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4

Moderators and Mediators of Treatments for Youth With Depression

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INTRODUCTION

Depression in Youth

Depression in youth is prevalent, disabling, and recurrent. Nearly 5% of children experience clinically significant mood disorder at any given time; this prevalence rate surges to 10%–20% in the teen years, with the result that nearly 1 in 5 youth will have experienced an episode of depression by the end of puberty (Avenevoli, Knight, Kessler, & Merikangas, 2008). Depressive disorder interferes markedly with peer and family relationships and school achievement (Jaycox et al., 2009; Kessler, Foster, Saunders, & Stang, 1995; Lewinsohn et al., 1994) and is associated with suicide attempt and completion (Barbe, Bridge, Birmaher, Kolko, & Brent, 2004a; Rao, Weissman, Martin, & Hammond, 1993), the third leading cause of death for adolescents and young adults (Centers for Disease Control and Prevention [CDC], 2010). Depression is linked to risky behavior and poorer physical health, including higher rates of obesity (Goodman & Whitaker, 2002; Jaycox et al., 2009; Lewinsohn et al., 1994). Depression also is highly comorbid with other mental health problems. Anxiety disorders may precede and follow depression, and they are the most closely associated form of psychopathology in terms of shared risk and etiological underpinnings (for discussion, see Garber & Weersing, 2010). Depression also may serve as a risk factor for the development of substance use and abuse (Gotlib, Lewinsohn, & Seeley, 1995; Rice, Lifford, Thomas, & Thapar, 2007). Perhaps most prominently, depression in youth is a

potent risk factor for the recurrence of depressive disorder in adulthood and across the lifespan. Of adolescents who experience an episode, 25% will have a recurrence within 1 year, 40% within 2 years, and 70% within 5 years (Mash & Wolfe, 2016).

Efficacy of Treatment

Given the major public health impact of youth depression, efforts have been made to develop efficacious treatments. The effect sizes in psychosocial clinical trials for youth depression have been quite variable, ranging from zero to over 1 (a very large effect), a pattern driven both by high variability in response within treatment groups and very substantial differences in control condition response rates. In addition to issues with variability, the youth depression treatment literature as a whole has experienced a notable contraction in the estimated *mean* effect of intervention over the past two decades, with mean effect sizes moving from some of the largest in the mental health literature to some of the smallest (see Weisz, McCarty, & Valeri, 2006).

This pattern of results has presented a challenge for crafting best practice recommendations for the treatment of youth depression, a task made even more difficult by uneven sampling of population characteristics in the literature. For example, as described earlier, the prevalence of depression rises dramatically in the teen years and, understandably, the majority of clinical trials have focused on depressed adolescents. For the most part, depressed children have been included only in (a) early-stage studies with small samples and less rigorous assessment (e.g., selecting youth screening high on self-reported of depression questionnaires, rather than conducting diagnostic assessment; Butler et al., 1980), or (b) studies with a very broad age range, but minimal power to examine age or developmental level as a moderator of response (e.g., Wood, Harrington, & Moore, 1996). In a similar fashion, cultural and ethnic groups have been unevenly represented across trials. Investigations of interpersonal psychotherapy (IPT) for adolescent depression have been largely conducted in samples of Latino youth, with two published randomized IPT trials conducted in Puerto Rico and the remaining trials including substantial representation of Latino youth living in the mainland United States. In contrast, the cognitive behavioral therapy (CBT) literature has historically included predominantly non-Hispanic Caucasian families (Huey & Polo, 2008).

However, despite these challenges, the literature does support some general conclusions about treatment efficacy (see Weersing & Gonzalez, 2009). For depressed adolescents with mild to moderate depression, treatment with CBT or IPT should be considered efficacious and likely superior to watchful waiting, simple attention from a caring adult, or non-directive therapy (see Brent et al., 1997; Mufson et al., 2004; Rohde et al., 2004). The definition of the terms *mild* and *moderate* vary across studies, but studies that characterized their samples in this fashion still tend to include teens that meet at least minimal diagnostic

criteria for a depressive disorder (usually Major Depression). In contrast, youth with moderate to severe levels of depression meet diagnostic criteria, with scores on normed symptom measures in the clinically significant range and also demonstrate impairment across several areas of their life (e.g., Children's Global Assessment Scale [CGAS; Shaffer et al., 1983] functioning score less than 50; TADS, 2004), have longer term histories of depressive illness (e.g., history of failed antidepressant treatment; Brent et al., 2008), or high levels of suicidality (e.g., Brent et al., 1997). For these moderately to severely depressed adolescents, the results of CBT alone are more mixed (cf. Brent et al., 1997; TADS, 2004) and combination treatment with CBT and medication may be a wise choice (Brent et al., 2008; March et al., 2004). The benefits of IPT and medication combination treatment remain untested. For depressed children, CBT appears to hold promise, although the evidence base is thinner than with depressed teens. The value of IPT remains largely unexplored in pre-pubertal depressed youth (although current trials are in progress; National Institute of Mental Health, 2014).

To move the field beyond these very general conclusions will require (a) better understanding of why the youth depression literature has produced such inconsistent findings, and (b) systematic, theoretically driven attempts to fill critical gaps in the literature. In an effort to aid this process, in the following critical review, we focus on the two efficacious interventions for youth depression—CBT and IPT—and attempt to answer two key questions. First, what is the underlying theory driving the treatment, and do the available data in the clinical trial literature support this theory of intervention? Second, what are the boundaries of these theories? Are these interventions universally applicable to the treatment of depressed youth, or should these treatments be expected to work more or less well with different types of depression, in the presence of comorbid disorders, and across demographic groups? This first question is a search for evidence of treatment mechanism and mediators of intervention effects, while the second is one of moderation. By examining the available evidence on mediators and moderators of CBT and IPT for youth depression, we aim to illuminate the current state of the field and provide useful guidance on developing an agenda for future research.

MEDIATION AND THEORIES OF INTERVENTION

Depression is often viewed as a prime example of a diathesis-stress model of psychopathology. Broadly, depression is thought to arise from (a) the experience of stressful life events (e.g., Kendler, Thornton, & Gardner, 2001); in combination with (b) genetic vulnerability toward mood dysregulation in response to stress (e.g., Caspi et al., 2003); (c) maladaptive behavioral responses to stress (avoidance, poor interpersonal problem-solving skills; e.g., Gazelle & Rudolph, 2004); and (d) inaccurate, overly negative cognitive interpretations of stressful events (e.g., Gladstone & Kaslow, 1995). This general theory of depressive psychopathology has spawned a range of intervention theories, each crafted to interrupt various

processes of disorder. Below, we describe the intervention theories underlying the two evidence-based psychosocial treatments for youth depression, CBT and IPT, and detail the extent to which the empirical literature has (or more often has not) tested the mediators targeted by these theories.

Mediators of CBT Effects

THEORY OF INTERVENTION

Two major cognitive theories have been proposed to explain the etiology and maintenance of depression: classic Beckian cognitive theory (Beck, Rush, Shaw, & Emery, 1979) and learned helplessness theory (Abramson, Metalsky, & Alloy, 1989). Both of these approaches are cognitive vulnerability models. In each, biased, overly negative cognitive processing is thought to arise from stressful early life experience. Individuals "learn" that the world is an unsafe and unpredictable place, that they are not adept at handling stress, and that the future is likely to be dark and filled with insurmountable challenges. When faced with stressful circumstances in the present, these beliefs (cf. schemas, explanatory styles) are activated, interfere with effective coping, and are associated with dysphoric mood, behavioral avoidance, and, eventually, clinical depression. Furthermore, depressogenic thinking is resistant to disconfirmation, in part, because of enduring styles of information processing that promote belief maintenance (e.g., selective abstraction of negative information). In addition to these cognitive vulnerability models, purely behavioral accounts of depression have been proposed. Lewinsohn and colleagues (1974; Lewinsohn, 1975) suggested that depression may result directly from low levels of positive reinforcement and high levels of punishment and aversive control. As a result, individuals withdraw from negative interactions and avoid situations that may produce low mood; this exacerbates the problem of low positive reinforcement, as withdrawal also diminishes opportunities for reinforcing feelings of pleasure and experiences of mastery. The resulting cycle of avoidance and negative mood induction leads to clinically impairing depression. The depressive cycle may be brought about through environmental change (e.g., a friend moving away) or a mismatch between environmental demands and behavioral skills (e.g., insufficient social skills to cope with onset of dating).

