https://doi.org/10.1016/j.apmr.2014.08.006

The following publication Mak, M. K., Wong, A., & Pang, M. Y. (2014). Impaired executive function can predict recurrent falls in Parkinson's disease. Archives of physical medicine and rehabilitation, 95(12), 2390-2395 is available at https://dx.doi.org/10.1016/j.apmr.2014.08.006

Title: Impaired executive function can predict recurrent falls in Parkinson's disease

Abstract

Objective: To examine whether impairment in executive function could independently predict recurrent falls in people with Parkinson's disease (PD).

Design: Prospective cohort study

Setting: University motor control research laboratory

Participants: A convenience sample of 144 community-dwelling people with PD was recruited from patients' self-help group and movement disorders clinics.

Intervention: Not applicable

Main outcome measures: Executive function was assessed by Mattis Dementia Rating Scale Initiation/Perseveration (MDRS-IP) subtest. Fear of falling was assessed by Activities-specific Balance Confidence (ABC) scale. All participants were followed up for 12 months to record the number of monthly fall events.

Results: Forty-two people with PD had at least two falls during follow-up and were classified as recurrent fallers. Multiple logistic regression analysis, after accounting for demographic variables and fall history ($p=0.001$), showed that ABC scores ($p=0.004$) and MDRS scores ($p=0.033$) were significantly associated with future recurrent falls in people with PD. The overall accuracy of the prediction was 83.1%. Using the same significant predictors identified in the above multiple logistic regression analysis, a prediction model as determined by the logistic function was generated. $Z = 1.814 + 1.352$ (fall history) $- 0.046$ (ABC) $- 0.018$ (MDRS-IP).

Conclusions: The results indicate that impaired executive function is a significant predictor of future recurrent falls in people with PD. Those with executive dysfunction and higher level of fear of falling upon baseline testing had a significantly higher risk of sustaining recurrent falls within the next 12 months.

Keyword: Accidental falls, executive function, Parkinson's disease, prediction

List of abbreviations

PD	Parkinson's disease
MDRS-IP	Mattis Dementia Rating Scale Initiation/Perseveration
ABC	Activities-specific Balance Confidence
HY	Hoehn and Yahr
UPDRS-III	Unified PD rating scale motor examination
GDS	Geriatric Depression Scale
PASE	Physical Activity Scale for the Elderly
FOGQ	Freezing of Gait Questionnaire
FoF	Fear of falling

Introduction

Falls are common among people with Parkinson's disease (PD) with a high fall incidence of 40-70%.[1] A long-term prospective study further reported an alarming fall rate of 87% during a 20-year period.[2] Among patients who experienced a fall, 35% of them sustained fractures.[2] In addition to physical injuries, PD fallers suffer adverse psychological effects, which can lead to functional restrictions, physical de-conditioning and increased risk of institutionalisation.[2] Identification of factors leading to falls has received considerable attention in recent years.

Fall-related risk factors in people with PD have been identified in various prospective studies. Significant physical fall risk factors include postural instability,[3] PD-specific impairment,[4] gait freezing,[5-7] and prolonged timed "up and go".[6] Self-perceived fear of falling has been found to be strongly associated with falls and reduced quality of life in people with PD.[4,8] Cognitive impairment such as impaired selective attention has been associated with increased postural instability and fall frequency.[9] Dementia and impaired fronto-executive function have been found to predict future falls in individuals with PD.[5] Executive function is an umbrella term that encompasses a host of higher cognitive abilities required to successfully perform goal-directed activities such as walking. Impaired executive function is a common cognitive feature of PD.[10] Executive dysfunction may disrupt organisation abilities and the performance of purposeful actions[11] and has been associated with increased gait variability and reduced gait speed during dual-task walking.[12] Hence, impaired executive function may increase the risk of falling. Indeed, impaired executive function has been found to predict future falls in community-dwelling older adults.[13,14] The association between executive dysfunction and falls, however, has not been examined in people with PD. This study used a 1-year prospective design to determine whether impaired executive function could predict recurrent falls in individuals with PD.

