

# Parkinson's Disease Current Awareness Bulletin

September 2020

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**Title: Physical activity and cognition in young-onset Parkinson's disease.**

**Citation:** Acta neurologica Scandinavica; Aug 2020; vol. 142 (no. 2); p. 151-160

**Author(s):** Biddiscombe, Karen J; Ong, Ben; Kalinowski, Pawel; Pike, Kerry E

**Background:** A relationship has been observed between physical activity and cognition in older-onset Parkinson's disease, as well as improvements in cognition after a physical activity intervention. To date, this has not been investigated in young-onset Parkinson's disease (YOPD).

**Objectives:** To examine the baseline relationship between physical activity and cognition in YOPD; and to examine whether a physical activity intervention can improve cognition in YOPD.

**Methods:** Two interrelated online studies were conducted. In the first study, 132 participants with YOPD completed self-reported measures of physical activity, and objective and subjective measures of cognition. A subset of 38 participants was then randomly allocated to either a six-week physical activity intervention or control condition. Following the intervention, participants repeated the objective and subjective cognitive measures.

**Results:** No relationship was found between self-reported physical activity and objective cognition; however, there was a relationship between physical activity and subjective cognition. Similarly, following the intervention subjective improvements were found for concentration, attention, and processing speed, but not for memory. Furthermore, medium effect sizes were evident for objective measures of processing speed and small-medium effect sizes for planning and cognitive flexibility, although statistical significance was not reached.

**Conclusions:** In this first study investigating physical activity and cognition in YOPD, the results suggest that increased physical activity relates to improved processing speed and attention. Replication is recommended with a larger sample size. A longer, more intense physical activity manipulation and utilizing the study's strengths of online recruitment and intervention delivery are also recommended.

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**Title: Parkinson's disease and hip fractures: Are complications and mortality rates increased?**

**Citation:** European journal of orthopaedic surgery & traumatology : orthopedie traumatologie; Aug 2020; vol. 30 (no. 6); p. 1083-1088

**Author(s):** Müller, Franz; Dobliger, Matthias; Füchtmeier, Bernd

**Purpose:** The aim of this study was to assess patients with Parkinson's disease (PD) in comparison with patients without PD for the treatment of hip fractures. Therefore, we performed a mono-centre study including 145 patients with PD and 2135 consecutive patients without PD as a concurrent group (C).

**Methods:** For analysis, we used our database, in which any type of hip fracture was enrolled. The study period ranged from 2007 to 2017, and the patient age was  $\geq 60$  years. Overall, 10 variables were included. The primary measures were operations for any reason, infection, dislocation, failure, and mortality. The secondary outcome was any de novo fracture based on a new fall. The follow-up period for every living patient was 2 years after the operation. Any missing data were retrospectively evaluated via telephone. The hypothesis was no effect between the two groups.

**Results:** No significant differences were observed regarding revision ( $p = 0.348$ ), infection ( $p = 0.207$ ), dislocation ( $p = 0.785$ ), failure of internal fixation ( $p = 0.368$ ), failure of replacement ( $p = 0.174$ ), and de novo fractures ( $p = 0.287$ ). However, patients with PD sustained a contralateral hip fracture significantly more often ( $p < 0.001$ ). Kaplan-Meier survival analysis demonstrated no effects up to 2 years after the operation (log rank 0.259).

**Conclusion:** Compared to a concurrent group, patients with PD demonstrated no more complications and similar mortality rates within 2 years after surgery. The rate of dislocation after hip replacement was also not increased. A contralateral hip fracture was the most common de novo fracture in PD. Further studies should investigate measures reducing the risk for any new falls in PD.

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**Title: Measuring impulsivity in Parkinson's disease: a correlational and structural neuroimaging study using different tests.**

**Citation:** European journal of neurology; Aug 2020; vol. 27 (no. 8); p. 1478-1486

**Author(s):** Marín-Lahoz, J; Martínez-Horta, S; Sampedro, F; Pagonabarraga, J; Horta-Barba, A; Bejr-Kasem, H; Botí, M Á; Fernández-Bobadilla, R; Pascual-Sedano, B; Pérez-Pérez, J; Aracil-Bolaños, I; Gironell, A; Gómez-Ansón, B; Kulisevsky, J

**Background and Purpose:** Impulsivity is an aspect of personality and a major component of multiple neuropsychiatric conditions. In Parkinson's disease, it has been associated with the expression of impulse control disorders, a highly prevalent non-motor complication. Even though multiple tests of impulsivity have been used in this context, the impact of test choice has not been addressed. The aim was to evaluate whether different impulsivity measures in Parkinson's disease share substantial inter-scale and anatomical correlations or rather mirror different underlying phenomena.

**Methods:** In a consecutive sample of 89 Parkinson's disease patients without impulse control disorders, four common tests were evaluated assessing different aspects of impulsivity: impulsiveness trait, decisions under implicit risk with and without losses, and delay discounting. Correlations among test scores were analysed and each score was used as a regressor in a set of grey matter volume (GMV) voxel-based morphometry analyses to explore their brain structural correlates.

**Results:** No significant correlations were found between the different impulsivity tests. Furthermore, their structural brain correlates were divergent. Impulsiveness trait appeared to be associated with lower GMV in dorsal-lateral prefrontal cortices, implicit risk (with losses) with higher GMV in the left nucleus accumbens and lower left insular GMV, implicit risk (without losses) with higher GMV in the left lingual gyrus and lower GMV in the gyri recti and delay discounting with higher GMV in the left nucleus accumbens.

