

Parkinson's Disease Current Awareness Bulletin

June 2020

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Title: Cognitive-Behavioral Therapy for Anxiety in Parkinson's Disease.

Citation: Behavior Modification; Jul 2020; vol. 44 (no. 4); p. 552-579

Author(s): Reynolds ; Saint-Hilaire, Marie; Thomas, Cathi A.; Barlow, David H.; Cronin-Golomb, Alice

Abstract: Parkinson's disease (PD) is characterized by motor symptoms, but nonmotor symptoms also significantly impair daily functioning and reduce quality of life. Anxiety is prevalent and debilitating in PD, but remains understudied and undertreated. Much affective research in PD focuses on depression rather than anxiety, and as such, there are no evidence-based treatments for anxiety in this population. Cognitive-behavioral therapy (CBT) has shown promise for treating depression in PD and may be efficacious for anxiety. This exploratory study implemented a multiple-baseline single-case experimental design to evaluate the utility and feasibility of CBT for individuals with PD who also met criteria for a DSM-5 anxiety disorder (n = 9). Participants were randomized to a 2-, 4-, or 6-week baseline phase, followed by 12 CBT sessions, and two post treatment assessments (immediately post treatment and 6-week follow-up). Multiple outcome measures of anxiety and depression were administered weekly during baseline and intervention. Weekly CBT sessions were conducted in-person (n = 5) or via secure videoconferencing (n = 4). At post treatment, seven of the nine participants showed significant reductions in anxiety and/or depression, with changes functionally related to treatment and most improvements maintained at 6-week follow-up. Effects of CBT on secondary outcomes varied across participants, with preliminary evidence for reduction in fear of falling. Adherence and retention were high, as were treatment satisfaction and acceptability. The findings of this pilot study provide preliminary evidence for the utility of CBT as a feasible treatment for anxiety and comorbid depressive symptoms in PD and highlight the potential of telehealth interventions for mood in this population.

Title: 'Mind the gap' — a scoping review of long term, physical, self-management in Parkinson's.

Citation: Physiotherapy; Jun 2020; vol. 107 ; p. 88-99

Author(s): Hulbert ; Goodwin, Victoria A.

Abstract : Parkinson's is a common progressive neurological condition characterised by impairments of movement and balance; and non-motor deficits. It is now accepted that physical activity is a fundamental for people with Parkinson's (PwP), despite this PwP remain inactive. There is a social and financial drive to increase physical activity for PwP through physical self-management, however little is known about this concept. This scoping review provides an overview of the literature concerning physical self-management for PwP and its provision, participation and uptake by PwP. Systematic search of the databases; Medline, EMBASE, HMIC, CDSR, Cochrane Methods Studies, DARE, CINAHL, PEDro, PsycINFO and Cochrane Library using the search terms 'Parkinson*' and 'self-manag*' was undertaken alongside citation and grey literature searching and a consultation exercise. A narrative summary was undertaken to describe the current state of the literature. 1959 studies were identified with nineteen papers from seventeen studies meeting the inclusion criteria - Three reviews, four experimental studies, three pre-post-test designs, six cross-sectional designs, one qualitative interview design and two mixed method designs. The findings of this scoping review suggest a need for clarity on what 'physical self-management' means and involves, with a gap between what the evidence promotes and what is being achieved by PwP. Further research should focus on the amount, type, intensity and duration

of physical self-management models including behavioural change approaches and how, where and by whom this should be implemented.

Title: Being limited by Parkinson's disease and struggling to keep up exercising; is the group the glue?

Citation: Disability & Rehabilitation; May 2020; vol. 42 (no. 9); p. 1270-1274

Author(s): Claesson ; Ståhle, Agneta; Johansson, Sverker

Background: People with Parkinson's disease find that exercise helps to improve their physical performance. However, when performed in a group, they also tend to appreciate each other's company.

Purpose: After people with Parkinson's disease participated in a community-based group balance exercise program, our aims were to explore the participants' general attitude to their balance ability and exercise, and specifically their experiences of participating in a group exercise.

Materials and Methods: Informants were people living with Parkinson's disease at an early stage (n = 15) who had participated in a community-based "Somatosensory Focused Balance Training without Cues." Each informant took part in one face-to-face interview. The interviews were transcribed, according to content analysis, coded independently by two researchers and triangulated together with a third experienced researcher. Categories and themes were derived in consensus.

Results: The participants felt limited by their body. They agreed that the group balance exercise program did help with their balance control. Moreover, the vast majority found that the group context implied a positive social contribution to their lives and to their ability to cope with living with the disease.

Conclusion: Group balance exercise might constitute a context with potential to improve quality of life for people with Parkinson's disease, not only by improving balance control, but also contributing to social connections, fellowship and the exchange of mutual experiences. Group-based exercise in early Parkinson seems to add more than just the physical effects of training, since it also gives a platform for meeting social and emotional needs, as well as addressing physical ability. The group dynamics and the support of peers seem to promote a positive attitude to life and enable people to learn coping strategies from each other. Community-based exercise groups for people with early Parkinson seem to be a way to get out in society and regain a feeling of being part of society. Due to body limits, people with Parkinson's disease must struggle daily, already at an early stage of their disease; this stresses the need to begin rehabilitation early.

