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AN EXAMINATION OF THE RELATIONSHIP BETWEEN ADOLESCENT DEPRESSION, ANHEDONIA, AND BEHAVIORAL THERAPY

by

Alison A. DeLizza

A dissertation submitted to the Graduate College
in partial fulfillment of the requirements
for the degree of Doctor of Philosophy
Psychology
Western Michigan University
August 2019

Doctoral Committee:

Scott Gaynor, Ph.D., Chair
Amy Damashek, Ph.D.
Sheryl Lozowski-Sullivan, Ph.D.
Amy Naugle, Ph.D.

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ACKNOWLEDGMENTS

I would like to begin by acknowledging my mentor, Dr. Scott Gaynor, for his continued support and willingness to continuously meet, work, and re-work this project. The countless theoretical and practical discussions about depression, the RDoC, and ACT made this dissertation possible.

I would next like to thank my committee, Drs. Amy Damashek, Amy Naugle, and Sheryl Lozowski-Sullivan, for their comments and suggestions on this project. In addition, a special thanks to Dr. Jon Sikorski for his assistance and support as I completed this project from afar.

I would also like to thank Lindsey Knot, Rebecca Rausch, McKenna Corlis, Carmelita Foster, Rachel Petts, and Tanya Douleh. They each contributed to this project in different but meaningful ways, from assisting with data collection to conceptual conversations. They are all invaluable and phenomenal researchers, friends, and women.

Finally, I would like to thank my family for their support not only as I completed this dissertation, but through the journey of graduate school. To my parents, who instilled a love of learning and asking questions, I cannot thank you enough. And to my husband, Jeff, thank you for your willingness to listen to me always talk about depression, disappear for hours to write, and yet keep our lives running. Thank you for sticking with me to the end.

Alison A. DeLizza

AN EXAMMINATION OF THE RELATIONSHIP BETWEEN ADOLESCENT DEPRESSION, ANHEDONIA, AND BEHAVIORAL THERAPY

Alison A. DeLizza, Ph.D.

Western Michigan University, 2019

Adolescent depression is a significant public health problem, however the current characterization of depression as a categorical label is problematic for understanding individual phenomenology, interindividual variability, and best treatment practices (Lewinsohn, Solomon, Seeley, & Zeiss, 2000). Anhedonia has been posited as a process underlying depression that may contribute to poorer outcomes (Gabbay, 2015). The current project examines large samples of adolescents diagnosed with depression to identify common features at a symptom level and the relationship these features have with behavioral therapy outcomes. Four phases of analyses were completed to 1) examine symptomology of multiple depressed adolescent samples in order to identify core features of depression in adolescents; 2) extend a factor analysis to a new sample to determine if the same factors on the Children's Depression Rating Scale emerge; 3) determine if a prior finding that anhedonia is predictive of poorer outcomes replicates in a new sample from a large scale clinical trial; and 4) explore whether behaviorally oriented treatments appear to specifically target and diminish anhedonia symptoms. Results suggest that anhedonic symptoms, such as difficulty having fun, are among the most severely rated by adolescents. Factor analyses show a consistent anhedonia factor including difficulty having fun, social withdrawal, and depressed mood. This factor is predictive of poorer quality of life at the end of treatment in a large randomized controlled trial, particularly for females. Finally, it was found that activation

oriented behavioral therapy significantly improved anhedonic symptoms of difficulty having fun, fatigue, and disturbed sleep. These results suggest that anhedonia may be a more clinically useful identifying feature and target for treatment in adolescents. Future research should examine anhedonia targeted treatments feasibility, efficacy, and effectiveness, as well as differences that may exist for males and females treated with behavioral therapy.

Key words: *adolescents, depression, anhedonia, RDoC, behavior therapy*

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CHAPTER I

INTRODUCTION

Adolescent Depression and the DSM

The lifetime rate of Major Depressive Disorder (MDD) in adolescents is 11% (Avenevoli, Swenson, He, Burstein, & Merikangas, 2015). Of those with a MDD diagnosis, 3% are considered to have severe MDD, and 30% report some form of suicidality, highlighting the significance of this problem. Epidemiological findings show the nature of the problem in terms of the number of youth struggling with symptoms that allow for the diagnostic label of depression to be applied. However, it may underestimate the number of youth struggling with symptoms of depression that would be considered "sub-threshold", though still impairing (Avenevoli, et al., 2015). An epidemiological approach also falls prey to treating depression as a *thing* that a certain percentage of youth *have,* when no research has determined a definitive pathogenesis or any sensitive and specific markers that allow for confirmatory diagnostics (Kapur, Phillips, & Insel, 2012). Plainly speaking, there is no way independent of the symptoms to verify a depression diagnosis. The problem of reification and its risks have been identified and described in detail elsewhere (Hyman, 2010). Briefly, reification occurs when one treats or converts a concept into a concrete object. In the practice of psychology, reification is seen in the treatment of categorical diagnoses with no clear etiology or physiological bases as true illnesses individuals "have." This is problematic, as diagnoses that lack validity are used as explanations for behavior, as well as outcomes in evaluating treatments (Hyman, 2010). Consider how adolescent depression is captured in the Diagnostic and Statistical Manual of Mental Disorders (DSM-5; APA, 2013). Diagnostic criteria for adolescent depression are identical to those for adult depression with only two minor differences: 1) the presence of irritable mood may replace depressed mood, and 2) the failure to meet expected weight gain may replace a significant

weight loss. Five out of nine symptoms are still required for a diagnosis; thus two individual adolescents may receive the same diagnosis with only one symptom in common. Beyond the stipulation that symptoms be present in the same 2 weeks or greater time period and represent a change in functioning, the individual frequency, duration, intensity, or impairment of each symptom is not taken into account, effectively treating each symptom as equally contributing to the final tally. This discounts the variability in impairment and severity across symptoms and individuals. There also is no specificity of symptoms to guide practitioners in what is developmentally typical versus pathological (i.e., what is hypersomnia over the common need for more sleep in adolescents). These problems have led some to point out that a threshold of symptoms (i.e. 5 out of 9) is not absolute, but that a continuum approach is more appropriate (Lewinsohn, Solomon, Seeley, & Zeiss, 2000; Blom, et al, 2015). While this approach may better capture group level data, at an individual level, even continuous symptom scores are often summed to provide an overall depression score, paying little attention to the individual symptom items themselves. Even the use of the term "symptom" implies that the experience reported is an indicator or piece of evidence suggestive of a larger problem- the disorder- rather than of importance in its own right.

The DSM criteria sets are intended as descriptive guidelines that summarize the relevant syndromes; that is, the clusters of symptoms that are considered to reasonably co-occur but for which the etiology or pathogenesis is unknown. Implementation requires clinical judgment (APA, 2013). In practice, clinicians are often left to sort out the relevant presenting symptoms as they formulate an idiographic treatment plan. As the DSM (APA, 2013) states: "it is not sufficient to simply check off the symptoms in the diagnostic criteria to make a mental disorder diagnosis. Although a systematic check for the presence of these criteria as they apply to each patient will assure a more reliable assessment, the relative severity and valence of individual

criteria and their contribution to a diagnosis require clinical judgment… The ultimate goal of a clinical case formulation is to use the available contextual and diagnostic information in developing a comprehensive treatment plan that is informed by the individual's cultural and social context" (p. 19). This leaves considerable variability in assessment and treatment of mental health, and, for the present purposes, adolescent depression especially. The question remains, what would an empirical examination of "the relative severity and valence of individual criteria" tell us and how might this inform us about the experiences currently labeled adolescent depression?

Anhedonia and Other Factors Linked to Depression

Consistent with the concerns about reification stated above, the National Institute of Mental Health instituted the Research Domain Criteria (RDOC) initiative (Insel, et al., 2010). The RDoC model seeks to identify the "fundamental underlying mechanisms of dysfunction" utilizing all levels of analysis (i.e. genetics, neuropathways, behavior, self-report, etc.; Insel, et al., 2010). Its goal is to identify potential targets for treatment, as well as to identify potential subgroups allowing for more precise treatment selection, and ultimately to afford providers with a better match between research findings and treatment decisions (Blom, et al, 2014). As an approach, RDoC is not bound by diagnostic labels but instead examines hypothesized transdiagnostic systems and processes along dimensions from adaptive function to impairment. RDoC seeks to identify processes across levels of analysis, from molecular or cellular factors through self-report (Insel, et al, 2010). It is hypothesized that if identified, these processes linking brain circuitry and corresponding behavioral and developmental manifestations may provide a more valid taxonomy and enhanced clinical utility.

Systems of particular interest for the present purposes are the negative and positive valence systems. The negative valence system is described as involving a state of motivation deprivation that may appear in many aspects of life and may be episodic or permanent (NIMH, 2017). A subsystem of the negative valence systems is loss, which may be manifested behaviorally as anhedonia, defined as the loss of interest or pleasure in previously enjoyed stimuli (NIMH, 2017). The positive valence system involves responses for positive motivational situations, such as reward seeking, reward/habit learning, and consummatory behavior (NIHM, 2017). The DSM criteria for a Major Depressive Episode contains an anhedonia item requiring "markedly diminished interest or pleasure in all, or almost all activities" (APA, 2015). Anhedonia, as such, may be referred to as deficits in experiencing rewarding stimuli (diminished pleasure), as well as blunted anticipatory pleasure leading t deficits in reward learning (diminished interest; Dillon, et al, 2014). As is apparent, the deficits may be anticipatory and/or consummatory; experienced either while awaiting reward or after receiving the reward (Shankman, Katz, DeLizza, Sarapas, Gorka, & Campbell, 2014). Thus, neuroscience investigations have focused on reward processing systems, and indeed many studies have linked neurobiological deficits in reward processing during both reward anticipation and consumption to depression and anhedonia (Nusslock & Alloy, 2017; Dillon, et al, 2015; Shankman, et al, 2014). Other studies have linked depression to a weakened response bias, where depressed individuals fail to continue adaptive behaviors and quit too quickly in the absence of immediate reward (Dillon, et al, 2015). This can also be conceptualized as decreased reward learning, or a failure to integrate reinforcement histories into current behavior. More recent research suggests that there might be benefits to distinguishing types of anhedonia, noting that some studies have documented a decreased motivation to pursue reward, while others have focused on decreased hedonic pleasure from reward (Nusslock & Alloy, 2017). Indeed, many studies have linked self-

reported anhedonia, decreased effort to gain reward in behavioral tasks, and decreased activation in neural areas related to reward seeking (see Nusslock & Alloy, 2017 for review). Whereas other studies have focused on the link between reported anhedonia and decreased activation in areas related to reward processing during consumption. However, this link seems less reliable in the literature, leading some to call for more focus on anticipatory reward hyposensitivity and its connection to anhedonia (Nusslock & Alloy, 2017; Dillon, et al, 2015).

Additionally, the positive attenuation hypothesis identifies a blunting of emotional responding, also termed decreased emotional reactivity, to positive stimuli in maintaining depressotypic functioning (Bylsma, et al, 2008). If the response to stimuli that previously signaled reinforcement is blunted (diminished interest) and the effect of previously reinforcing consequences is blunted (diminished pleasure), this could manifest as the classic anhedonic symptoms (Bylsma, et al, 2008). One meta-analysis of studies examining emotional reactivity in depression found consistent reductions in both positive and negative emotional reactivity (Bylsma, et al, 2008). In addition, the largest effect sizes were found for reductions in positive emotional reactivity, that is, depressed patients showed less emotional responding to consumption of positive or rewarding stimuli. These findings provide further support for the potential importance of anhedonic symptoms.

Buckner and colleagues (2008) found that only 8% of a sample of 546 young adults with a history of or current depression did not endorse the anhedonia, as defined by the DSM, as a primary symptom. In addition, anhedonia was found to be associated with other severe symptoms of depression, including social withdrawal and impairment, reactivity of mood, rumination, and diurnal mood variation. This symptom pattern was different from those related to sadness and individuals who did not experience anhedonia, suggesting that anhedonia may

play a unique role (Buckner, et al, 2008). These findings come from a sample of young adults enrolled in a longitudinal study of the course of depression beginning in adolescence and thus shows that anhedonia is a relevant process related to adult depression, but also the experience of adolescents as well. Recent research has sought to determine if anhedonia is indeed a core underlying factor that is of particular importance to better characterizing adolescent depression, and illuminate what role it plays not only in dysfunction, but treatment outcomes as well.