**Conclusions:** In Parkinson's disease, different impulsivity measures reflect very dissimilar behavioural and brain structural correlates. Our results suggest that parkinsonian impulsivity is not a unitary phenomenon but rather a heterogeneous entity.

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**Title: Association Between Stroke and Parkinson's Disease: a Meta-analysis.**

**Citation:** Journal of molecular neuroscience : MN; Aug 2020; vol. 70 (no. 8); p. 1169-1176

**Author(s):** Liu, Yumei; Xue, Li; Zhang, Yingying; Xie, Anmu

**Abstract:** Parkinson's disease (PD) and stroke are both associated with aging, but the relationship between these two disorders remains unclear. Recent evidence has shown that

they frequently co-occur and are influenced by each another, although some studies have found inconsistent results. We performed this meta-analysis of patients with PD on stroke risk to clarify the relationship between these two disorders on the basis of the studies published from 1975 to July 2019 in the PubMed, EMBASE, and Cochrane Library databases. In total, 13 case-control studies met the inclusion criteria for meta-analysis. The pooled odds ratio (OR) for PD in relation to the stroke risk was 1.72 (95% confidence interval (CI) 1.19-2.49). The OR for the presence of cerebral infarct among PD in the four studies was 1.35 (95% CI 1.04-1.74). Moreover, the OR for the presence of stroke pathology among PD in the four postmortem studies was 1.86 (95% CI 1.17-2.98). In conclusion, our meta-analysis suggests that there is an association between stroke and PD. Sensitivity analysis was used to test the robustness of our results through the sequential removal of each one study at time, in order to investigate if a single study was driving the study results. These results indicate that PD and stroke may have a common pathogenesis and may share preventive treatment measures.

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**Title: Sexual dysfunction in male patients with Parkinson's disease: related factors and impact on quality of life.**

**Citation:** Neurological sciences : official journal of the Italian Neurological Society and of the Italian Society of Clinical Neurophysiology; Aug 2020; vol. 41 (no. 8); p. 2201-2206

**Author(s):** Shalash, Ali; Hamid, Eman; Elrassas, Hanan; Abushouk, Abdelrahman Ibrahim; Salem, Haitham Hamdy

**Background:** Sexual dysfunction (SD) is a common, yet under-reported, non-motor symptom (NMS) of Parkinson's disease (PD). The present study investigated the sexual functions in PD male patients, its correlation with motor and other NMSs, and their impact on health-related quality of life (HRQoL).

**Methods:** The sexual functions of 40 PD male patients were assessed using the International Index of Erectile Function (IIEF) and compared to 25 healthy age-matched controls. Patients were evaluated using the NMS Scale (NMSS) and the Arabic version of the Parkinson's-Disease Questionnaire (PDQ-39). We compared the sexual functions of younger ( $\leq 55$  years) and elder ( $> 55$  years) males and tested the correlations between sexual functions and motor, other NMSs, and HRQoL.

**Results:** Seventy percent of PD male patients reported erectile dysfunction. They showed significantly worse total ( $p < 0.001$ ) and subscores of IIEF, compared to healthy controls. The total IIEF was inversely correlated to age of patients ( $p = 0.013$ ), age at onset ( $p = 0.043$ ), total, cognitive/mood, gastrointestinal and urinary domains of NMSS, and the cognitive domain of PDQ-39 ( $p = 0.013$ ). Age was the main predictor ( $\beta = -0.581$ ,  $p = 0.006$ ) of SD. Elder patients showed worse sexual functions, stronger correlations to other NMSs, and more impact on HRQoL than younger patients.

**Conclusion:** Sexual functions are worse among PD male patients with age as the main predictor. SD was associated with worse cognitive/mood and urinary domains of NMSS and has a negative impact on the patients' HRQoL among elder males.

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**Title: Levodopa/carbidopa/entacapone for the treatment of early Parkinson's disease: a meta-analysis.**

**Citation:** Neurological sciences : official journal of the Italian Neurological Society and of the Italian Society of Clinical Neurophysiology; Aug 2020; vol. 41 (no. 8); p. 2045-2054

**Author(s):** Liao, Xiaoli; Wu, Nian Yue; Liu, Dongfeng; Shuai, Bowei; Li, Shilei; Li, Ke

**Abstract:** Treatment of Parkinson's disease with levodopa/carbidopa/entacapone (LCE) has been studied for a long time. However, the efficacy and safety of LCE in the treatment of early Parkinson's disease (PD) still need to be assessed. Our objective was to do a meta-analysis of relevant randomized controlled trials (RCTs) to evaluate the efficacy and safety of LCE for early PD. PubMed, Embase, the Cochrane Library, and the Web of Science were searched for RCTs with "levodopa/carbidopa/entacapone" and "Parkinson's disease" as keywords. The search period was from inception to October 2018. The quality of included studies was strictly evaluated. We evaluated the quality of included studies strictly and six studies met all inclusion criteria. The results showed that LCE could improve activities of daily living and motor function in PD patients. However, LCE therapy was associated with higher risks of total AEs and single AEs compared with traditional therapy.

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**Title:** Two-year clinical outcomes associated with robotic-assisted subthalamic lead implantation in patients with Parkinson's disease.

