Supplemental Information

Brief Behavioral Activation Treatment for Depression (BATD)

Behavioral activation treatments for depression are theorized to work by encouraging patients to expose themselves to potentially reinforcing situations and to inhibit the behavioral withdrawal often characteristic of depression (1, 2). Behavioral activation treatments have gained increasing interest since Jacobson and colleagues' (3) seminal dismantling study of cognitive behavioral therapy in which behavioral activation appeared equally effective as full cognitive therapy in reducing depressive symptoms. At follow-up, behavioral activation was also as effective as cognitive therapy in preventing relapse (4), and a subsequent large-scale randomized controlled trial showed behavioral activation as equivalent to paroxetine in reducing symptoms in moderately to severely depressed individuals (5). As behavioral activation treatments have developed over time, the original focus on engagement with activities generally thought to be pleasant (e.g., watching a sunset) has shifted to a functional analytic model. This model aims to modify patient-specific behaviors that function to maintain depressive symptoms (e.g., avoiding family or friends; absence from work) by promoting goal-specific behaviors (3). Consistently engaging in ideographically functional behaviors is thought to coincide with or precede changes in thoughts and/or mood without direct attempts to modify cognition or emotion (2).

Following Jacobson's functional analytic model as well as traditional behavioral therapy models, Lejuez and Hopko have developed and tested their Brief Behavioral Activation Treatment for Depression (BATD) (6). Although sharing many common elements with previous approaches, BATD is unique in that it is shorter than traditional treatments (8-15 sessions) and does not require as extensive of skills in functional analysis on the part of the therapist or the patient (2). Treatment proceeds through a series of structured units that a) provide psychoeducation about depression and a rationale for the treatment approach; b) assess and monitor baseline activity levels; c) develop behavioral goals and a hierarchical plan for goal attainment; and d) monitor, support, and reward achieving behavioral goals. Preliminary studies have demonstrated that BATD effectively reduces depressive symptoms and is well-tolerated in both outpatient (6, 7) and inpatient (2) settings. In the current study, BATD was provided by author MJS (a licensed clinical psychologist) or by an advanced graduate student under her supervision.

Participant Inclusion/Exclusion Criteria

Inclusion and exclusion criteria have been reported previously (8). All participants received a Structured Clinical Interview for DSM-IV (SCID; 9) to confirm Axis I inclusion/exclusion criteria. At the time of consent, participants in the MDD group met DSM-IV criteria for a current episode of Major Depressive Disorder, no other current Axis I disorder other than dysthymia, and scored 15 or above on the Hamilton Rating Scale for Depression (HAM-D, 10). One MDD participant met criteria for concurrent dysthymia. Participants in the control group scored 6 or lower on the HAM-D, and did not meet criteria for a current Axis I disorder or current/lifetime episode of mood or anxiety disorder. One control participant and two MDD participants met criteria for past substance dependence; all were in remission for at least one year. Participant exclusion criteria for both groups included: 1) coexisting bipolar or psychotic disorder, 2) comorbid current Axis I diagnosis including substance dependence, 3) active suicidal ideation, 4) evidence of organicity, 5) estimate verbal IQ below 70 (as indicated by North American Adult Reading Test verbal IQ (NAART)), 6) magnetic resonance imaging contraindicated (e.g., metal in body), 7) history of neurological injury or disease, 8) current use of psychoactive medications including antidepressants, and 9) current pregnancy. Medical comorbidities were not assessed.

