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Cognitive Behavioral Therapy for Mood Disorders: Efficacy, Moderators and Mediators

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Synopsis

Cognitive behavior therapy (CBT) is efficacious in the acute treatment of depression and may provide a viable alternative to antidepressant medications (ADM) for even more severely depressed unipolar patients when implemented in a competent fashion. CBT also may be of use as an adjunct to medication treatment for bipolar patients, although the studies are few and not wholly consistent. CBT does appear to have an enduring effect that protects against subsequent relapse and recurrence following the end of active treatment, something that cannot be said for medications. Single studies that require replication suggest that patients who are married or unemployed or who have more antecedent life events may do better in CBT than in ADM, as might patients who are free from comorbid Axis II disorders, whereas patients with comorbid Axis II disorders appear to do better in ADM than in CBT. There also are indications that CBT may work through processes specified by theory to produce change in cognition that in turn mediate subsequent change in depression and freedom from relapse following treatment termination, although evidence in that regard is not yet conclusive.

Keywords

cognitive behavioral therapy; mood disorder; depression; efficacy; moderator; mediator

Introduction

Clinical depression is one of the most common and debilitating of the psychiatric disorders. [1] Lifetime prevalence has been estimated at 16.2% and rates of comorbidity and risk for suicide are high.[2] Up to one-third of all patients will have episodes that last longer than two years, and over three-quarters of all patients who recover from one episode will go on to have at least one more.[3] Although there are efficacious treatments for depression, many patients do not receive adequate treatment, and still more are refractory to available interventions.[4]

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Depression can be defined as both a syndrome and a disorder. As a syndrome it involves episodes of sadness, loss of interest, pessimism, negative beliefs about the self, decreased motivation, behavioral passivity, suicidal thoughts and impulses, and changes in sleep, appetite and sexual interest. As a disorder it comes in two forms. The unipolar type, which affects approximately 10% of men and 20% of women, includes only episodes of depression. Heritability estimates for unipolar depression have ranged from approximately 25% in less-severe samples up to 50% in more-severe samples.[5] In the bipolar form, which is commonly known as manic depression, patients also (or exclusively) experience episodes of mania or hypomania that are in many ways the opposite of depression. Manic episodes are marked by euphoria or irritability, sleeplessness, grandiosity, recklessness and uncontrollable impulses that can lead to buying sprees and sexual promiscuity.[6]

Cognitive behavioral therapy (CBT) refers to a family of interventions that are among the best-known empirically-supported treatments for depression. There are several different specific interventions that vary somewhat in their constituent components, with cognitive therapy (CT) being the most widely practiced, but all these interventions are closely related and the terms CBT and CT are used somewhat interchangeably in this paper. CBT is based on the premise that inaccurate beliefs and maladaptive information processing (forming the bases for repetitive negative thinking) have a causal role in the etiology and maintenance of depression. This 'cognitive model' posits that when maladaptive thinking is corrected, both acute distress and the risk for subsequent symptom return will be reduced.[7] In this paper, we focus on the efficacy of individual CBT in the treatment of acute phase depression and the prevention of subsequent symptom return in adult populations, with an emphasis on the moderation and mediation of response.

The efficacy of CBT in the acute phase of depression

Meta-analytic findings

CBT has a medium effect size (d = .67) relative to a variety of control conditions ranging from the absence of treatment to non-specific controls.[8] Translated into numbers needed to treat (NNT), this effect size corresponds to an NNT of 2.75. This means that for just under every three patients treated with CBT, one will get better solely because of having come into therapy. By way of comparison, medication treatment of severe hypertension produces an NNT of 15 and taking aspirin alone for myocardial infarction produces an NNT of 40 relative to no treatment (see NNT readings at www.evidence-based-medicine.co.uk). Effect sizes tend to be larger when CBT is compared to wait-list controls (d = 0.88) than when CBT is compared to care-as-usual (d = 0.38) or non-specific controls (d = 0.38).[8] These findings suggest that CBT is more efficacious than its absence and somewhat more efficacious than the mobilization of hope and therapist contact. Effect sizes tend to be lower in high-quality studies or when corrected for publication bias.[8] It has been reported that the efficacy of CBT when delivered individually did not differ from the efficacy of a group format (d = .15, nonsignificant), but the quality of the relevant studies is low, limiting our confidence in this conclusion.[9]

Gloaguen and colleagues found CBT superior to an assortment of other psychotherapies,[10] but this estimate was likely inflated by the inclusion of non-bona fide therapies intended only to control for nonspecific factors.[11] This is in line with Cuijpers and colleagues who found no significant differences when comparing CBT with other psychotherapies.[8] Gloaguen and colleagues also found CBT moderately superior to antidepressant medication although this estimate was likely to be inflated by the inclusion of early studies that did a questionable job of implementing pharmacotherapy.[12] For example, Rush and colleagues found CBT superior to the ADM imipramine in the treatment of depressed outpatients, but started medication withdrawal two weeks before the end of treatment,[13] and Blackburn and colleagues found CBT superior to either amitriptyline or clomipramine in a general practice sample, but had

such poor response to ADM (14%) as to raise questions about the adequacy of the pharmacotherapy as implemented by the general practitioners.[14] Subsequent studies that did a more adequate job of implementing pharmacotherapy typically found comparable outcomes between CBT and ADM.[15,16] This is in line with findings of a more recent meta-analysis by Cuijpers and colleagues that suggests that CBT and ADM are equally efficacious in the treatment of major depression.[8]

