

Parkinson's Disease Current Awareness Bulletin March 2019

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Title: Parkinson's disease: summary of updated NICE guidance

Citation: BMJ : British Medical Journal (Online); Feb 2019; vol. 364

Title: The use of commercially available games for a combined physical and cognitive challenge during exercise for individuals with Parkinson's disease - a case series report.

Citation: Physiotherapy Theory & Practice; Apr 2019; vol. 35 (no. 4); p. 355-362 **Author(s):** Pradhan, Sujata

Abstract: Complexity of an animal's environment has been shown to affect structural and functional changes in the brain. Evidence from animal models of Parkinson's disease (PD) suggests that exercising in an enriched environment may protect against the onset of Parkinsonian symptoms in rats that are exposed to 1-methyl-4-phenyl-1.2.3.6tetrahydropyridine. The variety of activities and visual interfaces that can be created using commercially available gaming devices provide cognitively stimulating as well as physically challenging environments for exercise. This case series will: 1) elaborate on the rationale behind selection of specific games to target common deficits seen in PD; and 2) present preliminary results on clinical outcomes from three pilot participants who each completed six sessions of exercise. All three participants had mild to moderate PD. They were functionally independent individuals leading an active lifestyle. Participants were tested on the outcome measures before and after the six exercise sessions. On average, participants showed a 33.8% (22.8) improvement in functional reach test, 12.7% (35.0) improvement in single limb stance (SLS) time—right leg, 55.2% (33.9) improvement in SLS time—left leg, 11.9% (7.3) improvement in 6-min walk test, 2% (6.8) improvement in self-selected gait speed (GS), and 8.0% (5.8) improvement in fastest possible GS. Further investigation is warranted to study if these effects can be replicated over a longer exercise intervention and in a larger group, and if these effects are maintained at follow-up testing after the enriched exercise intervention is discontinued.

Title: Multisystem Balance Training Reduces Injurious Fall Risk in Parkinson Disease: A Randomized Trial.

Citation: American Journal of Physical Medicine & Rehabilitation; Mar 2019; vol. 98 (no. 3); p. 239-244

Author(s): Wong-Yu, Irene S. K.; Mak, Margaret K. Y.

Abstract: Previous studies have shown that balance training could reduce falls in people with Parkinson disease. However, it remains unclear whether exercise can reduce injurious falls. The objective of present study was to determine whether multisystem balance training could reduce injurious falls and modify targeted fall risk factors in Parkinson disease nonfallers and single fallers. Participants were randomly assigned to an 8-wk balance group (experimental, n = 41) or an upper limbs group (control, n = 43). Outcomes examined at posttraining and 12-mo follow-up were: (1) injurious fall risk (ratio of noninjurious fallers to injurious fallers); (2) two potential fall risk factors based on Balance Evaluation Systems Test scores and dual-task timed-up-and-go times. At posttraining, results indicated that there were no injurious falls, and fewer experimental participants were found in high fall risk cohorts based on Balance Evaluation Systems Test scores and dual-task timed-up-and-go times. Test scores and dual-task timed-up-and-go times (P < 0.05). At 12-mo follow-up, the number of injurious fallers was lower in

experimental group (P < 0.05). There was also a marginally lower percentage of experimental group in the high fall risk cohort based on Balance Evaluation Systems Test scores (P = 0.059). The findings conclude that multisystem balance training potentially reduces injurious fall risk up to 12-mo posttraining and lowers balance-related fall risks in people with Parkinson disease.

Title: Factors to Consider in the Selection of Dopamine Agonists for Older Persons with Parkinson's Disease.

Citation Drugs & Aging; Mar 2019; vol. 36 (no. 3); p. 189-202 **Author(s):** Latt, Mark Dominic; Lewis, Simon; Zekry, Olfat; Fung, Victor S. C.

Abstract: Dopamine agonists (DAs) are frequently used in the management of Parkinson's disease (PD), a complex multisystem disorder influenced substantially by age-related factors. Over 80% of PD patients present after age 60 years and may have clinical features exacerbated by age-related comorbidities or decline in physiological compensatory mechanisms. Pharmacotherapy for motor symptoms in older persons is more likely to involve exclusive use of levodopa combined with a peripheral decarboxylase inhibitor throughout the course of the illness. Non-ergot DAs, such as pramipexole, rotigotine and ropinirole, may be used as de novo monotherapy for the control of motor symptoms in older persons, although they are less efficacious than levodopa therapy. DAs may also be considered as adjunct therapy in older persons when motor symptoms are no longer adequately controlled by levodopa or when motor fluctuations and dyskinesia appear. DAs may be used cautiously in older persons with cognitive impairment and orthostatic hypotension but should be avoided when there is a history or risk of psychosis or impulse control disorders.

Title: Regularly monitor neuropsychiatric symptoms in Parkinson's disease and adjust treatment as necessary.

Citation: Drugs & Therapy Perspectives; Mar 2019; vol. 35 (no. 3); p. 119-123 **Author(s):** Adis Medical Writers

Abstract: Neuropsychiatric disorders are frequent in Parkinson's disease (PD), but may be difficult to identify as they are closely related to other aspects of PD, such as motor impairment and non-motor fluctuations. While integral to PD treatment, dopaminergic therapies may contribute significantly to neuropsychiatric symptoms. Treatments in PD should be constantly reviewed and balanced, such as by adjusting doses appropriately, to minimize neuropsychiatric issues among other adverse events.

Title: Effects of Tai Chi Exercise on Reducing Falls and Improving Balance Performance in Parkinson's Disease: A Meta-Analysis.

Citation: Parkinson's Disease (20420080); Feb 2019 ; p. 1-8 **Author(s):** Liu, Hsin-Hsuan; Yeh, Nai-Chen; Wu, Yi-Fan; Yang, Yea-Ru; Wang, Ray-Yau; Cheng, Fang-Yu **Introduction:** Parkinson's disease (PD) is a common neurodegenerative disorder that may increase the risk of falls, functional limitation, and balance deficits. Tai Chi was used as an option for improving balance in people with PD. The aim of this meta-analysis was to evaluate the effects of Tai Chi on falls, balance, and functional mobility in individuals with PD.

