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Sequence of improvement in depressive symptoms across cognitive therapy and pharmacotherapy

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Abstract

Background—The authors examined the patterns of improvement in cognitive and vegetative symptoms of major depression in individuals treated with cognitive therapy (CT) or pharmacotherapy (PT).

Method—Outpatients diagnosed with major depressive disorder (n = 180) were randomized to receive either CT or PT. Cognitive and vegetative symptoms of major depression were measured by the Beck Depression Inventory - II at baseline and regularly throughout 16 weeks of treatment.

Results—Multivariate hierarchical linear modeling demonstrated the same patterns of change over time for cognitive and vegetative symptoms within CT and within PT.

Limitations—Self-report measures may not be sufficiently specific to capture subtle differences in improvements between vegetative and cognitive symptoms.

Conclusions—These results are consistent with Beck's (1984) hypothesis that CT and PT have a similar site of action, which when targeted, results in changes in both cognitive and vegetative features.

Keywords

Depression; Cognitive Therapy; Pharmacotherapy; Symptom Change

Although cognitive therapy (CT) and pharmacotherapy (PT) have been found to be similarly effective for treating major depression (DeRubeis et al., 1999; DeRubeis et al., 2005; Hollon et al., 2005), there is little research on the sequence of symptom improvement for each of the treatment modalities. One possibility suggested in the literature is that cognitive symptoms of depression improve before vegetative symptoms when patients are treated with CT, with the reverse pattern implicated for PT (DiMascio et al., 1979; Rush et al., 1981). Such distinct

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patterns of symptom remission are based on the theoretical assumptions underlying the different treatments (reviewed in Goldapple et al., 2004). CT is assumed to directly target cognitive processes such as dysfunctional attitudes and negative automatic thoughts (Beck et al., 1988), the improvement of which in turn would facilitate improvements in other symptoms of major depression. Conversely PT involving serotonin selective reuptake inhibitors (SSRIs) alters serotonin functioning (Hyman and Nestler, 1996) known to play a key role in the regulation of appetite, sleep and several other vegetative functions. Thus, SSRIs may improve vegetative functions, before other symptoms of depression.

Empirical results have been inconsistent with respect to whether CT and PT are associated with distinct patterns of symptom improvement. Rush and colleagues (1981) found that across the first four weeks of treatment, CT was associated with initial improvements in hopelessness, self beliefs and negative mood followed by the alleviation of vegetative and motivational symptoms while no discernable pattern of change was seen in patients treated with PT. DiMascio and colleagues (1979) found that vegetative symptoms of depression such as sleep disturbance improved before depression, anxiety and apathy for patients treated with PT, a pattern not observed for patients treated with interpersonal psychotherapy. Further, Haskell, DiMascio and Prusoff (1975) found that PT was associated with rapid improvements in sleep, appetite disturbances and suicidal feelings, but slower improvement in cognitive and behavioral symptoms such as hopelessness, interest and retardation.

However, other studies have not found discernible treatment specific differences in the rapidity of change of vegetative or cognitive symptoms. DeRubeis and colleagues (DeRubeis et al., 1990) found that cognitive constructs associated with vulnerability of depression (e.g., hopelessness, dysfunctional assumptions) were significantly reduced in the first half of treatment, regardless of whether patients were treated with CT (alone, or in combination with PT) or PT alone. Similarly, Simons, Garfield and Murphy (1984) found that CT and PT were associated with nearly identical patterns of improvement in negative automatic thoughts and dysfunctional assumptions. Accordingly, Mandell (1988) found that cognitive and vegetative symptoms of depression changed in a uniform manner across CT and PT.

With the exception of research by Rush et al. (1981) and Mandell (1988), researchers have not examined session-by-session changes in cognitive and vegetative symptoms of major depression in response to CT and to PT. Assessing symptoms over such short intervals is necessary to detect the pattern of change of symptoms over the course of treatment (DeRubeis et al., 1990; Laurenceau et al., 2007). The purpose of this study, therefore, was to examine the pattern of improvement in cognitive versus vegetative symptoms of major depression as a function of the form of treatment in a sample in which symptoms were measured repeatedly and relatively frequently.

