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Body Mass Index and Atypical Balance Score as Predictors of Treatment Outcomes for Seasonal Affective Disorder

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BODY MASS INDEX AND ATYPICAL BALANCE SCORE AS PREDICTORS OF TREATMENT OUTCOMES FOR SEASONAL AFFECTIVE DISORDER

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ABSTRACT

Efficacious treatments for winter seasonal affective disorder (SAD) include light therapy (LT) and cognitive-behavioral therapy (CBT-SAD); however, it is unknown whether patient baseline characteristics differentially predict treatment outcomes. The present study investigated body mass index (BMI) and atypical balance as prognostic and prescriptive predictors of SAD treatment outcomes using data from a parent study in which 177 adults diagnosed with Major Depression, Recurrent with Seasonal Pattern were randomized to either CBT-SAD (n = 88) or LT (n = 89). At pre-treatment, BMI was assessed and atypical balance was derived using the Structured Interview Guide for the Hamilton Rating Scale for Depression–Seasonal Affective Disorder Version (SIGH-SAD). Hierarchical linear and logistic regressions were used to investigate the main effects of treatment type, BMI, and atypical balance score and their interactive effects on SIGH-SAD depression outcomes at post-treatment and first and second winter follow-up. Linear mixed modeling was used to examine the effect of BMI and atypical balance on the rate of SIGH-SAD symptom improvement during the treatment period. BMI x treatment group interaction significantly predicted depression remission at second winter follow-up such that at BMI $\leq$ 26.1, the probability of depression remission was higher with CBT-SAD than LT. The atypical balance x treatment group interaction significantly predicted depression remission at second winter followup such that the probability of depression remission was higher with CBT-SAD than LT at atypical balance $\leq$ 40.3%. The linear mixed model analyses uncovered a significant interaction between time, BMI, and treatment group, indicating the rate of change in SIGH-SAD scores was slower in LT and faster in CBT-SAD as BMI increased. Taken together, results suggest that BMI and atypical balance are predictors of depression treatment outcomes, and thus may be useful in clinical decision making and efforts for precision medicine.

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CHAPTER 1: INTRODUCTION

Winter seasonal affective disorder (SAD) is a form of major depression characterized by the onset of depression symptoms in the fall and winter seasons that remit in the spring and summer. Although light therapy (LT) is the most long-standing treatment for this disorder, cognitive-behavioral therapy tailored to SAD (CBT-SAD; Rohan, 2008) is also an effective treatment. Rohan and colleagues conducted a randomized clinical trial comparing LT and CBT-SAD in 177 adult SAD patients. LT and CBT-SAD showed comparable improvements in depression and very similar remission rates at post-treatment (47.2% vs. 47.6%, respectively; Rohan et al., 2015); however, CBT-SAD was associated with less severe depressive symptoms and fewer depression recurrences two winters following treatment (27.3% vs. 45.6%; Rohan et al., 2016). These findings align with those of prior studies supporting CBT-SAD's superiority over LT on long-term outcomes (Rohan, Roecklein, Lacy et al., 2009).

When there are multiple effective treatments for a condition, it is imperative to understand which treatment may work best for specific individuals, as this can maximize positive treatment outcomes and improve healthcare cost-effectiveness. This process, called "precision medicine," involves elucidating both prognostic and prescriptive factors. Prognostic factors are predictive of treatment outcome, regardless of treatment type (i.e., the presence of a statistically significant main effect), whereas prescriptive factors are predictive of which treatment has better outcomes for a given patient profile (i.e., a moderator indicated by the presence of a statistically significant predictor × treatment interaction).

Much research has been dedicated to exploring baseline factors that impact treatment outcomes for Major Depressive Disorder. There is increasing interest in the examination of Body Mass Index (BMI) – a measure of body fat determined by weight and height – as a potential predictor of treatment outcomes for depression. This metric is inexpensive, easy-to-use, and commonly assessed in healthcare settings. Although not a diagnostic tool or independently indicative of individual health, BMI is strongly associated with cardiovascular disease (Global Burden of Disease 2015 Obesity Collaborators, 2017), Type II Diabetes (Holmes et al., 2014), and mortality (Aune et al., 2016). BMI categories are classified according to increasing health risk (Table 1) and are applicable for non-pregnant individuals 18 years of age or older.

Studies focusing on BMI as a predictor of treatment outcomes with antidepressant medications have produced mixed findings. For example, Toups et al. (2013) examined BMI as a moderator of depression response and remission for individuals with chronic or recurrent Major Depressive Disorder (MDD), and found no difference in outcome across BMI categories at 12-weeks (post-treatment) with escitalopram, bupropion, venlafaxine, mirtazapine, or a combination of these antidepressants. Similarly, a study exploring the association between the components of metabolic syndrome and treatment resistance to antidepressants found no relationship between high BMI (≤ 27.5 kg/m^2) and treatment-resistant depression (Sagud et al., 2013). On the other hand, several studies indicate an association between higher BMI and poor response to antidepressant medications. For example, a meta-analysis of three clinical trials of MDD patients treated with SSRIs or SNRIs found that individuals within the normal BMI range showed a better antidepressant response than those who were overweight or obese based on BMI

(Oskooilar et al., 2009). Further, in a study of sustained remission among participants with depressive disorders, Dennehy and colleagues (2015) found non-remitters had a higher average BMI and an increased likelihood of BMI-defined obesity when compared to remitters.

More current work extends this line of research by examining remission outcomes according to antidepressant combination and type. Green and colleagues (2017) found BMI differentially predicted remission according to antidepressant type. Specifically, morbidly obese patients were more likely to remit on venlafaxine-XR than those in the normal BMI range. In a different study (Jha et al., 2018), BMI differentially predicted antidepressant treatment outcomes, whereby normal-weight and underweight participants were less likely remit when treated with a bupropion-SSRI combination relative to SSRI-monotherapy. However, obese class II participants were *more* likely to experience remission when treated with the bupropion-SSRI combination than SSRI-monotherapy. These studies highlight the potential utility of BMI as a tool to aid clinical decision making regarding personalized treatment for depression, particularly when multiple efficacious treatments are available. Currently, we are not aware of any studies that have examined BMI as a prognostic or prescriptive factor in CBT for depression. Investigating BMI as a predictor of CBT for depression outcomes is critical, as this characteristic may aid in treatment decision-making.

There are several factors that may explain the inconsistent findings regarding BMI and depression treatment outcomes. Some researchers postulate that atypical depressive symptoms contribute to the heterogeneity of depressive profiles and, therefore, to treatment outcomes. Atypical depressive symptoms include significant weight gain,

increase in appetite, hypersomnia, and leaden paralysis (i.e., the feeling that one's limbs are weighed down; Lojko et al., 2015). Individuals with a higher proportion of atypical symptoms are more likely to have obesity-related health issues and increased levels of inflammatory markers (Lamers et al., 2013; Woo et al., 2016). As such, understanding the impact of excess bodyweight on atypical depressive symptoms may better clarify the relationship between body weight and antidepressant treatment outcomes. Toups et al. (2013) found that atypical features were more common among high-BMI participants, and melancholic features were more common among low-BMI participants. In this sample, increasing BMI was significantly associated with both higher atypical features and lower melancholic features. Furthermore, in a prospective population study of MDD subtypes and changes in adiposity, Lasserre and colleagues (2014) reported a significant association between MDD with atypical features and increased BMI over a 5.5-year period not explained by confounders (e.g., comorbid mental health disorders, sociodemographic or lifestyle traits, antidepressants, or weight-increasing medications). Taken together, this information suggests that BMI and atypical symptoms may interact in important ways that impact depression treatment outcomes.

