

Parkinson's Disease Current Awareness Bulletin January 2021

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Contact us: Academy Library 824897/98 Email: ruh-tr.library@nhs.net Title: Multitasking guardian of mitochondrial quality: Parkin function and Parkinson's disease.

Citation: Translational neurodegeneration; Jan 2021; vol. 10 (no. 1); p. 5 **Author(s):** Kamienieva, Iryna; Duszyński, Jerzy; Szczepanowska, Joanna

Abstract: The familial form of Parkinson's disease (PD) is linked to mutations in specific genes. The mutations in parkin are one of the most common causes of early-onset PD. Mitochondrial dysfunction is an emerging active player in the pathology of neurodegenerative diseases, because mitochondria are highly dynamic structures integrated with many cellular functions. Herein, we overview and discuss the role of the parkin protein product, Parkin E3 ubiquitin ligase, in the cellular processes related to mitochondrial function, and how parkin mutations can result in pathology in vitro and in vivo.

Title: Cross-talks among GBA mutations, glucocerebrosidase, and α -synuclein in GBA-associated Parkinson's disease and their targeted therapeutic approaches: a comprehensive review.

Citation: Translational neurodegeneration; Jan 2021; vol. 10 (no. 1); p. 4 **Author(s):** Behl, Tapan; Kaur, Gagandeep; Fratila, Ovidiu; Buhas, Camelia; Judea-Pusta, Claudia Teodora; Negrut, Nicoleta; Bustea, Cristiana; Bungau, Simona

Abstract: Current therapies for Parkinson's disease (PD) are palliative, of which the levodopa/carbidopa therapy remains the primary choice but is unable to modulate the progression of neurodegeneration. Due to the complication of such a multifactorial disorder and significant limitations of the therapy, numerous genetic approaches have been proved effective in finding out genes and mechanisms implicated in this disease. Following the observation of a higher frequency of PD in Gaucher's disease (GD), a lysosomal storage condition, mutations of glycosylceramidase beta (GBA) encoding glucocerebrosidase (GCase) have been shown to be involved and have been explored in the context of PD. GBA mutations are the most common genetic risk factor of PD. Various studies have revealed the relationships between PD and GBA gene mutations, facilitating a better understanding of this disorder. Various hypotheses delineate that the pathological mutations of GBA minimize the enzymatic activity of GCase, which affects the proliferation and clearance of α-synuclein; this affects the lysosomal homeostasis, exacerbating the endoplasmic reticulum stress or encouraging the mitochondrial dysfunction. Identification of the pathological mechanisms underlying the GBA-associated parkinsonism (GBA + PD) advances our understanding of PD. This review based on current literature aims to elucidate various genetic and clinical characteristics correlated with GBA mutations and to identify the numerous pathological processes underlying GBA + PD. We also delineate the therapeutic strategies to interfere with the mutant GCase function for further improvement of the related α -synuclein-GCase crosstalks. Moreover, the various therapeutic approaches such as gene therapy, chaperone proteins, and histone deacetylase inhibitors for the treatment of GBA + PD are discussed.

Title: An Innovative Personalised Management Program for Older Adults with Parkinson's Disease: New Concepts and Future Directions.

Citation: Journal of personalized medicine; Jan 2021; vol. 11 (no. 1)

Author(s): Varma, Piyush; Narayan, Lakshanaa; Alty, Jane; Painter, Virginia; Padmakumar, Chandrasekhara

Introduction: Parkinson's disease is a heterogeneous clinical syndrome. Parkinson's disease in older persons presents with a diverse array of clinical manifestations leading to unique care needs. This raises the need for the healthcare community to proactively address the care needs of older persons with Parkinson's disease. Though it is tempting to categorise different phenotypes of Parkinson's disease, a strong evidence based for the same is lacking. There is considerable literature describing the varying clinical manifestations in old age. This article aims to review the literature looking for strategies in personalising the management of an older person with Parkinson's disease.

Title: Sexual Disorders and Quality of Life in Parkinson's Disease.

Citation: Sexual medicine; Jan 2021; vol. 9 (no. 1); p. 100280

Author(s): Santa Rosa Malcher, Claudia Marques; Roberto da Silva Gonçalves Oliveira, Kleber; Fernandes Caldato, Milena Coelho; Lopes Dos Santos Lobato, Bruno; da Silva Pedroso, Janari; de Tubino Scanavino, Marco

Introduction: Sexual disorders are the most neglected nonmotor symptoms in Parkinson's disease (PD). Although doctors seek greater priority to motor manifestations, which are the basis for the diagnosis of PD, the nonmotor symptoms deserve to be highlighted as much as the motor problems because of their strong presence and discomfort in the patients, causing the important impairment in the quality of life (QoL) of the individual with PD.AIMProvide the prevalence of sexual disorders among patients with PD and alert the medical profession to investigate and be familiar with problems related to QoL and sexual disorders in PD.

