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Methodology and Research Protocols

# Behavioral Activation Augmented With Mobile Technology for Depression and Anxiety in Chronic Moderate-Severe Traumatic Brain Injury: Protocol for a Randomized Controlled Trial

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**KEYWORDS**
Anxiety disorders;
Brain injuries;
Depression;
Rehabilitation

**Abstract** *Objective:* To describe and provide the rationale for a randomized controlled trial for depression or anxiety after moderate to severe traumatic brain injury (TBI), which will test 2 treatments based on behavioral activation (BA), a promising model to promote both positive mood and increased activity in this population.
*Design:* Randomized controlled trial with masked outcome assessment.
*Setting:* Outpatient catchment area of 1 TBI treatment center.
*Participants:* Community-dwelling persons (N=60) with moderate-severe TBI at least 6 months prior to enrollment and greater than mild depression or anxiety.
*Interventions:* Participants will be randomized 2:1 into an 8-session treatment, behavioral activation with technology, consisting of 6 face-to-face sessions and 2 via phone, with mood and activity monitoring conducted via ecological momentary assessment on a smartphone;

*List of abbreviations:* ANOVA, analysis of variance; BA, behavioral activation; BADS, Behavioral Activation for Depression Scale; BAT, Behavioral Activation with Technology intervention arm; BSI-18, Brief Symptom Inventory-18; EMA, ecological momentary assessment; EROS, Environmental Reward Observation Scale; FTF, face-to-face; GSI, Global Severity Index; INT, intention; PART-O, Participation Assessment with Recombined Tools-Objective; PGIC, Patient Global Impression of Change; QOLIBRI, Quality of Life after Brain Injury; RCT, randomized controlled trial; SMS, short message service; SWLS, Satisfaction With Life Scale; TBI, traumatic brain injury.

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or a single session incorporating BA principles followed by 8 weeks of activity reminders in the form of implementation intentions, delivered as text messages.
*Main Outcome Measures:* Brief Symptom Inventory-18 (primary outcome); Environmental Reward Observation Scale, Behavioral Activation for Depression Scale, Participation Assessment with Recombined Tools-Objective, Diener Satisfaction With Life Scale, Quality of Life after Brain Injury scale, Patient Global Impression of Change. Outcomes are measured midway through intervention, after treatment cessation (primary outcome), and at 2-month follow-up. A treatment enactment interview is administered after the follow-up to ascertain to what extent participants continue to engage in activities and use strategies promoted during trial participation.
*Results:* N/A.
*Conclusions:* N/A.
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Depression and anxiety are prevalent after moderate-to-severe traumatic brain injury (TBI)[1-3] and are associated with diminished social and community activity and poor quality of life.[2-6] To date, there are no practice guidelines for treating these disorders in TBI.[7] Based on evidence that reduced activity precedes depression more than the reverse relation in TBI,[8,9] behavioral activation (BA) has been suggested as a promising treatment.[10] BA is based on the hypothesis that gradual, scheduled increases in rewarding activities alleviate depression and anxiety via environmental reinforcement.[11] A TBI depression trial revealed that increased exposure to environmental reward, in the form of pleasurable and meaningful activity, was the strongest predictor of improvement.[12] BA is particularly suited to activity restrictions due to medical conditions,[13,14] and even a brief *dose* can have a significant effect.[15] A key process is monitoring associations among activities and emotions, so that activities connected to positive states may be increased. Traditionally, paper diaries have been used for this purpose, but monitoring may also be achieved via ecological momentary assessment (EMA), consisting of periodic self-reports delivered by smartphones.[16]

