experiments are emphasised. Towards the end of treatment, patients make their own plan for relapse prevention. At the end of each module, patients are asked to explain what they learned in the module, how tasks and exercises were implemented in practice, and how they worked with treatment goals. The same therapist that provided the physical exercise therapy supervised the ICBT. Reports on exercises and weekly monitoring of symptoms were electronically sent to the therapist. The therapist provided feedback to the patient in the ICBT-program at least once a week. The therapist was a certified e-therapist by the Norwegian Association for Cognitive Therapy.

### Statistics

Means and standard deviations were computed with the SPSS version 20 to determine the values necessary to compute the reliable change index (RCI; Jacobson & Truax, 1991) and cut-off for clinically significant change. RCI was calculated according to the recommendations by Jacobson and Truax (1991) and Zahra and Hedge (2010). Standard deviations from the baseline values for the current sample were used, together with the Cronbach's  $\alpha$ s reported earlier for the different measures to determine RCI. Method C as described by Jacobson and Truax (1991) was used to determine clinical cut-offs for the different inventories. This cut-off denotes the transition point from healthy to clinical state and vice versa. Again, baseline values for means and standard deviations from the current sample were used in combination with reference values on means and standard deviations for the measure in question.

Analysis of data from the qualitative interview was performed by systematic text condensation (Malterud, 2001).

## Results

### Feasibility data

Table 1 displays the participants' adherence to the physical exercise. All participants were able to complete at least 80% of the supervised exercise sessions, and three of the four completed more than 80% of the unsupervised sessions. Two participants (1 and 2) completed 100% of the supervised sessions, and the same two participants completed more than the scheduled unsupervised sessions. The weekly

Table 1. *Participants' adherence to the physical exercise*

Participant	Completed supervised sessions <sup>a</sup>	Completed unsupervised sessions <sup>b</sup>	Total weekly average
1	12 (100%)	31 (129%)	3.6
2	11 (91%)	23 (96%)	2.8
3	10 (83%)	19 (79%)	2.4
4	12 (100%)	29 (121%)	3.4

<sup>a</sup>Proportion of the 12 scheduled weekly supervised sessions in parentheses.

<sup>b</sup>Proportion of the 24 weekly scheduled unsupervised sessions in parentheses.

average of these participants was higher than three sessions per week. Participant 3 was prohibited from taking part in exercise for two weeks during treatment, and therefore missed two supervised sessions, and five unsupervised sessions. The exercise diary also indicated that five of the recorded unsupervised sessions for this participant were completed below the expected intensity. The same was true for seven of the unsupervised sessions of participant 4.

For the ICBT, two participants (1 and 2) completed all modules, while participant 3 and 4 completed seven and eight modules, respectively.

### **Treatment outcomes**

*Clinician rating.* According to this rating, participants 1, 3 and 4 no longer met the criteria for PD or agoraphobia, while participant 2 retained the diagnosis of PD with agoraphobia.

*Primary outcome measures.* Table 2 displays the participants' results on the primary outcome measures. These show that the participants experienced reliable and clinically significant change on several measures, but these changes were not all consistent across measures. Participants 1 and 2 reported reliable change on several measures, and also scored below clinical cut-off on most measures. However, the scores also indicated that the initial values were below the estimated clinical cut-off on some of these measures. Participant 3 reported initial values above clinical cut-off, and had reliable and clinically significant change on all measures, except for the MIA-alone. Ratings of panic-related distress were greatly reduced for all but participant 3, whose initial score was low. Participant 4 reported little change in the primary outcome measures.

*Secondary outcome measures.* Two participants reported reliable and clinically significant change on the BAI. All participants reported change that was reliable and had scores that were below the clinical cut-off at post-treatment with none or minimal symptoms as recorded on the BDI-II.

### **Participant experiences and treatment satisfaction**

*Qualitative interview.* Data from the qualitative interviews indicated that all participants

saw the combination of physical exercise and ICBT as beneficial. None believed that either of the interventions in isolation would have been equally effective.

The main challenge described by all participants was making time for both behavioural experiments and physical workouts. Participant 1 and 3 said they would have liked the duration of treatment to be somewhat longer, to facilitate processing of the information in the self-help modules. Despite the commitment required, all participants thought that the current combination of treatment modalities was feasible and stated that they would recommend it to others with similar problems.

