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Predictors of Treatment Response to Cognitive-Behavioral Therapy for Depression in Parkinson's Disease

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Abstract

Objective—The purpose of this study was to examine predictors of treatment response to cognitive-behavioral therapy (CBT) for depression in Parkinson's disease (PD).

Methods—The sample comprised 80 depressed (DSM-IV criteria) adults with PD [60% male] and their caregivers who participated in an NIH-sponsored randomized-controlled trial of CBT vs. clinical monitoring from April 2007 until July 2010. Individually-administered CBT was provided to people with PD for 10 weeks, modified to address the unique needs of the medical population, and supplemented with up to 4 separate caregiver educational sessions. Treatment response was defined a priori as a rating of depression much improved or very much improved on the Clinical Global Impression-Improvement Scale or 50% reduction in the baseline Hamilton Depression Rating Scale score. It was hypothesized (a priori) that caregiver participation in treatment, motor disability, psychiatric comorbidity, and executive functioning would be significant predictors of response to CBT at end-of-treatment (week 10) and short-term follow-up (week 14).

Results—At week 10, caregiver participation was the only significant predictor of treatment response in the CBT group. At week 14, both caregiver participation and executive functioning predicted response to CBT. Treatment group, baseline depression severity, executive functioning,

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motor disability, psychiatric comorbidity, marital status, and caregiver burden were also related to change in depression scores, for all participants, in secondary and exploratory models.

Conclusions—Caregiver participation may enhance acute treatment response to psychosocial interventions for depression in PD. Further research is needed to extend and replicate these findings.

Keywords

Parkinson's disease; depression; cognitive-behavioral therapy; caregiver; predictors of treatment response

Parkinson's disease (PD) is a progressive neurodegenerative disorder characterized by tremor, rigidity, and bradykinesia. PD affects up to 1 million people in the United States and as many as 6 million individuals worldwide (National Parkinson Foundation, 2010). The majority of people with Parkinson's disease also experience non-motor complications such as depression, anxiety, sleep disturbance, psychosis, and cognitive changes (Weintraub & Burn, 2011). These neuropsychiatric features of the illness are larger determinants of disability and distress, for both people with PD and their family members, than are the physical aspects of the disease (Carter, Stewart, Lyons, & Archbold, 2008; Forsaa, Larsen, Wentzel-Larsen, Herlofson, & Alves, 2008).

Depression is the most frequently cited non-motor complaint in PD (Cummings, 1992). Affecting up to 50% of people with PD (Reijnders, Ehrt, Weber, Aarsland, & Leentjens, 2008), the incidence of depression in PD is more than double that observed in the general population and significantly higher than the rates reported in other medical conditions (Tandberg, Larsen, Aarsland, & Cummings, 1996). Depression in PD (dPD) may predate the onset of motor symptoms (Leentjens, Van den Akker, Metsemakers, Lousberg, & Verhey, 2003) and is often under-diagnosed (Shulman, Taback, Rabinstein, & Weiner, 2002) and inadequately managed by healthcare providers (Ravina et al., 2007). The sub-optimal treatment of dPD is of great clinical concern as depression is associated with more rapid physical and cognitive deterioration (Starkstein, Mayberg, Leiguarda, Preziosi, & Robinson, 1992), poorer quality of life (Forsaa et al., 2008), and increased caregiver distress in Parkinson's disease (Carter et al., 2008).

Despite these negative consequences of dPD, there is a paucity of controlled research to guide the treatment of this psychiatric complication. To date, pharmacological approaches for the treatment of dPD have received the most preliminary support (e.g., Menza et al., 2009). In contrast, little is known about the usefulness of psychosocial interventions for treating depression in the context of this comorbid medical condition. To the best of our knowledge, we recently conducted the first randomized-controlled trial (RCT) of cognitive-behavioral therapy (CBT) for depression in PD (Dobkin et al., 2011). In this RCT, we demonstrated that CBT was associated with notable improvements in depression, anxiety, coping, quality of life, and motor disability in people with PD, compared to clinical monitoring, over 14-weeks. Given the paucity of available research to guide the management of dPD, identifying factors that may facilitate depression treatment response in this medical population may have significant clinical implications.