In a recent randomized controlled trial (RCT), we examined the effects of one 2-hour session of BA, supplemented by 8 weeks of daily text (short message service [SMS]) messages in the form of *implementation intentions* developed collaboratively between patient and therapist, on depression or anxiety in people with chronic, moderate to severe TBI. Implementation intentions are if-then statements that, if rehearsed, serve to keep intentions in mind so that desired behaviors are more likely to occur in preidentified trigger situations: for example, "If I'm feeling groggy, sleepy, or bored, then I'll get down to the gym." Implementation intentions have shown robust effects on health-related and prosocial behaviors.[17-19] Our comparison treatment provided 1 educational session on the importance of motivation for achieving goals, followed by 8 weeks of daily motivational messages via SMS. Both conditions resulted in modestly improved emotional status, and BA participants reported greater exposure to environmental reward and increased productive activity.[20] Feasibility of the SMS delivery method was amply confirmed. Despite interesting qualitative findings suggestive of differential mechanisms of action in the 2 conditions, the gains in each were of questionable clinical significance, prompting us to design the present RCT using the prior BA treatment as a control condition (now called INT, for intentions) for a more intensive treatment, BA with technology (BAT). This includes more of the elements in traditional multisession BA, plus EMA and activity reminders delivered through SMS. We will examine persistence of treatment effects via a 2-month follow-up and a final interview to assess *treatment enactment*, the extent to which participants continue to use intervention content in everyday life.[20,21] We hypothesize that (1) the BAT intervention will lead to significantly greater positive change from baseline to post-treatment compared to the INT condition on measures of emotional distress (primary outcome) and secondary outcomes; and (2) the superiority of BAT will persist to the 2-month follow-up.

In this article, we present the details of the protocol for this RCT, including the interventions, measures, and data analytic plan.

## Method

### Overview of design

This study is an RCT with masked outcome assessment, registered at clinicaltrials.gov as [NCT02061553]. After screening for eligibility and informed consent, participants undergo a baseline assessment, T1, to characterize the population regarding the cognitive and functional status in addition to obtaining baseline values on the outcome measures (described later). Next, participants are randomized 2:1 into BAT or INT. The 2:1 randomization will allow a higher number of participants in the arm with the intervention thought to be more promising (BAT). It will also afford a secondary analysis that includes data for ~80 participants, 60 participants from this trial, and ~20 participants from the prior trial, because the INT condition in the current trial is identical to that of the prior trial[20] regarding the inclusion criteria and assessment or

treatment procedures. This secondary analysis will maximize experimental power by creating study groups of equivalent size (~40 in each condition) while optimizing the use of a limited participant pool. Intervention (described below) begins as soon as feasible after T1, typically in the afternoon of the same day. An interim assessment, T2, is performed via telephone after 4 weeks of treatment (INT) or 4 sessions (BAT). Post-treatment assessment, T3, is conducted after treatment, with T4 (follow-up) 8 weeks later. Finally, a treatment enactment interview is conducted via telephone to assess the extent to which participants are maintaining the use of learned principles, and still performing activities planned in therapy sessions, more than 2 months after cessation of intervention. Figure 1 shows the timeline of the study, including the assessment and treatment sessions.

## Participants

Participants are 60 persons who meet the following inclusion criteria: (1) age ≥18; (2) TBI (open or closed), sustained at least 6 months prior to enrollment, of at least complicated-mild injury severity as evidenced by (a) loss or alteration of consciousness not due to intoxication or sedation *and* documented prospectively from the injury (ie, not retrospectively self-reported); and/or (b) positive neuroimaging findings consistent with TBI; (3) at least mild depression or anxiety as evidenced by a score of >5 on the Patient Health Questionnaire-9 or Generalized Anxiety Disorder-7 screening tools,[22,23] but without suicidal ideation; (4) able to travel or arrange travel independently in the community (to maximize the probability that participants will be cognitively and physically able to engage in the treatment); (5) fluent in English and able to communicate adequately for participation in the treatment protocols; and (6) informed consent given by participant or legally authorized representative. Participants are excluded for (1) history of serious mental illness such as schizophrenia or well-documented bipolar disorder; (2) current psychiatric instability, including very severe depression and anxiety as indicated by Patient Health Questionnaire-9 or Generalized Anxiety Disorder-7 ≥20, current substance dependence, or active suicidal ideation; (3) significant cognitive disability for reasons other than TBI (eg, developmental disability); (4) concurrent involvement in one-to-one counseling or psychotherapy more than once per month for emotional issues; and (5) inability to use a smartphone due to sensorimotor limitations (eg, blindness, bimanual paresis). Participants who have been on a stable dose of a psychoactive medication for depression or anxiety for at least 4 weeks are not excluded, but concurrent medications and other nonexcluded treatments are measured at every assessment point throughout the trial, to allow for the possibility of post hoc analyses of the influence of these treatments on outcomes.

