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Q&A

How did you become involved in doing research?
In the spring of 2015, I approached Dr. Steve Ilardi to ask for advice on how to get more experience in academic research, writing, and data analysis. At the time, Dr. Ilardi's Therapeutic Lifestyle Change (TLC) program had generated data on participant adherence that had not yet been analyzed. This project is my analysis and interpretation of those data.

How is the research process different from what you expected?
This project afforded me a different perspective on the entire research process because I started "in the middle of things." Dr. Ilardi and his graduate students, Christina Williams and Yevgeny Botanov, developed TLC and collected the data that I used for this project before I came to KU. My work began with the analysis and assimilation of multiple spreadsheets and documents on the participant adherence data. From this experience, I learned that data are very much alive. Even though I was not there for the original data collection, I was able to come up with an independent hypothesis and examine the data to see whether or not it was supported.

What is your favorite part of doing research?
My favorite part of doing research is writing up the final product. It's so much fun to see everything come together in words.

Better Adherence, Better Outcome: Differences in Depressed Participants' Adherence to Elements of the Therapeutic Lifestyle Change Protocol

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Depression is a devastating illness. It is the leading cause of disability worldwide, and it afflicts 6.7% of Americans every year ((World Health Organization [WHO], 2012; National Institutes of Mental Health [NIMH], 2014). Worse, there is considerable evidence that traditional therapy—particularly drug therapy—is not particularly effective (Whitaker, 2010; Krystal, Sanacora, & Duman, 2013). The data from the STAR*D trials conducted by NIMH demonstrated that, among 4,000 depressed patients given standard antidepressant drugs, only slightly more than one quarter of these patients achieved remission after 3 months (Krystal et al., 2013).

Researchers have begun investigating new avenues for treating depression, in large part because of the inadequacy of standard antidepressant treatment. Omega-3 supplementation, bright light exposure, and exercise all have a positive impact on depressive symptoms (Grosso et al., 2014; Even, Schroder, Friedman, & Rouillon, 2008; Josefsson, Lindwall, & Archer, 2014). The Therapeutic Lifestyle Change (TLC) program combines these approaches, finding that they are even more effective together than separately (Ilardi et al., 2012).

A major problem for the success of any treatment is participant adherence (Centers for Disease Control [CDC], 2013). The CDC estimates that roughly 50% of medications are not continued as prescribed (2013), and others studies suggest that adherence to non-medication regimes—such as exercise plans—is even worse (Robison & Rogers, 1994; Findorff, Wyman, & Gross, 2009). It seems that not following the doctor's orders really makes a difference too. Research shows that adherence really matters for determining

patient outcomes across a wide variety of illnesses, with this relationship being strongest for chronic illness not treated with medication (DiMatteo, Giordani, Lepper, & Croghan, 2002).

Because depression is a chronic condition that the TLC program treats without medication, and because depression itself is known to be a risk factor for non-adherence (DiMatteo, Lepper, & Croghan, 2000), this research seeks to answer two major questions about the impact of participant adherence on depressive symptoms:

1. Are participants more likely to adhere to one element of the treatment than another?
2. Does overall adherence to the TLC protocol influence the degree of therapeutic effect?

METHOD

Participants

The sample considered here consists of 95 TLC participants aged 18-65 who met DSM-V criteria for clinical depression and did not have a comorbid *DSM-V* disorder. Trained clinicians administered a full Structured Clinical Interview for DSM Disorders (SCID) in order to confirm depression status.

The Protocol

The TLC protocol consisted of fourteen 1.5 hour-long group sessions over the course of 14 weeks. Two co-therapists led the sessions, which were split roughly in two. For the first half of the session, one co-therapist led a discussion of adherence to the protocol, while for the second half, the other therapist trained participants in the protocol. Each week, a different core component of TLC was presented. The protocol consisted of six core components: omega-3 supplementation, exercise, bright light exposure, anti-ruminative strategies, sleep habit improvement, and social support. Only adherence to omega-3 supplementation, exercise, and bright light exposure are considered in this presentation. This decision was made due to missing data and difficulty in calculating adherence indices for the other elements of the protocol. For the treatment elements examined in this work, the specific protocols were:

- Omega-3: one supplement containing 1000 mg EPA (eicosapentaenoic acid) and 500 mg of DHA (docosahexaenoic acid) every day.
- Exercise: 30 minutes per day, three times a week.
- Bright Light: 10,000 lux for 30 minutes per day, every day.

