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Continuation-Phase Cognitive Therapy's Effects on Remission and Recovery from Depression

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Abstract

We tested continuation-phase cognitive therapy's (C-CT) effects on remission and recovery from recurrent major depressive disorder (MDD), defined as 6 weeks and 8 months, respectively, of continuously absent or minimal symptoms. Responders to acute-phase cognitive therapy were randomized to 8 months of C-CT (n = 41) or assessment control (n = 43), and followed 16 additional months (Jarrett, Kraft, Doyle, et al., 2001). Relative to controls, a few more patients in C-CT remitted (88% vs. 97%) and significantly more recovered (62% vs. 84%). All patients without remission and recovery relapsed, but most patients who remitted (60%) and who recovered (75%) did not later relapse or recur. We discuss the importance of defining efficacious treatment as producing remission and recovery.

Key words/phrases

major depressive disorder; remission; recovery; cognitive therapy; continuation phase cognitive therapy

Major depressive disorder (MDD) is common (16% lifetime prevalence; Kessler, Berglund, Demler, Jin, & Walters, 2005), recurs frequently (Mueller et al., 1999), produces significant disability (Judd et al., 2000), and can be treated efficaciously with cognitive therapy (CT; Craighead, Sheets, Brosse, & Illardi, 2007). The major purpose of this report is to extend investigation of CT for MDD from the traditional emphasis on acute symptom reduction and prevention of relapse and recurrence, to examine extended periods of minimal or absent symptoms. We report rates of remission and recovery—6 weeks and 8 months, respectively, with few-to-no symptoms—after response to acute phase CT (A-CT) with and without continuation phase CT (C-CT) in a randomized clinical trial (Jarrett et al., 2001).

Considerable research supports CT's efficacy: Patients' average scores on the Hamilton Rating Scale for Depression (HRSD; Hamilton, 1960) decrease 8-16 points over A-CT, 50-70% of patients who complete A-CT no longer meet criteria for MDD (Craighead et al., 2007), and symptom reduction during A-CT is similar to that in other depression-specific treatments (e.g., behavior therapy, interpersonal psychotherapy, and pharmacotherapy;

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Butler, Chapman, Forman, & Beck, 2006; Craighead et al., 2007). A-CT offers some prophylaxis relative to discontinuing pharmacotherapy, but at least half of A-CT responders have a major depressive relapse or recurrence within 2 years (Vittengl, Clark, Dunn, & Jarrett, 2007). However, continuation phase CT (C-CT) reduces relapse and recurrence significantly (21-29% reduction compared to inactive comparison conditions; Vittengl et al., 2007) among responders to acute-phase treatments.

Although very valuable, an emphasis on short-term outcomes (e.g., symptom scores at the end of acute-phase treatment) and/or outcomes allowing significant sub-diagnostic symptoms (e.g., absence of relapse and recurrence) limits most research on A-CT and C-CT. For example, a primary outcome variable in major CT clinical trials is “remission” or “recovery” defined as minimal or absent symptoms (e.g., low HRSD scores) at the end of A-CT (e.g., DeRubeis et al., 2005; Dimidijian et al., 2006; Elkin et al., 1989). Low depressive symptoms mark clinically significant improvement, but analysis of a single or short period of assessment likely misses the fluctuating course of symptoms that characterizes most patients’ MDD. CT researchers also commonly report rates of “remission” or “recovery” defined as the absence of a major depressive episode over follow-up (e.g., Dobson et al., 2008; Hollon et al., 2005), although some reports define “recovery” as only 8 weeks of minimal or absent symptoms (e.g., Shea et al., 1992). Marking a higher standard than these traditional definitions, emerging criteria for evaluating treatments emphasize longer periods of minimal or absent depressive symptoms for defining remission (3+ weeks) and especially recovery (4+ months; Rush et al., 2006).

Defining remission and recovery as longer periods of few-to-no symptoms is important because—analogous to treatment of hypertension or cancer—being “less depressed” arguably is an inadequate benchmark for effective treatment of MDD (Rush, 2007) and evaluation of CT. For example, sub-diagnostic moderate depressive symptoms predict significant impairment in major social roles (e.g., work, social relationships) over the longitudinal fluctuating course of MDD (Judd et al., 2000). Moreover, moderate symptoms at the end of acute phase treatments are a common and potent risk factor for MDD relapse and recurrence, and so may be unsustainable for many patients (Fava, Fabbri, & Sonino, 2002). In short, failing to meet criteria for MDD too frequently does not mean experiencing good health (Fava, Ruini, & Belaise, 2007).

