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CBT for the treatment of depression in Parkinson's disease: A promising non-pharmacological approach

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Abstract

Depression is very common in PD and linked with a faster progression of physical symptoms, greater cognitive decline, and poorer quality of life. Non-pharmacological approaches, like cognitive-behavioral therapy (CBT), for the treatment of depression in Parkinson's disease (dPD) have received little experimental attention despite strong demonstrated efficacy in other geriatric and medical populations. Depressed PD patients often differ from the depressed non-PD elderly in that they present with increased rates of both executive dysfunction and co-morbid psychiatric diagnoses, may differ in their depressive symptom presentation, and typically have caregivers who are highly involved in their treatment. Therefore, it is not possible to conclude that empirically validated treatments in the depressed aged will generalize to those with Parkinson's disease. In order to be most effective for PD patients, CBT should be tailored to their unique needs. Additional controlled research is needed to further explore the efficacy of CBT for dPD.

Keywords

depression; Parkinson's disease; cognitive-behavioral therapy; non-pharmacological treatment

Introduction

Depression is very common in PD and linked with a faster progression of physical symptoms, greater cognitive decline, and poorer quality of life. Despite the fact that untreated depression accelerates the patients' disability in numerous domains, there is currently no evidence-based standard of care. Conclusions from scarce placebo-controlled trials that have evaluated the use of antidepressants (ADMs) for depression in Parkinson's disease (dPD) have been weakened by methodological and tolerability limitations. Similarly, non-pharmacological approaches for the treatment of dPD have received little experimental attention despite strong demonstrated efficacy in other geriatric populations [1,2].

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Cognitive-behavioral therapy (also known as CBT) is a type of psychotherapy that addresses behaviors and thought patterns that contribute to depression. CBT is a widely researched treatment that has been found to be very effective for treating depression in people without PD, including the elderly [1,2] and those with other physically disabling disorders [3,4,5,6]. However, there has been little work applying the cognitive-behavioral treatment approach to depression in Parkinson's disease. CBT has demonstrated efficacy for the treatment of depression when used alone [7,8,9,10] or in combination with antidepressant medication [11, 12]. Several comparison studies have also suggested that cognitive and behavioral interventions are as effective as antidepressant medications [13,14,15] and may be superior to medication for prevention of relapse of depressive symptoms [8,9,11,15,16]. A non-medication approach such as CBT may be a particularly useful option for PD patients who can't tolerate (i.e., had uncomfortable side effects), do not wish to take, or have not been sufficiently helped by antidepressant medication.

Depression and Parkinson's disease

Parkinson's disease (PD) is the second most common neurodegenerative disorder in the US [17]. Affecting approximately 500,000 – 1 million people [17], PD is a progressive illness that is associated with significant functional disability. Depression is the most frequently reported non-motor symptom in PD [18] and may present as major depressive disorder, dysthymia, or subthreshold symptoms that do not meet formal DSM-IV criteria for a depressive disorder [19], yet cause great distress and impairment. In addition, depression may co-occur with the motor "on-and-off" fluctuations frequently observed during dopaminergic treatment in PD patients. For example, some patients may experience mood fluctuations (i.e., brief periods of dysphoria or anxiety) in conjunction with motor fluctuations or "off time" (i.e., intermittent periods throughout the day when their motor symptoms are not well controlled by the anti-parkinson's medications- usually resulting from long term use of levodopa) [20,21,22].

While a wide range of statistics have been reported regarding the prevalence of depression in PD (i.e., depending on the type and setting of the assessment, definition of depression used), it has been suggested that some form of depression may affect up to 50% of patients [23,24, 25,26]. Early-onset PD may be a risk factor for depression [27] while research regarding the relationship between PD severity and depression has yielded mixed results [27,28,29]. Depression in PD (dPD) may precede the onset of motor symptoms [30], is often under-detected by medical professionals [31], and warrants significant attention from clinicians as it is related to a faster progression of physical symptoms, greater cognitive decline, poorer quality of life, increased caregiver burden, and decreased ability to care for oneself [32,33,34,35,36].

Despite these established pernicious effects, there is a dearth of well-designed research that can guide clinical care for these patients. Although some placebo-controlled studies have suggested that antidepressants may be beneficial for PD patients, conclusions have been weakened by methodological shortcomings [37]. Limitations include small sample size, low power, inadequate dosing, use of assessment tools with undocumented reliability and validity, inclusion of medically unstable patients, and lack of consideration of symptom overlap between depression and PD. In addition, a recent meta-analysis of limited studies suggests that antidepressants may not be as helpful for PD patients as they are for the non-PD depressed aged [38]. Several NIH sponsored clinical trials, including one at our site, are currently being conducted to further elucidate the efficacy of ADMs for dPD. Nevertheless, a paucity of empirical support regarding the efficacy and tolerability of antidepressant treatment in the PD population is currently available.