Combining CBT with ADM results in somewhat higher effect sizes than medication alone ($d = 0.27$, $p < .05$; NNT = 6.58).[8] This means that the combination produces a modest increment over medication monotherapy; combining CBT with ADM will improve acute response for one out of nearly every six patients. Combined treatment produces only a small nonsignificant effect relative to CBT alone ($d = 0.15$; ns; NNT = 11.9), an effect about half the magnitude of adding CBT to medications.[8] However, these estimates are based on controlled treatment trials that often provide greater training and supervision than is the case in actual practice. Whether most patients will have access to comparably trained CBT therapists is a matter of conjecture. It may still be the case that combining medications with CBT as typically practiced in applied settings will enhance treatment response.

In sum, CBT has been found to work better than its absence and may well work for specific reasons. CBT seems to be as efficacious as other active treatments, including medications. Adding CBT to ADM has resulted in a modest improvement of efficacy. The benefits of adding medication to CBT relative to CBT alone have been less apparent, although these effects might be larger in applied clinical practice than in the controlled setting of a treatment trial.

CBT for severe depression

The NIMH treatment of depression collaborative research program (TDRCP) was the first major trial comparing CBT to a pill-placebo control and the results were not supportive of CBT. Although there were no differences across the full sample,[17] CBT was no more efficacious than pill-placebo and less efficacious than either the ADM imipramine or interpersonal psychotherapy (IPT) among patients with more severe depressions.[18] The results of the TDRCP had a major impact on the field, because of the size of the sample and the rigor of the design. It led many to conclude that CBT was not efficacious with more severe depressions and subsequent guidelines strongly suggested that such patients should not be treated with psychotherapy alone.[19]

Despite the rigor of its design, questions have been raised about the adequacy of the implementation of CBT in the TDCRP.[20] Outcomes for CBT varied considerably across the three study sites, with CBT doing no better than pill-placebo at the two sites with less experienced therapists and as well as ADM at the remaining site where the cognitive therapists had prior experience with the approach.[21] Subsequent placebo-controlled trials that have done a better job of implementing CBT have shown it to be comparable to ADM and each superior to pill-placebo controls. For example, Jarrett and colleagues found cognitive therapy as efficacious as phenelzine (a monoamine oxidase inhibitor; MAOI) for the treatment of atypical depression.[22] This group has worked closely with the Center of Cognitive Therapy in Philadelphia to ensure that their cognitive therapists were well-trained and had session tapes rated for competence by an offsite consultant expert in the approach. Similarly, MAOIs are the medications of choice for atypical depression and were prescribed at dosage levels that were appropriate.

DeRubeis and colleagues attempted a direct replication of the TDCRP with respect to the comparison between CBT and ADM among more severely depressed patients.[23] Patients who met the TDCRP criterion for moderate to severe depression (scores of 20 or above for two consecutive weeks on the Hamilton Depression Rating Scale; HDRS) were randomly

assigned to 16 weeks of either CBT or paroxetine pharmacotherapy or 8 weeks of pill-placebo (a sufficient length of time to establish drug-placebo differences). Paroxetine is generally considered the best of the SSRIs for dealing with patients with more severe depressions. In addition, patients in the ADM condition who were not fully responsive by the end of eight weeks of treatment were augmented with either lithium or desipramine through the end of the sixteen-week trial. This is a more aggressive pharmacotherapy regime than is typically used in short-term treatment trials. The study was conducted at two sites, one of which was the original home of cognitive therapy (University of Pennsylvania), whereas the other had somewhat less experienced cognitive therapists (Vanderbilt University). Ratings conducted by experts at the Beck Institute suggested that the less experienced cognitive therapists at Vanderbilt were not performing at the same level of competence as the more experienced cognitive therapists at Penn. Therefore, the Vanderbilt therapists were provided with additional training through the extra-mural training program at the Beck Institute during the early years of the trail.

Both CBT and paroxetine pharmacotherapy were superior to pill placebo across the first eight weeks of the trial and virtually identical to one another by the end of the full 16-week acute treatment period. There were differences between the sites with CBT showing a nonsignificant advantage relative to ADM at Penn and ADM doing significantly better than CBT at Vanderbilt. Differences between the sites were more pronounced in the beginning of the trial with the less experienced cognitive therapists at Vanderbilt catching up to their more experienced colleagues at Penn across time with respect to both competence ratings and patient outcomes. There also were indications that patients with comorbid Axis II disorders did better on ADM than they did in CBT, whereas the opposite was true for patients without Axis II disorders.[24] Patients with Axis II disorders constituted a larger portion of the sample at Vanderbilt and differences in patient composition and therapist experience largely explained the differences between the sites. These findings suggest that CBT can be as efficacious as ADM with more severely depressed patients if provided by experienced cognitive therapists who are competent to implement that modality.