The purpose of the current study was to examine predictors of treatment response to CBT for depression in PD. It was hypothesized (a priori) that caregiver participation in treatment, motor disability, psychiatric comorbidity, and executive functioning would be significant predictors of response to CBT at end-of-treatment (week 10) and short-term follow-up (week 14). These a priori predictors were selected for several reasons. First, the inclusion of family members in psychosocial interventions for chronic medical conditions has been

linked with improved patient outcomes across a range of physical illnesses versus usual care (Martire, Lustig, Schulz, Miller, & Helgeson, 2004). Second, estimates suggest that informal caregivers assist people with PD an average of 11 times per day in early PD and up to 30 times per day in later stage disease (Carter et al., 1998). The beneficial impact of caregiver involvement on mental and physical health in PD has been well demonstrated (e.g., Ravenek & Schneider, 2009). Third, in addition to the physical disability observed in this medical group, dPD is characterized by high rates of executive dysfunction (Santangelo et al., 2009) and psychiatric comorbidity (Menza, Robertson-Hoffman, & Bonapace, 1993), factors which have been associated with depression treatment response in older adults (Andresscu et al., 2009; Mohlman & Gorman, 2005; Weinberger, Raue, Meyers, & Bruce, 2009) and in the few pharmacologic studies that have examined these relationships in PD (e.g., Dobkin et al., 2010). The extent to which these a priori factors moderated treatment effects and predicted change in depression scores over time across both study treatments, as well as the degree to which demographic and clinical variables (previously linked with dPD) influenced improvement in this trial, were also examined.

Method

Participants and Procedures

The sample comprised 80 depressed (DSM-IV criteria; SCID-I) people with Parkinson's disease (PWP) [60% male, 40% female; 5% Asian, 1% African-American, 1% Pacific Islander, 3% Hispanic Caucasian, 90% Non-Hispanic Caucasian] and their caregivers (e.g., a family member or friend) who participated in a randomized-controlled trial of CBT vs. clinical monitoring (with no new treatment) for dPD at an academic medical center in the Northeast. Sixty-five PWP (81%) had primary Major Depressive Disorder; 45 (56.3%) had a secondary anxiety disorder diagnosis. The spouse was the identified caregiver in 62% of cases. Additional participant characteristics, study inclusion criteria, recruitment strategies, flow of participants through the trial, sample size and power calculations, as well as study treatments and procedures are described in detail in the main outcome paper from this trial (Dobkin et al., 2011).

In brief, the study had full IRB approval. Written informed consent was obtained prior to the initiation of any study procedures. As described by Dobkin et al. (2011), participants were allocated to receive CBT plus clinical monitoring ($N = 41$) or clinical monitoring alone ($N = 39$) by computer-generated random assignment. The 10-session individually-administered CBT protocol was tailored to the unique needs of the PD population and supplemented with up to four separate caregiver educational sessions. CBT was provided by doctoral level psychologists. All participants received close clinical monitoring of their depressive symptoms by study staff (four, two-hour, in-person assessments and two, 30-minute phone calls) and their personal physicians.

Measures

Depression outcome measures—The Hamilton Depression Rating Scale (HAM-D 17; Hamilton, 1960), Beck Depression Inventory (BDI; Beck, Rush, Shaw, & Emery, 1979), and the Clinical Global Impression-Improvement Scale (CGI-I; Guy, 1976) were used to assess depression severity and change. CGI-I ratings for depression in the current trial were determined not only by symptom change but also by the impact of that change on quality of life and daily functioning, based in response to a scripted interview standardized at the outset of the trial. Treatment response was defined a priori as a score of 1 (very much improved) or 2 (much improved) on the CGI-I or 50% reduction in the baseline HAM-D 17 score (Frank et al., 1991). This categorical construct of treatment response was the primary depression outcome of interest in the current paper.