Similarly, there has been a paucity of investigations regarding non-pharmacological treatments for dPD. Deep brain stimulation (DBS) is often used as a late therapeutic option in the treatment

of PD when motor symptoms can not be adequately controlled with medication alone [39]. In addition to improving motor function, some studies have also found DBS to be associated with improvements in mood and depression [40,41,42]. The results of these studies are equivocal, however, as some reports have demonstrated adverse reactions, including significant worsening of depressive symptoms and suicidal ideation [41,43,44] and inducement of mania [45,46,47]. In addition, a randomized, controlled trial of Qigong exercise showed decreases in depression scores in both the control and treatment group, although those in the treatment group did experience a greater improvement in motor symptoms [48]. Two exploratory studies of bright light therapy for dPD, one of which was a randomized placebo-controlled double blind study, have demonstrated moderate improvement in depressive symptoms [49,50], but further research is necessary to replicate these findings.

The application of cognitive-behavioral therapy to the treatment of dPD has also received little experimental attention. To date, only one published pilot report (with a comparison condition) has examined the helpfulness of cognitive therapy for depressed PD patients. As participants were not randomly assigned to treatment condition, endorsed very mild depressive symptoms at baseline, and had comparison groups that were unequal in size, only very limited conclusions may be drawn from this study [51]. An uncontrolled 15-patient pilot study [52] and several case reports have also documented the feasibility of CBT for dPD [53,54]. Moreover, an eight-session group educational program for PD patients and their caregivers that introduced many of the skills covered in CBT, such as self-monitoring, stress management, dealing with negative thoughts, and appropriate use of social supports, was pilot tested with 36 participants [55]. While the program yielded short-term improvements in global ratings of mood, no significant effects on depression or quality of life were observed and it is unclear if patients with formal diagnoses of depression were enrolled [55]. Although educational programs have great merit, they are more diffuse by nature than individualized cognitive-behavioral therapy programs designed to treat patients with mood disorders.

This site is currently conducting a large study sponsored by the National Institutes of Health, to examine the impact of cognitive-behavioral therapy on major and minor depressive episodes, as well as dysthymia, in patients with Parkinson's disease. Eighty PD patients without evidence of dementia, psychosis, or significant motor fluctuations (i.e., "off" greater than 50% of waking hours) will be randomized to receive either 10 weeks of CBT or 10 weeks of standard medical care under the supervision of their personal physicians. Secondary outcomes regarding anxiety, sleep, motor function, quality of life, appropriate use of social supports, coping, dysfunctional attitudes, and cognitive functioning will also be explored. Additional trials of this nature are also in progress at other academic medical centers. Further research support for a cognitive-behavioral intervention for depression in PD would not only provide clinicians with one additional treatment option for their patients, but it would also meet a significant need for people living with PD who have expressed an interest in alternative treatments to help them cope with the unique cognitive, physical, and psychosocial issues that they face [101]. For example, in a recent psychosocial needs assessment, 65% of PD patients reported that they desired counseling to help them cope with their illness [56]. In a separate study conducted in a multidisciplinary clinic, 95% of patients sampled requested to speak with a mental health professional in order to deal with PD related concerns [57]. Empirically validated psychotherapies, such as CBT, are greatly needed to guide these efforts. The distinctive aspects of depression in Parkinson's disease, including executive dysfunction, psychiatric complexity, and highly involved caregivers, as well as how CBT can best be tailored in order to meet these needs, are further addressed below.

Expert Commentary

Unique features of dPD

Executive dysfunction—Evidence of marked frontal lobe impairment (i.e., problems with anticipation, planning, and the regulating and directing of purposeful behavior) [56] is frequently seen in PD. Difficulties with memory, attention, and language are also common in PD and are frequently aggravated by depression [8,59,60,61,62]. This widespread cognitive impairment has been noted despite the absence of clinically significant cognitive decline [8]. Some research has suggested that cognitive deficits may predict non-response to pharmacologic treatment, increased disability, relapse, and recurrence [63,64,65].