The participants saw computerised self-help as providing them with credible explanations of their problems, as well as tools to help them cope with anxiety.

With regard to physical exercise, one participant thought this had helped her become less afraid of bodily signals. The remaining three did not describe such a direct effect on their fearful interpretations of symptoms, but considered the physical exercise valuable in reducing tension, improving mood, and increasing energy.

All participants emphasised the role of the therapist, reporting that his supportive attitude, encouragement for them to push themselves, and help in explaining the rationale for treatment helped their motivation and understanding. Three participants expressed a wish that the treatment had included more face-to-face interaction.

Participants 1 and 3 reported feeling fully recovered after treatment. Participants 2 and 4 described some residual symptoms they needed to work on. Three out of four saw their mood as considerably improved. All participants reported that they had gained a new understanding of symptoms that had previously frightened them, with three out of four describing a new-found ability to let distress arise and pass without feeling that they needed to remove it or leave the situation.

*Treatment satisfaction.* Participants (case number in parentheses) reported being either *very satisfied* (1, 3), *satisfied* (2) or *mainly satisfied* (4) with the treatment they had received. They reported having either *changed very much* (1, 3), *Much* (2) or *Somewhat* (4). Three participants reported that treatment

Table 2. Participants scores and change on outcome measures

Participant	Pre-score	Post-score	Change	RCI
<b>BSQ</b>				
1	2.47	1.24 <sup>b</sup>	1.23	3.78*
2	2.29 <sup>a</sup>	1.41 <sup>b</sup>	0.88	2.70*
3	3.71	1.18 <sup>b</sup>	2.53	7.76*
4	3.06	2.65	0.41	1.26
<i>Clinical cut-off</i>		2.31	<i>Required change</i>	± 0.64
<b>ACQ</b>				
1	1.71 <sup>a</sup>	1.00 <sup>b</sup>	0.71	3.07*
2	2.00	1.50 <sup>b</sup>	0.50	2.16*
3	2.57	1.50 <sup>b</sup>	1.07	4.62*
4	1.93	2.14	-0.21	-0.91
<i>Clinical cut-off</i>		1.90	<i>Required change</i>	± 0.45
<b>MIA-alone</b>				
1	1.11 <sup>a</sup>	1.00 <sup>b</sup>	0.11	0.27
2	4.41	1.52 <sup>b</sup>	2.89	7.19*
3	2.15	1.65 <sup>b</sup>	0.50	1.24
4	1.85	2.04	-0.19	-0.47
<i>Clinical cut-off</i>		1.65	<i>Required change</i>	± 0.79
<b>MIA-accompanied</b>				
1	1.19 <sup>a</sup>	1.00 <sup>b</sup>	0.19	2.25*
2	1.27 <sup>a</sup>	1.15 <sup>b</sup>	0.12	1.42
3	1.92	1.64 <sup>b</sup>	0.28	3.32*
4	1.24	1.04 <sup>b</sup>	0.20	2.37*
<i>Clinical cut-off</i>		1.92	<i>Required change</i>	± 0.17
<b>Panic frequency</b>				
1	0	0	0	
2	1	0	1	
3	3	0	3	
4	1	1	0	
<b>Panic severity (distress)</b>				
1	6	0	6	
2	8	4	4	
3	8	2	6	
4	4	3	1	
<b>BAI</b>				
1	6.00 <sup>a</sup>	3.00	3.00	0.68
2	17.00	11.00 <sup>b</sup>	6.00	1.35
3	33.00	0.00 <sup>b</sup>	33.00	7.44*
4	19.00	10.00 <sup>b</sup>	9.00	2.03*
<i>Clinical cut-off</i>		13.52	<i>Required change</i>	± 8.69
<b>BDI-II</b>				
1	11.00 <sup>a</sup>	0.00 <sup>b</sup>	11.00	4.24*
2	8.00 <sup>a</sup>	2.00 <sup>b</sup>	6.00	2.31*
3	21.00	0.00 <sup>b</sup>	21.00	8.10*
4	20.00	4.00 <sup>b</sup>	16.00	6.17*
<i>Clinical cut-off</i>		13.63	<i>Required change</i>	± 5.08

Note. Clinical cut-off refers to the estimated transition point from healthy to clinical state and vice versa. Required change denotes the level of change estimated to constitute reliable change according to the RCI.