One purpose of this report is to raise standards of longitudinal evaluation of CT using rigorous definitions of remission and recovery (Jarrett et al., 2001). This report examined remission and recovery among patients with recurrent MDD who responded to A-CT, were assigned randomly to 8 months of C-CT or assessment control, and were followed 16 additional months. Jarrett et al. found that, compared to assessment control, C-CT reduced relapse (10% vs. 31%) over the 8 months, and reduced cumulative relapse and recurrence among patients at high risk (early-onset MDD, 16% vs. 67%; and unstable acute-phase remission, 37% vs. 62%) over the entire 2 years of post-A-CT follow-up. We extended Jarrett et al.’s analyses to test the hypothesis that compared to assessment control, C-CT increases remission and recovery, defined as minimal or absent depressive symptoms maintained continuously for at least 6 weeks and 8 months (35 weeks), respectively, after the end of A-CT. Compared to traditional research on CT, the long periods of wellness demanded by these definitions increase the clinical significance of treatment outcomes for MDD as an often recurrent and chronic, fluctuating illness.

Method

Participants

Participants were adult outpatients presenting with *DSM-IV* nonpsychotic, recurrent MDD with clear inter-episode recovery (≥2 months of at least nearly normal functioning; American Psychiatric Association, 1994) and scoring ≥16 on the 17-item HRSD. Diagnoses were made by a doctoral-level clinician using the Structured Clinical Interview for *DSM-III-R* (outpatient version; Spitzer, Williams, Gibbon, & First, 1989), with supplemental interview questions to assess *DSM-IV* disorders and subtypes. Eligible patients consenting to the experiment (C-CT vs. control; $N = 84$) had a mean age of 42.7 years ($SD = 10.4$) and education level of 15.4 years ($SD = 2.7$); 72.6% were women; and 3.6% were African American, 3.6% Hispanic, 2.4% Native American, and 90.5% Caucasian. Comorbid Axis I disorders at intake included social phobia (17.9%), specific phobias (10.7%), panic disorder without (9.5%) and with (1.2%) agoraphobia, posttraumatic stress disorder (8.3%), dysthymic disorder (4.8%), obsessive-compulsive disorder (1.2%), agoraphobia without a history of panic disorder (1.2%), and hypochondriasis (1.2%).

Procedure

Patients received 20 individual sessions (50-60 minutes each) of A-CT (Beck et al., 1979) in a 12-14 week protocol. A-CT is designed to reduce depressive symptoms by eliciting thoughts associated with negative affect, teaching patients to evaluate the validity of such thoughts through logical and empirical methods, and generating more realistic alternatives when negative thoughts are not supported. Consenting responders to A-CT (completed the A-CT protocol and had no MDD and HRSD ≤ 9 by an independent evaluator; 3 responders did not consent) were randomized to C-CT (Jarrett, 1989; Jarrett, Vittengl, & Clark, 2008; $n = 41$) or assessment control ($n = 43$). The C-CT protocol consisted of 10 sessions (60-90 minutes each) over 8 months provided by the patient's A-CT therapist. C-CT is designed to prevent relapse and recurrence of depression through maintenance and generalization of skills learned in A-CT, reduction of residual depressive symptoms, preparation for current or anticipated vulnerabilities, and enhancement of strengths. In C-CT, patients are taught to use emotional distress and symptoms as cues to implement skills learned in A-CT. The control condition consisted of 10 evaluation visits on the same schedule as C-CT. Evaluators of control patients had not provided A-CT and were prohibited from using psychosocial interventions. In both conditions, patients who relapsed were asked to complete all sessions and were referred for extra-protocol treatment if not receiving C-CT. The follow-up phase consisted of 10 assessments scheduled over 16 months (ending 24 months post A-CT). Pharmacotherapy was not provided in any study phase.

Therapists

Five doctoral-level therapists (PhD in clinical psychology or MD with training in psychiatry) completed ≥ 1 years of CT training and achieved competency scores ≥ 40 on the Cognitive Therapy Scale (CTS; Young & Beck, 1980) before treating study patients. During A-and C-CT, therapists received weekly group supervision, plus additional supervision as requested, from a PhD clinical psychologist with extensive experience in supervising CT. During both A- and C-CT, an offsite consultant (a PhD clinical psychologist with extensive experience evaluating CT) reviewed videotapes of the fourth and an additional randomly selected session using the CTS. Therapists received written feedback to facilitate competence and adherence with treatment manuals. All therapists achieved mean CTS scores > 40 during both A- and C-CT.