These cognitive and behavioral theories of depression were developed to explain the etiology and maintenance of adult depression. However, there is evidence that depressed youth exhibit patterns of information processing similar to depressed adults (e.g., Gladstone & Kaslow, 1995). Certainly, experiencing negative, uncontrollable events has been linked to helpless behavior and apathy in adults and in youth (and cross-species). In adolescents, first onset and recurrence of depression are often preceded by family conflict, physical illness, breakup of romantic relationships, and loss of friendships (Lewinsohn, Allen, Seeley, & Gotlib, 1999). Of these, familial stress may play a particularly important role; parental depression, parent-child conflict, parental divorce, low family

cohesion, and high levels of "expressed emotion" have all been found to significantly increase the risk of depression in adolescents (e.g., Goodman & Gotlib, 2002; Lewinsohn et al., 1994, 1996; Tompson et al., 2010).

Moving from intervention theory to implementation, CBT programs for youth depression typically begin with psychoeducation about depression and the theory of intervention, include an early application of behavioral techniques (such as pleasant activity scheduling) in order to bolster current mood, and then move into cognitive restructuring. Beyond this core structure, CBT manuals differ in (a) supplemental cognitive and behavioral techniques employed (e.g., problem-solving, social skills, relaxation), (b) relative focus on cognitive change versus behavioral skill building, (c) overall number of sessions and dosing of each technique, (d) format (from structured skills group to principle-based individual sessions), and (e) level of parental involvement. Across this diversity in manuals, improvement in negative cognitive style and behavioral mood regulation skills are hypothesized to be the mechanisms of action of CBT effects.

Empirical Evidence Supporting Mediation Model

To date, only four investigations have tested whether change in cognitive or behavioral processes mediated the impact of CBT on depression at post-treatment: (a) the Kolko and colleagues (2000) reanalysis of the Brent et al. (1997) comparative trial of cognitive, family, and supportive therapy; (b) the Ackerson et al. (1998) trial of cognitive bibliotherapy for teens with mild depression seen in primary care; (c) a secondary paper by Kaufman et al. (2005) examining the process and outcome of CBT adapted for youth with depression and comorbid conduct disorder; and (d) a secondary analysis by Jacobs et al. (2009) of the Treatment of Adolescents with Depression Study (TADS), a multi-site randomized trial of CBT and medication management, singly and in combination. All of these investigations focused on treatment of adolescent (versus child) depression and relied on youth self-report of cognitive (four studies) and behavioral processes (one study). Given the small size of this literature, we review each of these in some detail.

In the original Brent comparative efficacy trial (1997), CBT was tested against family and supportive therapies in a sample of moderately to seriously depressed adolescents with high levels of suicidality. Across multiple measures of depression, CBT was found to be more efficacious than these alternate interventions at post-treatment assessment. To probe mechanisms of intervention effects, Kolko et al. (2000) investigated the mediating role of several cognitive and family process variables, hypothesizing that CBT and family therapy should show specific effects on their theoretical mechanisms of action, and that change in these theoretically specific mechanisms should statistically mediate the impact of intervention on depression outcome. As hypothesized, CBT did have a significantly greater effect on cognitive distortions, but was not superior to family

or supportive therapy in changing hopelessness. Change in cognitive distortion did not mediate the effect of CBT on depression symptoms, although low power may have limited ability to find significant effects (e.g., the subsample youth with complete mediator data did not show a significant effect of the CBT on depression, unlike in the full sample). Interestingly, and contrary to hypotheses, CBT also had superior effects than alternate interventions on family functioning and marital satisfaction at post-treatment, suggesting that the most efficacious intervention overall (CBT) may have produced broad, general change rather than theoretically specific effects on mediators.

Stronger support comes from an investigation of a CBT bibliotherapy program for depressed teens. Ackerson et al. (1998) found that youth who were given a CBT self-help book demonstrated a reduction in depression symptoms 4 weeks later. Teens also had a significant reduction in depressogenic thinking as assessed by the Dysfunctional Attitudes Scale (DAS), but they did not show significant change in negative automatic thoughts, as assessed with the Automatic Thoughts Questionnaire (ATQ), despite a positive effect size for the measure. Change in dysfunctional attitudes did mediate the effects of the intervention on youth-reported depression symptoms, but the conditions for mediation were not met for other measures of depression (i.e., interviewer ratings). Again, power may have been a limiting factor in this investigation, as cell sizes were below 15 and only the largest effects demonstrated statistical significance.

In the Kaufman reanalysis of the Rohde et al. (2004) trial of CBT for youth with comorbid major depression and conduct disorder, CBT was found to significantly impact one cognitive process measure. Change in cognitions did statistically mediate program effects on depression symptoms (all constructs were measured post-treatment); however, effects were inconsistent across measures of cognition, and the specific pattern of findings was opposite to that of Ackerson—small but significant effects on the ATQ but non-significant results for the DAS, with an effect size near zero. Furthermore, Kaufman failed to find evidence of mediation for three additional measures tapping problem-solving, social skills, and involvement in pleasant activities—all of which were targeted by the CBT program under investigation.

The most recent analysis of mediators of adolescent depression treatment was based on the multi-site TADS study (2003) comparing CBT plus medication (combination treatment) to CBT alone, medication (fluoxetine) alone, and pill placebo. In the original TADS trial, CBT failed to outperform pill placebo, contrary to the authors' a priori hypotheses. Combination therapy was the most broadly efficacious intervention, although medication alone equaled combination on some depression metrics and did separate from placebo better than CBT. The TADS trial stirred no small level of controversy at the time of its publication, with questions raised about the sample (more ill, male, and comorbid than many trials) and quality and content of the specific CBT protocol (which was previously untested; see Weersing, Rozenman, Gonzalez, 2009, for discussion). In this context, Jacobs et al. (2009) sought to explore

mediators of the TADS effects, focusing on the DAS perfectionism subscale (measured pre- and post-treatment). In this analysis, DAS perfectionism did partially mediate the superior effects of combination treatment (compared to alternate arms) on interviewer-rated depression symptoms. Statistically, when DAS perfectionism change scores were included in models of depression outcome, combination therapy and medication alone had very similar rates of improvement, and these two conditions remained superior to CBT and placebo. DAS perfectionism also served as a mediator of the superior effect of combination (versus medication only) on suicidality. These results are consistent with a mediating role for cognitive change in CBT effects, although this conclusion is weakened by (a) the overall poor effects of CBT alone in TADS on both the outcomes and mediator, and (b) the lack of fine-grained data on the timing of change in cognitive process and outcomes. It is also possible that DAS perfectionism changes followed symptomatic improvement, and improvement in perfectionistic thinking was reflective of improved mood.

Mediators of IPT Effects

THEORY OF INTERVENTION

Interpersonal psychotherapy (IPT) is a well-established, efficacious treatment for adult unipolar depression (Klerman, Weissman, Rounsaville, & Chevron, 1984). Two research teams have adapted the adult IPT model to match the developmental presentation of adolescent depression. Mufson and colleagues (1999) produced the first adaptation of the model, while Rosello and colleagues (2008) independently developed a culturally adapted version of IPT for Puerto Rican adolescents. Both share a core theoretical framework; the Mufson model has been more elaborated in the literature (e.g., Mufson, Dorta, Moreau, & Weissman, 2011), and we thus use it as our base example of IPT intervention theory and techniques.