Title: Pain and Musculoskeletal Disorders: Common Nuisances in Parkinson Disease.

Citation: Journal for Nurse Practitioners; May 2020; vol. 16 (no. 5); p. 332-334

Author(s): Sin, Mo-Kyung; Khemani, Pravin

Abstract: Parkinson disease (PD) is a widespread neurodegenerative disorder with progressive motor and nonmotor features. Pain is one of the most frequent but ignored nonmotor features of the disease. Among several different types of pain in PD, musculoskeletal pain due to rigidity, rheumatologic disease, or skeletal deformity is the most frequently reported pain. Pain assessment with a reliable and valid tool is necessary to differentiate different types of pain. The King's Parkinson's Disease Pain Scale is a reliable

and valid tool for rating of various types of pain in PD. Treatment modalities for musculoskeletal pain in PD are based on a multidisciplinary approach, which includes modification of dopaminergic medications, botulinum toxin for dystonia, exercise and rehabilitative measures, and surgical options for select patients. An accurate diagnosis of pain subtype in PD is a prerequisite for optimal treatment. • Pain is one of the most frequent but ignored non-motor symptom of Parkinson disease (PD). • Musculoskeletal pain is the most commonly reported pain in PD. • A multidisciplinary approach is used to manage musculoskeletal pain in PD.

Title: Predicting falls in people with Parkinson's disease: impact of methodological approaches on predictors identified.

Citation: Aging Clinical & Experimental Research; Jun 2020; vol. 32 (no. 6); p. 1057-1066

Author(s): Almeida ; Heller, Gillian; Allen, Natalie E.; Canning, Colleen G.; Sherrington, Catherine; Valenca, Guilherme T.; Oliveira-Filho, Jamary; Paul, Serene S.

Background: Previous investigations of falls predictors in people with Parkinson's disease (PD) have used various statistical methods and categorization of falls outcomes. The impact of methodological differences on falls predictors has not been investigated.

Objectives: To describe similarities and differences in predictors modelled for fall rates [negative binomial (NB), Poisson Inverse Gaussian (PIG) and quantile regression] and previously-reported predictors of time to second fall (Cox regression), i.e. past falls, motor fluctuations, disability, levodopa dose and balance impairment. To investigate whether predictors from quantile regression vary across subsets of fallers based on fall frequency.

Methods: Participants with PD (n = 229) were followed-up for 12 months. NB and PIG regression were used to determine predictors of fall rates, with the best fitting model reported. Quantile regression was used to determine predictors at higher (62nd, 70th, 80th) percentiles of the falls distribution. Univariate and multivariate analyses were performed.

Results: Predictors of fall rates were the same in NB and PIG multivariate models, with the PIG model fitting our data better. Past falls, disability and levodopa dose were associated with fall rates from PIG and quantile regression. Freezing of gait was associated with fall rates from PIG regression. Disease severity predicted less (70th percentile, approximately 2–4) and more (80th percentile, approximately ≥ 5) frequent falls, and anteroposterior stability also predicted less frequent falls ($p < 0.05$), from quantile regression.

Conclusions: Not all predictors of time to second fall were predictors of fall rates. Quantile regression revealed some divergent predictors depending on the percentile of fall frequency examined.

Title: Effects of a core stabilization training program on balance ability in persons with Parkinson's disease: a randomized controlled trial.

Citation: Clinical Rehabilitation; Jun 2020; vol. 34 (no. 6); p. 764-772

Author(s): Cabrera-Martos ; Jiménez-Martín, Ana Teresa; López-López, Laura; Rodríguez-Torres, Janet; Ortiz-Rubio, Araceli; Valenza, Marie Carmen

Objective: To explore the effects of an eight-week core stability program on balance ability in persons with Parkinson's disease.

Design: Randomized controlled trial.

Setting: A local Parkinson's association. **Subjects:** A total of 44 participants with a clinical diagnosis of Parkinson's disease were randomly assigned to an experimental (n = 22) or control group (n = 22). **Intervention:** The experimental group received 24 sessions of core training, while the control group received an intervention including active joint mobilization, muscle stretching, and motor coordination exercises.

Main measures: The primary outcome measure was dynamic balance evaluated using the Mini-Balance Evaluation Systems Test. Secondary outcomes included the balance confidence assessed with the Activities-specific Balance Confidence Scale and standing balance assessed by the maximal excursion of center of pressure during the Modified Clinical Test of Sensory Interaction on Balance and the Limits of Stability test.

Results: After treatment, a significant between-group improvement in dynamic balance was observed in the experimental group compared to the control group (change, 2.75 ± 1.80 vs 0.38 ± 2.15 , $P = 0.002$). The experimental group also showed a significant improvement in confidence (change, 16.48 ± 16.21 vs 3.05 ± 13.53 , $P = 0.047$) and maximal excursion of center of pressure in forward (change, 0.86 ± 1.89 cm vs 0.17 ± 0.26 cm, $P = 0.048$), left (change, 0.88 ± 2.63 cm vs 0.07 ± 0.48 cm, $P = 0.010$), and right (change, 1.63 ± 2.82 cm vs 0.05 ± 0.17 cm, $P = 0.046$) directions of limits of stability compared to the control group.