RCI, reliable change index.

<sup>a</sup>Pre-score below clinical cut-off.

<sup>b</sup>Post-score below clinical cut-off.

\*RCI values greater than 1.96 in either direction denote statistical significant change at the  $p < .05$ .

had *only had a positive impact* (1, 2, 3) on them, while one reported treatment having *not had negative impact of any concern* (4). Two reported that the treatment they had received was the *altogether correct treatment* (1, 3) for their problems, while two reported it was *mainly the correct treatment* (2, 4). Participants reported either that the treatment *demanding a great deal* (2, 3, 4), or that it *demanding a good deal* (1).

### ***Manipulation check for physical exercise***

The fitness test indicated that three of the participants had moved to a higher fitness category. Participant 1 had changed fitness category from *above average* to *good/excellent*, with score increasing from 40.3 to 48.1. Participant 3 had changed from *below average* to *above average/good*, with score increasing from 32.1 to 41.8. Participant 4 stayed in *excellent*, with score increasing from 49.8 to 55.5. The group mean for these participants had increased to 48.5 (SD = 6.9). Participant 2 scored 39.3 at the pre-test, but suffered from a cold when post-treatment data were obtained. A valid fitness test could therefore not be conducted.

## **Discussion**

The preliminary results indicate that combining therapist-guided ICBT with one supervised and two unsupervised weekly sessions of physical exercise was feasible for the participants to complete. This study is the first to investigate the feasibility of combining ICBT with physical exercise, and these preliminary findings indicate that the beneficial and potentially augmenting properties of physical exercise, as an adjunct to ICBT can be further investigated.

According to the presented feasibility data, three out of four participants managed to complete the scheduled dose of physical exercise. All participants also managed to complete seven modules or more of the ICBT, and half of the participants completed all. In the previously cited study by Bergström et al. (2010) that utilised an equivalent ICBT program, the average number of modules completed by these participants was 6.7. The current findings seem to indicate that adhering

to the exercise protocol in this study does not negatively affect progression with the ICBT. In the qualitative interviews, participants reported that the combination of the two treatments was beneficial, with the general experience being that physical exercise provided them with increased energy and reduced tension. They did however report that it was challenging to find time for both exercises related to the ICBT and the unsupervised exercise sessions, and all participants reported that the treatment had been demanding. The participants were generally satisfied the treatment, reported positive change and impact, and importantly, no negative impact. They also considered the current treatment to be correct for their PD, and would recommend it to others with similar problems.

The outcome measures, including the clinical rating, did not provide a consistent picture. This is not to be unexpected given the small number of participants in these preliminary findings. As recommended, RCI and an estimated clinical cut-off were used to determine reliable and clinically significant change (Zahra & Hedge, 2010). Obviously, this method does not yield perfect specificity or sensitivity to clinical status, neither before nor after treatment, something that is obvious from these results. Furthermore, and a limitation of this study; the reliability of the clinical rating is not controlled, thus this can also explain these discrepancies. Still, the results on the primary outcome measures indicated reliable change for three of the four participants on most of these measures. They also scored below the clinical cut-offs on all measures. The fourth participant was also rated as being remitted from her PD although little change was reported on the primary outcome measures. Some participants also reported initial values below the clinical cut-off on some measures. Still, all participants were referred by their GP to treatment for PD indicating problems above a certain level of distress or disability for the participants. The treatment's impact on depression was uniform and noteworthy.

None of the first four participants included in the study dropped out during the treatment. This small data-set cannot generate any answers to the questions of whether this combined treatment influences dropout rate. As described under "Participants" in the

Methods section, subjects that were not included opted for ICBT without physical exercise with reference to having problems scheduling the supervised exercise session. This is a drawback with combining ICBT with regular attendance at a clinic. However, as described in the introduction, therapist contact could also be a protective factor against dropout. In the preliminary findings reported here, participants cited the importance of the therapist in supporting and encouraging them over the course of treatment. They also all expressed a wish for more face-to-face interaction. The ability of supervised exercise to reduce dropout from ICBT should be further investigated.