Method: The literature search was conducted in PubMed, the Cochrane Library, CINAHL, PEDro, Medline, Embase, sportDISCUS, Trip, and the National Digital Library of Theses and Dissertations in Taiwan. Randomized controlled trials (RCTs) analyzing the effects of Tai Chi, compared to no intervention or to other physical training, on falls, functional mobility, and balance in PD patients were selected. The outcome measurements included fall rates, Berg Balance Scale (BBS), Functional Reach (FR) test, and the Timed Up and Go (TUG) test. Two reviewers independently assessed the methodological quality and extracted data from the studies using the PEDro scale.

Results: Five RCTs that included a total of 355 PD patients were included in this review. The quality of evidence in these studies was rated as moderate to high. Compared to no intervention or other physical training, Tai Chi significantly decreased fall rates (odds ratio = 0.47, 95% confidence interval (CI) 0.30 to 0.74, and p=0.001) and significantly improved balance and functional mobility (BBS mean difference (MD) = 3.47, 95% CI 2.11 to 4.80, and p<0.001; FR MD = 3.55 cm, 95% CI 1.88 to 5.23, and p<0.001; TUG MD = -1.06 s, 95% CI -1.61 to -0.51, and p<0.001) in people with PD.

Conclusion: This meta-analysis provides moderate- to high-quality evidence from five RCTs that Tai Chi could be a good physical training strategy for preventing falls and improving balance and functional mobility in people with PD.

Title: Persuasive bodies: Testimonies of deep brain stimulation and Parkinson's on YouTube.

Citation: Social Science & Medicine; Feb 2019; vol. 222 ; p. 44-51 **Author(s):** Gardner, John; Warren, Narelle; Addison, Courtney; Samuel, Gabby

Abstract: Contemporary publics actively engage with diverse forms of media when seeking health-related information. The hugely popular digital media platform YouTube has become one means by which people share their experiences of healthcare. In this paper, we examine amateur YouTube videos featuring people receiving Deep Brain Stimulation (DBS) for the treatment of Parkinson's disease. DBS has become a widely implemented treatment, and it is surrounded by high expectations that can create difficulty for clinicians, patients and their families. We examine how DBS, Parkinson's disease, and DBS recipients themselves, are delineated within these YouTube videos. The videos, we demonstrate, contain common compositional and stylistic elements that collectively represent DBS as a technological fix, and which accentuate the autonomy of the DBS recipient. The relational, interpersonal dimensions of chronic illness, and the complex impact of DBS on family dynamics, are elided. We therefore shed light on the means by which high expectations regarding DBS are sustained and circulated, and more generally, we illustrate how potentially powerful representations of medical technologies can emerge from the intersection of social media platforms, afflicted bodies and patient narratives.

Highlights: • YouTube has become a forum for sharing experiences of deep brain stimulation (DBS). • Amateur YouTube videos configure DBS as a technological fix. • Videos often elide the complexity of chronic illness and its treatment. • Videos thus sustain expectations that technologies enhance patient independence. • Powerful portrayals emerge from intersections of social media, bodies & narratives.

Title: Optimism, Pessimism, Coping, and Depression: A Study on Individuals With Parkinson's Disease.

Citation: International Journal of Aging & Human Development; Apr 2019; vol. 88 (no. 3); p. 231-249

Author(s): Anzaldi, Kristen; Shifren, Kim

Abstract: Few published studies exist on how individuals with Parkinson's disease (PD) deal with their disease. We conducted this study to examine the relationship between optimism, pessimism, coping strategies, and depressive symptoms in individuals with PD. Specifically, we assessed the possible mediator role of optimism and pessimism on the relation between coping strategies and depressive symptoms in those with PD. Seventy individuals with PD (35 females and 35 males) were assessed with the Brief COPE scale, Life Orientation Test-Revised, and Center for Epidemiological Studies Depression Scale. Findings showed that individuals with PD used similar amounts of problem-focused coping strategies and emotion-focused coping strategies, and they reported more optimism than pessimism. There was only one gender difference: Females reported more problem-focused coping than males. Optimism was positively related to both emotion-focused and problem-focused coping. Optimism and pessimism fully mediated the relation between coping strategies and depressives and problem-focused and problem-focused coping. Optimism and pessimism fully mediated the relation between coping strategies and depressive symptoms.

Title: High-Cadence Cycling Promotes Sustained Improvement in Bradykinesia, Rigidity, and Mobility in Individuals with Mild-Moderate Parkinson's Disease.

Citation: Parkinson's Disease (20420080); Mar 2019 ; p. 1-7 **Author(s):** Ridgel, Angela L.; Ault, Dana L.

Introduction: Exercise has been shown to be an important adjunct therapy to medication in Parkinson's disease (PD). However, the optimal type, frequency, and intensity of exercise or physiotherapy are still being debated. An important part of understanding the optimal frequency is to examine how acute bouts of exercise affect motor function and mobility in this population. The purpose of this study is to assess if six bouts of high-cadence cycling improves motor function and mobility in individuals with PD.

Methods: Sixteen subjects with mild-moderate idiopathic PD were randomized into either a high-cadence cycling or a control (stretching) group. High-cadence cycling was completed on a custom motorized recumbent bicycle at a high cadence between 75 and 85 rpm. Cycling and stretching sessions were separated by 1 day of rest and took place over a 15-day period. Motor function and mobility were assessed after every cycling/stretching bout using the UPDRS Motor III scale, Kinesia ONE, and Timed up and Go (TUG).

Results: Six bouts of high-cadence cycling improved UPDRS scores (2.5 pts, P=0.002), hand movement amplitude (P=0.013), rapid alternating hand movement speed (P=0.003), gait (P=0.012), and TUG time (1.17 s, P=0.002) from baseline testing to end of treatment. The control group showed no improvements.