Method

Participants

The sample consisted of 180 depressed outpatients recruited at the Adult Psychiatry Clinic at Vanderbilt University Medical Center (n = 90) and at the Depression Research Unit at the University of Pennsylvania (n = 90). The majority of participants were Caucasian (82.8%) and the average education was 14.6 (SD = 2.4) years. Patients were randomized to receive either PT (n = 120; mean age = 39.8, SD = 11.6; 70 females), or CT (n = 60; mean age = 40.3, SD = 11.5, 35 females). Participants were recruited from the community and from clinical referrals (see DeRubeis et al., 2005 for further details about the sample).

Inclusion criteria included a DSM-IV diagnosis of major depressive disorder and a score of 20 points or higher on the 17-item version of the Hamilton Revised Scale for Depression (HRSD:

Hamilton, 1960) for two consecutive weeks. The Structured Clinical Interview for DSM-IV Axis I Disorders-Patient Version (SCID-I/P: First et al., 1995) was used to assess for Axis I disorders. Interrater reliability for the assessment of a major depressive episode was .80. Similar levels of depression as measured by the Beck Depression Inventory - II (Beck et al., 1996) were reported by participants in the PT condition (M = 32.6, SD = 10.0) and the CT condition (M = 30.9, SD = 8.6, t(175) = 1.1, p = .28] at intake. Exclusion criteria included a lifetime history of psychotic disorders or bipolar disorder, history of substance dependence in the past year, medical conditions if they interfered with study procedures, Axis I disorders requiring different treatment, high risk for suicide, treatment with certain psychoactive medications, and failure to respond to either paroxetine or CT within the preceding year. DeRubeis and colleagues (DeRubeis et al., 2005) provide a between-site comparison of patient characteristics and treatment effects.

Measures and Procedures

Beck Depression Inventory - II—(BDI-II: Beck et al., 1996) is a 21-item self-report instrument measuring the severity of depression in adults and adolescents. Each item is rated on a 4-point scale ranging from 0 to 3 and possible total scores range from 0 to 63. Support for the validity and reliability of the BDI is well established with samples from various populations (Beck et al., 1996). The items in the BDI have been found to segregate into two factors: nine items representing a cognitive dimension (e.g., pessimism, self-dislike, self criticalness) and twelve items representing a somatic-affective dimension (e.g., changes in sleeping patterns, changes in eating patterns, fatigue) of self-reported depression (Beck et al., 1996). In the current study, unweighted means of the items assigned to each factor were used as measures of cognitive and vegetative symptoms of depression respectively (COG and VEG). The BDI-II was assessed at baseline (i.e., the earliest available BDI-II score ranging from 2 weeks prior to treatment) and at weeks 1, 2, 3, 4, 6, 8, 10, 12, 14, and 16 of the active phase of treatment (for treatment procedures, see DeRubeis et al., 2005).

Treatment assignment was randomized. Cognitive therapy sessions were conducted in accordance with the treatment manuals by Beck et al. (1988). Sessions lasted 50 minutes and were twice per week for the first four weeks and then were gradually reduced to weekly for the second half of the active treatment phase. All participants in the PT condition were started on paroxetine and tapered up to a maximum of 50 mg daily by the end of week 6. For patients who did not respond by week 8, medication treatment was augmented. Clinical sessions for medication management and general support were held for approximately 20 minutes weekly for the first four weeks and biweekly after that. Implementation of PT was supervised by experienced pharmacotherapists. Data collection for the original study included a third condition, pill placebo, which is not included in the present study (see DeRubeis et al., 2005).