Conclusion: A program based on core stability in comparison with non-specific exercise benefits dynamic balance and confidence and increases center of mass excursion in patients with Parkinson's disease.

Title: Predictors of improved balance performance in persons with Parkinson's disease following a training intervention: analysis of data from an effectiveness-implementation trial.

Citation: Clinical Rehabilitation; Jun 2020; vol. 34 (no. 6); p. 837-844

Author(s): Joseph ; Leavy, Breiffni; Franzén, Erika

Objective: (1) To determine associated factors of improved balance performance after a 10-week HiBalance intervention period, and (2) to determine effects of the programme on modifiable factors found above, considering both groups.

Design: Pre-posttest substudy founded on the outcomes evaluation of an effectiveness-implementation trial. **Participants:** Sixty-one participants were allocated the HiBalance training, while 56 were controls.

Intervention: Participants received a 10-week, two times weekly, progressive balance training, that is, HiBalance intervention, led by physical therapists. The intervention was group based and gradually incorporated dual-tasking over the training period. Participants also performed, unsupervised, a 1×/week home exercise programme.

Main outcome: The Mini-Balance Evaluation Systems Test (Mini-BESTest) assessed balance performance, and those having improved by ≥ 2 points were classified as positive responders. Balance confidence was the secondary outcome.

Results: Fifty-three (87%) participants completed the intervention and 32 (60%) improved their balance scores by ≥ 2 points in the intervention group, with 11 (24%) in the control group. The multivariable logistic regression analysis revealed two independently associated factors of improved balance, which included balance confidence (odds ratio (OR) = 0.95; 95% confidence interval (CI) = 0.90–0.99) and attendance of $\geq 80\%$ of training sessions (OR = 10.10; 95% CI = 1.71–59.60). The final model demonstrated good fit and acceptable discrimination (area under the curve = 0.84). Secondary analysis revealed a fair relationship (Rho = 0.30; $P = 0.044$) between improvements in balance confidence and balance performance in the intervention but not control group.

Conclusion: Two personal factors were significantly associated with a higher likelihood of improvement in clinically measured balance performance. The HiBalance intervention appears to benefit those with lower balance confidence.

Title: Therapeutic Strategies to Treat or Prevent Off Episodes in Adults with Parkinson's Disease.

Citation: Drugs; Jun 2020; vol. 80 (no. 8); p. 775-796

Author(s): Vijiaratnam ; Foltynie, Thomas

Abstract: Parkinson's disease is a chronic, neurodegenerative disease, which manifests with a mixture of motor, cognitive and behavioural symptoms. Levodopa is the most effective antiparkinsonian treatment to date, although chronic use engenders a mixture of complications in a substantial proportion of patients. Amongst these is the occurrence of episodes of worsening symptoms—'off' phenomena. These episodes can manifest with either motor or non-motor symptoms or a combination of these features and have been found to have profound impacts on patients' quality of life. Although preventative measures are poorly evidenced, avoiding excessive total daily levodopa intake in selected populations that are deemed to be of a higher risk for developing these episodes warrants further exploration. Methods to improve levodopa bioavailability and delivery to the brain are currently available and are of value in addressing these episodes once they have become established. These include modifications to levodopa formulations as well as the use of complimentary agents that improve levodopa bioavailability. The deployment of device-assisted approaches is a further dimension that can be considered in addressing these debilitating episodes. This review summarises the clinical manifestations of 'off' phenomena and the current approaches to treat them. Although we briefly discuss clinical advances on the horizon, the predominant focus is on existing, established treatments.

Title: Evidence of Rehabilitative Impact of Progressive Resistance Training (PRT) Programs in Parkinson Disease: An Umbrella Review.

Citation: Parkinson's Disease (20420080); May 2020 ; p. 1-9

Author(s): Paolucci ; Sbardella, S.; La Russa, C.; Agostini, F.; Mangone, M.; Tramontana, L.; Bernetti, A.; Paoloni, M.; Pezzi, L.; Bellomo, R. G.; Santilli, V.; Saggini, R.

Abstract: Parkinson disease (PD) is a chronic neurodegenerative condition that leads to progressive disability. PD-related reductions in muscle strength have been reported to be associated with lower functional performance and balance confidence with an increased risk of falls. Progressive resistance training (PRT) improves strength, balance, and functional abilities. This umbrella review examines the efficacy of PRT regarding muscular strength in PD patients. The PubMed, PEDro, Scopus, and Cochrane Library databases were searched from January 2009 to August 2019 for systematic reviews and meta-analyses conducted in English. The populations included had diagnoses of PD and consisted of males and females aged >18 years old. Outcomes measured were muscle strength and enhanced physical function. Eight papers (six systematic reviews and meta-analyses and two systematic reviews) were considered relevant for qualitative analysis. In six of the eight studies, the reported severity of PD was mild to moderate. Each study analyzed how PRT elicited positive effects on muscle strength in PD patients, suggesting 10 weeks on average of progressive resistance exercises for the upper and lower limbs two to three times per week. However, none of the studies considered the postworkout follow-up, and there was no

detailed evidence about the value of PRT in preventing falls. The possibility of PRT exercises being effective for increasing muscle strength in patients with PD, but without comorbidities or severe disability, is discussed. Overall, this review suggests that PRT should be included in rehabilitation programs for PD patients, in combination with balance training for postural control and other types of exercise, in order to preserve cardiorespiratory fitness and improve endurance in daily life activities.