## Measures and procedures

Baseline (T1) measures include basic demographic information (age, sex, race and ethnicity, education) and available medical chart data pertaining to TBI etiology (mechanism) and severity. The latter may include such indices as the Glasgow Coma Scale[24] score on admission to emergency care, duration of unconsciousness, or duration of posttraumatic amnesia. Because primary medical records for participants with chronic TBI are often incomplete and inconsistent, we include in T1 a standardized interview used in our previous studies[20,25-29] to elicit a retrospective estimate of posttraumatic amnesia duration, as a measure of TBI severity common to all participants. *Cognitive/functional status* is measured using the Wechsler Abbreviated Scale of Intelligence (Vocabulary and Matrix Reasoning subtests),[30] the Rey Auditory Verbal Learning Test,[31] the Trail Making Test parts A and B,[32] and the Brixton Spatial Anticipation Test.[33] Functional status is assessed using the Extended Glasgow Outcome Scale.[34]

Measures related to *emotional status/behavioral activation* include the Global Severity Index (GSI) of the Brief Symptom Inventory-18 (BSI-18) items,[35] the Environmental Reward Observation Scale (EROS),[36] with the reference period adjusted to 4 weeks, and the Behavioral Activation for Depression Scale (BADS).[37] *Societal/community participation* is measured using the Participation Assessment with Recombined Tools-Objective (PART-O), with separate examination of the 3 subscales measuring social relations, community activity, and productivity.[38,39] *Satisfaction with life* is measured using the Diener Satisfaction With Life Scale (SWLS)[40] and health-related quality of life, specific to brain injury, with the Quality of Life after Brain Injury (QOLIBRI) scale.[41,42] Participant assessment of overall change and its effect is measured using the Patient Global Impression of Change (PGIC).[43] The BSI-18, EROS, BADS,

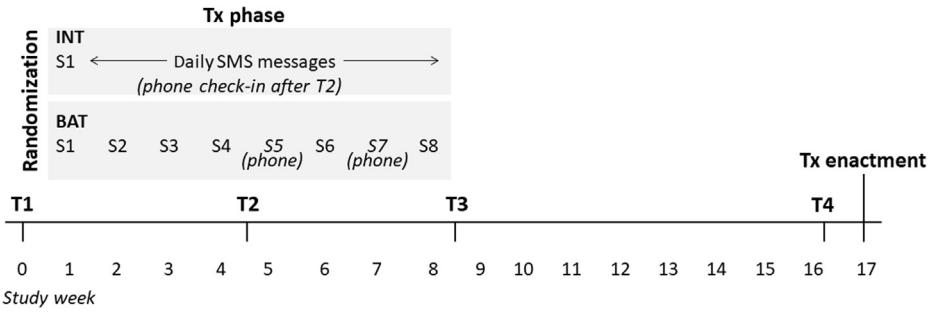


**Fig 1** Schematic of study timeline showing treatment phases and assessment intervals (labeled as T1-T4). Abbreviations: S, session; Tx, treatment.

PART-O, SWLS, and QOLIBRI are administered at all assessment points (T1-T4). The PGIC is administered at T2, T3, and T4.