Methods: This is a large literature review on sexual disorders in PD and impaired QoL.

Main Outcome Measures: Sexual disorders in PD and prevalence between genders have been described in epidemiological studies. Neuroanatomy, pathophysiology, risk factors, QoL, and etiologies were reviewed.

Results: The estimate of the prevalence of sexual dysfunction in the form of compulsive sexual behavior in PD is higher in men by 5.2% than in women by 0.5%. This diagnosis is a determinant of intense and persistent suffering and is related to several health problems of a social, economic, personal, family, psychological, and occupational nature, which can even culminate in sexual abuse. It is most commonly associated with the use of drugs commonly used in PD therapy in 98.1% of cases. In addition to this serious public health problem, another common condition of sexual dysfunction occur with the decreased libido by loss of the neurotransmitter dopamine proper of the pathophysiology of PD.

Conclusion: The presence of sexual disorders in PD should be tracked and monitored because of its harmful consequences, whether due to increased sexual behavior or associated psychological distress, as well as the impacts on QoL. Early recognition and adequate treatment of PD in its fullness and richness of associated symptoms are essential for improving QoL. Santa Rosa Malcher CM, Roberto da Silva Gonçalves Oliveira K, Fernandes Caldato MC, et al. Sexual Disorders and Quality of Life in Parkinson's Disease. Sex Med 2020;XX:XXX-XXX.

Title: Inflaming the Brain with Iron.

Citation: Antioxidants (Basel, Switzerland); Jan 2021; vol. 10 (no. 1)

Author(s): Urrutia, Pamela J; Bórquez, Daniel A; Núñez, Marco Tulio

Abstract: Iron accumulation and neuroinflammation are pathological conditions found in several neurodegenerative diseases, including Alzheimer's disease (AD) and Parkinson's disease (PD). Iron and inflammation are intertwined in a bidirectional relationship, where iron modifies the inflammatory phenotype of microglia and infiltrating macrophages, and in turn, these cells secrete diffusible mediators that reshape neuronal iron homeostasis and regulate iron entry into the brain. Secreted inflammatory mediators include cytokines and reactive oxygen/nitrogen species (ROS/RNS), notably hepcidin and nitric oxide (NO). Hepcidin is a small cationic peptide with a central role in regulating systemic iron homeostasis. Also present in the cerebrospinal fluid (CSF), hepcidin can reduce iron export from neurons and decreases iron entry through the blood-brain barrier (BBB) by binding to the iron exporter ferroportin 1 (Fpn1). Likewise, NO selectively converts cytosolic aconitase (c-aconitase) into the iron regulatory protein 1 (IRP1), which regulates cellular iron homeostasis through its binding to iron response elements (IRE) located in the mRNAs of iron-related proteins. Nitric oxide-activated IRP1 can impair cellular iron homeostasis during neuroinflammation, triggering iron accumulation, especially in the mitochondria, leading to neuronal death. In this review, we will summarize findings that connect neuroinflammation and iron accumulation, which support their causal association in the neurodegenerative processes observed in AD and PD.

Title: Effect of family history, occupation and diet on the risk of Parkinson disease: A casecontrol study

Citation: PLoS ONE; Dec 2020; vol. 15 (no. 12)

Author(s): Torti M.; Casali M.; Grassini P.; Radicati F.G.; Stirpe P.; Vacca L.; Stocchi F.; Fossati C.; De Pandis M.F.; Iavicoli I.; Leso V.; Ceppi M.; Bruzzone M.; Bonassi S.

Background: The aetiology of Parkinson's disease (PD) is still very controversial, with a peculiar lack of established risk factors or protective behavior.

Methods: We carried out a case-control study of 634 idiopathic PD patients admitted from 2011 to 2015 to two hospitals located in central Italy and 532 controls matched by hospital, gender and age (+/- 5 years). The study questionnaire included questions on host factors, family history, residence, occupation and lifestyle. Odds ratios (ORs) for PD and 95% confidence intervals (CIs) were estimated with logistic regression, adjusting for actual and potential confounders.

Results: A lower OR was observed in females (0.74; 95%CI:0.58-0.96), while older age classes showed a constantly increased risk for PD (p<0.005) starting from the class 65-69 years. Subjects who reported a first degree relative affected by PD showed a borderline increase which was more evident in those enrolled in the urban center of Rome (OR = 1.65; 95%CI: 1.09-2.50). Significant reduction of the risk was associated to current smoking (OR = 0.48; 95%CI: 0.24-0.54), and to vegetables consumption (p<0.03), while borderline increases were associated to meat and cold cut consumption. Occupational activities classified according to ISCO-08 categories did not show increased risk, while higher ORs' were found for pilots and physicians.