CBT (based on Beck et al., 1979) [66] has clearly defined treatment goals, incorporates agenda items for each session, applies concrete skills to address emotional concerns, and focuses on problematic thoughts and behaviors that are within the patients' range of conscious awareness. This structure and format of treatment may prove especially helpful to patients with problems initiating, organizing, and monitoring goal-directed activities as a result of frontal lobe dysfunction. CBT for dPD can also incorporate several behavioral strategies to facilitate memory retention (e.g., use of planners, handouts, audiotapes, streamlined presentation of information, reinforcement by the caregiver) more intensely than have been applied in the non-PD elderly, with the hope of enhancing treatment outcome. Preliminary functional imaging also suggests that CBT may result in significant metabolic changes in the cortical-limbic pathways that may positively impact several of the aspects of cognitive functioning that are aggravated by depression in PD [67]. Other research groups have also highlighted the importance of considering executive functioning when implementing CBT to treat psychiatric disturbances in PD [68], as well as in the non-PD aged [69].

Psychiatric complexity—In contrast to the non-PD depressed aged, PD patients report higher levels of somatic symptoms, anxiety, fatigue, sleep disturbance, pessimism and irrationality [8,70]. They also tend to be more psychiatrically complicated with high rates of co-morbid anxiety and depressive disorders found in this population [71,72,73]. The impact of co-morbid anxiety and depression on the course and treatment of PD is unclear. However, some have suggested that this psychiatric comorbidity in PD is linked with greater chronicity of depression, treatment resistance to depression interventions, increased rates of cognitive decline, decrements in quality of life, poorer PD prognosis, and greater PD symptom severity [74,75,76].

Because this unique symptom presentation affects quality of life, disease prognosis, and treatment response, it follows that a cognitive-behavioral treatment package for dPD should be tailored in the following ways. Relaxation techniques, which typically receive limited attention in depression treatment protocols, can be incorporated throughout treatment to more thoroughly address anxious mood, somatic symptoms, and insomnia. Additional attention can be directed to behavioral strategies for managing fatigue, such as increasing daily exercise, the pacing of daily activities, and setting realistic and achievable daily goals. A more intensive emphasis can be placed on behavioral activation in order to help patients increase and/or maintain their involvement in meaningful activities. Sleep hygiene techniques can be thoroughly addressed throughout treatment, given the high rate of insomnia in this population. In addition to the traditional cognitive restructuring that is conducted in the patient's individual treatment sessions, a supplemental caregiver educational program (described further below) can be implemented to help address patients' pessimism and irrational beliefs.

Social support and the role of the caregiver—PD patients often have a caregiver or support person that is intimately involved in their treatment. While it has been well documented that social support buffers against the development of depression [77], it is also important to

note that depression may lead to a deterioration of social support over time [78]. Specifically, there are negative types of social interactions that have been identified in the literature (e.g., criticism, rejection, minimizing worries and concerns), that are risk factors for the onset and maintenance of depressive symptoms [79]. These benefits and detriments of social interactions have been well documented in PD.

With family relationships often affected early in the illness, caregivers of PD patients often perceive high levels of personal burden due to the progressive nature of the disease [24]. Depression and other psychiatric disturbances in the patient have been identified as the strongest and most consistent predictors of caregiver distress [80,81]. Caregiver burden significantly increases the risk that caregivers will offer negative social feedback, exacerbating the patients' symptoms of both PD and depression [82,83,84]. Conversely, positive social support has been linked to improved coping [85], as well as less disability, depression, and anxiety in the PD population [86,87], even when controlling for disease severity [88].

Contact with the patients' family members often occurs within the cognitive-behavioral treatment framework (with the patients' permission). Thus, CBT has the ability to incorporate a standardized approach for working directly with caregivers, as one component of the PD patient's treatment, with the dual intent of alleviating the patients' depression and reducing caregiver burden. Such a program can provide caregivers with specific techniques for responding to the patient's negative thoughts in a constructive manner, thereby targeting two specific risk factors for depression (the patient's negative thoughts and the extent to which caregivers support or refute those thoughts) [89,90]. CBT can also teach friends and family members effective ways to offer social support in times of stress, as well as to reinforce the new coping skills that patients are trying to develop as part of their individualized treatment program.