**Citation:** Journal of robotic surgery; Aug 2020; vol. 14 (no. 4); p. 559-565

**Author(s):** Paff, Michelle; Wang, Alice S; Phielipp, Nicolas; Vadera, Sumeet; Morenkova, Anna; Hermanowicz, Neal; Hsu, Frank P K

**Abstract:** Few centers have routinely implemented robotic stereotactic systems for deep brain stimulator (DBS) placement. The present study compares clinical outcomes associated with robotic-assisted subthalamic nucleus (STN)-targeted DBS surgery in patients with Parkinson's disease (PD) to those of the traditional frame-based method. A retrospective chart review was performed (February 2013-June 2017). Thirty-three patients were implanted using the Cosman-Roberts-Wells (CRW) frame and 27 patients were implanted using the ROSA robot. Movement Disorder Society-Unified Parkinson's Disease Rating Scale (MDS-UPDRS) or UPDRS part III motor scores and levodopa equivalent daily doses (LEDD) were examined preoperatively and at 6, 12, and 24 months of follow-up. Operative times and complication rates were recorded. For the frame-based group, the reduction in the mean MDS-UPDRS part III motor score compared to baseline was 27% both at 6 and 12 months, and 36.7% at 24 months. For the robotic-assisted group, the reduction in the mean motor score from baseline was 17.6% at 6 months, 19% at 12 months and 21.4% at 24 months. The mean LEDD for the frame-based group decreased by 48.7% at 6 months, 56.7% at 12 months, and 29.7% at 24 months. For the robotic-assisted group, the mean LEDD decreased by 42% at 6 months, 45% at 12 months and 50% at 24 months. There were no significant differences in the mean motor scores and the LEDD reduction between the two groups. Operative times tended to be longer for robotic-assisted DBS surgery. Clinical outcomes associated with robotic-assisted surgery are comparable to those with frame-based surgery.

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**Title:** Is Parkinson's disease a chronic low-grade inflammatory bowel disease?

**Citation:** Journal of neurology; Aug 2020; vol. 267 (no. 8); p. 2207-2213

**Author(s):** Rolli-Derkinderen, Malvyne; Leclair-Visonneau, Laurène; Bourreille, Arnaud; Coron, Emmanuel; Neunlist, Michel; Derkinderen, Pascal

**Abstract:** While the pathogenesis of Parkinson's disease is not fully understood, there is increasing evidence that inflammatory responses in the brain are implicated in both disease initiation and progression. The inflammatory process in Parkinson's disease is, however, not limited to the brain but also involves the gastrointestinal tract. High amounts of cytokines and

inflammatory markers are found in the colon of Parkinson's disease patients and there is now strong epidemiological and genetical evidence linking Parkinson's disease to inflammatory bowel diseases. Recent findings obtained in both experimental inflammatory bowel diseases and Parkinson's disease further support a bidirectional link between gastrointestinal inflammation and brain neurodegeneration. Altogether, these observations suggest a role for gastrointestinal inflammation in the initiation and progression of Parkinson's disease.

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**Title: Nocturnal blood pressure changes in Parkinson's disease: correlation with autonomic dysfunction and vitamin D levels.**

**Citation:** Acta neurologica Belgica; Aug 2020; vol. 120 (no. 4); p. 915-920

**Author(s):** Arici Duz, Ozge; Helvacı Yilmaz, Nesrin

**Abstract:** Nocturnal blood pressure (BP) changes are an indicator of autonomic dysfunction. We aim to investigate the correlation between nocturnal blood pressure (BP) variability, vitamin D levels and Parkinson's disease severity (PD) in this study. Thirty-five patients with PD participated in the study. Disease severity was evaluated by United Parkinson's Disease Rating Scale (UPDRS) and Hoehn and Yahr Scale (HYS). Equivalent levodopa dose was calculated and 25-hydroxyvitamin D levels were measured. The Non-Motor Symptom Questionnaire (NMSQ) was applied to all patients. Ambulatory BP monitoring for 24 h was established. Patients were divided into three groups according to nocturnal BP results: dippers (normal finding-a decline in mean nighttime BP of more than 10%); non-dippers (pathological-a decline in mean nighttime BP of less than 10%); reverse dippers (pathological-an increase in mean nighttime BP). The mean score of the NMSQ was higher in the group with HYS > 2 ( $p = 0.050$ ). Four patients were dipper, 17 patients were non-dipper and 16 patients were reverse dipper. There was no significant difference between the three groups in terms of age, gender, disease duration, age of the disease onset, disease stage, disease duration, dopamine agonist usage, levodopa equivalent dose, vitamin D level and NMSQ scores. NMSQ scores are high in advanced PD. Ambulatory BP monitoring is useful in detecting autonomic dysfunction. The number of patients with non-dipping and reverse dipping is high in PD, independent from PD severity, drug dose, vitamin D and the other NMS symptoms.

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**Title: Coordinate based meta-analysis of motor functional imaging in Parkinson's: disease-specific patterns and modulation by dopamine replacement and deep brain stimulation.**

**Citation:** Brain imaging and behavior; Aug 2020; vol. 14 (no. 4); p. 1263-1280

**Author(s):** Xing, Yue; Tench, Christopher; Wongwandee, Monton; Schwarz, Stefan T; Bajaj, Nin; Auer, Dorothee P

**Objective:** To investigate factors affecting the pattern of motor brain activation reported in people with Parkinson's (PwP), aiming to differentiate disease-specific features from treatment effects.

**Methods:** A co-ordinate-based-meta-analysis (CBMA) of functional motor neuroimaging studies involving patients with Parkinson's (PwP), and healthy controls (HC) identified 126 suitable articles. The experiments were grouped based on subject feature, medication status (onMed/offMed), deep brain stimulation (DBS) status (DBSon/DBSoff) and type of motor initiation.

