ISRCTN95964384 https://doi.org/10.1186/ISRCTN95964384

Effectiveness of heart rate variability biofeedback training for improving psychological and cognitive functioning and quality of life in women with primary breast cancer

Submission date
08/07/2022

Recruitment status
No longer recruiting

Registration date
18/07/2022

Overall study status
Completed

Last Edited
05/10/2023

Condition category
Cancer

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[_] Record updated in last year

Plain English Summary

Background and study aims

Breast cancer is the most common cancer affecting women around the globe. Latest statistics estimate that 1 in 7 UK women will receive the diagnosis in her lifetime. The UK survivor rates have doubled over the past 40 years and continue increasing due to improvements in cancer treatment and screening. However, women recovering from breast cancer are shown to suffer from moderate to severe chronic mental and physical health conditions. Wide-ranging health conditions are caused by common breast cancer treatments and linked to the nature of the disease and various psychosocial and lifestyle factors. Growing research shows that women with a breast cancer diagnosis suffer profound and chronic emotional vulnerability with cognitive deficits which independently and adversely impact on quality of life and life expectancy. Accumulating findings suggest that common chronic mental and physical health comorbidities seen in breast cancer are linked to a common mechanism, specifically, an imbalance in the autonomic nervous system. This imbalance can be measured by heart rate variability (HRV). Lower levels of HRV have predicted anxiety and depression while individuals with higher HRV show an increased capacity to cope with stress and are characterised by better mental and physical health. Women with breast cancer show reduced HRV compared to women without the diagnosis. One of the ways of stimulating the autonomic nervous system balance and increasing HRV non-invasively is through paced breathing.

The main aim of this study is to assess the effectiveness of a 4-week heart rate variability biofeedback (HRVB) training which involves paced breathing for improving the emotional and cognitive functioning of women with a primary breast cancer diagnosis, and to explore the impact of training in other symptoms commonly seen in women with breast cancer, including cognitive dysfunction, anxiety and depression, sleep difficulties, menopausal hot flushes, and night sweats. Research shows that these symptoms are associated with reduced HRV, and early findings show that paced breathing interventions and/or HRVB have positive effects on these symptoms. It is expected that the 4-week HRVB training will result in a higher resting HRV and

improve emotional and cognitive functioning and wellbeing. This will be reflected in better self-reported emotion regulation, cognitive function, and an improved ability to shift attention and ability to respond to stress.
Sleep difficulties are amongst the most common complaints in women with breast cancer. Previous findings including studies in cancer patients show that HRVB may be a particularly helpful tool for improving insomnia and overall quality of sleep, it will therefore be expected that HRVB intervention will result in subjectively reported improvements of quality of sleep.
Menopausal hot flushes and night sweats are highly prevalent and distressing symptoms experienced by women recovering from breast cancer (i.e., endocrine therapy side effects). Current evidence-based psychological therapies recommended paced breathing as behavioural as a key coping strategy for managing these symptoms; this includes daily practice and application during symptom onset. Considering the effectiveness of paced breathing techniques on management of hot flushes, the HRVB intervention may lead to self-reported reductions in intensity and frequency of hot flushes and night sweats in women with primary breast cancer.
Based on numerous previous HRVB studies it is also expected that women who complete HRVB intervention will report reduced anxiety and depression symptoms, decreased levels of stress and fatigue, as well as enhanced overall wellbeing. These reports are expected to translate into improved daily functioning, self-management, and overall quality of life.

Who can participate?
Women with a primary breast cancer diagnosis between the ages of 18 and 65 years. The participants must have undergone chemotherapy as part of their treatment and be between 6 to 60 months post-treatment. They should not be receiving any active anti-cancer treatment(s) at the time of recruitment. The participants can be taking regular hormone replace therapy medications (e.g., tamoxifen, aromatase inhibitors) or receiving target treatment(s) (i.e. Herceptin injections). Participants must be currently experiencing sleep difficulties and hot flushes/night sweats. Participants must not have any serious neurological, cardiovascular, any seizure, substance misuse diagnosis or severe psychiatric diagnosis, and must also not be currently practicing breathing exercises/techniques which involve deep or slow-paced breathing (e.g., yogic breathing, Qi Gong breathing) etc on a regular basis.

What does this study involve?
Breast cancer survivors will be recruited on a voluntary basis through online advertisements placed on social media platforms including, Facebook and Twitter. Advertisements will also be placed on the Building Resilience in Breast Cancer (BRiC) and other relevant charities and support group pages.
Participants who express interest will be screened for study eligibility using a set of self-report measures online. Eligible participants must report experiencing difficulties with sleep and menopausal hot flushes/night sweats which are directly impacting their quality of life.
Eligible participants will be randomly assigned to one of three conditions. Treatment and active control groups will complete 4-week HRV biofeedback training which involves daily (5 days per week) paced breathing practice using a smart phone app displaying a visual breath pacer and a portable pulse monitor designed to be attached to the ear lobe. Participants randomly assigned to the wait list control group will receive training and materials to self-administer treatment upon completion of the 6-months follow-up.

