Telephone-linked Home-based Exercise Training in PD

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1. STUDY GOALS

Nonmotor symptoms in Parkinson's disease (PD) are thought to be present from the early stages of disease and are often more disabling and resistant to treatment than motor symptoms. One of the most important and serious of these symptoms is depression. However, there is no consensus on best pharmacological treatment for depression in PD as efficacy is lacking and there is much concern about polypharmacy and safety of various antidepressant medications. Therefore, it is essential that we characterize the effects of nonpharmacological interventions on depression in PD. A number of studies have shown significant benefits of exercise in reducing depressive symptoms. Emerging studies indicate similar benefits of exercise in the form of resistance training in limiting depression in older adults as well as in those with PD.

We propose to conduct a randomized, controlled trial of a novel program that uses resistance training coupled with real-time guidance delivered remotely in veterans 40 years of age or older with depression in PD. The recruitment goal of this VA RR&D SPiRE project was to recruit a total of 40 participants. The SPiRE award mechanism is intended to fund small pilot projects that lack preliminary data. Our aim was to determine whether there are differences in change on the Hamilton Rating Scale for Depression between patients in the resistance training intervention program and patients in a health education control program.

2. BACKGROUND AND SIGNIFICANCE

2.1 Depression in Parkinson's Disease

The Veterans Health Administration (VHA) treats an estimated 80,000 veterans with PD each year (1). This number is expected to increase significantly in the next decade (2). Motor features of PD (e.g., resting tremor, rigidity, bradykinesia) are well recognized; however, it is now realized that the majority of people with PD also experience nonmotor features such as depression, anxiety, sleep disturbance, and cognitive changes (3). Depressive disorders may affect up to 50% of patients with PD and contribute to accelerated disability and functional morbidity (4, 5).

It is important to treat depression in PD due to its high prevalence and negative impact on patient outcomes. Unfortunately, in certain clinical settings such as primary care, depressive disturbances are under-recognized and, even when identified, frequently undertreated (6). The efficacy and safety of various antidepressants in the management of depression in patients with PD have been addressed in multiple studies; however, there is no consensus on optimum pharmacological treatment (7, 8). An in depth review and meta-analysis of 10 studies showed uncertainty and a lack of strong systematic evidence supporting the clinical benefit of selective serotonin reuptake inhibitors for depression in PD (9). Another evidence-based review concluded that the secondary amine tricyclic antidepressants (e.g., desipramine, nortriptyline) are likely efficacious but common side effects limit their utility (10). Concerns about polypharmacy and safety of antidepressant treatment regimens have led to increasing interest in the utility of alternative and nonpharmacological treatments for depression in PD. These treatments may include repetitive transcranial magnetic stimulation (rTMS), cognitive behavioral therapy (CBT), and exercise. Although short-term benefits of rTMS and CBT have been seen, limitations include a shortage of programs or equipment at VA facilities and the need for patients with moderate levels of disability to frequently travel to these facilities (7, 11-14).

2.2 Exercise and Depression

A recent meta-analysis of exercise interventions and major depression indicated a pooled standardized mean difference (SMD) of -0.61 (95% CI, -0.88 to -0.33), based on 10 trials and 758 participants. Improvement of depressive symptoms was greater with strength training (SMD -0.96) than with aerobic training (SMD -0.52) (15). Similarly, a recent Cochrane review examined the effectiveness of exercise compared to no intervention for depression in adults (16). The pooled SMD for resistance exercise met the criteria for a large clinical effect (SMD -1.03, 95% confidence interval [CI], -1.52 to -0.53). This effect was greater than that observed with aerobic training (SMD -0.55, 95% CI -0.77 to -0.34) or with mixed aerobic and resistance exercise.