As discussed recently by Rozental et al. (2014), it is important to investigate side-effects of new clinical interventions, and little is so far known in terms of possible side-effects of Internet-based interventions, less so in the combination with physical exercise. None of the participants in the study reported negative effects in the qualitative interview, but one participant reported negative change on two of the outcome measures. These negative changes were not large enough to indicate reliable deterioration, but still indicate non-response, which can be regarded as a side effect (Rozental et al., 2014). A possible side effect from combining treatments comprises increased demands from the treatment that could lead to stress and scheduling difficulties. The latter is indeed reported by the participants in the study. However, they still report that the combination of the two treatments was beneficial and resulted in either improved exposure, or reduced tension, improved mood, and increased energy. A control group is required to properly investigate side effects from treatments (Rozental et al., 2014). However, this was beyond the aims and resources of this study. Future, controlled studies should also consider assessing possible side effects when combining ICBT with other treatments, such as physical exercise.

In this study, the therapist provided both the physical exercise and the ICBT. This solution was chosen for practical reasons. According to the participants' qualitative feedback, the therapist's ability to motivate and help them push themselves during the exercise sessions and treatment in general was important. The

therapist was a certified Internet therapist, but without prior experience in treating PD. The therapy was thus delivered through the ICBT program and the self-help modules in this program. However, this dual role of the therapist might have been beneficial for the patients' experiences with the treatment and their results. This could be considered a limitation of this study, and separating these functions would have created a more stringent design. As this study lacked a control group, we cannot be certain that the observed and reported changes have resulted from the treatment, as these changes could represent regression towards the mean/spontaneous recovery.

The manipulation check indicated that the participants had increased their physical fitness over the course of treatment. It is however a limitation of the current study that intensity was not monitored during the unsupervised sessions. The weekly supervised sessions were intended to ensure adherence to the physical exercise, both the supervised and the unsupervised, and assure continuous progress over the course of treatment. Participants were instructed to use the supervised session as a template for the following two unsupervised sessions in terms of intensity and duration. Yet the exercise diary indicated that for two of the participants, some sessions were below the recommended intensity. The fitness test also indicated that most participants were above average in their level of fitness, thus the continuing data collection will hopefully shed more light on the feasibility and appeal of the combined intervention for less fit subjects.

## Conclusion

The current preliminary results indicate that it is feasible for patients with PD to complete a combined treatment with ICBT and physical exercise. Combining physical exercise with ICBT does not appear to have a detrimental effect on the course of treatment, if anything; the combination seems to be beneficial. The complete data will provide more conclusive results.

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## Disclosure statement

The authors have declared that no conflict of interest exists.