**Results:** HC and PwP shared similar neural networks during upper extremity motor tasks but with differences of reported frequency in mainly bilateral putamen, insula and ipsilateral inferior parietal and precentral gyri. The activation height was significantly reduced in the bilateral putamen, left SMA, left subthalamus nucleus, right thalamus and right midial global pallidum in PwPoffMed (vs. HC), and pre-SMA hypoactivation correlated with disease severity. These changes were not found in patients on dopamine replacement therapy (PwPonMed vs. HC) in line with a restorative function. By contrast, left SMA and primary motor cortex showed hyperactivation in the medicated state (vs. HC) suggesting dopaminergic overcompensation. Deep-brain stimulation (PwP during the high frequency subthalamus nucleus (STN) DBS vs. no stimulation) induced a decrease in left SMA activity and the expected increase in the left subthalamic/thalamic region regardless of hand movement. We further demonstrated a disease related effect of motor intention with only PwPoffMed showing increased activation in the medial frontal lobe in self-initiated studies.

**Conclusion:** We describe a consistent disease-specific pattern of putaminal hypoactivation during motor tasks that appears reversed by dopamine replacement. Inconsistent reports of altered SMA/pre-SMA activation can be explained by task- and medication-specific variation in intention. Moreover, SMA activity was reduced during STN-DBS, while dopamine-induced hyperactivation of SMA which might underpin hyperdynamic L-dopa related overcompensation.

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**Title: A Mixed-Methods Approach to Understanding the Palliative Needs of Parkinson's Patients.**

**Citation:** Journal of applied gerontology : the official journal of the Southern Gerontological Society; Aug 2020; vol. 39 (no. 8); p. 834-845

**Author(s):** Prizer, Lindsay P; Gay, Jennifer L; Wilson, Mark G; Emerson, Kerstin G; Glass, Anne P; Miyasaki, Janis M; Perkins, Molly M

**Abstract:** Parkinson's disease (PD) is the second-most common age-related neurodegenerative disorder. Despite recommendations for a palliative approach, little is known about what palliative needs are unmet by standard care. This study aims to (a) identify palliative needs of PD patients, (b) determine the relationship between palliative needs and health-related quality of life (HRQoL), and (c) probe into factors affecting HRQoL. PD patients and neurologists were recruited for a survey on palliative need; a subset of patients was interviewed. Significant differences between physicians and patients were found in Physical, Psychological, Social, Financial, and Spiritual domains. Physical and Psychological needs predicted HRQoL. Primary themes across interviews included (a) lack of healthcare education and (b) need for care coordination. Secondary themes included (a) the importance of support groups, (b) the role of spirituality/religion, and (c) the narrow perceived role of the neurologist. Findings highlight the importance of coordinated individualized care.

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**Title: Automated Classification of Postural Control for Individuals With Parkinson's Disease Using a Machine Learning Approach: A Preliminary Study.**

**Citation:** Journal of applied biomechanics; Jul 2020 ; p. 1-6

**Author(s):** Li, Yumeng; Zhang, Shuqi; Odeh, Christina

**Abstract:** The purposes of the study were (1) to compare postural sway between participants with Parkinson's disease (PD) and healthy controls and (2) to develop and

validate an automated classification of PD postural control patterns using a machine learning approach. A total of 9 participants in the early stage of PD and 12 healthy controls were recruited. Participants were instructed to stand on a force plate and maintain stillness for 2 minutes with eyes open and eyes closed. The center of pressure data were collected at 50 Hz. Linear displacements, standard deviations, total distances, sway areas, and multiscale entropy of center of pressure were calculated and compared using mixed-model analysis of variance. Five supervised machine learning algorithms (ie, logistic regression, K-nearest neighbors, Naïve Bayes, decision trees, and random forest) were used to classify PD postural control patterns. Participants with PD exhibited greater center of pressure sway and variability compared with controls. The K-nearest neighbor method exhibited the best prediction performance with an accuracy rate of up to 0.86. In conclusion, participants with PD exhibited impaired postural stability and their postural sway features could be identified by machine learning algorithms.

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**Title: Update on the diagnosis and management of Parkinson's disease.**

**Citation:** Clinical Medicine; Jul 2020; vol. 20 (no. 4); p. 393-398

**Author(s):** Kobylecki

**Abstract:** Parkinson's disease (PD) is diagnosed where bradykinesia occurs together with rigidity or tremor, in the presence of supporting features. The diagnosis is clinical, and attention should be paid to exclusion criteria indicating an alternative diagnosis and to 'red flag' features. There is no cure or diseasemodifying treatment for PD, and the rate of progression is variable. The most effective symptomatic treatment remains levodopa, which has superior benefits for quality of life in early PD compared to other therapies. Motor fluctuations and dyskinesia later in the disease course can be improved with adjunctive treatments. Around 10% of patients per year with refractory motor fluctuations may be eligible for advanced therapies, including deep-brain stimulation surgery. There is emerging evidence for the management of non-motor symptoms in PD, and the importance of multidisciplinary care. In this article, the evidence base for optimal diagnosis and management of PD is discussed.

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**Title: The effects of yoga on depression and motor function in patients with Parkinson's disease: A review of controlled studies.**

**Citation:** Annals of clinical psychiatry : official journal of the American Academy of Clinical Psychiatrists; Aug 2020; vol. 32 (no. 3); p. 209-215

**Author(s):** Sagarwala, Raza; Nasrallah, Henry A

**Background:** Parkinson's disease (PD) is a neurodegenerative/neuropsychiatric disorder characterized by both motor and non-motor symptomology. The reported prevalence of depression in patients with PD is difficult to ascertain due to overlapping somatic symptoms and failure to self-report symptoms. Although antidepressants remain a first-line treatment, they can have adverse effects. Recently, literature has demonstrated that due to its anti-inflammatory properties, yoga may be an effective nonpharmacologic therapy for depression.

