RESEARCH ARTICLE

Interpersonal Psychotherapy for the Treatment of Depression in Parkinson's Disease: Results of a Randomized Controlled Trial

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ABSTRACT: Background: Depression is a common nonmotor complication in Parkinson's disease (PD). However, few studies have evaluated the efficacy of first-line psychological therapies for depression in this patient population.

Objectives: This randomized controlled trial evaluated the efficacy of interpersonal psychotherapy (IPT), an empirically validated intervention for depression that focuses on the bidirectional relationship between mood disturbance and interpersonal and social stressors. A secondary aim was to assess maintenance of treatment gains at 6-month follow-up.

Methods: Participants with PD stages I to III and a comorbid depressive disorder were randomly assigned to 12 sessions of IPT (n = 32) or supportive therapy (ST) (n = 31), our active control intervention. The primary outcome was the Hamilton Depression Rating Scale (HAM-D) administered blindly by telephone. Secondary outcomes included self-report depression and anxiety, quality of life, clinician-rated motor symptom, interpersonal relationships, and attachment style.

Results: IPT compared to ST resulted in a greater reduction in posttreatment HAM-D scores (least square mean difference = −3.77, 95% confidence interval [CI]: −6.19 to −1.34, $P = 0.003$) and was associated with a greater odds of meeting remission (odds ratio = 3.23, 95% CI: 1.10–9.51, $P = 0.034$). The advantage of IPT over ST on HAM-D scores and remission rates was not sustained at the 6-month follow-up. Both treatments improved self-report depression, anxiety, quality of life, and aspects of interpersonal functioning.

Conclusions: This trial demonstrates the benefits of acute treatment with IPT in reducing depressive symptoms in PD. Clinicians should consider psychotherapy, alone or in combination with medication, as an important treatment option for PD depression.

Key Words: Parkinson's disease; depression; psychotherapy; interpersonal psychotherapy; randomized controlled trial

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Depression is a common neuropsychiatric complication of Parkinson's disease (PD).[1] Depression in the context of PD is consequential[2-5] and an important predictor of poor quality of life.[6] Antidepressant medication is the mainstay approach for treating depressed PD patients because of an emphasis on neurobiological factors in the development of depressive symptoms.[7,8] However, antidepressant medications have limitations, and they do not address psychosocial factors that contribute to mood disturbance.[9] As well, PD patients attribute the cause of their mood disturbance to psychosocial rather than biological factors and have a preference for psychotherapy over pharmacotherapy.[10] Despite this favorable view toward psychotherapy, research on the safety and efficacy of psychosocial interventions for PD depression remains sparse.

Several evidence-based brief psychotherapies are available for the treatment of depression in the general population.[11] Among these, cognitive behavior therapy (CBT), which emphasizes the relationship between cognitions, emotions, and behaviors, is effective for PD depression.[12] Interpersonal psychotherapy (IPT) is another robust first-line treatment for depression.[13] IPT uses a medical model approach, and its central premise is that there is a bidirectional relationship between mood disturbance and psychosocial stressors, notably the death of a loved one, difficulty adjusting to life changes and role loss, conflict and disappointments in important relationships, and social isolation and loneliness.[14-16] Reduction in depressive symptoms is achieved by helping patients resolve the interpersonal stressor that is central to their mood disturbance.

IPT may be a suitable treatment for PD depression because PD results in loss and disruption in health, valued social roles and activities, future plans, and self-identity, and can present significant challenges to close relationships.[17,18] Social isolation, loneliness, loss of network supports and attachments due to death, relocation, and other circumstances are also relevant.[19,20] IPT's focus on cultivating and strengthening supportive relationships is important because living with a chronic illness is stressful, and supportive relationships can mitigate the negative effects of stress[21] and positively impact patient health, quality of life, and emotional well-being.[22-24]

We conducted the first feasibility trial of IPT adapted for PD and found that the therapy was well accepted and tolerated by patients.[25] IPT improved depressive symptoms, with half of the participants achieving remission at endpoint. PD quality of life also improved. These findings are encouraging, but a larger trial is needed to determine IPT's efficacy for PD depression.

Patients and Methods

The study was a single-site, prospective, evaluator-blinded, randomized clinical trial comparing the efficacy of IPT to nondirective supportive therapy (ST). The primary aim of the trial was to determine whether 12 sessions of IPT was superior to ST for PD depression. We also assessed whether treatment gains were maintained at 6-month follow-up. We chose ST as our control condition because it was frequently used in psychotherapy research to control for "nonspecific" or common ingredients that are central to all forms of psychotherapies and that contribute to patient improvement, such as therapist attention, opportunities for catharsis, and instilling expectancy for improvement.[26] Although ST can yield considerable clinical benefits in depressed medically ill patients,[27,28] it provides a rigorous test of whether IPT has specific effects in reducing depressive symptoms over and beyond common therapeutic factors. The trial was registered at ClinicalTrials.gov (ID: NCT02552836).