Title: Cognitive decline profiles differ in Parkinson disease dementia and dementia with Lewy bodies.

Citation: Neurology; May 2020; vol. 94 (no. 20); p. e2076

Author(s): Smirnov, Denis S; Galasko, Douglas; Edland, Steven D; Filoteo, J Vincent; Hansen, Lawrence A; Salmon, David P

Objective: To examine whether domain-specific patterns of cognitive impairment and trajectories of decline differed in patients with clinically diagnosed Parkinson disease dementia (PDD) (N = 29) and autopsy-confirmed dementia with Lewy bodies (DLB) (N = 58) or Alzheimer disease (AD) (N = 174) and to determine the impact of pooling patients with PDD and DLB in clinical trials targeting cognition.

Methods: Patients were matched on demographics and level of global cognitive impairment. Patterns of cross-sectional performance and longitudinal decline were examined in 4 cognitive domains: Visuospatial, Memory, Executive, and Language. Power analyses were performed to determine the numbers of participants needed to adequately power a hypothetical clinical trial to slow cognitive decline in pure PDD, pure DLB, or a mixed PDD/DLB group.

Results: Both DLB and PDD were more impaired and declined more rapidly than AD in the Visuospatial domain. Patients with PDD exhibited the most impairment and fastest decline in Executive, although patients with DLB also declined faster than AD. Memory was more impaired in AD than DLB and in both compared with PDD; however, all 3 groups declined at comparable rates. In contrast, PDD declined at a slower rate on Language measures than DLB or AD. Power analyses suggest that Visuospatial and Executive outcome measures would be most sensitive in PDD, but Memory and Language in DLB.

Conclusion: DLB and PDD differ from each other, and from AD, in a cognitive domain-specific manner. As such, different outcome measures may be most sensitive to detecting changes in DLB vs PDD, suggesting that the 2 should be analyzed separately in clinical trials.

Title: Current and Desired Quality of Life in People with Parkinson's Disease: the Calman Gap Increases with Depression.

Citation: Journal of clinical medicine; May 2020; vol. 9 (no. 5)

Author(s): Prell, Tino; Teschner, Ulrike; Witte, Otto W; Kunze, Albrecht

Abstract: Hopes and expectations often differ from current experiences. This so-called Calman gap influences quality of life (QoL). We investigated this gap in 77 elderly patients with Parkinson's disease (PD), 25 patients with epilepsy, and 39 age-matched healthy older adults using a novel QoL questionnaire, where current and desired states were marked on a visual analogue scale. We studied the relationships between (1) epidemiological factors, (2) current and desired QoL, as well as the difference between the latter two. Current QoL was determined by depression, education level, living situation, and condition (PD, epilepsy,

control). In contrast, desired QoL was essentially determined by the presence of a disease (condition), education level, and age, but not by depression. In particular, the presence of PD, lower education level, and higher age was correlated with lower expectations. In patients with PD, the gap between the current and desired QoL was largest for pain and physical functions. Accordingly, the significant effects of depression were observed only for mean current QoL, but not for desired QoL. Therefore, depression mainly influences current but not desired QoL in patients with PD. Depressed patients with PD had significantly worse QoL than PD patients without depression, although they both had almost the same desired QoL and hence, depressed PD patients had a larger Calman gap between current and desired QoL.

Title: Bright light improves sleep in patients with Parkinson's disease: possible role of circadian restoration.

Citation: Scientific reports; May 2020; vol. 10 (no. 1); p. 7982

Author(s): Endo, Takuyuki; Matsumura, Ritsuko; Tokuda, Isao T; Yoshikawa, Tomoko; Shigeyoshi, Yasufumi; Node, Koichi; Sakoda, Saburo; Akashi, Makoto

Abstract: Parkinson's disease (PD) is one of the most common neurodegenerative disorders. Among the most common manifestations of PD are sleep problems, which are coupled with the adverse effects of dopaminergic therapies (DT). A non-pharmacological solution for these sleep problems has been sought to avoid additional pharmacological intervention. Here, we show that bright light therapy (BLT) is effective for improving sleep in Japanese PD patients receiving DT. Furthermore, experimental evaluation of peripheral clock gene expression rhythms revealed that most PD patients receiving DT who experienced improved sleep following BLT showed a circadian phase shift, indicating the existence of a correlation between circadian modulation and sleep improvement. Conversely, this result indicates that sleep problems in PD patients receiving DT may arise at least in part as a result of circadian dysfunction. Indeed, we found that chronic dopaminergic stimulation induced a rapid attenuation of autonomous oscillations of clock gene expression in ex vivo cultured mouse suprachiasmatic nucleus (SCN) at the single neuron level. In conclusion, BLT is a promising medical treatment for improving sleep in PD patients receiving DT. This BLT-induced improvement may be due to the restoration of circadian function.