Despite the literature examining BMI as a predictor of nonseasonal MDD treatment outcomes, the research examining BMI as a predictor of treatment outcomes for specific subtypes of MDD – such as SAD – is quite limited. SAD is a particularly useful depression subtype to examine with respect to BMI, as SAD depressive episodes are recurrent and characterized by atypical symptoms (e.g., hypersomnia, increased appetite and food intake, carbohydrate cravings, heaviness in limbs, decreased energy). To our knowledge, only one published study (Dimitrova et al., 2017) investigated BMI as

a predictor of SAD treatment outcomes. Higher BMI emerged as a positive prognostic indicator for LT treatment outcomes, such that SAD patients with higher BMIs showed a larger reduction in scores on the Structured Interview Guide for the Hamilton Depression Rating Scale – Seasonal Affective Disorder version (SIGH-SAD) after six weeks of LT relative to those with lower BMIs (Dimitrova et al., 2017). Further, baseline atypical balance score, operationalized as (8-item atypical subscale score/total SIGH-SAD score) ×100, significantly predicted LT outcomes, such that individuals with higher atypical balance showed greater improvement with LT.

Dimitrova and colleagues' (2017) findings highlight higher BMI and a larger proportion of atypical symptoms in presenting symptoms as positive prognostic indicators of LT outcomes for SAD. The present study used data from Rohan et al.'s (2015, 2016) parent randomized clinical trial comparing LT to CBT-SAD to investigate BMI and atypical balance score as 1) prognostic and prescriptive predictors of acute and long-term SAD treatment outcomes and 2) predictors of rate of symptom improvement during treatment.

This project extends Dimitrova and colleagues' research in several ways. First, the parent trial includes a comparator treatment – CBT-SAD – that has demonstrated effectiveness in treating SAD (Rohan et al., 2015, 2016), allowing for examination of BMI and atypical balance as prescriptive factors to inform which treatment may prove more effective for specific individuals. Second, the parent study evaluated outcomes at treatment endpoint as well as at first and second winter follow-ups, allowing for an evaluation of the predictive ability of BMI and atypical balance with regard to longer term outcomes beyond treatment endpoint. Third, the project investigated BMI and

atypical balance score as predictors of the rate of improvement during treatment, thus extending scientific knowledge of the relationship between these constructs. Fourth, in addition to examining continuous depression scores as outcomes, the project adds to Dimitrova and colleagues' (2017) work by evaluating BMI and atypical balance as predictors of two clinically meaningful dichotomous outcomes: depression remission and (at follow-ups) recurrence. The public health burden of depression largely stems from the fact that it is recurring, and costly to both the individual and society. Therefore, the ability to predict remission or recurrence is useful for determining which treatment may be more long-lasting for a specific patient profile.

We view this work as exploratory given that there is only one prior study like this one using SAD patients (Dimitrova et al., 2017). Based on that study, we hypothesized that pre-treatment BMI and atypical balance score would predict SAD treatment outcomes (irrespective of treatment type) at post-treatment and at first and second winter follow-ups. Specifically, we predicted that higher BMI would be a positive prognostic indicator of outcomes in both treatments. However, our approach explored the empirical questions of whether BMI and atypical balance emerge as prescriptive factors that differentially predict: 1) depression outcomes between CBT-SAD and LT at post-treatment and first and second winter follow-ups, and 2) the rate of improvement in depression scores between CBT-SAD and LT across the six-week treatment period.

CHAPTER 2: METHOD

Participants

Participants were recruited via newspaper and radio announcements and referrals from Vermont area health providers. Eligible participants were 18 or older and met the following inclusion criteria: (a) DSM-IV-TR criteria for major depression, recurrent with seasonal pattern, (b) SIGH-SAD score of 20 or greater, indicative of a current SAD episode, and (c) no current antidepressant use or consistent use of the same antidepressant medication(s) for the past four weeks with no plans to change. Individuals were excluded for: (a) current treatment with light therapy or psychotherapy for depression; (b) prior LT or CBT-SAD; (c) diagnosis of psychosis, bipolar disorder, substance abuse/dependence, or other disorder requiring immediate treatment; (d) current and serious suicidal intent; (e) hypothyroidism, as indicated by a medical work-up; and (f) planned travel for a week or more through the end of March.

Treatments

Light Therapy (LT). Participants randomized to LT first attended an instructional session involving demonstrated assembly, positioning, and use of the light box, a 23x15½x3¼-in. SunRay that emits 10,000 lux of cool-white fluorescent ultraviolet-filtered light. The session included a review of the treatment rationale and possible side effects. The starting dose for all participants was 30 minutes upon waking, and after treatment week 1, treatment dose was titrated to maximize response and reduce side effects. If the treatment dose produced an insufficient response – defined as less than 30% reduction in SIGH-SAD score in week 1, less than 50% reduction in week 2, or non-remission on the SIGH-SAD at week 3 and beyond – LT duration was increased by 15-

minutes weekly to a maximum of two hours per day. If significant side effects were reported, LT duration was decreased by 15-minutes weekly to no less than 30 minutes per day. In the case of severe side effects (e.g., migraines), participants took a 1-day hiatus from LT, and resumed treatment the following day at 50% of the prescribed duration with subsequent increases until side effects were tolerable. For reports of early morning waking and/or sleepiness in the early evening, morning LT dose was reduced and/or a daily light session was added in the evening, starting with 10 minutes and increased as needed. Side effects were monitored using weekly self-report logs. Each week, the principal investigator and a chronobiological psychiatrist met to review each light therapy subject's file and adjust LT dose. Recommended clinical adjustments to dosage were relayed to LT participants within 24 hours. Participants were encouraged to continue LT on their own post the six weeks of monitored treatment until spontaneous springtime remission. Light boxes were collected from the participants in May. Access to light boxes was offered again the following fall.

Cognitive-Behavioral Therapy for Seasonal Affective Disorder (CBT-SAD*).* CBT-SAD (Rohan, 2008) was adapted from traditional CBT for depression and specifically addresses behaviors and cognitions related to depression in the winter season. CBT-SAD utilizes behavioral activation and cognitive restructuring. Behavioral activation, which involves the identification, scheduling, and completion of pleasant events, is used to target wintertime anhedonia. Cognitive restructuring consists of identifying and reframing negative automatic thoughts, including thoughts about the winter season, lack of light, and inclement weather, and core beliefs. The program concludes with the creation of a personalized relapse-prevention plan, in which

participants are taught to implement CBT skills upon their first signs of negative thoughts, feelings, and behaviors related to the winter season to prevent recurrence. Although CBT is typically delivered weekly as 20 1-hour long sessions over 16 weeks, CBT-SAD is condensed into 12 1.5-hour sessions delivered twice weekly to accommodate the winter season. Sessions were facilitated by one of three licensed doctoral-level clinical psychologists, with a clinical psychology graduate student co-facilitator. Group sized ranged between four to eight participants, and sessions were audio-recorded to assess treatment fidelity.

Measures

Body Mass Index (BMI). At pre-treatment, body weight was measured with a calibrated scale to the nearest 0.01 kilogram, and height was measured to the nearest 0.01 centimeter. A trained study nurse, who also documented medical comorbidities (e.g., hypertension, diabetes, etc.), collected BMI data. BMI was analyzed primarily as a continuous variable. When analyzed as a categorical variable, BMI was categorized according to Centers for Disease Control and Prevention (2019) guidelines as follows: $BMI < 18.5$ is underweight, $18.5 \leq BMI \leq 24.9$ is normal/healthy weight, $25.0 \leq BMI \leq 29.9$ is overweight, and $BMI \geq 30.0$ is obese.

SIGH-SAD. Depressive symptoms were assessed with the 29-item SIGH-SAD (Williams et al. 1992). The current study uses SIGH-SADs from pre-treatment to obtain the atypical balance predictor and SIGH-SADs from post-treatment and at first and second winter follow-up as outcomes. The measure includes two subscales – the 21-item Hamilton Rating Scale for Depression (HAM-D; Williams et al., 1998), and an 8-item subscale assessing atypical symptoms. Higher scores indicate more depressive severity.

Training for SIGH-SAD administration included listening to, rating, and discussing item scores for several audiotaped SIGH-SADs with the group of raters, and administering a mock SIGH-SAD with the study principal investigator. Interviews were audio-recorded and re-rated by a second blind rater; inter-rater reliability was high at each time point (Rohan, Rough et al., 2016).

Atypical balance was calculated with the SIGH-SAD as *8-item atypical score / total SIGH-SAD score x 100* (Terman et al., 1996). Atypical symptoms captured on the SIGH-SAD include social withdrawal, weight gain, appetite increase, increased eating, carbohydrate craving and eating, hypersomnia, fatigue, and mood and/or energy slumps in the afternoon and/or evening.