Participants

Participants were recruited from a large movement disorders clinic between May 2016 and January 2023, with a 4-month pause in recruitment due to the COVID pandemic in 2020. The study was approved by the Ottawa Health Science Network Research Ethics Board (20150743-01H) and the Montfort Hospital Research Ethics Office (DK-04-07-16), and all participants provided written informed consent. To be included in the study, participants had to have idiopathic PD with Hoehn and Yahr stages I to III[29]; be on a stable dose of dopaminergic replacement, or if not currently on dopamine replacement therapy, assessed as not likely to require therapy for at least 12 weeks; live independently at home or a retirement facility; meet the *Diagnostic and Statistical Manual of Mental Illnesses*, edition 5, criteria for a depressive disorder (major depressive episode or persistent depressive disorder) confirmed by structured interview[30]; and obtain a score ≥12 on the 17-item Hamilton Depression Rating Scale (HAM-D)[31] at baseline visit.

Exclusion criteria were substance misuse in the past 12 months, current or past psychosis and bipolar disorder, and high suicide risk. Other psychiatric disorders were allowed so long as the depressive disorder was the primary presenting complaint. Participants with a score ≤ 24 on the Mini-Mental State Exam[32] and those with other significant neurological problems, unstable comorbid medical conditions, and poor hearing acuity that could affect communication in therapy were also excluded. Concurrent treatment with psychotherapy or counseling was proscribed, but concurrent use of

psychotropic medications was allowed if the medication type and dose remained stable for 8 weeks prior to starting treatment.

Treatment Allocation and Masking

Participants were randomly allocated to the interventions in a 1:1 ratio. An independent statistician generated the allocation schedule using a randomly permuted block design with randomly varying block lengths of 2, 4, or 6. A centralized randomization system was used to ensure treatment allocation concealment. The study was designed to evaluate face-to-face therapy, with some virtual sessions allowed if attendance was difficult due to poor health, transportation problems, or caregiver burden. However, due to COVID-related public health restrictions participants who started face-to-face therapy were switched to virtual sessions, and the remainder of participants who were recruited for the study received all of their sessions virtually.

The 17-item HAM-D, our primary efficacy measure, was administered by telephone by clinical raters who were blind to treatment allocation. A standard procedure was adopted for the assessment. If the blind was inadvertently broken, the participant was switched to a different rater.

Intervention

Interpersonal Psychotherapy

Participants received 12 50-minute therapy sessions. Treatment was based on the IPT manual of Weissman et al,[33] with some modifications made to meet the needs of PD patients. These modifications are described in detail elsewhere.[25] The therapy is semistructured and has three phases (beginning, middle, and termination), with each phase involving specific tasks and strategies. Similar to all psychotherapies, common factors, particularly the therapeutic alliance, play a key role in IPT's success. Although IPT is designed as a one-to-one therapy, occasional joint sessions with close members of the patient's social network are allowed. Participants were encouraged to invite a primary support person to up to two joint sessions. These sessions were intended to educate the support person about PD depression, explore ways they can support the participant, and discuss challenges they may face as a primary support person.

Supportive Therapy

ST was similar to IPT in number and duration of sessions. Unlike IPT, ST is nondirective and unstructured, and it does not use a medical model illness or target specific social and interpersonal problems that contribute to mood disturbance. The therapy did not include a joint session with a support person. The goal of ST is to reduce symptoms, restore and bolster self-esteem and self-confidence, and promote adaptive coping with life challenges.[28] The ST used in the current study emphasized a common factors therapeutic approach described in previous research,[34,35] focusing on the therapeutic alliance as a vehicle for patient improvement and use of general therapist skills such as empathic listening, encouraging expression of affect, and helping the patient feel understood. Therapists also provided psychoeducation about depression and encouraged adherence to treatment and lifestyle recommendations for PD. Therapists were instructed not to engage in therapeutic strategies that overlap with IPT or use techniques that are unique to other psychotherapeutic approaches. A treatment protocol outlined general techniques and skills used in ST.

Study Therapists and Treatment Fidelity

Therapists were master's (n = 3) and doctoral (n = 4) level licensed clinicians. All the study therapists had knowledge of and skills in common factors prior to participating in the study. Therapists were trained in the respective treatments and supervised throughout the trial by the principal investigator. Therapy sessions were audio-recorded and reviewed to ensure therapist treatment adherence throughout the trial.