A recent study revealed evidence that progressive strengthening exercises can reduce depression in patients with PD (17). Thirty-one patients with mild PD were randomly assigned to an early start group consisting of 48 weeks of exercise (weeks 1 to 48) or a delayed start group consisting of 24 weeks of exercise (weeks 24 to 48). Both groups exercised for one hour, three days per week. At 48 weeks, both groups experienced improvements in depression, as measured by the Beck Depression Inventory. Importantly, the early start group experienced significantly ($p=0.04$) greater improvements in depression, as compared with the delayed start group. This suggests that higher doses of strengthening exercises – both longer duration exercise and greater progression of exercise intensity over time – contributed to larger beneficial effects. Exercise-related increases in neurotrophic factors (e.g., glial-derived neurotrophic factor [GDNF] and brain-derived neurotrophic factor [BDNF]) may represent underlying biological mechanisms consistent with these effects. Coelho et al. (18) showed significant increases in plasma concentrations of BDNF after a 10-week strength training program in community-dwelling elderly women. A recent clinical trial found that strength training, but not aerobic training, significantly increased plasma BDNF levels and reduced depressive symptoms (change in Geriatric Depression Scale scores: -0.85 [strength training], -0.54 [aerobic training]) in elderly women (19).

2.3 Significance

PD tends to be managed clinically using pharmacological interventions with little evidence of efficacy and significant concerns regarding polypharmacy and safety of multiple antidepressant medicines. The importance of identifying effective nonpharmacological interventions is escalating. Several studies in older adults with depression have shown significant and clinically meaningful reductions in depression with participation in progressive resistance exercise programs. Recently, similar findings have been reported in PD.

We propose to conduct a randomized, controlled trial (RCT) of a home-based resistance training program that uses state-of-the-art information technology. Our team has used this program successfully in an RCT of older adults (n=103) with high retention rates and positive results (see Section 3 below). The program has several notable features that overcome limitations of prior studies: 1) it does not require specialized clinical facilities or highly skilled personnel to administer the program; 2) it can be used in the home setting, eliminating the need to travel to a clinical facility; 3) it costs very little to set up and operate; 4) it can be sustained for an indefinite period of time; 5) it incorporates motivational and problem-solving strategies to promote increased adherence to exercise; and 6) it can be implemented independent of certain external barriers such as weather or the season.

3. PRELIMINARY STUDIES

We have experience successfully implementing a remote home-based resistance exercise training program in older veterans (age range, 50 to 94 years) (20). By the end of the 12-month program, 86% retention of the participants was achieved. This program, the Telephone-Linked Computer-based Long-term Interactive Fitness Trainer (TLC-LIFT), significantly increased lower extremity strength and decreased depressive symptoms over levels in the health education control arm. There were no serious adverse events related to the TLC-LIFT intervention. Further, there was virtually no difference in nonserious adverse events (musculoskeletal injury and discomfort) between the intervention and control groups.

The TLC-LIFT program uses advanced interactive voice response (IVR) technology, including speech-recognition software, to facilitate communication with TLC-LIFT. The TLC-LIFT program provides verbal instructions on what exercises to do and how to do them, guiding the participants through the exercises as they perform them in their home. The TLC-LIFT system asks the participant to begin a given exercise and to count each repetition out loud. Voice recognition of each counted repetition allows the system to monitor the number of repetitions for each exercise. Because TLC-LIFT is fully automated and administered by telephone in the participant's home, TLC-LIFT offers great flexibility and sufficiently low cost to continue indefinitely. To facilitate this approach, participants are supplied with a wireless headset (with microphone) that connects with their existing phone, thus allowing for hands-free communication with TLC-LIFT as they exercise. TLC-LIFT utilizes speech-recognition technology that we have customized to recognize wide variations in speech clarity, in addition to variations in speech during exercise (e.g., variations counting repetitions out loud due to changes in breathing patterns). Furthermore, TLC-LIFT facilitates interactive communication (e.g., "Are you ready to set

a higher goal for your next exercise?") tailored to each individual to optimize engagement and a person-centered approach. Participants are provided with an illustrated booklet that converts to a desktop easel, allowing them to see the exercises while simultaneously listening to the audio instructions.

The tailored resistance exercise training program comprises three 60-minute sessions per week consisting of a warm-up phase (10 minutes), a stimulus phase (40 minutes), and a cool-down phase (10 minutes). The stimulus phase is made up of eight exercises to address the following key muscle groups: hip extensors, knee extensors, plantar flexors, trunk extensors, elbow flexors, elbow extensors, shoulder flexors and extensors. Exercises (e.g., biceps curls, front shoulder raises, heel raises) are performed with dumbbells to provide increased resistance and as a means of progressing the exercise program over time.