Measures

All participants completed our measures of depression and adherence at the beginning of each meeting. Depression was measured using the Beck Depression Index (BDI), and adherence was measured using weekly record forms. On the weekly record form, each treatment element was listed beneath each day of the week, and participants indicated with a yes or no whether or not they adhered to the given treatment element for each day listed.

Adherence Indices

In this study, adherence specifically refers to the percent of the time participants followed the TLC protocol for each treatment element. The adherence index for omega-3 supplementation was calculated as the number of days out of 7 that participants took the supplement. For exercise, the adherence index was the percent of minutes out of 90 that participants reported for that week. For bright light exposure, the adherence index was calculated as the percentage of days out of 7 that participants reported obtaining at least 30 minutes of bright light exposure. The mean of these weekly scores was taken over fourteen weeks to calculate a mean percent adherence score for each client on each individual element. Finally, an overall adherence score for each client was calculated by taking the mean of the individual element adherence scores.

Results

Omega-3 supplementation had the highest mean percent adherence (M = 63.9%) followed by exercise (M = 54.5%), and then bright light exposure (M = 48.2%). We conducted a within-subjects analysis of variance (ANOVA) to test if mean adherence significantly differed among the three treatment elements. The overall model was significant, $F(2, 188) = 51.65$, $p < .001$. Pairwise comparisons revealed that the mean adherence scores for each element significantly differed from one another, with all *p-values* <0.001. Figure 1 depicts the differences in mean percent adherence scores for each treatment element.

The different types of adherence were highly correlated with one another (all r values > 0.8). This finding suggested that all three adherence variables were measuring the same construct—overall adherence. For this reason, we first conducted a linear regression of final BDI score on overall adherence with pretreatment BDI as a covariate. The overall model was significant, with F (4, 90) = 6.245 and p-value: 0.000176. This regression found that

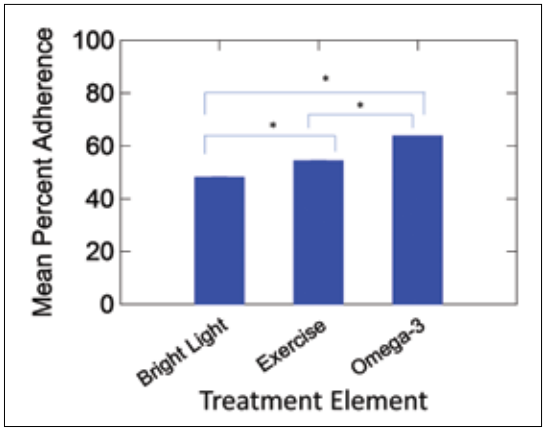

Figure 1. Mean Percent Adherence Scores for Each Treatment Element

overall adherence had a statistically significant impact on reducing final BDI score, $\beta = -0.31$, $p = 0.002$. Our multiple R^2 for this regression equaled 0.2172, signaling that overall adherence and pretreatment BDI score explained 21% of the variance in final BDI. Pretreatment BDI was added as a covariate in order to control for the fact that people who began the TLC program with lower BDI scores were more likely to complete treatment with lower BDI scores as well, even though the scores would have improved. See Table 1.

	Standardized Beta Coefficient	P-Value
Pretreatment BDI	0.30	0.002*
Overall Adherence	-0.31	0.002*

Table 1: Linear regression of final BDI score on overall adherence with pretreatment BDI as a covariate

Separate regressions of final BDI score on participant mean weekly exercise, bright light, and omega-3 adherence with pretreatment BDI as a covariate were also conducted. These results are displayed in Table 2. Since adherence to one treatment element was highly correlated with adherence to the other treatment elements, a model containing all three types of adherence had high multicollinearity. In order to avoid this problem, we regressed BDI on each individual treatment element. These regressions show that adherence to each treatment element was predictive of outcome, but not *uniquely* predictive.