## References

- American Psychiatric Association (2000). *Diagnostic and statistical manual of mental disorders* (4th ed., text revision). Washington, DC: Author.
- Andersson, G., Cuijpers, P., Carlbring, P., Riper, H., & Hedman, E. (2014). Guided Internet-based vs. face-to-face cognitive behavior therapy for psychiatric and somatic disorders: A systematic review and meta-analysis. *World Psychiatry, 13*, 288–295. doi:10.1002/wps.20151
- Andrews, G., Creamer, M., Crino, R., Hunt, C., Lampe, L., & Page, A. (2003). *The treatment of anxiety disorders—Clinician guides and patient manuals* (2 ed.). Cambridge: University Press.
- Beck, A.T., & Steer, R.A. (1993). *Beck anxiety inventory manual*. San Antonio, TX: The Psychological Corporation.
- Beck, A.T., Steer, R.A., & Brown, G.K. (1996). *Beck depression inventory-II manual*. San Antonio, TX: The Psychological Corporation.
- Bergstrom, J., Andersson, G., Ljotsson, B., Ruck, C., Andreevitch, S., Karlsson, A., ... Lindfors, N. (2010). Internet-versus group-administered cognitive behaviour therapy for panic disorder in a psychiatric setting: A randomised trial. *BMC Psychiatry, 10*, 54. doi: 10.1186/1471-244X-10-54
- Bijl, R.V., Ravelli, A., & van Zessen, G. (1998). Prevalence of psychiatric disorder in the general population: Results of the Netherlands mental health survey and incidence study (NEMESIS). *Social Psychiatry and Psychiatric Epidemiology, 33*, 587–595. doi:10.1007/s001270050098
- Broman-Fulks, J.J., & Storey, K.M. (2008). Evaluation of a brief aerobic exercise intervention for high anxiety sensitivity. *Anxiety, Stress & Coping, 21*, 117–128. doi:10.1080/10615800701762675
- Broocks, A., Bandelow, B., Pekrun, G., George, A., Meyer, T., Bartmann, U., ... R  ther, E. (1998). Comparison of aerobic exercise, clomipramine, and placebo in the treatment of panic disorder. *American Journal of Psychiatry, 155*, 603–609. doi:10.1176/ajp.155.5.603
- Carlbring, P., Bohman, S., Brunt, S., Buhrman, M., Westling, B.E., Ekselius, L., Andersson, G. (2006). Remote treatment of panic disorder: A randomized trial of Internet-based cognitive behavior therapy supplemented with telephone calls. *American Journal of Psychiatry, 163*, 2119–2125. doi:10.1176/ajp.2006.163.12.2119
- Carlbring, P., Gustafsson, H., Ekselius, L., & Andersson, G. (2002). 12-month prevalence of panic disorder with or without agoraphobia in the Swedish general population. *Social Psychiatry and Psychiatric Epidemiology, 37*, 207–211. doi:10.1007/s00127-002-0542-y
- Carlbring, P., Westling, B.E., Ljungstrand, P., Ekselius, L., & Andersson, G. (2001). Treatment of panic disorder via the Internet: A randomized trial of a self-help program. *Behavior Therapy, 32*, 751–764. doi:10.1016/S0005-7894(01)80019-8
- Cavanagh, K. (2014). Geographic inequity in the availability of cognitive behavioural therapy in England and Wales: A 10-year update. *Behavioural and Cognitive Psychotherapy, 42*, 497–501. doi:10.1017/S1352465813000568
- Chambless, D.L., Caputo, G.C., Bright, P., & Gallagher, R. (1984). Assessment of fear of fear in agoraphobics: The body sensations questionnaire and the agoraphobic cognitions questionnaire. *Journal of Consulting and Clinical Psychology, 52*, 1090–1097. doi:10.1037/0022-006X.52.6.1090
- Chambless, D.L., Caputo, G.C., Jasin, S.E., Gracely, E.J., & Williams, C. (1985). The mobility inventory for agoraphobia. *Behaviour Research and Therapy, 23*, 35–44. doi:10.1016/0005-7967(85)90140-8
- Chignon, J.-M., Lepine, J.-P., & Ades, J. (1993). Panic disorder in cardiac outpatients. *American Journal of Psychiatry, 150*, 780–785. doi:10.1176/ajp.150.5.780
- Clark, D.M. (1986). A cognitive approach to panic. *Behaviour Research and Therapy, 24*, 461–470. doi:10.1016/0005-7967(86)90011-2
- Clark, D.M., Salkovskis, P.M., Hackmann, A., Middleton, H., Anastasiades, P., & Gelder, M. (1994). A comparison of cognitive therapy, applied relaxation and imipramine in the treatment of panic disorder. *The British Journal of Psychiatry, 164*, 759–769. doi:10.1192/bjp.164.6.759
- Cohen, H., Benjamin, J., Geva, A.B., Matar, M.A., Kaplan, Z., & Kotler, M. (2000). Autonomic dysregulation in panic disorder and in post-traumatic stress disorder: Application of power spectrum analysis of heart rate variability at rest and in response to recollection of trauma or panic attacks. *Psychiatry Research, 96*(1), 1–13. doi:10.1016/S0165-1781(00)00195-5
- Craig, P., Dieppe, P., Macintyre, S., Michie, S., Nazareth, I., & Petticrew, M. (2008). Developing and evaluating complex interventions: The new Medical Research Council guidance. *BMJ, 337*, a1655. doi:10.1136/bmj.a1655
- Emmelkamp, P.M., David, D., Beckers, T., Muris, P., Cuijpers, P., Lutz, W., ... Vervliet, B. (2014). Advancing psychotherapy and evidence-based psychological interventions. *International Journal of Methods in Psychiatric Research, 23*, 58–91. doi:10.1002/mpr.1411
- Esquivel, G., D  az-galvis, J., Schruers, K., Berlanga, C., Lara-Mu  oz, C., & Griez, E. (2008). Acute exercise reduces the effects of a 35% CO<sub>2</sub> challenge in patients with panic disorder. *Journal of Affective Disorders, 107*, 217–220. doi:10.1016/j.jad.2007.07.022