Assessment masking at T2-T4 is achieved through precautions such as a script read by the examiner at the start of all data collection sessions, reminding participants not to discuss any details of treatments or messages they have received. Treatment staff also remind participants of this during any contacts preceding an assessment. Any instances of inadvertent unmasking are recorded for later analysis of their influence.

The treatment enactment interview is conducted via telephone by a master-trained research assistant with prior experience in interviews of this type, but with no other role in the project (ie, no previous contact with participants). In the interview, BAT participants are asked whether and how frequently they are continuing to use an activity schedule and whether they have added any new activities since the study ended. INT participants are asked whether their implementation intention messages still occur to them and whether they have created additional reminders for themselves in that format. Participants in both conditions are asked to rate from 1 (no, or almost no) to 10 (optimal) the level of meaningful and pleasurable activity in daily life (a) currently, (b) at the end of the study 2 months before, and (c) before the study began. Participants are also asked to describe "the #1 most helpful thing about being in the study."

This study is approved and overseen by an institutional review board and complies in full with all protections for human participants as required by the Helsinki Declaration.

## Randomization

As in the previous trial,[20] the 2:1 randomization to BAT or INT, respectively, is stratified by severity of emotional distress, using a cut score of T=60 on the BSI GSI. The randomization process uses a sequence of permuted blocks randomly selected from sizes 6, 9, and 12. Only study therapists may access a secure randomization spreadsheet, which keeps all but the current treatment assignment obscured from view. Randomization is performed by the therapist immediately after baseline assessment (T1) is completed.

## Interventions

Study therapists include 1 master-trained and 3 doctoral-level clinicians with extensive experience in neuropsychological rehabilitation. All therapists are trained to deliver both treatments, which are supported by detailed manuals, minimizing the possibility of contamination across conditions. Therapists meet weekly to elicit peer feedback on clinical issues as well as to discuss procedural aspects of the trial.

Both interventions require the use of a smartphone. For participants who do not own one, we provide an LG Fiesta 2 smartphone with an unlimited texting plan for the duration of the trial. For participants who do not already use SMS, we provide training and hands-on practice in how to send and receive text messages. We also provide an illustrated manual with step-by-step instructions for using the study phone to send and receive messages.

Both interventions also make use of a secure cloud-based system, called MossGoal, that was created for the previous RCT.[20] MossGoal allows users to enter SMS messages as free text, to preschedule them for specified dates and times, and to edit both messages and schedules at will. The system also stores all replies to messages as date- and time-stamped texts.

### SMS condition

Participants assigned to the SMS condition receive 1 face-to-face (FTF) and 1 telephone-based session supplemented by 8 weeks of daily SMS messaging (see fig 1). The FTF session begins with lay-language education on the underlying assumption of BA: that mood disorders can result in part from a *vicious cycle* in which inactivity and low mood reinforce one another. Participants are shown and encouraged to comment on a list of common reasons for inactivity after TBI, including physical limitations, cognitive problems, loss of opportunity through work or school or preinjury social contacts, and logistical reasons such as limitations in finances and transportation. Participants are counseled that the vicious cycle may be gradually reversed by countering avoidance and undertaking increases in pleasurable and meaningful activities, rather than waiting until mood or circumstances might motivate such change. They are then encouraged to brainstorm a list of possible activities to engage in during the trial. These can be previously rewarding activities that participants might want to resume, do more of, or do differently, or new activities that they would like to try. To assist with this brainstorming, participants are asked to consider 7 life areas that might invoke desired activities; these are presented one at a time on tent cards labeled recreation, relaxation, and creativity; relationships and social life; physical health and fitness; spirituality and mental health; learning and developing interests; working and contributing; and daily responsibilities.