What are the possible benefits and risks of participating?
All participants in this study will be given the opportunity to receive an intervention which is not currently available through health care services. Participants will be paid a total sum of £100 in Amazon vouchers by the completion of the 6-months follow-up point; payment will be made in two instalments, £50 immediately after training and £50 after the 6-months follow-up. All participants, including treatment, active control and waitlist participants will also be offered

access to relevant free resources and will have a 20% discount on biofeedback technology utilised in this study.
There are no known risks associated with the present intervention (HRV biofeedback training) and measures and tasks used in this study. Each participant will be monitored by the lead researcher throughout the study.

Where is this study run from?
This is a fully remote study. Recruitment and relevant assessments will take place via secure online platforms, interviews will take place via telephone. Participants will complete the intervention in their home environment. The research team is based at Birkbeck College, University of London (UK)

When is the study starting and how long is it expected to run for?
May 2022 to May 2024

Who is funding the study?
Economic and Social Research Council (ESRC) (UK)

Who is the main contact?
1. Prof. Nazanin Derakhshan, n.derakhshan@bbk.ac.uk
2. Prof. Beth Grunfeld, e.grunfeld@bbk.ac.uk

Contact information

Type(s)
Principal Investigator

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
Nil known

Study information

Scientific Title
A randomised control trial investigating the efficacy of heart rate variability biofeedback training for improving psychological and cognitive functioning and quality of life in women with primary breast cancer

Acronym
HRVBBC

Study hypothesis
Hypotheses:
1. Women who receive the intervention will show reduced baseline resting heart rate and improved resting HRV parameters (i.e., increased root mean square of successive differences, RMSSD) as compared to active control and waitlist control groups after the 4-week training and at a follow-up time of 6-months after the intervention.
2. Women who receive the intervention will report greater improvements in self-reported measures of cognitive and emotional wellbeing, and quality of life, as compared to the active control and waitlist control groups, after the 4-week training and at the 6-month follow-up.
3. Women in the intervention group will show better cognitive and emotional functioning on objective measures of stress reactivity using the internet-based Trier Social Stress Test, and cognitive flexibility using the cued task-switching task compared with the active control and waitlist groups after the intervention and at the 6-months follow-up.
4. Women who receive the intervention will report a greater improvement in their quality of sleep, and improvements in their experience of hot flushes and/or night sweats compared with the active control and wait list control groups after intervention and at 6-months follow-up.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 25/06/2022, the Department of Psychological Science Research Ethics Committee at Birkbeck College, University of London (Malet Street, London, WC1E 7HX, UK; Tel: not available; ethics@psychology.bbk.ac.uk), ref: 2122088

Study design
Single-centre interventional longitudinal 6-month randomized control trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Home

Study type(s)
Quality of life

Participant information sheet
Not available in web format, please use contact details to request a participant information sheet

Condition
Breast cancer

Interventions
Training intervention:
The intervention involves a 4-week Heart Rate Variability biofeedback (HRVB) training which involves paced breathing. Numerous studies across health and clinical populations have shown that around 4 weeks of daily HRVB training increases baseline heart rate variability, reflecting improved increased parasympathetic tone and autonomic balance, and that these effects are associated with improvements across a wide range of mental and physical health symptoms. HRVB training is associated with reduced anxiety and depression, improved stress management, improvements in chronic sleep, fatigue, and pain symptoms, as well as improvements in cognitive and cardiorespiratory function. The present study will be the first to look for similar intervention effects in primary breast cancer. Findings so far suggest that HRVB could be a useful complementary intervention for the management of a wide range of chronic conditions. In this trial HRVB intervention will be facilitated using widely used biofeedback technology, the Inner Balance smartphone application and a portable Inner Balance Bluetooth pulse monitor (designed to measure pulse from participants' ear lobe non-invasively; HeartMath Inc.). The training protocol involves daily breathing training, 5 days per week, starting with 10 minutes twice daily training and ending with 20 minutes twice daily training by week 4 (training protocol adapted from Lehrer et al., 2013). Sealed Envelope simple randomisation software (https://www.sealedenvelope.com) will be used to randomly allocate the recruited women with primary breast cancer (n = 90) to one of three conditions:
1. HRV biofeedback training intervention (six breaths per minute) (n =30)

2. HRV biofeedback training active control (12 breaths per minute) (n = 30)
3. Wait list control group (n = 30)

Identical to the intervention and active control groups, participants in the wait list group but will complete all relevant tasks and assessments at the set time intervals, i.e., pre-intervention, post-intervention (around 4 weeks after the pre-intervention assessment), and 6 months after the intervention, but without completing any experimental intervention. Waitlist control participants will be offered to complete the intervention after the trial completion, i.e., after the 6-months follow-up. All necessary training and materials including a Bluetooth pulse monitor will be provided to enable them to self-administer the intervention. There will be no planned follow-up on the waitlist control group participants.