During each exercise session, participants are instructed to perform 2 sets of 12 repetitions of the 8 exercises. Each participant starts the program using 2 lb vinyl-coated dumbbells. Weight is increased by 2 lb per limb each succeeding session for a given exercise as long as the participant is able to complete 2 sets of 10 or more repetitions. The TLC-LIFT system provides participants with detailed instructions on the proper technique for each of the 8 exercises. Family members or caretakers are encouraged to assist the participant with the exercise program as appropriate. To reduce the risk of any injury from exercising, participants are instructed in every call to stop exercising if they experience symptoms suggestive of a musculoskeletal injury or cardiac problem or significant deterioration of neurologic function.

The TLC-LIFT program includes dialogues that have a strong behavioral theoretical underpinning in social cognitive theory (22, 23). At the conclusion of each exercise session, one interactive counseling module is delivered to the participant by the TLC-LIFT system. One important construct that is included in the counseling dialogues is self-efficacy, the expectation that one has the capacity to successfully perform a behavior required for a desired outcome to occur. Motivational messages aimed to increase self-efficacy are presented to participants regularly. These messages are designed to get participants to recognize their own exercise abilities, to reinforce good exercise performance, and to target areas of low confidence in order to promote self-confidence in exercise. Prior research indicates that level of self-efficacy predicts level of participation in physical activity promotion programs (24-27). Real-time monitoring of adherence permits continual reinforcement of goals and promotion of self-efficacy, motivational techniques known to increase adherence.

Another important construct contained in the modules is outcome expectations, or the results that one would anticipate after performing a particular behavior (28, 29). As expected, the extent to which individuals perceive they will be able to perform a behavior is related to the outcomes they anticipate. Three major forms of outcome expectations have been identified (23): 1) positive and negative physical effects; 2) positive and negative social effects; and 3) positive and negative self-evaluative reactions to the change in behavior. Within each major form, positive expectations function as incentives and negative expectations as disincentives to changing behavior. Information is offered to participants about the typical results that they could expect from participation in the TLC-LIFT exercise program in each of these three areas. Positive outcomes, for example, the known benefits of exercise, are highlighted often throughout the course of the program. Negative outcomes are discussed with an emphasis on how to overcome or resolve them; for example, if exercise is taking time away from social activities, participants are reminded about the benefits of exercise and the positive impact it can have on their social activities.

Other important behavioral techniques that are incorporated into the dialogues are goal setting and reinforcement. Goal setting has been identified as an important construct for changing behavior and increasing compliance (30). For TLC-LIFT, each week participants are prompted to set a goal in one of the exercise areas, thus providing participants with an endpoint on which to focus and helping to build self-efficacy when accomplished. The use of reinforcement techniques is also effective for behavior change and maintenance of the change (30). Therefore, reinforcement, which can incorporate tangible rewards (such as purchasing DVD movie or going out to dinner) and verbal rewards (praise, supportive comments), is another behavioral technique included in the TLC-LIFT dialogues.

4. RESEARCH DESIGN AND METHODS

4.1 Participants for the Randomized, Controlled Trial

We will conduct an RCT of our home-based resistance training program (TLC-LIFT) in patients with depression in PD. Forty patients will be randomized to the TLC-LIFT program for 6 months or to a health education control program for 6 months. Patients with depression in PD who meet eligibility criteria will be recruited into this study. Specific inclusion criteria will include a physician diagnosis of idiopathic, typical PD; at least 2 of the 3 cardinal signs of PD (resting tremor, rigidity, bradykinesia); response to dopaminergic medication; absence of secondary causes of Parkinsonism; a diagnosis of major depression, dysthymic disorder, or minor depressive disorder; and an age of 40 years or older. Exclusion criteria will include a diagnosis of angina pectoris (unless symptomatically resolved post-revascularization); a history of myocardial infarction (MI) within 6 months, or remote (>6 months) MI with current ischemia on an exercise stress test; and a history of ventricular dysrhythmia requiring current therapy, or current atrial fibrillation without adequate rate control (resting HR <90).