Potential predictor measures—All potential predictors of treatment response and symptom change, except caregiver participation in CBT, were evaluated at baseline.

A priori model

Caregiver participation: The number of caregiver sessions attended were tabulated.

Motor disability: The Unified Parkinson's Disease Rating Scale (UPDRS; Fahn et al., 1987) is a 42-item clinician-administered scale used to evaluate the severity of PD symptoms. The motor subscale assesses key motor symptoms including bradykinesia, resting and action tremor, rigidity, postural instability and gait disorder. Higher scores indicate greater severity.

Psychiatric comorbidity: The number SCID Axis I diagnoses were tabulated.

Executive functioning: The Trail-making Test (TMT) is a timed neuropsychological test comprised of two parts (Bowie & Harvey, 2006). In Part A, the patient is asked to connect a series of consecutively numbered circles (1–25) in ascending order. In Part B, the patient must connect a series of numbered (1–13) and lettered (A–L) circles in ascending order while alternating between numbers and letters (i.e., 1-A-2-B-3-C, etc.). Parts A and B are timed separately. The time difference between parts B and A is a reflection of executive functioning.

Exploratory models

Demographic variables: Age, gender, marital status, highest level of education, race and ethnicity (per NIH guidelines), and work status were assessed.

Clinical variables: Information on the following clinical variables relevant to the treatment of dPD was also obtained: primary mood disorder diagnosis, length of the current depressive episode, number of past depressive episodes, current use of an antidepressant medication, number of past antidepressant medication trials, history of psychotherapy, comorbid medical conditions, age of PD onset, new onset of PD (in the past year), anxiety (Hamilton Rating Scale for Anxiety; Hamilton, 1959), caregiver burden (Caregiver Distress Scale; Cousins, Davies, Turnball, & Playfer, 2002), global cognition (Dementia Rating Scale Total Score; Mattis, 1988), and negative thoughts (Inference Questionnaire; Alloy & Abramson, 1999).

Results

Data was analyzed with SPSS Version 18. The a priori predictor model was separately examined at end-of-treatment (week 10) and short-term follow-up (week 14) on the following depression outcomes: 1) treatment response (yes/no) [primary outcome], 2) HAM-D ratings [secondary outcome], and 3) BDI scores [secondary outcome]¹. The primary outcome of treatment response was examined in the CBT group only with stepwise logistic regression. Secondary and exploratory² outcomes were tested with stepwise linear regression in the entire sample, controlling for treatment group and baseline score on each respective secondary outcome measure (HAM-D or BDI). We also tested the interaction (i.e., moderating effects) between treatment group and each a priori predictor (controlling for the main effects of each variable and baseline depression severity) on HAM-D and BDI

¹As caregiver participation is confounded with treatment arm (i.e., caregivers in the clinical monitoring group did not have the option to attend sessions), this variable was removed from the a priori model for analyses of secondary outcomes.

²Exploratory correlations between demographic and clinical factors that have been previously linked to dPD and each respective depression outcome measure (at weeks 10 and 14) were conducted. Variables that correlated with outcome at $p < .025$ were tested in exploratory regression models. Those that contributed unique variance above and beyond the a priori model (p levels $< .05$ adjusted via the Holm Method) were retained in the final exploratory models.

scores. All available participant data, coupled with a multiple imputation approach to missing data, was used to compute all reported statistics.