Conclusions: These findings suggest that they are both acute and sustained improvements in motor function and mobility after high-cadence cycling. Future research should examine how exercise type, frequency, and intensity can be optimized for each individual.

Title: Motor Improvement-Related Regional Cerebral Blood Flow Changes in Parkinson's Disease in Response to Antiparkinsonian Drugs.

Citation: Parkinson's Disease (20420080); Mar 2019 ; p. 1-8 **Author(s):** Taguchi, Soutarou; Tanabe, Nachi; Niwa, Jun-ichi; Doyu, Manabu

Abstract: Little is known about the relationship between regional cerebral blood flow (rCBF) change and clinical improvement in patients with Parkinson's disease (PD). Single-photon emission computed tomography (SPECT) measurement of cerebral blood flow allows evaluation of temporal changes in brain function, and using SPECT, we aimed to identify motor improvement-related rCBF changes in response to the administration of antiparkinsonian drugs. Thirty PD patients (16 without dementia; 14 with dementia) were scanned with technetium-99m labeled ethyl cysteinate dimer SPECT and were rated with the Movement Disorder Society-Unified Parkinson's Disease Rating Scale part III, both before and after a single administration of antiparkinsonian drugs. The SPECT data were processed using Statistical Parametric Mapping 2, the easy Z-score Imaging System, and voxel-based Stereotactic Extraction Estimation. The rCBF responses in the deep brain structures after administration of antiparkinsonian drugs tended to be larger than those in cortical areas. Among these deep brain structures, the rCBF increases in the substantia nigra (SN), lateral geniculate (LG) body, and medial geniculate (MG) body correlated with drug efficacy (p<0.05, respectively). A subgroup analysis revealed that the motor improvement-related rCBF change in the MG was statistically significant, irrespective of cognitive function, but the significant changes in the LG and SN were not found in subjects with dementia. In conclusion, our SPECT study clearly exhibited drug-driven rCBF changes in PD patients, and we newly identified motor improvement-related rCBF changes in the LG and MG. These results suggest that rCBF changes in these regions could be considered as candidates for clinical indicators for objective evaluation of disease progression. Furthermore, functional studies focusing on the LG and MG, especially in relation to therapies using audio-visual stimuli, may bring some new clues to explain the pathophysiology of PD.

Title: The Effectiveness of Reality Orientation Therapy in the Treatment of Parkinson Disease Dementia.

Citation: American Journal of Alzheimer's Disease & Other Dementias; Mar 2019; vol. 34 (no. 2); p. 124-130

Author(s): Camargo, Carlos Henrique Ferreira; Ladeira, Marcelo Araújo; Serpa, Rafael Arthur; Jobbins, Vinicius Aguiar; Filho, Carlos Rory Pucci; Welling, Leonardo Christiaan; Teive, Hélio Afonso Ghizoni

Abstract: Patients with Parkinson disease dementia (PDD) have deficits resulting mainly from frontostriatal dysfunction. The aim of this study was to assess the effectiveness of reality orientation therapy (ROT) combined with drug therapy (acetylcholinesterase inhibitors) in PDD treatment and compare it with that of drug therapy alone. Patients (n = 12) with a diagnosis of PDD were divided into 2 groups: group A--drug therapy and ROT; group B--drug therapy alone. Reality orientation therapy was applied weekly for 6 months, and patients were assessed during the same period. Significant improvements in frontostriatal deficits were observed in the group that received the combined therapy, as shown mainly by the scores in verbal fluency in the Consortium to Establish a Registry for Alzheimer's Disease (CERAD) battery (P = .02) and in attention in Scales for outcomes of Parkinson's Disease-Cognition (P = .021) and Clock Drawing Test (P = .037). Patients who received only

medication had worse results in constructional praxis recall in the CERAD battery (P = .037). Our results indicate that ROT may help in the treatment of frontostriatal cognitive deficits and can potentially be used to complement drug therapy.

Title: "It's like having an evil twin": an interpretative phenomenological analysis of the lifeworld of a person with Parkinson's disease.

Citation: Journal of Research in Nursing; Mar 2019; vol. 24 (no. 1/2); p. 49-58 **Author(s):** Eatough, Virginia; Shaw, Karen

Background: This paper offers an understanding of the lifeworld of a person with Parkinson's Disease derived from interpretative phenomenological analysis (IPA). Aims The paper has two main aims: firstly, to demonstrate how a focus on individual experience chimes with and can inform current ideas of a more personalised humanised form of healthcare for people living with Parkinson's disease; and secondly, to demonstrate how an IPA study can illuminate particularity whilst being able to make, albeit cautiously, more general knowledge claims that can inform wider caring practices. Methods It achieves these aims through the detailed description and interpretation of one person's experience of living with Parkinson's disease using the IPA approach. Results Three analytic themes point to how the various constituents of the lifeworld, such as embodiment, selfhood, temporality and relationality are made manifest. These enable the IPA researcher to make well-judged inferences, which can have value beyond the individual case. Conclusions A key feature of IPA is its commitment to an idiographic approach that recognises the value of understanding a situated experience from the perspective of a particular person or persons.

Title: The Association between Toxoplasma gondii Infection and Risk of Parkinson's Disease: A Systematic Review and Meta-Analysis.

Citation: BioMed Research International; Feb 2019 ; p. 1-8

Author(s): Zhou, Zonglei; Zhou, Ruzhen; Li, Kunpeng; Wei, Wen; Zhang, Zengqiao; Zhu, Yan; Luan, Rongsheng

Background: Several studies have investigated the association between Toxoplasma gondii (T. gondii) infection and risk of Parkinson's disease (PD) with inconsistent results. Clarifying this relation might be useful for better understanding of the risk factors and the relevant mechanisms of PD, thus a meta-analysis was conducted to explore whether exposure to T. gondii is associated with an increased risk of PD.

