Study Protocol

Effects of high ventilation breathwork with retention on mental health and wellbeing: A randomised placebo-controlled trial (NCT06064474)

Guy William Fincham, Elissa Epel, Alessandro Colasanti, Clara Strauss, Kate Cavanagh

Document date: October 09, 2023

Background & rationale

There has been an unprecedented surge in public/scientific interest in a style of breathwork that incorporates hyperventilation (high ventilation) with breath-holds (retention). This technique has similarities to Tibetan Tummo meditation and Yogic Pranayama but has been popularised in the West by the Wim Hof Method (Kox et al., 2014). Despite emerging research there are no well-controlled studies exploring effects of high ventilation breathwork with retention (HVBR) on mental health and wellbeing. We plan to complete the first robust randomised-controlled trial (RCT) comparing HVBR (20 minutes/day) for three weeks to a well-designed placebo (paced breathing at 15 breaths/min with retentions). The metric of 15b/min aligns with guidance from the British Journal of Nursing, Royal College of Physicians and Johns Hopkins Medicine which state that the average, healthy rate should range from: 12-20, 12-18 and 12-16b/min, respectively.

Slow breathwork has received most research attention so far; in our recent meta-analysis (Fincham et al., 2023) we found significant small-medium effects, showing breathwork was associated with lower subjective stress (primary outcome), anxiety and depression (secondary outcomes) compared to non-breathwork controls. For the primary outcome, 10 and only 2 studies respectively comprised slow and fast breathwork; these were of moderate and high risk of bias, suggesting more robust tests of their potential effects are needed. Nonetheless, fast breathwork may offer potential therapeutic benefit as temporary voluntarily induced stress has been suggested as, and could possibly be, beneficial for health (Petraskova Touskova et al., 2022). High-intensity physical exercise can improve health by inducing a sympathetic response (stress) initially, subsequently followed by adaptation. Similarly, HVBR may induce short-term stress that can improve mental health and provisional evidence has shown it may confer beneficial therapeutic effects regarding perceived stress (Kopplin & Rosenthal, 2022). While increasing stress seemingly mitigates the improved health claims of HVBR, it might be elucidated more clearly through the notion of hormesis, an adaptive response to states of moderate bodily stress (Mattson, 2008). The key, perhaps, is that it is not done reflexively (i.e., responsive hyperventilation during a panic attack), but is performed deliberately in a controlled manner (i.e., hyperventilation during an intentional breathwork practice); and only five min/day of HVBR for four weeks has also been associated with improvements on state anxiety along with positive and negative affect (Balban et al., 2023). For example, exercise is voluntarily induced and thus is a different stressor to reactive states in response to negative stressors in life. Both RCTs of Kopplin and Rosenthal (2022) and Balban et al. (2023) display positive effects of HVBR on mental health outcomes, however such findings are limited by the quality of trial design and study methods used. For example, neither included a *placebo* control, making it difficult to establish for these studies whether the interventions had specific active effects on mood beyond attention/expectation effects. Further, more research is needed to gauge the safety profile of fast breathwork. Whilst our meta-analysis did not find negative effects directly attributed to breathwork, only six studies in total (for all outcomes) out of 26 actively reported on this. Thus, we will actively do so.

The theoretical rationale for our study is: Identifying if HVBR exerts effects on mental health and wellbeing related outcomes via a well-designed RCT within a young (18-39), healthy general population. The appropriate placebo used here may help disentangle effects of the breathwork intervention (Sevoz-Couche & Laborde, 2022), if any. The practical rationale is: Using data collected to help develop time- and cost-effective remote interventions for lowering stress and improving wellbeing. Studies included in our meta-analysis were deemed as being at moderate or high risk of bias, including all RCTs using fast breathwork, hence we plan to complete the first low risk-of-bias fast breathwork RCT. We wish to share findings through publication in a reputable open-access journal to inform practice and hopefully benefit others.

Objectives & endpoints

The main question our study attempts to address is: Does HVBR lead to improved mental health and wellbeing? Participants will be randomised to a guided audio of HVBR (four rounds with longer retentions) or placebo breathwork (15b/min with four shorter retentions) for 20min/day, for 21 days, both pre-recorded by a trained breathwork facilitator, delivered remotely. Participants will be asked whether negative effects (both short- and long-term) occurred. The study will be conducted online through Prolific (all data will be anonymous). We will collect self-reports of mental health and wellbeing pre-post and at three-week follow-up.

Research Questions

Primary research question

- Does HVBR lead to improved subjective stress (primary outcome) in comparison to an active placebo control in a general population adult sample at post-intervention (primary timepoint)?