Use of CBT to Target Specific Symptoms of dPD

Depression in PD may be characterized by any combination of the following symptoms: sad, low, or irritable mood, feelings of guilt, agitation, helplessness, or hopelessness, loss of interest in activities or other people, decreased motivation to get things done, sleep problems (i.e., difficulties falling or staying asleep, waking up too early, sleeping too much), appetite changes (i.e., loss of desire for food, decreased enjoyment from eating, forcing oneself to eat, overeating), problems with memory and concentration, feelings of fatigue or low energy, weight loss or gain, and most seriously, thoughts that life is not worth living. Even though there may be symptom overlap between the medical diagnosis of PD and the psychiatric diagnosis of depression (i.e., somatic symptoms such as insomnia, slowness of movement and thought, weight loss, and fatigue are common to both disorders) experts recommend using an inclusive approach in the evaluation and treatment of dPD [19]. Thus, all overlapping symptoms should be counted towards a diagnosis of depression, assuming the presence of low mood or loss of interest (necessary criteria for the diagnosis of major depression or dysthymia) and the DSM-IV diagnostic exclusion criteria of not counting symptoms towards a psychiatric diagnosis that may be "due to a general medical condition" should be disregarded when assessing for dPD. While this "inclusive" approach favors sensitivity of the diagnosis over specificity, it increases the likelihood that dPD will be appropriately identified and treated. Moreover, if cognitive symptoms of depression such as low mood, loss of interest, feelings of guilt, worthlessness, helplessness, or hopelessness, or suicidal ideation are present, it is likely that at least some of the variance in the somatic symptoms common to both PD and depression are accounted for the mood disorder.

While the exact cause of depression in PD can not be neatly pinpointed, the high incidence of depressive symptoms in this population likely results from the interaction of neurodegeneration, and how patients and families think, feel, and react to living with this

medical condition. It is also important to note that even for patients with depression of a hypothesized neurochemical etiology, addressing the behavioral and cognitive sequelae of this phenomenon can prove helpful [40].

Therefore, several different CBT strategies (based on Beck et al., 1979; Lewinsohn et al., 1986) [40,91,92] can be used to help PD patients cope more effectively with the numerous symptoms of depression described above, as well as with the daily stress of living with PD. Examples described below were derived from a past pilot study conducted by our group [28]. CBT can help people develop strategies to increase their involvement in meaningful, pleasurable, and/or social activities, as well as ways to safely increase daily exercise. In doing so, it is important to help patients recognize that just because they might need to modify the manner in which they participate in certain tasks, it is critical for them to increase, rather than decrease, the amount of time they spend in structured activities that they find rewarding. Beginning volunteer work, increasing time with grandchildren, painting, and photography are just a few examples of activities that PD patients in past studies have utilized to help cope with depression. CBT can help individuals to problem-solve about their physical limitations (i.e., order ziti in a public restaurant if they have difficulty cutting meat; walk for 10-minutes three times a day, instead of 30 minutes at one time), as well as address barriers to medication adherence (i.e. use of external reminders such as watch or cell-phone alarms that improve compliance to dopaminergic replacement regimens). Problem-solving can also be conducted to help patients appropriately pace daily activities, set more realistic daily goals, place less rigid demands on themselves, and to identify coping skills to be utilized during “off-time.”

CBT can also help PD patients maximize control over their emotional reactions to stressful life circumstances through the development of healthier ways of dealing with negative feelings such as sadness, irritability, anxiety, and anger. For example, patients are taught techniques for catching, labeling and re-evaluating negative thoughts that lead to increased depression. Thoughts regarding excessive disability, feelings of dependency, burden, loneliness, isolation, lack of intimacy, and loss of control were a main target of treatment. CBT can also help patients to modify their maladaptive cognitive and behavioral responses to physical symptoms. For example, the following excerpt details the way in which cognitive restructuring techniques helped a patient who viewed himself as “helpless” when he experienced freezing to re-evaluate the situation.

Situation: Freezing in the bathroom

Automatic Thought: I’m helpless

Evidence For: I was alone in the bathroom in the middle of the night and unable to move.

Evidence Against: This happens quite a bit, so I planned in advance. I had my cell phone in my pocket. I called my wife on the house phone and she helped me back to bed.

Rationale Response: Even though I was physically unable to move my feet, I was able to help myself out of the situation (thus I am not helpless).

In order to help patients manage insomnia, good sleep habits can be reviewed and incorporated into the patient’s routine. Specifically, daily exercise, relaxing before bedtime, keeping regular sleep hours (i.e., going to bed and getting up at the same time everyday), and avoiding excess time in bed, daytime naps, caffeine or alcohol in the evening, and large evening meals may be helpful. And most importantly, individuals suffering from insomnia are taught to only use their bed for sleep and not for other activities such as paying bills, watching TV, or trying to solve the problem of the day. Finally, relaxation techniques such as diaphragmatic breathing,

progressive muscle relaxation, and guided visualization can be sequentially introduced into the treatment in order to target both somatic and emotional symptoms of anxiety.

It should be noted that techniques described above represent an overview of strategies that may prove helpful for Parkinson's patients who present with major depression, dysthymia, as well as subthreshold symptoms. As variability does exist in depressive symptom presentation between PD patients, the CBT techniques employed in any given treatment plan should be selected to address each patient's specific needs. For example, it might not be reasonable to encourage patients who follow a healthy exercise regimen to modify their workout routine. Finally, it should be noted that appropriate training in CBT and sufficient knowledge of PD are necessary prerequisites to the successful implementation of this treatment approach. See Table 1 for a breakdown of specific CBT techniques that can be used to target each specific symptom of dPD.