Materials and methods

Subjects

One hundred and seventy community-dwelling individuals with PD volunteered for the study and 144 PD individuals completed the study (Fig. 1). These PD individuals were recruited from the Hong Kong Parkinson's Disease Association, a patient self-help group, and the movement disorders clinics of two local hospitals. All patients were diagnosed by neurologists to have idiopathic PD.[15] To be included in the study, patients were required to be above 40 years of age, medically stable and able to walk 6 metres at least three times with or without an assistive device. Patients were excluded if they had neurological conditions other than idiopathic PD, a Mini Mental State Examination score < 24,[16] postural hypotension, visual disturbance or vestibular dysfunction affecting balance, or significant cardiovascular or musculoskeletal disorder limiting locomotion or balance.Informed consent was obtained from each participant in accordance with the 1964 Declaration of Helsinki. The experimental procedure and the use of human subjects were approved by the ethics committees and IRB of the involved university and hospitals.

Procedure

All assessments were carried out at the University motor control research laboratory. All participants were tested during the "on" phase of the anti-Parkinsonian medication cycle. Each subject underwent evaluation of the following outcome measures at baseline.

Baseline measurements

The demographic data including age, gender, time since the diagnosis of PD and daily dosage of levodopa were recorded. Disease severity and PD-specific motor impairment and disability were assessed by Hoehn and Yahr (HY) staging scale[17] and Unified PD rating scale motor examination (UPDRS-III) respectively.[18] Depressive symptoms were measured by the Chinese version of the short-form Geriatric Depression Scale (GDS).[19] The questionnaire contains 15 items with a "YES" or "NO" response for each item. The GDS score ranges from 0 to 15, with a score >6 being suggestive of clinical depression. Information on the number of fall events over the prior 12 months was obtained via patient interview. Subjects were classified as having a fall history if they had suffered at least one fall in the past 12 months. A fall is defined as an event during which a patient comes to rest on the ground or at some lower level, not as the result of a major intrinsic event e.g. syncope, stroke or seizure, or an overwhelming hazard.[20]

The recent physical activity level of each subject was assessed with the Physical Activity Scale for the Elderly (PASE).[21] This questionnaire consists of 10 items that assess the frequency and duration of an individual's leisure, household and work-related activities in the past 7 days. The total PASE score ranges from 0 to 400, with higher scores indicating a higher physical activity levels.

The Freezing of Gait Questionnaire (FOGQ) was used to detect and rate patients' subjective perception of the severity and impact of freezing on their gait performance.[22] It consists of six items that assess FOG severity and walking difficulties in general. FOGQ is rated from 0 to 4, with the total score ranging from 0 to 24. Higher scores indicate that walking performance is more affected by freezing.

The balance performance of subjects was assessed with the Mini-BESTest.[23] The Mini-BESTest includes 14 items representing four domains of dynamic balance: anticipatory postural adjustments, postural responses, sensory orientation and balance during gait activities. The Mini-BESTest items are rated from 0 to 2, with the total score ranging from 0 to 28. Higher scores represent better balance performance.

The validated Chinese version of the Activities-specific Balance Confidence (ABC) scale was used to estimate fear of falling (FoF).[24] The subjects were asked to rate their self-perceived balance confidence from 0 (no confidence at all) to 100 (full confidence) in completing 16 activities of daily living. The mean score of the 16 activities was calculated for each subject, with a minimum score of 0 and a maximum of 100.

Executive function was assessed by the Mattis Dementia Rating Scale (MDRS),[25] which is a neuropsychological instrument designed for the assessment of cognitive functions. The MDRS comprises five subsets that measure abilities in different cognitive domains: attention, initiation/perseveration (IP), construction, conceptualisation and memory. Of these subsets, the IP subset has been validated as an executive function measure in PD patients.[26] The MDRS-IP comprises 11 items that survey different executive abilities including verbal fluency, verbal programming, motor programming and perseverations in drawing, yielding a score between 0 and 37, with a higher scores indicating better executive function. Tests including FOGQ, Mini-BEST test, ABC and MDRS scales were carried out in a randomised order. All tests were completed in 1.5 hours and intermittent rests were given to subjects to prevent fatigue.

Prospective assessment of falls

After the baseline assessment, PD participants were instructed to complete a fall diary and were also contacted by phone by the end of each month to record any fall events.[20] Each participant was followed up for 12 months after the initial assessment. A person was classified as a recurrent faller (RF) if he or she had more than one fall within the 12-month follow-up period.