Guo and colleagues (2006) sought to investigate the underlying components of adolescent depression through a factor analysis of the Children's Depression Rating Scale-Revised (CDRS-R; Poznanski & Mokros, 1996). The CDRS-R is a 17- item semi-structured interview for children and adolescents that assesses symptoms of depression in the past month. It is considered the gold standard for assessing depression in children and adolescents and is useful both in research and clinical practice. The CDRS-R has been used in multiple large scale clinical trials of child and adolescent depression including the Treatment of Adolescent Depression Study (TADS; TADS Team, 2005) and the Treatment of Resistant Depression in Adolescents (TORDIA; Brent, et al, 2008). Guo and associates conducted an exploratory factor analysis on the CDRS-R symptom scores of 314 adolescents enrolled in SSRI treatment trials. Patients enrolled had a primary diagnosis of major depressive disorder, indicated by a CDRS-R total score of $\geq$40. In their exploratory factor analysis, Guo et al. (2006), found 5 factors made up of 15/17 CDRS-R items: observed depressive mood, anhedonia, morbid thoughts, somatic symptoms, and reported depressive mood. The anhedonia factor was specifically made up of two items, difficulty having fun and social withdrawal. These items were argued to hang together conceptually in suggesting a degradation of reward system function particular in the interpersonal domain. However other items, such as impaired school work may also theoretically align with anhedonia. Deconstructing the criteria into factors may provide a way to move beyond

a construct label, and better address and reduce heterogeneity. An initial step is to determine whether, and which factors are consistently observed; that is, if they reliably appear across samples. Guo et al.'s (2006) factors have not yet been replicated and therefore require further exploration and confirmation in different samples, particularly to determine if the anhedonia factor remains a consistent feature across other groups of adolescents diagnosed with depression.

Some research suggests that anhedonia may not only be an important feature for best characterizing the heterogeneous experiences described currently with the term depression, but also for predicting treatment outcome. Uher and associates (2012) examined what symptom dimensions of depression predicted of response to treatment with antidepressant medication. Their study examined outcomes from two large antidepressant trials in adults, the Genome-based Therapeutic Drugs for Depression study and the Sequenced Treatment Alternatives to Relieve Depression study. Combined, the authors looked at outcomes (measured using the Hamilton Depression Rating Scale and the clinician rating of the Quick Inventory of Depression Symptomology) of over 4,400 adults treated with antidepressant medications. The only symptom dimension that significantly predicted treatment outcome across both samples was one they called "interest-activity" (Uher, et al, 2012). The interest-activity dimension was created with symptoms reflecting low interest, reduced activity, indecisiveness, and lack of enjoyment. Interestingly, high scores on this anhedonia dimension were more predictive of poorer outcomes than any other symptom dimension, even when controlling for baseline depression severity and other clinical covariates (such as type of medication, age of onset, and number of past depressive episodes; Uher, et al, 2012). These findings suggest the importance of anhedonia in predicting (poorer) treatment outcomes for adults treated with antidepressant medication.

Gabbay and colleagues (2015) conducted a similar study examining the role anhedonia plays in outcomes for adolescents with depression. They used the CDRS-R and Beck Depression Inventory (BDI) items measuring anhedonia (i.e. “loss of pleasure”, “difficulty having fun”, “loss of interest”) and irritability to predict clinical outcomes in a sample of adolescents with a current diagnosis of MDD. Anhedonia and irritability scores were normally distributed with a wide range of severity. Gabbay, et al. (2015) found that anhedonia and irritability scores were correlated with overall severity, suicidality, duration of current MDD episode, number of MDD episodes, and past suicide attempts. However, when included in a multiple regression model, high levels of anhedonia alone were associated with worse clinical outcomes, including greater overall severity as well as suicidality, longer duration, and more MDD episodes. Irritability did not predict any of these outcomes (Gabbay, et al., 2015). These findings further highlight the potential importance of specifically assessing and targeting anhedonia in treatment. These findings challenge the essentialist views requiring a necessary symptom for a diagnosis of adolescent depression and instead direct attention to interindividual variability and a more nuanced understanding of symptom presentation (Gabbay, et al., 2015).

McMakin and colleagues (2012) also suggest anhedonia may be and unique and central feature in adolescent depression. This study used data from the Treatment of Resistant Depression in Adolescents (TORDIA; Brent, et al., 2008) trial of 334 teens who had failed to improve with previous antidepressant medication treatment. Teens were randomized to either a medication switch or medication switch plus Cognitive Behavioral Therapy (CBT). In this study, the five dimensions of the CDRS-R found by Guo and colleagues (2006) were used as predictors for time to remission (measured in days) and the number of depression free days. While multiple dimensions were associated with outcomes independently, when included together only anhedonia significantly predicted outcomes. Higher scores on the anhedonia dimension predicted

fewer depression free days as well as a longer time to remission. In fact, anhedonia served as a better predictor for poorer clinical outcomes than overall depression score on the CDRS-R, highlighting its potential as an important prognostic indicator for depressed adolescents and as a target for treatment.

Blom and colleagues (2014) proposed a model of behavioral intervention for adolescent depression constructed to target specific RDoC domains implicated in depression (named "TARA", Training for Awareness Resilience, and Action). When recommending treatment strategies for the positive valence system domains of approach motivation and reward learning (part of the reward circuitry linked to anhedonia; Dillon et al., 2014), they suggest behavioral activation strategies targeting the practice of approach behavior (rather than avoidance) toward goals determined by core values (Blom, et al., 2014). These techniques centering on values-based behavioral activation and are drawn from contemporary cognitive behavioral therapies including Mindfulness Based Cognitive Behavioral Therapy, Acceptance and Commitment Therapy, Behavioral Activation, Dialectical Behavioral Therapy, and Compassion Therapy. An initial single arm clinical trial of TARA was conducted with 26 adolescents with mild-moderate depression. After 12 weeks of behavioral treatment, adolescents had significantly reduced symptoms of depression, which remained at 6 month follow up (Blom, et al, 2017). In addition, the anhedonia subscales of the Reynolds Adolescent Depression Scale (RADS-2) and Avoidance and Fusion Questionnaire for Youth (AFQ-Y) showed small, but significant decreases after treatment. This study is promising, and the authors hypothesize that the small effect sizes found may be attributable to the shorted amount of time spent on activation practices (Blom, et al 2017). Further research is required to determine if more targeted behaviorally based treatments have a larger impact on anhedonic symptoms. For example, studies utilizing treatment focused on behavioral activation, have shown promising results. In one such study, an activation focused

protocol of Acceptance and Commitment Therapy was found to significantly improve depression scores on the CDRS-R, Beck Depression Inventory (BDI-II), and the Behavioral Activation for Depression Scale- Short Form (BADS-SF) in a group of 11 teenagers with clinical depression (Petts, et al, 2017). Similarly, Gaynor & Harris (2008) found that improvements in activation scores on the BADS-SF mediated treatment response in a trial of Values-Based Behavioral Activation. Both of these studies represent small, single-subject studies of behavioral therapy for depression and provide promising initial evidence for activation-focused treatments as potentially effective in targeting anhedonia and depression.

Taken together, the studies reviewed above suggest that anhedonia is a signature feature of adolescent depression. It is linked to reward circuitry and reward processing and is represented in the RDoC initiative's focus on approach motivation and reward learning (Nusslock & Alloy, 2017; Shankman, et al., 2015; Dillon, et al., 2014). Several studies have demonstrated its predictive influence in treatment outcome for both adolescents and adults, specifically as a negative predictor of response to antidepressant medication and cognitively-focused therapies (Gabbay, et al., 2015; Blom, et al., 2014; McMakin, et al., 2012; Uher, et al., 2012). However, initial findings suggest that anhedonia may indeed be successfully targeted by behaviorally-oriented treatments emphasizing activation (Gaynor & Harris, 2008; Petts, et al., 2017).

The Present Study

The present study has multiple aims addressed in four phases. The first aim is to examine item-level symptom ratings on the CDRS-R across multiple depressed adolescent samples in order to identify, and rank order, the most highly endorsed features of depression in adolescents. Of particular interest is whether the item-level ratings will be consistent across samples and

where in the rank ordering of symptom endorsements will the items that are considered to represent anhedonia fall. The second aim is to determine whether the factors identified by Guo et al. (2006) are also identified in the Treatment for Adolescents with Depression Study (TADS; TADS Team, 2005) dataset. Again, the anhedonia factor is of particular interest. Next, this study seeks to replicate and extend McMakin et al.'s (2012) finding that anhedonia is predictive of poorer outcomes, again using the TADS sample. Finally, this study explores whether behaviorally oriented treatments targeting values-based behavioral activation diminish the individual anhedonia symptoms in adolescents from a racially diverse sample generated from treatment outcome studies in the Behavioral Research and Treatment lab at Western Michigan University.

CHAPTER II

PHASE ONE

Rank Ordering the Symptoms of Depression

Phase 1 entails an item analysis of the CDRS-R (Poznanski & Mokros, 1996) to provide a characterization of the most highly endorsed symptoms of adolescent depression. As reviewed above, the DSM criteria for adolescent depression are largely those used with adults. However, adolescents experience unique developmental challenges that may alter the presentation of depression (Zeiss, 2006). Current research and clinical descriptions emphasize the presence of low mood, irritability, and anhedonia in teenagers diagnosed with depression (Gabbay et al, 2015). A clearer understanding of what symptoms are most and least endorsed will contribute to our understanding of how to best characterize the experience of adolescent depression, allow for comparisons with adult samples, and potentially contribute to identification of targets to guide treatment research for adolescent depression. Furthermore, this phenomenology may serve to guide the creation of treatments in an RDoC consistent manner, looking at specific targets of dysfunction as opposed to generalized labels (Blom, et al, 2014). In addition, this phase aimed to examine the consistency of item level rank orderings across multiple large samples. This analysis also sought to identify where anhedonia linked items appear in the rank ordering to determine if their placement supported the central role anhedonia has been accorded in recent research.

Methods

Participants

CDRS-R item scores were taken directly from publications by Guo et al. (2006) and Mayes et al. (2010). Guo's sample consisted of 314 adolescents enrolled in two clinical trials of

fluoxetine. All participants had a primary diagnosis of depression utilizing the CDRS-R with a score of ≥40. Participants were aged 7-17, and 48% identified as female. Racial/ethnic data were not provided in the publication. The sample from Mayes et al. (2010) included 94 adolescents with a diagnosis of depression included in a relapse prevention trial of fluoxetine. The sample included adolescents aged 12-17, and 46% identified as female. It was predominantly Caucasian (75%), followed by 12% Hispanic, 10% African American, and 2% other. The current project will utilize the published item means from the baseline evaluations, as participants had not yet received any treatment for depression.

Two other datasets were also for analysis. The first was the Treatment for Adolescents with Depression Study (TADS; TADS Team 2004). The TADS database is freely accessible through the NIMH with permission. Detailed explanations of recruitment procedures and treatment outcomes have been widely published elsewhere (TADS Team, 2003, 2005). In brief, the TADS randomized controlled trial compared Cognitive Behavioral Therapy, fluoxetine, the combination of the two, and a placebo control as treatment for depression in teens ages 12-17 years. TADS inclusion criteria required a score ≥45 on the CDRS-R at initial assessment and resulted in a randomization of a total of 439 teens. The first fourteen items of the CDRS-R were used. The TADS sample was 54% female, with 12% African American, 73% Caucasian, and 8% Hispanic (TADS Team, 2005).

The second database is compiled from four open clinical trials of behavior therapy (Acceptance and Commitment Therapy and Behavioral Activation) for adolescent depression conducted through the Behavior Research and Therapy Lab at Western Michigan University (Petts, et al., 2016; 2017). Teens enrolled in all four trials had a primary diagnosis of depression evidenced by a CDRS-R score of ≥45. This sample included 59 diverse and often

socioeconomically disadvantaged adolescents aged 14-18. The WMU sample was 67.8% female, with 47% African American, 7% Arab, 15% Caucasian, 4% Hispanic, and 19% multiracial.

Measures

Children's Depression Rating Scale-Revised (CDRS-R*;* Poznanski and Mokros, 1996). The CDRS-R is a semi-structured interview that assesses the presence and severity of depression in youth. It may be administered with either the adolescent or their parent. The 17 items are rated by an evaluator on a seven-point Likert-type scale, with the exception of two items (Sleep Disturbance and Appetite Disturbance) rated on a five-point scale (the higher the score, the more severe the symptom). Scores ≥ 40 are considered to indicate depressive disorder is likely and a score ≤ 28 indicates remission. Although initially developed in children, the administration to adolescents is indicated, with acceptable to excellent internal consistency (*Cronbach's* α = .74-.92; Mayes, Bernstein, Haley, Kennard, & Emslie, 2010). The CDRS-R is considered the gold standard for assessment of depression in children and teens and has been used in multiple large scale randomized controlled trials of adolescent depression treatments (TADS Team, 2004; TORDIA Team, 2008). Typical inclusion criteria for outcome studies is a total score of $\geq$ 45.The 14 self-report items may be ranked at the individual item level to provide a nomothetic sense of "the relative severity and valence of individual criteria" (APA, 2015, pg. 19) among adolescents who meet criteria for a diagnosis.