	Standardized Beta Coefficient	P-Value
Pretreatment BDI	0.30	0.002*
Exercise Adherence	-0.31	0.002*

	Standardized Beta Coefficient	P-Value
Pretreatment BDI	0.31	0.002*
Exercise Adherence	-0.26	0.001*

	Standardized Beta Coefficient	P-Value
Pretreatment BDI	0.31	0.002*
Omega-3 Adherence	-0.30	0.002*

Table 2a, b, and c: Separate regressions of final BDI score on participant mean weekly exercise, bright light, and omega-3 adherence with pretreatment BDI as a covariate

DISCUSSION

Previous studies have shown that adherence directly relates to outcome, particularly for illnesses that are chronic and not treated with medication (DiMatteo et al., 2002). The linear regression in Table I suggests that this finding extends to depression treated with the TLC protocol. Better adherence generally meant a better outcome for participants.

Our finding that omega-3 supplementation had the best adherence, followed by exercise, and then bright light exposure is fairly consistent with the broader literature on adherence. To our knowledge, no previous work has been done to examine the rate of adherence to omega-3 supplementation, making it difficult to find a true reference point for our finding. However, taking an omega-3 supplement is the element of the protocol most like taking a medication or an antidepressant. A study by Lingam and Scott found that median non-adherence for antidepressant medications was 53% (Lingam & Scott, 2002), while studies of medication adherence for chronic conditions in non-depressed individuals ranges from 43% to 78% depending on the ailment being treated (Osterberg & Blaschke, 2005). Our mean percent adherence for omega-3 supplementation of 63.9% falls within this range. For exercise, our mean percent of 54.5% is similar to that found by studies of exercise adherence among specific populations, such as women and the elderly (Miranda et al., 2014; Findorff, Wyman, & Gross, 2009). However, to our knowledge, no studies rigorously examine adherence to an exercise regime among depressed patients. A study by Michalak et al. finds that average adherence to bright light exposure among patients diagnosed with seasonal affective disorder was 59.3%, which is substantially higher than our mean of 48.2% (2007). However, this study contained only 19 participants and was conducted over four weeks, limiting its generalizability.

One factor influencing the pattern of adherence observed is the amount of time required to follow each element of the protocol. Conceivably, omega-3 supplementation had the best adherence because it required the least amount of time per week. Taking an omega-3 supplement takes less than 30 seconds each day. In contrast, following the exercise protocol required 90 minutes of participants' time per week, while following the bright light protocol

required participants' time every day—a total of 210 minutes per week. Thus, the element that required the most time had the poorest adherence, while the one that required the least time had the best.

Another factor possibly influencing the pattern observed is American culture. In the U.S., we tend to prefer to treat sickness with medication rather than with lifestyle changes. So, it would follow that the element of the protocol that just requires taking a "pill" would have the best adherence. Americans also generally seek to avoid publicizing any psychiatric or psychological conditions. While one can easily take a pill without alerting a close friend or a loved one, it is much more difficult to begin a regular exercise regime or to spend 30 minutes each day obtaining bright light exposure without someone noticing. It is possible that we observed lower adherence for the exercise and bright light elements because some participants were attempting to hide their depression status from others.

A major limitation of this research is that it relied exclusively on a weekly self-report measure of adherence. It is possible that from one week to the next participants did not accurately remember on which days they followed the protocol versus on which days they did not. It is also possible that participants may have intentionally misrepresented their adherence. Future research should include additional measures of adherence to improve these issues. For example, in order to verify exercise adherence, participants could be given a heart rate monitor that records the amount of time spent exercising. A clever method of verifying bright light adherence comes from the Michalak et al. study mentioned above. In this work, the light boxes given to clients were outfitted with hidden recording devices that monitored the amount of time the boxes were turned on. However, since TLC permits clients to obtain their bright light exposure from outside, we would still rely on a self-report measure of outdoor bright light exposure.

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