Summary and Conclusions

Depressed PD patients often differ from their non-PD counterparts in that they present with increased rates of both executive dysfunction and co-morbid psychiatric diagnoses, may differ in their depressive symptom presentation, and typically have caregivers who are highly involved in their treatment. Therefore, it is not possible to conclude that empirically validated treatments in the depressed aged will generalize to those with Parkinson's disease. Unique modifications may need to be made to maximize treatment response in this population. These modifications include a more intensive focus on behavioral activation, relaxation training, and sleep hygiene throughout the course of treatment than typically occurs in traditional CBT protocols, the development of standardized procedures to help caregivers refute the patients' pessimistic thoughts, facilitate behavioral changes, and reinforce the application of all newly acquired coping skills, the streamlined presentation of study material, and the application of behavioral strategies to help patients organize their thoughts and facilitate memory retention more intensively than have been applied in the non-PD depressed elderly. Given the physical and emotional costs of depression in PD and the uncertainty as to the tolerability and effect of medication treatments as highlighted above, the need for an efficacious non-pharmacological approach, such as cognitive-behavioral therapy, seems paramount.

CBT incorporates a variety of techniques that can specifically target each of the depressive symptoms that PD patients may experience and may help patients cope more effectively with the complications of chronic therapy. CBT has been shown to be an effective treatment for depression in the aged as well as for those with comorbid medical conditions. Through the targeting of problematic thoughts and behaviors, CBT has the potential to help PD patients cope most effectively with the physical, psychosocial, and cognitive aspects of their medical condition- a need of great importance to both patients and families. Additional controlled research is needed to further explore the efficacy of this approach for dPD.

5-year view

Over the next five years, we will learn the results of several randomized controlled trials designed to evaluate the efficacy of CBT for dPD. Predictors of treatment response, such as age of onset, executive dysfunction, motor disability, and social support, to non-pharmacological interventions like CBT will be identified. More conclusive scientific data regarding the safety, efficacy, and tolerability of antidepressants for the treatment of dPD should also be available and the benefits of combination treatment (CBT and ADMs) versus monotherapy will be explored. If the efficacy of CBT for dPD is established, it will be critical to identify effective strategies for making the treatment readily available and accessible within the PD community. Towards this end, it may prove beneficial to train nurses and social workers to provide the treatment both in movement disorders clinics as well as to establish a mechanism

for the treatment to be delivered at the patients' homes (for those who are unable to travel). We will also see the development of specialized CBT treatment protocols for other disabling non-motor symptoms in PD, such as anxiety and sleep.

Key issues

- Depression in PD is associated with significant disability and distress
- There is currently no evidence based standard of care for dPD
- CBT holds promise as a non-pharmacological intervention
- CBT addresses problematic thoughts and behaviors that contribute to depression.
- CBT has the potential to help PD patients cope more effectively with physical, emotional, and cognitive aspects of their medical condition.
- CBT should be tailored to meet the unique needs of PD patients.
- Additional controlled research is needed to further explore the efficacy of cognitive-behavioral therapy for depression Parkinson's disease

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Table 1
CBT strategies to target specific symptoms of dPD

Depressed Mood	<ul style="list-style-type: none"> • Behavioral activation • Increasing meaningful and pleasurable activities • Cognitive restructuring • Mobilizing social supports
Loss of interest	<ul style="list-style-type: none"> • Behavioral activation • Increasing meaningful and pleasurable activities • Setting realistic and achievable daily goals • Problem-solving for physical limitations
Insomnia	<ul style="list-style-type: none"> • Relaxation techniques • Review and incorporation of sleep hygiene approaches • Increasing meaningful and pleasurable activities
Appetite changes	<ul style="list-style-type: none"> • Planning for weekly meals to include favorite foods • Scheduling of daily meals and snacks • Problem-solving for physical limitations • Identifying emotional triggers to over/under eating and generating an appropriate alternative response • Substituting unhealthy food choices with healthier selections
Fatigue	<ul style="list-style-type: none"> • Increasing daily exercise • Pacing of daily activities • Review and incorporation of sleep hygiene approaches • Setting realistic and achievable daily goals
Guilt/worthlessness	<ul style="list-style-type: none"> • Cognitive restructuring
Concentration	<ul style="list-style-type: none"> • Focusing on one task at a time • Appropriate pacing of daily activities • Setting realistic and achievable daily goals
SI	<ul style="list-style-type: none"> • Cognitive restructuring