- First, M.B., Spitzer, R.L., Gibbon, M., & Williams, J.B.W. (1995). *Structured clinical interview for DSM-IV axis I disorders-patient edition (SCID-I/P, version 2.0)*. New York, NY: Biometric Research Department, New York State Psychiatric Institute.
- Garber, C.E., Blissmer, B., Deschenes, M.R., Franklin, B.A., Lamonte, M.J., Lee, I., . . . , Swain, D.P., (2011). Quantity and quality of exercise for developing and maintaining cardiorespiratory, musculoskeletal, and neuromotor fitness in apparently healthy adults. *Medicine & Science in Sports & Exercise*, *43*, 1334–1359. doi:10.1249/MSS.0b013e318213febf
- Gloster, A.T., Witthen, H., Einsle, F., Lang, T., Helbig-Lang, S., Fydrich, T., . . . , Arolt, V., (2011). Psychological treatment for panic disorder with agoraphobia: A randomized controlled trial to examine the role of therapist-guided exposure *in situ* in CBT. *Journal of Consulting and Clinical Psychology*, *79*, 406–420. doi:10.1037/a0023584
- Gomes, R., Sardinha, A., Araújo, C., Nardi, A., & Deslandes, A. (2014). Aerobic training intervention in panic disorder: A case-series study. *Medical Express*, *1*, 195–201.
- Gomez-Caminero, A., Blumentals, W.A., Russo, L. J., Brown, R.R., & Castilla-Puentes, R. (2005). Does panic disorder increase the risk of coronary heart disease? A cohort study of a national managed care database. *Psychosomatic Medicine*, *67*, 688–691. doi:10.1097/01.psy.0000174169.14227.1f
- Haug, T., Nordgreen, T., Öst, L.G., & Havik, O.E. (2012). Self-help treatment of anxiety disorders: A meta-analysis and meta-regression of effects and potential moderators. *Clinical Psychology Review*, *32*, 425–445. doi:10.1016/j.cpr.2012.04.002
- Hovland, A., Nordhus, I.H., Sjøbø, T., Gjestad, B. A., Birknes, B., Martinsen, E.W., . . . , Pallesen, S., (2013). Comparing physical exercise in groups to group cognitive behaviour therapy for the treatment of panic disorder in a randomized controlled trial. *Behavioural and Cognitive Psychotherapy*, *41*, 408–432. doi:10.1017/S1352465812000446
- Hovland, A., Pallesen, S., Hammar, Å., Hansen, A. L., Thayer, J.F., Tarvainen, M.P., & Nordhus, I. H. (2012). The relationships among heart rate variability, executive functions, and clinical variables in patients with panic disorder. *International Journal of Psychophysiology*, *86*, 269–275. doi:10.1016/j.ijpsycho.2012.10.004
- Jacobson, N.S., & Truax, P. (1991). Clinical significance: A statistical approach to defining meaningful change in psychotherapy research. *Journal of Consulting and Clinical Psychology*, *59*, 12–19. doi:10.1037/0022-006X.59.1.12
- Kessler, R.C., Berglund, P., Demler, O., Jin, R., Merikangas, K.R., & Walters, E.E. (2005). Lifetime prevalence and age-of-onset distributions of DSM-IV disorders in the National Comorbidity Survey Replication. *Archives of General Psychiatry*, *62*, 593. doi:10.1001/archpsyc.62.6.593