4.1.1 Recruitment

We will recruit 40 patients with depression in PD into our study. Specifically, this approach will involve identifying patients in VISN 1 who are 40 years of age or older with an ICD code for PD, prescription for a dopaminergic, anti-cholinergic, or NMBA receptor medication, and clinical evidence indicating depression. To access electronic medical records we will use the CAPRI system, which provides one interface into the VISTA systems within VISN 1. We will review these data to confirm specific eligibility criteria. Patients with PD typically have an initial Neurology consultation and then are seen in Neurology Clinic every 6 months. A standardized VA note format is utilized which includes HPI, medications, and detailed neurologic examination at each visit. The initial VA Neurology consultation will be reviewed with as many subsequent clinic notes as needed to establish the diagnosis of PD and responsiveness to dopaminergic therapy. The two most recent Neurology Clinic notes will also be reviewed to determine current medication use and functional status. Also, Primary Care provider notes and any hospital discharge summaries from the previous year will be reviewed for evidence of exclusionary conditions.

4.1.2 Baseline Evaluation

We will administer the Structured Clinical Interview for DSM-IV (SCID) (31) and confirm the diagnosis of depression based on published criteria (32). Patients with confirmed depression will then complete the Hamilton Rating Scale for Depression (33). This measure will be repeated later as described in detail in Section 4.3. Half of the 40 participants will be randomized to each experimental arm.

4.2 The Study Interventions

4.2.1 TLC-LIFT Intervention

Patients randomized to receive the TLC-LIFT intervention will be instructed on how to use the TLC-LIFT system (Section 3) and will perform an abbreviated exercise session (1 set of 3 repetitions of each of the 8 exercises) under the guidance of a trained staff member. The exercise program is progressive (weight is increased) and also tailored to the ability of each participant. This allows some participants to progress faster than others to ensure each participant is adequately challenged. Participants will be given a booklet containing colored pictures of all the exercises, serving as a reference of the specific components of the exercise program. These pictures provide visual cues that will complement the audio instructions provided through the TLC-LIFT system. Participants are encouraged to carry out exercises during an optimal time in their medication schedule to increase successful implementation and reduce risk.

Adherence to this intervention will be encouraged by intermittent newsletters, birthday cards, holiday greeting cards, and certificates of study participation. Another method to promote adherence will be through the use of incentives (36); incentives to reward adherence will include key chains, mugs, hats, t-shirts, and movie passes.

4.2.2 Health Education Control

The group randomized to receive health education will serve as an attention control. Participants will be

asked to use the health education control system 3 times a week, which will deliver general information about a variety of health topics including content on exercise. This system, similar to the TLC-LIFT system, provides auditory instructions/content via the participant's home telephone. The health education control system uses advanced IVR technology, including speech-recognition software, to facilitate communication with the system. There are opportunities for participant interaction while the content is delivered by the system, for example, the participant can request subtopics about which they desire more information while skipping others of less interest. Near the end of the baseline visit, the initial health education session is completed with a staff member who has experience working with patients with PD.

During the first four weeks of the intervention, content on exercise based on the Fitness Counts program developed by the National Parkinson Foundation (Chapters 3 & 4) (37) will be presented focusing on the benefits of exercise for persons with PD (1 session), the types of exercises important for persons with PD (1 session), principles of stretching and strengthening exercises (2 sessions), descriptions of safe stretching and strengthening exercises for persons with PD (6 sessions), and strategies to overcome barriers to exercise (2 sessions). Participants will be provided with illustrations of the exercise program with written instructions to accompany the auditory content. Subsequently, during each session, participants will select a topic from 4 content areas: common symptoms, medical conditions, preventive medicine topics, and tips for healthy living with PD. These PD-specific tips include mobility strategies, such as strategies for moving from lying down to a sitting position, and from sitting to standing position, and tips to help with performance of daily activities including organization of the physical environment and reducing time pressure. A similar approach as described above (see Section 4.2.1) will be used in the control group to encourage and maintain study adherence.