Title: Benign versus malignant Parkinson disease: the unexpected silver lining of motor complications.

Citation: Journal of neurology; Jun 2020

Author(s): Merola, Aristide; Romagnolo, Alberto; Dwivedi, Alok K; Padovani, Alessandro; Berg, Daniela; Garcia-Ruiz, Pedro J; Fabbri, Margherita; Artusi, Carlo Alberto; Zibetti, Maurizio; Lopiano, Leonardo; Pilotto, Andrea; Bonacina, Sonia; Morgante, Francesca; Zeuner, Kirsten; Griewing, Christopher; Schaeffer, Eva; Rodriguez-Porcel, Federico; Kauffman, Marcelo; Turcano, Pierpaolo; de Oliveira, Lais M; Palermo, Giovanni; Shanks, Emily; Del Sorbo, Francesca; Bonvegna, Salvatore; Savica, Rodolfo; Munhoz, Renato P; Ceravolo, Roberto; Cilia, Roberto; Espay, Alberto J

Objective: We sought to evaluate demographic, clinical, and habits/occupational variables between phenotypic extremes in Parkinson's disease (PD).

Methods: Databases from nine movement disorders centers across seven countries were retrospectively searched for subjects meeting criteria for very slowly progressive, benign, PD (bPD) and rapidly progressive, malignant, PD (mPD). bPD was defined as Hoehn and Yahr (H&Y) stage ≤ 3 , normal cognitive function, and Schwab and England (S&E) score ≥ 70 after ≥ 20 years of PD (≥ 10 years if older than 60 at PD onset); mPD as H&Y > 3 , S&E score < 70 , and cognitive impairment within 10 years from PD onset. We performed between-group analysis of demographic, habits/occupational, and clinical features at baseline and follow-up and unsupervised data-driven analysis of the clinical homogeneity of bPD and mPD.

Results: At onset, bPD subjects ($n = 210$) were younger, had a single limb affected, lower severity and greater asymmetry of symptoms, and lower prevalence of depression than mPD ($n = 155$). bPD was associated with active smoking and physical activity, mPD with agricultural occupation. At follow-up, mPD showed higher prevalence of depression, hallucinations, dysautonomia, and REM behaviour disorder. Interestingly, the odds of mPD were significantly reduced by the presence of dyskinesia and wearing-off. Data-driven analysis confirmed the independent clustering of bPD and mPD, with age at onset emerging as a critical discriminant between the two groups (68-year-old).

Conclusions: Phenotypic PD extremes showed distinct demographic, clinical, and habits/occupational factors. Motor complications may be conceived as markers of therapeutic success given their attenuating effects on the odds of mPD.

Title: COVID-19 in Parkinson's Disease Patients Living in Lombardy, Italy.

Citation: Movement disorders : official journal of the Movement Disorder Society; Jun 2020

Author(s): Fasano, Alfonso; Cereda, Emanuele; Barichella, Michela; Cassani, Erica; Ferri, Valentina; Zecchinelli, Anna Lena; Pezzoli, Gianni

Background: It is unknown whether patients with Parkinson's disease (PD) are at greater risk of COVID-19, what their risk factors are and whether their clinical manifestations differ from the general population.

Methods: In a case-controlled survey, we interviewed 1486 PD patients attending a single tertiary centre in Lombardy, Italy and 1207 family members (controls).

Results: 105 (7.1%) and 92 controls (7.6%) were identified as COVID-19 cases. COVID-19 patients were younger, more likely to suffer from chronic obstructive pulmonary disease, to be obese and vitamin D non-supplemented than unaffected patients. Six patients (5.7%) and seven family members (7.6%) died from COVID-19. Patients were less likely to report shortness of breath and require hospitalization.

Conclusions: In an unselected large cohort of non-advanced PD patients, COVID-19 risk and mortality did not differ from the general population but symptoms appeared to be milder. The possible protective role of vitamin D supplementation warrants future studies. This article is protected by copyright. All rights reserved.

Title: The evidence for multidisciplinary care in Parkinson's disease.

Citation: Expert review of neurotherapeutics; Jun 2020 ; p. 1-11

Author(s): Lidstone, Sarah C; Bayley, Mark; Lang, Anthony E

Introduction: Parkinson's Disease (PD) is a chronic and slowly progressive neurodegenerative disease. Team-based care is required to address and manage the

diverse array of motor and non-motor symptoms in PD and related conditions. As the evidence base for the efficacy of non-pharmacological treatment of PD is expanding, many different centers are implementing interdisciplinary models of care with allied health professionals trained in PD.

Areas Covered: In this review, the authors outline these various models and review the evidence for multidisciplinary approaches to care in PD. They begin by defining the terms used to describe the spectrum of multidisciplinary and integrated care models, followed by synthesizing the evidence for these models in PD. The authors then highlight some representative models to illustrate the variety of multidisciplinary care interventions: a community network-based model, a day-hospital model, an academic clinic-based model, and an intensive inpatient rehabilitation model. The authors synthesize these results and suggest directions for team-based PD care for the future.