All participants will complete the following measures remotely (online, using a video-conferencing platform): a questionnaire battery to capture a subjective measure of cognitive, mental, and physical wellbeing and quality of life, objective measures of cognitive flexibility task (task-switching task, Ciobotaru et al., 2021) online via Gorilla platform (https://gorilla.sc), and internet-based Trier Social Stress Test (iTSST; Eagle et al., 2021) and resting baseline heart rate variability (HRV) assessment, via secure video conferencing platform Zoom (https://zoom.us). These measures will be collected at three timepoints: before training, after the 4-week training period, and 6 months after training.

Interview intervention:
A sub-group of participants from the three groups (n = 45) will also complete 1-hour semi-structured telephone interviews during the assessment phases outlined before, i.e., before training, after training and 6 months after training. Fifteen participants from each group will be selected sequentially, i.e., in order of application until the required number is reached) The aim of the interviews is to understand in detail how women living with primary breast cancer diagnosis experience and manage some of the common difficulties associated with the diagnosis and treatment. Questions will focus on the following well-being areas a) cognitive functioning and mood, b) quality of sleep, and c) menopausal hot flushes and night sweats. Baseline interviews will focus on current symptom experience, management, impact on quality of life and daily functioning; 4-week follow-up interviews will focus on current symptom experience, management and impact, and intervention experience and effects for relevant groups; 6-months follow-up interviews will focus on current symptom experience and management, any changes in lifestyle and symptom management in the last 6 months, and short-term and long-term intervention effects for relevant groups. An in-depth qualitative investigation will help understand the effectiveness and application of HRVB training for the management of difficulties and chronic symptoms commonly experienced by women with primary breast cancer. Framework analysis will be used to develop any common themes based on individual verbatim transcripts.

Intervention Type
Behavioural

Primary outcome measure
Assessed at three timepoints - pre-training [baseline], post-training, and at 6-month follow-up:
1. Resting heart rate and heart rate variability assessed using a portable pulse monitor
2. Cognitive flexibility assessed using computerised Cued Task-Switching task
3. Psychological stress reactivity assessed by heart rate and heart rate variability measurements and subjective mood ratings during an Internet-based Trier Social Stress Test (iTSST)
4. Perceived quality of sleep assessed using Pittsburgh Sleep Quality Index (PSQI) and qualitative

interview measures
5. Self-reported frequency of hot flushes and night sweats and associated problem rating assessed using the Hot Flush Rating Scale (HFRS) and qualitative interview measures
6. Perceived emotion regulation assessed using the Emotion Regulation Questionnaire (ERQ) and qualitative interview measures

Secondary outcome measures
Assessed at three timepoints - pre-training [baseline], post-training, and at 6-month follow-up.
1. Perceived cognitive functioning measured using the Functional Assessment of Cancer Therapy-Cognitive Scale (FACT-Cog, version 3) and qualitative interview measures
2. Perceived stress level assessed using the Perceived Stress Scale (PSS)
3. Anxiety and depression symptoms assessed using the Hospital Anxiety and Depression Scale (HADS).
4. Perceived cancer-specific distress assessed using the Revised Impact of Events Scale for cancer care (IES-R)
5. Perceived fatigue symptomatology and its impact on daily functioning assessed using the Functional Assessment of Chronic Illness Therapy – Fatigue (FACIT-F, version 4)
6. Subjective measure of health morbidity and mortality risk assessed using Charlson Comorbidity Index (CCI; modified version)
7. Perceived quality of life, emotional, cognitive, and daily functioning and coping with common difficulties including sleep difficulties and hot flushes assessed using qualitative semi-structured interviews, analysed using a Framework approach

Overall study start date
01/05/2022

Overall study end date
31/05/2024

Eligibility

Participant inclusion criteria
Breast cancer survivors with a primary diagnosis of breast cancer who have finished active treatment:
1. Primary breast cancer diagnosis
2. Completed chemotherapy between 6 – 60 months ago
3. 18 – 65 years of age
4. Currently not practicing breathing exercises/techniques which involve deep or slow-paced breathing e.g., yogic breathing, Qi Gong Breathing etc on a regular basis
5. Currently experiencing sleep difficulties and hot flushes and/or night sweats (any frequency, i. e., frequent >30, or infrequent <7 per week)
6. English literate; able to complete tasks and questionnaires in English independently
7. Basic IT skills and access to laptop/desktop/tablet and smartphone