4.3 Outcome Data Collection

We will assess the Hamilton Rating Scale for Depression (HAM-D) (33) at baseline and 6 months at the Jamaica Plain campus of the VA Boston healthcare system with participants in an optimally medicated (on) dopaminergic state. HAM-D is the most widely used and accepted measure for evaluating depression severity (38). The 17-item version of the HAM-D results in scores ranging from 0 to 54, with higher scores representing more severe depression. The scale has been found to be sensitive to change in patients with PD (38).

4.4 Data Management and Security

For the purposes of this study, each subject will be assigned a unique randomly generated ID number, which will be used on all electronic data stored locally. A walk across file will be maintained to link the subject with the random ID number and will be stored in a separate location from all other data extracted. Only the study coordinator and PI will have access permissions to this file.

All electronic databases related to this protocol will be stored locally on a VA server in an entry controlled, locked room at the Jamaica Plain campus of the VA Boston Healthcare System. There are multiple levels of security to ensure the integrity and confidentiality of all data. The computer system operates entirely within the VA network, which is protected by a firewall maintained by the VA Office of Information Technology. Part of the maintenance of the VA server is that it is backed up regularly; therefore, all data related to this protocol will be routinely backed up and stored behind the VA firewall. Only authorized users can log on to the server. An additional layer of restrictions is at the file and directory level. Users can only access portions of the data to which they are entitled. Access to all data on the server is password protected. Access permissions will be removed and passwords will be changed whenever study personnel are no longer part of the research team.

All paper forms will be secured in a locked fireproof study cabinet. Only the PI will have keys to the study cabinet. All data will be kept indefinitely or until the law allows their destruction in accordance with the VA Record Control Schedule. Records will be destroyed, when allowed, in the following manner: paper records will be shredded and electronic records will be destroyed in a manner in which they cannot be retrieved. All suspected or identified information security incidents (e.g. theft or loss of data or unauthorized access) will be reported to the PI, ISO, and PO immediately upon suspicion by study staff.

To minimize data entry errors, all data collected on paper forms will be entered twice by a staff member using software that allows specification of valid responses for each entry field. Upon second entry of each record, the software will analyze each field to check for discrepancies in the two entries. Entry errors will be corrected on the spot and any errors requiring more extensive review will be deleted and re-keyed after the errors are resolved. In addition, the study coordinator will perform a careful quality assessment of all measures through logic and consistency checks and distributional assessment of overall distributions of responses. Data at follow-up exams will be compared to previous data for longitudinal consistency. Any patterns in missing or erroneous data will be discussed with the staff members collecting the data to determine the cause of the problem and what corrective measures will be taken. Databases will be carefully versioned so that all analyses can be clearly audited.

4.5 Statistical Analysis

Change in the Hamilton Rating Scale for Depression (HAM-D) was analyzed with the use of PROC MIXED (SAS) to estimate intervention effects based on a mixed-effects longitudinal model (40). The unstructured covariance model was used to allow for different variances at each time point (baseline, 6 months) and different correlations between outcomes for each pair of visits. The home-based exercise intervention program improved HAM-D score at the 6-month follow-up, as compared with the health education program with a between group difference of -3.4 points ($p < 0.05$; total $N = 40$). The standardized mean difference (SMD) was -0.6, which is between a medium and large effect. This SMD is very similar to that observed in a meta-analysis of major depression and exercise interventions in non-PD, which indicated a pooled SMD of -0.61 (15). However, we are not aware of any published data providing a minimal clinically important difference (MCID) on the HAM-D against which to compare our results.