Expert Opinion: The future of medicine is team-based care that is decentralized and integrated vertically and horizontally across health systems. Building an evidence base for these complex interventions will require alternative models of evaluation other than randomized controlled trials.

Title: Nintendo Wii™ versus Xbox Kinect™ for functional locomotion in people with Parkinson's disease: a systematic review and network meta-analysis.

Citation: Disability and rehabilitation; Jun 2020 ; p. 1-6

Author(s): Marotta, Nicola; Demeco, Andrea; Indino, Angelo; de Scorpio, Gerardo; Moggio, Lucrezia; Ammendolia, Antonio

Purpose: To investigate the effectiveness of commercial exergames treatments on people with Parkinson's disease (PD), a systematic review and network meta-analysis (NMA) of randomised controlled trials (RCT) was performed to evaluate functional locomotion effects in patients with PD.

Methods: A comprehensive search on PubMed, Embase, Cochrane Controlled Trials Register, the Cochrane, and other databases without language restrictions was conducted. References and reviews were cross-checked for possible studies. RCTs from 2012 were included. Seven studies with 236 participants were included in the NMA that used a random-effect Frequentist model to investigate the standard mean difference of pooled effect sizes change in functional locomotion between baseline and delayed retention tests on six comparisons.

Results: The direct comparisons Kinect: Control (n = 4), Wii: Control (n = 5) and the indirect-network comparison Kinect: Wii (n = 1) determine that Nintendo Wii™ may be the best choice in functional locomotion improvements.

Conclusions: These network meta-analytic findings show that Kinect and Wii show immediate positive effects on functional locomotion in people with PD. Compared with Kinect RCTs, Wii may be considered the best therapy for providing functional recovery in PD.

Implications for rehabilitation: Exergames rehabilitation reveals intervention benefits for functional locomotion in people with PD. In patients with cognitive disorders, Wii's platform can be considered a visual reference and a cue to facilitate patients with freezing. Nintendo Wii seems to be a better device for locomotion rehabilitation in people with PD than Xbox Kinect.

Title: Therapeutic Strategies to Treat or Prevent Off Episodes in Adults with Parkinson's Disease.

Citation: Drugs; Jun 2020; vol. 80 (no. 8); p. 775-796

Author(s): Vijiaratnam, Nirosen; Foltynie, Thomas

Abstract: Parkinson's disease is a chronic, neurodegenerative disease, which manifests with a mixture of motor, cognitive and behavioural symptoms. Levodopa is the most effective antiparkinsonian treatment to date, although chronic use engenders a mixture of complications in a substantial proportion of patients. Amongst these is the occurrence of episodes of worsening symptoms-'off' phenomena. These episodes can manifest with either motor or non-motor symptoms or a combination of these features and have been found to have profound impacts on patients' quality of life. Although preventative measures are poorly evidenced, avoiding excessive total daily levodopa intake in selected populations that are deemed to be of a higher risk for developing these episodes warrants further exploration. Methods to improve levodopa bioavailability and delivery to the brain are currently available and are of value in addressing these episodes once they have become established. These include modifications to levodopa formulations as well as the use of complimentary agents that improve levodopa bioavailability. The deployment of device-assisted approaches is a further dimension that can be considered in addressing these debilitating episodes. This review summarises the clinical manifestations of 'off' phenomena and the current approaches to treat them. Although we briefly discuss clinical advances on the horizon, the predominant focus is on existing, established treatments.

Title: Parkinson disease and the immune system - associations, mechanisms and therapeutics.

Citation: Nature reviews. Neurology; Jun 2020; vol. 16 (no. 6); p. 303-318

Author(s): Tan, Eng-King; Chao, Yin-Xia; West, Andrew; Chan, Ling-Ling; Poewe, Werner; Jankovic, Joseph

Abstract: Multiple lines of evidence indicate that immune system dysfunction has a role in Parkinson disease (PD); this evidence includes clinical and genetic associations between autoimmune disease and PD, impaired cellular and humoral immune responses in PD, imaging evidence of inflammatory cell activation and evidence of immune dysregulation in experimental models of PD. However, the mechanisms that link the immune system with PD remain unclear, and the temporal relationships of innate and adaptive immune responses with neurodegeneration are unknown. Despite these challenges, our current knowledge provides opportunities to develop immune-targeted therapeutic strategies for testing in PD, and clinical studies of some approaches are under way. In this Review, we provide an overview of the clinical observations, preclinical experiments and clinical studies that provide evidence for involvement of the immune system in PD and that help to define the nature of this association. We consider autoimmune mechanisms, central and peripheral inflammatory mechanisms and immunogenetic factors. We also discuss the use of this knowledge to develop immune-based therapeutic approaches, including immunotherapy that targets α -synuclein and the targeting of immune mediators such as inflammasomes. We also consider future research and clinical trials necessary to maximize the potential of targeting the immune system.

Title: Enhanced Obstacle Contrast to Promote Visual Scanning in Fallers with Parkinson's Disease: Role of Executive Function.