Methods: We conducted this meta-analysis according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement. A rigorous literature selection was performed by using the databases of PubMed, Embase, Web of Science, Cochrane Library, and ScienceDirect. Odds ratio (OR) and corresponding 95% confidential interval (CI) were pooled by using fixed-effects models. Sensitivity analysis, publication bias test, and methodological quality assessment of studies were also performed.

Results: Seven studies involving 1086 subjects were included in this meta-analysis. Pooled data by using fixed-effects models suggested both latent infection (OR, 1.17; 95% CI, 0.86 to 1.58; P=0.314) and acute infection (OR, 1.13; 95% CI, 0.30 to 4.35; P=0.855) were not associated with PD risk. Stable and robust estimates were confirmed by sensitivity analysis. No publication bias was found by visual inspection of the funnel plot, Begg's, and Egger's test.

Conclusions: This meta-analysis does not support any possible association between T. gondii infection and risk of PD. Researches are still warranted to further explore the underlying mechanisms of T. gondii in the pathogenesis of PD and their causal relationship.

Title: Everyday Language Difficulties in Parkinson's Disease: Caregiver Description and Relationship With Cognition, Activities of Daily Living, and Motor Disability.

Citation: American Journal of Speech-Language Pathology; Feb 2019; vol. 28 ; p. 165-173 **Author(s):** Wolff, Logan; Benge, Jared

Purpose: Parkinson's disease (PD) impacts language in multiple ways, though important questions remain. The current article explores 2 main issues: what type of everyday language difficulties (ELDs) are noted by care partners and how do ELDs relate to cognition, daily activities, and motor disability in PD.

Method: Care partner reports of ELD were collected in 42 community-dwelling individuals with PD. Descriptive information of ELD was tallied, and the relationship of cognitive decline, activities of daily living (ADLs), and motor disability with ELD was evaluated.

Results: Forty-two percent of patients were described by care partners as having at least 1 consistent ELD, and the frequency of ELD increased in the presence of dementia, $\chi^2(2) = 14.37$, p = .0008. The most commonly described ELDs by caregivers were related to comprehension of instructions and deriving the point of conversations. ELD was correlated with worse cognition (rs = -.524, p < .001), increased difficulty with daily activities (rs = .634, p < .001), and increased motor dysfunction (rs = .554, p < .001). Mild ADL decline (Functional Assessment Questionnaire score of 4); an area under the curve of .81 (SE = .07) was highly specific to the presence of ELD (95.4%).

Conclusions: Care partners note a variety of ELDs in patients with PD, most commonly comprehension difficulties. These difficulties increase with overall cognitive decline but are described in 30%-40% of those without significant cognitive deficits. ADL difficulties correlate with functional, motoric, and cognitive status, with even mild functional declines predictive of the presence of ELD. Implications for research and practice in this population are discussed.

Title: Influence of alarming auditory cues on viscoelastic stiffness of skeletal muscles in patients with Parkinson's disease.

Citation: Clinical Biomechanics; Feb 2019; vol. 62 ; p. 93-95 **Author(s):** Rätsep, Tõnu; Asser, Toomas

Background: Patients with Parkinson's disease can show brief normalization of motor activity in response to intense external stimuli – a phenomenon known as paradoxical kinesis. The purpose of the present study was to examine the effect of alarming auditory signals on the level of viscoelastic stiffness of skeletal muscles as an indicator of parkinsonian rigidity.

Methods: Myotonometry was used to determine the changes of viscoelastic stiffness of skeletal muscles in ten patients in an advanced stage of Parkinson's disease, treated with deep brain stimulation, and ten healthy controls. The measurements were repeated and compared during the stimulation-on and stimulation-off periods, with and without auditory alarming signals.

Findings: The mean values of stiffness measured in the stimulation-off phase (370.4 N/m) were significantly higher than the values obtained in the stimulation-on phase (339.2 N/m) (q = 6.05; P < 0.01) but also in the stimulation-off with alarming signals phase (349.6 N/m) (q = 4.04; P < 0.05). In the normal controls, exposure to the auditory alarming signals did not change the values of viscoelastic stiffness.

Interpretation: These findings demonstrate that the phenomenon of paradoxical kinesis is associated with the changes of muscular rigidity in parkinsonian patients.

Results: from the study may help to establish new strategies for addressing motor disabilities in patients with Parkinson's disease.

Highlights: • Viscoelastic stiffness is elevated in patients with higher parkinsonian rigidity. • The values of viscoelastic stiffness decreased due to alarming signals. • Paradoxical kinesis is accompanied by decrease of muscular rigidity.

Title: Efficacy of safinamide on non-motor symptoms in a cohort of patients affected by idiopathic Parkinson's disease.

Citation: Neurological Sciences; Feb 2019; vol. 40 (no. 2); p. 275-279 **Author(s):** Bianchi, Maria Laura Ester; Riboldazzi, Giulio; Mauri, Marco; Versino, Maurizio

Abstract: The primary endpoint of this work was to evaluate the effect of safinamide on nonmotor symptoms (NMS) in patients affected by idiopathic Parkinson's disease (PD) complicated by motor fluctuations. We retrospectively collected data from 20 subjects affected by idiopathic PD in treatment with L-dopa alone or in combination with dopamine agonists, who began to be treated with safinamide due to the occurrence of motor fluctuations. Secondary endpoints included SCales for Outcomes in Parkinson's disease (SCOPA) Motor Scale, cognitive assessment, the Hoehn and Yahr stage, Clinical Impression of Severity Index for Parkinson's Disease, Hospital Anxiety And Depression Scale, Physical and Mental Fatigue, Parkinson's disease Sleep Scale, Parkinson's Disease Questionnaire-8 (PDQ-8) and EQ-5D. Each one of these scales/questionnaires was performed at baseline and T1. For efficacy analyses, continuous variables were treated with descriptive statistics, using mean and standard deviations. A non-parametric test (the Friedman test) was carried out to evaluate the statistical significance of the results observed. We found a statistically significant reduction of the total score of NMS, of 6 domains out of 9. and 13 items out of 30. A statistically significant reduction of SCOPA Motor Scale, PDQ-8, and CISI was also detected. In conclusion, our data showed a positive effect of safinamide on NMS and confirm its positive effect on motor symptomatology.