Conclusions: The results from this study confirmed the higher risk of PD in males and in elderly, and the inverse association with smoking habit. The possible etiological role of familial clustering, dietary habit, and some job tasks is suggested.

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distribution, and reproduction in any medium, provided the original author and source are credited.

Title: Variations in hospitalization rates across Parkinson's Foundation Centers of Excellence

Citation: Parkinsonism and Related Disorders; Dec 2020; vol. 81 ; p. 123-128 **Author(s):** Zeldenrust F.; Lidstone S.; Marras C.; Wu S.; Dai Y.; Okun M.S.; Cubillos F.; Beck J.; Davis T.; Lyons K.; Nelson E.; Rafferty M.; Schmidt P.

Introduction: Patients with Parkinson's disease (PD) are at increased risk for hospitalization and often experience worsening of PD when hospitalized. It is therefore important to identify strategies to prevent hospitalization.

Method(s): Hospital encounter rates in different Parkinson's Foundation Centers of Excellence in United States, Canada, Israel and the Netherlands were analyzed as part of the Parkinson Foundation Parkinson's Outcomes Project (PF-POP). Multivariate logistic regression was used to estimate the odds ratio for hospitalization, adjusted for risk factors.

Result(s): Baseline age, disease duration, other relative than spouse/partner as care giver, cancer, arthritis, other comorbidities, falls, use of levodopa, use of dopamine agonist, use of COMT inhibitor, occupational therapy before the baseline visit, PDQ-39, MSCI total score and time between visits were significantly associated with the risk of hospital encounters. After adjustment for these factors, two centers had significantly lower odds for hospitalization admission and ER visit (minimum OR 0.3) and four centers had significantly higher odds (maximum OR 1.5) than the average center. Four centers had significantly lower hazard ratios for time to re-hospitalization compared to the average center. Reducing hospital admission rates in those centers with higher than average rates would reduce overall hospitalizations by 11%. Applied to PD patients over 65 nationwide this represents a potential for cost savings of greater than \$1 billion over 48 months.

Conclusion(s): Encounter rates vary even across expert centers and suggest that practices carried out in some centers may reduce the risk of hospitalization. Further research will be necessary to identify these practices and implement them more widely to improve care for people with PD. Copyright © 2020 Elsevier Ltd

Title: Tai Chi and Qi Gong therapies as a complementary treatment in Parkinson's disease - a systematic review

Citation: Complementary Therapies in Medicine; Jan 2021; vol. 56 **Author(s):** Kamieniarz A.; Grzybowska-Ganszczyk D.; Juras G.; Milert A.; Opara J.

Highlights: The effectiveness of Tai Chi and Qigong training on motor function in PD was evaluated with functional tests, and only a few articles included objective methods.

The articles included in the review showed several limitations, such as a small sample size, heterogeneity of stages of PD, and diversified duration of the intervention.

Current state of knowledge shows that both Tai Chi and Qigong interventions might be a promising complementary therapy in PD.

Future research is required to establish the optimal training program for each stage of Parkinson's disease.

Title: Retinal Thickness Predicts the Risk of Cognitive Decline in Parkinson Disease

Citation: Annals of Neurology; Jan 2021; vol. 89 (no. 1); p. 165-176

Author(s): Murueta-Goyena A.; Del Pino R.; Acera M.; Carmona-Abellan M.; Fernandez-Valle T.; Tijero B.; Gomez-Esteban J.C.; Gabilondo I.; Galdos M.; Arana B.; Lucas-Jimenez O.; Ojeda N.; Ibarretxe-Bilbao N.; Pena J.; Cortes J.; Ayala U.; Barrenechea M.

Objective: This study was undertaken to analyze longitudinal changes of retinal thickness and their predictive value as biomarkers of disease progression in idiopathic Parkinson's disease (iPD).

Method(s): Patients with Lewy body diseases were enrolled and prospectively evaluated at 3 years, including patients with iPD (n = 42), dementia with Lewy bodies (n = 4), E46K-SNCA mutation carriers (n = 4), and controls (n = 17). All participants underwent Spectralis retinal optical coherence tomography and Montreal Cognitive Assessment, and Unified Parkinson's Disease Rating Scale score was obtained in patients. Macular ganglion cell-inner plexiform layer complex (GCIPL) and peripapillary retinal nerve fiber layer (pRNFL) thickness reduction rates were estimated with linear mixed models. Risk ratios were calculated to evaluate the association between baseline GCIPL and pRNFL thicknesses and the risk of subsequent cognitive and motor worsening, using clinically meaningful cutoffs.

Result(s): GCIPL thickness in the parafoveal region (1- to 3-mm ring) presented the largest reduction rate. The annualized atrophy rate was 0.63microm in iPD patients and 0.23microm in controls (p < 0.0001). iPD patients with lower parafoveal GCIPL and pRNFL thickness at baseline presented an increased risk of cognitive decline at 3 years (relative risk [RR] = 3.49, 95% confidence interval [CI] = 1.10-11.1, p = 0.03 and RR = 3.28, 95% CI = 1.03-10.45, p = 0.045, respectively). We did not identify significant associations between retinal thickness and motor deterioration.