**Methods:** A search was conducted to identify randomized controlled trials (RCTs) published from January 2000 to January 2019 that assessed the effects of yoga on depression and motor functioning in PD.



**Results:** Three studies met the criteria for inclusion. In one RCT, biweekly yoga resulted in a decrease in depression score ( $P = .056$ ). In another RCT, weekly yoga resulted in a significant decrease in depression and demonstrated that its therapeutic effects are long-lasting. Finally, in a third RCT, no significant difference was found between control and experimental groups in depression after biweekly yoga. However, yoga was found to be protective against worsening of depression.

**Conclusions:** Our review suggests that the practice of yoga may be a useful nonpharmacologic adjunctive treatment for depression in patients with PD. However, more controlled RCTs are needed to validate our conclusions.

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**Title: Virtual reality in research and rehabilitation of gait and balance in Parkinson disease.**

**Citation:** Nature reviews. Neurology; Aug 2020; vol. 16 (no. 8); p. 409-425

**Author(s):** Canning, Colleen G; Allen, Natalie E; Nackaerts, Evelien; Paul, Serene S; Nieuwboer, Alice; Gilat, Moran

**Abstract:** Virtual reality (VR) technology has emerged as a promising tool for studying and rehabilitating gait and balance impairments in people with Parkinson disease (PD) as it allows users to be engaged in an enriched and highly individualized complex environment. This Review examines the rationale and evidence for using VR in the assessment and rehabilitation of people with PD, makes recommendations for future research and discusses the use of VR in the clinic. In the assessment of people with PD, VR has been used to manipulate environments to enhance study of the behavioural and neural underpinnings of gait and balance, improving understanding of the motor-cognitive neural circuitry involved. Despite suggestions that VR can provide rehabilitation that is more effective and less labour intensive than non-VR rehabilitation, little evidence exists to date to support these claims. Nevertheless, much unrealized potential exists for the use of VR to provide personalized assessment and rehabilitation that optimizes motor learning in both the clinic and home environments and adapts to changes in individuals over time. Design of such systems will require collaboration between all stakeholders to maximize useability, engagement, safety and effectiveness.

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**Title: Evaluation of causality between ADHD and Parkinson's disease: Mendelian randomization study.**

**Citation:** European neuropsychopharmacology : the journal of the European College of Neuropsychopharmacology; Aug 2020; vol. 37 ; p. 49-63

**Author(s):** Li, Gloria Hoi-Yee; Ge, Grace Mengqin; Cheung, Ching-Lung; Ip, Patrick; Coghill, David; Wong, Ian Chi-Kei

**Abstract:** In a retrospective cohort study, patients with attention-deficit hyperactivity disorder (ADHD) and psychostimulant prescription were associated with increased risk of Parkinson's disease (PD). It is unclear whether ADHD per se or psychostimulant prescription is associated with PD. We aim to determine if genetic correlation or/and causal association exists between ADHD and PD using summary statistics obtained from the largest meta-analysis of genome-wide association studies of ADHD (20,183 cases; 35,191 controls) and PD (26,421 cases; 442,271 controls). Genetic correlation was tested between ADHD and PD by linkage disequilibrium score regression. Causal estimate was assessed by inverse-variance weighted (IVW) method as the main mendelian randomization analysis, with

sensitivity analyses to detect horizontal pleiotropy. Weak and inverse genetic correlation existed between ADHD and PD ( $r=-0.100$ ;  $SE=0.045$ ;  $P=0.026$ ). Univariable IVW analysis with 10 and 77 genetic instruments respectively revealed null association for ADHD with PD ( $OR=0.930$  per doubling in odds of ADHD; 95% CI:0.792-1.092) and PD with ADHD ( $OR=0.986$  per doubling in odds of PD; 95% CI:0.956-1.015). Multivariable IVW analyses adjusted for BMI/smoking also revealed null association of ADHD with PD. Using 58 PD-associated genetic instruments, multivariable IVW analysis with/without adjustment for BMI/smoking suggested a weak and inverse causal association for PD on ADHD, but cautious interpretation is required. This well-powered study did not support causality between ADHD and PD. The observed positive association between ADHD and PD is more likely to be caused by unmeasured confounders. As psychostimulant use is associated with high risk of early-onset PD, future research should focus on this area.

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**Title: Management of Sleep Disturbances in Parkinson's Disease Patients, Carers and the Patient and Carer Dyadic Relationship: A Scoping Review.**

**Citation:** Clinical Gerontologist; Oct 2020; vol. 43 (no. 5); p. 499-507

**Author(s):** Wade ; Pachana, Nancy A.; Dissanayaka, Nadeeka

**Abstract:** Sleep disturbances are a debilitating non-motor symptom in Parkinson's disease (PD) and negatively impact patients, their carers and the patient-carer dyadic relationship. This review outlines the phenomenology, as well as factors associated with and treatment of sleep disturbances, in PD patients and their informal carers. The following terms were used in four databases: Parkinson\*, sleep\* disturbance\*, carer\*, dyad\*, intervention\* and treatment\*. Across the articles reviewed, the frequency of reported sleep disturbances in PD ranged between 60% and 98%. Common sleep problems in PD included insomnia, excessive day time sleepiness, REM sleep behavior disorder (RBD), sleep apnoea, periodic limb movements and sleep attacks. Within dyads, significant correlations were found with depression, anxiety and carer burden relating to night time care in particular. Despite the negative impact of sleep disturbance in PD, the evidence-base for treatment remains limited. While addressing individual factors associated with sleep disturbances, it is also important to emphasize the needs arising from the patient-carer dyadic relationship. While a number of non-pharmacological interventions were suggested in the literature, further well-controlled trials are still required. Multiple approaches are required to reduce sleep disturbances and associated burden in PD.