Analytic Strategy

All analyses were conducted using IBM SPSS version 24. Item means were first ranked in each sample to allow for similarities and differences across samples to be determined. Then, Pearson product moment correlations were conducted to examine the consistency of item ratings across the four samples. Based on the significant correlations, the samples were combined into

one set of ranked item means. Item means were averaged across the 4 samples, using weighted averages to account for the variable sample sizes, to create total mean scores. These weighted item means were then ranked to determine which symptoms were rated as most severe.

Results

The orderings of the item means from the individual study samples were similar and highly correlated (see Tables 1 and 2). Across all four samples, the mean ratings on the items impaired school work, difficulty having fun, and depressed mood were ranked in the top 5 most severe symptoms. In addition, fatigue, irritability, and low self-esteem were in the top 5 in 3 out of the 4 samples. All four samples were highly and significantly correlated (Pearson *r's* between .874-.983, all *p's* = .000; see Table 2). Thus, the samples were combined to create a dataset including scores from 906 adolescents. Item means were calculated using weighted averages based on the size of each sample. When combined, the most severe symptoms were (in order): difficulty having fun, fatigue, depressed mood, irritability, and low self-esteem (see Table 3).

Because two items (sleep disturbance and appetite disturbance) are scored on a 5-point Likert scale rather than a 7-point scale, thus suppressing their means, these items were re-scored to convert them to a 7-point rating. To do this, the item score was divided by 5, then multiplied by 7 (i.e. for the Mayes sleep disturbance item, it was (3.80/5)*7 = 5.32). Item means with the two converted scores are listed in Table 4. With this conversion, sleep disturbance now became the highest ranking items in each sample, and the highest ranked item in the combined, weighted sample.

Table 1: Item Means and Standard Deviations for Mayes, Guo, TADS, and WMU Samples

Item	Mayes N=94		Guo N=314		TADS N=439		WMU N=59	
	M (SD)	Rank	*M (SD)*	Rank	*M (SD)*	Rank	*M (SD)*	Rank
1. Impaired Schoolwork	4.20 (1.30)	5	4.54 (1.71)	5	4.35 (1.82)	4	4.20 (1.87)	4
2. Difficulty Having Fun	4.50 (1.10)	3	4.69 (1.30)	3	4.62 (1.59)	2	5.05 (1.50)	1
3. Social Withdrawal	3.80 (1.20)	7	3.84 (1.43)	8	3.47 (1.60)	7	3.95 (1.72)	6
4. Sleep Disturbance	3.80 (1.20)	7	3.69 (1.41)	9	3.39 (1.67)	8	3.78 (1.39)	7
5. Appetite Disturbance	2.90 (1.20)	10	2.88 (1.30)	11	2.73 (1.51)	9	2.92 (1.50)	10
6. Excessive Fatigue	4.60 (1.30)	2	4.51 (1.54)	6	4.67 (1.85)	1	4.46 (1.92)	2
7. Physical Complaints	3.20 (1.50)	9	3.44 (1.61)	10	2.51 (1.69)	10	2.66 (1.75)	11
8. Irritability	4.40 (1.00)	4	4.92 (1.39)	1	4.22 (1.73)	6	4.29 (1.45)	3
9. Excessive Guilt	2.50 (1.30)	12	2.76 (1.41)	13	1.97 (1.40)	12	2.27 (1.43)	14
10. Low Self-Esteem	4.20 (1.10)	5	4.72 (1.34)	2	4.26 (1.82)	5	3.46 (1.78)	9
11. Depressed Feelings	4.70 (.90)	1	4.68 (1.19)	4	4.48 (1.94)	3	4.17 (1.51)	5
12. Morbid Ideation	2.40 (1.20)	13	2.83 (1.61)	12	1.93 (1.53)	13	2.56 (1.30)	12
13. Suicidal Ideation	2.10 (1.30)	14	2.52 (1.42)	14	1.68 (1.34)	14	2.56 (1.63)	12
14. Excessive Weeping	2.80 (1.50)	11	4.10 (1.83)	7	2.50 (1.85)	11	3.49 (2.01)	8

Table 2: Sample Correlations

	Guo	Mayes	TADS
Mayes	.983**		
TADS	.923**	.920**	
WMU	.878**	.874**	.909**

*** Correlation is significant at the .001 level (2-tailed)*

Table 3: Ranked CDRS-R Weighted Item Means		
Rank	Item	Mean
1	2. Difficulty Having Fun	4.66
2	6. Excessive Fatigue	4.55
3	11. Depressed Mood	4.52
4	8. Irritability	4.52
5	10. Low Self-Esteem	4.40
6	1. Impaired School Performance	4.39
7	3. Social Withdrawal	3.71
8	4. Sleep Disturbance	3.55
9	14. Excessive Weeping	3.25
10	7. Physical Complaints	2.88
11	6. Appetite Disturbance	2.80
12	12. Morbid Ideation	2.34
13	9. Excessive Guilt	2.31
14	13. Suicidal Ideation	2.10

Discussion

In this phase, symptomology of adolescent depression was examined by assessing the severity of individual items across a large sample of teenagers. Notably, difficulty having fun was found as one of the most severe items in each sample individually, and when the samples were combined was the most strongly endorsed CDRS-R item. Other symptoms potentially consistent with anhedonia were also found to be highly rated, including excessive fatigue, impaired school performance, and social withdrawal. Thus, a phenomenology that includes severe symptoms of anhedonia is seen as potentially characteristic of depression in adolescents. That difficulty having fun, depressed mood and irritability were all among the highest rated symptoms is consistent with the DSM-5 criteria where a diagnosis of MDD requires the presence

Table 4: Item Means and Standard Deviations for Mayes, Guo, TADS, and WMU Samples with Items 4 and 5 Converted to 7-point Scale

Item	Mayes N=94		Guo N=314		TADS N=439		WMU N=59		Total Sample N= 906	
	M (SD)	Rank	*M (SD)*	Rank	*M (SD)*	Rank	*M (SD)*	Rank	*M*	Rank
1. Impaired Schoolwork	4.20 (1.30)	6	4.54 (1.71)	6	4.35 (1.82)	5	4.20 (1.87)	5	4.39	7
2. Difficulty Having Fun	4.50 (1.10)	4	4.69 (1.30)	4	4.62 (1.59)	3	5.05 (1.50)	2	4.66	2
3. Social Withdrawal	3.80 (1.20)	9	3.84 (1.43)	10	3.47 (1.60)	9	3.95 (1.72)	7	3.71	9
4. Sleep Disturbance	5.32 (1.20)	1	5.17 (1.41)	1	4.74 (1.67)	1	5.29 (1.39)	1	5.02	1
5. Appetite Disturbance	4.06 (1.20)	8	4.03 (1.30)	9	3.82 (1.51)	8	3.20 (1.50)	10	3.88	8
6. Excessive Fatigue	4.60 (1.30)	3	4.51 (1.54)	7	4.67 (1.85)	2	4.46 (1.92)	3	4.55	3
7. Physical Complaints	3.20 (1.50)	10	3.44 (1.61)	11	2.51 (1.69)	10	2.66 (1.75)	11	2.88	11
8. Irritability	4.40 (1.00)	5	4.92 (1.39)	2	4.22 (1.73)	7	4.29 (1.45)	4	4.52	4
9. Excessive Guilt	2.50 (1.30)	12	2.76 (1.41)	13	1.97 (1.40)	12	2.27 (1.43)	14	2.31	13
10. Low Self-Esteem	4.20 (1.10)	6	4.72 (1.34)	3	4.26 (1.82)	6	3.46 (1.78)	9	4.40	6
11. Depressed Feelings	4.70 (.90)	2	4.68 (1.19)	5	4.48 (1.94)	4	4.17 (1.51)	6	4.52	4
12. Morbid Ideation	2.40 (1.20)	13	2.83 (1.61)	12	1.93 (1.53)	13	2.56 (1.30)	12	2.34	12
13. Suicidal Ideation	2.10 (1.30)	14	2.52 (1.42)	14	1.68 (1.34)	14	2.56 (1.63)	12	2.10	14
14. Excessive Weeping	2.80 (1.50)	11	4.10 (1.83)	8	2.50 (1.85)	11	3.49 (2.01)	8	3.25	10

of at least one of these symptoms. This is also a limitation, as all of the samples used were from studies recruiting and enrolling adolescents who met criteria for depression, potentially ensuring these would be among the most prevalent symptoms. However, just because these symptoms were required to be present by the DSM-5 does not mean that they must be the most severely rated. In addition, the consistently low ranking of suicidal ideation was likely influenced by data

coming from studies where acute suicidality would result in immediate intervention and often removal from, or ineligibility for, the study protocol.

The finding that fatigue was the second most severely rated is consistent with the metaphor of being "pressed down" or depression that involves not only mood change and difficulty experiencing pleasure but also being low energy. Reports of fatigue may also be related to sleep disturbance, which was the most highly rated item when re-scored on a 7-point scale. Unfortunately, the CDRS-R does not differentiate hypersomnia from sleep onset insomnia, middle awakening, or early morning awakening, as all sleep disturbances are coded on this single item. Sleep disturbance might well contribute to feeling fatigued, heightened emotional sensitivity and reactivity, and changes in the reinforcing and punishing effects of consequences. Indeed, most theories of depression postulate a "downward spiral" or "vicious cycle" wherein the effects of life events begin a cascade of interacting effects (Zeiss, 2006). To capture these interactions would require finer-grained time series data. The cross sectional data available here can only examine the severity of reported symptoms and whether certain symptoms appear to reliably cluster. In addition, it is unclear if sleep disturbance is a specific characteristic of adolescent depression. Disturbed sleep is a common feature of adolescent development as well as a broad range of psychiatric disorders (APA, 2015). Having identified and rank ordered the most severely rated symptoms by adolescents meeting criteria for depression, the relationships between symptoms can be examined. Thus, in Phase 2 the TADS CDRS-R data were subjected to principal components analyses to identify factors- items that were correlated with one another, but somewhat orthogonal from the others.

CHAPTER III

PHASE 2

Factor Analysis of the CDRS-R

Phase 2 sought to extend the findings of Guo and colleagues (2006) to determine what CDRS-R items appeared to cluster into factors. Guo et al. conducted an exploratory factor analysis of the CDRS-R teen self-report from 314 youth (demographics described above), utilizing a Maximum Likelihood extraction method with Promax rotation. In order to determine the number of factors, Guo et al. (2006) considered the scree test as well as the Chi-square measure of fit test based on the ML estimation. Factors were maintained if they had at least two salient loading items and accounted for 5% of the common variance. Items were maintained on a factor if they had a loading greater than .35, shared conceptual meaning, and did not cross-load on multiple factors. If an item did cross-load, it was excluded. This analytic method resulted in five factors. The first, *Observed Depressive Mood*, was made up of the three clinician rated items: Tempo of Speech, Hypoactivity, and Depressed Facial Affect. The second factor was *Anhedonia* and was composed of Social Withdrawal and Difficulty Having Fun. The third factor Guo and colleagues titled *Morbid Thoughts* and included Morbid Ideation and Suicidal Ideation. The *Somatic Symptoms* factor included Excessive Fatigue, Impaired Sleep, Physical Complaints, and Impaired Schoolwork). The final factor, *Reported Depressive Mood*, was composed of Weeping, Depressed Feelings, and Low Self-Esteem (see Table 5). As is apparent, not all items in the CDRS-R loaded onto a factor; namely Irritability, Change in Appetite, and Guilt. These items reportedly had low correlations with multiple factors, and no loading that exceeded .35. It is notable that irritability did not appear in a factor given its prominence in certain conceptualizations of adolescent depression, and the authors note this requires further

exploration and explanation. Of particular interest is the emergence of an anhedonia factor comprised of social withdrawal and difficulty having fun. In RDoC, anhedonia is typically related to the negative valence system and social withdrawal is related to the RDoC construct of loss of social relationships; that is, responding to aversive interpersonal contexts by withdrawing. The experience of difficulty having fun may also be understood in terms of an aversive context, but also may implicate the positive valence system and sensitivity to reinforcement in positive contexts. Importantly, both may link to dysregulated reward circuitry (Nusslock & Alloy, 2017; Dillon, et al., 2015). Thus, more examination is needed to shed light on these constructs.