Interpretation(s): Our results provide evidence of the potential use of optical coherence tomography-measured parafoveal GCIPL thickness to monitor neurodegeneration and to predict the risk of cognitive worsening over time in iPD. ANN NEUROL 2021;89:165-176.Copyright © 2020 The Authors. Annals of Neurology published by Wiley Periodicals LLC on behalf of American Neurological Association.

Title: Discordant Monozygotic Parkinson Disease Twins: Role of Mitochondrial Integrity

Citation: Annals of Neurology; Jan 2021; vol. 89 (no. 1); p. 158-164

Author(s): Dulovic-Mahlow M.; Trinh J.; Diaw S.H.; Knappe E.; Kuhnke N.; Ingwersen L.-C.; Hinrichs F.; Weber J.; Kupnicka P.; Balck A.; Grunewald A.; Klein C.; Seibler P.; Lohmann K.; Konig I.R.; Urban P.P.; Delcambre S.; Vollbrandt T.

Objective: Even though genetic predisposition has proven to be an important element in Parkinson's disease (PD) etiology, monozygotic (MZ) twins with PD displayed a concordance rate of only about 20% despite their shared identical genetic background.

Method(s): We recruited 5 pairs of MZ twins discordant for idiopathic PD and established skin fibroblast cultures to investigate mitochondrial phenotypes in these cellular models

against the background of a presumably identical genome. To test for genetic differences, we performed whole genome sequencing, deep mitochondrial DNA (mtDNA) sequencing, and tested for mitochondrial deletions by multiplex real-time polymerase chain reaction (PCR) in the fibroblast cultures. Further, the fibroblast cultures were tested for mitochondrial integrity by immunocytochemistry, immunoblotting, flow cytometry, and real-time PCR to quantify gene expression.

Result(s): Genome sequencing did not identify any genetic difference. We found decreased mitochondrial functionality with reduced cellular adenosine triphosphate (ATP) levels, altered mitochondrial morphology, elevated protein levels of superoxide dismutase 2 (SOD2), and increased levels of peroxisome proliferator-activated receptor-gamma coactivator-alpha (PPARGC1A) messenger RNA (mRNA) in skin fibroblast cultures from the affected compared to the unaffected twins. Further, there was a tendency for a higher number of somatic mtDNA variants among the affected twins.

Interpretation(s): We demonstrate disease-related differences in mitochondrial integrity in the genetically identical twins. Of note, the clinical expression matches functional alterations of the mitochondria. ANN NEUROL 2021;89:158-164.Copyright © 2020 The Authors. Annals of Neurology published by Wiley Periodicals LLC on behalf of American Neurological Association.

Title: Rivastigmine in Parkinson's Disease Dementia with Orthostatic Hypotension

Citation: Annals of Neurology; Jan 2021; vol. 89 (no. 1); p. 91-98

Author(s): Espay A.J.; Marsili L.; Sturchio A.; Mahajan A.; Pathan R.; Pilotto A.; Elango D.S.; Pezous N.; Masellis M.; Gomez-Mancilla B.

Objective: The purpose of this study was to evaluate if the cognitive benefit of rivastigmine is affected by the presence of orthostatic hypotension (OH) in patients with Parkinson's disease dementia (PDD).

Method(s): We conducted a post hoc analysis on 1,047 patients with PDD from 2 randomized controlled trials comparing rivastigmine versus placebo at week 24 (n = 501) and rivastigmine patch versus capsule at week 76 (n = 546). A drop >= 20 mm Hg in systolic blood pressure (SBP) or >= 10 in diastolic blood pressure (DBP) upon standing classified subjects as OH positive (OH+); otherwise, OH negative (OH-). The primary end point was the Alzheimer's Disease Assessment Scale - Cognitive subscale (ADAS-Cog) at week 24 and the Mattis Dementia Rating Scale (MDRS) at week 76, using intention-to-treat with retrieved dropout at week 24 and observed cases at week 76, consistent with the original analyses.

Result(s): Overall safety was comparable between OH+ (n = 288, 27.5%) and OH- (n = 730, 69.7%), except for higher frequency of syncope (9.2%) in the OH+ placebo arm. The placebo-adjusted effect of rivastigmine on ADAS-Cog at week 24 was 5.6 +/- 1.2 for OH+ and 1.9 +/- 0.9 in OH- (p = 0.0165). Among subjects with OH, the MDRS change from baseline at week 76 was higher for rivastigmine capsules versus patch (10.6 +/- 2.9 vs -1.5 +/- 3.0, p = 0.031). The overall prevalence of OH was lower for rivastigmine than placebo at week 24 (28.3% vs 44.6%, p = 0.0476).