Once a participant has generated a list of potential activities, the therapist works with him or her to identify at least 4-5 that are (1) important to the participant; (2) realistic (ie, doable without extensive planning or additional resources); and (3) capable of being repeated over the succeeding 8 weeks (eg, a *one-shot* activity of taking a vacation would not be selected). The therapist then assists participants to develop 8-10 implementation intentions, phrased as if-then statements, specifying the actions to be implemented (the *then* portions) and under what conditions they should be done (the *if* portions). These implementation intentions may either specify action plans directly, or coping plans, which specify what to do if obstacles are encountered (thus overcoming avoidance patterns). The therapist assists the participant in creating a weekly schedule for receiving the messages; we encourage receipt of each one at least several times per week, but there is considerable flexibility permitted. Participants are asked to reply to each message by sending a brief paraphrase or keyword(s); this is to help ensure that messages are being received and read, and replies are stored for later calculation of response rate. The final procedure in the FTF session is a practice message sent in real time to the

**Table 1** Custom EMA protocol for the BAT condition

| Items Viewed by Participants | Response Options |
|---|---|
| (PANAS items, each rated separately): Interested, Distressed, Excited, Upset, Strong, Guilty, Scared, Hostile, Enthusiastic, Proud, Irritable, Alert, Ashamed, Inspired, Nervous, Determined, Attentive, Jittery, Active, Afraid | (one per PANAS adjective)<br>Not at all<br>A little<br>Moderately<br>Quite a bit<br>Extremely |
| (Additional item recommended by consultants): Bored | Not at all<br>Somewhat<br>Moderately<br>Quite a bit<br>Extremely |
| What have you been doing over the past hour or so? | (choose all that apply)<br>Learning/school activity<br>Working<br>Household chores/pet care<br>Leisure activity<br>Pray/worship/meditate<br>Resting/sleeping<br>Watching TV/video<br>Walking<br>Shopping/errands<br>Talking or socializing<br>Reading<br>Listening to music/radio/podcast<br>Playing videogames/E-games<br>Active play/sports/exercise<br>Intimate relations<br>Social media/Internet/e-mail/texting<br>Preparing food/cooking<br>Care of children<br>Other |
| How enjoyable was this activity? | (choose one)<br>Not at all<br>A little<br>Moderately<br>Quite a bit<br>Extremely |
| Did this activity give you a sense of accomplishment? | (choose one)<br>Not at all<br>A little<br>Moderately<br>Quite a bit<br>Very much so |
| Who were you *primarily* doing this activity with? | (choose one)<br>Alone<br>Family<br>Friends<br>Spouse or significant other<br>Mixed group of family and friends<br>Peers or coworkers<br>Professionals<br>Strangers<br>Pets<br>Others |
| Where are you? | (choose one)<br>Learning facility<br>Health care facility<br>Entertainment facility<br>Gym or exercise facility<br>Home<br>Work<br>Park/forest/out in nature<br>Public sidewalk/street<br>Religious facility<br>Store or mall<br>Someone else's home<br>Restaurant/bar<br>Other |

Abbreviations: PANAS, Positive and Negative Affect Scale; TV, television.

participant's phone. The participant replies to the message under the therapist's supervision with guidance as needed.

After 4 weeks of receiving the messages and after the T2 assessment has been completed, the therapist contacts the participant by telephone to review the relevance or helpfulness of each message and the overall schedule. Participants are given the opportunity to change, remove, or add messages or change the schedules of receipt. The resulting schedule is then maintained for the second 4-week period of study participation, after which messages are terminated and the T3 or T4 assessments administered.

### BAT condition

The manual for this treatment arm was based on published models of BA[11,44] as well as input from 2 consumer consultants, people with chronic severe TBI who had experienced depression and/or anxiety after injury. These consultants provided invaluable input on the *flow* of treatment sessions as well as guidance regarding the verbiage to be used and the incorporation of EMA data.