Outcome Measures

The 17-item HAM-D[31] was administered at baseline, sessions 6 and 12, and 6-month follow-up. The HAM-D is the most widely used primary outcome in clinical trials of depression. It assesses the core symptoms of depression, is sensitive to change in psychosocial interventions for PD depression,[36-38] and can be administered centrally by phone interview to improve reliability.[39] A semistructured version of the scale was used.[40] The self-report Beck Depression Inventory-II (BDI-II)[41] was used as a secondary measure of depression, with higher scores reflecting greater symptom severity. The BDI-II is frequently used as a complementary measure to the HAM-D in clinical trials because it assesses subjective experiences and includes items related to cognitive symptoms of depression (eg, self-dislike, self-criticalness).[42] Other secondary clinical outcomes included remission, defined as a score ≤7 on the HAM-D and the self-report Beck Anxiety Inventory (BAI),[43] with higher scores reflecting higher levels of anxiety. The BDI-II and BAI were administered at baseline, sessions 6 and 12, and 6-month follow-up.

Quality of life was assessed using the 39-item Parkinson's Disease Questionnaire (PDQ-39),[44] which assesses eight distinct dimensions. We used the PDQ-39-Summary Index (PDQ-39-SI) as a secondary outcome, with higher scores reflecting poorer quality of life. The individual dimensions of the PDQ-39

were also analyzed to explore which dimensions improved with treatment. The Movement Disorders Society-Unified Parkinson's Disease Rating Scale (MDS-UPDRS)[45] was used to evaluate PD motor symptoms, with higher scores reflecting more severe symptoms. This scale was administered by clinicians who were blind to treatment assignment. The PDQ-39 and MDS-UPDRS were administered at baseline, session 12, and 6-month follow-up.

To assess the impact of treatment on interpersonal functioning, we used the Interpersonal Relationships Inventory (IPRI)[46] that measures three dimensions of interpersonal relationships: social support, reciprocity, and conflict. Sum scores for each subscale as well as standard means are reported. Higher scores reflect higher levels of perceived social supports, reciprocity, and conflict. The Experiences in Close Relationships Scale-Revised (ECR-R)[47] was used to assess attachment anxiety and attachment avoidance in adult relationships. High scores on attachment anxiety reflect concern about the availability and responsiveness of close relationships, and high scores on attachment avoidance reflect a discomfort with closeness and dependence on others. Sum scores for each subscale as well as standard means are reported. These scales were administered at baseline, session 12, and 6-month follow-up.

Additional measures included the self-report Activities of Daily Living section of the MDS-UPDRS,[45] which was administered at baseline to assess motor aspects of experiences in daily life at baseline.

Sample Size Calculation

Sample size calculation was based on our pilot work on IPT for PD depression. We considered a three-point difference between the groups at posttreatment to be clinically significant (ie, a standardized difference of 0.60). This is comparable to the standardized difference of 0.70 used to calculate the equivalent sample size in Dobkin et al's[37] randomized controlled trial (RCT) of CBT for PD depression. After having accounted for correlation ($r = 0.5$) with the baseline measure in the analysis of covariance analysis, we needed to recruit 68 participants (34 per group) to detect this difference with 80% power using a two-sided test at the 5% level of significance. Assuming a dropout rate of about 15%, our recruitment target was 80 participants. However, due to recruitment challenges we were able to recruit 63 participants.

Data Analysis

Baseline characteristics in the treatment and control arms were described using mean and standard deviation (SD) and frequency and proportion. Analyses of efficacy were by intent to treat (ITT), with all randomly assigned patients included in all analyses. Repeated measures of the primary and secondary continuous outcomes from baseline to 6-month follow-up were analyzed using general linear models, with treatment group, time, and interaction specified as independent variables. The models were estimated using restricted maximum likelihood, and degrees of freedom were computed using the between-within approximation. Suitable covariance structures to account for correlation among repeated measures over time, that is, exchangeable, Toepliz, autoregressive, spatial power, or unstructured, were identified using information criteria (Akaike information criterion and Bayesian information criterion). Within this framework, all available observations of each patient were included in the analysis without having to use an imputation procedure such as last-observation carried forward. To explore whether transitioning to virtual sessions affected our primary outcome, the aforementioned analysis was performed, with treatment type (in person vs. virtual) included as a factor in the analysis. Least square (LS) means, standard errors, and LS mean differences with 95% confidence intervals (CI) between the groups at posttreatment were obtained from the model and are reported in the paper. A supplemental table (Table S1) provides the observed means and SDs for primary and secondary outcomes. For analysis of the dichotomous outcome, remission, treatment groups were compared using a generalized linear model with the logit link function and binomial variance function. The generalized estimating equations approach was used to account for correlation among repeated measures over time using robust (sandwich) covariance estimators for the regression coefficients.

Data Sharing

Trial data will be available with the first author (D.K.) at reasonable request and with ethics approval.