Measures

Longitudinal Interval Follow-Up Evaluation (LIFE)—The LIFE (Keller et al., 1987) is a semi-structured interview assessing *DSM-IV* Axis I psychopathology and extra-protocol treatment retrospectively. Independent evaluators completed the LIFE 4, 8, 12, 16, 20, and 24 months post-A-CT (each assessment covered the preceding 4 months), at study exit, and when patients, therapists, or follow-up evaluators suspected major depressive relapse or recurrence. Independent evaluators were highly experienced clinicians trained in the application of *DSM-IV* criteria, depressive symptom measures, and the LIFE, and did not provide A- or C-CT in this study. Independent evaluators were blind to group assignment at all LIFE assessments except months 16 and 20, due to the high cost of blind evaluations. As defined a priori by Jarrett et al. (2001), weekly psychiatric status ratings (PSR) of *DSM-IV* MDD (on a 1-6 scale) defined remission and recovery, respectively, as ≥ 6 and ≥ 35 continuous weeks of PSR of 1 (no symptoms) or 2 (one or two mild symptoms); and relapse and recurrence as ≥ 2 weeks of PSR of 5 (meets MDD criteria) or 6 (meets MDD criteria with severe impairment and/or psychosis) before and after, respectively, meeting criteria for recovery. Other researchers have also used these PSR cutoffs (e.g., Shea et al., 1992). Patients who relapsed before remission or recovery were coded as not achieving remission or recovery, respectively. Assessments were scheduled to maximize protocol data collection, and the same or different evaluators (39% and 61% of pairs of assessments, respectively) coded adjacent weeks' PSR at separate 4-month administrations of the LIFE (i.e., weeks 18-19, 35-36, 52-53, 69-70, and 86-87). We corrected the median intraclass correlation for different evaluators (.73) by dividing it by the square root of the median retest *r* for same evaluators (.83) to estimate the interrater reliability of the PSR as .80.

Extra-Protocol Treatment

Participants agreed to postpone or to report (via the LIFE) all extra-protocol psychiatric and psychosocial treatment during the study. Before they remitted, a control patient received 2 weeks of pharmacotherapy (zolpidem), and a C-CT patient received 1 week of pharmacotherapy (chlorazepate). Five patients received extra-protocol treatment before they recovered. In the control group, one patient received 2 weeks of pharmacotherapy (codimal), and a second received 9 marital-therapy sessions. In the C-CT group, one patient received 9 weeks of pharmacotherapy (methylphenidate), a second received 1 week of pharmacotherapy (melatonin), and a third received 3 weeks of pharmacotherapy (chlorazepate 1 week and Darvocet 2 weeks) plus four psychosocial treatment sessions for weight loss. The small amount of extra-protocol pharmacotherapy and psychosocial treatment received before remission or recovery did not differ significantly between the control and C-CT groups (Wilcoxon test *p*s > .28, two-tailed).

Results

Product-limit survival analyses indicated that 92% of A-CT responders remitted (i.e., achieved 6 continuous weeks of minimal or absent depressive symptoms) between weeks 6-16, and 73% recovered (i.e., achieved 35 continuous weeks of minimal or absent depressive symptoms) between weeks 35-70, post-A-CT. Analyses excluding patients who received extra-protocol treatment produced similar estimates of remission (92%) and recovery (71%).

Remission and recovery were partly distinct from the absence of relapse and recurrence (see Figure 1). Between the extremes of MDD (relapse and recurrence) and minimal or absent symptoms (remission and recovery), patients could have maintained moderate symptoms below the MDD diagnostic threshold. None did so in the current dataset. Except for patients who attrited (5 before relapse or remission, 10 before relapse or recovery), all patients who

failed to achieve remission (6/6) and recovery (19/19) relapsed. Further, 40% (27/68) of patients who remitted later relapsed or recurred, and 25% (14/55) of patients who recovered later recurred. The overall correlations of remission (r = -.34, p < .01, n = 79) and recovery (r = -.66, p < .01, n = 74) with a negative outcome (relapse or recurrence) were moderate.