That being said, Dimidjian and colleagues found a pattern of results in a subsequent placebo-controlled trial that was reminiscent of the one found in the TDRCP, but that might still be consistent with the notion that competence matters with respect to CBT for more severely depressed patients.[25] In that trial, patients with major depression representing a full range of severity were randomly assigned to 16 weeks of CBT, behavioral activation (BA), paroxetine pharmacotherapy (without augmentation), or pill placebo (8 weeks only). As in the TDRCP, there were no differences between any of the treatment conditions among less severely depressed patients. Among the more severely depressed patients (those with HDRS scores of 20 or above), both ADM and BA were found to be superior to either pill-placebo (at week 8) or CBT (both at week 8 and week 16). In point of fact, the advantage of BA over CBT was largely a consequence of a subset of patients who showed extremely poor response to CBT. [26] These patients were severely depressed, functionally impaired, and had problems with their primary support group; most also described themselves as having life-long depressions. Although Dimidjian et al. did not assess the full array of personality disorders, these patients were similar in many respects to the Axis II patients that did poorly in CBT in the Penn/Vandy trial.[24] There were as many such patients in that earlier study and although they did not do necessarily do all that well in CBT, they did not show the extreme non-response that they showed in the study by Dimidjian and colleagues. The cognitive therapists started the Dimidjian et al. study with about the same level of experience as the less-experienced cognitive therapists at the Vanderbilt site in DeRubeis et al., but did not have the advantage of the additional training through the Beck Institute during the study proper.

By and large, CBT seems to be as efficacious as ADM in the treatment of depression. Two studies found that CBT did less well than either ADM or other psychotherapy among more severely depressed patients.[18,25] It is not clear that the cognitive therapists were all that experienced with the approach in those two trials and CBT has done as well as ADM in other placebo-controlled trials when therapist experience was not an issue.[22,23] Thus, CBT seems to work as well as ADM for more severely depressed patients, if conducted by well-trained therapists.

It is not clear just how much experience and training is necessary to ensure therapist competence but it does appear that much of the variation in the CBT literature is related to the skill with which the modality is implemented. We have emphasized the role played by such variability in determining outcomes in the handful of placebo-controlled trials precisely because they are the most influential studies found in the literature and (one would hope) the most carefully conducted. The bulk of these trials were efficacy studies and it is likely that variability is even greater (and competence less likely to be assured) in the effectiveness literature. Those studies that found the best outcomes for CBT typically selected experienced cognitive therapists (as was the case at the University of Pennsylvania) or provided extended training coordinated with Philadelphia (as at the Vanderbilt site in that same study or in the study of atypical depression); studies that depended on more limited training and off-site supervision typically produced less impressive findings relative to alternative interventions (especially medications). These differences were most apparent with severe and complicated patients and it is likely that therapist competence is more an issue with such patients since that is where treatment differences are usually found. Just how much training and supervision is required and whether it varies as a function of patient difficulty are clearly issues that deserve further exploration.

Cognitive-Behavioral Analysis System of Psychotherapy (CBASP) for chronic depression

CBASP was developed specifically for the treatment of chronic depression and combines techniques from cognitive, behavioral, psychodynamic and interpersonal psychotherapies. It shares with CBT its structured approach, the use of home-work assignments and the systematic focus on assessing and changing behaviors or interpretations of a situation. It differs from CBT, however, by its primary focus on interpersonal interaction. Keller and colleagues compared the efficacy of CBASP with that of nefazodone, and with the combination of CBASP and nefazodone and found that after 12 weeks of acute treatment CBASP and nefazodone resulted in equal response-rates (both 48%), while combined treatment significantly outperformed both mono-treatments (response-rate 73%).[27] However, these analyses were based on a modified intention-to-treat in which patients who either didn't start treatment or who could not achieve a minimum dose of 300 milligrams of nefazodone by week 3 were dropped from the analyses; it would have been better if the analyses would have been conducted on the full intention-to-treat sample.

CBT to prevent relapse and recurrence

Depression is a chronically recurrent disorder. Although up to two-thirds of all patients respond to acute treatment with ADM (about half of whom will fully remit), a sizable number will experience a return of symptoms after treatment is over.[28] According to conventions developed in the pharmacotherapy literature, symptom return during the first six-to-twelve months among remitted patients is assumed to represent a return of the treated episode (relapse) and treatment provided during that interval is called continuation treatment. Patients who go more than twelve months without relapse following remission are said to be recovered; symptom return following that interval among recovered patients is said to represent the onset of a wholly new episode (recurrence) and treatment provided after the end of that interval is called maintenance treatment.[29] Although ADM can suppress the expression of symptoms (a purely palliative effect), there is no evidence that it can shorten the duration of the underlying

episode or reduce subsequent risk for recurrence,[28] and current medical practice calls for keeping patients with a history of recurrent or chronic depression on medication indefinitely.[19] On the other hand, if CBT has an enduring effect it can be said to be more than purely palliative.[30] Whether it is truly curative depends on how long this enduring effect can be said to last and how and to what extent it actually prevents subsequent episodes.