Recruitment and follow-up occurred between April 2007 and July 2010. Ninety percent of participants completed the study (88% in CBT; 92% in clinical monitoring) and treatment fidelity was high (Dobkin et al., 2011). Detailed results regarding predictors of treatment response to CBT and depression change over time (HAM-D and BDI) across both treatment conditions can be found in Table 1, Table 2, Table 3, and Table 4. In brief, stepwise logistic regression revealed that caregiver involvement accounted for significant variance [21% at week 10 ($p = .012$) and 25% at week 14 ($p = .008$)] in CBT response status. Moreover, results of stepwise linear regression suggested that treatment group, baseline depression severity, executive functioning, motor disability, psychiatric comorbidity, marital status, and caregiver burden also influenced change in depression scores over time across both study conditions, while executive functions (in addition to caregiver participation) were related to the short-term maintenance of treatment gains in the CBT group (as demonstrated by stepwise logistic regression). Of note, relationship to patient (i.e., spouse, friend) was also a significant predictor of week 14 HAM-D score when used in place of marital status in the exploratory model. Having a spouse involved in treatment was more beneficial than another family member or friend. No significant moderators of treatment effects were revealed.

Discussion

This was the first study to examine predictors of treatment response to CBT for dPD. Results suggest that caregiver participation in treatment may positively influence acute depression response to CBT in PD. While several additional factors (as described above) also predicted depression change over time for all participants, the effect sizes for these measures were small, relative to treatment group and baseline depression severity.

The findings from this study provide preliminary support for supplementing individually-administered CBT with a standardized caregiver educational intervention in the treatment of dPD. Further research is needed to determine if the impact of caregiver involvement is specific to CBT or if these results will generalize to any active treatment for depression in PD. However, the skills-based nature of treatment, the focus on tangible thoughts and behaviors, and the importance of homework and practice (i.e., behavioral experiments, cognitive restructuring) between sessions (and after therapy has ended) may make CBT especially well-suited for the inclusion of PD caregivers in treatment.

The study has several limitations. First, the sample size is modest by clinical trial standards and it is possible that additional variables of clinical relevance and moderators of treatment response would have been identified in a larger sample. Second, the specific mechanisms (i.e., practicing CBT skills, increased treatment adherence, non-specific factors) by which caregivers positively impacted patient outcomes cannot be elucidated from the current data. Third, because the follow-up period was limited to one-month, it is not possible to explore predictors of long-term outcomes or to identify patterns of relapse or recurrence in this medical population. Lastly, our results may not generalize to all individuals with dPD as the majority of participants were Caucasian and highly educated with no evidence of dementia.

In sum, despite the negative effects of depression in PD, there is a dearth of information available to guide clinical care. The results of the current study offer preliminary guidance regarding treatment strategies, such as caregiver participation, that may help to optimize the acute management of dPD. Further research is needed to extend and replicate these findings given the modest sample size and small effects observed across several outcome measures.