References

1. Parkinson's Disease Research, Education and Clinical Centers. VA Establishes Six Parkinson's Disease Centers [online]. Accessed August 10, 2014.
2. Dorsey ER, Constantinescu R, Thompson JP, Biglan KM, Holloway RG, Kieburtz K, Marshall FJ, Ravina BM, et al. Projected number of people with Parkinson disease in the most populous nations, 2005 through 2030. Neurology. 2007;68(5):384-38.
3. Weintraub D, Burn DJ. Parkinson's disease: the quintessential neuropsychiatric disorder. Mov Disord 2011;26:1022-31.
4. Ravina B, Camicioli R, Como PG, et al. The impact of depressive symptoms in early Parkinson's disease. Neurology. 2007;69:342-347.
5. Pontone GM, Bakker CC, Chen S, et al. The longitudinal impact of depression on disability in Parkinson disease. Int J Geriatr Psychiatry. 2015, in press.
6. Dobkin RD, Rubino JT, Friedman J, Allen LA, Gara MA, Menza M. Barriers to mental health care utilization in Parkinson's disease. J Geriatr Psychiatry Neurol. 2013;26:105-16.
7. Dobkin RD, Menza M, Allen LA, Gara MA, Mark MH, Tiu J, Bienfait KL, Friedman J. Cognitive-behavioral therapy for depression in Parkinson's disease. Am J Psychiatry. 2011;168:1066-74.
8. Barone P, Poewe W, Albrecht S, Debieuvre C, Massy D, Rascol O, Weintraub D. Pramipexole for the treatment of depressive symptoms in patients with Parkinson's disease. Lancet Neurol. 2010;9:573-80.
9. Skapinakis P, Bakola E, Salanti G, Lewis G, Kyritsis AP, Mavreas V. Efficacy and acceptability of selective serotonin reuptake inhibitors for the treatment of depression in Parkinson's disease: a systematic review and meta-analysis of randomized controlled trials. BMC Neurol 2010;10:49.
10. Seppi K, Weintraub D, Coelho M, Perez-Lloret S, Fox SH, Katzenschlager R, Hametner EM, Poewe W, et al. The Movement Disorder Society Evidence-Based Medicine Review Update: Treatments for the non-motor symptoms of Parkinson's disease. Mov Disord 2011;26 Suppl 3:S42-80.
11. Lefaucheur JP, Andre-Obadia N, Antal A, et al. Evidence-based guidelines on the therapeutic use of repetitive transcranial magnetic stimulation (rTMS). Clin Neurophysiol. 2014;125:2150-206.
12. Pal E, Nagy F, Aschermann Z, Balazs E, Kovacs N. The impact of left prefrontal repetitive transcranial magnetic stimulation on depression in Parkinson's disease: a randomized, double-blind, placebo-controlled study. Mov Disord. 2010;25(14):2311-7.
13. Dobkin RD, Allen LA, Menza M. Cognitive-behavioral therapy for depression in Parkinson's disease: a pilot study. Mov Disord. 2007;22:946-52.
14. Pachana NA, Egan SJ, Laidlaw K, et al. Clinical issues in the treatment of anxiety and depression in older adults with Parkinson's disease. Mov Disord. 2013;28:1930-1934.
15. Silveira H, Moraes H, Olivera N, Coutinho ES, Laks J, Deslandes A. Physical exercise and clinically depressed patients: a systematic review and meta-analysis. Neuropsychobiology. 2013;67:61-8.
16. Cooney GM, Dwan K, Greig CA, Lawlor DA, Rimer J, Waugh FR, McMurdo M, Mead GE. Exercise for depression. Cochrane Database of Systematic Reviews 2013, Issue 9. Art. No.: CD004366.
17. Park A, Zid D, Russell J, Malone A, Rendon A, Wehr A, Li X. Effects of a formal exercise program on Parkinson's disease. Parkinsonism Relat Disord. 2014;20:106-11.
18. Coelho FM, Pereira DS, Lustosa LP, Silva JP, Dias JM, Dias RC, Queiroz BZ, Teixeira AL, et al. Physical therapy intervention (PTI) increases plasma brain-derived neurotrophic factor (BDNF) levels in non-frail and pre-frail elderly women. Arch Gerontol Geriatr. 2012;54:415-20.
19. Pereira DS, de Queiroz BZ, Miranda AS, Rocha NP, Felicio DC, Mateo EC, Favero M, Coelho FM, et al. Effects of physical exercise on plasma levels of brain-derived neurotrophic factor and depressive symptoms in elderly women—a randomized clinical trial. 2013;94:1443-50.
20. Sparrow D, Gottlieb DJ, Demolles D, Fielding RA. Increases in muscle strength and balance using a resistance training program administered via a telecommunications system in older adults. J Gerontol A Biol Med Sci Med Sci. 2011;66:1251-7.
21. Borg G. Psychophysical bases of perceived exertion. Med Sci Sports Exerc. 1982;14:377–381.
22. Bandura A. Self-efficacy: Toward a unifying theory of behavior change. Psychol Review 1977; 84: 191-215.
23. Bandura A. Social foundations of thought and action: A social cognitive theory. Englewood Cliffs, NJ: Prentice-Hall, 1986.
24. Bandura A. Exercise of personal agency through the self-efficacy mechanism. In R. Schwarzer (Ed.), Self-