Title: Factors associated with freezing of gait in patients with Parkinson's disease.

Citation: Neurological Sciences; Feb 2019; vol. 40 (no. 2); p. 293-298 **Author(s):** Choi, Seong-Min; Jung, Hyun-Jung; Yoon, Geum-Jin; Kim, Byeong C.

Title: The performance of patients with Parkinson's disease on the Face-Name Associative Memory Examination.

Citation: Neurological Sciences; Feb 2019; vol. 40 (no. 2); p. 405-407 **Author(s):** Kormas, Constantinos; Zalonis, Ioannis; Evdokimidis, Ioannis; Potagas, Constantin **Abstract:** In this study, we examined the performance of patients with Parkinson's disease (PD) with different cognitive profiles on the Face-Name Associative Memory Examination (FNAME). We evaluated 71 patients with a comprehensive neuropsychological battery. The results revealed that the group with executive and additional visuospatial deficits demonstrated significantly lower scores on FNAME. This finding indicates the possible clinical utility of FNAME for screening patients with PD with distinct cognitive profiles. Further longitudinal studies are needed to consider the prognostic adequacy of FNAME in detecting high-risk Parkinson's disease dementia (PDD).

Title: Understanding multifactorial architecture of Parkinson's disease: pathophysiology to management.

Citation: Neurological Sciences; Jan 2019; vol. 40 (no. 1); p. 13-23 **Author(s):** Kaur, Ramandeep; Mehan, Sidharth; Singh, Shamsher

Abstract: Parkinson's disease (PD) is the second most common multifactorial neurodegenerative disorder affecting 3% of population during elder age. The loss of substantia nigra, pars compacta (SNpc) neurons and deficiency of striatal dopaminergic neurons produces stables motor deficient. Further, increase alpha-synuclein accumulation, mitochondrial dysfunction, oxidative stress, excitotoxicity, and neuroinflammation plays a crucial role in the pathogenesis of PD. Alpha-synuclein protein encodes for SNCA gene and disturbs the normal physiological neuronal signaling via altering mitochondrial homeostasis. The level of α -synuclein is increased in both normal aging and PD brain to a greater extent and secondly reduced clearance results in accumulation of Lewy bodies (LB). Emerging evidences indicate that mitochondrial dysfunction might be a common cause but pathological insult through protein misfolding, aggregation, and accumulation leads to neuronal apoptosis. The observation supporting that expression of DJ-1, LLRK2, PARKIN, PINK1, and excessive excitotoxicity mediated by dysbalance between GABA and glutamate reduced mitochondrial functioning and increased neurotoxicity. Therefore, the present review summarizes the various pathological mechanisms and also explores the therapeutic strategies which could be useful to ameliorate movement disorder like Parkinsonism.

Title: Concordance for Parkinson's Disease in Twins: a 20-Year Update.

Citation: Annals of neurology; Feb 2019

Author(s): Goldman, Samuel M; Marek, Kenneth; Ottman, Ruth; Meng, Cheryl; Comyns, Kathleen; Chan, Piu; Ma, Jinghong; Marras, Connie; Langston, J William; Ross, G Webster; Tanner, Caroline M

Abstract: During the 1990s we estimated the genetic contribution to Parkinson's disease risk in a large population-based twin registry. Because many unaffected twins were still alive, prior concordance estimates were based on incomplete information. 95% of twins are now deceased. Here we update concordance and heritability through 2015 using National Death Index data. In total, we identified 30 concordant and 193 discordant pairs. Probandwise concordance was 0.20 in monozygotic and 0.13 in dizygotic pairs. Heritability was 0.27 overall, 0.83 in pairs diagnosed 50. High concordance in dizygotic twins suggests shared effects of early childhood environment. This article is protected by copyright. All rights reserved.

Title: A palm-worn device to quantify rigidity in Parkinson's disease.

Citation: Journal of neuroscience methods; Feb 2019; vol. 317; p. 113-120

Author(s): Perera, Thushara; Lee, Wee-Lih; Jones, Mary; Tan, Joy L; Proud, Elizabeth L; Begg, Angus; Sinclair, Nicholas C; Peppard, Richard; McDermott, Hugh J

Background: Parkinsonian rigidity is identified on clinical examination as resistance to passive movement. Measurement of rigidity commonly relies on ordinal rating scales (MDS-UPDRS), however instrumented objective measures may provide greater mechanistic insight.

New Method: We present a palm-worn instrument to objectively quantify rigidity on a continuous scale. The device employs a miniature motor to flex the third digit of the hand about the metacarpophalangeal joint whilst transducers record flexion/extension forces. We aim to determine congruence with the MDS-UPDRS, investigate sensitivity to the impact of deep brain stimulation (DBS) and contralateral movement, and make comparisons with healthy individuals. Eight participants with Parkinson's disease underwent evaluation during conditions: on and off DBS, and with and without contralateral limb movement to activate rigidity. During each DBS condition, wash-in/out effects were tracked using both our instrument and two blinded clinical raters. Sixteen healthy volunteers (age-matched/young) served as controls.

Results: Rigidity measured using our instrument had moderate agreement with the MDS-UPDRS and showed differences between therapeutic state, activation conditions, and disease/healthy cohorts. Rigidity gradually worsened over a one-hour period after DBS cessation, but improved more rapidly with DBS resumption.

Comparison with Existing Methods: Previous attempts to quantify rigidity include manual approaches where a clinician is required to manipulate limbs while sensors passively gather information, or large automated instruments to move the wrist or elbow.

Conclusion: Given its ability to track changes in rigidity due to therapeutic intervention, our technique could have applications where continuous measurement is required or where a suitably qualified rater is absent.