Enduring effects of CBT

There is evidence that CBT has an enduring effect that lasts beyond the end of treatment. Among patients who respond to acute treatment, relapse rates are lower following treatment termination after acute CBT than after acute ADM and also lower for patients treated with combined treatment than for patients treated with ADM alone.[31] This suggests that it is not so much the withdrawal of medication that provokes relapse in remitted patients as that prior exposure to CBT prevents it. It remains unclear whether this effect is specific to CBT, since other psychotherapies have rarely been tested against medication withdrawal.

A pair of recent studies found that the magnitude of the CBT's enduring effect was at least as large as keeping patients on continuation ADM.[32,33] In both these studies patients who responded to CBT were essentially withdrawn from that treatment and compared with ADM responders randomized to either ADM continuation or withdrawal onto pill-placebo. CBT responders were significantly less likely to relapse following treatment termination than ADM responders withdrawn from ADM and no more likely to relapse than ADM responders kept on continued medication. Both studies found prior CBT superior to medication withdrawal even after patients were continued on ADM for up to a year after initial response.

Although these results suggest that prior exposure to acute CBT prevents subsequent symptom return, it is possible that these findings may be an artifact of differential mortality. As described by Klein, acute treatment may act as a "differential sieve" if high risk patients are more likely to respond to one treatment than another.[34] Although there is no evidence that this was the case in either study, the fact that only about half of the patients initially randomized both completed and responded to treatment leaves open the possibility that what appears to be an enduring effect might actually be nothing more than the differential retention of high risk patients. Therefore, while the existing evidence is consistent with the notion that CBT has an enduring effect, it is less than wholly conclusive.

Studies that provide CBT following the end of acute treatment are not subject to the possible biasing effects of differential mortality so long as all patients receive the same acute phase treatment. Fava and colleagues found that adding a version of CBT including well-being therapy and life-style modification resulted in lower subsequent recurrence rates following medication discontinuation among patients with recurrent depression who were first treated to recovery with ADM [35] with enduring effects evident up to six years later.[36] Similarly, Paykel and colleagues found that adding CBT reduced rates of relapse and subsequent recurrence relative to ADM alone in patients with residual depressive symptoms following initial medication treatment,[37] with enduring effects found up to 3.5 years after the completion of CBT.[38] Bockting and colleagues found that among patients in remission after various types of treatment adding CBT resulted in significantly lower rates of relapse/recurrence than treatment-as-usual (TAU) alone for patients with a history of five or more depressive episodes; no such differences were evident for patients with less than five prior episodes.[39] In a pair of studies, Teasdale and colleagues found that adding mindfulness-based cognitive therapy (MBCT) reduced subsequent rates of relapse/recurrence relative to TAU over a one-year period for patients with three or more previous episodes of depression; no such differences were evident for patients with two or fewer prior episodes.[40,41] MBCT is a group intervention that combines CBT with meditation techniques aimed at teaching patients to relate to depressive thoughts and feelings as mental events, rather than as accurate reflections of

reality in order to prevent relapse as a result of dysphoric mood. Only Perlis and colleagues failed to find an advantage for adding CBT, but did so in the context of providing ongoing ADM with dose increase for all patients that should have reduced rates of relapse and recurrence regardless of whether CBT was added.[42] These studies suggest that CBT has an enduring effect that is robust to the biasing effects of differential mortality.

CBT as a continuation and maintenance treatment

In addition to the enduring effects of acute CBT treatment, research has focused on the efficacy of keeping patients in CBT after they first respond to that treatment. Jarrett and colleagues focused on whether extending the duration of CBT adds to the efficacy of acute treatment by comparing CBT with and without a continuation phase for CBT-responders with a history of recurrent depression.[43] During the ensuing 8 months significantly fewer patients relapsed when CBT was continued than when it was not. Patient characteristics moderated the effects of extending CBT over the full 24-month follow-up period such that patients with an earlier age of depression onset or who showed an unstable pattern of remission were less likely to relapse or recur if provided with continuation/maintenance treatment than if not, whereas extending CT treatment did not matter for patients with a later age of depression onset or who showed a stable pattern of remission. These findings suggest that extending CT might be necessary only for patients at higher risk for relapse. Jarrett and colleagues also examined the efficacy of CBT as continuation treatment after acute treatment for patients with atypical depression, but sample sizes were so small that no meaningful conclusions could be drawn. [44]

Klein and colleagues examined the efficacy of CBASP as a maintenance treatment for chronic depression. Treatment responders to 12 weeks of acute and 16-weeks of continuation CBASP treatment in their earlier trial were randomly assigned to CBASP maintenance treatment versus an assessment-only control.[45] Over 52 weeks, CBASP maintenance treatment resulted in lower recurrence rates. Moreover, patients in the CBASP condition experienced a small reduction in depressive symptoms, while depressive symptoms increased somewhat for patients in the control condition. It must be borne in mind that this sample consists solely of patients that showed a sustained response to CBASP (all chronically depressed). For this group of patients CBASP maintenance treatment after 28 weeks of acute and continuation phase treatment seems is more efficacious than its absence.