Table 5. Factors and Loadings of Guo, et al. (2006)

Factor	Salient Loading Item	Loading
Factor 1:	Observed Depressed Mood	
	16. Tempo of Speech	.86
	17. Hypoactive	.69
	18. Depressed Facial Affect	.58
Factor 2:	Anhedonia	
	3. Social Withdrawal	.81
	2. Difficulty Having Fun	.60
Factor 3:	Morbid Thoughts	
	12. Morbid Ideation	.87
	13. Suicidal Ideation	.44
Factor 4:	Somatic Symptoms	
	6. Excessive Fatigue	.58
	4. Sleep Disturbance	.43
	7. Physical Complaints	.42
	1. Impaired Schoolwork	.40
Factor 5:	Reported Depressive Mood	
	14. Excessive Weeping	.63
	11. Depressed Feelings	.45
	10. Low Self-Esteem	.38

Taken from Guo, Nilsson, Heiligenstein, Wilson, and Emslie, 2006

Methods

Participants

Data were from 439 teens in the TADS sample, which was described above (TADS Team, 2004). Data used in these analyses included the first 14 items on the CDRS-R for those participants who were randomized into a treatment condition and met inclusion criteria (minimum CDRS-R total score of 45). The TADS protocol did not score the 3 clinician rated items of the CDRS-R; thus, analyses did not include Tempo of Speech, Hypoactivity, or Depressed Facial Affect. In addition to the interviews conducted with the teen as the informant, analyses were also conducted using the CDRS-R scores from interviews where the informant was a primary caregiver.

Analytic Strategy

Analyses were first conducted using the approach described by Guo and colleagues (2006). A Maximum Likelihood extraction and Promax rotation was conducted on the raw (non-imputed) TADS pretreatment CDRS-R data collected from interviews with the teen using SPSS version 24 (Dimension Reduction -> Factor Analysis procedure). However, with every attempt at this procedure, a communalities error was reported, stating that communalities values were greater than one. Errors with communality estimates over one are known as "ultra- Heywood Cases" and imply there is some unique factor with a negative valence and indicates a problem with the analytics (SAS/STAT 9.22 User's Guide, 2010). This error renders a factor solution invalid, and thus calls any interpretation into question. Because the procedure used by Guo and colleagues (2006) was not the standard/default method for carrying out factor analysis, we next attempted the analysis with a conventional approach following the recommendations of Tabachnick & Fidell (2013). A factor analysis using a Principal Components extraction with

Varimax rotation (Tabachnick & Fidell, 2013) was used and did not result in the communalities error. For these principal components analyses, the number of factors maintained in the model was determined by eigenvalues greater than 1, and items with loadings of >.35 were maintained in a factor. In addition, and unlike Guo et al. (2006), when items cross-loaded on multiple factors, they were represented in the component on which they had the highest loading. After initial analysis with the teen informant data was conducted, the same analytic method was used to examine the pre-treatment parent informant CDRS-R scores. Unique principal component analyses were also conducted based on male or female gender identification, to determine if any gender differences in factors were present.

Results

Item means for each group (full sample, parents, males, and females) are presented in Table 6.

Table 6. Item means for CDRS-R in TADS Groups

Item	Full Sample *M(SD)* N= 429	Parent Sample *M(SD)* N= 431	Males *M(SD)* N= 194	Females *M(SD)* N= 235
1. Impaired Schoolwork	4.36 (1.81)	4.54 (1.94)	4.46 (1.82)	4.25 (1.82)
2. Difficulty Having Fun	4.61 (1.60)	4.69 (1.61)	4.45 (1.69)	4.77 (1.51)
3. Social Withdrawal	3.45 (1.59)	3.61 (1.68)	3.41 (1.72)	3.52 (1.51)
4. Sleep Disturbance	3.41 (1.67)	3.22 (1.66)	3.36 (1.70)	3.42 (1.66)
5. Appetite Disturbance	2.73 (1.51)	2.55 (1.48)	2.55 (1.54)	2.88 (1.47)
6. Excessive Fatigue	4.69 (1.84)	4.61 (1.92)	4.27 (1.91)	5.01 (1.73)
7. Physical Complaints	2.54 (1.70)	2.47 (1.68)	2.09 (1.43)	2.87 (1.82)
8. Irritability	4.22 (1.72)	4.41 (1.68)	4.11 (1.78)	4.31 (1.70)
9. Excessive Guilt	1.98 (1.41)	1.69 (1.20)	1.73 (1.21)	2.17 (1.52)
10. Low Self-Esteem	4.25 (1.82)	4.51 (1.66)	3.92 (1.94)	4.54 (1.68)
11. Depressed Feelings	4.50 (1.64)	4.56 (1.51)	4.15 (1.74)	4.76 (1.52)
12. Morbid Ideation	1.93 (1.54)	1.50 (1.19)	1.71 (1.33)	2.12 (1.67)
13. Suicidal Ideation	1.67 (1.34)	1.34 (.94)	1.53 (1.18)	1.80 (1.45)
14. Excessive Weeping	2.51 (1.85)	2.12 (1.60)	1.71 (1.21)	3.16 (2.03)

Teen Informant

Prior to conducting the principal components analysis, data were assessed for normality. Skewness was .22 with a nonsignificant test statistic ($Z_{skewness}$ = skewness/standard error of skewness, Field, 2009), $Z = 1.87$, $p > .05$, suggesting the distribution of values was relatively symmetrical around the mean. Likewise, kurtosis was .30 with a nonsignificant test statistic ($Z_{kurtosis}$ = kurtosis/standard error of kurtosis, Field, 2009), $Z = 1.29$, $p > .05$, indicating a distribution that while slightly peaked was generally close to normal. The D 'Agostino-Pearson test of normality was also nonsignificant ($\chi^2 = 5.17$, $p = .08$), further indicating the relative normality of data. The Kaiser-Meyer-Olkin (KMO) Measure of Sampling Adequacy and Bartlett's Test of Sphericity provide minimum standards for conducting a principal components analysis. The KMO result, which can vary between 0 and 1, was .82, indicating the degree of common variance among the CDRS-R items was acceptable (Kaiser & Rice, 1974). Likewise, Bartlett's test was significant, suggesting that the items were correlated, $\chi^2 = 1200.94$, $p < .001$. Based on these outcomes, principal components analyses were conducted.

Using the Dimension Reduction platform in IBM SPSS 24, a principal component analysis using varimax rotation with Kaiser normalization was conducted on the CDRS-R item scores from the TADS teen self-report sample. The principal components analysis resulted in three factors with eigenvalues greater than 1.0, which together accounted for 47.14% of the variance. All 14 items loaded onto one of the three factors. Factor 1, which we labeled Somatic Complaints, accounted for 17.04% of the variance and was comprised of items 4, 5, 6, 7, 8, and 14 which all had loadings greater than .35 (see Table 7). Factor 2, which we called Anhedonia, accounted for 15.41% of the total variance and was comprised of items 1, 2, 3, and 11 all of which had loadings greater than .35 (see Table 7). Finally, Factor 3, which we labeled Negative

Ideation, accounted for 14.71% of the variance and included items 9, 10, 12, and 13 all of which had loading greater than .35 (see Table 7).

Table 7. Teen Self-report Factors and Variance Explained

Factor	Salient Loading Item	Loading	% Variance
Factor 1:	Somatic Complaints		17.04
	4. Sleep Disturbance	.47	
	5. Appetite Disturbance	.64	
	6. Excessive Fatigue	.46	
	7. Physical Complaints	.64	
	8. Irritability	.48	
	14. Excessive Weeping	.60	
Factor 2	Anhedonia		15.41
	1. Impaired Schoolwork	.62	
	2. Difficulty Having Fun	.77	
	3. Social Withdrawal	.70	
	11. Depressed Feelings	.52	
Factor 3:	Negative Ideation		14.71
	9. Excessive Guilt	.42	
	10. Low Self-Esteem	.45	
	12. Morbid Ideation	.82	
	13. Suicidal Ideation	.81	

Parent Report

Prior to conducting the principal components analysis on the parent report, data were assessed for normality. Skewness was .207 with a nonsignificant test statistic ($Z_{skewness}$ = skewness/standard error of skewness, Field, 2009), $Z = 1.74$, $p > .05$, suggesting the distribution of values was relatively symmetrical around the mean. Likewise, kurtosis was .242 with a nonsignificant test statistic ($Z_{kurtosis}$ = kurtosis/standard error of kurtosis, Field, 2009), $Z = 1.02$, $p > .05$, indicating a normal distribution. The D 'Agostino-Pearson test of normality was nonsignificant ($\chi^2 = 4.07$, $p = .13$), further indicating the relative normality of data. The KMO result, which can vary between 0 and 1, was .77, indicating the degree of common variance among the CDRS-R items was acceptable (Kaiser & Rice, 1974). Likewise, Bartlett's test was

significant, suggesting that the items were correlated, $\chi^2 = 874.61$, $p < .001$. Based on these outcomes, principal components analyses were conducted.

Using the same analytic method described above (Dimension Reduction -> Principal Component), a principal components analysis using varimax rotation with Kaiser normalization was conducted on the parent reports. The principal components analysis resulted in four factors with eigenvalues greater than 1.0 which accounted for 52.28% of the total variance and included all 14 items. Factor 1 accounted for 24.28% of the total variance and was comprised of items 2, 3, 8, 10, and 11 which all had loadings greater than .35 (see Table 8). Factor 2 accounted for 11.24% of the total variance and included items 1, 4, and 6 with loadings greater than .35 (see Table 8). Factor 3 accounted for 9.05% of the variance and was comprised of items 7, 9, and 14 which had loadings greater than .35 (see Table 8). Lastly, Factor 4 accounted for 7.71% of the total variance and was made up of items 12 and 13 which both had loadings greater than .35.

Table 8. Parent -reported Factors and Variance Explained

Factor*	Salient Loading Item	Loading	% Variance
Factor 1:			24.28
	2. Difficulty Having Fun	.73	
	3. Social Withdrawal	.73	
	8. Irritability	.44	
	10. Low Self-Esteem	.66	
	11. Depressed Feelings	.57	
Factor 2:			11.24
	1. Impaired Schoolwork	.49	
	4. Sleep Disturbance	.70	
	6. Excessive Fatigue	.52	
Factor 3:			9.05
	7. Physical Complaints	.54	
	9. Excessive Guilt	.65	
	14. Excessive Weeping	.63	
Factor 4:			7.71
	12. Morbid Ideation	.77	
	13. Suicidal Ideation	.86	

*In Principal Components Analysis, the names applied to the empirically determined factors are decided by the researchers. The parent factors were left untitled, as the items contributing to each factor did not make clear conceptual sense, and thus are identified simply by their factor number

Analysis by Gender

Prior to conducting the principal components analysis by gender, data from males and females were assessed for normality separately. Skewness for males was .06 with a nonsignificant test statistic ($Z_{skewness}$ = skewness/standard error of skewness, Field, 2009), Z = .35, $p > .05$, suggesting the distribution of values was relatively symmetrical around the mean. Likewise, kurtosis for males was .106 with a nonsignificant test statistic ($Z_{kurtosis}$ = kurtosis/standard error of kurtosis, Field, 2009), $Z = 31$, $p > .05$, indicating a distribution that while slightly peaked is generally close to normal. The D 'Agostino-Pearson test of normality was also nonsignificant ($\chi^2 = .22$, $p = .90$), further indicating the relative normality of data from the male sample. The KMO result was .768, indicating the degree of common variance among the CDRS-R items for males was acceptable (Kaiser & Rice, 1974). Likewise, Bartlett's test was significant, suggesting that the items were correlated, $\chi^2 = 566.09$, $p < .001$. For females, skewness was .268 with a nonsignificant test statistic ($Z_{skewness}$ = skewness/standard error of skewness, Field, 2009), $Z = 1.71$, $p > .05$, suggesting the distribution of values was relatively symmetrical around the mean. Likewise, kurtosis for females was .30 with a nonsignificant test statistic ($Z_{kurtosis}$ = kurtosis/standard error of kurtosis, Field, 2009), $Z = .96$, $p > .05$, indicating a distribution that while slightly peaked is generally close to normal. The D 'Agostino-Pearson test of normality was also nonsignificant ($\chi^2 = 3.83$, $p = .15$), further indicating the relative normality of data for females. The KMO result was .807, indicating the degree of common variance among the female CDRS-R items was acceptable (Kaiser & Rice, 1974). Similarly, Bartlett's test was significant in females, suggesting the items were correlated, $\chi^2 = 641.07$, $p < .001$. Based on these outcomes, principal components analyses were conducted.