Interpretation(s): The cognitive benefit from rivastigmine is larger in patients with PDD with OH, possibly mediated by a direct antihypotensive effect. ANN NEUROL 2021;89:91-98.Copyright © 2020 American Neurological Association

Title: Neuromechanical Assessment of Activated vs. Resting Leg Rigidity Using the Pendulum Test Is Associated With a Fall History in People With Parkinson's Disease

Citation: Frontiers in Human Neuroscience; Dec 2020; vol. 14 **Author(s):** Martino G.; McKay J.L.; Ting L.H.; Factor S.A.

Abstract: Leg rigidity is associated with frequent falls in people with Parkinson's disease (PD), suggesting a potential role in functional balance and gait impairments. Changes in the neural state due to secondary tasks, e.g., activation maneuvers, can exacerbate (or "activate") rigidity, possibly increasing the risk of falls. However, the subjective interpretation and coarse classification of the standard clinical rigidity scale has prohibited the systematic, objective assessment of resting and activated leg rigidity. The pendulum test is an objective diagnostic method that we hypothesized would be sensitive enough to characterize resting and activated leg rigidity. We recorded kinematic data and electromyographic signals from rectus femoris and biceps femoris during the pendulum test in 15 individuals with PD, spanning a range of leg rigidity severity. From the recorded data of leg swing kinematics, we measured biomechanical outcomes including first swing excursion, first extension peak, number and duration of the oscillations, resting angle, relaxation index, maximum and minimum angular velocity. We examined associations between biomechanical outcomes and clinical leg rigidity score. We evaluated the effect of increasing rigidity through activation maneuvers on biomechanical outcomes. Finally, we assessed whether either biomechanical outcomes or changes in outcomes with activation were associated with a fall history. Our results suggest that the biomechanical assessment of the pendulum test can objectively guantify parkinsonian leg rigidity. We found that the presence of high rigidity during clinical exam significantly impacted biomechanical outcomes, i.e., first extension peak, number of oscillations, relaxation index, and maximum angular velocity. No differences in the effect of activation maneuvers between groups with clinically assessed low rigidity were observed, suggesting that activated rigidity may be independent of resting rigidity and should be scored as independent variables. Moreover, we found that fall history was more common among people whose rigidity was increased with a secondary task, as measured by biomechanical outcomes. We conclude that different mechanisms contributing to resting and activated rigidity may play an important yet unexplored functional role in balance impairments. The pendulum test may contribute to a better understanding of fundamental mechanisms underlying motor symptoms in PD, evaluating the efficacy of treatments, and predicting the risk of falls.© Copyright © 2020 Martino, McKay, Factor and Ting.

Title: Acupuncture Treatment Reduces Incidence of Parkinson's Disease in Patients With Depression: A Population-Based Retrospective Cohort Study in Taiwan

Citation: Frontiers in Aging Neuroscience; Dec 2020; vol. 12 **Author(s):** Huang C.-H.; Hsieh C.-L.; Lin M.-C.

Abstract: Depression is a risk factor for subsequent Parkinson's disease (PD). Some patients with depression undergo acupuncture treatment because of other diseases in Taiwan. Therefore, the present study used data from Taiwan's National Health Insurance Research Database (NHIRD) to investigate the incidence of PD in patients having depression with and without acupuncture treatment. We conducted a retrospective study of a matched cohort of 48,981 patients with newly diagnosed depression between 2000 and 2012 who were selected from the NHIRD. The 1:1 propensity score method was utilized to match an equal number of patients (N = 9,189) in the acupuncture and non-acupuncture cohorts. We employed Cox proportional hazard models to evaluate the risk of PD. The

cumulative incidence of PD in both cohorts was estimated using the Kaplan-Meier method, and the difference was examined through a log-rank test. Patients with depression who received acupuncture treatment demonstrated a lower risk of PD [adjusted hazard ratio (aHR) = 0.39, 95% confidence interval = 0.31-0.49] than those who did not undergo acupuncture treatment, after adjusting for age, sex, insurance amount, geographic region, urbanization levels, comorbidities, and drugs. The cumulative incidence of PD was significantly lower in the acupuncture cohort than in the non-acupuncture cohort (log-rank test, p < 0.001). The database did not indicate the severity of depression and acupoints. The results suggest that acupuncture treatment significantly reduced the development of PD in patients with depression; however, a future study should be conducted to provide more objective evidence.© Copyright © 2020 Huang, Lin and Hsieh.

Title: People with Parkinson's disease are more willing to do additional exercise if the exercise program has specific attributes: a discrete choice experiment

Citation: Journal of Physiotherapy; Jan 2021; vol. 67 (no. 1); p. 49-55

Author(s): Paul S.S.; Canning C.G.; Lee D.C.; Bampton J.; Lofgren N.; Sherrington C.; Howard K.