IPT models conceptualize depression as occurring within an interpersonal matrix and target the resolution of psychosocial stresses that coincide with the onset of teen patients' index depressive episode. As discussed previously, depressed youth experience a high level of severe psychosocial stress, are exposed to family and parental conflict, and are dependent for their needs on parents with high rates of psychopathology (see Hammen et al., 1999). In addition, specific, aversive family communication styles have been identified as significant predictors of depression in youth (e.g., Asarnow et al., 1993). Furthermore, in adolescents, depression is often preceded by negative interpersonal events separate from the family, such as the breakup of romantic relationships and loss of friendships (Lewinsohn et al., 1999). Unlike CBT, IPT does not claim a causal role for these environmental stresses in creating depression (e.g., by specifically triggering depressogenic thinking, or by directly reducing opportunities for positive reinforcement). Instead, patients are taught that depression and life stress frequently co-occur and that, regardless of the cause of depression (adversity,

biology), the alleviation of interpersonal problems will likely result in an attenuation of depressive symptoms.

In the first phase of IPT, the difficult environmental context of teen patients' lives is categorized into one of five common problem areas: grief, role disputes, role transitions, interpersonal deficits, or issues with single-parent families (an adaptation from adult IPT; see Mufson et al., 2011). In the remainder of treatment, specific strategies are specified for working through each of the problem areas over the course of 12 sessions, with an overall emphasis on restoring (or creating) meaningful, low-conflict social relationships. For example, in working with a stressful role transition (such as changing from elementary to middle school), an IPT therapist may help a teen (a) mourn the loss of his or her old, comfortable role; (b) discuss the challenges involved in the transition; (c) attempt to discover the benefits of the new role or, at least, form reasonable expectations about the new role; and (d) help the teen's interpersonal system adjust to the role transition. This final task—interacting directly with the adolescent's family—is a modification of the adult IPT model, similar to the increased involvement of parents in developmental adaptations of CBT. IPT formulation and techniques are not fundamentally incompatible with the cognitive view of depression. In fact, there are several similarities, including problem-solving and skill-building activities, albeit infused with specific, recent social experiences.

Empirical Evidence Supporting the Mediation Model

There has yet to be a randomized controlled trial of IPT that has tested the mediating processes thought to underlie the effects of the intervention. Some indirect evidence on the mechanisms of IPT action comes from a review by Weersing, Rozenman, and Gonzalez (2009). In this review, the authors coded secondary outcomes of randomized trials for adolescent depression along cognitive, behavioral, and interpersonal dimensions. Effect sizes for treatment versus control were calculated, and IPT, CBT, and family therapy were compared in terms of their relative impact on these theoretically relevant outcomes. At post-treatment assessment, IPT did produce changes in self-reported social functioning by the adolescents, although the specific interpersonal domains that demonstrated improvement varied across studies. IPT appeared to show the most consistently positive effects on dating relationships and the most variable effects on family functioning (ES ranging from -0.29 to 0.60). Interestingly, IPT also significantly impacted purportedly "cognitive" measures, at a level similar to CBT; however, the cognitive outcomes assessed in IPT studies did tend to have a social component (e.g., measures of social problem-solving). Taken together, these results suggest that IPT does impact the interpersonal targets underlying intervention theory, although it is unclear whether these interpersonal outcomes are functioning as mediators. It is possible, of course, that change in depression symptoms improves social relations, rather than change in social relationships serving as a mechanism of depression recovery. Additional data on the timing of change in interpersonal process and depression symptom reduction are clearly needed.

MODERATION AND BOUNDARIES OF EFFECTS

As discussed in detail in Chapter 1 of this volume, the study of moderators is a search for the boundaries of theory. In understanding the effects of youth depression treatments, we have found it useful to define three classes of moderators. First, we consider *match-to-intervention moderators*, namely baseline characteristics of youth who are a theoretical "match" to one of the existing evidence-based interventions for depression. In CBT for youth depression, cognitive distortions and behavioral mood regulation skills are the core targets of intervention, and change in these process are presumed to mediate intervention effects. Accordingly, it might be hypothesized that youth demonstrating deficits in these domains would be particularly good candidates for CBT treatment versus alternate interventions, such as IPT. CBT would provide a "match" to the hypothesized diatheses that formed the basis of the youth's depression, and, thus, baseline levels of cognitive and behavioral deficits should moderate treatment response *in favor* of CBT (a compensation model of treatment response, see Rude & Rehm, 1991). In contrast, interpersonal relationships and functioning are the central targets of intervention in IPT. Deficits and disruptions in this domain are hypothesized to co-occur with depression and may be linked to the onset and maintenance of episodes. Interpersonal functioning and relationship quality at the beginning of treatment, therefore, serve as theoretically interesting moderators of IPT effects. It could be hypothesized that IPT would be a particularly good match to youth with deficits in these domains or experiencing high levels of interpersonal conflict.

Second, we focus on *contextual moderators* of intervention effects. As discussed earlier, depression is viewed as a stress-sensitive disorder. Both CBT and IPT focus on improving the ability of youth to cope with current stressors by applying the skills learned in treatment (e.g., problem-solving in CBT, social role play and rehearsal in IPT). This structured focus on current stressors and assistance in applying skills should stand in sharp contrast to non-directive, attention only, or placebo control comparison conditions. Youth may especially benefit from CBT or IPT (versus these control conditions) when they are actively experiencing stressful life circumstances. Furthermore, some of the more cognitively focused CBT manuals (e.g., Brent et al., 1997) also may address the lingering impact of past stressors by targeting youths' core beliefs about themselves and the world around them. We thus explore the potential moderating impact of stressful life events and trauma history on response.

Third, we review *generalizability moderators* of CBT and IPT effects to assess whether these interventions are robust to clinical complexity and perform well across diverse family demographic characteristics. In terms of clinical complexity, we probe the effect of these evidence-based interventions versus control in the face of high levels of depressive symptom severity, presence of suicidality, low functioning, comorbidity with other mental health symptoms, and familial

comorbidity (e.g., current depression in the parent). We further examine intervention response by youth age, gender, ethnicity and family income.

To aid in interpretation of effects across this complex literature, we provide a summary of moderator findings in Table 4.1, organized under these three categories (match to intervention, context, and generalizability). Investigators have seldom used precisely the same measure of cognitive distortions or family processes across studies. As these different operationalizations of moderators may influence findings (and help to explain divergent results across studies), we have retained this level of complexity by grouping, rather than collapsing, similar variables. For each variable, we indicate whether the potential moderator was significantly associated with superior or inferior effects of active treatment compared to control or whether the test of the *treatment x moderator* interaction was not statistically significant. The majority of trials tested CBT as the active intervention, and CBT effects are presented in the table in standard font. When IPT was tested as the active intervention, results are coded in the table in *italics*. In the following section, we provide a critical review of these findings.

Moderators of CBT Effects

MATCH TO INTERVENTION

Below, we review the empirical literature on cognitive, behavioral, and interpersonal moderators of CBT effects in randomized controlled trials for youth depression. We highlight evidence (or lack of evidence) for treatment specificity and matching effects. As discussed in the overview, matching hypotheses would suggest that CBT should outperform control conditions and alternate treatment models for youth with "matching" deficits in cognitive and behavioral processes at baseline. In contrast, significant moderation in favor of CBT would not be expected for youth with interpersonal deficits, when CBT is compared to models that focus explicitly on interpersonal processes as their mechanism of action (e.g., active IPT, family therapy control conditions).

COGNITIVE MODERATORS

Clinical trials of CBT frequently include measures of cognitive processes as outcomes, and five papers have tested whether baseline levels of these processes served as moderators of intervention effects. As can be seen in Table 4.1, studies employed a diversity of measures of cognitive processes, complicating interpretation of results across the literature. To aid in our review, we group these measures as primarily focusing on (a) cognitive distortions/negative bias, (b) problem-solving skills, or (c) coping style, when coping is defined by cognitive processes (e.g., cognitive reappraisal of stressors) or when coping style involves appropriately choosing and applying strategies (e.g., reflecting executive functioning).