Attrition from C-CT and assessment control was similar before remission (2 and 3 patients, respectively; exact p = 1.0) and recovery (4 and 6 patients, respectively; exact p = .74). Figure 2 shows from product-limit survival analyses that a numerically larger proportion of patients in C-CT vs. control achieved remission (97% vs. 88%), but the effect was not significant, log-rank $\chi^2(1) = 2.52$, p = .11, r = .17. However, C-CT produced significantly more recovery than control (84% vs. 62%), log-rank $\chi^2(1) = 4.20$, p = .04, r = .22. When controlling the presence vs. absence of extra-protocol treatment in stratified analyses, the effects of C-CT on remission, log-rank $\chi^2(1) = 2.52$, p = .11, r = .17, and recovery, log-rank $\chi^2(1) = 4.72$, p = .03, r = .24, were similar.

Discussion

Previous research indicates that A-CT reduces depressive symptoms (Butler et al., 2006; Craighead et al., 2007) and C-CT reduces relapse and recurrence among A-CT responders (Vittengl et al., 2007). We expanded the CT evidence base by examining remission and recovery, defined as relatively long periods of minimal or absent symptoms. Many recurrent-MDD patients who respond to A-CT and then discontinue A-CT will remit (88%) and recover (62%), with these outcomes defined rigorously as 6 and 35 continuous weeks, respectively, of minimal or absent symptoms. Further, patients treated with C-CT have a modestly better chance of remitting (97%) and a significantly better chance of recovering (84%) relative to stopping A-CT.

At the same time, our analyses reveal limitations of A-CT and C-CT in producing and protecting health. Some patients who remitted and recovered experienced a major depressive episode later in the study (40% and 25%, respectively). Response to A-CT, even when followed by remission and recovery, clearly does not guarantee freedom from MDD among patients with a history of recurrent illness. Perhaps more importantly, 100% of patients who failed to achieve remission and recovery later relapsed. In this sample, being “less depressed” was not a state that our patients with recurrent MDD could sustain (cf. Fava et al., 2002).

Important limitations include reduced statistical power to detect effects on remission due to its high base rate (92%). In addition, results from our patient sample with carefully diagnosed recurrent MDD, rigorously defined remission and recovery, and highly experienced cognitive therapists may not generalize to other populations, settings, and outcome definitions. Whereas many have used less rigorous definitions, some advise that recovery include positive markers of well-being (e.g., autonomy, mastery, self-acceptance), not just low symptoms (Fava et al., 2007).

Our results clarify the importance of treating patients through to remission and recovery and discovering how long to treat with which treatments. Although many A-CT responders will remit and recover, the addition of C-CT increases the chance of recovery. Our data suggest that absence of remission and recovery portend relapse among recurrent-MDD patients and reinforce calls for persistence and flexibility in treatment to achieve sustained absent or low depressive symptoms (Rush, Trivedi, Wisniewski, et al., 2006). Because A-CT’s power to reduce symptoms and C-CT’s ability to prevent relapse for many patients are well-established, research emphasizing extended wellness is now more viable and urgent. Our field has not identified a “cure” for depression, but our goal should be no less.

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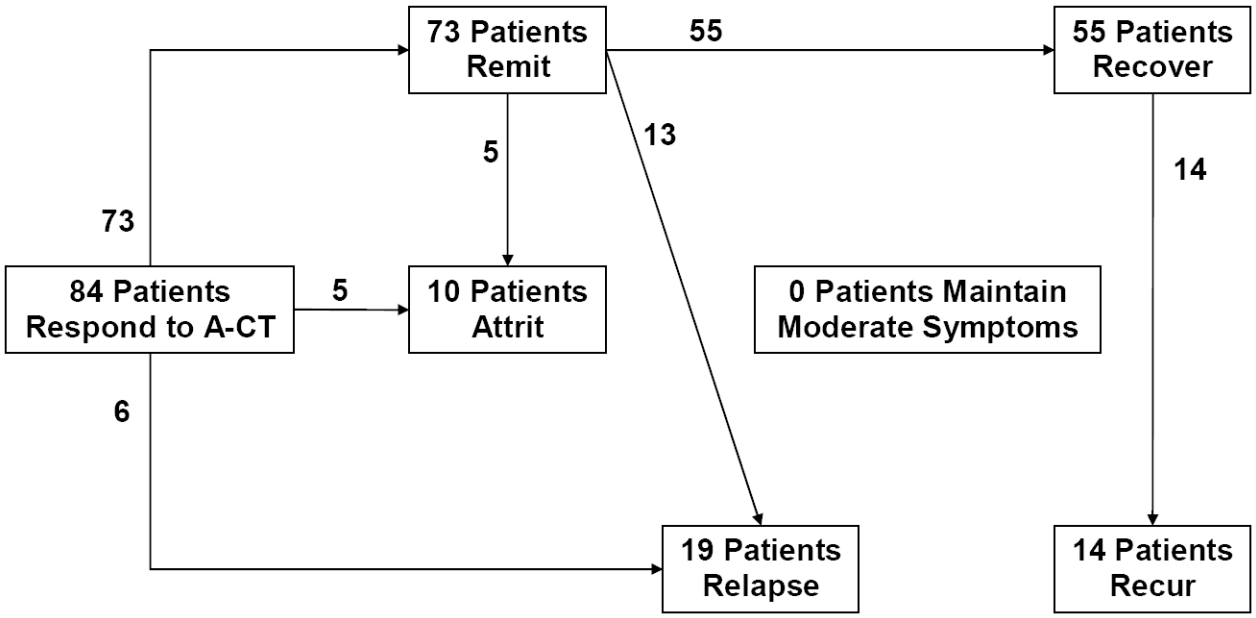