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**Title: Factors Associated With Uncertainty in Illness Among People With Parkinson's Disease.**

**Citation:** Clinical Nursing Research; Sep 2020; vol. 29 (no. 7); p. 469-478

**Author(s):** Choi ; Lee, JuHee; Oh, Eui Geum; Chu, Sang Hui; Sohn, Young H.; Park, Chang Gi

**Abstract:** People with Parkinson's disease (PD) reported to experience uncertainty because of gradually progressive disease characteristics with no cure, and variably manifesting and unpredictable symptoms. This study was designed to identify illness-related variables influencing uncertainty in PD patients and to analyze direct and indirect paths between these variables. Data were collected from 206 participants using a structured questionnaire. Path analysis revealed the direct and/or indirect effects of economic status, disease severity, social support, and resilience on uncertainty in people with PD. Disease severity, social

support, and resilience were shown to have significant direct effects on uncertainty. Economic status and disease severity had indirect effects on uncertainty, which were mediated by social support. Disease severity and social support also had indirect effects on uncertainty, which were mediated by resilience. Therefore, the efforts of health care professionals should be directed not only toward managing PD symptoms, but also toward facilitating social support and resilience.

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**Title: Effects of self-management education for persons with Parkinson's disease and their care partners: A qualitative observational study in clinical care.**

**Citation:** Nursing & Health Sciences; Sep 2020; vol. 22 (no. 3); p. 741-748

**Author(s):** Hellqvist ; Berterö, Carina; Hagell, Peter; Dizdar, Nil; Sund-Levander, Märta

**Abstract:** Persons with Parkinson's disease and their care partners want support from health care to develop the skills to handle everyday life with the long-term condition. Earlier findings indicate that participants of the self-management program Swedish National Parkinson School experience several benefits of the program. The purpose of this qualitative observational study was to explore if participants had implemented the strategies of self-monitoring included in the program and use them to communicate health care status and needs in clinical encounters. Data were collected 3 to 15 months after participation in the program and analyzed using constant comparative analysis. Three categories were evident: "Self-observation in everyday life," "Self-care activities to promote health," and "Managing emotional impact of Parkinson's Disease." Categories were linked together in a core category that highlight the use of self-management strategies described by participants during clinical encounters. Results confirmed that persons with Parkinson's disease and care partners use the techniques of self-observation in their everyday lives. Observations of effects in clinical care can be a valuable approach to evaluate the outcomes educational interventions and their benefits for individuals and health care.

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**Title: Progression of fatigue in Parkinson's disease -A nine-year follow-up.**

**Citation:** European journal of neurology; Sep 2020

**Author(s):** Ongre, Solgunn Odinsen; Dalen, Ingvild; Tysnes, Ole-Bjørn; Alves, Guido; Herlofson, Karen

**Background:** Though highly disabling, the pathogenesis and evolution of fatigue in Parkinson's disease (PD) is largely unknown, and no sufficiently documented treatment currently exists. The aim of the present study is to investigate the evolution of fatigue during the first nine years after diagnosis.

**Methods:** This study is part of the Norwegian ParkWest collaboration, a prospective population-based longitudinal cohort study. The present study comprised 191 newly diagnosed patients and 170 control participants. Fatigue was assessed by the Fatigue Severity Scale, with examinations at baseline and then every other year up to nine years follow-up. Linear mixed models were applied to investigate possible variables associated with fatigue.

**Results:** We found that there was a statistically significant increase in the proportion of PD patients with fatigue during the first nine years after diagnosis. A large proportion of patients had a significant increase or decrease in fatigue score between consecutive visits. In addition, the relative risk of persistent fatigue and ever having fatigue was higher than for the controls. There were statistically significant longitudinal associations between higher levels

of fatigue and female gender, comorbidity at baseline, depressive symptoms, dependency in activities of daily living, and better cognitive functioning. Lower levels of fatigue were associated with the use of dopamine agonists.

**Discussion:** Fatigue is a common, severely limiting symptom in PD. This study demonstrates associations with other factors that could yield a better understanding of the symptom and thus possible treatment strategies, though further investigations are necessary to establish causal relationships.

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**Title: Physiotherapy in Parkinson's Disease: A Meta-Analysis of Present Treatment Modalities.**

**Citation:** Neurorehabilitation and neural repair; Sep 2020 ; p. 1545968320952799

**Author(s):** Radder, Danique L M; Lgia Silva de Lima, Ana; Domingos, Josefa; Keus, Samyra H J; van Nimwegen, Marlies; Bloem, Bastiaan R; de Vries, Nienke M

**Background:** Physiotherapy is a commonly prescribed intervention for people with Parkinson's disease (PD). Conventional types of physiotherapy have been studied extensively, while novel modalities are being developed and evaluated.

**Objective:** To evaluate the effectiveness of conventional and more recent physiotherapy interventions for people with PD. The meta-analysis performed as part of the 2014 European Physiotherapy Guideline for PD was used as the starting point and updated with the latest evidence.