In the examination of cognitive distortions, evidence for the matching hypothesis was mixed. In the TADS study (2004, described earlier), the combination of CBT

Table 4.1. MODERATORS OF TREATMENT EFFECTS IN YOUTH DEPRESSION CLINICAL TRIALS

	Intervention Superior	Intervention Inferior	Not Statistically Significant
MATCH TO INTERVENTION			
Cognitive factors			
Cognitive distortions	7		
Negative thoughts			17
Hopelessness	2		6, 7, 17, 20
Self-esteem			21
Dysfunctional Attitudes Scale (DAS)			17
DAS: Perfectionism			12
Coping style	17		
SPSI-R Positive Problem Orientation	5		
SPSI-R Negative Problem Orientation		5	
SPSI-R Rational Problem-Solving			5
SPSI-R Impulsivity-Carelessness Style			5
SPSI-R Avoidant Style			5
Behavioral factors			
Pleasant events schedule			17
Social adjustment	*10*		10, 17
Perceived social support			9
Interpersonal and family factors			
Sociotropy vs. achievement orientation	*11*		11
Family conflict (more)	*10*		7, 17
Marital discord			1
Marital discord x gender	1		
Marital discord x oppositionality	1		
Tx x marital discord x gender			1
FAM task accomplishment			8
FAM role performance (good functioning)	8		

(continued)

Table 4.1. CONTINUED

	Intervention Superior	Intervention Inferior	Not Statistically Significant
FAM communication (more clear)	8		
FAM affective expression			8
FAM involvement	8		
FAM control	8		
FAM values and norms	8		
CONTEXTUAL FACTORS			
Stressful life events		9	
No trauma history (youth)	2, 3, 15, 18		
Exposure to traumas, non-abusive (youth)			15
History of abuse (youth)		2, 20	
Exposure to physical abuse (youth)		18	15
Exposure to sexual abuse (youth)		3	15, 18
GENERALIZABILITY			
Features of depression			
Severity of symptoms (high)	2, 7, 11, *11*		9, 17, 20
Global functioning (poor)			7, 17, 20
Age of onset of first MDE (younger)			17
Total number of past MDE	17		
Duration of MDE (shorter)			7, 20
Melancholic features (less)			7
Suicidality (current or lifetime)			4, 7, 17, 20
Non-suicidal self-harm	2		20
Comorbidity			
No. of comorbid disorders (fewer)		2	7
CBCL total problem score			17
Comorbid anxiety (any)	2, 6		7, 17, 20, *22*
Comorbid probable GAD			*22*
Comorbid probable social phobia			*22*
Comorbid probable panic disorder	*22*		
Comorbid disruptive behavior (CD, ODD)			2, 7, 20
Comorbid ADHD	2, 13		17
Comorbid substance abuse		9	17, 20

(continued)

Table 4.1. CONTINUED

	Intervention Superior	Intervention Inferior	Not Statistically Significant
Demographic factors			
Sex (female)			1, 7, 11, 17, 19, 20
Developmental level (younger/lower)	2, 7		7, 17, 19, 20
Ethnicity (minority status)	2, 17		7, 20
SES (income)	7		2

NOTE: In cases where authors indicated that they planned to test a variable as a moderator but did not report the results, it was presumed that the variable was tested but was not statistically significant. Studies are numbered by first author in alphabetical order: 1. Amaya et al. (2011); 2. Asarnow et al. (2009); 3. Barbe et al. (2004a); 4. Barbe et al. (2004b); 5. Becker-Weidman et al. (2010); 6. Brent et al. (1998); 7. Curry et al. (2006); 8. Feeny et al. (2009); 9. Gau et al. (2012)*; 10. Gunlicks-Stoessel et al. (2011); 11. Horowitz et al. (2007)*; 12. Jacobs et al. (2009); 13. Kratochvil et al. (2009); 14. Lewis et al. (2009); 15. Lewis et al. (2010); 16. Rohde et al. (2001); 17. Rohde et al. (2006); 18. Shamseddeen et al. (2011); 19. Stice et al. (2010); 20. Vitiello et al. (2011); 21. Vostanis et al. (1996); 22. Young, Mufson, & Davies (2006). In the body of the table, moderation results in favor of CBT are presented in plain text; moderation results in favor of IPT are indicated by ***bold italic*** formatting. Also note CBCL = Child Behavior Checklist (Achenbach, 1991); DAS = Dysfunctional Attitude Scale (Spanier, 1976); FAM = Family Assessment Measure (Skinner et al., 1983); SPSI-R = Social Problem Solving Inventory-Revised (D'Zurilla et al., 1996).

and medication was, on average, the most efficacious intervention for depressed adolescents. The superiority of combination treatment on clinician-rated depression symptoms was maintained in the subset of depressed teens with high levels of cognitive distortions, as assessed by the Children's Negative Cognitive Error Questionnaire (CNCEQ). In contrast, participants with lower baseline CNCEQ scores (< 63) responded equally well to combination treatment or to fluoxetine alone, both of which were significantly more effective than CBT or pill placebo (Curry et al., 2006). This ordering of conditions suggests that high levels of cognitive distortion may be an indication for adding on CBT to medication; however, high cognitive distortion did not substantially improve the efficacy of CBT alone in this sample, undercutting a more generalized application of the matching hypothesis. Furthermore, additional analyses in the TADS sample by Jacobs et al. (2009) failed to find evidence of moderation for an alternate measure of cognitive distortion, the DAS perfectionism subscale (also see discussion of this study in the section on mediation in this chapter). High DAS perfectionism scores at baseline predicted poorer outcomes across all treatment groups and pill placebo, but

did not moderate the effects of combination or CBT. Rohde and colleagues (2006) also probed the moderating effect of the DAS in a trial testing the efficacy of CBT (a version of the well-known Coping with Depression for Adolescents [CWD-A] program) versus a life skills/tutoring control condition. This sample is unique in the youth depression treatment literature, in that the depressed teen sample was recruited from a juvenile justice center and in addition to meeting diagnostic criteria for Major Depressive Disorder (MDD), all youth met diagnostic criteria for Conduct Disorder as well. As in the TADS sample, in this trial, DAS scores at baseline did not moderate outcome, operationalized in this study as weeks to MDD recovery. Vostanis et al. (1996) also failed to find evidence of moderation in a comparison of a brief CBT model to non-directive therapy; both treatment modalities improved participant self-esteem.

Four additional studies probed for moderating effects of hopelessness. Hopelessness is a core cognitive component of learned helplessness models of depression and conveys a generally negative or empty outlook on the future, due to the abandonment of expectation of potential contentment or success. In a reanalysis of the Brent et al. (1997) trial, hopelessness was associated with poor outcomes across CBT, family therapy, and non-directive treatment (Brent et al., 1998), and larger changes in hopelessness in CBT helped to explain the superiority of CBT over supportive therapy on the outcome of suicidality (Barbe et al., 2004a). However, baseline levels of hopelessness did not change the magnitude of the CBT effect on depression outcomes, relative to comparison treatments. The same team of investigators later examined hopelessness as a predictor and moderator in a major, multi-site clinical trial of Treatment-Resistant Depression in Adolescents (TORDIA; Brent et al., 2008). In this trial, seriously depressed teens who had failed to respond to an initial course of antidepressants were randomly assigned to medication switch, with or without add-on CBT. Hopelessness was tested as a potential moderator of treatment response, which was defined by ≥ 50% improvement on clinician-rated depression symptoms and global ratings of functional improvement (Clinical Global Impressions [CGI]; Guy, 1976). Contrary to the matching hypothesis, *lower* levels of hopelessness at baseline were associated with better response to CBT add-on at the 12-week assessment (Asarnow et al., 2009). However, the moderating effect of hopelessness was not maintained over long-term follow-up in TORDIA (Vitiello et al., 2011), nor was it replicated in the TADS sample (Curry et al., 2006) or CWD-A application to teens with depression and conduct problems (Rohde et al., 2006). As with the original Brent et al. (1997), these investigations found that hopelessness predicted poor response across conditions, leaving the TORDIA trial as the sole investigation finding a moderating relationship.