Title: Overview of the cholinergic contribution to gait, balance and falls in Parkinson's disease.

Citation: Parkinsonism & related disorders; Feb 2019

Author(s): Morris, Rosie; Martini, Douglas N; Madhyastha, Tara; Kelly, Valerie E; Grabowski, Thomas J; Nutt, John; Horak, Fay

Abstract: Mobility deficits, including gait disturbance, balance impairments and falls, are common features of Parkinson's disease (PD) that negatively impact quality of life. Mobility deficits respond poorly to dopaminergic medications, indicating a role for additional neurotransmitters. Due to the critical role of cortical input to gait and balance, acetylcholinean essential neurotransmitter system for attention-has become an area of interest for mobility. This review aimed to identify the role of cholinergic function on gait, balance, and falls in PD using three techniques; pharmacological, imaging, and electrophysiological. Studies supported the role of the cholinergic system for mobility in PD, with the most promising evidence indicating a role in falls. Imaging studies demonstrated involvement of anterior cholinergic (basal forebrain) systems in gait, and posterior (brainstem) systems in balance. However, this review identified a small number of studies which used varying protocols, making comparisons difficult. Further studies are warranted, measuring comprehensive gait and balance characteristics as well as gold standard falls detection to further quantify the relationship between ACh and mobility in PD.

Title: Deep Brain Stimulation and Cognitive Outcomes Among Patients With Parkinson's Disease: A Historical Cohort Study.

Citation: The Journal of neuropsychiatry and clinical neurosciences; Feb 2019 ; p. appineuropsych18050118

Author(s): Hansen, Allison L; Krell-Roesch, Janina; Kirlin, Kristin A; Limback-Stokin, Martin M; Roesler, Kimberly; Velgos, Stefanie N; Lyons, Mark K; Geda, Yonas E; Mehta, Shyamal H

Objective: Deep brain stimulation (DBS) is an effective treatment for motor symptoms of Parkinson's disease; however, there is conflicting literature about the effect of DBS on cognitive function. The authors conducted a historical cohort study involving patients with Parkinson's disease who underwent DBS of the globus pallidus pars interna (GPi; N=12) or subthalamic nucleus (STN; N=17).

Methods: The authors investigated differences in four neuropsychological test scores at 6 months post-DBS (follow-up) as compared with baseline (i.e., Boston Naming Test, WAIS Verbal Comprehension Index [WAIS-VCI], Working Memory Index [WAIS-WMI], and Processing Speed Index [WAIS-PSI]).

Results: GPi DBS patients showed no difference between baseline and follow-up on any neuropsychological test. STN DBS patients had lower scores indicating decreased performance at follow-up as compared with baseline on WAIS-PSI (mean [SD], 91.47 [10.42] versus 81.65 [12.03]; p=0.03). There was a significant (p=0.008) difference between the change in baseline to follow-up scores on the WAIS-VCI for the STN DBS and GPi DBS groups (i.e., STN DBS patients scored lower at the 6-month follow-up compared with baseline, whereas GPi DBS patients scored higher).

Conclusions: GPi may be a preferred target for DBS in patients with Parkinson's disease when considering cognitive outcomes.

Title: Immune system and new avenues in Parkinson's disease research and treatment.

Citation: Reviews in the neurosciences; Feb 2019

Author(s): Nasrolahi, Ava; Safari, Fatemeh; Farhoudi, Mehdi; Khosravi, Afra; Farajdokht, Fereshteh; Bastaminejad, Saiyad; Sandoghchian Shotorbani, Siamak; Mahmoudi, Javad

Abstract: Parkinson's disease (PD) is a progressive neurological disorder characterized by degeneration of dopaminergic neurons in the substantia nigra. However, although 200 years have now passed since the primary clinical description of PD by James Parkinson, the etiology and mechanisms of neuronal loss in this disease are still not fully understood. In addition to genetic and environmental factors, activation of immunologic responses seems to have a crucial role in PD pathology. Intraneuronal accumulation of α -synuclein (α -Syn), as the main pathological hallmark of PD, potentially mediates initiation of the autoimmune and inflammatory events through, possibly, auto-reactive T cells. While current therapeutic regimens are mainly used to symptomatically suppress PD signs, application of the disease-modifying therapies including immunomodulatory strategies may slow down the progressive

neurodegeneration process of PD. The aim of this review is to summarize knowledge regarding previous studies on the relationships between autoimmune reactions and PD pathology as well as to discuss current opportunities for immunomodulatory therapy.

Title: A study of the validity of the Six-Spot Step Test in ambulatory people with Parkinson's disease.

Citation: Clinical rehabilitation; Feb 2019 ; p. 269215519833016 **Author(s):** Brincks, John; Callesen, Jacob; Johnsen, Erik; Dalgas, Ulrik

Objective: The aim of this study was to evaluate the concurrent and divergent validity of the Six-Spot Step Test in mild to moderately impaired people with Parkinson's disease.

Design: Cross-sectional cohort study.

Setting: Outpatient clinics.

Subjects: Fifty-eight people with Parkinson's disease.

Main Measure: The Six-Spot Step Test, the Timed "Up and Go" test, the mini-Balance Evaluation Systems Test (mini-BESTest), and postural sway were tested on the same day, and the Spearman's Rank Correlation Coefficient (ρ) was used for data analysis.

Results: Subjects had a median age of 68 years (Q1-Q3: 62-73), a median Hoehn and Yahr score of 2.5 (Q1-Q3: 2-3), a median Six-Spot Step Test score of 7.9 seconds (Q1-Q3: 6.5-9.2), a median Timed "Up and Go" test score of 7.0 seconds (Q1-Q3: 5.6-7.9), a median mini-BESTest score of 22.5 (Q1-Q3: 19.8-25.0), and a median postural sway score of 27.9 mm2 (Q1-Q3: 15.0-53.5) and 22.5 mm/s (Q1-Q3: 14.6-39.8). Statistical significant correlations were found between the Six-Spot Step Test and the Timed "Up and Go" test ($\rho = 0.81$) and the mini-BESTest ($\rho = -0.64$), whereas no significant relations were identified between the Six-Spot Step Test and postural sway ($\rho = 0.18$, P > 0.05).