Results

Participant Characteristics

A CONSORT diagram describing the flow of participants during the trial is shown in Figure 1. Eighty-three participants were assessed for eligibility. Of these, 63 (75.9%) met study criteria and were randomly assigned to either IPT ($n = 32$) or ST ($n = 31$). Table 1 presents the demographic and baseline clinical characteristics of the ITT sample. There was no significant difference between the treatment groups on baseline demographic and clinical characteristics. Eighteen participants (30%) who started treatment received some or all

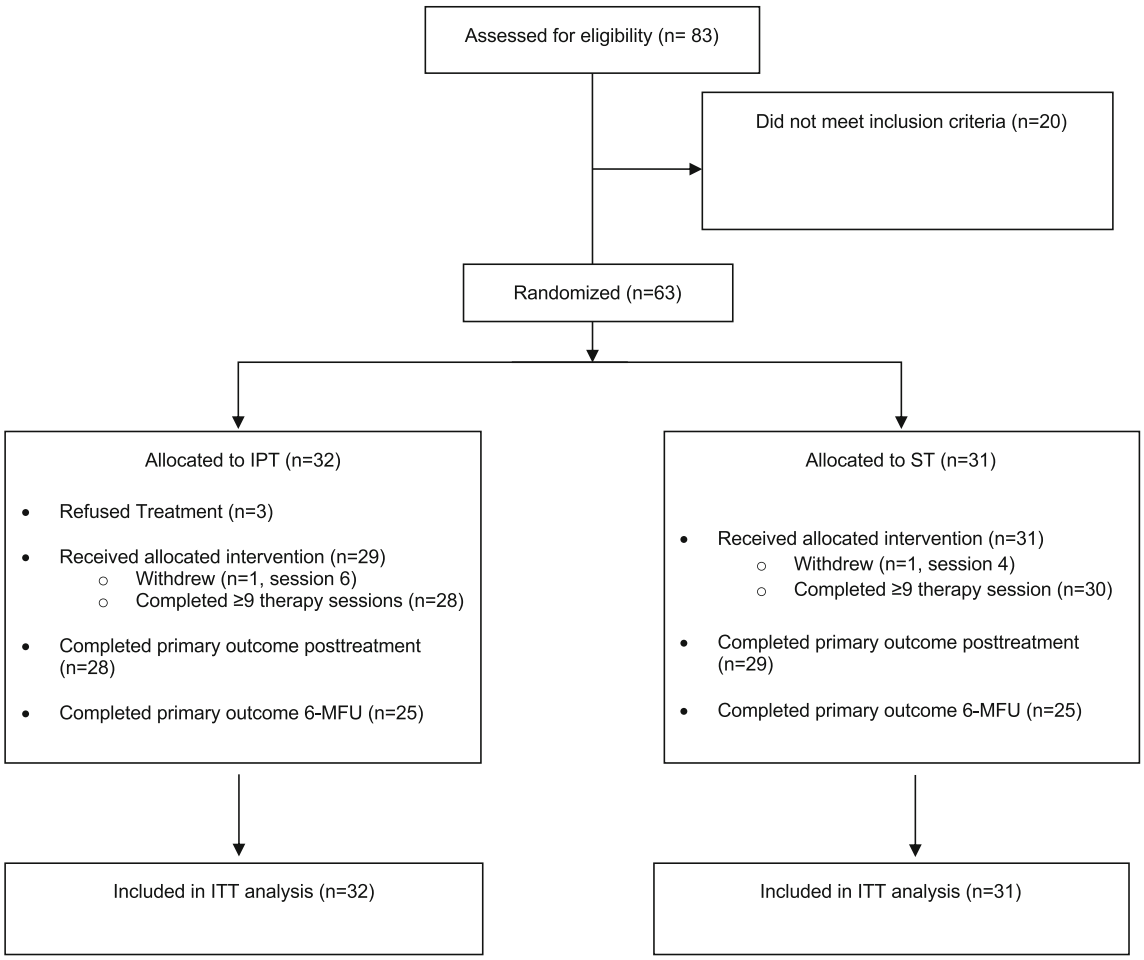

FIG. 1. Consort diagram.

of their therapy sessions virtually. No important difference was found between participants who received their treatment face-to-face or virtually on baseline demographic and clinical characteristics.

Attrition and Treatment Compliance

Primary outcome data at posttreatment were obtained for 28 (87.5%) of the ITT sample assigned to IPT and 29 (93.5%) assigned to ST. Participants who completed at least nine therapy sessions were considered a priori as treatment completers. After randomization, 3 participants refused treatment and 2 discontinued therapy prematurely. Fifty-eight participants completed at least 9 therapy sessions, with 57 attending all 12 sessions. The mean number of sessions attended did not differ between the groups (IPT = 11.79 ± 1.1 vs. ST = 11.65 ± 1.5, $P = 0.67$). Participants who completed treatment had lower baseline BAI scores than those who refused or discontinued treatment (19.61 ± 9.30 vs. 31.25 ± 14.9, $t = -2.31$, $P = 0.025$), but no other baseline differences were found. Twelve participants who started IPT (41.4%) included a support person in a conjoint session. Baseline characteristics and session attendance did not differ between participants with and without a conjoint session.