Three studies focused on the efficacy of CBT continuation treatment as compared to ADM continuation. First, Blackburn and colleagues compared 6 months of continuation treatment with CBT or ADM or their combination for patients who had responded to acute phase treatment in those same modalities.[46] No differences were found across the six months of continuation treatment, suggesting a continuation effect of CBT comparable to medication. Across a 2-year follow-up (the last 18 months of which was treatment-free) the number of patients that relapsed or recurred were significantly higher following withdrawal from medication alone than for prior CBT with or without medication, suggesting an enduring effect of CBT. However, given that patients were randomized to different treatments during the acute phase, it is possible that acute treatment could have served as a “differential sieve” that systematically unbalanced the groups of treatment responders and thereby produced a spurious enduring “effect” that accounted for the results observed. Second, Blackburn and Moore examined the relative efficacy of CBT and ADM maintenance treatments. Patients were randomly assigned to acute ADM followed by maintenance ADM, acute ADM followed by maintenance CBT, and acute CBT followed by maintenance CBT.[47] There were no differences in the reduction of acute phase symptoms and no significant differences between maintenance CBT and maintenance ADM, regardless of whether maintenance CBT followed acute treatment with CBT or with ADM. These results suggest that maintenance CBT can have

prophylactic effects similar to maintenance ADM, although it is always treacherous to draw causal inferences from null findings in a small sample and medication doses were reduced during the maintenance phase. While it may be the case that maintenance CBT is as efficacious as maintenance ADM, these studies do little to contribute to our confidence for the reasons cited.

Finally, Kuyken and colleagues compared MBCT plus ADM discontinuation with ADM maintenance treatment in patients with a history of multiple depressive episodes that were fully or partially remitted after initial treatment with ADM.[48] No significant differences in relapse/recurrence rate were found over a 15-month period. It should be noted that only about three-quarters of the MBCT patients actually discontinued medications, but that group contained most of the high-risk patients and comparisons between those in the MBCT group who did discontinue and patients in the ADM maintenance group who were fully compliant also found no differences. In sum, while MBCT might be as efficacious as keeping patients on continuation antidepressant medication, methodological problems limit the interpretation of similar findings with regard to CBT.

CBT to prevent relapse in bipolar disorder

Whereas the distinction between relapse and recurrence is relevant to unipolar depression (patients are either in episode and thus at risk for relapse when asymptomatic or not in episode and thus at risk for recurrence), bipolar disorder is thought of as a chronic disorder that never goes away and is marked by periodic symptomatic relapses into mania and depression. Although stabilization on medications is the cornerstone of treatment for bipolar disorder, there has been considerable interest in recent years in using CBT to treat existing symptoms (particularly depression) and to prevent subsequent relapse when euthymic. In addition to such general features as examining the accuracy of dysfunctional beliefs and improving communication and problem-solving skills, CBT also focuses on teaching skills to cope with prodromes (periods when symptoms first emerge but have not yet reached maximum severity) and disruption of routines (especially sleep) that contribute to the onset of an episode in bipolar disorder. These are features that it shares with other promising adjunctive psychosocial interventions like interpersonal social rhythm therapy and family-focused therapy.[49] In a pilot study, Lam and colleagues found that adding CBT reduced the frequency of bipolar episodes across the following year relative to TAU alone in euthymic bipolar I patients who continued to have relapses despite the use of mood stabilizers, but were not currently facing an acute bipolar episode.[50] The authors subsequently replicated this finding in a larger sample across the course of a one-year[51] and two-year follow-up, although the differential relapse prevention effects occurred mainly in the first year after treatment.[52] CBT patients also reported fewer days in episode and better mood ratings, social functioning, and coping with bipolar prodromes. Subsequent studies typically found benefits for CBT over TAU in medicated patients, either at the level of a nonsignificant trend [53] or in terms of days free from depression and reductions in medication use [54].

It should be noted that a recent multicenter trial by Scott and colleagues largely failed to replicate these effects.[55] The investigators studied a more heterogeneous sample, including patients who were currently in episode, and found that the addition of CBT did not result in lower relapse rates or symptom levels for the full sample. Post hoc analyses did suggest an interaction with previous episodes (moderation), such that adding CBT was significantly more effective for patients with fewer than 12 previous episodes, but less efficacious for those with 12 or more previous episodes. This led the authors to conclude that CBT might be helpful for only the minority of bipolar patients with relatively fewer previous episodes and the authors of a recent meta-analysis to conclude that CBT was of little use for bipolar patients.[56] However, Lam has criticized this study for including a mixed patient sample; almost a third of

the patients were currently in episode and the focus on acute symptom reduction rather than relapse prevention might have undercut any possible relapse prevention effect.[57] It should be possible to reanalyze the data for only those patients not in episode at the start of the trial to see whether that subsample replicated the effects found in the Lam studies, but that has not yet been done. It also would have been helpful to know whether medication dosing varied between the two conditions in the Scott study, since such confounds sometimes obscure the effects of added treatments [54]. That being said, more research is clearly needed to determine whether CBT truly has an adjunctive role to play in the treatment or prevention of bipolar disorder and, if so, whether those beneficial effects of CBT (if any) are due to its specific content or to non-specific treatment factors like therapist contact and the mobilization of hope and expectation.