Statistical Analysis

Descriptive statistics were used to examine the central tendency and variability of all measured variables. The data normality was checked using the Shapiro-Wilk test. To avoid the inflated risk of making a type I error associated with multiple comparisons, multivariate analysis of variance was used to compare the differences in continuous variables such as age, duration of PD, daily dosage of levodopa, UPDRS score, GDS score, Mini-BESTest score, ABC score and MDRS-IP score between RFs and non-RFs. Mann-Whitney U test and Chi-square test were used to analyse differences between these two groups in ordinal variables (i.e. HY stage), and nominal variables (i.e. gender, fall history) respectively. Pearson product correlation coefficient was used to establish the association between MDRS-IP and ABC score. Hierarchical logistic regression analysis was first used to determine whether executive function (MDRS-IP) could significantly predict recurrent falls after adjusting for the effects of other relevant factors. The selection of independent variables for the regression analysis was based on physiological relevance and findings from previous studies on fall prediction in patients with PD.[3-7] Demographic data (i.e. age, gender, duration of PD, UPDRS score, prior fall history, HY stage, GDS score, madopar dosage, and PASE score) were entered first (step 1). Next, balance and mobility function, which have been shown to influence fall rate in patients PD[3-7] (i.e. FOG, Mini-BESTest score, ABC score) was entered into the model (step 2). Finally, the variable of interest, MDRS-IP score, was entered in the regression model (step 3). In each step, we employed the “Enter” method whereby the variables selected were forced into the same regression model. For daily clinical practice, it would be more useful to have an equation that enables the prediction of the probability of recurrent falls in individuals with PD. Using the same significant predictors identified in the above multiple logistic regression analysis, a logistic function was generated.

$$Z = a + b_1X_1 + b_2X_2 + b_3X_3 + \ldots$$

Where Z is the logit (natural logarithm of the odds), *a* is a regression constant, and *b* is the regression coefficient. [27]

The predicted probability of recurrent falls can then be estimated by the following formula[27]

$$\text{Probability of recurrent falls} = e^z/(1 + e^z)$$

Where e is the base of the natural logarithm.

The probability value could range from 0 to 1. A value closer to 1.0 (above 0.5) predicts that recurrent falls are likely to occur, whereas a value closer to 0 (below 0.5) indicates that the individual is not likely to have recurrent falls. All statistical tests were performed with SPSS 20.0 (SPSS Inc., Chicago, USA). A significance level of 0.05 was set for all statistical tests.

Results

A total of 144 PD individuals completed the study (Table 1). At the end of the 12-month follow-up period, 42 participants (29.2%) reported more than one fall and were thus classified as RFs. RFs had significantly higher HY scores (p=0.001), higher FOGQ scores (p=0.004), and lower Mini-BESTest (p=0.017), ABC (p<0.001), and MDRS-IP scores (p=0.018) than non-RFs Thus, upon baseline testing, RFs had more advanced disease, more severe gait freezing, greater postural instability, higher level of fear of falling, and more impaired executive function. There was no association between MDRS-IP and ABC score for RFs ($p>0.05$) and a significant correlation between MDRS-IP and ABC score for non-RFs ($r=0.403$, $p<0.001$).

According to the multiple logistic regression analysis used to identify significant predictors for recurrent falls among individuals with PD (Table 2), fall history ($p=0.001$), a low ABC score ($p=0.014$) and a low MDRS-IP score ($p=0.006$) were significantly associated with recurrent falls. The overall accuracy of the prediction was 85.9%. Using the same significant factors, the prediction model as determined by the logistic function is expressed as

$$Z = 1.544 + 0.378\ (\text{fall history}) - 0.045\ (\text{ABC}) - 0.145\ (\text{MDRS-IP})$$

This formula suggests that PD individuals with a fall history and low ABC and MDRS-IP scores have a higher risk of falling.

Discussion

Our prediction formula highlights the importance of evaluating both self-perception of balance confidence and executive function in predicting future falls in PD individuals Our results also suggest the potential role of treatment interventions that enhance balance confidence and executive function in preventing recurrent falls in individuals with PD.

A number of prospective studies have already found that prior falls are strongly predictive of future falls.[1,4,6,7] Thus, it is somewhat expected that a positive fall history would be the most significant predictor of future recurrent falls in our study. fall history cannot be altered, therefore the identification of modifiable factors prior to patients' first fall (ie. In newly diagnosed patients) could be more meaningful in formulating fall prevention programmes. Our finding that more fear of falling was a significant fall predictor confirmed previous reports.[4,28]

The association between fear of falling and lower postural control and mobility level could contribute to increased fall risk in people with PD .[29,30] However, our logistic regression model showed that fear of falling has independent effect on recurrent fall risk after adjusting for other relevant factors.