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References

- Alloy LB, Abramson LY. The Temple-Wisconsin Cognitive Vulnerability to Depression (CVD) Project: Conceptual background, design, and methods. *Journal of Cognitive Psychotherapy*. 1999; 13:227–262.
- Andreescu C, Lenze EJ, Mulsant BH, Wetherell JL, Begley AE, Mazumdar S, Reynolds CF III. High worry severity is associated with poorer acute and maintenance efficacy of antidepressants in late-life depression. *Depression and Anxiety*. 2009; 26:266–272. [PubMed: 19212971]
- Beck, AT.; Rush, AJ.; Shaw, BF.; Emery, G. *Cognitive Therapy of Depression*. New York, NY: Guilford Press; 1979.
- Bowie CR, Harvey PD. Administration and interpretation of the Trail Making Test. *Nature Protocols*. 2006; 1:2277–2281.
- Carter JH, Stewart BJ, Archbold PG, Inoue I, Jaglin J, Lannon M, Zoog K. Living with a person who has Parkinson's disease: the spouse's perspective by stage of disease. *Movement Disorders*. 1998; 13:20–28. [PubMed: 9452321]
- Carter JH, Stewart BJ, Lyons KS, Archbold PG. Do motor and nonmotor symptoms in PD patients predict caregiver strain and depression? *Movement Disorders*. 2008; 23:1211–1216. [PubMed: 18528898]
- Cousins R, Davies ADM, Turnball CJ, Playfer JR. Assessing caregiver distress: conceptual analysis and brief scale. *British Journal of Clinical Psychology*. 2002; 41:387–403. [PubMed: 12437793]
- Cummings JL. Depression and Parkinson's disease. *American Journal of Psychiatry*. 1992; 149:443–454. [PubMed: 1372794]
- Dobkin RD, Menza M, Allen LA, Gara MA, Mark MH, Tiu J, Friedman J. Cognitive-behavioral therapy for depression in Parkinson's disease: a randomized, controlled trial. *American Journal of Psychiatry*. 2011; 168:1066–1074. [PubMed: 21676990]
- Dobkin RD, Menza M, Bienfait KL, Gara M, Marin H, Mark MH, Tröster A. The impact of antidepressant treatment on cognitive functioning in depressed patients with Parkinson's disease. *The Journal of Neuropsychiatry and Clinical Neurosciences*. 2010; 22:188–195. [PubMed: 20463113]
- Fahn, S.; Elton, RL. UPDRS program members. Unified Parkinsons Disease Rating Scale. In: Fahn, S.; Marsden, CD.; Goldstein, M.; Calne, DB., editors. *Recent Developments in Parkinson's Disease*. Vol. 2. Florham Park, NJ: Macmillan Healthcare Information; 1987. p. 153-163.
- Forsaa EB, Larsen JP, Wentzel-Larsen T, Herlofson K, Alves G. Predictors and course of health-related quality of life in Parkinson's disease. *Movement Disorder*. 2008; 23:1420–1427.
- Frank E, Prien RF, Jarrett RB, Keller MB, Kupfer DJ, Lavori PW, Weisman MM. Conceptualization and rationale for consensus definitions of terms in major depressive disorder. *Archives of General Psychiatry*. 1991; 48:851–855. [PubMed: 1929776]
- Guy, W. *ECDEU Assessment Manual for Psychopharmacology*. Washington, DC: U.S. Department of Health, Education, and Welfare; 1976.
- Hamilton M. The assessment of anxiety status by rating. *British Journal of Medical Psychology*. 1959; 32:50–55. [PubMed: 13638508]
- Hamilton M. A rating scale for depression. *Journal of Neurology, Neurosurgery, and Psychiatry*. 1960; 23:56–62.
- Leentjens AF, Van den Akker M, Metsemakers JF, Lousberg R, Verhey FR. Higher incidence of depression preceding the onset of Parkinson's disease: a register study. *Movement Disorders*. 2003; 18:414–418. [PubMed: 12671948]