Using the same analytic method described above (Dimension Reduction -> Principal Component), a principal components analysis using varimax rotation with Kaiser Normalization was conducted first on the male only sample, then the female sample. The principal components analysis of the male sample resulted in five factors with eigenvalues greater than 1.0 which accounted for 61.44% of the total variance and included all 14 items. Factor 1, Mood and Affect, accounted for 24.48% of the total variance and was comprised of items 6, 8, 10, 11, and 14 which all had loadings greater than .35 (see Table 9). Factor 2, Extreme Negative Ideation, accounted for 11.19% of the total variance and included items 12 and 13 with loadings greater than .35 (see Table 9). Factor 3, Anhedonia, accounted for 9.27% of the variance and was comprised of items 2 and 3 which had loadings greater than .35 (see Table 9). Factor 4 accounted for 7.27% of the total variance and was made up of items 1 and 4 which both had loadings greater than .35 (see Table 9). Lastly, Factor 5 accounted for 7.20% of the total variance and was composed of items 5, 7, and 9, all with factor loadings greater than .35 (see Table 6).

The principal components analysis of the female sample resulted in three factors with eigenvalues greater than 1.0 which accounted for 46.88% of the total variance and included all 14 items. Factor 1, Somatic and Negative Ideation, accounted for 27.59% of the total variance and was comprised of items 4, 5, 7, 8, 9, 10, and 14, which all had loadings greater than .35 (see Table 10). Factor 2, Anhedonia, accounted for 10.82% of the total variance and included items 1, 2, 3, 6, and 11 with loadings greater than .35 (see Table 10). Factor 3, Extreme Negative Ideation, accounted for 8.46% of the variance and was comprised of items 12 and 13 which had loadings greater than .35 (see Table 10).

Table 9. Factors and Variance Explained for Males only

Factor*	Salient Loading Item	Loading	% Variance
Factor 1:	Mood and Affect		24.48
	6. Excessive Fatigue	.71	
	8. Irritability	.55	
	10. Low Self-Esteem	.58	
	11. Depressed Feelings	.58	
	14. Excessive Weeping	.52	
Factor 2:	Extreme Negative Ideation		11.19
	12. Morbid Ideation	.85	
	13. Suicidal Ideation	.86	
Factor 3:	Anhedonia		9.27
	2. Difficulty Having Fun	.70	
	3. Social Withdrawal	.87	
Factor 4:			7.27
	1. Impaired Schoolwork	.62	
	4. Sleep Disturbance	.81	
Factor 5:			7.20
	5. Appetite Disturbance	.79	
	7. Physical Complaints	.48	
	9. Excessive Guilt	.52	

*In Principal Components Analysis, the names applied to the empirically determined factors are decided by the researchers. Two factors were left untitled, as the items contributing to each factor did not make clear conceptual sense, and thus are identified simply by their factor number

Table 10. Factors and Variance Explained for Females Only

Factor	Salient Loading Item	Loading	% Variance
Factor 1:	Somatic and Negative Ideation		27.59
	4. Sleep Disturbance	.55	
	5. Appetite Disturbance	.64	
	7. Physical Complaints	.59	
	8. Irritability	.57	
	9. Excessive Guilt	.40	
	10. Low Self-Esteem	.46	
	14. Excessive Weeping	.63	
Factor 2:	Anhedonia		10.82
	1. Impaired Schoolwork	.62	
	2. Difficulty Having Fun	.79	
	3. Social Withdrawal	.72	
	6. Excessive Fatigue	.41	
	11. Depressed Feelings	.49	
Factor 3:	Extreme Negative Ideation		8.46
	12. Morbid Ideation	.79	
	13. Suicidal Ideation	.81	

Discussion

Several interesting findings emerge from these factor analyses. First, Guo and colleagues' (2006) factors were not explicitly replicated in the TADS sample. However, an anhedonia factor did consistently appear in each of these analyses. In each iteration of the factor analysis, the two items from the Guo et al. (2006) anhedonia factor consistently loaded together onto a factor: difficulty having fun and social withdrawal. In the full TADS sample as well as the female sample, impaired school work also loaded with these symptoms and may demonstrate another manifestation of anhedonia as a loss of interest in school. Indeed, the female sample did almost replicate the anhedonia factor from the full sample, with the addition of fatigue. In the male sample, the two anhedonia items loaded together on their own factor, just as in Guo and colleagues (2006). In addition, in the male sample, depressed feelings did cross-load with the anhedonia items, coming close to a replication of the full sample factor, however it loaded more strongly on the Mood and Affect factor.

An anhedonia factor consisting of at least the difficulty having fun and social withdrawal items was identified across both teen and parent informants and among both males and females, consistent with the anhedonia findings of Guo et al. (2006). One other factor appeared to emerge consistently across the various iterations and also replicated a factor from Guo and colleagues (2006): morbid thoughts. Suicidal ideation and morbid thoughts loaded together in each of the samples. This finding makes theoretical sense, as morbid thoughts and thoughts of suicide are highly related clinically (Lewinsohn, Rhode, & Seeley, 1996).

Overall, the parent reported factors differed from the full sample of teen reports. Indeed, as noted in the tables, we declined to name the parent factors, as they were so divergent from the factors derived from the teen reports and instead seemed to be mixed versions of the full teen sample. This finding is not surprising, given that parent and child reports often differ as parents

and their children seem to see things differently (Eickshtain & Gaynor, 2009). Indeed, research shows that correlations between teen and parent reported symptoms are often quite low (Eickshtain & Gaynor, 2009). However, when looking at parent ratings of item severity, it is important to note that again difficulty having fun was rated as the second most severe item by parents. This rating of difficulty having fun as one of the most severe symptoms was also seen in the full sample, as well as in the samples broken down by gender.

In addition, the samples differed greatly by gender, again highlighting the heterogeneity of depressive symptoms. For females, the factors were more similar to the full sample, however the male factors showed more factors made up of fewer items in each factor. As stated above, even with these differences, both males and females did show an anhedonia factor made up of difficulty having fun and social withdrawal. However, the female anhedonia factor had additional items of impaired school work, fatigue, and depressed feelings. The differences in these factors raise questions surrounding differences between males and females in their experience of depressive symptoms and impairment.

Interestingly, in the parent sample and the full teen informant sample (apparently driven by the females), difficulty having fun, social withdrawal, and depressed feelings loaded together onto a factor. That anhedonic symptoms and depressed feelings relatively consistently appeared on the same factor is interesting, given their role as "gate-keeper" symptoms of a depression diagnosis. This introduces an interesting question. Do these items load together because they are more likely to be rated together by assessors who are looking for their presence to assign a diagnosis, or are they truly linked, therefore justifying their central role in diagnosis?

It is important to note that the above factor analyses do account for less than 50% of the variance in each iteration. Thus, while these factors do show interesting patterns in how depressive symptoms may relate into underlying factors, a considerable amount of variability is

left unaccounted for and requires further investigation. However, the above factor analyses do provide further support for anhedonia as a core feature of adolescent depression. Paired with the findings from Phase 1, a picture emerges that shows anhedonia as a severe and consistent symptom for adolescents. It is next necessary to determine what impact these symptom has on outcomes for this population, which is the purpose of Phase 3.

CHAPTER IV

PHASE 3

Anhedonia as a Predictor of Outcome

McMakin and colleagues (2012) utilized the factors found by Guo et al. (2006) to predict outcomes for participants in the Treatment of Resistant Depression in Adolescents (TORDIA) study. In this study, treatment outcome was measured using overall score on the CDRS-R, an interviewer assessment of remission status, and number of depression free days calculated by the CDRS-R. Depression free days were calculated by summing each day in between assessments that a participant met criteria for remission (i.e. between assessments at 6 and 12 weeks). The symptom factors were calculated by summing the items that made up the factor on the CDRS-R at treatment entry. It was found that the anhedonia factor (comprised of two items: social withdrawal and difficulty having fun) was predictive of longer time to remission and fewer depression free days, over and above all other factors and total CDRS-R severity at 24 weeks post-treatment entry (McMakin, et al., 2012). An exact replication of McMakin et al. (2012) using the TADS data was not possible for several reasons. First, the TADS study did not measure number of depression free days. Second, while the TADS study did measure remission status, and this variable could be transformed to determine the time to remission, remission was rated by assessors with explicit instructions to ground their ratings in the participants' CDRS-R scores (TADS Team, 2005). Thus, to predict remission status similarly to McMakin and colleagues, CDRS-R factor scores at entry would be used to predict CDRS-R remission status at subsequent time points. Rather than relying on factors derived from the CDRS-R to predict subsequent status derived from the CDRS-R, another outcome variable was selected: quality of life. The present analyses used the pre-treatment CDRS-R factors identified in the principal components analyses

to prospectively predict participant self-reported quality of life at the end of treatment (12 weeks) and across two follow up assessments (18 and 24 weeks post-treatment entry). Thus, clinician-rated pre-treatment factors were used to predict participant-rated outcome.

Method

Participants

Data for these analyses were taken from the TADS dataset described above and in detail elsewhere (TADS Team, 2003; 2005). Data included the CDRS-R factor scores based on the three factors found in Phase 2 with the full sample. The factors were Somatic Complaints (sleep disturbance, appetite disturbance, fatigue, physical complaints, irritability, and excessive weeping), Anhedonia (impaired school work, difficulty having fun, social withdrawal, and depressed feelings), and Morbid Ideation (excessive guilt, low self-esteem, morbid ideation, suicidal ideation). Factor scores were generated by summing scores of each item in the factor (consistent with the method of McMakin, et al., 2012). Depression outcomes were measured using scores on the Pediatric Quality of Life Enjoyment and Satisfaction Questionnaire (PQ-LES-Q; Endicott, Nee, Yang, & Wohlberg, 2006) collected at end of treatment (12 weeks) and at 18 and 24 week follow up assessments.

Measures

Pediatric Quality of Life Enjoyment and Satisfaction Questionnaire (PQ-LES-Q; Endicott, Nee, Yang, & Wohlberg, 2006). The PQ-LES-Q is a 15 item self-report measure that assesses various aspects of quality of life and is summed to create an overall quality of life score. The PQ-LES-Q has high internal consistency (Cronbach α=.89) and test-retest reliability (.78; Endicott, et al, 2006). It is also moderately correlated with global measures of illness severity

(the Children's Global Assessment Scale and Clinical Global Index of Severity; .36 and -.40 respectively; Endicott, et al, 2006). However, these correlations are not so high as to indicate redundancy with these measures. The PQ-LES-Q was administered to participants in the TADS study at all major assessment points. It was found that participants receiving either medication or the combination of medication and CBT showed significant changes on the PQ-LES-Q at the end of treatment, compared to those receiving pill placebo or CBT alone (Vitiello, et al, 2006).

Analytic Strategy

As described above, while McMakin and colleagues (2012) used depression free days as a measure of improvement and remission, these data are not available for the TADS dataset. Clinician rated remission status was not used in these analyses, as the TADS protocol grounds these ratings in the adolescent's CDRS-R score. Thus, to use any clinician rating of remission as an outcome would have included CDRS-R score and would involve predicting an outcome using the same measure. Therefore, PQ-LES-Q scores were used as a measure overall functioning at the end of treatment and at 6 and 12 weeks follow up. Linear regression analyses were carried out with SPSS version 23 using the three CDRS-R factors from Phase 2 as predictors for PQ-LES-Q total score at end of treatment, 6 weeks post-treatment, and 12 weeks post-treatment (hereafter referred to as "week 12," "week 18," and "week 24" respectively). First, multivariate models were estimated that used the three CDRS-R factors generated from the full sample. Next, multivariate models were analyzed for males and females separately, using the separate pre-treatment CDRS-R factors for each sex as predictors of PQ-LES-Q total score at each of the three time points.