**Methods:** We performed a systematic search in PubMed, CINAHL, Embase, and Web of Science. Randomized controlled trials comparing any physiotherapy intervention with no intervention or sham treatment were included. Trials were classified into 12 categories: conventional physiotherapy, resistance training, treadmill training, strategy training, dance, martial arts, aerobic exercises, hydrotherapy, balance and gait training, dual tasking, exergaming, and Nordic walking. Outcomes included motor symptoms, balance, gait, and quality of life, and are presented as standardized mean differences. The GRADE (Grading of Recommendations, Assessment, Development and Evaluation) approach was used to systematically appraise methodological quality.

**Results:** A total of 191 trials with 7998 participants were included. Conventional physiotherapy significantly improved motor symptoms, gait, and quality of life. Resistance training improved gait. Treadmill training improved gait. Strategy training improved balance and gait. Dance, Nordic walking, balance and gait training, and martial arts improved motor symptoms, balance, and gait. Exergaming improved balance and quality of life. Hydrotherapy improved balance. Finally, dual task training did not significantly improve any of the outcomes studied.

**Conclusions:** This meta-analysis provides a comprehensive overview of the evidence for the effectiveness of different physiotherapy interventions in the management of PD, allowing clinicians and patients to make an evidence-based decision for specific treatment modalities. Further work is needed to directly compare the relative efficacy of the various treatments.

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**Title: Exercise for Older Adults Improves the Quality of Life in Parkinson's Disease and Potentially Enhances the Immune Response to COVID-19.**

**Citation:** Brain sciences; Sep 2020; vol. 10 (no. 9)

**Author(s):** Hall, Mary-Frances E; Church, Frank C

**Abstract:** Parkinson's disease (PD) is a progressive neurodegenerative disorder brought about due to dopaminergic neuronal cell loss in the midbrain substantia nigra pars compacta region. PD presents most commonly in older adults and is a disorder of both motor and nonmotor dysfunction. The novel SARS-CoV-2 virus is responsible for the recent COVID-19 pandemic, and older individuals, those with preexisting medical conditions, or both have an increased risk of developing COVID-19 with more severe outcomes. People-with-Parkinson's (PwP) of advanced age can have both immune and autonomic nervous problems that potentially lead to pre-existing pulmonary dysfunction and higher infection risk, increasing the probability of contracting COVID-19. A lifestyle change involving moderate-intensity exercise has the potential to protect against SARS-CoV-2 through strengthening the immune system. In addition to a potential protective measure against SARS-CoV-2, exercise has been shown to improve quality-of-life (QoL) in PD patients. Recent studies provide evidence of exercise as both neuroprotective and neuroplastic. This article is a literature review investigating the role exercise plays in modifying the immune system, improving health outcomes in PwP, and potentially acting as a protective measure against SARS-Cov-2 infection. We conclude that exercise, when correctly performed, improves QoL and outcomes in PwP, and that the enhanced immune response from moderate-intensity exercise could potentially offer additional protection against COVID-19.

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**Title: Minority Enrollment in Parkinson's Disease Clinical Trials: Meta-Analysis and Systematic Review of Studies Evaluating Treatment of Neuropsychiatric Symptoms.**

**Citation:** Journal of Parkinson's disease; Sep 2020

**Author(s):** Di Luca, Daniel G; Sambursky, Jacob A; Margolesky, Jason; Cordeiro, Joacir Graciolli; Diaz, Anthony; Shpiner, Danielle S; Moore, Henry P; Singer, Carlos; Luca, Corneliu

**Background:** Randomized clinical trials (RCTs) in Parkinson's disease (PD) have historically enrolled a low number of underrepresented minorities, lessening the generalizability of therapeutic developments. Although there are racial disparities in PD, little is known regarding neuropsychiatric symptoms and other nonmotor manifestations across all races/ethnicities.

**Objective:** To assess minority participation in PD trials evaluating the treatment of neuropsychiatric symptoms and explore underlying reasons.

**Methods:** We systematically searched PubMed and Embase for RCTs with a primary goal of treating neuropsychiatric symptoms in PD patients from 2000-2019. The pooled prevalence and 95% confidence interval (CI) of being white and enrolled in a clinical trial was calculated using the inverse variance method. I-square was calculated as a measure of heterogeneity and meta-regression was used to evaluate temporal trends.

**Results:** We included 63 RCTs with a total of 7,973 patients. In pooled analysis, 11 (17.5%) RCTs reported race/ethnicity. Of studies reporting this data, 5 African American (0.2%), 16 Hispanics (0.64%), and 539 Asians (21.44%) were enrolled. The pooled prevalence of being white in clinical trials was 98% (CI 0.97-0.98,  $p < 0.001$ ), with 1,908 patients (75.8%). NIH-funded studies were most likely to report racial data when compared to non-NIH trials ( $p = 0.032$ ).

**Conclusion:** This large pooled analysis found a small percentage of RCTs reporting race/ethnicity when evaluating treatment of neuropsychiatric symptoms in PD. There was a disproportionately high number of white patients when compared to African Americans and Hispanics. More studies are needed to investigate this discrepancy and improve rates of & minority enrollment in PD trials.