Secondary research questions

- Does HVBR lead to improved subjective stress in comparison to an active placebo control in a general population adult sample at follow-up?
- Does HVBR lead to improved subjective anxiety in comparison to an active placebo control in a general population adult sample at: a) post-intervention, b) follow-up?
- Does HVBR lead to improved subjective depression in comparison to an active placebo control in a general population adult sample at: a) post-intervention, b) follow-up?
- Does HVBR lead to improved subjective mental wellbeing in comparison to an active placebo control in a general population adult sample at: a) post-intervention, b) follow-up?
- Does HVBR lead to improved subjective sleep-related impairment in comparison to an active placebo control in a general population adult sample at: a) post-intervention, b) follow-up?
- Does HVBR lead to improved subjective positive affect in comparison to an active placebo control in a general population adult sample: a) immediately after the first session of breathwork, b) at post-intervention.
- Does HVBR lead to improved subjective negative affect in comparison to an active placebo control in a general population adult sample: a) immediately after the first session of breathwork, b) at post-intervention.

Exploratory Hypotheses

Additionally, we want to see if pre-post changes are correlated with a) adherence (amount of breathwork practice, i.e., is there a dose response?), and b) credibility and expectancy of the breathwork intervention given. We would expect both greater adherence (in the HVBR practice arm) and credibility/expectancy to be associated with greater improvements on the outcome measures listed. If there are significant differences between groups on credibility/expectancy then covariance analysis will be explored, to test whether differences between groups in credibility/expectancy are accounting for any measured differences in outcomes at post-intervention.

Methods

Participants

200 people (100 per group) will be recruited. We will also select the balanced sample filter option on Prolific so as to distribute the study evenly across gender. A moderate effect size, statistical power and significance level of 0.50, 0.80 and 0.05, respectively, requires a sample of 128 participants (64 per group). PsyDAO, a decentralised organisation funding research at the intersection of psychedelics and mental health, provided funding for participant payments for a sample size of 200 participants, so this was the largest sample possible, and also allows for potential attrition. The two previous published RCTs of Balban et al. (2023) and Kopplin and Rosenthal (2022) had final samples of N=108 (4 groups; HVBR condition n=33) and N=86 participants (4 groups; HVBR condition n=20), respectively. The former study was adequately powered statistically, but the latter was not (actually required a sample size of 100).

The (self-assessed) inclusion criteria are as follows: -Comfortable with holding breath, -Comfortable with faster breathing, -Willing to only practice breathwork in safe environment, lying down in soft area (i.e., bed, sofa, carpet/mat), and always away from water and hard ground, -Willing to only practice the breathwork away from large meals (i.e., before or one hour after) and bedtime (i.e., at least one hour before if practicing in evening), -Have access to headphones. The following pre-screeners on Prolific will also be set so only those eligible on Prolific will see the study: 18-39 years of age (18 is the automatic minimum age on Prolific), Located/living in UK, Fluent in English, approval rate of 98% and at least 20 previous submissions (as recommended by Prolific to increase retention and reduce dropout rates in longitudinal and multi-part studies).

The comprehensive (self-assessed) exclusion criteria are as follows: -Hypotension or hypertension (low or high blood pressure), -History of respiratory or cardiovascular/heart problems or disease, -History of fainting or syncope, -Epilepsy or seizures, -History of panic disorder or panic attacks, Cerebral aneurysm, -Have had problems with prior breathwork sessions (i.e., fainting), -Pregnancy or think one might be pregnant, trying to get pregnant, or are breastfeeding, -Any problems which affect one's ability to pace their breathing (i.e., active/chronic respiratory infection including blocked nose/cough/cold/fever, etc.), breathlessness, abnormally slow breathing (bradypnea), or abnormally fast breathing (tachypnoea), -Any other physical/mental health conditions or current life events which impair or affect one’s ability to engage in activities involving breath control, -Taking any regular medication other than the contraceptive pill, including medications to reduce blood pressure (i.e., Ramipril or other ACE-inhibitors), beta blockers (i.e., Propranolol), antidepressants, anxiolytics, or any other psychotropic medications.

Outcome measures

All outcomes (primary, secondary, other) are mentioned below.