- Martire LM, Lustig AP, Schulz R, Miller GE, Helgeson VS. Is it beneficial to involve a family member? A meta-analysis of psychosocial interventions for chronic illness. *Health Psychology*. 2004; 23:599–611. [PubMed: 15546228]
- Mattis, S. Dementia Rating Scale. Odessa, FL: Psychological Assessment Resources; 1988.
- Menza M, Dobkin RD, Marin H, Mark MH, Gara M, Buyske S, Dicke A. A controlled trial of antidepressants in patients with Parkinson's disease and depression. *Neurology*. 2009; 72:886–892. [PubMed: 19092112]
- Menza MA, Robertson-Hoffmann DE, Bonapace AS. Parkinson's disease and anxiety: comorbidity with depression. *Biological Psychiatry*. 1993; 34:465–470. [PubMed: 8268331]
- Mohlman J, Gorman JM. The role of executive functioning in CBT: a pilot study with anxious older adults. *Behavioral Research and Therapy*. 2005; 43:447–465.
- National Parkinson Foundation. Parkinson's disease overview. 2010 Mar 30. Retrieved from <http://www.parkinson.org>
- Ravenek MJ, Schneider MA. Social support for physical activity and perceptions of control in early Parkinson's disease. *Disability and Rehabilitation*. 2009; 31:1925–1936. [PubMed: 19479519]
- Ravina B, Camicioli R, Como PG, Marsh L, Jankovic J, Weintraub D, Elm J. The impact of depressive symptoms in early Parkinson disease. *Neurology*. 2007; 69:342–347. [PubMed: 17581943]
- Reijnders MA, Ehrt U, Weber WEJ, Aarsland D, Leentjens AF. A systematic review of prevalence studies of depression in Parkinson's disease. *Movement Disorders*. 2008; 23:183–189. [PubMed: 17987654]
- Santangelo G, Vitale C, Trojano L, Longo K, Cozzolino A, Grossi D, Barone P. Relationship between depression and cognitive dysfunctions in Parkinson's disease without dementia. *Journal of Neurology*. 2009; 256:632–638. [PubMed: 19370301]
- Shulman LM, Taback RL, Rabinstein AA, Weiner WJ. Non-recognition of depression and other non-motor symptoms in Parkinson's disease. *Parkinsonism and Related Disorders*. 2002; 8:193–197. [PubMed: 12039431]
- Starkstein SE, Mayberg HS, Leiguarda R, Preziosi TJ, Robinson RG. A prospective longitudinal study of depression, cognitive decline, and physical impairments in patients with Parkinson's disease. *Journal of Neurology, Neurosurgery and Psychiatry*. 1992; 55:377–382.
- Tandberg E, Larsen JP, Aarsland D, Cummings JL. The occurrence of depression in Parkinson's disease: a community-based study. *Archives of Neurology*. 1996; 53:175–179. [PubMed: 8639068]
- Weinberger MI, Raue PJ, Meyers BS, Bruce ML. Predictors of new onset depression in medically ill, disabled older adults at 1 year follow-up. *American Journal of Geriatric Psychiatry*. 2009; 17:802–809. [PubMed: 19700952]
- Weintraub D, Burn DJ. Parkinson's disease: the quintessential neuropsychiatric disorder. *Movement Disorders*. 2011; 26:1022–1031. [PubMed: 21626547]

Table 1

Predictors of Treatment Response to CBT

Variables	M (SD)	Wald χ^2	df	Exp(B)	[95% CI]	P	Nagelkerke R^2 Change
Baseline UPDRS Motor Subscale	22.39 (9.99)	0.76	1	0.97	[0.90, 1.04]	.383	8%
Axis I Diagnoses (number)	1.88 (0.81)	0.49	1	0.72	[0.28, 1.81]	.482	1%
Trail-making test B-A Time (seconds)	82.15 (71.20)	3.37	1	0.99	[0.97, 1.00]	.067	4%
Caregiver Sessions Attended (number)	2.90 (1.42)	6.25	1	2.20	[1.18, 4.08]	.012	21%
Baseline UPDRS Motor Subscale	22.39 (9.99)	0.23	1	0.98	[0.91, 1.05]	.633	6%
Axis I Diagnoses (number)	1.88 (0.81)	0.21	1	1.24	[0.50, 3.09]	.648	1%
Trail-making test B-A Time (seconds)	82.15 (71.20)	4.74	1	0.98	[0.97, 1.00]	.029	7%
Caregiver Sessions Attended (number)	2.90 (1.42)	7.02	1	2.41	[1.26, 4.60]	.008	25%