Primary Outcome

Figure 2 shows the LS means for the HAM-D from baseline to 6-month follow-up. The groups did not differ on baseline scores. The time × treatment interaction was significant ($F = 3.60$, $df = 3, 61$, $P = 0.013$), with treatment differences favoring IPT at session 6 (LS mean difference = −2.90, 95% CI: −5.58 to −0.22, $t = -2.17$, $P = 0.034$) and posttreatment (LS mean difference = −3.77, 95% CI: −6.19 to −1.34, $t = -3.11$, $P = 0.003$). However, the advantage of IPT over ST was not sustained at 6-month follow-up (LS mean difference = −2.37, 95% CI: −8.11 to 3.36, $t = -0.83$, $P = 0.41$). Receiving therapy face-to-face or virtually had no impact on HAM-D scores (session type: $F = 0.48$, $df = 1, 59$, $P = 0.49$; time × treatment × session type: $F = 1.26$ $df = 3, 59$, $P = 0.30$).

TABLE 1 *Baseline demographic and clinical characteristic of the ITT sample*

Variable	IPT (n = 32)	ST (n = 31)	*P*-value
Age (mean ± SD)	64.84 ± 7.6	64.65 ± 9.4	0.93
Gender (% men)	75	51.5	0.054
Ethnicity (% white)	93.8	96.8	0.57
Marital status (% married)	75	77.4	0.82
Living arrangements			0.95
Lives at home with another person	81.3%	83.9%	
Lives at home alone	16%	12.9%	
Lives in a senior's residence	3.1%	3.2%	
Age-of-onset PD	58.44 ± 9.5	56.10 ± 10.0	0.35
MDS-UPDRS Patient Questionnaire-Motor Experiences of Daily Living (mean ± SD)	16.45 ± 7.8	15.96 ± 7.8	0.82
MMSE (mean ± SD)	28.81 ± 1.5	29.12 ± 1.3	0.40
Prior history depression (%)	43.75%	58.1%	0.26
History of psychotherapy (%)	53.1%	64.5%	0.36
Depressive disorder subtype			0.094
MDE	53.1%	32.3%	
PDD	46.9%	67.5%	
PDD specifiers			
With pure dysthymic syndrome	18.8%	51.6%	
With intermittent MDEs, current episode	28.1%	16.1%	
Current use of psychotropic medication	65.6%	61.3%	0.72
Comorbid psychiatric disorder*	56.3%	45.2%	0.38
Generalized anxiety disorder	43.8%	41.9%	
Social anxiety disorder	25.0%	9.7%	
Panic disorder ± agoraphobia	15.6%	12.9%	
Specific phobias	3.0%	0%	

Abbreviations: IPT, interpersonal psychotherapy; ST, supportive therapy; SD, standard deviation; PD, Parkinson's disease; Movement Disorders Society-Unified Parkinson's Disease Rating Scale; MMSE, Mini-Mental State Exam; MDE, major depressive episode; PDD, persistent depressive disorder. *Some participants had more than one anxiety disorder.

Secondary Outcomes

Participants in the IPT condition were more likely to achieve remission posttreatment (odds ratio [OR] = 3.23, 95% CI: 1.10–9.51, $P = 0.034$), but the effects were attenuated at 6-month follow-up (OR = 1.18, 95% CI: 1.10–3.74, $P = 0.78$). Table 2 presents the results for the BDI-II, BAI, PDQ-39-SI, and MD-UPDRS. Baseline scores did not differ between the treatments. The time × treatment interaction was significant for the BDI-II, with the difference between treatments favoring IPT at session 6 (LS mean difference = −5.27, 95% CI: −9.81 to −0.72, $t = -2.43$, $P = 0.024$) but not at posttreatment (LS mean difference = −4.14, 95% CI: –8.73 to 0.45, $t = -1.80$, $P = 0.076$) or 6-month follow-up (LS mean difference = −2.13, 95% CI: −6.95 to 2.69, $t = -0.88$, $P = 0.38$). The time × treatment interaction was also statistically significant for the BAI, with IPT having an advantage over ST at session 6 (LS mean difference = −6.55, 95% CI: −12.46 to −0.63, $t = -2.22$, $P = 0.03$) but not at posttreatment (LS mean difference = −0.09, 95% CI: −5.85 to 5.66, $t = -0.03$, $P = 0.97$) or 6-month follow-up (LS mean difference = −2.37, 95% CI: −8.11 to 3.36, $t = -0.83$, $P = 0.41$). The time × treatment interaction was significant for the clinician-rated MDS-UPDRS, but the pairwise comparisons were not statistically significant at posttreatment (LS mean = 5.44, 95% CI: −0.20 to 11.08, $P = 0.058$) or 6-month follow-up (LS mean = −2.14, 95% CI: −8.73 to 4.43, $P = 0.52$).