The EMA data are collected via the LifeData System,[a] a flexible mobile platform which allows researchers to custom-design assessment or intervention protocols and deliver them using a smartphone app called RealLife Exp. Participants are assisted in downloading RealLife Exp to their device via the Apple App Store or Google Play. For this study, we program the app to *ping* (notify the participant to answer) a set of questions 5 times per day, pseudo-randomized within a 14-hour window to correspond with participants' typical waking hours. Each set of questions includes the 20-item Positive and Negative Affect

Schedule,[45] a reliable, valid, and widely used self-report measure of mood states. For later correlation to mood states, we follow these items with questions about the participant's activity, context, and location during the past hour. Table 1 lists all questions and response options delivered in each *ping*. Options are selected with radio buttons displayed on their screens; there is also the option to supplement all choices with free text entries.

Participants' responses are uploaded via the cloud or WiFi, such that updated data are available to the therapist between appointments. Prior to each FTF session, the participant's EMA data are downloaded from the secure LifeData website and converted to graphics which may be used from Session 2 onward (see below). These graphics include pie charts depicting time spent in various kinds of activities and bar graphs showing the associations among activity categories and levels of positive or negative affect and perceived reward.

As shown in fig 1, the BAT condition comprises 8 weekly sessions: 6 FTF (wk 1, 2, 3, 4, 6, 8) and 2 by telephone (wk 5 and 7). Session 1 begins identically to the INT session, with an overview of the vicious cycles of inactivity, avoidance and low mood, and an explanation of how BA acts to reverse these cycles. The process of EMA is introduced with examples, the RealLife app is installed on the participant's phone, and the therapist provides guided practice until the participant is comfortable and accurate in using the app. No changes to participants' activities are recommended in this session, because the purpose of the first week is to begin collecting data on current activity patterns and their associations to feeling states. Participants are given a binder that includes an illustrated manual with reminders for how to respond to RealLife *pings*, a troubleshooting guide, and a contact number for reporting any problems to the therapist.

Session 2 introduces the concept of values as guiding principles by which to choose activities that give a sense of purpose and meaning to life. Participants are prompted to identify their core values and to link both current and desired activities. They are assisted by visual aids prompting consideration of 6 life areas that overlap with, but are not identical to, those in the INT condition: relationships and social life; learning and developing interests; mental health and spirituality; physical health and well-being; recreation and relaxation; and productive community involvement. The therapist assists in recording values and activities on a worksheet, which is completed at the start of Session 3. This worksheet is used in succeeding sessions as a source of ideas for new, values-based activities to pursue. Next, the graphics from the previous week's RealLife output are reviewed and examined for patterns. A written schedule for the succeeding week is created collaboratively between therapist and participant, who is encouraged to add 1 or 2 new activities to his or her routine. Finally, SMS messages are developed to remind the participant of key activities and, often, the values they fulfill. A schedule is then created for these messages to be sent via MossGoal in the coming week.

Sessions 3-7 follow the same general pattern, as follows (Sessions 3, 4, 6 are FTF, 5 and 7 are by phone): (1) Review of the activities scheduled for the previous week, with discussion of any obstacles and the participant's reaction to new activities (whether they were easy or difficult, enjoyable, etc). (2) (in FTF sessions) Review of the RealLife data outputs to date, with discussion of any notable patterns, including longitudinal changes in positive or negative affect and feelings of enjoyment and accomplishment as more data become available. (3) Creation of a written schedule for the coming week, with more activities gradually added, and the participant gradually given more responsibility or less prompting for planning and troubleshooting as well as writing into the schedule form. (4) Creation and scheduling of reminder SMS messages to be sent via MossGoal, as above. In Session 6, the participant is told that these reminder messages will cease after Session 7, and the therapist prompts him or her to develop a system for replacing them.

Session 8 includes a personalized review of the rationale for BA and the importance of activities linked to values. RealLife data outputs collected during the first and last weeks of treatment are compared and discussed, after which the app is deleted from the participant's phone. The last part of the session is devoted to planning for the future: participants are encouraged to keep scheduling activities, to keep adding activities linked to their values, and to maintain a system for reminding themselves of plans and intentions.