Citation: Neuroscience; Jun 2020; vol. 436 ; p. 82-92

Author(s): Alcock, Lisa; Galna, Brook; Hausdorff, Jeffrey M; Lord, Sue; Rochester, Lynn

Abstract: The ability to perceive differences in environmental contrast is critical for navigating complex environments safely. People with Parkinson's disease (PD) report a multitude of visual and cognitive deficits which may impede safe obstacle negotiation and increase fall risk. Enhancing obstacle contrast may influence the content of visual information acquired within complex environments and thus target environmental fall risk factors. 17 PD with a history of falls and 18 controls walked over an obstacle covered in a high and low contrast material in separate trials whilst eye movements were recorded. Measures of visual function and cognition were obtained. Gaze location was extracted during the approach phase. PD spent longer looking at the obstacle compared to controls regardless of contrast ($p < .05$), however group differences were largest for the low contrast obstacle. When accounting for group differences in approach time, PD spent longer looking at the low contrast obstacle and less time looking at the ground beyond the low contrast obstacle compared to controls ($p < .05$). The response to obstacle contrast in PD (high-low) was significantly associated with executive function. Better executive function was associated with spending longer looking at the low contrast obstacle and at the ground beyond the high contrast obstacle. Enhancing the contrast of ground-based trip hazards may improve visual processing of environmental cues in PD, particularly for individuals with better executive function. Manipulating contrast to attract visual attention is already in use in the public domain, however its utility for reducing fall risk in PD is yet to be formally tested in habitual settings.

Title: Young-onset and late-onset Parkinson's disease exhibit a different profile of fluid biomarkers and clinical features.

Citation: Neurobiology of aging; Jun 2020; vol. 90 ; p. 119-124

Author(s): Schirinzi, Tommaso; Di Lazzaro, Giulia; Sancesario, Giulia Maria; Summa, Susanna; Petrucci, Simona; Colona, Vito Luigi; Bernardini, Sergio; Pierantozzi, Mariangela; Stefani, Alessandro; Mercuri, Nicola Biagio; Pisani, Antonio

Abstract: Young-onset Parkinson's disease (YOPD) is a relevant condition whose neurobiology is questioned if different from those of typical late-onset Parkinson's disease (LOPD). Here, we explored whether the clinical-biochemical profile of Parkinson's disease (PD) could be affected by the age-of-onset (AO), as a possible result of a distinct neurodegenerative process. A panel of fluid biomarkers (CSF lactate, 42-amyloid- β peptide, total and 181-phosphorylated tau; serum uric acid) and the standard scores for motor and nonmotor signs were assessed in 76 idiopathic PD patients (genetic cases excluded; YOPD, $AO \leq 50$, $n = 44$; LOPD, $AO > 50$, $n = 32$) and 75 sex/age-matched controls, adjusting the models for the main confounding factors. In PD, AO directly correlated to either CSF lactate and tau proteins or the nonmotor symptoms scale score. Specifically, a younger AO was associated with lower levels of biomarkers and minor burden of nonmotor symptoms. Our findings indicate that clinical-biochemical features of idiopathic PD may vary depending on the AO, accounting for different profiles in YOPD and LOPD whose recognition is fundamental for further pathophysiological implications and clinical applications.

Title: Sleep in Parkinson's disease: A systematic review and meta-analysis of polysomnographic findings.

Citation: Sleep medicine reviews; Jun 2020; vol. 51 ; p. 101281

Author(s): Zhang, Ye; Ren, Rong; Sanford, Larry D; Yang, Linghui; Zhou, Junying; Tan, Lu; Li, Taomei; Zhang, Jihui; Wing, Yun-Kwok; Shi, Jie; Lu, Lin; Tang, Xiangdong

Abstract: Polysomnographic studies have been conducted to explore sleep changes in Parkinson's disease (PD), but the relationships between sleep disturbances and PD are imperfectly understood. We conducted a systematic review of the literature exploring polysomnographic differences between PD patients and controls in EMBASE, MEDLINE, All EBM databases, CINAHL, and PsycINFO. 67 studies were identified for systematic review, 63 of which were used for meta-analysis. Meta-analyses revealed significant reductions in total sleep time, sleep efficiency, N2 percentage, slow wave sleep, rapid eye movement sleep (REM) percentage, and increases in wake time after sleep onset, N1 percentage, REM latency, apnea hypopnea index, and periodic limb movement index in PD patients compared with controls. There were no remarkable differences in sleep continuity or sleep architecture between PD patients with and without REM sleep behavior disorder (RBD). Our study suggests that PD patients have poor sleep quality and quantity. Sex, age, disease duration, presence of RBD, medication status, cognitive impairment, and adaptation night are factors that contributed to heterogeneity between studies.

Title: Non-pharmacological treatment for Parkinson disease patients with depression: a meta-analysis of repetitive transcranial magnetic stimulation and cognitive-behavioral treatment.

Citation: The International journal of neuroscience; Apr 2020 ; p. 1-14

Author(s): Chen, Jianing; He, Peikun; Zhang, Yuhu; Gao, Yuyuan; Qiu, Yihui; Li, You; Zhang, Qingxi; Wang, Limin; Huang, Zhiheng; Zhao, Jiehao; Nie, Kun; Wang, Lijuan

Background: Nowadays, antidepressants still are the mainstay of treatment for depression in Parkinson's disease (PD) but some recent studies report that medication might aggravate motor symptoms in PD patients. This meta-analysis aims to assess the effect of non-pharmacological treatments for depression in patients with PD.