Pre-post intervention and follow-up questionnaires will be self-completed by participants online via the survey platform Qualtrics, which will be linked to Prolific. Three short scales will be used to measure trait outcomes of mental health, wellbeing and sleep-related impairment at these timepoints (baseline/pre-intervention, post-intervention, three-week follow-up): the Depression Anxiety Stress Scale (DASS-21) (Lovibond, & Lovibond, 1995), Short Warwick-Edinburgh Mental Wellbeing Scale (SWEMWBS) (Ng Fat et al., 2017), and PROMIS Item Bank v. 1.0 - Sleep-Related Impairment - Short Form 4a (PROMIS-4a) (Hanish, Lin-Dyken & Han, 2017). The primary outcome will be stress (measured using the DASS-21 stress subscale), and the primary timepoint will be post-intervention (three weeks

post-randomisation). The secondary outcomes will include: anxiety and depression (from DASS-21), mental wellbeing (SWEMWBS) and sleep-related impairment (PROMIS-4a). State measures of positive and negative affect using the Positive and Negative Affect Schedule (PANAS-20) (Watson, Clark & Tellegen, 1988) (secondary outcomes) will also be completed during the baseline survey. Immediately after starting the breathwork (first session of breathwork), participants will be asked about the credibility and expectancy of the intervention randomly allocated to them to assess if the intervention and placebo are seen as equally credible and thus merit equal expectation of benefit. This will be measured using the Credibility/Expectancy Questionnaire (CEQ-6), which is another secondary outcome. The PANAS-20 will also be completed once at this timepoint, to gauge a sense of state change due to the breathwork, in addition to once more at post-intervention. The last secondary outcomes, which will be measured post-intervention, are: negative side effects (to judge the safety and tolerability profile of the breathwork) and adherence to protocol (number of times participants self-reported practicing breathwork out of the 21 days assigned). Other outcomes include general sentiment towards the protocol (i.e., positive, negative, neutral) and open-ended questions on participants overall experiences of the protocol and/or study period. Pre-intervention, simple demographics (Age, Gender and Ethnicity) will be collected and, at follow-up, participants will be asked if they can guess which condition they were allocated to (to tentatively see if blinding was successful—see Procedure section).

Primary outcome measure

1. Subjective stress (DASS-21 stress subscale)

Secondary outcome measures:

2. Subjective anxiety (DASS-21 anxiety subscale)
3. Subjective depressive symptoms (DASS-21 depression subscale)
4. Subjective mental wellbeing (SWEMWBS)
5. Subjective sleep-related impairment (PROMIS-4a)

[All of above outcomes measured pre-post-follow-up]

6. Subjective positive affect (PANAS-20 positive affect subscale). Measured pre-intervention, after first breathwork session, and post-intervention.
7. Subjective negative affect (PANAS-20 negative affect subscale). Measured pre-intervention, after first breathwork session, and post-intervention.
8. Self-reported credibility and expectancy of protocol (CEQ-6). Measured after completing first session of breathwork.
9. Negative side effects due to protocol (whether participants experienced unpleasant/unwanted a) short-term effects, and/or b) lasting bad effects from the breathwork, to gauge safety and tolerability). Measured post-intervention.
10. Self-reported adherence to breathwork protocol (number of sessions participants self-report practicing out of 21 days assigned). Measured post-intervention.

Other—Overall experience, Hypothesis guessing, Attention checks

Optional questions on participants' perspectives and overall experience of the protocol (post-intervention) / study-period (follow-up), and if they can correctly guess which condition they were allocated to (follow-up). Lastly, The DASS-21, SWEMWBS, PROMIS-4a, and PANAS-20 will all have one attention-check question in them to ensure participants are completing the surveys properly.

Procedure

Participants will be recruited entirely online via the research study platform Prolific to gain a general population sample. Participants will see a title of the study, a description (describing what participants will be doing in the study), including the participant information sheet and consent form with all key information that will help them to decide if they wish to participate. It will also be specified that the study requires audio. Participants will see all this information before they choose to take part in the study, allowing them to make an informed choice as to whether they'd like to participate. Again, pre-screeners on Prolific will also be set so only those eligible on Prolific will see the study on the platform: 18-39, Located/living in UK, Fluent in English, approval rate of 98% and at least 20 previous submissions (as recommended by Prolific to increase retention and reduce dropout rates in longitudinal and multi-part studies). Participants will be paid to complete the surveys (30min total for all parts) at the hourly rate of 9GBP/hour (4.50GBP in total) which is deemed as a good, recommended amount by Prolific. We unfortunately do not have funds to pay participants to complete the daily breathwork (classed as low effort activity by Prolific). Daily reminder messages will be sent through Prolific to practice breathwork over the 21 days and keep a record of number of times practiced. All participant data will be anonymous (only Prolific user IDs will be seen). No identifiable personal information will be collected. When the first (baseline/pre-intervention) survey is complete we will get the participant IDs of the relevant Prolific participants. We will then invite these participants to the subsequent surveys (e.g., post-intervention) using a custom allowlist on Prolific (only those on the allowlist will see the study on their Prolific profile). As we have two conditions and want to keep these conditions consistent between surveys, separate identical surveys for each condition are set up. However, only one pre-intervention survey is needed as Qualtrics supports allocation to conditions from one URL. Messages will also be sent through Prolific to complete post-intervention and follow-up questionnaires when required.