Results

A standard multivariate linear regression was run with all three CDRS-R factors as predictors of PQ-LES-Q scores at week 12 on the full TADS sample. The full model was found to be significant, F (3, 379) = 9.68, p =.000, and accounted for roughly 7% of the variability (R^2 = .071, Adjusted R^2 =.064). Of the three factors included, two were found to be significant predictors: Somatic Complaints (t = -2.02, p =.044) and Anhedonia (t = -2.09, p = .036; see Table 11). Because the Anhedonia factor was the most significant predictor of PQ-LES-Q score, we next examined the relationship between the four individual items that made up the Anhedonia factor and the PQ-LES-Q at 12 weeks using Pearson's r. Using a Bonferroni corrected alpha level (α = .013), two of the CDRS-R items were significantly related to PQ-LES-Q total score. Difficulty Having Fun was significantly negatively related to quality of life at the end of treatment (r = -.185, p = .000), as was Depressed Feelings (r = -.195, p = .000; see Table 12). Thus, those who had higher scores on these symptoms of anhedonia at the start of treatment had lower scores on quality of life at the conclusion of treatment.

Table 11. Baseline CDRS-R Factors and PQ-LES-Q at 12 Weeks (N=382)

	β (SE)	t	*p*
Somatic Complaints	-.22 (.11)	-2.02	.04
Anhedonia	-.28 (.13)	-2.09	.03
Negative Ideation	-.21 (.15)	-.08	.16

Table 12. Baseline CDRS-R Items and PQ-LES-Q at 12 Weeks

	PQ-LES-Q Total Score *r*
Impaired Schoolwork	-.12
Difficulty Having Fun	-.18*
Social Withdrawal	-.11
Depressed Feelings	-.19*

**p<.013*

A second multivariate linear regression was run to determine if the CDRS-R factors remained predictive at week 18, 6 weeks after treatment ended in the TADS protocol. The full model was significant, F (3, 329) = 4.12, p = .007, accounting for approximately 3% of the variability (R^2 = .036, Adjusted R^2 = .027). However, none of the three predictors were independently significant any longer (see Table 13). Similarly, at week 24 (12 weeks post-treatment) the full model was significant, F (3,288) = 3.37, p =.019, accounting for roughly 3% of the variability (R^2 = .034, Adjusted R^2 = .024), but none of the individual factors remained significant (see Table 13).

Table 13. Baseline CDRS-R Factors and PQ-LES-Q at 18 and 24 Weeks

	18 weeks (N=333)			24 weeks (N=292)		
	β (SE)	t	*p*	β (SE)	t	*p*
Somatic Complaints	-.22 (.11)	-1.86	.06	-.14 (.13)	-1.08	.28
Anhedonia	-.21 (.14)	-1.45	.14	-.19 (.17)	-1.11	.26
Negative Ideation	.001 (.15)	.01	.99	-.18 (.18)	-1.01	.31

Analyses were next run on the sample split by gender, using the factors found in Phase 2 analyses for males and females. A multivariate linear regression was run first on only the males from the TADS sample with the five CDRS-R factors as predictors of PQ-LES-Q total score at weeks 12, 18, and 24. At week 12, the full model with all five factors was significant, F (5,158) = 3.033, p = .012, accounting for 9% of the variance (R^2 = .09, Adjusted R^2 = .06). Of the five factors included, only factor one (Mood and Affect) was an individually significant predictor, t = -2.435, p = .016 (see Table 14). At 18 weeks, the full male model remained significant (F (5, 128) = 2.345, p = .045), as did factor one (t = -2.592, p = .011; see Table 14). The model accounted for roughly 8% of the variance (R^2 = .084, Adjusted R^2 = .048). Again, none of the other factors were significant individual predictors of PQ-LES-Q score at 18 weeks. At 24

weeks, the full model of five factors was no longer significant, F (5, 106) = .672, p = .645. Similar to the full sample, correlations between individual items at pre-treatment and 12 week PQ-LES-Q scores were calculated using Pearson's r. Using a Bonferroni corrected alpha (α = .013), four CDRS-R items were significantly negatively related to quality of life at 12 weeks: Low Self-Esteem, Difficulty Having Fun, Depressed Mood, and Physical Complaints (see Table 15).

Table 14. Baseline Male CDRS-R Factors and PQ-LES-Q at 12 and 18 Weeks

	12 weeks (N= 159)			18 weeks (N= 134)		
	β (SE)	t	*p*	β (SE)	t	*p*
Mood and Affect	-.45 (.18)	-2.43	.00	-.51 (.19)	-2.59	.01
Extreme Negative Ideation	-.36 (.38)	-.945	.34	-.21 (.42)	-.51	.60
Anhedonia	-.23 (.30)	-.75	.45	.45 (.33)	1.35	.17
Factor 4	-.01 (.30)	-.03	.97	-.43 (.32)	-1.30	.19
Factor 5	.06 (.30)	.22	.81	.20 (.32)	.63	.87

Table 15. Baseline CDRS-R Items and PQ-LES-Q at 12 Weeks for Males Only

	PQ-LES-Q Total Score
	r
Low Self-Esteem	-.301*
Difficulty Having Fun	-.194*
Depressed Mood	-.236*
Physical Complaints	-.221*

* $p \leq .013$

For females, a different picture began to emerge. Again analyses were run using the 3 CDRS-R factors found for females in Phase 2 as predictors of PQ-LES-Q total score at 12, 18, and 24 weeks. At twelve weeks, the full model with all three factors was found to be significant, F (3, 211) = 4.52, p = .004, and accounted for approximately 6% of the variability (R^2 = .06, Adjusted R^2 = .05). Of the three factors, anhedonia was the only factor found to be a significant

predictor, t = -2.07, p = .04 (see Table 16). Similarly, at week 18, the full model remained significant, F (3, 186) = 2.88, p = .04, accounted for roughly 4% of the variance (R^2 = .04, Adjusted R^2 = .03), and the anhedonia factor remained the only significant predictor, t = -2.15, p = .03 (see Table 16). Finally, at week 24 for females, the model remained significant, F (3, 167) = 3.82, p = .01, and accounted for approximately 6% of the variance (R^2 = .06, Adjusted R^2 = .05). However, the anhedonia factor was trending toward, but no longer statistically significant, t = -1.57, p = .09 (see Table 17). Again, correlations between individual CDRS-R items and PQ-LES-Q scores at 12 weeks were calculated using Pearson's *r*. Using a Bonferroni corrected alpha (α = .013), only two pre-treatment symptoms were significantly negatively related to quality of life at end of treatment: Difficulty Having Fun and Physical Complaints (see Table 18).

Table 16. Baseline Female CDRS-R Factors and PQ-LES-Q at 12 and 18 Weeks

	12 weeks (N= 213)			18 weeks (N= 190)		
	β (SE)	t	*p*	β (SE)	t	*p*
Somatic and Mild Negative Ideation	-.17 (.13)	-1.33	.18	-.09 (.13)	-.66	.50
Anhedonia	-.36 (.17)	-2.07	.04	-.38 (.17)	-2.15	.03
Extreme Negative Ideation	-.09 (.31)	-.29	.77	.39 (.30)	1.30	.19

Table 17. Baseline Female CDRS-R Factors and PQ-LES-Q at 24 Weeks (N= 171)

	β (SE)	t	*p*
Somatic and Mild Negative Ideation	-.21 (.15)	-1.42	.15
Anhedonia	-.32 (.19)	-1.67	.09
Extreme Negative Ideation	.001 (.32)	.003	.99

Table 18. Baseline CDRS-R Items and PQ-LES-Q at 12 Weeks for Females Only

	PQ-LES-Q Total Score
	r
Difficulty Having Fun	-.167*
Physical Complaints	-.238*

* $p \leq .013$

Discussion

From multiple standard multivariate linear regressions, it was found that anhedonic symptoms were the most predictive of quality of life at the end of treatment. In the full sample, only the anhedonia factor was found to significantly predict PQ-LES-Q score at the end of treatment. Of note, while these models may account for a small portion of variance, updated guidelines suggest that these correlations may demonstrate reasonable effect sizes within the literature (Gignac & Szodorai, 2016). Notably, Gignac & Szodorai (2016) recommend effect sizes of .10, .20, and .30 as relatively small, typical, and relatively large, given updated meta-analyses of derived correlations showing that less than 3% of correlations in the literature were found to be as large as $r = .50$.

While it did not remain a significant predictor in post-treatment follow up for the full sample, for females, anhedonia was the only significant predictor of quality of life at post treatment and 6 week follow up. At the individual symptom level, difficulty having fun and physical symptoms were the only items significantly related to quality of life at the end of treatment. In males, somatic symptoms were the only significant predictor of quality of life at the end of treatment. It is interesting to note, however, that while the males' anhedonia factor was not a significant predictor of quality of life at follow up, the individual symptom of difficulty having fun was. Thus, across the entire sample, and by gender, at the individual symptom level, difficulty having fun appears to be an important predictor of quality of life at the end of treatment. These findings point to potential gender differences that require further investigation, particularly at the symptom level. It may be that for males, attending to symptoms such as low self-esteem, depressed mood, and physical complaints, in addition to anhedonia, can provide

valuable information regarding potential outcomes. Whereas for females it seems anhedonic symptoms and physical complaints may provide the more valuable predictor of outcome.

The findings of Phase 3 fit within the literature on anhedonia as an important predictor of treatment outcome in adolescent depression. Both Gabbay et al. (2015) and McMakin et al. (2012) demonstrated that individuals with higher levels of anhedonia at the start of treatment had poorer outcomes as measured by symptom severity, suicidality, and remission status. The current study found that higher anhedonia scores were predictive of poorer quality of life scores at the end of treatment, and into follow up for females. Quality of life is an important component of determining treatment success, as it may be viewed as an indicator of functional impairment (Vitiello, et al, 2006; Endicott, et al., 2006). Thus, it appears that anhedonia impacts not only symptom remission, but overall quality of life and functioning as well. Taken together, these findings point to the necessity of targeting anhedonia in treatment.

CHAPTER V

PHASE 4

Behavioral Therapy and Anhedonic Symptoms

Phase four examined which symptoms are most impacted by activation-based behavioral treatment of adolescent depression. This phase was modeled on previous work using a smaller sample (N=36) of depressed adolescents (DeLizza et al., 2012). This pilot work suggested that behavioral activation may indeed target theoretically consistent symptoms, specifically difficulty having fun and social withdrawal. Using paired sample t-tests, it was found that difficulty having fun, excessive fatigue, and social withdrawal showed the largest change from pre- to post-treatment after receiving behavior therapy explicitly targeting values-based activity scheduling, which were influenced by Behavioral Activation and ACT (Petts et al., 2016; Petts et al., 2017). This phase sought to replicate these findings using a larger group of diverse teens (including those from the pilot work).

Method

Participants

CDRS-R pre-treatment and post-treatment data were from 38 adolescents enrolled in one of three open clinical trials of behavior therapy conducted in large, Midwest public high schools. The behavior therapy offered always explicitly targeted values-based behavioral activation as its foundation and in some protocols strategies for addressing verbal barriers to activation. Thus, the behavior therapy offered represented an assimilation of BA (Martell et al., 2001) and ACT (Hayes et al., 1999). Adolescents were aged 14-18 (M=15.86), had a baseline CDRS-R score of $\geq$ 45, and 60% identified as female. The sample was diverse with 43% African American, 21%

Caucasian, 4% Latinx, 23% Multiracial, and 9% other. In addition, the sample identified as socioeconomically disadvantaged, with a mean score on the MacArthur Scale of Subjective Social Status (MSSSS; Adler, Stewart, et al., 2007) of 5.02. This score falls roughly 2 standard deviations below the normative mean of the MSSSS. The students were additionally assessed using the Mini International Neuropsychiatric Interview for Children and Adolescents (MINI-KID; Sheehan, et al., 2010) to determine if any exclusionary diagnoses were present. Exclusionary diagnoses included bipolar disorder, psychotic disorder, pervasive developmental disorder, anorexia nervosa, obsessive compulsive disorder, and autism. Students could not receive additional psychotherapy, though individuals taking antidepressant medications were included if they were on a stable dosage for eight weeks at the time of intake with no change during treatment.

Behavior Therapy

Each of the three behavior therapy trials followed a similar protocol. Participants were initially assessed using the CDRS-R before entering treatment. They then entered a baseline phase of Motivational Interviewing Assessment (MIA) for 3 weeks after which they were re-assessed. Participants then received up to 8- 10 sessions of ACT. The ACT protocol used in each of the trials focused heavily on increasing activity in values based areas. Participants scheduled values based activities each week with their therapist, and were taught skills (i.e. mindfulness, acceptance, defusion) to deal with any barriers that arose. Participants were finally assessed again at the end of treatment. All three trials were conducted at local public high schools in Kalamazoo, MI and were approved by the University's Human Subjects Institutional Review Board. Assessments were conducted by independent assessors.