Materials and Methods: Only randomized controlled trials (RCTs) were included. The participants were PD patients with comorbid depression (dPD). The interventions had the equivalent effect of non-pharmacological treatments alone compared with control(s). Scores of depression scale were selected as the primary outcome, while scores of Unified Parkinson's Disease Rating Scale part III and the incidence of side effects were the secondary outcome. The statistics were pooled and presented as weighted mean differences (WMDs), standardized mean differences (SMDs), or risk ratios (RRs) with their 95% confidence intervals (CIs).

Results: Fifteen articles were eventually included; twelve studies reported on repetitive transcranial magnetic stimulation (rTMS) and three used cognitive behavioral therapy (CBT). Other interventions failed to have qualified studies. Our data indicated that both rTMS and CBT could significantly improve depression scores in a short term (SMD = -0.621, 95% CI [-0.964, -0.278]; SMD = -1.148, 95% CI [-1.498, -0.798], respectively). In addition, rTMS could alleviate motor symptom (WMD = -2.617, 95% CI [-4.183, -1.051]) and was relatively safe (RR = 1.054, 95% CI [0.698, 1.592]).

Conclusion: Our data suggest that rTMS can safely alleviate depression and motor symptoms in dPD at least for a short period. Moreover, compared with clinical monitoring, CBT can improve depressive symptoms.

Title: Frequency of and risk factors for potentially inappropriate medication use in Parkinson's disease.

Citation: Age and ageing; Apr 2020

Author(s): Abraham, Danielle S; Pham Nguyen, Thanh Phuong; Hennessy, Sean; Weintraub, Daniel; Gray, Shelly L; Xie, Dawei; Willis, Allison W

Background: impairments in neurotransmitter pathways put Parkinson's disease (PD) patients at risk for drug-disease interactions and adverse medication events.

Objective: to determine the prevalence and risk factors for potentially inappropriate medication (PIM) prescriptions, as defined by the 2015 Beers List, in PD.

Methods: cross-sectional analysis was conducted on 2014 Medicare beneficiaries with PD who had parts A, B and D coverage. The prevalence of PIM prescriptions for older adults was determined overall, and specifically for medications that can exacerbate motor symptoms or cognitive impairment in PD. Logistic regression models were constructed to determine the association between age, sex, race, geography and poverty with PIM prescriptions.

Results: the final sample included 458,086 beneficiaries. In 2014, 35.8% of beneficiaries with PD filled a prescription for at least one PIM for older adults. In total, 8.7% of beneficiaries received a PIM that could exacerbate motor symptoms and 29.0% received a PIM that could worsen cognitive impairment. After adjustment, in all models, beneficiaries who were younger, female, white, urban-dwelling and eligible for Medicaid benefits were more likely to receive a PIM.

Conclusion: PIM prescriptions are not uncommon in PD, particularly for medications that can exacerbate cognitive impairment. Future research will examine underlying drivers of sex and other disparities in PIM prescribing. Additional studies are needed to understand the impact of PIMs on disease symptoms, healthcare utilisation and patient outcomes.

Title: Seeing ophthalmologic problems in Parkinson disease: Results of a visual impairment questionnaire.

Citation: Neurology; Apr 2020; vol. 94 (no. 14); p. e1539

Author(s): Borm, Carlijn D J M; Visser, Femke; Werkmann, Mario; de Graaf, Debbie; Putz, Diana; Seppi, Klaus; Poewe, Werner; Vlaar, Annemarie M M; Hoyng, Carel; Bloem, Bastiaan R; Theelen, Thomas; de Vries, Nienke M

Objective: To determine the prevalence and clinical effect of ophthalmologic symptoms in patients with Parkinson disease (PD), compared with controls, using a standardized questionnaire.

Methods: In this observational, cross-sectional, multicenter study, 848 patients with PD and 250 healthy controls completed the Visual Impairment in Parkinson's Disease Questionnaire (VIPD-Q). The VIPD-Q addressed 4 domains according to structures: (1) ocular surface; (2) intraocular; (3) oculomotor; and (4) optic nerve. The questionnaire also assessed the effect of ophthalmologic symptoms on daily activities.

Results: One or more ophthalmologic symptoms were reported by 82% (95% confidence interval [CI], 80-85) of patients, compared with 48% (95% CI, 42-54) of controls ($p < 0.001$). Patients with PD experienced more ophthalmologic symptoms across all domains than controls ($p < 0.001$), as reflected by a higher VIPD-Q total score among patients (median 10 [interquartile range (IQR) 13]) than controls (median 2 [IQR 5]; $p < 0.001$). Ophthalmologic

symptoms interfered with daily activities in 68% (95% CI, 65-71) of patients, compared with 35% (95% CI, 29-41) of controls ($p < 0.001$).

Conclusion: Patients with PD have a higher prevalence of ophthalmologic symptoms than controls. Moreover, these frequently interfere with daily activities. A screening questionnaire such as the VIPD-Q may help with identifying ophthalmologic symptoms in PD, thereby enabling more timely treatment.

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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