The most interesting finding is that impaired executive function independently increases the fall risk in people with PD. There was also a lack of significant association between executive function and fear of falling in RFs, further suggesting that that both of these entities have to be addressed in fall prediction. Most falls occur during walking, and the common perceived causes are tripping and loss of concentration.[28,32] A previous study reported a low score (<17/18) on the Frontal Assessment Battery i.e. fronto-executive impairment, led to a more than threefold increase in fall risk.[5] We are the first to report that impaired executive function, expressed as relatively poor performance on the MDRS-IP, is a significant predictor of recurrent falls in people with PD. Successful performance on the MDRS-IP requires intact cognitive processes including initiation, perseverance, inhibition of inappropriate responses, set-shifting, task monitoring and attention. These cognitive processes are essential for initiating and monitoring gait and other upright functional activities that require balance control. Executive dysfunction contributes to increased risk of falling possibly through delayed initiation, poor attention and task monitoring, impaired task switching and failed inhibition of motor responses.[5,9] A delay in initiating postural responses to restore an upright position could lead to falls upon tripping or slipping. Difficulties or delay in task switching such as turning or avoiding obstacles while walking and inappropriate planning or programming of walking tasks in a complex environment can increase the risk of falling. A subtle failure to inhibit inappropriate responses and/or difficulties in prioritising postural tasks during dual-task walking have been found in PD individuals,[33] especially those with executive dysfunction.[19] These difficulties may lead to increased risk of falling.

Our results showed that RFs had significantly lower FoG questionnaire and Mini-BESTest scores but that these two factors do not have independent predictive power in the presence of demographic data, fall history, fear of falling and executive function. These findings are in contrast with reported findings of association between increased gait freezing and increased risk of falling (OR=3.5-4.2).[5-7] These studies predicted fallers whilst our study predicted RF. The mean FoG score of the non-faller group in Kerr et al.[6] was 3.1 whilst that of our non-RF was 8.5, implying that some non-RF had gait freezing and therefore this measure might not be able to discriminate RF and non-RF. A low Mini-BESTest score has been found to predict future falls in PD individuals.[3] However, the reported studies did not include ABC or executive function in the models. Our results suggest that perceived and/or cognitive fall risk factors could be stronger than the physiological factors for prediction of falls.

Clinical implications

Our study suggests that physiological, psychological and cognitive risk factors should be included in fall risk assessments for people with PD. The prediction model developed in this study may be useful in estimating the probability of recurrent falls. For example, if an individual has experienced 3 falls in the past 12 months, with a low balance confidence (ABC score = 30) and impaired executive function (MDRS-IP score = 6), the Z value (logit) would be 0.458. The resulting estimated probability of recurrent falls would be 0.61, indicating that the individual will likely have recurrent falls. Further study is required to validate this prediction model using a different sample of PD patients. Our findings also suggest that interventions that manage PD individuals' executive functioning and enhance their self-perceived balance confidence could be useful in reducing future falls. Behavioural interventions and computer games have been found to enhance attention and executive function in individuals with PD,[34] Exercises that improve the feedforward and feedback mechanisms of postural control have been reported to enhance balance confidence in people with PD[35 (add Shen 2014)]. Cognitive behavioural therapy has been shown to reduce fear of falling in older people.[36] Further study is needed to examine the short- and long-term effects of these treatment interventions in fall prevention for people with PD.

Study limitations

We included subjects who were cognitively intact (MMSE ≥ 24) and results of the study could not be applied to those who have cognitive deficits. One major limitation of the study is that executive function is an umbrella term that encompasses a host of abilities. In this study, we used the MDRS-IP as the measure of executive function. Although the MDRS-IP contains test items for a number of important executive abilities such as set shifting and motor programming, it is by no means a comprehensive measure of executive function. A number of neuropsychological tests have been used to investigate executive function in PD. For instance, the Wisconsin Card Sorting Test, the Trail Making Test and the Tower of London test have shown sensitivity for detecting executive impairments in the PD population.[37,38] However, these tests have not been used to predict falls in people with PD. The present study showed that the MDRS-IP, which requires a short period of training for administration and scoring and can be completed in 10 minutes, is adequately sensitive for predicting risk of recurrent falls. The use of a simple executive function assessment increases the applicability of the results to a wide variety of clinical and research settings.