**Title: Targeting COVID-19 in Parkinson's patients: Drugs repurposed.**

**Citation:** Current medicinal chemistry; Sep 2020

**Author(s):** Anwar, Firoz; Naqvi, Salma; Al-Abbasi, Fahad A; Neelofar, Nauroz; Kumar, Vikas; Sahoo, Ankit; Kamal, Mohammad Amjad

**Abstract:** The last couple of months have witnessed the world in a state of virtual standstill. The SARS-CoV-2 virus has overtaken globe to economic and social lockdown. Many patients with COVID-19 have compromised immunity, especially in an aged population suffering from Parkinson disease (PD). Alteration in dopaminergic neurons or deficiency of dopamine in PD patients is the most common symptoms affecting 1% population above the age of 60 years. The compromised immune system and inflammatory manifestation in PD patients make them an easy target. The most common under trial drugs for COVID-19 are Remdesivir, Favipiravir, Chloroquine and Hydroxychloroquine, Azithromycin along with adjunct drugs like Amantadine with some monoclonal antibodies. Presently, clinically US FDA approved drugs in PD includes Levodopa, catechol-O-methyl transferase (COMT) inhibitors, (Entacapone and Tolcapone), Dopamine agonists (Bromocriptine, Ropinirole, Pramipexole, and Rotigotine), Monoamine oxidase B (MAO-B) inhibitors (Selegiline and Rasagiline), Amantadine and Antimuscarinic drugs. The drugs have established mechanism of action on PD patients with known pharmacodynamics and pharmacokinetic properties along with dose and adverse effects. Conclusion and relevance of this review focus on the drugs that can be tried for the PD patients with SAR CoV-2 infection, in particular, Amantadine approved by all developed countries a common drug possessing both antiviral properties by downregulation of CTSL, lysosomal pathway disturbance and change in pH necessary to uncoat the viral proteins and antiParkinson properties. The significant prognostic adverse effect of SARS-CoV-2 on PD and the present-day treatment options, clinical presentation and various mechanism is warrant need of the hour.

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**Title: A walking dance to improve gait speed for people with Parkinson disease: a pilot study.**

**Citation:** Neurodegenerative disease management; Sep 2020

**Author(s):** Harrison, Elinor C; Earhart, Gammon M; Leventhal, David; Quinn, Lori; Pietro Mazzoni

**Aim:** To determine the effectiveness of a targeted dance intervention to improve walking speed for people with Parkinson disease (PD) by increasing motor motivation.

**Materials and Methods:** 11 participants with PD participated in a 6-week pilot study in which they learned a contemporary dance composed of walking steps and designed to mimic everyday walking. 1 h classes occurred twice-weekly.

**Results:** Pre- and post-intervention assessments revealed a significant increase in gait speed ( $t_9 = 3.30$ ;  $p = 0.009$ ), cadence ( $t_9 = 2.345$ ;  $p = 0.044$ ), and stride length ( $t_9 = 3.757$ ;  $p = 0.005$ ), and a significant decrease (improvement) in single support time variability ( $t_9 = -2.744$ ;  $p = 0.022$ ). There were no significant changes in other measures of gait variability nor in motor symptoms, mood and anxiety, extent of life-space mobility, or quality of life. No adverse events were reported.

**Conclusion:** Joywalk provides preliminary evidence that a targeted physical intervention for people with PD may specifically counter bradykinesia.

**Title: Prevalence and impact of COVID-19 in Parkinson's disease: evidence from a multi-center survey in Tuscany region.**

**Citation:** Journal of neurology; Sep 2020

**Author(s):** Del Prete, Eleonora; Francesconi, Alessio; Palermo, Giovanni; Mazzucchi, Sonia; Frosini, Daniela; Morganti, Riccardo; Coleschi, Piero; Raglione, Laura Maria; Vanni, Paola; Ramat, Silvia; Novelli, Alessio; Napolitano, Alessandro; Battisti, Carla; Giuntini, Martina; Rossi, Carlo; Menichetti, Chiara; Ulivelli, Monica; De Franco, Valentino; Rossi, Simone; Bonuccelli, Ubaldo; Ceravolo, Roberto; Tuscany Parkinson COVID-19 Participants

**Background:** If Parkinson's Disease (PD) may represent a risk factor for Coronavirus disease 2019 (COVID-19) is debated and there are few data on the direct and indirect effects of this pandemic in PD patients.

**Objective:** In the current study we evaluated the prevalence, mortality and case-fatality of COVID-19 in a PD cohort, also exploring possible risk factors. We also aimed to investigate the effect of lockdown on motor/non-motor symptoms in PD patients as well as their acceptability/accessibility to telemedicine.

**Method:** A case-controlled survey about COVID-19 and other clinical features in PD patients living in Tuscany was conducted. In non-COVID-19 PD patients motor/non-motor symptoms subjective worsening during the lockdown as well as feasibility of telemedicine were explored.

**Results:** Out of 740 PD patients interviewed, 7 (0.9%) were affected by COVID-19, with 0.13% mortality and 14% case-fatality. COVID-19 PD patients presented a higher presence of hypertension ( $p < 0.001$ ) and diabetes ( $p = 0.049$ ) compared to non-COVID-19. In non-COVID-19 PD population ( $n = 733$ ) about 70% did not experience a subjective worsening of motor symptoms or mood, anxiety or insomnia. In our population 75.2% of patients was favorable to use technology to perform scheduled visits, however facilities for telemedicine were available only for 51.2% of cases.

**Conclusion:** A higher prevalence of COVID-19 respect to prevalence in Tuscany and Italy was found in the PD population. Hypertension and diabetes, as for general population, were identified as risk factors for COVID-19 in PD. PD patients did not experience a subjective worsening of symptoms during lockdown period and they were also favorable to telemedicine, albeit we reported a reduced availability to perform it.

#### **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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