## Data analysis

### Primary results of RCT

For each of the 6 endpoints measured at baseline (BSI-18 GSI, EROS, BADS, PART-O, SWLS, QOLIBRI), the 8-week change from the baseline will be analyzed using a 2-way ANOVA model with treatment group and strata as 2 factors. The interaction between treatment group and strata will be evaluated. The same model will be used for the analysis of the PGIC at 8 weeks, because PGIC is defined as a measure of change from the baseline.

Hypothesis 1 will be considered supported if the difference in 8-week change in the BSI GSI T-score between BAT and INT groups is significant at the level $\alpha = 0.05$ using the model-based F test for treatment group. The same hypothesis will be tested for all secondary endpoints controlling for family-wise Type I error at the 0.05 level. If the assumption of a normal distribution is not appropriate for some of the endpoints, such endpoints will be analyzed using a stratified 2-sample van Elteren test[46] (an extension of the Wilcoxon rank-sum test) instead of 2-way ANOVA model.

The primary analysis will be conducted on the study sample in the current trial (40 in the BAT group and 20 in the INT group). For secondary analysis, we will include additional participants who received the INT intervention in the previously conducted trial. For these analyses, the models described above will also include the main effect of study time (current vs previous) to adjust for the possibility of overall differences between the previous study and current study populations. This will allow us to factor out these possible differences for the purpose of estimating the effect of BAT in comparison to INT in the previous and current cohorts.

**Sample size and power considerations**
In the prior study of the INT treatment,[20] a mean change of 2.6 (SD = 6.7) was observed in the stratum with BSI-18 GSI < 60, and a mean change of 6.2 (SD = 8.6) was observed in the stratum with BSI-18 GSI ≥ 60. Our proposed sample N = 60 (40 in the BAT group and 20 in the INT group) will provide 80% power to detect a mean difference of 6.71 between the mean changes in BAT and INT groups assuming a 2-sided *t* test, alpha = 0.05, and a conservative common standard deviation of 8.6 (effect size of 0.78). If there is 10% attrition (N = 57; 38 in the BAT group and 19 in INT group), then there will be 80% power to detect a mean difference of 6.89 between BAT and INT groups (effect size of 0.80).

**Trajectory and persistence of change due to treatment**
For each of the 6 endpoints measured at baseline (BSI-18 GSI, EROS, BADS, PART-O, SWLS, QOLIBRI), all longitudinal repeated measures (in wk 0, 4, 8, 8-week follow-up) of the primary and secondary outcome measures will be analyzed using a linear mixed effects model incorporating the fixed effect of treatment group and strata, and the random effect of participant and possible serial correlation among repeated measures. The models will be used to (1) test the difference between treatment groups in terms of changes from baseline to 8-week follow-up (*hypothesis 2*) and (2) evaluate 4- and 8-week changes and to compare the changes in the first 4 weeks to those in weeks 5-8 using appropriate model-based contrasts. The PGIC measured at T2, T3, and T4 will be analyzed similarly as the other endpoints. Assuming that the standard deviation of the T1-T4 changes in BSI-18 GSI is similar to the standard deviation of the T1-T3 changes in BSI-18 GSI, the power analysis provided in Aim 2 is applicable here.

**Examination of treatment enactment**
Analyses of data from the treatment enactment interviews will involve mostly descriptive and exploratory methods, intended to generate hypotheses for future research. We will calculate the proportions of participants who are continuing to use the therapeutic techniques presented in treatment (eg, activity scheduling, self-reminding of intentions). We will compare the treatment groups as to the self-reported degree of meaningful activity in participants' daily lives at various time points (present time, end of study, pretreatment) and compare conditions as appropriate using nonparametric statistical tests.