Remission was defined as either: 1) a $\geq$ 50% reduction in total SIGH-SAD score relative to pre-treatment with a HAM-D score $\leq$7 and an atypical score $\leq$7, or 2) HAM-D score $\leq$2 and an atypical score $\leq$10 (Terman et al., 1990). Recurrence was assessed at first and second winter follow-up and was defined as a total SIGH-SAD score of $\geq$ 20 with the HAM-D score $\geq$10 and the atypical scale score $\geq$5 (Terman et al., 1990).

Data Analytic Plan

The project is a secondary data analysis of a randomized clinical trial on treatment for SAD conducted at the University of Vermont in the Mood and Seasonality Laboratory. The study was approved by the University's Institutional Review Board. Study procedures are published elsewhere (Rohan et al., 2013).

Analyses were conducted in SPSS 24 for Macintosh. Analysis of variance (ANOVA) tested for baseline differences between CBT-SAD and LT groups in BMI and atypical balance score. Correlations were run between BMI, atypical balance, and SIGH-

SAD score at pre-treatment. We used a Chi-Square to test whether the proportions of participants in the three BMI categories (normal weight, overweight, and obese) differed between CBT-SAD and LT.

To address Aim 1, hierarchical multiple regression analyses were used to test the main effect of each predictor (pre-treatment BMI and atypical balance), treatment type (CBT-SAD or LT), and their interaction in predicting continuous SIGH-SAD depression scores at post-treatment, first winter follow-up, and second winter follow-up. Given that remission status (assessed at post-treatment and first and second winter follow-ups) and recurrence status (assessed at first and second winter follow-ups) are dichotomous outcomes, logistic regression analyses were used to test the main effects of BMI and atypical balance, treatment type (CBT-SAD or LT), and the interaction in predicting SIGH-SAD remission and recurrence.

Regression analyses utilized all available data. Missing data was minimal, as 174/177 (98.3%) participants provided post-treatment data (Rohan et al. 2015), and 170/177 (96.0%) and 169/177 (95.5%) participants provided data at first and second winter follow-up, respectively (Rohan, Meyerhoff et al., 2016). As such, missing data was handled via listwise deletion.

We used the procedures outlined by Kraemer and colleagues (2002) to test pre-treatment BMI and atypical balance as predictors and moderators of treatment outcome. Both pre-treatment BMI and atypical balance were centered on the grand mean before calculating subsequent interaction terms (Cohen, Cohen, West & Aiken, 2003). Significant interactions were plotted using a simple slopes analysis and investigated using the Johnson-Neyman technique to determine regions of statistical significance ($p < .05$).

Prognostic indicators (i.e., non-specific predictors of treatment outcome) are defined as variables with significant main effects. Prescriptive factors (i.e., moderators of treatment outcome) are variables with significant treatment by predictor interactions. In all models, we utilized dummy coded treatment variables (CBT-SAD = 1, LT = 0). Models for testing the moderators included first-order terms and interaction terms to examine the effect of pre-treatment BMI and atypical balance on treatment outcome in CBT-SAD vs. LT. Parameter estimates for the treatment effects indicate differences between CBT-SAD and LT, parameter estimates for the interaction terms indicate treatment group differences in the effect of pre-treatment BMI or atypical balance on treatment outcome.

Pre-treatment depression severity (as measured by the SIGH-SAD) was included as a covariate. Antidepressant medication status, presence of a physical comorbidity, presence of a mental health comorbidity, gender, education, marital status, and race/ethnicity (White/non-Hispanic vs. all others) were investigated as potential covariates. Variables that were significantly correlated with a depression outcome at post-treatment, first winter, or second winter follow-up, were included as covariates in the relevant analysis of that outcome at that timepoint.

To address Aim 2, growth curve modeling was used to examine the impact of the BMI and atypical balance on rate of improvement in depression symptoms from baseline over the six-week treatment period. The intercept will represent individual pre-treatment depression symptom scores. The main effect of BMI represents the relationship between BMI and pre-treatment SIGH-SAD depression symptomatology. In these mixed effects models, the slope represents the rate of change in depression symptoms over the six-week

treatment period after pre-treatment (intercept). The dependent variables are seven SIGH-SADs administered weekly. Here, an association between BMI and the slope would reflect a relationship between BMI and the rate of improvement in depression symptoms over the six-week treatment period. We also examined the interactions between BMI, treatment group, and time. As such, a 3-way interaction between BMI, treatment group, and time would signify that the effect of BMI on the rate of improvement in depression symptoms differs by treatment group. Similar modeling was used to assess the impact of baseline atypical balance on rate of improvement in depression symptoms from baseline over the six-week treatment period.

Depression scores at pre-treatment and over the six-week treatment period were first modeled as a random effect of time with a random intercept to allow individual growth curves for each person. Next, the main effects (BMI and treatment group), followed by the interactions between BMI, treatment group, and slope were entered into the model. Plotted simple slopes were used to examine significant interactions.

CHAPTER 3: RESULTS

Descriptive Findings

Table 1 presents predictor variable means and baseline medical comorbidities by treatment group. There were no significant differences by treatment group in baseline BMI, baseline atypical balance, or medical comorbidities. Study participant baseline characteristics and descriptives are published elsewhere (Rohan et al., 2015). Medical comorbidity and BMI data were collected on 153/177 participants. The remaining 24 participants were part of a pilot study conducted prior to implementation of the medical screening visit.

The average BMI across study participants was in the overweight range (M = 27.6, SD = 5.66). Average baseline atypical balance was 40.8%, meaning that atypical symptoms comprised approximately 41 percent of a participant's pre-treatment SIGH-SAD score, on average. Nearly two-thirds (62.1%) of participants had a medical comorbidity. The most common physical issues included cardiovascular conditions (23.5%), gastrointestinal issues (14.5%), and asthma/respiratory conditions (14.5%).

Correlations between predictor variables, possible covariates (e.g., gender, marital status, education level, race, antidepressant use) and depression outcome measures are presented in Table 2. Of note, pre-treatment depression scores were significantly correlated with nearly all depression outcomes; as such, we adjusted for baseline depression score in all regression analyses. Neither BMI nor baseline atypical balance were significantly correlated with depression outcomes at any time point. Presence of a physical comorbidity at baseline was significantly associated with post-treatment SIGH-

SAD score, $r(147) = .17$, $p = .040$. The presence of a mental health comorbidity was correlated with Winter 2 SIGH-SAD depression recurrence, $r(166) = .20$, $p = .010$.

Regression diagnostics revealed non-normal distribution of BMI across the sample. We ran analyses using the appropriate transformation of BMI (log BMI), but found that this transformation did not change the general pattern of findings. As such, for ease of understanding, results are presented from analyses conducted with BMI data in their original (raw score) form.

BMI Predicting SIGH-SAD Scores

The results of hierarchical regression models with BMI predicting SIGH-SAD scores at post-treatment, Winter 1, and Winter 2 are presented in Table 3. The overall model with BMI predicting post-treatment SIGH-SAD score was significant throughout all regression steps in the model, $F[5, 143] = 3.97$, $p = .002$. The variables included in Step 1 of the model, pre-treatment SIGH-SAD score and presence of a medical comorbidity, significantly predicted post-treatment SIGH-SAD score, and together accounted for 11% of the variance in the outcome, $\Delta R^2 = .11$, $\Delta F = 9.47$, $p < .001$. Neither the variables added in step 2 (BMI and treatment group) nor the BMI x treatment group interaction term added in Step 3 were significantly associated with post-treatment SIGH-SAD score.

The overall model with BMI predicting Winter 1 SIGH-SAD score was statistically significant at Step 1, $F[1, 169] = 12.05$, $p < .001$, and remained significant through subsequent steps in the model. Pre-treatment SIGH-SAD score, included in Step 1, explained 7% of the variance in Winter 1 SIGH-SAD score, $\Delta R^2 = .067$, $\Delta F = 12.05$, $p < .001$. None of the variables included in Step 2, BMI and treatment group, nor the BMI

x treatment group interaction term in Step 3, were significantly associated with Winter 1 SIGH-SAD score.