Imaging Data Analysis

Functional data were preprocessed using FEAT 5.92 within FSL 4.0.4 (Oxford Centre for Functional Magnetic Resonance Imaging of the Brain (FMRIB), Oxford University, U.K.). Preprocessing was applied in the following steps: (i) brain extraction for non-brain removal (11), (ii) motion correction using MCFLIRT (12), (iii) slice-timing correction; (iv) spatial smoothing using a Gaussian kernel of FWHM 5 mm, (v) mean-based intensity normalization of all volumes by the same factor, and (vi) high-pass filtering (13). No subject had greater than a 1.5-mm deviation in the center-of-mass in any dimension. Functional images were co-registered to structural images in native space, and structural images were normalized to a standard stereotaxic space (Montreal Neurological Institute). The same transformation matrices used for structural-to-standard transformations were then used for functional-to-standard space transformations of co-registered functional images. All registrations were carried out using an intermodal registration tool (11, 13). Voxel-wise temporal autocorrelation was estimated and corrected using FMRIB's Improved Linear Model (14).

Onset times of events were used to model a signal response containing a regressor for each response type, which was convolved with a double-γ function to model the hemodynamic response. Model fitting generated whole brain images of parameter estimates and variances, representing average signal change from baseline. Group-wise random effects activation images were calculated by a mixed effects higher level analysis using Bayesian estimation techniques, FMRIB Local Analysis of Mixed Effects (FILM, 15) with a significance threshold of $p<0.0001$ (FLAME 1, 16) and a minimum extent of eight uninterpolated voxels.

Wheel of Fortune (WoF) Outcomes

The average (SD) number of wins for each group at each timepoint were: Depressed Time 1: 73.9 (23.8); Depressed Time 2: 63.8 (23.8); Control Time 1: 74.4 (19.7); Control Time 2: 73.3 (17.1). The average (SD) number of non-wins for each group and timepoint were: Depressed Time 1: 78.0 (23.7); Depressed Time 2: 75.4 (23.7); Control Time 1: 82.7 (24.7); Control Time 2: 81.1 (15.4). A 2 (Group: Depressed, Nondepressed) X 2 (Type: Win, Non-Win) X 2 (Time 1, Time 2) repeated measure MANOVA revealed no significant main effects or interactions, *p*s>.10.

The average (SD) number of maximum consecutive win trials for each group at each timepoint were: Depressed Time 1: 4.7 (1.6); Depressed Time 2: 5.0 (1.6); Control Time 1: 4.9 (2.0); Control Time 2: 5.2 (2.2). The average (SD) number of maximum consecutive non-win trials for each group and timepoint were: Depressed Time 1: 5.9 (2.5); Depressed Time 2: 5.2 (2.5); Control Time 1: 5.5 (2.0); Control Time 2: 5.8 (2.3). A 2 (Group: Depressed, Nondepressed) X 2 (Type: Win, Non-Win) X 2 (Time 1, Time 2) repeated measure MANOVA revealed no significant main effects or interactions, *p*s>.15.

At each scan session, WoF conditions were presented in the same proportions: 17.4% 50/50 wheels, 30.4% 30/70 wheels, 34.7% 10/90 wheels, and 17.4% control wheels.

Wheel of Fortune In-Scanner Selections

Figure 2 illustrates reward choice selections, confidence ratings, and feedback valence ratings for both diagnostic groups. Analyses of selection data (i.e., whether high- or low-probability pie slices were chosen) did not include the 50/50 condition. A 2 (Group: Depressed, Nondepressed) X 2 (Condition: 10/90, 30/70) X 2 (Time 1, Time 2) repeated measure MANOVA on the percent of risky choices revealed a main effect of Condition, multivariate $F(1,25)=6.53$, $p<0.02$, reflecting that across groups and timepoints, more high-probability selections were made with the 90/10 than 70/30 pies, but no other significant main effects or interactions. Analyses of square-root-transformed reaction times (RTs) (including the 50/50 condition) revealed a main effect of Time, multivariate $F(1,23)=9.69$, $p<0.005$, reflecting that RTs were faster at Time 2 [mean(SD)=1461 (189)] than at Time 1 [mean(SD)=1599 (234)], but no other main effects or interactions.