Figure 1.
Outcomes of patients who responded to acute phase cognitive therapy (A-CT) for depression over two years of follow-up.

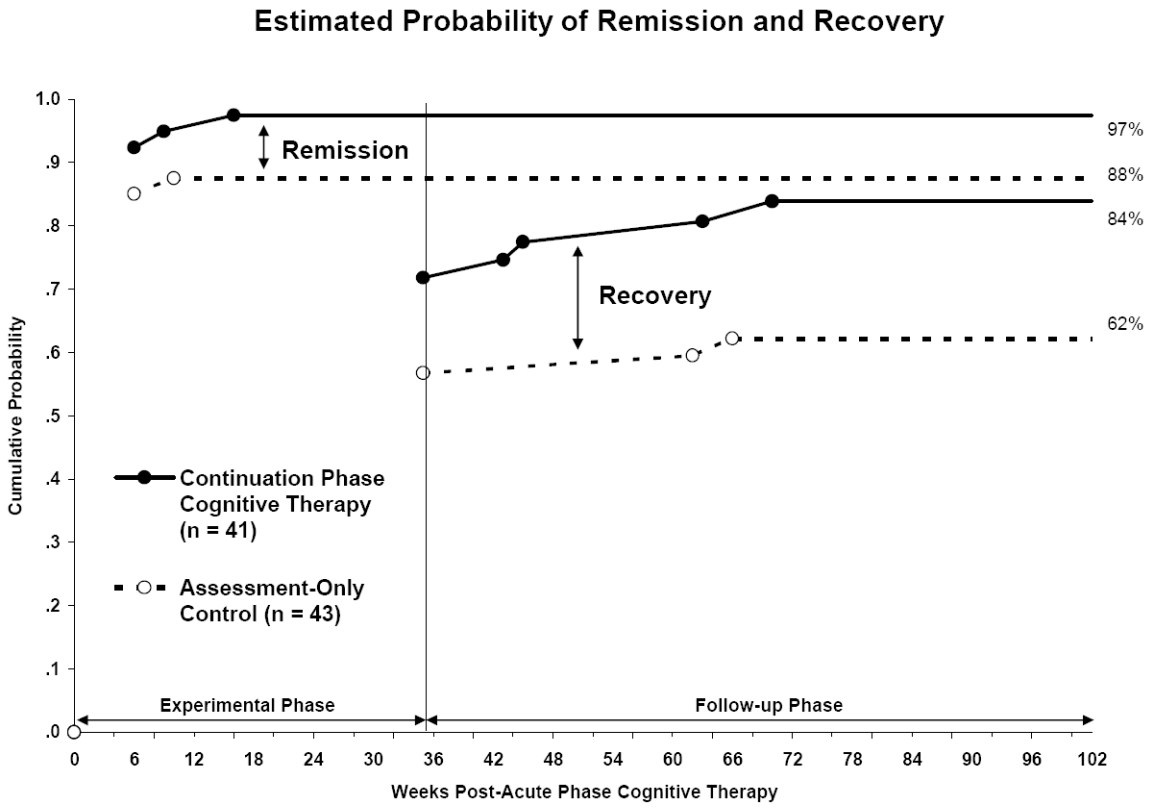

Figure 2.
Rates of remission and recovery (6 and 35 weeks of absent or minimal depressive symptoms, respectively) estimated from Kaplan-Meier product-limit survival analyses.