Participant type(s)
Patient

Age group
Adult

Lower age limit

18 Years

Upper age limit
65 Years

Sex
Female

Target number of participants
90

Total final enrolment
60

Participant exclusion criteria
Breast cancer survivors with a primary diagnosis of breast cancer who has finished active treatment and who are:
1. Receiving concurrent treatment for cancer (except endocrine or biologic therapy)
2. Cardiovascular disorders that affect HRV parameters (paroxysmal supraventricular tachycardia, atrial fibrillation, myocardial infarction within 12 months, unstable angina, bradyarrhythmias, atrial flutter)
3. Receiving medications that affect cardiac rhythm (angiotensin-converting enzyme [ACE] inhibitors), calcium channel blockers, or beta-adrenergic inhibitors)
4. Pacemaker or defibrillator in situ
5. Had a heart transplant or by-pass surgery within 1 year
6. Any active seizure disorder or use of antiseizure or anticonvulsant medication prescribed specifically for seizure disorder
7. Pre-existing dementia prior to cancer diagnosis or other organic mental disorders
8. Moderate (without good recovery) or severe head injury or stroke in last 6 months
9. Evidence of active substance misuse or dependence
10. Any use of long-acting (extended-release) opioid medications
11. Severe and enduring major psychiatric disorder (including bipolar disorder, schizophrenia, other psychosis, and personality disorders)
12. Persisting developmental disorders including autism spectrum disorders and attention-deficit /hyperactivity disorder
13. History of brain metastases, primary brain cancer, or other neurological conditions which altered cognitive abilities
14. Moderate to severe breathing difficulties including COPD, asthma or any other pulmonary condition which may affect or prevent ability to perform paced breathing

Recruitment start date
22/07/2022

Recruitment end date
01/08/2023

Locations

Countries of recruitment
England

United Kingdom

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Birkbeck, University of London
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ROR
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Funder(s)

Funder type
Research council

Funder Name

Economic and Social Research Council

Alternative Name(s)
ESRC

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Funder Name
Birkbeck, University of London

Alternative Name(s)
Birkbeck College, Birkbeck, Collegium Birkbeck Londiniense

Funding Body Type
Government organisation

Funding Body Subtype
Research institutes and centers

Location
United Kingdom

Results and Publications

Publication and dissemination plan
Planned publication in a high-impact peer-reviewed journal.

Intention to publish date
01/09/2024

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are not expected to be made available due to an ethics agreement.

Collected data will only be accessible to the three researchers involved in this study (Professor Nazanin Derakhshan, Professor Beth Grunfeld and Karina Dolgilevica).

Informed consent will be collected from participants at the start of every experimental phase, written electronic consent will be collected for each individual measurement (including online questionnaires, telephone interviews, baseline measurements of heart rate variability), at pre-intervention, post-intervention, 6-months post-intervention.

All participant data files will be encrypted and kept on a password-protected computer to ensure confidentially. An encrypted email account will be used to send and store email communication between the researcher (KD) and participants, and this content will be kept only for the duration of the study. Telephone interview audio recordings with be downloaded into the encrypted files on the computer immediately after the interview has finished and removed from the recording device (this device will be stored in a locked drawer when not in use). All audio recording files will be deleted one year after study completion.

To keep all participant data strictly anonymous a randomly generated participant number will be assigned to each recruited participant. The participant reference number will be used instead of their name on all the materials/measures collected. Upon unintentional disclosure of any personally identifiable information during audio-recorded telephone interviews the information will be removed from the final interview transcript.

Heart rate data will also be anonymised and identified by the randomly generated participant number which will be used for all other data/materials. Each participant will be provided with a sham email address which will contain their participant number to use as a username for the creation of a cloud account (HeartCloud) to enable anonymised heart rate data collection using a Bluetooth device and Inner Balance app which will sync the data from each participant's cloud account to cloud account of the lead researcher KD to be stored temporarily to enable data collection and analysis. Any data stored on HeartCloud storage and other software used for heart rate data analysis (emWave Pro, and Kubios software) will be removed after 1 year of study completion. The heart rate data will be kept for one year after the end of the last study phase i.e., the 6-months follow-up, for data analysis purposes.

Contact for inquiries regarding access to the datasets: Miss Karina Dolgilevica (kdolgi01@student.bbk.ac.uk).

IPD sharing plan summary

Not expected to be made available