In conclusion, impaired executive function can independently predict recurrent falls in people with PD. Prediction model indicates that a positive fall history, more fear of falling and impaired executive function increases fall risk in people with PD. These findings suggest that psychological and cognitive risk factors should be considered in fall risk assessment. Fall prevention programmes for people with PD should be multi-dimensional, addressing the physical, psychological and cognitive domains of function.

References

1. Pickering RM, Grimbergen YM, Rigney U, et al. A meta-analysis of six prospective studies of falling in Parkinson's disease. Mov Disord 2007; 22: 1892-1900.
2. Hely MA, Reid WG, Adena MA, Halliday GM, Morris JG. The Sydney multicenter study of Parkinson's disease: the inevitability of dementia at 20 years. Mov Disord 2008; 3: 837-844.
3. Duncan RP, Leddy AL, Cavanaugh JT, et al. Accuracy of fall prediction in Parkinson disease: six-month and 12-month prospective analyses. Parkinsons Dis. 2012; 2012: 237673.
4. Mak MK, Pang MY. Fear of falling is independently associated with recurrent falls in patients with Parkinson's disease: a 1-year prospective study. J Neurol 2009; 256: 1689-1695.
5. Latt MD, Lord SR, Morris JG, Fung VS. Clinical and physiological assessments for elucidating falls risk in Parkinson's disease. Mov Disord 2009; 24: 1280-1289.
6. Kerr GK, Worringham CJ, Cole MH, Lacherez PF, Wood JM, Silburn PA. Predictors of future falls in Parkinson's disease. Neurology 2010; 75:116-124.
7. Paul SS, Canning CG, Sherrington C, Lord SR, Close JCT, Fung VSC. Three simple clinical tests to accurately predict falls in people with Parkinson's disease. Mov Disord 2013;28:655-662.

8. Brozova H, Stochl J, Roth J, Ruzicka E. Fear of falling has greater influence than other aspects of gait disorders on quality of life in patients with Parkinson's disease. Neuro Endocrinol ogy Letters 2009; 30: 453-457.
9. Allcock LM, Rowan EN, Steen IN, Wesnes K, Kenny RA, Burn DJ. Impaired attention predicts falling in Parkinson's disease. Parkinsonism Relat Disord 2009; 15: 110-115.
10. Goldman JG, Weis H, Stebbins G, Bernard B, Goetz CG. Clinical differences among mild cognitive impairment subtypes in Parkinson’s disease Mov Disord 2012;27:1129-1136
11. Fasano A, Plotnik M. Neurologic aspects and falls. Clinical Cases in Mineral and Bone Metabolism 2012; 9: 17-20.
12. Yogev G, Giladi N, Peretz C, Springer S, Simon ES, Hausdorff JM. Dual tasking, gait rhythmicity and Parkinson’s disease: which aspects of gait are attention demanding? Eur J Neurosci 2005; 22: 1248-1256.
13. Mirelman A, Herman T, Brozgol M et al, et al. Executive Function and Falls in Older Adults: New Findings from a Five-Year Prospective Study Link Fall Risk to Cognition. PLoS ONE 2012; 7: e40297. doi:10.1371/journal.pone.0040297
14. Buracchi, TJ, Mattek NC, Dodge HH, et al. Executive function predicts risk of falls in older adults without balance impairment, BMC Geriatrics 2011; 11:74.
15. Hughes AJ, Daniel SE, Kilford L, Lees AJ. Accuracy of clinical diagnosis of idiopathic Parkinson’s disease: a clinico-pathological study of 100 cases. J Neurol Neurosurg Psychiatry 1992; 55: 181-184.
16. Folstein MF, Folstein SE, MeHugh PR. Mini-mental state: a practical method for grading the state of patients for the clinician. J Psychiatr Res 1975; 12: 189-198.

17. Hoehn MM, Yahr MD. Parkinsonism: onset, progression and mortality. Neurology 1967; 17: 427-442.

18. Fahn S, Elton RL, members of the UPDRS Development Committee. Unified Parkinson’s Disease Rating Scale. In: Fahn D, Marsden CD, Calne D, Goldstein M, editors. Recent Development in Parkinson’s disease, vol. 2. Florham Park, NJ: Maacmillan Healthcare Information. 1987; p153-163,293-304.

19. Lee HCB, Chiu HFF, Kwong PPK. Cross-validation of the Geriatric Depression Scale short form in the Hong Kong elderly. Bull Hong Kong Psychol Soc 1994; 32: 72-77.

20. Tinetti ME, Speechley M, Ginter SF. Risk factors for falls among elderly persons living in the community. N Engl J Med 1988; 319:1701-1707.