Predictors of CBT efficacy

Since different patients respond differently to different treatments, it is important to know who responds best to what with particular reference to CBT. Two types of information are relevant to this question: prognostic information in which you hold treatment constant and allow patient characteristics to vary, and prescriptive information in which you hold patient characteristics constant and allow treatment to vary.[58] Prognostic factors predict outcome to a given treatment (or to treatment in general) and can be used to determine which patients are more likely to respond to CBT relative to other patients. However, although it is useful to know what to expect when starting treatment, prognostic factors are of little use in deciding what treatment to select. On the other hand, prescriptive information (also known as moderators) can detect different patterns of outcomes between different treatments for different types of patients and provide a basis for choosing the best treatment for a given patient.[59]

Demographic factors

Little research has focused on age, gender, education and other demographic predictors of response to CBT for depression while adequately controlling for pre-treatment severity.[60] A notable exception is a study by Fournier and colleagues that found that older age and lower intelligence each predicted relatively poor response to both CBT and ADM and were therefore purely prognostic factors, whereas being unemployed and having more antecedent life events predicted superior response to CBT relative to ADM and were therefore potentially prescriptive.[58] For whatever reason, married patients seem to do better in CBT than unmarried patients.[61–64] This is an example of prognostic information that allows a prediction of likely outcome but does not (on its own) provide a basis for choosing CBT over other treatments for such patients. However, Barber and Muenz reanalyzed data from the TDCRP and found that married patients did better in CBT than they did in IPT, whereas unmarried patients showed the opposite pattern.[65] Similarly, Fournier and colleagues found that patients who were married or cohabiting did better in CT than they did in ADM.[58] Both sets of findings are potentially prescriptive and could be used to select CBT over either IPT or ADM if replicated. Thus, marital status appears to be both prognostic (married patients do better than unmarried patients in CBT) and prescriptive (married patients do better in CBT than they do in at least some other treatments) with respect to CBT efficacy. In addition, more antecedent life events and unemployment are potentially prescriptive factors, associated with better response to CBT relative to ADM.

Illness characteristics

Chronic depression was found to be prognostic of poor response to either CBT or ADM in one study[58] and brief duration of the current depressive episode, a later age of depression onset, absence of a family history of affective disorder, and a history of more previous episodes of depression predictive of good response to CBT in another.[63] All these indices were purely

prognostic and should not be used as a basis for treatment selection. Leykin and colleagues found that the more prior medication exposures that patients had the less well they did in ADM; no such relationship was evident for CBT.[66] Although the authors did not report tests for treatment differences as a function of number of prior exposures, they did report an effect size favoring CBT over ADM for patients with two or more prior exposures of sufficient magnitude (d = .46) to suggest that the difference would have been significant if tested. There is little evidence to support the long-standing belief that patients with melancholic depression would be less responsive to CBT than to ADM.[67] It also is widely assumed that ADM is to be preferred to CBT in the treatment of patients with more severe depressions.[19] In their review, Hamilton & Dobson conclude that depression severity is associated with poor response to CBT (prognostic), but that there is no reason to conclude that alternative treatments such as ADM are any more efficacious than CBT for severely depressed patients (prescriptive).[60] When CBT has failed relative to ADM it has been with patients with more severe depressions,[18, 25] but as previously discussed, questions can be raised about the quality with which CBT was implemented in those studies. When CT has been adequately implemented, it appears to be about as efficacious as ADM with such patients.[22,23] In sum, both chronicity and severity appear to be prognostic only and melancholia does not appear to be prescriptive, while patients with more prior medication exposures may do better in CBT than on ADM.

Personality characteristics/disorders

The presence of a comorbid personality disorder (PD) might be relevant from both a prognostic and prescriptive perspective. Fournier and colleagues found that depressed patients with Axis II personality disorders (excluding antisocial, schizotypal, and borderline) were less responsive to CBT than to paroxetine ADM (44% vs 66% response), whereas patients without comorbid Axis II personality disorders showed the opposite pattern (70% vs 49%).[24] Moreover, only patients with Axis II disorders showed a medication discontinuation effect (they were more likely to relapse if withdrawn onto pill-placebo than if continued on active medications); patients without Axis II disorders showed no such effect. Axis II patients who did respond to CT were no more likely to relapse following treatment termination than patients without Axis II disorders, suggesting that the PD patients who did respond to CT tended to sustain their response. Treatment guidelines published by the American Psychiatric Association suggest that CBT is superior to ADM in the treatment patients with personality disorders [19], but that claim was based on a misreading of findings from the TDCRP that Axis II disorder was predictive of poor response within ADM or IPT but not in CBT. In point of fact, it was not that patients with personality disorders did better in CBT than they did in the other treatments, it was that patients without personality disorders did worse in CBT.[68] Hardy and colleagues similarly found that cluster C personality disorders predicted differential response within an interpersonal intervention but not within CBT (prognostic).[69] However, the treatment by personality disorder interaction was non-significant and authors did not conduct the kinds of direct treatment comparisons within patients subgroups required to establish moderation. Barber and Muenz found CBT superior to IPT for patients with avoidant personality traits and IPT superior to CBT for patients with obsessive personality traits.[65] Similarly, McBride and colleagues found that patients with high levels of attachment avoidance (a reluctance to initiate intimate contact and a tendency to withdraw when facing an attachment threat) had better outcomes to CBT than to IPT [70] and Joyce and colleagues found that avoidant and schizoid symptoms predicted poorer response to IPT but not to CBT.[71] Despite the differences in study design and the measures used in each, this approaches a conceptual replication of the Barber and Muenz findings with regard to avoidant personality, although Joyce and colleagues did not replicate the finding that IPT might be more efficacious than CBT for patients with obsessive-compulsive traits. In sum, there are consistent indications that presence of personality disorders dimensions may be prescriptive although the exact nature of that

prediction may depend on the specific comparison (CBT may be superior to IPT on some and inferior to ADM on others).