The overall model predicting Winter 2 SIGH-SAD score, which included pre-treatment SIGH-SAD score, race, BMI, treatment group, and the BMI x treatment group interaction was statistically significant, $F[5, 140] = 3.52$, p = .005. Treatment group, added in Step 2, significantly predicted the outcome such that Winter 2 SIGH-SAD scores for those who received CBT-SAD were, on average, 3 points lower than that of those who received LT. The addition of the BMI x treatment group interaction at Step 3 did not significantly predict Winter 2 SIGH-SAD scores.

Baseline Atypical Balance Predicting SIGH-SAD Scores

Table 3 presents the results of hierarchal regression models with baseline atypical balance predicting SIGH-SAD scores at post-treatment, Winter 1, and Winter 2. The overall model predicting post-treatment SIGH-SAD score was statistically significant at Step 1, $F[2, 146] = 9.47$, $p < .001$, and remained significant throughout additional steps in the model. In Step 1, pre-treatment SIGH-SAD score and presence of a medical comorbidity significantly predicted post-treatment SIGH-SAD score and together explained 12% of the variance in post-treatment SIGH-SAD score, $\Delta R^2 = .115$, $\Delta F = 9.47$, $p < .001$. In Step 2, neither pre-treatment atypical balance nor treatment group predicted post-treatment SIGH-SAD score. Similarly, the pre-treatment typical balance x treatment group interaction term included in Step 3 was not statistically significant.

The final model predicting Winter 1 SIGH-SAD score included pre-treatment SIGH-SAD score, baseline atypical balance, treatment group, and the baseline atypical balance x treatment group interaction term and was statistically significant, $F[4, 164] =$

5.03, p < .001. While the addition of baseline atypical balance at Step 2 significantly predicted Winter 1 SIGH-SAD score, treatment group did not. The pre-treatment atypical balance x treatment group interaction term was not statistically significant.

The model predicting Winter 2 SIGH-SAD score was statistically significant at Step 1 $F[2, 162] = 4.46$, $p < .001$, and remained significant throughout all subsequent steps. The addition of baseline atypical balance and treatment group at Step 2 explained an additional 4% of the variance in the model after accounting for pre-treatment SIGH-SAD score and race at Step 1, $\Delta R^2 = .045$, $\Delta F = 4.043$, $p = .019$. The pre-treatment atypical balance x treatment group interaction term added at Step 3 did not significantly predict Winter 2 SIGH-SAD score.

BMI Predicting SIGH-SAD Remission

The overall model predicting SIGH-SAD derpression remission at post-treatment, which included pre-treatment SIGH-SAD score (Step 1), BMI and treatment group (Step 2), and the BMI x treatment group interaction term (Step 3), was not statistically significant, Likelihood ratio $\chi^2(4) = 3.51$, $p = .061$, Pseudo $R^2 = .017$.

The overall model predicting Winter 1 SIGH-SAD remission status, which included pre-treatment SIGH-SAD score at Step 1, BMI and treatment group at Step 2, and the BMI x treatment group interaction at Step 3, did not significantly predict Winter 1 SIGH-SAD depression remission, Likelihood ratio $\chi^2(4) = 3.79$, $p = .43$, Pseudo $R^2 = .019$.

The overall model predicting Winter 2 SIGH-SAD depression remission was statistically significant, Likelihood ratio $\chi^2(4) = 10.02$, $p = .040$, Pseudo $R^2 = .057$. We observed a significnat effect of BMI on Winter 2 depression remission, $OR = 1.12$, $Z =$

2.16, p = .031. Further, findings from Step 3 revealed a statistically significant BMI x treatment group interaction term, OR = .855, Z = -2.14, p = .032. A decomposition of this interaction term (see Figure 1), followed by further probing using the Johnson-Neyman technique, revealed that the probability of depression remission was higher with CBT-SAD than LT for those with a BMI of 26.1 or lower. There was no significant difference in depression remission between CBT-SAD and LT for individuals with BMI greater than 26.1.

Baseline Atypical Balance Predicting SIGH-SAD Remission

The overall model predicting SIGH-SAD remission at post-treatment, which included pre-treatment SIGH-SAD score (Step 1), pre-treatment atypical balance and treatment group (Step 2), and the pre-treatment atypical balance x treatment group interaction term (Step 3), did not significantly predict SIGH-SAD depression remission at post-treatment, Likelihood ratio $\chi^2(4) = 4.45$, p = .349, Pseudo R^2 = .019.

The final model predicting SIGH-SAD depression remission at Winter 1 incldued pre-treatment SIGH-SAD score (Step 1), pret-treatment atypical balance and treatment group (Step 2), and the pre-treatment atypical balance x treatment group interaction term (Step 3), and was also not statistically significant, Likelihood ratio $\chi^2(4) = 9.20$, p = .056, Pseudo R^2 = .041.

The overall model predicting Winter 2 SIGH-SAD depression remission was statistically significant, Likelihood ratio $\chi^2(4) = 13.22$, p = .010, Pseudo R^2 = .066. At Step 3, pre-treatment atypical balance, OR = 1.08, Z =2.52, p = .012, and the pre-treatment atypical balance x treatment group interaction term, OR = .90, Z = -2.70, p = .007, significantly predicted Winter 2 SIGH-SAD depression remission. Decomposing

this interaction (Figure 2) and probing it using the Johnson-Neyman procedure revealed that the probability of depression remission at Winter 2 was higher with CBT-SAD than LT for those with pre-treatment atypical balance of 40.3 percent or lower. There was no significant difference in the probability of depression remission at Winter 2 between CBT-SAD and LT for individuals with pre-treatment atypical balance greater than 40.3 percent.

BMI Predicting SIGH-SAD Depression Recurrence

The binary logistic regression predicting Winter 1 SIGH-SAD depression recurrence was statistically significant, Likelihood ratio $\chi^2(4) = 12.03$, $p = .017$, Pseudo $R^2 = .071$, however, pre-treatment SIGH-SAD score was the only statistically significant predictor, $OR = 1.16$, $Z = 3.00$, $p = .003$.

Similarly, the overall model predicting Winter 2 SIGH-SAD depression recurrence was statistically significant, Likelihood ratio $\chi^2(5) = 18.77$, $p = .002$, Pseudo $R^2 = .096$. Although treatment group, $OR = .44$, $Z = -2.23$, $p = .026$, emerged as a significant predictor of Winter 2 SIGH-SAD depression recurrence, consistent with the primary efficacy results showing CBT-SAD's superiority to LT (Rohan et al., 2016), neither BMI, $OR = .96$, $Z = -.85$, $p = .396$, nor the BMI x treatment group interaction term, $OR = 1.03$, $Z = .53$, $p = .598$, was statistically significant.

Baseline Atypical Balance Predicting SIGH-SAD Depression Recurrence

The final model predicting Winter 1 SIGH-SAD depression recurrence was statistically significant, Likelihood ratio $\chi^2(4) = 11.59$, $p = .021$, Pseudo $R^2 = .059$, and pre-treatment SIGH-SAD score, $OR = 1.10$, $Z = 2.88$, $p = .004$, was the only significant predictor.

Further, the final model predicting SIGH-SAD depression recurrence at Winter 2 was statistically significant, Likelihood ratio $\chi^2(4) = 14.44$, $p = .006$, Pseudo $R^2 = .065$; while pre-treatment SIGH-SAD score, $OR = 1.09$, $Z = 2.64$, $p = .008$, and treatment group, $OR = .38$, $Z = -2.78$, $p = .005$, were significant predictors in this model, pre-treatment atypical balance, $OR = 1.00$, $Z = .21$, $p = .835$, and the pre-treatment atypical balance x treatment group interaction, $OR = 1.01$, $Z = -.43$, $p = .665$, were not.

Sensitivity Analyses: BMI and Baseline Atypical Balance as Predictors of Depression Treatment Outcomes after Adjusting for Each Other

Additional analyses were also conducted to determine if the significant findings persisted after controlling for BMI and atypical balance in their respective models. To remain parsimonious, these analyses were only run for models with an observed significant predictor x treatment group interactive effect.

The overall model examining BMI as a predictor of Winter 2 SIGH-SAD remission after adjusting for pre-treatment SIGH-SAD score and atypical balance was not statistically significant, Likelihood ratio $\chi^2(5) = 10.64$, $p = .059$, Pseudo $R^2 = .061$.