Conclusion: In patients with Parkinson's disease, the Six-Spot Step Test showed promising concurrent validity to other recommended clinical tests for encompassing balance capacity and capacity of functional mobility, making it a reasonable and easily administered alternative to existing assessment tools when measuring walking agility. As expected, weak correlates to postural sway revealed that the Six-Spot Step test is not a valid measure of standing balance.

Title: Long-term outcomes of deep brain stimulation in Parkinson disease.

Citation: Nature reviews. Neurology; Feb 2019 **Author(s):** Limousin, Patricia; Foltynie, Tom

Abstract: The efficacy of deep brain stimulation (DBS) for Parkinson disease (PD) is well established for up to 1 or 2 years, but long-term outcome data are still limited. In this Review, we critically discuss the evidence on the long-term outcomes of DBS and consider the clinical implications. Although many patients are lost to follow-up, the evidence indicates that subthalamic nucleus DBS improves motor function for up to 10 years, although the magnitude of improvement tends to decline over time. Functional scores recorded during on-medication periods worsen more quickly than those recorded in off periods, consistent with the degeneration of non-dopaminergic pathways. Dyskinesia, motor fluctuations and activities of daily living in off periods remain improved at 5 years, but quality-of-life scores have usually fallen below preoperative levels. The incidence and severity of dementia

among patients receiving DBS are comparable to those among patients who receive medical treatment. Severe adverse events are rare, but adverse events such as dysarthria are common and probably under-reported. Long-term data on the outcomes of globus pallidus interna DBS are limited and mostly confirm the efficacy for dyskinesia. A trend towards offering DBS in the earlier stages of PD creates a need to identify factors that predict long-term outcomes and to discuss realistic expectations with patients preoperatively.

Title: Does outpatient palliative care improve patient-centered outcomes in Parkinson's disease: Rationale, design, and implementation of a pragmatic comparative effectiveness trial.

Citation: Contemporary clinical trials; Feb 2019

Author(s): Kluger, Benzi M; Katz, Maya; Galifianakis, Nicholas; Pantilat, Steven Z; Kutner, Jean S; Sillau, Stefan; Gritz, Mark; Jones, Jacqueline; Fairclough, Diane; Sumrall, Malenna; Hall, Kirk; Miyasaki, Janis

Abstract: Patients with Parkinson's disease and related disorders (PDRD) and their families have considerable unmet needs including non-motor symptom management, caregiver support, spiritual wellbeing, advance care planning, and end-of-life care. There is increasing interest in applying palliative care (PC) models to better meet these needs. While PC has been shown to improve care and quality of life (QOL) for people with cancer and heart failure, few studies have evaluated the role of PC for people with PDRD. Well-designed clinical trials are needed to optimize the PC approach for PDRD and to influence policy and implementation efforts. We initiated a randomized multicenter comparative effectiveness trial of team-based outpatient PC versus usual care for people with PDRD and their caregivers. The primary aims of this study are to determine the effects of PC on patient QOL and caregiver burden. Qualitative interviews will be utilized to gain additional insights into the impact of PC on participants, the outcomes that matter most to this population, and to find opportunities to refine future interventions and trials. As a novel application of PC, challenges involved in the design of this study include choosing appropriate inclusion criteria, standardizing the intervention, defining usual care, and choosing outcome measures suitable to our research questions. Challenges involved in implementation include participant recruitment, retention, and management of participant burden. We anticipate the results of this trial will have relevance for both clinical care and future clinical research trial design in evaluating models of PC for people with PDRD and other serious illnesses.

Title: Parkinson's Disease Is Associated with Risk of Sexual Dysfunction in Men but Not in Women: A Systematic Review and Meta-Analysis.

Citation: The journal of sexual medicine; Mar 2019; vol. 16 (no. 3); p. 434-446 **Author(s):** Zhao, Shankun; Wang, Jiamin; Xie, Qiang; Luo, Lianmin; Zhu, Zhiguo; Liu, Yangzhou; Luo, Jintai; Zhao, Zhigang

Background: Mounting evidence has emerged suggesting that patients with Parkinson's disease (PD) are susceptible to sexual dysfunction (SD).AIMTo better clarify the relationship between PD and SD.

Methods: PubMed, Embase, Cochrane Library database, and PsychINFO database were systematically searched for pertinent studies evaluating sexual function in the patients with PD. This systematic review and meta-analysis have been registered on PROSPERO (ID: CRD42018108714; http://www.crd.york.ac.uk/PROSPERO).

Outcomes: The association between PD and SD was assessed using relative risk (RR) with 95% CI. The quality of evidence was ranked by the GRADE profiler.RESULTS11 observational studies met the predefined criteria for inclusion, enrolling 30,150 subjects from both the PD group and healthy control group (mean age 54.6-75.1 years). Synthesis results revealed that PD was associated with an elevated risk of SD in males (7 studies; 1.79; 95% CI = 1.26-2.54, P = .001; heterogeneity: I2 = 73.2%, P < .001). However, when restricted to female subjects, the combined RR from 3 eligible studies suggested a lack of significant association between PD and SD (RR = 1.3, 95% CI = 0.64-2.61, P = .469; heterogeneity: I2 = 80.0%, P = .007). The GRADE profiler indicated the overall quality of the evidence was low in studies including males and very low in studies including females.

Clinical Implications: The current meta-analysis indicated that men with PD were more likely to experience SD than those without PD. In female subjects, however, PD seemed to not be associated with a high prevalence of SD compared with healthy controls. Based on these findings, patients with PD should be routinely assessed for sexual functioning, especially males.

Strengths & Limitations: This is the first systematic review and meta-analysis of the association between PD and the risks of SD in both males and females. However, substantial heterogeneities were detected across the included studies.