Data Analysis

Multivariate hierarchical linear modeling (HLM) (MacCallum et al., 1997; Verbeke and Molenberghs, 2000) was conducted using SAS® PROC MIXED to examine the change trajectories for COG and VEG in the CT condition and in the PT condition. Curvilinear trends were visible in each trajectory. Therefore, we examined the extent to which each trajectory was fitted to a model that included quadratic as well as linear terms. Random intercepts, linear coefficients and unstructured error variance/covariance matrices were estimated. The assessment of model fit was based on the likelihood index which represents the joint probability that the data fit the assumed model. The -2 Log-Likelihood indices for the quadratic and linear models were 2488.5 and 2797.0 respectively, indicating a substantially improved fit for the quadratic model (a better fit between two sequential models corresponds to the model with the smaller index). Similar results were found using other indices of fit for linear versus quadratic models, such as the AIC (2510.5 vs. 2819.0), the AICC (2510.6 vs. 2819.1) and the BIC (2545.5

vs. 2854.0). An adequate fit of the quadratic model was also inferred from visual inspection of the plotted means and the distribution of residuals at each time point. A Bonferroni corrected alpha of 0.05/4 = 0.0125 was employed, given that four comparisons were of interest (COG vs. VEG for linear and quadratic components within CT and PT).

Results

Figure 1 shows the observed means for COG and VEG and the values predicted by the multivariate HLM model. There were no statistically significant differences between the linear or quadratic terms in the estimated change trajectories for COG and VEG in either of the treatment conditions (see Table 1). Visually, VEG appeared to improve more rapidly than COG between weeks -2 (two weeks prior to the start of treatment) and week 1 in the PT condition. Therefore, we conducted an additional test of the difference between the COG and VEG trajectories in PT between weeks -2 and 1 (using a random intercepts model without quadratic terms). This additional test did not achieve statistical significance (t = .27, df = 290, p = .78). Overall, the trajectories of improvement were similar for COG and VEG in the CT condition, and in the PT condition. 1

Discussion

This study examined the change trajectories of cognitive and vegetative symptoms of major depression in individuals treated with CT or with PT. No significant difference was detected in the pattern of change between these two types of symptoms in either treatment condition. The absence of statistical evidence for a temporal lag between the cognitive and vegetative symptoms of major depression, along with the roughly parallel time trends for these symptoms, suggest that changes may occur simultaneously at both cognitive and vegetative levels of depression irrespective of the type of treatment received by the patient.

While inconsistent with some theory-driven expectations (Goldapple et al., 2004; Rush et al., 1981), these results are consistent with Beck's (Beck, 1984, November) suggestion that vegetative and cognitive features of depression do not represent different systems of depression, but rather different *levels* of analyses of the same system. Beck suggests that the site of action of both PT and CT is the informational processing system, which, when targeted, results in changes in both cognitive and vegetative features of major depression. Our findings correspond with the proposal that although CT and PT may be associated with different primary mechanisms of change (DeRubeis et al., 1990; DeRubeis et al., 1999; DeRubeis et al., 2005; Goldapple et al., 2004; Hyman and Nestler, 1996), these mechanisms serve to activate changes in the informational processing system, which in turn leads to uniform improvement across vegetative and cognitive dimensions of depression.

The outcomes of this study are consistent with past research that found vegetative and cognitive symptoms changed in unison in response to PT (Rush et al., 1981) or to a psychosocial treatment (DiMascio et al., 1979). However, our findings are also discrepant from research showing that different patterns of improvement are evident in such symptoms in response to PT (DiMascio et al., 1979; Haskell et al., 1975) or CT (Rush et al., 1981). The discrepant findings may be due to differences in how patterns of change were analyzed. Rush et al. conducted cross lagged correlations to determine which symptoms improved before others across the first four weeks of treatment. This method of analysis has been since criticized as inadequate for examining

 $^{^{1}}$ As for the full sample, the trajectories of means for COG and VEG appeared roughly parallel in the PT condition and in the CT condition at each site (Vanderbilt University and University of Pennsylvania) as well as in the sub-sample of treatment responders (69 patients in PT, 35 in CT; see DeRubeis et al. 2005 for the classification of treatment response). No significant differences were found between the linear or quadratic term estimates for COG and VEG in any of these subgroups. Thus, only results for the full sample, collapsed across sites and response status, are reported.