The overall model with baseline atypical balance as a predictor of Winter 2 SIGH-SAD remission after adjusting for pre-treatment SIGH-SAD score and BMI was significant, Likelihood ratio $\chi^2(5) = 14.30$, $p = .014$, Pseudo $R^2 = .082$. Baseline atypical balance maintained a significant predictive effect on the outcome, $OR = 1.08$, $Z = 2.51$, $p = .012$. Further, the baseline atypical balance x treatment group interaction also remained significant, $OR = .892$, $Z = -2.77$, $p = .006$. The direction of the interactive effect was consistent with the direction seen in the model that did not adjust for BMI.

Sensitivity Analyses: Categorical BMI as a Predictor of Depression Remission at Winter 2 Followup

Analyses were also conducted to determine whether the significant effects of BMI as a predictor of depression remission at second winter followup were still observed with BMI entered as a categorical variable. Categorical BMI (with normal weight as the reference group) did not significantly predict depression remission at second winter followup, Likelihood ratio $\chi^2(6) = 9.20$, $p = .16$, Pseudo $R^2 = .05$.

Aim 2 Findings

Linear mixed models (LMM) investigating the main effects of between-subjects factors, within-subjects factors, and their interactions on SIGH-SAD score at post-treatment were examined. The final models included the intercept, time, predictor, treatment group, time x treatment group, time x predictor, and time x predictor x treatment group, in which the predictor was either BMI or atypical balance at pre-treatment. After fitting the models with multiple covariance structures, using unstructured covariance structure among random effects provided the best model fit as measured by the AIC and BIC fit statistics, in which lower numbers denote better fit. For instance, fit statistics were better with the unstructured covariance structure (AIC = 6314.3, BIC = 6333.9) than diagonal covariance structure (AIC = 6322.3, BIC = 6371.0). These analyses are reported in Table 6.

Predicting Post-treatment SIGH-SAD Scores Using Linear Mixed Modeling

In the BMI model, we observed a main effect of time (slope) such that participants reported a decrease (negative slope) in SIGH-SAD score across repeated measurements, $F(1, 145.3) = 772.85$, $p < .001$. There were no significant main effects for

BMI and treatment group, and no significant interactive effects for time x treatment group or time x BMI. A significant three-way time x treatment group x BMI interaction, $F(1, 141.8) = 4.95$, $p = .028$, suggested that SIGH-SAD scores at each week varied by treatment group and BMI.

The interaction was investigated by graphing the marginal effects of BMI on the rate of change of SIGH-SAD scores over the six weeks of treatment by treatment group (Figure 3). Plotting the interaction revealed a negative BMI x time interaction for light therapy such that as BMI increases, the rate of change in SIGH-SAD score decreases. However, there was a positive association between BMI and time for CBT-SAD, such that as pre-treatment BMI increases, the rate of change in SIGH-SAD scores increases.

In the model examining baseline atypical balance as a predictor of SIGH-SAD scores, we observed a main effect of time (slope) in that SIGH-SAD scores decreased approximately 2.5 points per week across repeated measurements, $F(1, 169.1) = 800.5$, $p < .001$. We observed no other significant main effects or interactive effects.

CHAPTER 4: DISCUSSION

To our knowledge, this is the first study to investigate BMI and atypical balance at baseline as prescriptive predictors of different SAD treatment outcomes at post-treatment and at follow-ups one and two winters later. BMI was a prescriptive predictor of the probability of depression remission at Winter 2, such that the probability of remission was significantly higher with CBT-SAD than LT at BMI $\leq$ 26.1. Furthermore, pre-treatment atypical balance was a prescriptive predictor of Winter 2 depression remission, whereby the probability of remission was significantly higher with CBT-SAD than LT when atypical balance score was $\leq$ 40.3 at pre-treatment.

Of note, all three of these significant findings were prescriptive of more remissions in CBT-SAD than in LT at or below the cutpoint, but were not prescriptive of more remissions in LT than in CBT-SAD above the cutpoint. This is evident in Figures 1 and 2, illustrating the magnitude of the difference between CBT-SAD and LT is much larger at one standard deviation below the mean on the predictor, where the difference favors CBT-SAD, than it is at one standard deviation above the mean, where the difference favors LT. If the goal is remission in future winters, these results have the potential to inform treatment algorithms for recommending CBT-SAD over LT for patients with SAD who are at or below these values. However, the probability of remission for patients with SAD who are above these mean values did not differ depending on whether the initial treatment was CBT-SAD or LT, offering no guidance to the clinician in selecting one treatment over the other. Therefore, these results inform personalized medicine only for patients with SAD at or below these mean values.

The overall pattern of results differs from the Dimitrova et al. (2017) study, which found higher atypical balance and BMI at pre-treatment predicted a greater decrease in depression scores after LT. We observed a significant advantage of CBT-SAD over LT for SAD patients with relatively lower BMI and atypical balance, but no significant advantage of LT over CBT-SAD for SAD patients with relatively higher BMI and atypical balance. In addition, our pattern of significant findings was observed at winter follow-ups (not at post-treatment) and on the outcome of depression remission (rather than continuous depression scores). The current study has several methodological improvements over Dimitrova et al. (2017), including a comparator treatment for LT (i.e., CBT-SAD), a larger sample size, and the longitudinal follow-up interval spanning two winters beyond treatment endpoint.

Our significant prescriptive findings are concentrated on the dichotomous outcome of depression remission. Remission is the accepted desired clinical endpoint for depression treatment, defined as a state in which there are minimal or no depression symptoms present with a return to normative psychosocial and occupational function (Zajacka, 2003). Depression remission is the desired clinical treatment outcome because research demonstrates that failure to achieve remission is associated with greater likelihood of depression relapse or recurrence (Lovieno et al., 2010), more severe functional impairment, and poorer long-term outcomes (Olchanski et al., 2013). Given that remission is an important benchmark of treatment effectiveness, our finding that relatively lower BMI and atypical balance prescriptively predicted lower risk of remission following CBT-SAD relative to LT is clinically useful.

We also examined baseline BMI and atypical balance as prescriptive predictors of the average weekly rate (i.e., slope) of change in SIGH-SAD score across the six-week treatment period. This analysis was largely exploratory, as prior work has not examined these predictors in relation to rate of depression change during treatment. We uncovered a significant interaction between time, BMI, and treatment group, indicating the rate of change in SIGH-SAD scores was slower in LT and faster in CBT-SAD as BMI increased. Based on Dimitrova et al. (2017), we speculated that perhaps LT would be associated with a faster rate of depression change than CBT-SAD as BMI increased—the opposite of what was observed here. In considering this short-term advantage of higher BMI in CBT-SAD (i.e., for greater rate of depression change during the six weeks of treatment) against the long-term advantage of lower BMI in CBT-SAD (i.e., for greater likelihood of remission two winters later), we argue the latter is more important, particularly because BMI was not a prescriptive predictor of post-treatment depression scores.

One framework that may be useful for understanding these results is the "seasonal thrifty phenotype" hypothesis (Levitan et al. 2006), which purports that due to an early gene-environment interaction, individuals make predictions about seasonal scarcity of food resources, resulting in increased risk of obesity with SAD. According to the hypothesis, the gene-environment interaction occurs via in utero signals that involve melatonin, which readily crosses the placenta and can provide photoperiodic information that can then impact rhythms related to seasonality and the circadian clock (Levitan et al. 2006). The core features of this phenotype include seasonal cravings, increased food intake, reduced activity, marked weight gain, and hypersomnia in preparation for

predictable seasonal famine, but currently maladaptive in environments with an abundance of food (Levitan et al., 2006).