efficacy: Thought control of action (pp. 3-38). Washington, DC: Hemisphere, 1992.
25. Marcus BH, Selby VC, Niaura RS, Rossi JS. Self-efficacy and the stages of exercise behavior change. Res Q Exerc Sport 1992; 63: 60-66.
26. Sallis JF, Hovell MF, Hofstetter CR, Faucher P, Elder JP, Blancher E, Caspersen CJ, Powell KE, Christenson H. A multivariate study of determinants of vigorous exercise in a community sample. Prev Med 1989; 18: 20-34.
27. Ellis T, Cavanaugh JT, Earhart GM, Ford MP, Foreman KB, Fredman L, Boudreau JK, Dibble LE. Factors associated with exercise behavior in persons with Parkinson Disease. Phys Ther. 2011;91:1838-48.
28. Bandura A. Self efficacy: The exercise of control. New York: WH Freeman and Company, 1997.
29. Ellis T, Boudreau JK, DeAngelis TR, Brown LE, Cavenaugh JT, Earhart GM, Ford MP, Foreman KB, et al. Barriers to exercise in people with Parkinson disease. Phys Ther. 2013;93:628-36.
30. O'Leary KD, Wilson GT. Behavior therapy: Application and outcome. Second edition. Englewood Cliffs, NJ: Prentice Hall, 1987.
31. Spitzer RL, Gibbon M, Williams JBW. Structured clinical interview for Axis I DSM-IV disorders: Biometrics Research Department. New York State Psychiatric Institute 1994.
32. Marsh L, McDonald WM, Cummings J, Ravina B. Provisional diagnostic criteria for depression in Parkinson's disease: report of an NINDS/NIMH Work Group. Mov Disord 2006;21:148-158.
33. Hamilton M. A rating scale for depression. J Neurol Neurosurg Psychiatry 1960;23:56-62.
34. Peto V, Jenkinson C, Fitzpatrick R, Greenhall R. The development and validation of a short measure of functioning and well being for individuals with Parkinson's disease. Qual Life Res 1995;4:241-248.
35. Goetz CG, Tilley SR, Shaftman GT, et al. Movement Disorder Society-sponsored revision of the Unified Parkinson's Disease Rating Scale (MDS-UPDRS). Mov Disord.2008;23:2129-2170.
36. Robinson KA, Dennison CR, Wayman DM, Pronovost PJ, Needham DM. Systematic review identifies number of strategies important for retaining study participants. J Clin Epidemiol. 2007;60:757-765.
37. Cianci H. Parkinson Disease: Fitness Counts. 3rd ed. Miami, FL: National Parkinson Foundation; 2006.
38. Schrag A, Barone P, Brown RG, Leentjens AFG, McDonald WM, Starkstein S, Weintraub D, Poewe W, et al. Depression rating scales in Parkinson's disease: critique and recommendations. Mov Disord. 2007;22:1077-1092.
39. Rosner B. Percentage points for a generalized ESD many-outlier procedure. Technometrics. 1983;25:165-172.
40. Diggle PJ, Heagerty P, Liang KY, Zeger SL. Analysis of Longitudinal Data. New York: Oxford University Press Inc.; 1994.
41. Shirota Y, Ohtsu H, Hamada M, Enomoto H, Ugawa Y. Supplementary motor stimulation for Parkinson disease: a randomized controlled study. Neurology. 2013;80:1400-5.