Analyses of confidence ratings for the 30/70 and 10/90 conditions were subdivided by choice selections (i.e., did participants chose the high- or low-probability pie slice) and included the 50/50 condition. A 2 (Group: Depressed, Nondepressed) X 3 (Condition: safe, 50/50, risky) X 2 (Time 1, Time 2) repeated measure MANOVA on confidence ratings revealed a main effect of Condition, multivariate $F(2,24)=98.67$, $p<0.0001$, reflecting that safe selections resulted in higher confidence ratings, but no other main effects or interaction. Analyses of square-root-transformed RTs revealed a main effect of Time, multivariate $F(1,23)=7.51$, $p<0.03$, reflecting that RTs were faster at Time 2 [mean(SD)=1179 (312)] than at Time 1 [mean(SD)=1367 (384)], and a main effect of Condition, multivariate $F(2,22)=7.24$, $p<0.004$, indicating that responses to the safe condition [mean(SD)=1372 (394)] took longer than to the other conditions [mean(SD)=1289 (329)], p's<.001, but no other main effects or interactions.

For analyses of feedback ratings, win and non-win trials were examined separately. For non-win trials, a 2 (Group: Depressed, Nondepressed) X 3 (Condition: risky, 50/50, safe) X 2 (Time 1, Time 2) repeated measure MANOVA revealed a significant Time X Condition interaction, multivariate F(2,24)=4.04 $p<0.05$, reflecting a trend towards an effect of Condition (i.e., higher valence ratings when not winning during high-risk trials) at Time 1, $p<.10$, but not at Time 2, $p>.51$, but no other main effects or interactions. For win trials, there was another Time X Condition interaction, multivariate F(2,24)=4.97 $p<0.01$, reflecting, once again, an effect of Condition at Time 1, $p<.02$, but not at Time 2, $p>.21$, but no other significant effects. Square-root-transformed RTs revealed a main effect of Condition, multivariate F(2,22)=5.84, $p<0.01$, reflecting that RTs were faster during outcomes to safe [mean(SD)=1672 (325)] relative to risky choices [mean(SD)=1503 (283)] for both wins and non-wins but no other main effects or interactions.

Potential Relations between Socioeconomic Status and Caudate Activations during WoF Anticipation

As reported in the *Participants* section, diagnostic groups differed in socioeconomic status (SES), (17) [MDD mean(SD)= 36.8 (12.0); Control mean(SD)= 45.8 (2.4)]. To verify whether the central finding of this study (i.e., increased caudate activation during reward anticipation in the depressed group after BATD) was related to SES, Pearson partial bivariate correlations were run between SES and extracted signal intensity from the left caudate cluster identified by the significant Group (Depressed, Nondepressed) X Time (Time 1, Time 2) interaction during monetary anticipation (money vs control) (see Table 3 and the bottom of Figure 3) across all participants and separately within diagnostic groups. Across all participants, correlations between left caudate activation at Time 1, at Time 2, and the difference between Time 1 and Time 2 were not significant, r's<.30, p's>.10. Within groups separately, correlations between left caudate activation at Time 1, at Time 2, and the difference between Time 1 and

Time 2 were not significant, *r*'s<.35, *p*'s>.20 within the nondepressed group, and *r*'s<.35, *p*'s>.30 within the MDD group.

Treatment-Outcomes and In-Scanner Behavioral Responses

Consistent with previous studies of BATD effectiveness (2), 75% of adults with MDD were treatment responders, achieving post-treatment HAM-D scores of 6 or below. Consistent with the HAM-D findings, BDI scores showed a highly significant decline after treatment. Not surprisingly, two measures of trait anhedonia, the Jackson Appetitive Motivation Scale (18) and the Behavioral Activation Scale (19), did not, consistent with the conceptualization of these measures as tapping deficits in trait-like affective styles that would expect to be stable markers of a depression diathesis rather than state markers of illness severity (20-22).

Diagnostic groups did not differ in their behavioral responses across all three stages of the task. Most critical is the lack of evidence of changes in reward-related behavior and subjective experience due to BATD in the MDD group. These results suggest that fMRI effects were not epiphenomena of behavior or subjective states.

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