Treatment preference

Two studies have examined the role of a patient's preference as a moderator of treatment efficacy. Leykin and colleagues found no differences in symptom reduction or likelihood of attrition between patients who received their preferred treatment versus those who did not (CBT vs ADM).[72] On the other hand, Kocsis and colleagues found that patients who preferred either CBT alone or ADM alone had higher rates of remission and fewer depressive symptoms if they got what they preferred than if they got combined treatment.[73] Thus, patient preferences in that study appeared to be driven more by a disaffection for a specific monotherapy than a preference for the other.

Dysfunctional attitudes

A number of studies have reported that high levels of pretreatment dysfunctional attitudes predict poorer response to CBT (prognostic).[62–64,74] Furthermore, Sotsky and colleagues found that patients with lower dysfunctional attitudes did better in CBT (or ADM) than in pill-placebo.[63] Thus, lower levels of dysfunctional attitudes were prescriptive relative to pill-placebo (but not to ADM) in that study. It is unclear whether levels of dysfunctional attitudes are prescriptive relative to other alternative treatments.[60]

Mediators of CBT efficacy

Although CBT has been found to be efficacious in the treatment and prevention of depression, questions remain about precisely how it works (mediation). Such questions are relevant to the identification of both the active ingredients in the treatment process and the mechanisms of change within the patient. Cognitive theory posits that negative automatic thoughts and maladaptive information processing proclivities play a causal role in the etiology and maintenance of depression.[7] According to this theory, CBT works by virtue of implementing efforts (process) to correct these errors in thinking (mechanism). To the extent that this is true then efforts to help patients learn how to examine the accuracy of their own beliefs should help ameliorate the level of existing distress and reduce risk for future episodes. Others factors that also are believed to mediate the efficacy of psychotherapy are the quality of the therapeutic relationship and facilitative conditions, such as therapist warmth and empathy. If cognitive theory is correct, then adherence to the specific components of CBT should drive symptom change and subsequent freedom from relapse over and above whatever contribution is made by nonspecific factors common to other therapies.

Treatment process

Several studies have shown that nonspecific factors are correlated with change across the course of cognitive therapy.[75–77] Conversely, several studies have found that homework compliance (assessed retrospectively at the end of treatment) was associated with better response to CBT.[61,77,78] However, these studies did not adequately control for reverse causality (that it was symptom change that drove treatment process rather than the other way around); doing so would have required controlling for symptom change up until the point at which homework compliance was measured. Shaw and colleagues found only limited support for the role of therapist competence (it was the ability to structure treatment rather than CBT skills that best predicted outcome), but also did not examine the pattern of temporal relations over time (again doing so would have required controlling for prior symptom change at the point at which competence was measured).[79] DeRubeis and Feeley revisited these issues in a pair of studies that controlled for symptom change prior to the assessment of treatment process and then monitored the effects of treatment process on subsequent symptom change.[80,81]

What they found was that after controlling for prior symptom change, the extent to which therapists used concrete symptom-focused CBT methods in early sessions predicted subsequent change in depression, whereas nonspecific processes like the helping alliance and facilitative conditions did not. Moreover, ratings of the helping alliance in subsequent sessions were predicted by prior depression change. This suggests that concrete symptom-focused techniques may play a causal role in the alleviation of depressive symptoms in CBT, whereas the quality of the therapeutic relationship may be more a consequence than a cause of change. Neither study ruled out possible third variable causality (that some unmeasured patient characteristic both facilitated concrete symptom-focused techniques and led to subsequent symptom change with no direct causal link between the two), but they did suggest that specific CBT techniques were predictive of (and possibly causal to) subsequent symptom change in a manner that nonspecific processes were not.