We turn next from cognitive distortions to problem-solving. Becker-Weidman and colleagues (2010) utilized the Social Problem Solving Inventory-Revised (SPSI-R; D'Zurilla, Nezu, & Maydeu-Olivares, 1996) to identify how different problem-solving styles impacted treatment outcome in the TADS sample of depressed teens. The scale assessed five approaches or orientations toward the process of problem-solving: a generally positive

orientation to the process of solving problems (e.g., belief that problems can be solved), a negative problem orientation (e.g., frustration in the face of difficulty implementing solutions), a rational approach to solving problems (e.g., a desire to break problems into small, logical steps), an avoidant style, and an impulsive/careless style. None of these subscales significantly moderated group differences when clinician-rated depression symptoms were the outcome. However, when using the Suicidal Ideation Questionnaire as the outcome measure (SIQ-Jr; Reynolds, 1987), both positive and negative problem orientations were significant moderators. Depressed youth with high levels of positive problem orientation at baseline had lower levels of suicidality in CBT in comparison to alternative treatments (SSRI alone or combination treatment). Treatment groups did not significantly differ from each other for teens with low positive problem orientation. In a similar pattern, treatment groups did not differ in efficacy for individuals with high baseline negative problem orientation, but teens with lower levels of negative problem orientation showed significantly greater improvement in suicidality when treated with CBT. The other treatment groups did not differ from one another. Notably, although this measure was designed to assess many styles of problem-solving, the results collapsed into a positive-negative contrast, with teens who indicated greater affiliation with problem-solving as a skill making better use of CBT as a tool for reducing suicidality.

Finally, coping style was assessed as a predictor and moderator in the CDW-A trial testing the efficacy of CBT for teens with depression and conduct problems. In contrast to the null findings for hopelessness and the DAS, coping style was a significant moderator of effects (Rohde et al., 2006). Youth with positive coping skills at baseline performed dramatically better than youth in control (a life skills/tutoring condition), recovering from MDD in 6 weeks versus 16 weeks. In contrast, no treatment effect was identified in the subsample of teens who reported poor coping skills. This finding points in the opposite direction from that hypothesized by a match-to-diathesis model, suggesting instead that CBT was most effective with youth who already had strengths in coping to build upon (a capitalization versus compensation model; Rude & Rehm, 1991). The coping measure included in this report serves as a useful bridge to our next section on behavioral skill moderators; "coping" included both cognitive and behavioral elements, such as escapism/avoidance in the face of stress.

BEHAVIORAL MODERATORS

Despite the importance of behavioral techniques to the CBT model, very few studies include measures of behavioral mood regulation skills at baseline, and even fewer test whether deficits in these skills moderate treatment. In the Rohde sample of depressed and disruptive teens (Rohde et al., 2006), baseline frequency of pleasant activities was investigated as a potential moderator of the CBT versus life skills/tutoring comparison. Teens' baseline use of pleasant activities to regulate mood was not related to differential response to CBT.

INTERPERSONAL FUNCTIONING AND RELATIONSHIPS

We next turn to an examination of interpersonal moderators. Two investigations have focused on adolescents social networks. In the Rohde trial of CBT for youth with depression and disruptive behavior, baseline social adjustment did not moderate CBT outcome, relative to the life skills control condition (Rohde et al., 2006). Gau et al. (2012) also failed to find a moderating relationship between adolescents' perceived social support from friends and family and the relative benefit of CBT versus an educational control condition.

Three published reports have explored the moderating effects of family conflict. In an analysis of the TADS data, Curry and colleagues (2006) examined whether the relation between treatment assignment and outcome (severity of depression) would vary as a function of parent-child conflict. Parent-child conflict was measured using a combination of scores from both parent and youth baseline reports on Conflict Behavior Questionnaire (CBQ; Prinz, 1977) and did not moderate response to treatment. Family conflict in the TADS sample was further explored by Feeny et al. (2009), using a slightly different operationalization focusing on both the CBQ and specific ratings of contentious issues. Again, conflict did not moderate response to intervention in this sample, although, in this analysis, conflict predicted poor response across all treatments. In a reanalysis of the Rohde trial, family cohesion (defined as low parent-child conflict) did not moderate response to CWD-A (Rohde et al., 2006).

In contrast to these null moderator findings for family conflict, marital discord did appear to be linked to intervention response in the TADS sample through complex interactions between conflict, gender, and youth externalizing behavior. Contrary to their expectations, Amaya and colleagues (2011) found that marital discord alone did not significantly impact differential response to combination of fluoxetine and CBT (COMB), fluoxetine (FLX) alone, CBT alone, or placebo. However, when gender and externalizing problems were added to this model, two distinct, significant three-way interactions were found, moderating acute treatment response. Examining *treatment x discord x gender*, COMB outperformed placebo across all levels of the moderating variables. In high-discord households, FLX also was superior to placebo, regardless of gender. These findings mirror the overall results of TADS, where interventions involving medication outperformed placebo across metrics. Results involving CBT and females were more complex. In high-conflict households, COMB outperformed CBT alone for males but not for female adolescents; indeed, female adolescents in high-conflict homes showed a uniform and undifferentiated response to all active treatments (versus PBO). In contrast, females in low-conflict homes showed a significantly worse response to CBT alone compared to COMB and FLX, with CBT failing to separate from placebo. Unpacking the *treatment x discord x externalizing* symptoms interaction yielded similar effects for combination treatment. Across all levels of moderators, COMB separated from placebo. However, within the subset of highly oppositional adolescents, marital conflict moderated response to intervention. Under conditions of high discord, both treatments involving medication—COMB and FLX—produced superior effects for oppositional

youth relative to CBT and placebo. Under conditions of low discord, depressed and oppositional youth benefited significantly more from COMB than all other treatments, with FLX failing to separate from placebo and CBT alone also showing a very poor response rate. Across these many analyses, combination treatment emerged as a robust intervention, and, interestingly, CBT alone appeared to fare particularly poorly under conditions of low marital discord.

Feeney et al. (2009) also explored the moderating role of seven indices of family functioning, drawn from the Family Assessment Measure (FAM-II; Skinner, Steinhauer, & Santa-Barbara, 1983). Notably, parent report of family functioning was not statistically related to outcome for any of the FAM subscales, and all moderator findings are based on adolescent report. Moderator results varied by definition of outcome, with the strongest pattern of moderation for clinician-reported depression severity (CDRS-R). Across analyses, adolescents who reported good family functioning (e.g., stronger agreements and more clarity on values and norms and control/rules, better communication and involvement) were more likely to benefit from combination therapy than FLX alone, CBT alone, or placebo. Conversely, among adolescents who reported worse family functioning, combination and FLX generally showed similar effects, with these conditions separating from CBT alone and placebo. As discussed previously with marital discord, combination therapy emerged as relatively robust to negative interpersonal moderators.

Contextual Moderators

STRESSFUL LIFE EVENTS

Only one CBT trial has investigated the moderating role of stressful life events, an indicated prevention study by Gau et al. (2012) targeting high school students with elevated depression symptoms. In this sample, a significant interaction was observed between treatment type, stress, and substance abuse. The CBT prevention program separated well from the education control for teens with low or moderate levels of stressful life events and substance use. However, for teens with either high levels of stress or significant substance use, the CBT program was not statistically superior to control.