- Kessler, R.C., Chiu, W.T., Demler, O., & Walters, E.E. (2005). Prevalence, severity, and comorbidity of 12-month DSM-IV disorders in the National Comorbidity Survey Replication. *Archives of General Psychiatry*, *62*, 617–627. doi:10.1001/archpsyc.62.6.617
- Klein, E., Cnaani, E., Harel, T., Braun, S., & Ben-Haim, S.A. (1995). Altered heart rate variability in panic disorder patients. *Biological Psychiatry*, *37*, 18–24. doi:10.1016/0006-3223(94)00130-U
- Kobayashi, K., Shimizu, E., Hashimoto, K., Mitsumori, M., Koike, K., Okamura, N., . . . , Iyo, M., (2005). Serum brain-derived neurotrophic factor (BDNF) levels in patients with panic disorder: As a biological predictor of response to group cognitive behavioral therapy. *Progress in Neuro-Psychopharmacology and Biological Psychiatry*, *29*, 658–663. doi:10.1016/j.pnpbp.2005.04.010
- Leclercq, Y., Sheehan, D., Weiller, E., Amorim, P., Bonora, I., Harnett Sheehan, K., . . . , Dunbar, G., (1997). The Mini International Neuropsychiatric Interview (MINI). A short diagnostic structured interview: Reliability and validity according to the CIDI. *European Psychiatry*, *12*, 224–231. doi:10.1016/S0924-9338(97)83296-8
- Malterud, K. (2001). Qualitative research: Standards, challenges, and guidelines. *The Lancet*, *358*, 483–488. doi:10.1016/S0140-6736(01)05627-6
- Martinsen, E.W., Medhus, A., & Sandvik, L. (1985). Effects of aerobic exercise on depression: A controlled study. *BMJ*, *291*, 109. doi:10.1136/bmj.291.6488.109
- McManus, F., Grey, N., & Shafran, R. (2008). Cognitive therapy for anxiety disorders: Current status and future challenges. *Behavioural and Cognitive Psychotherapy*, *36*, 695–704. doi:10.1017/S135246580800475X
- Melville, K.M., Casey, L.M., & Kavanagh, D.J. (2010). Dropout from Internet-based treatment for psychological disorders. *British Journal of Clinical Psychology*, *49*, 455–471. doi:10.1348/014466509X472138
- Merom, D., Phongsavan, P., Wagner, R., Chey, T., Marnane, C., Steel, Z., . . . , Bauman, A., (2008). Promoting walking as an adjunct intervention to group cognitive behavioral therapy for anxiety disorders—A pilot group randomized trial. *Journal of Anxiety Disorders*, *22*, 959–968. doi:10.1016/j.janxdis.2007.09.010
- Meyer, T., & Brooks, A. (2000). Therapeutic impact of exercise on psychiatric diseases. *Sports Medicine*, *30*, 269–279. doi:10.2165/00007256-200030040-00003
- National Collaborating Centre for Mental Health (2011). *Generalised anxiety disorder in adults: Management in primary, secondary and community care*. Leicester: British Psychological Society.
- National Institute for Health and Clinical Excellence (2011). *Generalised anxiety disorder and*