Question: What specific attributes of exercise programs influence the preferences of people with Parkinson's disease for additional exercise compared with their current practice? What trade-offs are participants willing to make between exercise program attributes?

Design: Discrete choice experiment.

Participant(s): Five hundred and forty people with Parkinson's disease.

Intervention(s): Participants decided whether they would adopt a hypothetical program in addition to their current exercise routine.

Outcome measures: Exercise program attributes included: type, number of sessions/week, location, travel time/session, delivery mode, supervisor's expertise, extent of supervision, benefits for physical and psychological function and out-of-pocket cost/session.

Result(s): Participants preferred additional exercise when programs: provided physical (OR 1.85, 95% CI 1.61 to 2.13) or psychological (OR 1.45, 95% CI 1.26 to 1.67) benefit, involved less travel time (ORs 1.50 to 2.02) and were supervised by qualified professionals with Parkinson's disease expertise (ORs 1.51 to 1.91). Participants were most willing to add multimodal exercise to their exercise routine (ORs 2.01 to 2.19). Participants were less likely to prefer higher cost programs (OR 0.65, 95% CI 0.60 to 0.71, per AU\$10 cost increase) or group sessions compared to individual sessions (OR 0.72, 95% CI 0.54 to 0.96). Men preferred adding strengthening exercises (OR 2.00, 95% CI 1.23 to 3.26) and women had a preference against adding aerobic exercise (OR 0.33, 95% CI 0.15 to 0.73). Participants not currently exercising were more likely to prefer adding exercise compared with those already exercising 300 minutes weekly (OR 1.74, 95% CI 1.15 to 2.63).

Conclusion(s): People with Parkinson's disease were more willing to participate in exercise programs that cost less, involve less travel, provide physical or psychological benefits and are supervised by qualified professionals. To enable more people with Parkinson's disease to exercise, health services should provide programs addressing these factors and account for sex differences. Copyright © 2020 Australian Physiotherapy Association

Title: Effects of cadence-compatible melodic rhythmic auditory stimulation implementation on gait in patients with Parkinson's disease

Citation: Somatosensory and Motor Research; 2020

Author(s): Carikci S.; Unluer N.O.; Torun S.

Purpose: Progressive loss of dopaminergic neurons in basal ganglia is blamed as the main source of gait disturbance in Parkinson's disease (PD). It is known that the normal step pattern does not disappear in PD, but there is a problem in activating the correct step response. The aim of this study was to investigate the effect of Rhythmic Auditory Stimulation (RAS), which is an external stimulus, on gait in individuals with PD.

Material(s) and Method(s): Twenty-six individuals, 13 in the PD group and 13 in the control group, participated in the study. All individuals were asked to walk under four different RAS conditions configured with beat frequency and melodic variations. Time-distance parameters and gait performance of the individuals were evaluated.

Result(s): RAS significantly increased the gait speed of the individuals with PD compared to the control group. RAS set to 10% increase in the cadence of the patient with melody (10M+) was found to be more effective than the RAS set to normal cadence of the patient without melody (0 M-) (p < 0.05). While all RAS implementations increased the stride length of the individuals with PD (p < 0.05), there was no change in the control group. RAS did not affect the return time in both groups.

Conclusion(s): Our study has shown that RAS implementation improves gait in individuals with PD both in terms of time-distance parameters and performance, especially when set to 10% more than the patient's gait cadence. It was concluded that cadence-compatible melodic RAS can be safely included in PD rehabilitation programs. Copyright © 2020 Informa UK Limited, trading as Taylor & Francis Group.

Title: Autonomic Dysfunctions in Parkinson's Disease: Prevalence, Clinical Characteristics, Potential Diagnostic Markers, and Treatment.

Citation: Parkinson's Disease (20420080); Dec 2020 ; p. 1-10 **Author(s):** Zhang ; Chen, Sheng-Di

Abstract: Parkinson's disease (PD) is a common neurodegenerative disease in the middleaged and the elderly. Symptoms of autonomic dysfunctions are frequently seen in PD patients, severely affecting the quality of life. This review summarizes the epidemiology, clinical manifestations, and treatment options of autonomic dysfunctions. The clinical significance of autonomic dysfunctions in PD early diagnosis and differential diagnosis is also discussed.

Title: The achievement and prospect of deep brain stimulation for the treatment of movement disorders.