Analytic Strategy

CDRS-R scores from the post-MIA and post-behavior therapy assessments of each sample were analyzed. This allowed for control of any initial change on the CDRS-R prior to entering behavior therapy. Paired samples t-tests were conducted on scores for each item across groups utilizing a Bonferroni corrected alpha level ($p \leq .003$). Effect sizes of item change were also calculated and guidelines from recent research by Gignac & Szodorai (2016) was used to interpret effect sizes.

Results

Data were available from 23 behavior therapy participants. These teens experienced a significant decreased in CDRS-R 14-item scores from prior to behavior therapy (M = 43.91, SD = 9.25) to after behavior therapy (M = 29.23, SD = 12.09), $t(22) = 14.70$, $p < .001$. Item mean differences are reported in Table 19. A Bonferroni correction of $p \leq .003$ was used to account for multiple correlations. Five items showed significant change after behavior therapy: difficulty having fun, sleep disturbance, excessive fatigue, physical complaints and morbid ideation. In addition, excessive fatigue, difficulty having fun, sleep disturbance, and physical complaints all showed very large (>.90) within-group effect sizes. Of the anhedonia symptoms, difficulty having fun showed one of the largest mean decreases of all items (1.43 points), which was statistically significant and associated with a large effect size (g=.97). Social withdrawal also showed a large mean decrease (1.40 points), which approached significance (t=3.006, p=.006), and was associated with a large effect size (g= .53). The item with the largest mean difference was excessive fatigue, with a 2-point decrease from pre- to post- behavioral intervention, associated with a large effect (g=1.41).

Table 19. Item Mean Difference on CDRS-R scores from Pre to Post-Behavioral Intervention (N=23)

Item	Mean Difference	SD	t	g
Impaired School Work	.78	1.95	1.92	.50
Difficulty Having Fun	**1.44**	**1.90**	**3.62***	**.97**
Social Withdrawal	1.40	1.67	3.01	.53
Sleep Disturbance	**1.13**	**1.63**	**3.32***	**.95**
Appetite Disturbance	.96	1.79	2.55	.74
Excessive Fatigue	**2.00**	**2.15**	**4.46***	**1.41**
Physical Complaints	**1.44**	**1.75**	**3.92***	**.93**
Irritability	1.13	1.84	2.94	.70
Excessive Guilt	.52	1.12	2.23	.46
Low Self-Esteem	1.39	2.23	2.99	.81
Depressed Feelings	1.10	1.94	2.79	.76
Morbid Ideation	**.91**	**1.13**	**3.89***	**.58**
Suicidal Ideation	.17	1.40	.59	.18
Excessive Weeping	.74	2.03	1.75	.47

*$p \leq .003$

Given the findings of gender differences in Phase 3, paired- samples t-tests were run on the sample broken out by gender. Only one significant difference was found when using the Bonferroni corrected alpha level of $p \leq .003$. In the female sample, a significant decrease in sleep difficulties was found, with a mean difference of 1.43, $t(13) = 3.98$, $p = .002$ (see Table 20). There were no other significant changes for the female or male samples using the Bonferroni corrected alpha. This is likely due to the small sample sizes of the groups. However, there were some differences at the conventional alpha level. In males, difficulty having fun, social withdrawal, fatigue, and morbid ideation all showed decreases after behavior therapy that were significant at the $p \leq .05$ level (see Table 21). In females, difficulty having fun, appetite disturbance, fatigue, physical complaints, irritability, low self-esteem, and morbid ideation all showed decreases after behavior therapy that were significant at the $p \leq .05$ level (see Table 20).

Table 20. Item Mean Difference on CDRS-R scores from Pre to Post-Behavioral Intervention in Females only (N=14)

Item	Mean Difference	SD	t	*p*
Impaired School Work	0.36	1.95	0.69	.50
Difficulty Having Fun	1.21	1.89	2.41	.03
Social Withdrawal	0.79	1.63	1.81	.09
Sleep Disturbance	**1.43**	**1.34**	**3.98***	**.002**
Appetite Disturbance	1.14	1.70	2.51	.03
Excessive Fatigue	1.50	2.18	2.58	.02
Physical Complaints	1.64	1.91	3.23	.007
Irritability	1.21	1.48	3.08	.009
Excessive Guilt	0.29	0.83	1.30	.22
Low Self-Esteem	1.64	2.10	2.93	.01
Depressed Feelings	1.00	2.04	1.84	.09
Morbid Ideation	0.79	1.19	2.47	.03
Suicidal Ideation	0.57	1.02	2.10	.06
Excessive Weeping	0.86	2.51	1.28	.22

Bonferroni corrected α is p≤.003.

Table 21. Item Mean Difference on CDRS-R scores from Pre to Post-Behavioral Intervention in Males only (N=8)

Item	Mean Difference	SD	t	*p*
Impaired School Work	1.25	1.91	1.85	.11
Difficulty Having Fun	1.75	2.12	2.33	.05
Social Withdrawal	1.00	1.20	2.37	.05
Sleep Disturbance	0.37	1.92	0.55	.60
Appetite Disturbance	0.5	2.07	0.68	.52
Excessive Fatigue	2.62	2.07	3.59	.01
Physical Complaints	1.00	1.60	1.76	.12
Irritability	0.62	2.26	0.78	.46
Excessive Guilt	0.75	1.49	1.43	.20
Low Self-Esteem	0.62	2.39	0.74	.48
Depressed Feelings	1.00	1.70	1.67	.14
Morbid Ideation	1.00	1.07	2.65	.03
Suicidal Ideation	-0.50	1.85	-0.76	.47
Excessive Weeping	0.37	.92	1.16	.29

Bonferroni corrected α is p≤.003.

Discussion

The results of Phase 4 showed significant change in theoretically consistent CDRS-R items targeted by behavioral intervention. The items that showed the largest and most significant change (excessive fatigue, difficulty having fun, physical complaints, and sleep disturbance) align with the targets of an activation oriented treatment of depression. Difficulty having fun is explicitly targeted by scheduling activities the participant finds meaningful and enjoyable. Excessive fatigue, sleep disturbance, and physical complaints may be indirectly targeted through activity scheduling. As a result of scheduling more activities for the participant, daytime sleeping and other passive activities (i.e. watching TV, surfing the internet) are reduced. This in turn may improve night time sleep, which could decrease feelings of fatigue and physical complaints. It is also important to note that while social withdrawal did not show statistically significant change using the Bonferroni corrected alpha level, it did approach significance and showed a large effect size. Thus, these findings suggest that behavioral treatments that emphasize behavioral activation do successfully target symptoms of anhedonia, particularly difficulty having fun.

When the sample was separated by gender, similar results began to emerge. Females showed a significant decrease in sleep difficulties from pre- to post- behavior therapy. Both males and females showed changes in difficulty having fun, as well as fatigue and morbid ideation, though these changes did not reach statistical significance when using the Bonferroni corrected alpha. This is likely due to the small size of the separated groups, given that items did show change that was significant at the conventional alpha level. Future research utilizing larger samples should be carried how to further elucidate what differences may exist in symptom change for males and females.

CHAPTER VI

GENERAL DISCUSSION

Across the four phases of analyses above, anhedonia was found to be an important hallmark of and target for treatment of adolescent depression. In the first phase, anhedonia was found to be one of the most severely rated symptoms of depression in adolescence on the CDRS-R. This was seen in the consistently high rating of the Difficulty Having Fun, Excessive Fatigue, Impaired School Performance, and Social Withdrawal items across four samples of depressed adolescents.

In phase two, anhedonia was found to be one of the only consistent factors in multiple principal component analyses. Difficulty Having Fun and Social Withdrawal loaded onto the same factor in the full sample of adolescents from the TADS study, as well as in the samples broken down by gender and in the sample of parent-reported ratings. In the third phase, high anhedonia scores at the start of treatment were found to significantly predict self-reported quality of life at the end of treatment. In females, this effect was maintained at 6 weeks post-treatment. Finally, in phase four, behavioral activation focused treatment significantly reduced the anhedonic symptoms of Difficulty Having Fun, Fatigue, and Sleep Disturbance.

Anhedonia appears to be an important component of adolescent depression that has the potential as a more useful construct to target than overall diagnosis, particularly for females. The RDoC initiative emphasizes objective and measurable areas of dysfunction that can be targeted for research and treatment (Insel, et al, 2010). Indeed, anhedonia fits this description far better than the vague and heterogeneous diagnosis of depression. It appears as one of the most significant and impairing symptoms rated by adolescents on the CDRS-R. In addition, it appears predictive of poorer outcomes related not only to symptom remission (McMakin, et al., 2012),

but also symptom severity (Gabbay, et al., 2015). Here it was found to predict poorer quality of life at the end of treatment, particularly for females, thus demonstrating that high levels of anhedonia are a significant problem for adolescents and should therefore be targeted explicitly. In addition to these clinical applications, anhedonia has been linked with neurobiological systems of reward processing (Nusslock & Alloy, 2017; Dillon, et al, 2015). Difficulty having fun may be conceptualized as a deficit in both reward anticipation (i.e. things don't sound enjoyable) and reward consumption (i.e. activities are not experienced as enjoyable). Clinically, this distinction may be useful in so far as it orients treatment toward either overcoming barriers to re-engage in rewarding activities (anticipation) or in finding activities that are experienced as reinforcing (consumption). Along these lines, research has demonstrated that activation oriented behavioral treatments successfully targeted anhedonic symptoms. These treatments (i.e. Behavioral Activation, Acceptance and Commitment Therapy) are effective in treating adolescent depression as a whole (Hayes, et al., 2011; Petts, et al., 2017), as well as specific anhedonic symptoms, and have been demonstrated as effective in shorter durations (i.e. less than 6 sessions; Ritchel, Ramirez, Jones, & Craighead, 2011). Therefore, activation oriented behavioral therapies may provide a brief and effective alternative to traditional CBT. In addition, these treatments are not bound by a diagnostic category and therefore are more broadly applicable to individuals experiencing distress and dysfunction (Hayes, et al., 1999; Hayes, et al., 2011).

This study demonstrates a potential mechanism by which these treatments effect change: reduction in anhedonia through activation. ACT and Behavioral Activation focus on explicitly enhancing engagement in meaningful activities, while less time is devoted to changing/challenging thoughts or other skills. Petts, Duenas, and Gaynor (2017) found that teens who completed activation oriented protocol of ACT demonstrated statistically significant

increases in activation as measured by the Behavioral Activation for Depression Scale (BADS-SF; Kanter, Mulick, Busch, Berlin, & Martell, 2007), which was associated with a significant decrease in CDRS-R total scores. Similarly, Gaynor & Harris (2008) found that increased activation (measured using a weekly activity log as well as therapist ratings) plausibly mediated change in depressive symptoms. The above therapy protocols vary dramatically from the format of CBT used in many large-scale therapy trials such as TADS or TORDIA. In such trials, the therapy is formatted with less time spent on activity scheduling (i.e. only 1 or 2 sessions) and more devoted to mood tracking, cognitive restructuring, or relaxation training (TADS Team, 2000; McMakin, et al., 2012). This "kitchen sink" and negative affect focused approach may explain why therapy alone in these trials has less success in reducing symptoms such as social withdrawal or difficulty having fun (McMakin, et al., 2012). More explicit research examining the role of activation as a mechanism of change in these therapies is needed.

As mentioned above, difficulty having fun and depressed mood were found to be significant symptoms in phase one, and loaded onto the same anhedonia factor in phase two. This finding is interesting in that it provides support for the DSM core criteria of depression and may represent an important prognostic tool for clinicians. Indeed, while the DSM provides guidance that adolescent depression may be marked by more irritability than depressed mood or lack of interest, the findings of this study indicate this may not be the case. That the anhedonia factor was most predictive of quality of life at the end of treatment is similar to findings by Gabbay and colleagues (2015) where anhedonia, not irritability, was the strongest predictor of outcome. From these findings, it is possible that anhedonia and depressed mood may serve as more important indicators for clinicians and health care providers than overall diagnosis or irritability. This approach has many benefits. By focusing on a more specific symptom, more adolescents may be identified before a full episode of depression develops, improving prognosis.

In addition, a specific symptom such as difficulty having fun is something that non-mental health professionals such as pediatricians or school personnel can identify without having to assess for a full diagnosis. Again, this provides potential to catch individuals early, as well as those who may not have access to mental health providers. Future research should examine the plausibility of such models and treatments for those who are experiencing high levels of anhedonia without full criteria for major depression.