- panic disorder (with or without agoraphobia) in adults. *Clinical guideline 113*. London: Author. Retrieved from <http://www.guidance.nice.org.uk/CG113>
- Nes, B., Janszky, I., Wisløff, U., Støylen, A., & Karlsen, T. (2013). Age-predicted maximal heart rate in healthy subjects: The HUNT fitness study. *Scandinavian Journal of Medicine & Science in Sports*, *23*, 697–704. doi:10.1111/j.1600-0838.2012.01445.x
- Noonan, V., & Dean, E. (2000). Submaximal exercise testing: Clinical application and interpretation. *Physical Therapy*, *80*, 782–807.
- Nordgreen, T., Standal, B., Mannes, H., Haug, T., Sivertsen, B., Carlbring, P., . . . , Havik, O., (2010). Guided self-help via Internet for panic disorder: Dissemination across countries. *Computers in Human Behavior*, *26*, 592–596. doi:10.1016/j.chb.2009.12.011
- Peters, J., Dieppa-Perea, L.M., Melendez, L.M., & Quirk, G.J. (2010). Induction of fear extinction with hippocampal-infralimbic BDNF. *Science*, *328*, 1288–1290. doi:10.1126/science.1186909
- Roy-Byrne, P.P., Stang, P., Wittchen, H.-U., Ustun, B., Walters, E., & Kessler, R.C. (2000). Lifetime panic-depression comorbidity in the National Comorbidity Survey: Association with symptoms, impairment, course and help-seeking. *The British Journal of Psychiatry*, *176*, 229–235. doi:10.1192/bjp.176.3.229
- Rozental, A., Andersson, G., Boettcher, J., Ebert, D.D., Cuijpers, P., Knaevelsrud, C., . . . , Carlbring, P., (2014). Consensus statement on defining and measuring negative effects of Internet interventions. *Internet Interventions*, *1*, 12–19. doi:10.1016/j.invent.2014.02.001
- Sardinha, A., Araújo, C.G.S., Soares-Filho, G.L.F., & Nardi, A.E. (2011). Anxiety, panic disorder and coronary artery disease: Issues concerning physical exercise and cognitive behavioral therapy. *Expert Review of Cardiovascular Therapy*, *9*, 165–175. doi:10.1586/erc.10.170
- Smits, J.A.J., Berry, A.C., Rosenfield, D., Powers, M.B., Behar, E., & Otto, M.W. (2008). Reducing anxiety sensitivity with exercise. *Depression and Anxiety*, *25*, 689–699. doi:10.1002/da.20411
- Stein, J.M., Papp, L.A., Klein, D.F., Cohen, S., Simon, J., Ross, D., . . . , Gorman, J.M., (1992). Exercise tolerance in panic disorder patients. *Biological Psychiatry*, *32*, 281–287. doi:10.1016/0006-3223(92)90109-D
- Ströhle, A., Feller, C., Strasburger, C.J., Heinz, A., & Dimeo, F. (2006). Anxiety modulation by the heart? Aerobic exercise and atrial natriuretic peptide. *Psychoneuroendocrinology*, *31*, 1127–1130.
- Ströhle, A., Graetz, B., Scheel, M., Wittmann, A., Feller, C., Heinz, A., & Dimeo, F. (2009). The acute antipanic and anxiolytic activity of aerobic exercise in patients with panic disorder and healthy control subjects. *Journal of Psychiatric Research*, *43*, 1013–1017. doi:10.1016/j.jpsychires.2009.02.004
- Ströhle, A., Kellner, M., Holsboer, F., & Wiedemann, K. (2001). Anxiolytic activity of atrial natriuretic peptide in patients with panic disorder. *The American Journal of Psychiatry*, *158*, 1514–1516.
- Ström, M., Uckelstam, C.-J., Andersson, G., Hassmén, P., Umefjord, G., & Carlbring, P. (2013). Internet-delivered therapist-guided physical activity for mild to moderate depression: A randomized controlled trial. *PeerJ*, *1*, e178.
- Swain, D.P. (2014). *ACSM's resource manual for guidelines for exercise testing and prescription* (7th ed.). Philadelphia, PA: Lippincott Williams & Wilkins.
- Szuhany, K.L., Bugatti, M., & Otto, M.W. (2015). A meta-analytic review of the effects of exercise on brain-derived neurotrophic factor. *Journal of Psychiatric Research*, *60*, 56–64. doi:10.1016/j.jpsychires.2014.10.003
- Trivedi, M.H., Greer, T.L., Church, T.S., Carmody, T.J., Grannemann, B.D., Galper, D.I., . . . , Blair, S.N., (2011). Exercise as an augmentation treatment for nonremitted major depressive disorder. *The Journal of Clinical Psychiatry*, *72*, 677–684. doi:10.4088/JCP.10m06743
- Veale, D., Le Fevre, K., Pantelis, C., De Souza, V., Mann, A., & Sargeant, A. (1992). Aerobic exercise in the adjunctive treatment of depression: A randomized controlled trial. *Journal of the Royal Society of Medicine*, *85*, 541–544.
- Weissman, M.M., Markowitz, J.S., Ouellette, R., Greenwald, S., & Kahn, J. (1990). Panic disorder and cardiovascular/cerebrovascular problems: Results from a community survey. *American Journal of Psychiatry*, *147*, 1504–1508. doi:10.1176/ajp.147.11.1504
- Zahra, D., & Hedge, C. (2010). The reliable change index: Why isn't it more popular in academic psychology. *Psychology Postgraduate Affairs Group Quarterly*, *76*, 14–19.