It may be the case that the two treatments compared in this study, CBT-SAD and LT, target different etiologic components of SAD onset. Perhaps CBT-SAD does not target individuals with SAD who fit the seasonal thrifty phenotype, who would be expected to have relatively higher BMIs and atypical symptoms. The Dual Vulnerability Model (Young et al. 2008) states that separate but interconnected biological and psychological processes are involved in the development and maintenance of SAD symptoms. The physiological vulnerability to environmental changes (e.g., shortened photoperiod) leads to vegetative symptoms (e.g., increased appetite, hypersomnia). Then, due to a psychological vulnerability to the experience of vegetative symptoms, SAD symptoms related to mood and cognition ensue, such as sadness and guilt. It is possible that CBT-SAD and LT target different points of vulnerability in this model. While LT targets the biological vulnerability by artificially lengthening photoperiod, CBT-SAD impacts the psychological vulnerability by improving coping with seasonal changes. Thus, it could be that individuals with lower BMI and lower atypical balance show increased likelihood of remission at follow-up with CBT than LT because CBT targets the factors at which they are most vulnerable (i.e., psychologically).

The predictive effects of BMI and atypical balance observed in this study could be explained by dysregulation in immunological or metabolic functioning. Specifically, meta-analyses suggest levels of specific inflammatory markers, including C-reactive protein (CRF), tumor necrosis factor (TNF), and interleukin-6 (IL-6), are higher in depressed individuals than their non-depressed counterparts (Dowlati et al., 2010;

Howren et al., 2009). Moreover, this effect is substantially attenuated after controlling for BMI (Howren et al. 2009), suggesting that weight may be an important factor in the relationship between depression and increased inflammatory response. In their recent work, Kappelmann et al. (2020) investigated the association between inflammatory markers, metabolic dysregulation, and specific depression symptoms using genetic correlation and 2-sample mendelian randomization. Their work found positive associations between IL-6 activity and suicidality, and that higher BMI, but not inflammatory markers, was associated with anhedonia, fatigue, appetite change, and feelings of inadequacy. Together, these results suggest that immune and metabolic factors may represent separate symptom-specific pathways that increase risk for depression. Rudolf and colleagues (2014) found levels of IL-6 were higher in individuals with atypical depression, but not in those with typical depression. Further, those with atypical depression had significantly higher BMIs, and increased CRP levels compared to their counterparts with typical depression.

The relationship between immune functioning and depression may be especially important to consider with SAD, as there is a preponderance of both human and non-human animal studies that suggest seasonality impacts immune function. In non-human animals, immune function is elevated during the shortened photoperiods of the winter season in response to energetic stress, which involves changes that alter the body's energetic state or demand, such as lowered food availability and colder temperatures (Harrell et al., 2016, Song et al., 2015;). In humans, more inflammatory cells (e.g., macrophages) and proinflammatory cytokines (e.g., IL-6), are present in the winter as compared to the summer (Kulwein & Irwin 2001; Maes et al., 1994; Song et al., 2015).

Given the relationship between seasonality and immune response, it is useful to examine how immune response changes with SAD treatment. Investigation of the relationship between immune functioning and SAD treatment outcomes is limited to LT and shows mixed results (Avissar et al. 1999; Lue et al. 2001, Song et al., 2015). As such, future research should examine immune functioning as a potential mechanism of the relationship between BMI (and atypical balance) and SAD treatment outcomes and whether this varies by treatment type (e.g., LT vs. CBT-SAD vs. medication).

Given that prior research demonstrates an association between BMI and some atypical symptoms of depression (Lamers et al. 2017; Lojko et al., 2015), one promising avenue for future research is to elucidate the underlying common biological mechanisms common to both factors and explore how they may influence depression treatment outcomes. For example, Akram and colleagues (2020) investigated the relationship between adiponectin – a hormone important for insulin and anti-inflammatory action – and SAD symptoms among an Old Older Amish sample. They found that participants with syndromal or subsyndromal SAD had significantly lower adiponectin plasma levels that those without SAD symptoms (Akram, 2020), suggesting that this hormone may be an important target for treatment. As such future research can examine how this hormone changes in response to treatment for SAD and major depressive disorder more broadly.

While there is much utility in examining the underlying biological mechanisms that may explain the observed relationship between BMI, atypical balance, and depression treatment outcomes, future research should also take a broader, more sociological perspective. Depression and obesity are highly comorbid (Levitan et al., 2012; Luppino et al., 2010), and both are stigmatized (Ebneter et al. 2013; Mooney et al.,

2016). Luck-Skiroriki et al. (2018) conducted a telephone-based study in which participants were presented with vignettes of women with depression, obesity, or both, and followed by semantic differentials (i.e., the Depression Stigma Scale and the Fatphobia Scale) to capture stigma towards these conditions. They found that the co-occurrence of obesity and depression was associated with increased levels of stigma as compared to the occurrence of obesity or depression independently. As such, future research should also examine how the stigma surrounding obesity and depression may impact treatment outcomes.

Several limitations to this work must be acknowledged. First, the SIGH-SAD is an interview that relies on self-report to capture the intensity and frequency of depression symptoms. Although the accepted measure of SAD symptom severity, the items that comprise the atypical subscale (e.g., hypersomnia, increased eating, fatigue) capture the perception of these constructs, which may differ from the data captured by means that track behavioral or physiological data. A second limitation surrounds the use of BMI as a moderator. Other metrics, such as waist-to-height ratio (Ashwell et al. 2012), may be more accurate/useful markers of metabolic dysregulation, as BMI does not account for muscle mass or distribution of adipose tissue. Finally, study data were collected in the state of Vermont with a predominantly older, white population, which may impact generalizability of the findings. Future research should involve multi-site data collection with individuals from various racial and ethnic backgrounds to improve generalizability. Despite these shortcomings, this paper makes an important contribution to the literature on how different factors impact depression treatment outcomes.

Table 1: Descrptive statistics on predictors variables and baseline medical comorbidities

	Total		Treatment Group		*t*	*p*
	Mean	SD	CBT-SAD M (SD)	LT M (SD)		
BMI (*N*= 153)	27.56	5.66	27.8 (5.94)	27.3 (5.40)	-.603	.547
Atypical balance (*N*= 177)	40.8	10.07	41.7 (10.09)	39.9 (10.02)	-1.17	.244
	Total (N =153)		CBT (*N* = 76)	LT (*N* = 77)		
	No.	%	No. (%)	No. (%)	Chi-square	*p*
BMI (categorized)					2.31	.314
Normal range	56	36.6	28 (36.8)	28 (36.4)		
Overweight	54	35.3	23 (30.3)	31 (40.3)		
Obese	43	28.1	25 (32.9)	18 (23.4)		
Any Comorbidity	95	62.1	52 (68.4)	43 (55.8)	2.57	.109
Asthma/respiratory	16	10.5	11 (14.5)	5 (6.5)	2.60	.107
Bones/joints/muscles	16	10.5	8 (10.5)	8 (10.4)	.001	.978
Cardiovascular	36	23.5	21 (27.6)	15 (19.5)	1.41	.235
Diabetes	6	3.9	5 (6.6)	1 (1.3)	2.83	.092
Gastrointestinal	26	17.0	11 (14.5)	15 (19.5)	.680	.410
Genitourinary	8	5.2	5 (6.6)	3 (3.9)	.556	.456
Head injury	2	1.3	1 (1.3)	1 (1.3)	.000	.993
Headache/migraine	9	5.9	5 (6.6)	4 (5.2)	.132	.716
Nervous System	16	10.5	9 (11.8)	7 (9.1)	.309	.578
Cancer History	9	5.9	3 (4.0)	6 (7.8)	1.02	.312
Skin	10	6.5	6 (7.9)	4 (5.2)	.456	.499
Sleep	6	3.9	4 (5.3)	2 (2.6)	.721	.396
Thyroid function	18	11.8	10 (13.2)	8 (10.4)	.282	.595
Other	10	6.5	7 (9.2)	3 (3.9)	1.77	.184

Notes.
BMI = body mass index; CBT-SAD = Cognitive Behavioral Therapy for Seasonal Affective Disorder; LT = Light therapy. Note that N for Medical comorbidities is smaller than overall N.