Intervention & Comparator

Participants in the intervention group will be randomised to a guided audio of HVBR pre-recorded by a trained breathwork facilitator for ~20min/day over 21 days (three weeks). This will be delivered remotely online through audio link, and comprises evocative music and four rounds of hyperventilation with four separate retentions (breath holds), progressively increasing in length (from ~45seconds up to ~90 seconds). The average number of HVBR rounds used is usually 3-4, so four rounds were chosen for the intervention group. The duration of ~20min was deemed as a manageable time for participants, and several studies (ranging from days to weeks) on meditation have shown benefit can be derived from this low-to-moderate length of practice.

Participants in the control group will be randomised to a guided audio of placebo ‘sham’ HVBR pre-recorded by a trained breathwork facilitator for ~20min/day over three weeks. This will be delivered remotely through audio link, comprising music and four rounds of paced breathing at 15b/min (equal inhale:exhale without pauses) with four separate (shorter) retentions, slightly increasing in length (from ~10secs to ~25secs). The metric of 15b/min is in line with guidance from the British Journal of Nursing, Royal College of Physicians, and Johns Hopkins University which state that the average, healthy rate should range from: 12-18, 12- 20, and 12-16b/min, respectively.

Randomisation & blinding

The type of study is participant blinded RCT with assessor blinded data collection (that is, assessor is not present for data collection which is self-completed by the participant on a survey software platform). After completing the pre-intervention survey, participants will be

randomly assigned, via the online survey software Qualtrics using block randomisation (1:1), to receive either the intervention (HVBR), or placebo (15b/min). Participants will be blinded to their intervention (concealment)—the study is referred to as the Sussex Fast Breathwork Study and the technique of breathwork will be referred to as 'rhythmic breathing' in both the active intervention and placebo control breathwork audios, in an attempt to blind participants to the intervention being used.

Safety & ethical considerations

This study has been approved by the Research Ethics Committee at the University of Sussex Sciences & Technology C-REC (reference: ER/GF221/5).

References

Balban, M. Y., Neri, E., Kogon, M. M., Weed, L., Nouriani, B., Jo, B., ... & Huberman, A. D. (2023). Brief structured respiration practices enhance mood and reduce physiological arousal. *Cell Reports Medicine*, *4*(1).

Devilly, G. J., & Borkovec, T. D. (2000). Psychometric properties of the credibility/expectancy questionnaire. *Journal of behavior therapy and experimental psychiatry*, *31*(2), 73-86.

Fincham, G. W., Strauss, C., Montero-Marin, J., & Cavanagh, K. (2023). Effect of breathwork on stress and mental health: A meta-analysis of randomised-controlled trials. *Scientific Reports*, *13*(1), 432.

Hanish, A. E., Lin-Dyken, D. C., & Han, J. C. (2017). PROMIS sleep-related impairment and sleep-related impairment in adolescents: examining psychometrics using self-report and actigraphy. *Nursing research*, *66*(3), 246.

Kopplin, C. S., & Rosenthal, L. (2022). The positive effects of combined breathing techniques and cold exposure on perceived stress: a randomised trial. *Current Psychology*, 1-13.

Kox, M., Van Eijk, L. T., Zwaag, J., Van Den Wildenberg, J., Sweep, F. C., Van Der Hoeven, J. G., & Pickkers, P. (2014). Voluntary activation of the sympathetic nervous system and attenuation of the innate immune response in humans. *Proceedings of the National Academy of Sciences*, *111*(20), 7379-7384.

Lovibond, S.H. & Lovibond, P.F. (1995). *Manual for the Depression Anxiety & Stress Scales*. (2 Ed.) Sydney: Psychology Foundation.

Ng Fat, L., Scholes, S., Boniface, S., Mindell, J., & Stewart-Brown, S. (2017). Evaluating and establishing national norms for mental wellbeing using the short Warwick–Edinburgh Mental Well-being Scale (SWEMWBS): findings from the Health Survey for England. *Quality of Life Research*, *26*, 1129-1144.

Mattson, M. P. (2008). Hormesis defined. *Ageing research reviews*, *7*(1), 1-7.

Petraskova Touskova, T., Bob, P., Bares, Z., Vanickova, Z., Nyvlt, D., & Raboch, J. (2022). A novel Wim Hof psychophysiological training program to reduce stress responses during an Antarctic expedition. *Journal of International Medical Research*, *50*(4), 03000605221089883.

Sevoz-Couche, C., & Laborde, S. (2022). Heart rate variability and slow-paced breathing: when coherence meets resonance. *Neuroscience & Biobehavioral Reviews*, 104576.

Watson, D., Clark, L. A., & Tellegen, A. (1988). Development and validation of brief measures of positive and negative affect: the PANAS scales. Journal of personality and social psychology, 54(6), 1063.