Protocol V2

Amendment 01, changes are after recruitment and intervention ended and before analysing the data, resulting in Protocol V2 (registered before start of analysis).

Date 20.07.23

1. Changes to hypothesis: changes are to specify the hypothesis.

   Hypothesis 2. Elevated belief updating about one's self-efficacy in interoceptive control (as compared to their prior at T0 and quantified using different computational methods (see https://psyarxiv.com/rntsf/) will mediate the expected primary outcomes change fromT0 to T1 in the InMe arm (primary mechanism see secondary outcomes 15.2.1.1).

2. Changes to the secondary outcome: changes are to specify the measure.

   Measures of Interoception:

   a. Updating of prospective interoceptive self-efficacy beliefs about one's ability to downregulate their HB (hereafter referred to as interoceptive control) will be tested as one of the primary mechanisms of change. We will first develop and compare different indexes, and secondarily computational models of this updating under a Bayesian learning framework (using an existing approach; see https://osf.io/x4ysv). These indexes will be used in subsequent analysis of the mechanisms of action on observed behavioural changes, while the models yielding the best model fit and values of validity testing will be used to determine some of the latent parameters that may be driving belief updating differences between the arms of the trial, or between participants. We anticipate that the beneficial effects of the target intervention, in comparison with those of the control arm, will be mediated by greater effects on self-efficacy beliefs.

   b. Interoception accuracy (as measured by the HRD) at T1b and T2 (as compared to T0)

   c. Interoceptive global Metacognitive sensitivity (as measured by the HRD) at T1b and T2 (and compared to T0)

   d. Perceptual self-efficacy beliefs on interoception (global perceptual metacognition indexes, asked before and after the HRD)

3. Changes to the Planned data analysis: Changes are to specify the statistical analysis plan (SAP).

   Analyses will be conducted following the intention-to-treat principle by a data analyst (blind to treatment allocation) with oversight from a senior statistician (blind to treatment allocation). All analyses relating to the objectives stated in this protocol will

be prespecified in a statistical analysis plan (SAP), which will be finalised and approved by an external trial statistician before data collection is completed. The data set not containing group allocations for blinded analyses will be provided to the data analyst only after the final SAP has been signed off by the chief investigator, senior statistician and an independent to the trial statistician. All analyses will be conducted using R. Note that before finalisation of the SAP, we will use mock randomisation to verify the plan. Means/standards deviations and frequencies with percentages will be used to describe the baseline characteristics of the sample and the post-randomisation outcome measures at each time point by group.

Intervention effects, at each time point, will be estimated using linear mixed-effects models with random effects accounting for repeated observations. Covariates will include, age, BMI and gender. Other sociodemographic covariates such as ethnicity, as well as prior experience/practice with biofeedback or other mindfulness techniques will be explored in a post-hoc analysis. Unstandardized and standardised effects estimates will be presented with 95% CIs.

Sensitivity analysis will be conducted for the primary outcome to assess the impact of missing data, using a multiple imputation approach, to deal with missing data due to loss to follow up. In this approach, models are run under a range of plausible scenarios with missing data imputed.

For mediation analysis, the mechanisms of action of the intervention will be examined for the primary outcome and key secondary outcomes (e.g., mental health symptoms see section 15.2.2), using mediator analysis in a structural equation modelling framework using the intention-to-treat sample. Specifically, the mediatory role of interception self-efficacy beliefs (see 15.2.1), will be assessed to explain any treatment effects at T1 (compared to T0) and T2 (compared to T0) on the primary outcome and key secondary outcomes (e.g., mental health symptoms see section 15.2.2). Analyses will estimate the total effect, indirect effect and proportion of the treatment effect on the outcomes that occurs via this putative mediator variable. These effects will be presented with 95%CIs only, as not powered to detect.

For moderation analysis, we will consider the following variables as possible treatment modifiers of our primary and key secondary outcomes: core dimensions of compulsivity, intolerance of uncertainty at baseline.

Following correlation analyses, we will also conduct exploratory moderation analyses with these variables: HRV at baseline, emotion regulation at baseline, general self-efficacy at baseline, perceptual self-efficacy beliefs updating (from HDT).

Analysis for each putative moderator will include the main effect and intervention group by moderator interaction term in the mixed-effects model used to estimate the

treatment effect for the primary/secondary outcome, based on the intention-to-treat sample. These effects will be presented with 95%CIs only, as not powered to detect.

In addition, Initial analysis of the expected heartrate increase/decrease following the intervention will be conducted to ensure that aberrant responses in this respect are taken into account in our final analyses. For example, the above analyses will be conducted also without participants who did not respond to the stressor/intervention (i.e., insufficient increase/decrease (2.5sd change below/above the average or change of at least 5 heart beats) of their heart rate during the stressor or following the intervention).

Note that analysis aiming to investigate the hypothesis on the maintenance of the effects (T2 from T0) for the primary and secondary outcomes will include only those who completed the follow-up testing no more than 10 days before the expected due date of follow-up (7-9 weeks from T0) and no more than 10 days after the expected due date of follow-up.