Citation: Chinese Journal of Contemporary Neurology & Neurosurgery; Dec 2020; vol. 20 (no. 12); p. 1027-1031

Author(s): Department of Neurosurgery, The First Affiliated Hospital of University of Science and Technology of China, Anhui Provincial Stereotactic Neurosurgical Institute; Anhui Province Key Laboratory of Brain Function and Brain Disease, Hefei 230001, Anhui, China; XIONG Chi

Abstract: Deep brain stimulation (DBS) was first used in the treatment of essential tremor in 1987, and later used in the treatment of advanced Parkinson's disease (PD), drug-refractory dystonia, other types of tremor and Tourette's syndrome, which can reduce the clinical symptoms and improve quality of life of patients for a long time, as a major progress in

surgical treatment of movement disorders in past 30 years. However, there are also limitations that can not effectively improve the axial system symptoms of PD, secondary dystonia, or related side effects such as cognitive impairment and balance disorder. In recent years, the exploration of new targets and innovation of DBS equipment have further promoted the treatment of DBS for movement disorders. This article reviews relevant research to provide clinical guidance.

Title: Advances in neural circuit mechanism in Parkinson's disease.

Citation: Chinese Journal of Contemporary Neurology & Neurosurgery; Dec 2020; vol. 20 (no. 12); p. 1032-1036

Author(s): Department of Neurosurgery, The First Affiliated Hospital of University of Science and Technology of China, Anhui Provincial Stereotactic Neurosurgical Institute; Anhui Province Key Laboratory of Brain Function and Brain Disease, Hefei 230001, Anhui, China; NIU Chao-shi

Abstract: Parkinson's disease (PD) is a common neurodegenerative disease with strong heterogeneity of clinical symptoms and progressive aggravation. The core pathological feature is the apoptosis of dopaminergic neurons in substantia nigra and striatum, but this pathological feature can only explain part of the symptom. With the development of electrophysiological recording, fMRI, optogenetics and other technologies, it has been found that neural circuit dysfunction after dopaminergic neuron apoptosis is an important mechanism for the occurrence and development of PD, as well as many therapeutic measures such as deep brain stimulation (DBS) intervention target. This article reviews the research progress of PD neural circuit mechanism in recent years, including common symptoms of PD, neural circuit models, and abnormal electrical activity patterns, to provide ideas for clinical research.

Title: Research progress of functional brain-neuroimaging technology in Parkinson's disease with gait disorder.

Citation: Chinese Journal of Contemporary Neurology & Neurosurgery; Dec 2020; vol. 20 (no. 12); p. 1104-1108

Author(s): Department of Rehabilitation Medicine, Tianjin Huanhu Hospital, Tianjin 300350, China; YU Yang; YU Ning-bo; WU Jia-ling

Abstract: Gait disorder appears in the whole process of Parkinson's disease (PD), which causes disability and serious affects in PD patients. The mechanism of gait disorder in PD is still unclear. Functional brain - neuroimaging can be used to analyse the characteristics and rules of brain functional activity related to gait disorder in PD, and has important clinical significance in revealing the neural physiopathologia mechanism of gait disorder, guiding the treatment and evaluating the curative effect. This paper briefly summarizes the research progress of fMRI and functional near-infrared spectroscopy (fNIRS) in gait disorder of PD, to provide reference for future research.

Title: The Spectrum of Sleep Disorders in Parkinson Disease: A Review.

Citation: CHEST; Feb 2021; vol. 159 (no. 2); p. 818-827 **Author(s):** Lajoie ; Lafontaine, Anne-Louise; Kaminska, Marta **Abstract:** There is increasing interest in the effects of sleep and sleep disturbances on the brain, particularly in relation to aging and neurodegenerative processes. Parkinson disease (PD) is the second most common neurodegenerative disorder, with growing prevalence worldwide. Sleep disorders, including sleep-disordered breathing (SDB), are among the most frequent non-motor manifestations of PD. They can substantially impair quality of life and possibly affect the course of the disease. This article reviews the etiology, implications, and management of sleep disturbances in PD, such as excessive daytime sleepiness, insomnia, restless legs syndrome, rapid eye movement sleep behavior disorder, and SDB. Also briefly explored is the potential role of sleep disorders, including SDB, in the progression of neurodegeneration.

Title: The effects of exercise on sleep quality in persons with Parkinson's disease: A systematic review with meta-analysis.

Citation: Sleep Medicine Reviews; Feb 2021; vol. 55

Author(s): Cristini ; Weiss, Maxana; De Las Heras, Bernat; Medina-Rincón, Almudena; Dagher, Alain; Postuma, Ronald B.; Huber, Reto; Doyon, Julien; Rosa-Neto, Pedro; Carrier, Julie; Amara, Amy W.; Roig, Marc