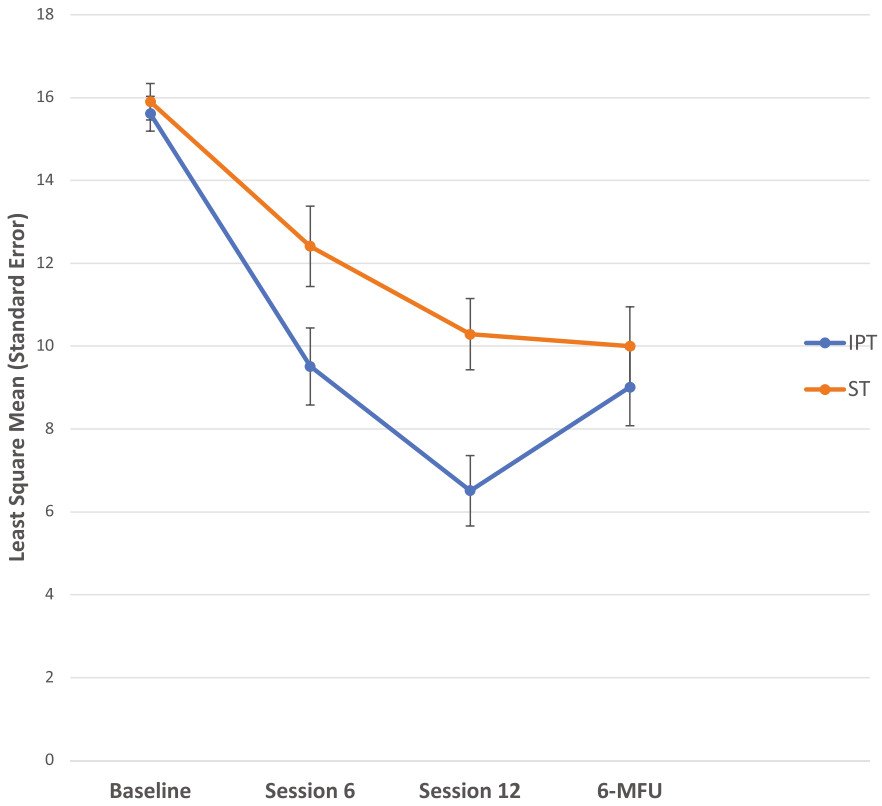

FIG. 2. Effect of treatment on HAM-D (Hamilton Depression Rating Scale) scores. [Color figure can be viewed at wileyonlinelibrary.com]

The time main effect was significant for the PDQ-39-SI, but no significant interaction with treatment was found. Examination of PDQ-39 dimensions (Table S2) revealed significant time main effects but no time × treatment interactions for six dimensions, with improvement noted for emotional well-being, stigma, social supports, cognition, communication, and body discomfort.

Table 3 presents the IPRI and ECR-R results. There were no significant treatment × time interactions for these outcomes. The time main effect was significant for the IPRI conflict subscale, with participants in both treatments reporting decreased interpersonal conflict. There was no treatment effect for the IPRI social support and reciprocity subscales or the ECR-R subscales.

Discussion

Both IPT and ST improved depressive symptoms over the course of acute treatment. As predicted, IPT was superior to ST, with differences in depression ratings apparent by session 6. At posttreatment, scores on our primary outcome were significantly lower with IPT, with a greater number of participants achieving remission. Posttreatment BDI-II scores were also lower in the IPT condition, with treatment differences just short of significance. The 4.14-point difference between the treatments on BDI-II scores is considered clinically important[48] and compares well with other research on IPT for depressed medically ill patients.[49] Although the HAM-D was more sensitive in detecting statistically significant treatment effects in this study, IPT exhibited consistent effects across the two depression measures. Overall, these findings suggest that improvement in depression may be attributed to specific strategies associated with IPT rather than nonspecific factors shared by all forms of therapy.

Depression scores remained lower at 6-month follow-up relative to baseline for both interventions. However, the advantage of IPT over ST on our primary outcome was not sustained at follow-up due to a small increase in depressive symptoms in the IPT condition. One explanation for this finding is that our sample comprised mainly older adults, many of whom suffered from chronic depression and comorbid anxiety. Depression in older medically ill patients often has a chronic and recurring course, and they may be less likely to maintain treatment gains with IPT over time.[50] Providing monthly maintenance IPT sessions may improve the likelihood of sustained improvement and reduce relapse, and help patients resolve chronic psychosocial stressors that influence mood.[51] A study of CBT for PD depression that included monthly sessions after acute treatment demonstrated that the advantage of CBT over usual care was sustained at 6-month follow-up.[52]

TABLE 2 *Least square means (±standard error) for secondary clinical outcomes for the intent-to-treat sample*