This study does have some limitations which require attention. First, while a promising first step in examining mechanisms of action, phase four's sample was small and drawn from three different studies with different therapy protocols. While the protocols of each study were very similar, results from a single study with a larger sample explicitly designed to examine symptom change from activation is needed. The small sample size in this phase likely also accounts for the lack of significant differences in symptoms when analyzing groups by gender. Second, the factor analyses in phase 2 did not replicate those of Guo and colleagues (2006). While not directly a limitation of the current paper, this does require further exploration to determine if there are consistent factors on the CDRS-R. Similarly, given the design of the TADS study, a direct replication of McMakin and colleagues (2012) was not possible. Thus, whether anhedonia predicted symptom change or diagnostic outcome in the TADS sample is unknown. However, using a measure of quality of life did provide an interesting addition to the literature on the role of anhedonia in treatment outcome, and adds an important component of treatment outcome that is not always reported in clinical trials. In addition, the gender differences between males and females found in phases 2 and 3 do require further exploration. That males and females may experience different depressive symptoms fits the larger understanding of depression as a very heterogeneous condition across individuals. However, further exploring the

role that somatic and physical symptoms play for males, and anhedonic and social symptoms play for females is needed.

From the four sets of analyses presented here, it is clear that anhedonia is an important component of adolescent depression. Future research should continue to examine it as a prognostic indicator and potential target for treatment. As the RDoC initiative continues to grow and direct research and treatment development, it appears that anhedonia should be a viable construct for exploration. Following from the treatment developed by Blom and colleagues (2017), treatment of anhedonia specifically using activation oriented therapies should be examined. Finally, given the movement toward brief, target interventions such as behavioral activation for depression in adults, future research should examine the efficacy of such treatments for adolescents.

References

Adler, N.E., Stewart, J., et al. (2004). The MacArthur Scale of Subjective Social Status. In *Psychosocial Research Notebook.* Retrieved from http://macses.ucsf.edu/research/psychosocial/subjective.php.

American Psychiatric Association: *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition.* Arlington, VA, American Psychiatric Association, 2013.

Avenevoli, D, Swendsen, J, He, JP, Burstein, M, & Merikangas, KR. (2015). Major depression in the National Comorbidity Survey- adolescent supplement: Prevalence, correlates, and treatment. Journal of the American Academy of Child and Adolescent Psychiatry, 54(1). 37-44.

Blom, E.H., Duncan, L.G., Ho, T.C., Connolly, C.G., LeWinn, K.Z., … & Yang, T.T. (2014). The development of an RDoC-based treatment program for adolescent depression: "Training for awareness, resilience, and action" (TARA). *Frontiers in Human Neuroscience, 8,* 1-19.

Blom, E.H., Tymofiyeva, O., Chesney, M.A., Ho, T.C., Moran, P., Connolly, C.G., et al. (2017). Feasibility and preliminary efficacy of a novel RDoC-based treatment program for adolescent depression: "Training for awareness resilience and action" (TARA) - A pilot study. *Frontiers in Psychiatry, 7:* 208. doi: 10.3389/pfpst.2016.00208.

Buckner, J.D., Joiner, Jr, T.E., Pettit, J.W., Lewinsohn, P.M., & Schmidt, N.B. (2008). Implications of the DSM's emphasis on sadness and anhedonia in major depressive disorder. *Psychiatry Research, 159,* 25-30.

Brent, D., Emslie, G., Clarke, G., Wagner, K.D., Asarnow, J.R., Keller, M., et al. (2008). Switching to another SSRI or to venlafaxine with or without cognitive behavioral therapy for adolescents with SSRI-resistant depression: the TORDIA randomized controlled trial.

JAMA, 299(8), 901-913. doi: 10.1001/jama.299.8.901.

Bylsma, L.M., Morris, B.H., Rottenberf, J. (2008). A meta-analysis of emotional reactivity in major depressive disorder. *Clinical Psychology Review, 28,* 676-691.

DeLizza, A.A., Petts, R.A., Foster, C.S., Duenas, J.A., Douleh, T. & Gaynor, S.T. (2015, November). *An item-level analysis of adolescent depressive symptoms prior to and after successful behavioral treatment among diverse, often socioeconomically disadvantaged, sample.* Poster presented at the 49th annual meeting of the Association of Behavioral and Cognitive Therapy, Chicago, IL.

Eickshtain, D. & Gaynor, S.T. (2009). Assessing outcome in cognitive behavior therapy for child depression: An illustrative case series. *Child & Family Behavior Therapy, 31*(2), 94-116.

Endicott, J., Nee, J., Yang, R., & Wohlberg, C. (2006). Pediatric quality of life enjoyment and satisfaction questionnaire (PQ-LES-Q): Reliability and validity. *Journal of the American Academy of Child and Adolescent Psychiatry, 45*(4), 401-407.

Field, A.P. (2009). *Discovering statistics using SPSS* (3rd Ed.). London, England: Sage.

Gabbay, V, Johnson, AR, Alonso, CM, Evans, LK, Babb, JS, & Klein, RG. (2015). Anhedonia, but not irritability, is associated with illness severity outcomes in adolescent major depression. *Journal of Child and Adolescent Psychopharmacology, 25*(3), 194-200. doi:10.1089/cap.2014.0105

Gignac, G.E. & Szodorai, E.T. (2016). Effect size guidelines for individual differences researchers. *Personality and Individual Differences, 102,* 74-78. doi: 10.1016/j.paid.2016.06.069.

Guo, Y., Nilsson, M.E., Heiligenstein, J., Wilson, M.G., Emslie, G. (2006). An exploratory factor analysis of the Children's Depression Rating Scale-Revised. *Journal of Child and Adolescent Psychopharmacology, 16*(4), 482-491.

Hayes, L., Boyd, C. P., & Sewell, J. (2011). Acceptance and commitment therapy for the treatment of adolescent depression: A pilot study in a psychiatric outpatient setting. *Mindfulness, 2,* 86-94.

Hayes, S. C., Strosahl, K. D., & Wilson, K. G. (1999). *Acceptance and commitment therapy: An experiential approach to behavior change*. New York: Guilford Press.

Hayes, S.C., Strosahl, K.D., & Wilson, K.G. (2011). *Acceptance and commitment therapy: The process and practice of mindful change* (2nd Ed.) New York: The Guilford Press.

Hyman, S.E. (2010). The diagnosis of mental disorders: The problem of reification. *Annual Review of Clinical Psychology, 6,* 155-179.

Insel, T., Cuthbert, B., Garvey, M., Heinssen, R., Pine, D.S., … Wang, P. (2010). Research Domain Criteria (RDoC): Toward a new classification framework for research on mental disorders. *American Journal of Psychiatry, 167*(7), 748-751.

Jacobson, N. S., Dobson, K. S., Truax, P. A., Addis, M. E., Koerner, K., Gollan, J. K., Gornter, E., & Prince, S. E., (1996). A component analysis of cognitive-behavioral treatment for depression. *Journal of Consulting and Clinical Psychology, 64,* 295-304.

Kaiser, H.F. & Rice, J. (1974). Little Jiffy, Mark IV. *Educational and Psychological Measurement, 34,* 111-117.

Kanter, J. W., Mulick, P. S., Busch, A. M., Berlin, K. S., & Martell, C. R. (2007). The Behavioral Activation for Depression Scale (BADS): Psychometric properties and factor structure. *Journal of Psychopathology and Behavioral Assessment, 29,* 191-202.

Kapur, S., Phillips, A.G., & Insel, T.R. (2012). Why has it taken so long for biological psychiatry to develop clinical tests and what to do about it? *Molecular Psychiatry, 17*(12), 1174-1179. doi: 10.1038/mp.2012.105

Lewinsohn, P.M., Rohde, P., & Seeley, J.R. (1996). Adolescent suicidal ideation and attempts: Prevalence, risk factors, and clinical implications. *Clinical Psychology Science and Practice, 3*(1), 25-46. doi: 10.1111/j.1468-2850.1996.tb00056.x

Lewinsohn, P.M., Solomon, A., Seeley, J.R., & Zeiss, A. (2000). Clinical implications of "subthreshold" depressive symptoms. *Journal of Abnormal Psychology, 109*(2), 345-351.

Mayes, TL, Bernstein, IH, Haley, CL, Kennard, BD, & Emslie, GJ. (2010). Psychometric properties of the children's depression rating scale-revised in adolescents. Journal of Child and Adolescent Psychopharmacology, 20 (6), 513-516. doi: 10.1089/cap.2010.0063

McMakin, D.L., Olino, T.M., Porta, G., Dietz, L.J., Emslie, G., … & Brent, D.A. (2015). Anhedonia predicts poorer recovery among youth with selective serotonin reuptake inhibitor treatment-resistant depression. *Journal of the American Academy of Child and Adolescent Psychiatry, 51*(4), 404-411.

NIMH. RDoC Snapshot: Version 3. (2017, May 18). Retrieved October 16, 2017, from https://www.nimh.nih.gov/research-priorities/rdoc/constructs/rdoc-snapshot-version-3-saved-5-18-17.shtml.

Nusslock, R. & Alloy, L.B. (2017). Reward processing and mood-related symptoms: An RDoC and translational neuroscience perspective. *Journal of Affective Disorders, 216,* 3-16. doi: 10.1916/j.jad.2017.02.001.

Petts, R.A., Duenas, J.A., & Gaynor, S.G. (2017). Acceptance and Commitment Therapy for adolescent depression: Application with a diverse and predominantly socioeconomically disadvantaged sample. *Journal of Contextual Behavioral Science, 6,* 134-144.

Poznanski, E. O. & Mokros, H. B. (1996). *Children's Depression Rating Scale, Revised (CDRS-R) Manual*. Los Angeles, CA: Western Psychological Services

Ritschel, L.A., Ramirez, C.L., Jones, M., & Craighead, W. E. (2011). Behavioral activation for depressed teens: A pilot study. *Cognitive and Behavioral Practice, 18,* 281-299.

SAS/STAT(R) 9.22 User's Guide. (2010, June 22). Retrieved May 03, 2018, from https://support.sas.com/documentation/cdl/en/statug/63347/HTML/default/viewer.htm#statug_chap0_sect002.htm

Shankman, S.A., Katz, A.C., DeLizza, A.A., Sarapas, C., Gorka, S.M., & Campbell, M.L. (2014). The different components of anhedonia and their associations with different psychopathologies. In *Anhedonia: A Comprehensive Handbook Volume 1: Conceptual Issues and Neurobiological Advances* (pp. 3-22). Spring Netherlands. doi: 10.1007/978-94-017-8591-4_1.

Tabachnick, B.G. & Fidell, L.S. (2013). *Using Multivariate Statistics,* 6th edition. Pearson Education, Inc. New Jersey.

TADS Team. (2000). Treatment for adolescents with depression study (TADS): Protocol version 8.

TADS Team. (2003). Treatment for adolescents with depression study (TADS): Rationale, design, and methods. *J. Am. Acad. Child Asolesc. Psychiatry, 42*(5). 1-13.

TADS Team. (2004). Fluoxetine, Cognitive Behavioral Therapy, and their combination for adolescents with depression: Treatment for adolescents with depression study (TADS) randomized controlled trial. *JAMA*, 292(7), 807- 820.

TADS Team. (2005). The Treatment for Adolescents with Depression Study (TADS): Demographic and clinical characteristics. *Journal of American Academy of Child and Adolescent Psychiatry, 44*(1), 28-40.

TADS Team. (2005). Independent Evaluator (IE) Manual: Treatment for Adolescents with Depression Study (TADS) Final version (4.1).

Uher, R., Perlis, R.H., Henigsberg, N., Zobel, A., Rietschel, M., Mors, O., et al. (2012). Depression symptom dimensions as predictors of antidepressant treatment outcome: replicable evidence for interest-activity symptoms. *Psychological Medicine, 42*(5), 967-980.

Vitiello, B., Rohde, P., Silva, S., Wells, K., Casat, C, Waslick, B.,…The TADS Team. (2006). Functioning and quality of life in the Treatment for Adolescents with Depression Study (TADS). *Journal of the American Academy of Child and Adolescent Psychiatry, 45*(12), 1419-1426. doi: 10.1097/01.chi.0000242229.52646.6e.

Zeiss, A.M. (2006). The theoretical implications of research findings on adolescent depression: Implications for Lewinsohn's integrative model of depression and for a lifespan developmental theory of depression. In Essau, C.A. (Ed.) *Child and Adolescent Psychopathology: Theoretical and Clinical Implications*. New York: Routledge.