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Extreme Nonresponse to Acute Phase Cognitive Therapy for Depression: An Attempt to Replicate and Extend

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As with other interventions for major depressive disorder (MDD), cognitive therapy (CT) results in treatment failure for about half of all participants. In 2007, Coffman and colleagues in Seattle studied this topic by identifying a group of patients who demonstrated an extremely poor response to CT (i.e., posttreatment BDI score ≥ 31). They called these patients "extreme nonresponders" (ENR) and described the pretreatment characteristics that predicted response status.

In the current study, we attempt a replication of the Seattle study with a larger sample of adults with recurrent MDD (N = 473) who received a 16–20 session (12–14 week) course of CT.

The rate of ENR in this large sample was only 6.3% (30/473), compared to 22.2% (10/45) in the Seattle sample. Four pretreatment measures of symptom severity and functioning differed significantly among ENR and non-ENR participants. In each case, higher symptoms or poorer functioning were associated with ENR status. However, the combination of these factors in a regression model did not predict actual ENR status with the high degree of sensitivity or specificity observed in the Seattle study.

These findings suggest that extreme nonresponse to CT is not as common as previously described and, although poor outcomes are associated with pretreatment clinical status, it is difficult to predict posttreatment symptom severity with a high degree of accuracy across different research samples.

Keywords: cognitive therapy (CT); major depressive disorder (MDD); nonresponse; predictors of response

COGNITIVE THERAPY (CT) IS THE MOST EXTENSIVELY studied psychological treatment for major depressive disorder (Butler, Chapman, Forman, & Beck, 2006) and evidence from randomized controlled trials suggests that its efficacy is comparable to that of antidepressant medications across 12–16 weeks of acute-phase treatment (DeRubeis, Gelfand, Tang, & Simons, 1999; DeRubeis et al., 2005; Roth & Fonagy, 1996). Like all acute-phase interventions for major depression, however, CT is far from universally effective. Approximately 40% to 50% of patients will not respond to a standard 12–16 week course of CT for depression, eventually requiring the initiation

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of a second treatment step such as a switch to, or addition of, an antidepressant medication (Schulberg, Pilkonis, & Houck, 1998). Given the time, expense, and morbidity associated with failed treatment trials, the identification of "prognostic factors" that predict successful treatment (preferably before treatment is started) is an important and clinically relevant area of research. This is particularly true within the field of CT, given the mismatch between high demand for the intervention and the relative scarcity of available providers (Shafran et al., 2009). As such, the early identification of individuals who are likely to benefit from this model of psychotherapy is advantageous not only for patients in treatment, but also for future clients who are waiting to utilize the services of cognitive therapists. This issue is particularly relevant from a public health perspective, since depression is one of the world's greatest public health concerns and is a leading cause of disability (Whiteford et al., 2013).

In a 2007 manuscript, Coffman and colleagues at the University of Washington in Seattle (Coffman, Martell, Dimidjian, Gallop, & Hollon, 2007) identified a pretreatment clinical profile associated with "extreme nonresponse" to acute-phase CT for depression. In their research sample ($N = 45$), Coffman and colleagues found that depressed patients who ended CT with Beck Depression Inventory (BDI) scores of 31 or higher—roughly analogous to the "severe" depression category originally defined by Beck et al. (Beck, Ward, Mendelson, Mock, & Erbaugh, 1961)—had higher pretreatment depressive symptoms and poorer levels of interpersonal and global functioning prior to the onset of treatment. Furthermore, the Seattle group found that a multivariate combination of four specific pretreatment variables—greater symptom scores on the BDI, the Hamilton Rating Scale for Depression, the Global Assessment of Functioning, and a measure of interpersonal problem severity—accurately identified 90% of individuals in the "extreme nonresponse" (ENR) category.

If replicable, the ENR construct would have important clinical implications. Perhaps most importantly, Coffman and colleagues (2007) did not find a subgroup of extreme nonresponders in the other psychosocial treatment group (i.e., Behavioral Activation) evaluated in their study, which might suggest that the characteristics that identified ENR patients have uniquely ominous implications for CT response. Furthermore, as there are few replicable pretreatment predictors of differential response to psychosocial interventions for depression, this would be a useful development that could enable clinicians to identify patients who are unlikely to benefit from Beck's model of therapy and might have a better chance of responding to an alternate intervention (e.g., Behavioral Activation or antidepressant pharmacotherapy).

In an effort to gain a better understanding of the phenomenon of ENR to CT, we attempted to replicate the findings of the Seattle group in a much larger cohort of depressed outpatients ($N = 473$) treated with a standard 12–14 week acute course of CT. Although our study did not include an active comparison group, such a replication would afford the opportunity to ascertain if a pattern of ENR did exist within this larger group of depressed outpatients and, if so, if these individuals had similar pretreatment characteristics to extreme nonresponders in the Seattle study. In addition, we explored other ways to classify ENR to CT, as well as the pretreatment measures that may help to predict it.

Material and Methods

Summary of the C-CT-RP Trial (Parent Study)

This report is a secondary analysis of data from the *Continuation Phase Cognitive Therapy Relapse Prevention [C-CT-RP] Trial*, which is registered at ClinicalTrials.gov (NCT00118404, NCT00183664, and NCT00218764; Jarrett & Thase, 2010). The purpose of the C-CT-RP trial was to evaluate the efficacy and durability of continuation phase CT for prophylaxis against major depressive disorder (MDD) relapse, and consisted of two phases: an initial 12–14 week "acute-phase" of CT for adult outpatients with recurrent MDD, followed by an 8-month "continuation-phase" of CT for participants considered to be at high risk for MDD relapse. For the current report, results from only the "acute-phase" of the study were examined, and the results of the continuation-phase (main outcomes) of the study are reported elsewhere (Jarrett, Minhajuddin, Gershenfeld, Friedman, & Thase, 2013).

Participant Recruitment and Inclusion/Exclusion Criteria

The C-CT-RP protocol was approved by the Institutional Review Boards (IRB) of the University of Texas Southwestern Medical Center and the University of Pittsburgh Medical Center, and all participants provided informed consent for evaluation and treatment. Outpatient male and female subjects, aged 18 to 70, were recruited from clinical referrals and advertisements between January 3, 2000, and July 30, 2008. Recruitment methods included project promotion through IRB-approved advertisements on the Internet and in newspapers, churches, hospitals, clinics, and other community settings. Patients were eligible to participate if they (a) presented with a principal diagnosis of recurrent MDD, as diagnosed by the Structured Clinical Interview for DSM-IV; (b) remitted between depressive episodes or had