Outcome	Baseline	Session 6	Session 12	6-MFU	Treatment effect			Time effect			Treatment–time interaction		
					F	*df*	*P*	F	*df*	*P*	F	*df*	*P*
BDI-II					2.12	1,61	0.15	23.25	1,61	<0.0001	2.76	3,61	0.05
IPT	24.48 ± 1.3	17.00 ± 1.6	13.82 ± 1.6	14.90 ± 1.7									
ST	23.67 ± 1.4	22.15 ± 1.6	17.96 ± 1.6	17.02 ± 1.7									
BAI					0.83	1,60	0.36	4.59	3,60	0.006	4.27	3,60	0.008
IPT	20.22 ± 1.8	16.40 ± 2.1	16.51 ± 2.0	15.74 ± 2.0									
ST	20.41 ± 1.9	22.90 ± 2.2	16.61 ± 2.1	18.12 ± 2.0									
PDQ-39-SI					0.19	1,56	0.66	18.62	2,80	<0.0001	1.04	2,80	0.36
IPT	38.31 ± 2.8	–	27.53 ± 2.9	28.69 ± 3.1									
ST	37.50 ± 2.7	–	30.82 ± 2.8	30.89 ± 3.1									
MDS-UPDRS					0.21	1,60	0.65	0.16	2,60	0.85	5.77	2,60	0.005
IPT	21.22 ± 2.6	–	23.26 ± 2.0	20.09 ± 2.3									
ST	20.48 ± 2.7	–	17.82 ± 2.0	22.23 ± 2.3									

Abbreviations: 6-MFU, 6-month follow-up; BDI-II, Beck Depression Inventory; IPT, interpersonal psychotherapy; ST, supportive therapy; BAI, Beck Anxiety Inventory; PDQ-39-SI, Parkinson's Disease Questionnaire-Summary Index; MDS-UPDRS, Movement Disorders Society-Unified Parkinson's Disease Rating Scale.

TABLE 3 *Least square means (±SE) for interpersonal relationships and attachment outcomes for the intent-to-treat sample*

				Treatment effect			Time effect			Treatment–time interaction		
Outcome	**Baseline**	**Session 12**	**6-MFU**	**F**	***df***	***P***	**F**	***df***	***P***	**F**	***df***	***P***
IPRI												
Social support				0.76	1,59	0.39	2.52	2,59	0.09	1.28	2,59	0.28
IPT	46.87 ± 1.4 **(3.61 ± 0.1)**	50.53 ± 1.2 **(3.89 ± 0.1)**	49.59 ± 1.3 **(3.81 ± 0.1)**									
ST	49.90 ± 1.4 **(3.84 ± 0.1)**	50.46 ± 1.3 **(3.88 ± 0.1)**	50.69 ± 1.4 **(3.90 ± 0.1)**									
Reciprocity				0.14	1,59	0.71	2.82	2,59	0.07	2.20	2,59	0.12
IPT	45.88 ± 1.1 **(3.53 ± 0.1)**	47.88 ± 1.1 **(3.68 ± 0.1)**	47.65 ± 1.1 **(3.67 ± 0.1)**									
ST	47.38 ± 1.2 **(3.65 ± 0.1)**	46.65 ± 1.1 **(3.59 ± 0.1)**	48.86 ± 1.1 **(3.76 ± 0.1)**									
Conflict				0.19	1,59	0.66	4.86	2,87	0.01	0.13	2,87	0.88
IPT	35.62 ± 1.4 **(2.74 ± 0.5)**	33.52 ± 1.4 **(2.58 ± 0.1)**	31.86 ± 1.5 **(2.45 ± 0.1)**									
ST	36.17 ± 1.4 **(2.78 ± 0.1)**	33.92 ± 1.5 **(2.6 ± 0.1)**	33.19 ± 1.6 **(2.55 ± 0.1)**									
ECR-R												
Attachment anxiety				2.44	1,60	0.12	1,74	2,82	0.18	0.13	2,82	0.88
IPT	66.91 ± 4.1 **(3.72 ± 0.2)**	63.72 ± 4.3 **(3.54 ± 0.2)**	59.17 ± 4.6 **(3.29 ± 0.2)**									
ST	57.27 ± 4.3 **(3.18 ± 0.2)**	54.84 ± 4.3 **(3.05 ± 0.2)**	52.72 ± 4.9 **(2.93 ± 0.2)**									
Attachment avoidance				2.89	1,59	0.09	0.66	2,59	0.52	1.60	2,59	0.21
IPT	62.68 ± 3.8 **(3.48 ± 0.2)**	56.81 ± 3.5 **(3.12 ± 0.2)**	56.46 ± 2.8 **(3.14 ± 0.2)**									
ST	50.64 ± 4.0 **(2.81 ± 0.2)**	51.97 ± 3.5 **(2.89 ± 0.2)**	51.97 ± 3.0 **(2.89 ± 0.2)**									

Values in bold font represent standard least square means ± SE.
Abbreviations: SE, standard error; 6-MFU, 6-month follow-up; IPRI, Interpersonal Relationships Inventory; IPT, interpersonal psychotherapy; ST, supportive therapy; ECR-R, Experiences in Close Relationships Scale-Revised.