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1 error rates.

models of change and causality (Rogosa, 1980). DiMascio et al. conducted a series of analyses of covariance to investigate significant differences between baseline scores of the HRSD and evaluations during treatment (week 1, 4, 8, 12 and 16). However, they did not correct for family wise type 1 error rates, thereby allowing for an inflated chance of falsely rejecting the null

The difference in findings may also relate to the different ways in which symptoms were defined and measured. Compared to the current study, previous researchers measured symptoms more specifically (e.g., sleep problems, appetite problems, negative self-views,) and examined problems that encompassed both vegetative and cognitive aspects (e.g., apathy, anxiety). For example, in order to measure the speed by which various symptoms changed in context of PT, Haskell and colleagues (1975) examined the change patterns of each item on a modified version of the HRSD. In the current study, we consolidated depressive symptoms as either vegetative or cognitive and measured these with established factors on the BDI-II. Given that Haskell et al. found some vegetative features to change more quickly than others in PT, it is possible that certain symptoms change faster than others, but that this effect is not observed when symptoms are grouped into broad categories such as vegetative or cognitive.

hypotheses. In contrast, the current study used more appropriate analyses to investigate change trajectories of cognitive and vegetative symptoms (i.e., HLM), and controlled for inflated type

Four issues related to this study can be addressed by further research. First, this study did not compare the trajectories of change of symptoms between patients in treatment and those not in treatment Researchers have suggested that antidepressant treatments activate a trajectory of improvement similar to that observed for patients not in active treatment (Stassen et al., 1993). It is argued that antidepressant treatments simply increase the probability of, but not the trajectory of, improvement in depressive symptoms, compared to the course observed for untreated depression. Further research can examine whether both cognitive and vegetative dimensions of depression show similar trajectories of change for patients in active treatment versus those not in treatment for depression.

Second, given that patients receiving PT were provided clinical management which involved support and advice, it is important to further examine whether non-specific factors play a role in influencing the pattern of response of symptoms to pharmacotherapy. Third, as it is a self-report measure, the BDI-II provides information about the participants' perceptions of their symptoms, rather than more objective indices of difficulties (e.g., hours of sleep, weight gain). Further research could investigate differences in the pattern of response of symptoms in CT and PT using observer-rated measures of depression such as the HRSD, or objective findings such as sleep lab reports. Finally, both BDI-II factors included items measuring affect and behavior, which may have affected the validity with which the factors measured purely cognitive and vegetative symptoms respectively. Future research should include measures of individual symptoms such as negative mood or appetite problems, in order to examine divergent patterns of change in specific depressive symptoms.

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Figure 1.

Changes in cognitive (COG) and vegetative (VEG) symptoms of depression over time for patients in the pharmacotherapy condition (PT) and cognitive therapy condition (CT).

	Table 1
Multivariate HLM Estimates of Fixed Effects (df = 252)

Parameter	Estimate	SE	t Value
РТ			
Intercept			de de de
COG	1.22	0.04	29.10****
VEG	1.34	0.04	33.75***
Linear slope			
COG	-0.12 _a	0.01	-22.15****
VEG	-0.11	0.01	-19.51***
Quadratic	ŭ		
COG	0.00 _b	0.00	14.20***
VEG	0.00 _b	0.00	12.16***
CT	0		
Intercept			
COĞ	1.16	0.06	20.70 ***
VEG	1.29	0.06	23.58 ^{***}
Linear slope			
COG	-0.08 _c	0.01	-10.17***
VEG	-0.08 _c	0.01	-10.32***
Quadratic	· ·		
COG	0.00 _d	0.00	4.74***
VEG	0.00 ^d	0.00	5.56***

Note. PT = Pharmacotherapy, CT = Cognitive therapy, COG = Cognitive symptoms of depression, VEG = Vegetative symptoms of depression. Pairs of COG and VEG parameter estimates sharing the same subscript are not significantly different at p < .0125.

Intercepts are estimated at week 0.

* p<.05.

** p < .01.

*** p < .001.