Conclusion: A hazardous effect of PD for developing SD was detected in men but not in women. As a result, sexual function assessment and appropriate therapy are recommended for men with PD in clinical practice. Zhao S, Wang J, Xie Q, et al. Parkinson's Disease Is Associated with Risk of Sexual Dysfunction in Men but Not in Women: A Systematic Review and Meta-Analysis J Sex Med 2019;16:434-446.

Title: A randomized controlled study of whether setting specific goals improves the effectiveness of therapy in people with Parkinson's disease.

Citation: Clinical rehabilitation; Mar 2019; vol. 33 (no. 3); p. 465-472

Author(s): Cabrera-Martos, Irene; Ortiz-Rubio, Araceli; Torres-Sánchez, Irene; Rodríguez-Torres, Janet; López-López, Laura; Valenza, Marie Carmen

Objective: To evaluate the effects of an intervention based on a specific set of goals on goal attainment, manual dexterity, hand grip strength and finger prehension force compared to a standardized approach in patients with Parkinson's disease.

Design: Randomized controlled trial.

Setting: Home-based.

Participants: Fifty patients with a clinical diagnosis of Parkinson's disease acknowledging impaired manual ability were randomized into two groups.

Interventions: Patients in the experimental group (n = 25) were included in an intervention focused on task components that involved goals proposed by participants. Patients in the control group (n = 25) received a standard intervention focused on impairments in range of motion, grasp and manipulation. Home condition and duration (four weeks, twice a week) were similar in both groups.

Main Outcome Measures: The primary outcome measure was goal achievement assessed with the Goal Attainment Scaling. Secondary outcomes were manual dexterity evaluated with the Purdue Pegboard Test and hand grip strength and finger prehension force assessed using a dynamometer.

Results: After four weeks, significant between-group improvement in goal attainment was observed in the experimental group (change 17.36 ± 7.48 vs. 4.03 ± 6.43 , P < 0.001).

Compared to the control group, the experimental group also showed a significant improvement (P < 0.05) in manual dexterity (postintervention values in the most affected arm 10.55 ± 1.95 vs. 7.33 ± 3.63 pins, P < 0.001) and finger prehension force (postintervention values in the most affected arm 8.03 ± 1.93 vs. 6.31 ± 1.85 kg, P = 0.010).

Conclusions: Targeting therapy toward specific goals leads to greater changes in arm function than a standardized approach in people with Parkinson's disease.

Title: Bright light therapy for depression in Parkinson disease: A randomized controlled trial.

Citation: Neurology; Mar 2019; vol. 92 (no. 11); p. e1145

Author(s): Rutten, Sonja; Vriend, Chris; Smit, Jan H; Berendse, Henk W; van Someren, Eus J W; Hoogendoorn, Adriaan W; Twisk, Jos W R; van der Werf, Ysbrand D; van den Heuvel, Odile A

Objective: To assess the efficacy of bright light therapy (BLT) in reducing depressive symptoms in patients with Parkinson disease (PD) and major depressive disorder (MDD) compared to a control light.

Methods: In this double-blind controlled trial, we randomized patients with PD and MDD to treatment with BLT (±10,000 lux) or a control light (±200 lux). Participants were treated for 3 months, followed by a 6-month naturalistic follow-up. The primary outcome of the study was the Hamilton Depression Rating Scale (HDRS) score. Secondary outcomes were objective and subjective sleep measures and salivary melatonin and cortisol concentrations. Assessments were repeated halfway, at the end of treatment, and 1, 3, and 6 months after treatment. Data were analyzed with a linear mixed-model analysis.

Results: We enrolled 83 participants. HDRS scores decreased in both groups without a significant between-group difference at the end of treatment. Subjective sleep quality improved in both groups, with a larger improvement in the BLT group (B [SE] = 0.32 [0.16], p = 0.04). Total salivary cortisol secretion decreased in the BLT group, while it increased in the control group (B [SE] = -8.11 [3.93], p = 0.04). CONCLUSIONBLT was not more effective in reducing depressive symptoms than a control light. Mood and subjective sleep improved in both groups. BLT was more effective in improving subjective sleep quality than control light, possibly through a BLT-induced decrease in cortisol levels.

Clinical trials Gov Identifier: NCT01604876.

Classification of Evidence: This study provides Class I evidence that BLT is not superior to a control light device in reducing depressive symptoms in patients with PD with MDD.

Title: Effectiveness of the Botulinum Toxin for Treating Sialorrhea in Patients with Parkinson's Disease: A Systematic Review.

Citation: Journal of clinical medicine; Mar 2019; vol. 8 (no. 3) **Author(s):** Ruiz-Roca, Juan Antonio; Pons-Fuster, Eduardo; Lopez-Jornet, Pia

Abstract: The main objective was to assess the efficacy of botulinum toxin-based treatment for sialorrhea in adult patients with Parkinson's disease. The search was performed by using the Medline-PubMed, EMBASE and Cochrane Library databases from January 2000⁻December 2017, in English/Spanish in patients with Parkinson's disease and sialorrhea. The methodological quality of trials was carried out by following the PRISMA

(Preferred Reporting Items for Systematic Reviews and Meta-Analyses) criteria and the Newcastle⁻Ottawa Scale (NOS). Finally, a total of 21 articles were identified as fulfilling the inclusion criteria. There is no consensus regarding the site of injection of the toxin (single or multiple points), toxin dose or follow-up period. In all cases there was a reduction of sialorrhea. Treatment safety increases with the use of ultrasonography. Effects approximately occur at one week post-injection and for 3⁻5 months. Botulinum toxin is an effective therapeutic strategy or option in treating sialorrhea in adult patients with Parkinson's disease. More studies with a better design, larger samples and a longer follow-up period are required to confirm these data.

Sources Used:

The following databases are searched on a regular basis in the development of this bulletin: Amed, British Nursing Index, Cinahl, Medline

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