This finding highlights the importance of maintenance psychotherapy and continued attention to mood symptoms in the treatment of PD depression.

Participants in the IPT condition exhibited an earlier decline in self-report anxiety, but no treatment differences emerged at posttreatment. The observed difference in anxiety at session 6 may have been partly accounted for by a worsening of anxiety in the ST condition. Despite improvement in depressive symptoms, neither treatment produced clinically important changes in clinician-rated motor symptoms. Scores were somewhat lower in the ST condition at posttreatment, but the change was minimal based on estimates that determine clinically meaningful change.[53] On the contrary, both interventions reduced the impact of PD on quality of life, with no specific advantage for IPT. The reduction in PDQ-39-SI scores exceeded the minimal clinical important difference of −4.72 points suggested by Horvath and colleagues.[54] Improving quality of life is an important criterion for antidepressant treatment success,[55] and our findings suggest that IPT and ST have important secondary benefits for the treatment of PD depression.

Despite IPT's interpersonal focus, there was no benefit of IPT over ST in improving domains of interpersonal functioning. Both interventions reduced perception of interpersonal conflict. As well, participants reported

improvement in social support on the PDQ-39. Results are consistent with prior findings that improved interpersonal functioning is not specific to IPT.[49,56] Improvement in aspects of interpersonal functioning with ST is not entirely surprising given that most patients raised relational issues during their sessions. Although ST did not focus on these issues in a systematic way as IPT, helping participants reflect and express emotions about relationships, learn to better cope with interpersonal challenges, and access environmental supports likely contributed to improved interpersonal functioning in ST-treated participants. Given that social relationships are a significant domain of quality of life in PD,[57] attending to relationship concerns and social supports should be an important component of all psychosocial intervention for PD.

The ECR-R subscales showed no significant improvement with treatment. It is plausible that 12 therapy sessions are insufficient to yield meaningful changes in attachment style in older adults. Research on attachment experiences in PD patients is sparse. Given that attachment insecurities can influence illness behavior, interactions with health-care providers, and outcome,[58-60] more research is needed to better understand attachment orientation in PD patients and the extent to which psychotherapy can increase attachment security in close relationships.

Similar to RCTs of CBT for PD depression,[37,38] attrition was low in this study, with 7.5% of participants either refusing treatment or dropping out before completing at least nine sessions. This is an important finding as receiving an optimal dose of psychotherapy is associated with better outcome.[61] The participants who refused or dropped out of the study had significantly higher levels of baseline anxiety than those who did not, and this may have influenced their motivation to start or continue with treatment. Adding a pretreatment engagement session that integrates motivational enhancement techniques has been found to improve treatment engagement with IPT[62] and may be an important supplement to reduce resistance and foster positive therapeutic engagement in depressed PD patients.

This first RCT of IPT has several advantages, including the use of a centralized randomization system, an active but nonspecific control intervention that focuses on common therapeutic factors, blind clinical raters for our primary outcome, a high completion of our primary outcome, and a low attrition rate. This study's limitations should also be noted. First, our sample was primarily white and comprised patients with stage I to III PD with no cognitive impairment. Thus, results cannot be generalized to other ethnic groups or to patients with a more advanced stage of the disease. Second, similar to other research on psychotherapy for PD depression,[63] this study faced recruitment difficulties, and we were unable to recruit the targeted number of participants. Although the 3.77-point difference in our primary outcome exceeded the 3-point difference that was used to calculate power for this study, it is possible that posttreatment differences in some secondary outcomes would have reached statistical significance if the sample size was larger. Third, the COVID-19 pandemic caused some disruption to the study, and the method of therapy delivery shifted from face-to-face to remote therapy. However, we found no impact of this shift on our primary outcome, which is consistent with other studies that found switching to virtual sessions during the pandemic had no negative impact on therapy outcome or process.[64,65]

In summary, this study showed that acute treatment with IPT has robust antidepressant effects relative to a potent control. Although less effective than IPT, ST was well accepted by participants and fared as well as IPT in improving scores on some secondary outcomes. Findings contribute to the accumulating evidence that first-line psychological interventions are of benefit to depressed PD patients. To optimize the benefits of IPT for PD depression, future research should examine strategies that maintain acute treatment gains and address how IPT works and for whom the therapy works best. Future research should also evaluate how well IPT and ST compare to CBT, the best-studied treatment for PD depression to date. ■

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Data Availability Statement

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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Supporting Data

Additional Supporting Information may be found in the online version of this article at the publisher's web-site.