Table 2: Bivariate correlations between predictor and depression outcome measures

	1.	2.	3.	4.	5.	6.	7.	8.	9.	10.	11.	12.	14.	15.	16.	17.	18.	19.	20.
1. Sex	---																		
2. Age	-.10	---																	
3. Race	-.05	.08	---																
4. Antidepressant Use	.01	.14	.08	---															
5. Education	-.04	.14	.00	-.04	---														
6. Marital Status	-.02	-.13	.04	-.07	-.12	---													
7. MH Comorbidity	-.11	-.15*	-.16*	.09	.10	-.09	---												
8. PH Comorbidity	.01	.31**	-.04	.17*	-.03	.07	.10	---											
9. BMI	-.16*	.06	-.12	.09	.00	-.09	.19*	.10	---										
10. Atypical balance	.09	-.09	.04	.08	.07	-.13	.02	-.16	.08	---									
11. Pre-tx SIGH-SAD	.03	.00	-.03	.08	-.01	-.06	.17*	.01	.07	.18*	---								
12. Post-tx SIGH-SAD	.03	.05	-.06	.06	-.04	.10	.12	.17*	.01	.04	.27**	---							
14. W1 SIGH-SAD score	-.04	.06	-.10	-.02	-.09	.00	.11	.11	-.05	-.14	.26**	.27**	---						
15. W2 SIGH-SAD score	.05	.13	-.17*	-.03	.05	.05	.14	.08	-.05	-.06	.18*	.22**	.54**	---					
16. Post-tx SIGH-SAD remission	.05	.00	.07	.00	.00	-.12	-.10	-.13	-.11	.04	-.14	-.77**	-.27**	-.25**	--				
17. W1 SIGH-SAD remission	.05	-.06	.02	.09	.06	.02	-.07	-.15	.01	.12	-.10	-.22**	-.75**	-.44**	.22**	--			
18. W2 SIGH-SAD remission	-.08	-.11	.07	.01	-.03	.01	-.14	-.16	.07	.06	-.09	-.15*	-.39**	-.74**	.15*	.41**	---		
19. W1 SIGH-SAD recurrence	-.04	.03	-.07	-.04	-.08	.07	.03	.09	-.10	-.11	.21**	.16*	.79**	.39**	-.16*	-.46**	-.19*	--	
20. W2 SIGH-SAD recurrence	.07	.13	-.12	-.01	.09	-.04	.20*	.07	.00	.05	.19*	.13	.46**	.83**	-.17*	-.36**	-.49**	.38**	--

PH = physical health; MH = mental health; Pre-tx = pre-treatment; Post-tx = post-treatment; SIGH-SAD = Structured Interview Guide for the Hamilton Depression Rating Scale – Seasonal Affective Disorder Version; W1 = first winter followup; W2 = second winter followup

*Correlation is significant at the .05 level (2-tailed).

**Correlation is significant at the .01 level (2-tailed).

Table 3: Regression Analyses Predicting Depression Scores

Outcome: SIGH-SAD	Post-tx SIGH-SAD				Winter1 SIGH-SAD score				Winter 2 SIGH-SAD score			
	B	S.E.	t	*p*	*b*	S.E.	t	*p*	*b*	S.E.	t	*p*
Predictor: BMI												
Intercept	10.8	.97	11.06	<.001	15.2	.98	15.57	<.001	26.0	4.13	6.29	<.001
Pre-tx SIGH-SAD	.38	.10	3.84	<.001	.46	.13	3.64	<.001	.38	.14	2.76	.007
CBT-SAD vs. LT	.47	1.1	.436	.662	-.52	1.4	-.379	.705	-3.4	1.5	-2.20	.029
Physical Comorbidity	2.2	1.1	1.98	.049	--	--	--	--	--	--	--	--
Race	--	--	--	--	--	--	--	--	-1.3	.72	-1.76	.081
BMI	-.12	.14	-.874	.383	-.14	.19	-.732	.465	-.28	.20	-1.43	.155
BMI x txgroup	.18	.19	.961	.338	.05	.25	.184	.855	.25	.29	.868	.387
Predictor: Atypical Balance (AB)												
Intercept	10.7	.96	11.09	<.001	15.13	.89	16.94	<.001	25.7	3.99	6.46	<.001
Pre-tx SIGH-SAD	.35	.10	3.49	.001	.46	.12	3.92	<.001	.34	.13	2.71	.007
CBT-SAD vs. LT	.40	1.08	.37	.715	-.21	1.3	-.160	.870	-3.59	1.4	-2.62	.010
Physical Comorbidity	2.2	1.13	1.97	.051	--	--	--	--	--	--	--	--
Race	--	--	--	--	--	--	--	--	-1.2	.69	-1.80	.074
Atypical balance	-.02	.078	-.208	.835	-.22	.09	-2.49	.014	-.19	.09	-2.04	.043
AB x txgroup	.09	.11	.842	.401	.11	.13	.915	.362	.25	.13	1.88	.061

Notes:
txgroup = treatment group (CBT-SAD vs. LT), AB = atypical balance

Table 4: Regression Analyses Predicting Depression Remission

Outcome: SIGH-SAD	Post-treatment Remission				Winter 1 remission				Winter 2 remission			
	b	S.E.	*Z*	*p*	*b*	S.E.	Z	*p*	*b*	S.E.	Z	*p*
Predictor: BMI												
Intercept	-.20	.23	-.84	.402	-.57	.24	-2.34	.019	-1.2	.28	-4.27	<.001
Pre-tx SIGH-SAD	-.06	.03	-1.86	.063	-.06	.03	-1.65	.098	-.07	.04	-1.78	.075
CBT-SAD vs. LT	.12	.34	.350	.728	.09	.34	.27	.790	.56	.38	1.50	.134
BMI	-.02	.04	-.346	.729	.05	.05	1.02	.308	.11	.05	2.16	.031
BMI x txgroup	-.04	.06	-.701	.483	-.07	.06	-1.14	.255	-.16	.07	-2.14	.032
Predictor: Atypical Balance (AB)												
Intercept	-.12	.22	-.56	.572	-.61	.24	-2.56	.011	-1.3	.28	-4.66	<.001
Pre-tx SIGH-SAD	-.06	.03	-1.98	.048	-.05	.03	-1.53	.126	-.05	.03	-1.51	.131
CBT-SAD vs. LT	.03	.31	.107	.915	.12	.33	.37	.709	.68	.37	1.86	.064
Atypical balance	.02	.02	.842	.400	.07	.03	2.56	.010	.07	.03	2.52	.012
AB x txgroup	-.01	.03	-.269	.788	-.07	.03	-2.05	.041	-.10	.04	-2.70	.007

Table 5: Regression Analyses Predicting SIGH-SAD Depression Recurrence

	Winter 1 Recurrence				Winter 2 Recurrence			
	b	S.E.	Z	*p*	*b*	S.E.	Z	*p*
Predictor: BMI								
Intercept	-1.35	.30	-4.58	<.001	-.42	.27	-1.57	.117
Pre-tx SIGH-SAD	.11	.04	3.00	.003	.074	.035	2.13	.033
CBT-SAD vs. LT	.299	.396	.753	.451	-.83	.37	-2.23	.026
Mental health comorbidity	--	--	--	--	1.02	.41	2.49	.013
BMI	-.05	.06	-.874	.382	-.04	.05	-.848	.396
BMI x txgroup	-.01	.08	-.145	.885	.04	.07	.527	.598
Predictor: Atypical balance								
Intercept	-1.25	.275	-4.55	<.001	-.097	.223	-.43	.665
Pre-tx SIGH-SAD	.097	.034	2.88	.004	.085	.03	2.64	.008
CBT-SAD vs. LT	.309	.367	.842	.400	-.961	.345	-2.78	.005
Atypical balance	-.04	.03	-1.50	.13	.00	.02	.208	.835
Atypical balance x txgroup	.01	.04	.242	.809	.01	.03	.215	.830

Table 6: Linear Mixed Models Predicting Depression Post-Treatment Scores

	DV: SIGH-SAD score			
	β	*df*	*t*	*p*
Predictor: BMI				
Intercept	26.68	155	39.55	<.001
Time (Slope)	-2.48	150	-19.01	<.001
Treatment Group	-.826	151	-.875	.383
BMI	.022	151	.264	.792
Time (slope) x Treatment Group	-.058	145	-.320	.749
Time (slope) x BMI	.025	168	1.176	.241
Time (slope) x Treatment Group x BMI	-.064	142	-2.22	.028
Predictor: Baseline atypical balance				
Intercept	26.73	181	41.82	<.001
Time (Slope)	-2.48	174	-19.34	<.001
Treatment Group	-1.05	177	-1.17	.245
Pre-tx atypical balance	.0723	175	1.625	.106
Time (slope) x Treatment Group	-.067	168	-.375	.708
Time (slope) x Pre-tx atypical balance	-.004	191	-.384	.701
Time (slope) x Treatment Group x Pre-tx atypical balance	-.003	162	-.196	.845