Cognitive mechanisms

In a similar fashion, early studies assessing whether cognitive change mediated CBT's effects typically reported that ADM produced as much change in cognition as CBT[82,83], leading authors to conclude that cognitive change was more of a nonspecific consequence of change in depression rather than a cause.[83] However, as was the case in the treatment process literature, these early studies did not assess the temporal pattern of change between cognition and subsequent depression and therefore were unable to address the possibility that cognitive change mediated change in depression in one treatment but was a consequence of change in depression in another.[84] In point of fact, DeRubeis and colleagues found that early change in cognition was predictive of subsequent change in depression in CBT but not in ADM despite the fact that both produced comparable change in cognition across the course of treatment, a pattern that is consistent with differential mediation in CBT but not in ADM.[85] Recent studies have extended this line of inquiry by examining the relation between cognitive change and subsequent relapse. Strunk and colleagues found that among treatment responders, patient competence in CBT coping skills and their independent implementation predicted the risk of relapse in the year following treatment termination.[86] Among partially remitted patients, Teasdale and colleagues found that CBT reduced the tendency to use an absolutist, dichotomous thinking style, and that this change (rather than simply becoming more positive) reduced the likelihood of subsequent relapse.[87] Moreover, there is evidence that CBT reduces the extent to which patients think negatively with increased dysphoria (cognitive reactivity) [88] and that this reduction in cognitive reactivity predicts subsequent risk for relapse.[89] Collectively, these studies support the notion of cognitive mediation in CBT by ruling out reverse causality (that cognitive change is caused by change in depression); although as for the process studies they do not rule out third variability causality (that some unmeasured patient factor both caused change in cognition and change in depression with no causal link between the two). Thus, some ambiguity still remains as to whether CBT works by virtue of changing cognitions, although the existing evidence is consistent with that notion.

Sudden gains

Tang and DeRubeis described a pattern of substantial stable decreases in depressive symptoms in CBT with implications for both treatment process and the mechanisms of change that they termed *sudden gains*.[90] A number of studies have replicated the presence of sudden gains during CBT since.[91–93] Sudden gains seem to appear in 30 to 50% of the patients, accounting for 50 to 60% of the total improvement in these patients. They generally have a magnitude of 10 or more points on the Beck Depression Inventory and appear in the first half of treatment (between sessions 4 and 8). Although the presence of sudden gains during CBT has been consistently associated with better end-of-treatment outcomes, nearly as many patients respond to treatment who show a more gradual course of change.[90–93] Most striking is the finding that sudden gains predict freedom from relapse among treatment responders.[93] Earlier

studies had found an inconsistent relation between sudden gains and levels of depression following treatment termination, but had relied on cross-sectional assessments that did not take into account inter-current relapses that could lead to subsequent treatment.[90,91] Conversely, Vittengl and colleagues found little evidence that sudden gains predicted differential relapse following successful treatment, but used a different definition that allowed only modest gains to pass the threshold.[94] Using the original more stringent definition, Tang and colleagues found that sudden gains predicted freedom from subsequent relapse among treatment responders even when controlling for end-of-treatment depression scores, and that that effect disappeared when they applied the less stringent definition used by Vittengl and colleagues.[93] What makes these findings relevant to mediation (and possibly process) is that Tang and DeRubeis found more cognitive change in the session preceding the sudden gains than in control sessions from the same patients (with no differences found for other therapeutic factors),[90] and replicated this in a subsequent study.[92] This suggests that sudden gains might be triggered by cognitive change which in turn is likely related to CBT-specific processes on the part of the therapist, as posited by cognitive theory. However, given the correlational nature of this finding, third variable causality cannot be ruled out, and sudden gains also have been found in other types of treatments that are less likely to be mediated by cognitive change.[91,94]

Cognitive change versus behavioral activation

The studies just described all relied on correlational analyses to identify the causal mechanisms of change in CBT. Jacobson and colleagues used a more experimental approach to dismantle CBT in an effort to identify its active ingredients and came up with a somewhat different answer.[95] In that study, the investigators compared the efficacy of different three different CBT components by comparing 1) behavioral activation only (BA), 2) BA plus the activation and modification of dysfunctional thoughts (AT), and, 3) BA plus AT plus the identification and modification of core schemes (CT), and found no differences in efficacy between these different components. This was surprising because cognitive theory posits that direct efforts to change beliefs are necessary to maximize change in depression and the BA condition did not address those beliefs directly. Moreover, no differences were found on purported mediators hypothesized to be differentially affected by the respective components (pleasant events, automatic thoughts, and attributional style) and early change in cognition was associated with subsequent change in BA (but not in CT) and early change in pleasant events was associated with subsequent change in CT (but not in BA). This study suggests that specific efforts to change beliefs may not be necessary to produce cognitive change, while at the same time leaving open the possibility that cognitive change (no matter how it is produced) may still play a meditational role in the subsequent reduction of distress. Clearly more research is needed in this regard.

Conclusion

CBT has been found superior to control conditions and as efficacious as other psychotherapies and ADM in the acute treatment of depression. When adequately implemented, CBT can be as efficacious as ADM for patients with more severe depressions. CBT may also be of use as an adjunct to medications in the treatment of bipolar disorder, although the evidence there is not so clear or extensive. CBT reduces relapse/recurrence rates, with a magnitude of effect that might be comparable to keeping patients on medications, which is particularly noteworthy in a chronic recurrent disorder. Patients who are married or show low levels of pre-treatment dysfunctional attitudes seem to be more likely to respond to CBT than patients who are unmarried or show high levels of dysfunctional attitudes. Unemployment, more antecedent life events and prior ADM exposures, and the absence of Axis II comorbidity are prescriptive factors associated with better response to CBT compared to medications. CBT appears to work

through concrete CT-specific strategies and may well be mediated by changes in cognition as specified by theory, although it remains unclear whether it is necessary to deal directly with cognition in order to produce those changes.

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