**Correlates of treatment response**
We will examine participant characteristics for their association to treatment response. We will combine the data from this study (40 in the BAT group and 20 in the INT group) with the data from the 38 participants in the INT condition in the previous trial.[20] Because the 2 trials will have to be completed in different time periods and the randomization established for the current trial will be applied only to the current 60 participants, it is possible that the 2 participant groups may not be balanced with respect to some baseline characteristics. The balance in all baseline characteristics will be investigated, and all analyses will incorporate any covariates that are found to be unbalanced. For each of the endpoints (BSI-18 GSI, EROS, BADS, PART-O, SWLS, QOLIBRI, PGIC), longitudinal repeated measures at times T2-T4 will be analyzed using a linear mixed effects model incorporating random effect of participant and possible serial correlation among repeated measures. The fixed effects will include the treatment group and strata, baseline characteristics such as cognitive status, severity of pretreatment emotional dysfunction, demographic characteristics, and the baseline measure (T1), except for PGIC which is not measured at T1. The models will be used to investigate the associations between baseline characteristics and magnitude of the treatment response at various time points (T2-T4). These analyses are exploratory and primarily intended to develop further hypotheses about the factors influencing treatment effects that might inform the design of a subsequent trial.

## Data and safety monitoring

We have enlisted a data safety and monitoring board consisting of an academic psychiatrist with expertise in treatment of anxiety and depression in persons with TBI and a biostatistician with expertise in clinical trials. Monitoring includes annual review of adverse and serious adverse events by treatment group, as well as projected versus actual participant enrollment and completion, to assess progress toward recruitment goals.

## Discussion

We have presented the rationale and design for an RCT comparing 2 interventions based on principles of BA, for people with chronic moderate to severe TBI and at least mild depression and/or anxiety. Treatments for emotional difficulties in this population are sorely needed, but there is little evidence supporting their efficacy.[7] The interventions tested in this RCT are based on a BA model that has been recommended for TBI[10] and are supported by a previous RCT[20] showing modest improvement in emotional status after a single session of BA followed by theoretically motivated SMS messages to support participant intentions for new or increased activity. We are now testing this single-session treatment against an intervention that incorporates more features of traditional BA, including multiple sessions to reinforce activity scheduling. Novel features of the intervention include the use of EMA, which has been shown to be feasible with persons with TBI,[47] for analysis of the relations among activities and their contexts with emotional states, and the use of input from people with the target problem (chronic, moderate to severe TBI and depression or anxiety) to develop the intervention protocol. The inclusion of a treatment enactment interview is also a novel feature that we encourage other researchers to adopt.[48]

## Study limitations

There are limitations of the current trial. Notably, our plan to combine data from 2 intervention trials runs the risk of bias due to historical factors. For example, 2 study therapists will have administered the INT treatment in both trials, whereas 1 will be treating only the cohort in the

current trial. The INT cohorts may be treated differently from one another by virtue of having a different therapist in the mix, or because of the greater experience of the other 2 therapists in treating the second cohort compared to the first. In addition, comparisons will be limited to the data collection waves common to both trials (T1-T3) because the first trial lacked an extended follow-up.

It might also be argued that we have stacked the deck in favor of the BAT treatment by offering 8 sessions versus the 1 session in INT and by incorporating in BAT more of the features of traditional BA, such as activity scheduling, self-monitoring of the emotional effect of various activities, and exploration of personal values to guide activity selection. However, the INT treatment is already known to lead to modest benefit for many participants.[20] We view the creation of the BAT treatment as an incremental step toward developing a treatment for emotional difficulties related to TBI that has more robust and long-lasting effects.

## Conclusions

Depression and anxiety are common and deleterious after moderate to severe TBI, yet evidence-based treatment guidelines are lacking. We propose an RCT to test a treatment based on principles of BA, which have been recommended in systematic reviews and supported by previous studies. The incorporation of commonly used technology in the form of smartphone apps has the potential to enhance the delivery of treatment in this population.

## Supplier

a. LifeData System; LifeData.

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