TRAUMA

Three different CBT trials have probed the moderating impact of trauma history on treatment outcomes among depressed adolescents. In a reanalysis of the Brent et al. (1997) comparative efficacy trial of CBT, Barbe et al. (2004b) found a significant interaction between treatment and history of sexual abuse. Too few participants in the family therapy arm had experienced sexual abuse to allow for analysis. When examining the remaining sample, CBT was reliably superior to supportive therapy for youth without a history of sexual abuse; however, for youth with an abuse history, CBT did not outperform the supportive therapy control. In the TADS sample, Lewis et al. (2010) identified four subgroups of

youth: those with no trauma history ($n = 201$); those with trauma history but with no abuse ($n = 148$); those with experience of physical abuse ($n = 40$); and those with experience of sexual abuse ($n = 38$). Reports of trauma were assessed using the PTSD section from the KSADS-PL interview. A significant *trauma x treatment x time* interaction revealed that adolescents with no trauma history had equally positive outcomes in COMB and FLX with worse outcomes observed in CBT and PBO, replicating the findings in the TADS sample as whole. Youth with a trauma history (but not abuse) and youth with a history of physical abuse had similar outcomes, with all four arms failing to statistically separate from each other (combination, FLX, CBT, and placebo). In contrast, youth with a history of sexual abuse had particularly poor outcomes in CBT alone, with all other arms outperforming this condition. Trauma history also was found to moderate short-term (Asarnow et al., 2009; Shamseddeen et al., 2011) and long-term (Vitiello et al., 2011) outcomes of the TORDIA trial. In the main effects findings of the TORDIA study, adjunctive CBT was found to be superior to medication switch alone in a sample of seriously depressed adolescents who had already failed a trial of antidepressant medication. The PTSD portion of the KSADS-PL was used to assess abuse history in this sample, with 13.15% ($n = 43$) of youth reporting a history of physical abuse (PA) and 15.9% ($n = 55$) a history of sexual abuse (SA). As in the rest of the CBT literature, youth without a trauma history had superior outcomes in combination (medication switch + adjunctive CBT) therapy in comparison to medication monotherapy (switch to a new antidepressant; Asarnow et al., 2009). However, trauma history significantly moderated response to (a) flatten out the superior effects of combination therapy for youth with sexual abuse and (b) reverse the relative benefits of combination and monotherapy for youth with physical abuse. Indeed, at both post-treatment (Shamsedden et al., 2011) and 18-month follow-up (Vitiello et al., 2011), youth with a history of physical abuse had a statistically superior response to medication monotherapy over combination, even after controlling for differences between PA and non-PA groups on negative clinical indicators such as depression severity, suicidality, and post-traumatic stress symptoms.

Generalizability Moderators

We next turn to an examination of clinical and demographic moderators of CBT response. These results speak to the potential generalizability of CBT effects across the population of depressed youth and limits to the effectiveness of CBT as an intervention when applied to diverse samples.

FEATURES OF DEPRESSION

Five clinical trials examined whether baseline severity moderated youth outcome; of these, three found a significant relationship. In the TADS trial, combination treatment was most efficacious in the mild/moderate depression subgroup; however, combination did not significantly differ from medication

monotherapy in the severe depression subgroup, although both were still superior to CBT alone and placebo (Curry et al., 2006). In the TORDIA trial, combination therapy (adjunctive CBT plus medication switch) was consistently more efficacious than medication monotherapy, but depression symptom severity moderated treatment effects in a quadratic pattern (Asarnow et al., 2009). The participants with low and high symptoms (CDRS-R < 52 or CDRS-R > 66) had the largest magnitude of CBT effects at post-treatment, although this effect was not present at 18-month follow-up (Vitiello et al., 2011). In a prevention study, Horowitz and colleagues (2007) tested baseline scores on two youth-reported depression scales (CDI and CES-D) as moderators of response to CBT, IPT, and control. For youth with initially high CDI scores (operationalized a variety of ways), CBT was significantly more efficacious than control condition and IPT showed a mixed pattern of generally positive effects; however, the two active treatments did not separate from control for youth with low symptoms. This moderating relationship was not found when analyzing the interactions using the CES-D as the severity measure, nor was it maintained at the 6-month follow-up (Horowitz et al., 2007). In addition, two trials that utilized youth-report on the Beck Depression Inventory (BDI; Beck, Steer, & Garbin, 1988) did not find significant moderation effects, post-treatment (Gau et al., 2011; Rohde et al., 2006). Finally, three of these investigations (TADS, Curry et al., 2006; CWD-A, Rohde et al., 2006; TORDIA, Vitiello et al., 2011) broadened their definition of severity to include global functioning, rated by trained clinicians using the C-GAS. Level of functioning at intake did not significantly moderate outcome in any of the three trials.

In addition to severity, various features of depressive illness also have been tested as potential moderators. In the Rohde et al. (2006) trial of CDW-A, age of onset of first major depressive episode (MDE) did not significantly moderate effects; however, those reporting multiple MDEs prior to study enrollment (i.e., recurrent depression) saw recovery in 6 weeks when receiving CWD-A, which is over 6 times faster than the recovery time of participants with recurrent depression who were randomized to the life skills control group (recovery = 38 weeks). CDW-A did not separate from life skills control in participants who reported a single depressive experience at intake. Both TADS and TORDIA trials investigated the impact of duration of depressive illness, but neither trial obtained significant results (Curry et al., 2006; Vitiello et al., 2011). The TADS team (2004) further used the CDRS-R to create a five-item summative measure of melancholic features (anhedonia, insomnia, appetite disturbance, guilt, psychomotor retardation). This summed score predicted treatment outcome, where participants with fewer/less severe melancholic features improved more overall, but the scale did not moderate treatment outcome (Curry et al., 2006). Four studies investigated the moderating effects of suicidality on treatment outcome: none of the trials found statistically significant effects (Barbe et al., 2004b; Curry et al., 2006, Rohde et al., 2006; Vitiello et al., 2011). In the TORDIA sample, youth with a history of non-suicidal self-injury had poorer outcomes across arms, and youth without a history of self-harm experienced greater response in combination

treatment than teens with such a history (Asarnow et al., 2009). However, these moderation results were not maintained at follow-up (Vitiello et al., 2011).

COMORBIDITY

As discussed earlier, comorbidity is the rule in depression, with 90% of youth diagnosed with major depression meeting diagnostic criteria for at least one additional disorder and 50% for two or more (Simonoff et al., 1997). The most common comorbidity with depression is anxiety, and four trials have explored the effects of comorbid anxiety on treatment outcome (Asarnow et al., 2009; Brent et al., 1998; Curry et al., 2006; Rohde et al., 2006, Vitiello et al., 2011). In general, the presence of anxiety disorder predicts worse outcomes over time across treatment and control conditions. However, two of the four trials found that outcome for anxious youth were *relatively* better in arms including CBT compared to other treatments (Asarnow et al., 2009; Brent et al., 1998), although superior effects of adjunctive CBT in TORDIA were not maintained at follow-up (Vitiello et al., 2011).

Clinical trials of depression in youth frequently exclude participants who meet diagnostic criteria for serious externalizing comorbidity, such as Conduct Disorder. In this context, trials generally have not found moderating effects of comorbid externalizing symptomatology on depression outcome (Asarnow et al., 2009; Curry et al., 2006; Vitiello et al., 2011). The Rohde et al. trial (2006) recruited depressed and disruptive teens from the juvenile justice system and assessed the impact of comorbid substance use on depression treatment outcome. Though substance use and abuse was more likely to occur in this sample than a general treatment-seeking sample, the study did not identify any moderating effects as a result of comorbid substance use disorder, with CBT separating from life skills control across levels of substance use. In the TORDIA trial, substance use predicted poor treatment outcome overall, but there was no significant interaction with treatment group to indicate a moderating effect. As discussed earlier, Gau and colleagues (2012) did find moderating effects of substance use in their indicated prevention study of CBT for high school students with elevated symptoms of depression. In this investigation, CBT was more efficacious than control for youth scoring in the low to medium range of substance use. However, group differences disappeared when youth exhibited high levels of substance use at baseline. In order to tease apart the "disruptive behavior" category with the TADS sample, Kratochvil and colleagues (2009) extracted and analyzed the subset of externalizing youth meeting criteria for comorbid ADHD (14% of the enrolled sample). Results suggested that depressed youth with ADHD experienced similar improvements in all active intervention arms (COMB = FLX = CBT) compared to placebo. However, youth without ADHD who received combination therapy had greater improvement in their depression symptoms at post-treatment (COMB > (FLX > CBT) = PBO), although by week 36, outcomes across arms were similar (Kratochvil et al., 2009). In contrast, TORDIA participants *with* comorbid ADHD (16% of the sample) had a superior response to combination therapy compared to medication monotherapy, while

those without comorbid ADHD did not show significant group differences in outcome (Asarnow et al., 2009).