Note. CI= confidence interval; UPDRS= Unified Parkinson's disease Rating Scale

Table 2

Hamilton Depression Rating Scale (HAM-D) A Priori Models

Variables	M (SD)	B [95% CI]	β	P	R ² Change
Treatment Condition		6.20 [4.57, 7.83]	.59	.000	37%
Baseline HAM-D Total	20.18 (4.27)	0.55 [0.35, 0.76]	.44	.000	18%
Week 10 Baseline UPDRS Motor Subscale Score	22.80 (9.51)	0.10 [0.02, 0.19]	.16	.046	2%
Axis I Diagnoses (number)	1.80 (0.92)	0.90 [-0.04, 1.85]	.15	.061	2%
Trail-making Test B-A Time (seconds)	91.61 (70.62)	0.01 [0.00, 0.02]	.16	.054	2%
Treatment Condition		5.66 [3.90, 7.43]	.50	.000	26%
Baseline HAM-D Total	20.18 (4.27)	0.88 [0.65, 1.11]	.66	.000	34%
Week 14 Baseline UPDRS Motor Subscale Score	22.80 (9.51)	0.03 [-0.08, 0.13]	.04	.623	0%
Axis I Diagnoses (number)	1.80 (0.92)	0.28 [-0.81, 1.37]	.04	.614	0%
Trail-making Test B-A Time (seconds)	91.61 (70.62)	0.00 [-0.01, 0.02]	.04	.662	0%

Note. CI= confidence interval; UPDRS= Unified Parkinson's disease Rating Scale; HAM-D= Hamilton Depression Rating Scale

Table 3

Hamilton Depression Rating Scale (HAM-D) Exploratory Models

Variables	M (SD)	B [95% CI]	β	P	R ² Change
Treatment Condition		6.13 [4.56, 7.70]	.58	.000	37%
Baseline HAM-D Total	20.18 (4.27)	0.51 [0.31, 0.71]	.40	.000	18%
Baseline UPDRS Motor Subscale Score	22.80 (9.51)	0.08 [−0.01, 0.17]	.14	.091	2%
Axis I Diagnoses (number)	1.80 (0.92)	1.06 [0.13, 1.98]	.18	.025	2%
Trail-making Test B-A Time (seconds)	91.61 (70.61)	0.01 [0.00, 0.02]	.16	.031	2%
Caregiver Burden	5.66 (3.75)	0.28 [0.07, 0.49]	.20	.008	4%
Treatment Condition		5.23 [3.48, 6.98]	.46	.000	26%
Baseline HAM-D Total	20.18 (4.27)	0.85 [0.63, 1.08]	.63	.000	34%
Baseline UPDRS Motor Subscale Score	22.80 (9.51)	0.03 [−0.06, 0.13]	.07	.497	0%
Axis I Diagnoses (number)	1.80 (0.92)	0.32 [−0.74, 1.38]	.05	.556	0%
Trail-making Test B-A Time (seconds)	91.61 (70.61)	0.00 [−0.01, 0.02]	.04	.606	0%
Marital Status		0.84 [0.17, 1.51]	.18	.014	3%

Note. CI= confidence interval; UPDRS= Unified Parkinson's disease Rating Scale; HAM-D= Hamilton Depression Rating Scale

Table 4

Beck Depression Inventory (BDI) A Priori Models

Variables	M (SD)	B [95% CI]	β	P	R ² Change
Treatment Condition		6.76 [3.70, 9.82]	.43	.000	20%
Baseline BDI Total	19.30 (7.97)	0.34 [0.15, 0.54]	.36	.001	12%
Week 10 Baseline UPDRS Motor Subscale Score	22.80 (9.51)	0.16 [-0.02, 0.33]	.18	.078	4%
Axis I Diagnoses (number)	1.80 (0.92)	0.94 [-0.87, 2.75]	.11	.309	1%
Trail-making Test B-A Time (seconds)	91.61 (70.61)	0.01 [-0.01, 0.03]	.10	.345	0%
Treatment Condition		3.72 [1.06, 6.39]	.26	.006	10%
Baseline BDI Total	19.30 (7.97)	0.46 [0.29, 0.63]	.51	.000	21%
Week 14 Baseline UPDRS Motor Subscale Score	22.80 (9.51)	0.13 [-0.02, 0.29]	.16	.085	5%
Axis I Diagnoses (number)	1.80 (0.92)	0.05 [-1.59, 1.68]	-.01	.957	0%
Trail-making Test B-A Time (seconds)	91.61 (70.61)	0.03 [0.01, 0.04]	.26	.011	5%

Note. CI= confidence interval; UPDRS= Unified Parkinson's disease Rating Scale; BDI= Beck Depression Inventory