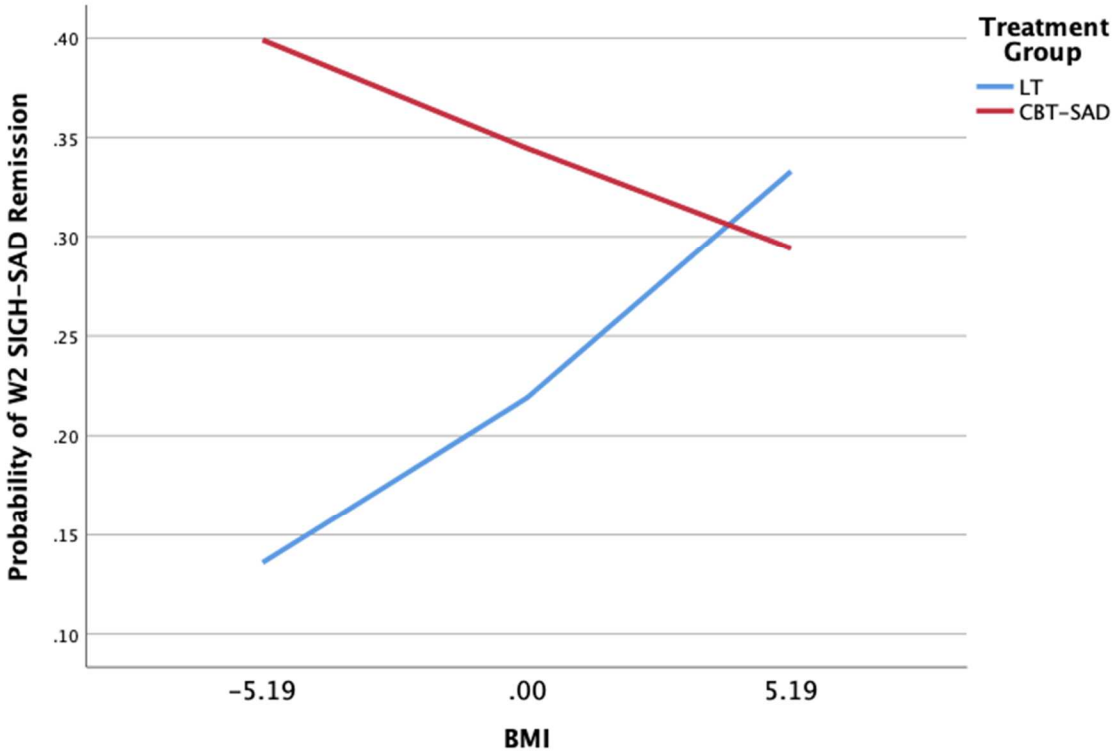

Figure 1: Decomposed BMI by Treatment Group Interaction on Probability of Winter 2 SIGH-SAD Remission

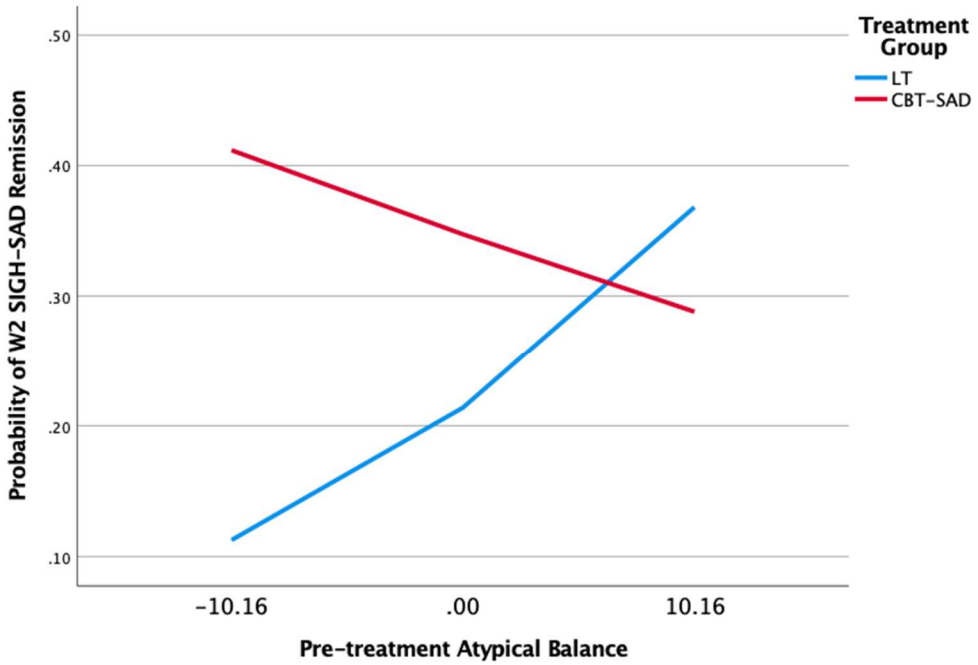

Figure 2: Decomposed Pre-treatment Atypical Balance by Treatment Group Interaction on Probability of Winter 2 SIGH-SAD Remission

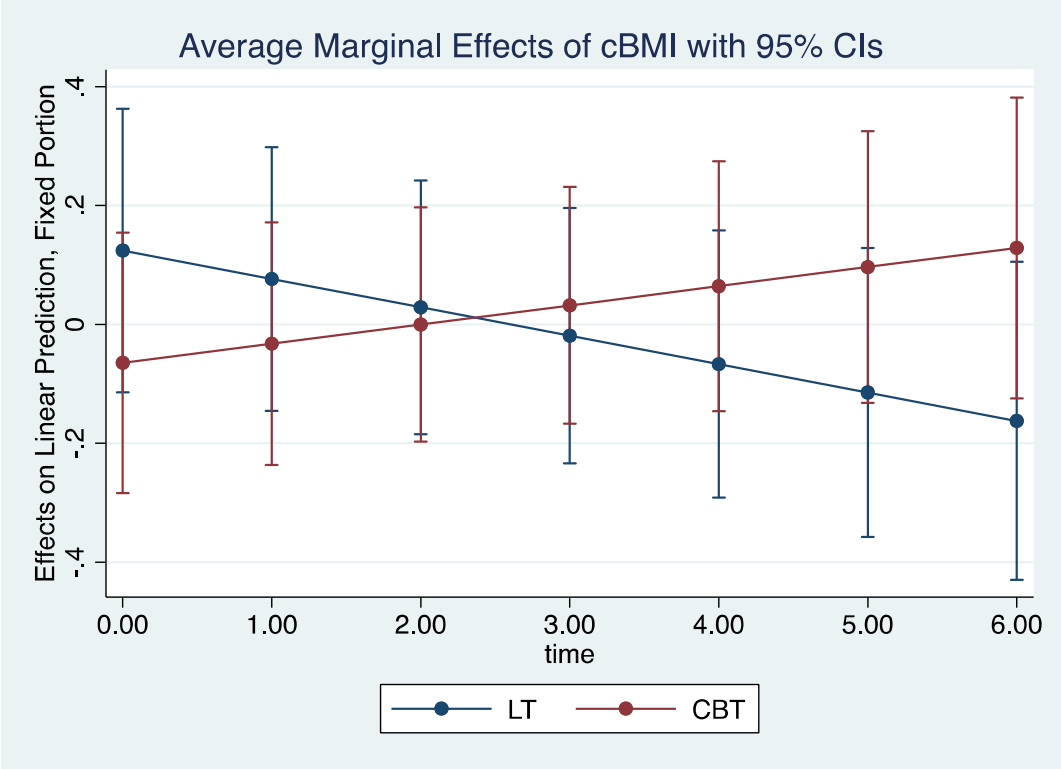

Figure 3: Marginal Effects of Centered BMI on Change in SIGH-SAD Score by Treatment Group

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