21. Ngai SP, Cheung RT, Lam PL, Chiu JK, Fung EY. Validation and reliability of the Physical Activity Scale for the Elderly in Chinese population. J Rehabil Med 2012; 44: 462-465.

22. Giladi N, Tal J, Azulay T, et al. Validation of the freezing of gait questionnaire in patients with Parkinson's disease. Mov Disord 2009; 24: 655-661.

23. Franchignoni F, Horak F, Godi M, Nardone A, Giordano A. Using psychometric techniques to improve the Balance Evaluation Systems Test: The Mini-BESTest. J Rehabil Med 2010; 42: 323-331.

24. Mak MK, Lau AL, Law FS, Cheung CC, Wong IS. Validation of the Chinese translated activities-specific balance confidence scale. Arch Phys Med Rehabil 2007; 88: 496-503.

25. Mattis S. Mental Status Examination for organic mental syndrome in the elderly patients. In L. T. Bellack L (Ed.), Geriatric Psychiatry: A Handbook for Psychiatrists and Primary Care Physicians, New York, Grune & Stratton, 1976, pp77-121.

26. Villeneuve S, Rodrigues-Brazete J, Joncas S, Postuma RB, Latreille V, Gagnon JF. Validity of the Mattis Dementia Rating Scale to detect mild cognitive impairment in Parkinson's disease and REM sleep behavior disorder. Dement Geriatr Cogn Disord 2011; 31: 210-217.
27. Portney LG, Watkins MP. Foundations of clinical research. Applications to practice. 3rd ed. Upper Saddle River, NJ: Pearson Education, Inc. 2009
28. Bloem BR, Grimbergen YA, Cramer M, Willemsen M, Zwinderman AH. Prospective assessment of falls in Parkinson’s disease. J Neurol 2001; 248: 950-958.
29. Franchignoni F, Velozo CA. Use of the Berg Balance Scale in rehabilitation evaluation of patients with Parkinson's disease. Arch Phys Med Rehabil 2005; 86: 2225-2226.
30. Mak MK, Pang MY. Balance self-efficacy determines walking capacity in people with Parkinson's disease Mov Disord 2008; 23: 1936-1939.
31. Mak MK, Pang MY, Mok V. Gait difficulty, postural instability, and muscle weakness are associated with fear of falling in people with Parkinson's disease. Parkinsons Dis 2012; 2012: 901721.
32. Mak MK, Pang MY. Parkinsonian single fallers versus recurrent fallers: different fall characteristics and clinical features. J Neurol 2010; 257: 1543-1551.
33. Bloem B, Grimbergen Y, Gert van Dijk J, Munneke M. The ‘posture second’ strategy: a review of wrong priorities in Parkinson’s disease. J Neurol Sci 2006; 248: 196-204.
34. Witt K, Daniels C, Daniel V, Schmitt-Eliassen J, Volkmann J, Deuschl G. Patients with Parkinson’s disease learn to control complex systems-an indication for intact implicit cognitive skill learning. Neuropsychologia 2006; 44: 2445-2451.
35. Smania N, Corato E, Tinazzi M, et al. Effect of balance training on postural instability in patients with idiopathic Parkinson's disease. Neurorehabil Neural Repair 2010; 24: 826-834.

36. Zijlstra GAR, Van Haastregt JCM, Ambergen T, Van Rossum E, Van Eijk JTM, Tennstedt SL, et al. Effects of a multicomponent cognitive behavioral group intervention on fear of falling and activity avoidance in community-dwelling older adults: results of a randomized controlled trial. J AmGeriatr Soc 2009; 57: 2020-2028.

37. Vingerhoets G, Verleden S, Santens P, Miatton M, De Reuck J. Predictors of cognitive impairment in advanced Parkinson's disease. J Neurol Neurosurg Psychiatry 2003; 74: 793-796.

38. Lewis SJ, Cools R, Robbins TW, Dove A, Barker RA, Owen AM. Using executive heterogeneity to explore the nature of working memory deficits in Parkinson's disease. Neuropsychologia 2003; 41: 645-654.

39. Shen X, Mak MKY**.** Balance and gait training with augmented feedback improves balance confidence in people with Parkinson's disease: A randomised controlled trial. Neurorehabil Neural Repair 2014:DOI: 10.1177/1545968313517752

40. **Figure Legend:**

Fig. 1 Flow chart showing the selection procedure of PD subjects.