DEMOGRAPHIC CHARACTERISTICS

Age, gender, ethnicity, and socioeconomic status have all been investigated as potential moderators of CBT response. With regard to age and development, investigators have hypothesized that (a) younger youth may show a superior response to CBT, given that they are earlier in the trajectory of disorder and may have less ingrained depressogenic cognitive and behavioral habits, or (b) older youth may benefit more from CBT, given their more developed abstract reasoning and general cognitive skills. More often than not, age has not been found to moderate response in either direction (Curry et al, 2006; Rohde et al., 2006; Stice et al., 2010), with the TORDIA trial being the sole study to find a greater benefit of adjunctive CBT (versus medication monotherapy) for older youth (Asarnow et al., 2009). In a different operationalization of development, Curry and colleagues (2006) did not find that verbal intelligence moderated outcomes of the TADS trial. Notably, all investigators testing development as a moderator have been conducted in adolescent-only samples, with significant restriction of range on this variable.

Gender also has been suggested as a moderator of CBT effects, with male participants hypothesized to benefit more than female participants given the structure and activity level found in most CBT models. However, three different trials using various CBT manuals reported that gender did not moderate treatment outcome (Amaya et al., 2011; Curry et al., 2006; Rohde et al., 2006, Stice et al., 2010). As discussed in a later section, gender also has been explored as a potential matching variable for choosing between IPT and CBT for depressed youth; results of these analyses have been inconclusive and not statistically significant.

The results for race/ethnicity and socioeconomic status have been more mixed. The TADS trial did not find significant moderating effects of race/ethnicity on the relative ordering of treatments (i.e., combination therapy remained the most efficacious intervention across groups; Curry et al., 2006); however, within TADS, income significantly moderated response. Results suggested that adolescents of families that earned less than $75,000 per year found combination and medication alone to be equally effective in reducing CDRS-R scores and both more effective than CBT alone or placebo (COMB = FLX > CBT = PBO). In the high-income subgroup (> $75,000), the three active treatment groups did not significantly differ from one another, but only combination and CBT alone were more efficacious than placebo (Curry et al., 2006). In contrast, the TORDIA trial (Asarnow et al., 2009; Vitiello et al., 2011) did not find moderating effects of socioeconomic status but did so for ethnicity. In TORDIA, stronger effects for combined treatment (CBT + medication switch) were found for Caucasian adolescents relative to adolescents from other racial and ethnic groups. Similarly, the Rodhe et al. (2006) investigation of CBT for youth with depression and disruptive behavior found that CBT was substantially superior than control for Caucasian teens (recovery in 11 versus 27 weeks, respectively; Rohde et al., 2006) but that

CBT and control did not statistically separate for minority participants. Notably, across all these studies, absolute representation of minority group participants was low (less than 30%), and all youth were again adolescents.

Moderators of IPT Effects

As discussed previously, the IPT clinical trial literature for youth depression is substantially smaller than the literature on CBT effects. As available, we next review moderators of IPT effects, following the same structure as our CBT review.

MATCH TO INTERVENTION

Matching hypotheses would suggest that IPT should outperform control conditions and alternate treatment models for youth with "matching" deficits in interpersonal skills, relationship quality, and family functioning at baseline. In contrast, significant moderation in favor of IPT would not be expected for youth with cognitive distortions or behavioral mood regulation deficits.

COGNITIVE AND BEHAVIORAL MODERATORS

While some investigations of IPT have included measures of social problem-solving (see Weersing, Rozenman, & Gonzalez, 2009), baseline levels of cognitive process variables have yet to be assessed as potential moderators of outcome. Furthermore, none of the published investigations of IPT in youth has included measures of behavioral mood regulation skills.

INTERPERSONAL MODERATORS

Data are available that are directly relevant to the interpersonal matching hypothesis. Gunlicks-Stoessel, Mufson, Jekal, and Turner (2010) performed a secondary analysis of an IPT-A effectiveness trial to understand the role of social functioning in IPT treatment outcome. In the primary investigation (Mufson et al., 2004), school counselors were randomized to provide IPT-A or supportive therapy (usual care in this setting) to depressed adolescents; teens receiving IPT-A had superior outcomes for both depression and global functioning. As would be predicted by a match-to-intervention model, IPT-A was especially effective when teens had significant interpersonal problems, with a medium effect size found for mother-child conflict and a large effect size for problems with peer relationships. Quality of dating relationships was not a significant moderator of outcome in this sample, although authors reported problems with reliability of this scale. Global quality of family functioning predicted poor outcomes in both IPT-A and supportive therapy but did not moderate response, suggesting some specificity to the family conflict finding (note that role disputes are a core content area of IPT intervention).

In addition, one IPT prevention study (Horowitz et al., 2009) tested whether the personality characteristics of orientation to social relationships

or achievement orientation moderated response to IPT versus CBT in a sample of high school students. Moderation analyses were not performed in the high symptom subsample, and the results thus are not directly comparable to outcomes of treatment trials. Consistent with a match-to-intervention compensation model, higher levels of baseline sociotropy predicted lower levels of depression symptoms in IPT, but this relationship was not present for CBT or control. However, contrary to expectations, achievement orientation also moderated response to IPT and control (but not to CBT), such that individuals with higher levels of achievement orientation evidenced lower levels of depressive symptoms over time.

CONTEXTUAL MODERATORS

To date, no study has examined the moderating effects of stressful life events or trauma history on the efficacy of IPT for depression in children or adolescents.

GENERALIZABILITY MODERATORS

Features of Depression

Depression severity and functioning were tested as moderators in the IPT-A effectiveness trial discussed earlier (Mufson et al., 2004). For both of these variables, IPT was statistically superior to usual school counseling services for the youth who were most severe. In the less severe/higher functioning group, IPT-A and usual care did not separate from each other. The Horowitz et al. (2007) prevention study also tested whether baselines levels of self-reported depression symptoms moderated response to IPT versus CBT or control. As discussed previously in this chapter in the section on CBT, the pattern of results across measures suggested that active interventions were superior to control in youth with elevated symptoms (more analogous to a treatment sample), with CBT effects perhaps being marginally stronger than IPT effects.

Comorbidity

Young, Mufson, and Davies (2006) also reanalyzed data from the IPT-A school effectiveness trial (Mufson et al., 2004) to probe the effects of comorbid anxiety in IPT treatment outcome. Comorbid anxiety disorders (generalized anxiety disorder, social phobia, panic disorder) were present in 68% of teens, and anxiety generally predicted more severe depression at baseline and worse post-treatment outcomes. At a global level, the presence of anxiety did not significantly moderate outcome, although descriptive statistics were in the direction of superior effects of IPT for anxious youth. Among teens with probable panic disorder, moderating effects were statistically significant for both depression symptoms and functioning. IPT-A was significantly superior to supportive therapy control for teens with panic, and the two treatments did not statistically separate for youth without comorbid panic. These results were in line with investigator hypotheses and parallel findings in CBT on the superior efficacy of active interventions (versus control) in the presence of clinically complicating comorbid anxiety.

Demographic Characteristics

Significant moderation by age, gender, ethnicity, or socioeconomic status has not been formally assessed in the IPT youth depression treatment literature. The IPT prevention study discussed earlier (Horowitz et al., 2009) also assessed whether gender moderated the comparative efficacy of IPT, CBT, and control, hypothesizing that female participants would particularly benefit from the interpersonal focus of IPT (and boys from CBT). Gender analyses were not performed in the subsample of youth with high symptoms, a sample analogous to the treated group in many other depression clinical trials; however, in the unselected sample as a whole, gender was not a significant moderator.

CHALLENGES AND FUTURE DIRECTIONS

In this chapter, we have sought to answer two key questions about CBT for depression in youth and IPT for depression in adolescents—the evidence-based psychosocial interventions for this population. The first question is one of mediation. What are the underlying theories driving our efficacious treatments, and to what extent do data on mediators of treatment effects support these theories of intervention? Data on this question are sparse at best. Despite nearly 30 years of CBT clinical trial research in this area, we were able to find only four studies that formally tested whether the cognitive and behavioral processes hypothesized to drive intervention effects statistically mediated the impact of intervention on depression outcomes. All four of these studies focused on depressed adolescents (to the exclusion of children) and self-report of key constructs, and, more often than not, the design of the mediation tests left directionality of effects unclear (i.e., failure to establish temporal precedence of changes). Furthermore, all four studies utilized different CBT treatment manuals that varied in their relative focus on cognitive versus behavioral techniques and number of sessions, and the trials had very different inclusion criteria in terms of level of severity and comorbidity. It is perhaps not surprising that this weak foundation has not yielded a definitive set of results. Cognitive change may be related to change in depression symptoms, depending on the study and the measure, and the field still awaits a positive mediational finding for a behavioral process in CBT for depressed youth. Furthermore, no data are yet available on mediators of IPT effects. Meta-analytic data suggest that CBT and IPT both *may* have theory-specific impacts on potential mediators of intervention effects when these candidate mediators are measured as simple, post-treatment outcomes (Weersing, Gonzalez, & Rozenman, 2009), but there is clearly a need for additional, programmatic research, with a focus on the replication of effects across manuals and investigations (as in multi-site trials) designed to clarify mechanisms of action for our efficacious interventions for youth depression.

The second question examined in this review is that of moderation. Are CBT and IPT broadly applicable to depressed youth, or should these interventions be expected to work more or less well with different types of depression, in the

presence of comorbid disorders, and across demographic groups? We began by examining evidence for *match-to-intervention* factors—cognitive, behavioral, or interpersonal characteristics of youth that map onto the theoretical diatheses targeted by CBT and IPT protocols. In the case of CBT, the modal moderator result was a non-significant finding (see Table 4.1); youth with high levels of cognitive distortions or behavioral deficits were generally no more likely to benefit from CBT than youth with lower scores on these measures. When significant results were found, the data were less consistent with a compensation model of CBT effects (match to diathesis) than a capitalization model, in which youth benefited the most when CBT protocols built on their strengths (e.g., good coping skills, positive problem orientation, less hopelessness). Data on match-to-intervention moderators for IPT were more sparse but more consistently supportive of the importance of interpersonal factors in IPT success. One randomized treatment trial indicated that baseline difficulties in social relationships were related to a more positive response to IPT (a compensation model), while an indicated prevention study suggested that heightened importance of interpersonal relationships (sociotrophic personality orientation) also moderated response in favor of IPT (a capitalization model). Although three studies in the literature include both CBT and IPT conditions (Horowitz et al., 2007; Rossello & Bernal, 1999; Rossello, Bernal, & Rivera-Medina, 2008), only the Horowitz prevention trial tackled the interesting question of differential response to these evidence-based treatments. A priori the authors hypothesized significant moderation such that girls and youth with high orientation to relationships would have superior outcomes in IPT, while boys and youth with high achievement orientation would perform better in CBT. Of these, only sociotrophy was significantly related to intervention effects in the hypothesized direction (predicted outcome within IPT).

Indeed, demographic factors as a whole were not strong moderators of intervention effects, despite theoretical reasons to suspect that gender (as above) and developmental level might predict differential response to intervention. With regard to developmental level, and to a lesser extent ethnicity and socioeconomic status, the field suffers from serious problems with restriction of range. As discussed in the introduction to this chapter, the clinical trial literature is dominated by studies of depression in adolescents, and a major direction for future research is the extension of mediator and moderator research into early adolescence and childhood.

CBT and IPT also were largely robust to negative clinical indicators that might be expected to reduce the effects of intervention relative to control. IPT may perform particularly well (compared to supportive therapy) with more severe youth, and the combination of CBT and medication appears to be robust to a wide range of severity indicators (results for CBT monotherapy follow this trend but are more mixed). With regard to comorbidity, there is evidence to suggest that the positive effects of CBT and IPT may be amplified compared to control when youth suffer from comorbid anxiety, and CBT effects have generally remained statistically significant and have been undiminished when youth suffer from significant externalizing comorbidity (with the possible exception of

substance abuse). Data are not available on the moderating impact of PTSD, but evidence on the effects of negative family context and trauma history suggest that these factors may diminish the efficacy of CBT. Trauma history has not been investigated as a moderator of IPT efficacy, although this is a theoretically interesting question. IPT has performed well under conditions of current family conflict; IPT could prove to be a particularly relevant intervention and positive match to youth suffering from the effects of past trauma or, equally plausibly, youth with trauma may be better matched to interventions such as CBT that build on strengths in other domains, rather than focusing primarily on interpersonal relationships.

IMPLICATIONS FOR PRACTICE

As discussed in the introduction, developing best-practice recommendations for youth depression has been limited by substantial gaps in the research literature. Data on depressed pre-pubertal children are sorely lacking, and all of the mediator and moderator results reviewed are based on studies of depressed adolescents. Within this essential limitation, there are areas of good news for the effective treatment of depression in youth. First, both CBT and IPT appeared to have reasonable generalizability in their effects—moderation of efficacy by demographic characteristics was rarely significant; intervention effects were robust to comorbidity and many indices of severity; and the combination of CBT and antidepressant treatment, in particular, was consistently superior to control and superior or equivalent to other active interventions, even when significant moderators were present. Second, while the literature is quite small, available data suggest that IPT may be a theoretically coherent intervention. Meta-analytic data indicate that IPT impacts interpersonal relationships (see the section on mediation in this chapter), and moderation findings for interpersonal factors are supportive of the intervention model theory. Compared to many multi-skill CBT protocols, IPT also may be a simpler intervention with a clearer single focus, both for delivering to youth and for training providers under conditions of low resources (cf. Bolton et al., 2003). In contrast, while CBT protocols have clearly demonstrated positive effects for youth depression, clinical trial data have not provided clear support for the CBT theories underlying these manuals. Mediation data are quite mixed, and moderator findings suggest that CBT may perform best as a capitalization intervention rather than as implied by the diathesis models central to CBT theory. As a result, practitioners are left with an efficacious set of CBT tools, but the rationale for why, when, and how to apply these tools in the care of individual youth becomes less clear. Research probing the question of strengths-based versus deficit-based models of CBT may better inform practice recommendations and aid in the development of future interventions for depressed children and adolescents.

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5

Moderators and Mediators of Treatments for Youth Who Show Externalizing Problem Behavior

MAJA DEKOVIĆ AND SABINE STOLTZ ■

INTRODUCTION

Externalizing problem behavior (EPB), broadly defined as oppositional behavior (non-compliance, disruptive behavior) and conduct problems (antisocial behavior, aggression, delinquency), is one of the most common reasons for referral to inpatient and outpatient child and adolescent mental health clinics. A large body of longitudinal research conducted in the past 30 years has shown that EPB is relatively stable and, if left untreated, leads to adverse outcomes such as school failure, unemployment, crime involvement, and serious pathology such as antisocial personality disorder later in life (Kimonis & Frick, 2011). The high prevalence, chronic course, and serious risk for later adverse outcomes have led to the development of different treatments aimed to decrease these problems. Among these treatments, approaches that involve parents, parental training for younger children, and multisystemic therapy for adolescents, have been most extensively studied, and their effectiveness has been demonstrated in a number of controlled outcome studies (e.g., Eyberg, Nelson, & Boggs, 2008; McCart, Priester, Davies, & Azen, 2006).

In this chapter, we begin with a brief definition of externalizing problems and we provide an overview of developmental trajectories and the most important factors that play a role in the development and maintenance of such problems. Next, we describe the theoretical background, assumptions, and approaches of two evidence-based treatments for these problems: behavioral and cognitive behavioral parental training (PT) and multisystemic therapy (MST). Although other treatments, such as child-focused individual and group-based cognitive