Abstract: We conducted a systematic review with meta-analysis to determine the evidence in support of exercise to improve sleep quality assessed subjectively and objectively in Parkinson's Disease (PD). Standardized mean differences (SMD) comparing the effects of exercise and control interventions on sleep quality with 95% confidence intervals (CI) were calculated. Data from 10 randomized and 2 non-randomized controlled trials, including a total of 690 persons with PD were included. Exercise had a significant positive effect on sleep quality assessed subjectively (SMD = 0.53; 95% CI = 0.16-0.90; p = 0.005). However, the methodological quality of the studies showing positive effects on sleep quality was significantly poorer than the studies showing no effects. Only one study assessed the impact of exercise on objective sleep quality, showing improvements in sleep efficiency assessed with polysomnography (SMD = 0.94; 95% CI = 0.38-1.50; p = 0.001). Exercise performed at moderate to maximal intensities (SMD = 0.46; 95% CI = 0.05-0.87; p = 0.03) had significant effects on subjective sleep quality. In contrast, exercise performed at mild to moderate intensities showed non-significant effects (SMD = 0.76; 95% CI = -0.24-1.76; p = 0.14). These results support the use of exercise to improve sleep quality in persons with PD and reinforce the importance of achieving vigorous exercise intensities. Biases, limitations, practice points and directions for future research are discussed.

Title: The effects of non-invasive brain stimulation on sleep disturbances among different neurological and neuropsychiatric conditions: A systematic review.

Citation: Sleep Medicine Reviews; Feb 2021; vol. 55

Author(s): Herrero Babiloni ; Bellemare, Audrey; Beetz, Gabrielle; Vinet, Sophie-A.; Martel, Marc O.; Lavigne, Gilles J.; De Beaumont, Louis

Abstract: Sleep disturbances (e.g., difficulty to initiate or maintain sleep) and poor sleep quality are major health concerns that accompany several neurological and neuropsychiatric clinical conditions where different brain circuitries are affected (e.g., chronic pain, Parkinson's disease or depression), having a great impact in the individual's well-being, quality of life, and the socioeconomic system. Sleep disturbances in absence of breathing or neurological disorders are mainly treated with medications (e.g., benzodiazepines,

hypnotics, etc.) and cognitive behavioral therapy, which are associated with side-effects and adherence issues, respectively. Moreover, these therapies do not seem to work effectively for some individuals. Repetitive transcranial magnetic stimulation (rTMS) and transcranial direct current stimulation (tDCS) are non-invasive stimulation techniques used to treat several conditions and symptoms. Results from this systematic review indicate that rTMS and tDCS are safe and have potential to improve insomnia symptoms and sleep disturbances across different types of neurological and neuropsychiatric diseases. However, uncontrolled and quasi experimental studies with high risk of bias were included. Thus, although these results can help developing the field, caution in interpreting them is advised. Additional research efforts are needed to reduce bias, improve quality, and characterize optimal brain stimulation parameters to promote their efficacy on sleep related outcomes.

Title: Non-invasive brain stimulation targets and approaches to modulate gamblingrelated decisions: A systematic review.

Citation: Addictive Behaviors; Jan 2021; vol. 112

Author(s): Pettorruso ; Miuli, Andrea; Di Natale, Chiara; Montemitro, Chiara; Zoratto, Francesca; De Risio, Luisa; d'Andrea, Giacomo; Dannon, Pinhas N.; Martinotti, Giovanni; di Giannantonio, Massimo

Introduction: Despite intense neuroscience research on the neurobiological underpinnings of Gambling Disorder (GD) and gambling-related decision-making, effective treatments targeting these dysfunctions are still lacking. Non Invasive Brain Stimulation (NIBS) techniques, such as transcranial Direct Current Stimulation (tDCS) and Transcranial Magnetic Stimulation (TMS), selectively modulate activity of brain circuits and have the potential to reverse alterations sustaining GD symptoms. Therefore, the aim of this systematic review was to determine the impact of different NIBS interventions on gambling-related decision processes.

Methods: We conducted a comprehensive and translational search in three online databases (MEDLINE via PubMed, Scopus, Web of Science), in accordance with the PRISMA guidelines. We included studies applying neuromodulation (TMS, tDCS) techniques in GD patients or assessing gambling-related decision-making in healthy subjects. In addition, we explored the potential impact of NIBS in drug-induced GD (e.g., Parkinson's Disease).

Results: Twenty-seven studies have been included. We summarized results to detect the impact of different targets and stimulation/inhibition protocols in terms of gambling-related decision-making. The majority of both tDCS and TMS studies targeted the dorsolateral prefrontal cortex. Although heterogeneous in protocols and parameters, results from tDCS and TMS studies converge in indicating that the stimulation (instead of inhibition) of prefrontal regions could be beneficial to contrast dysfunctional gambling-related decision processes.

Conclusion: NIBS interventions show promise to be further tested in controlled clinical settings for the treatment of behavioral addictions. Further studies are also necessary to investigate connectivity changes and laterality issues (unilateral versus bilateral; left versus right) of NIBS application in GD.

Title: Ten Unsolved Questions About Neuroinflammation in Parkinson's Disease.

Citation: Movement Disorders; Jan 2021; vol. 36 (no. 1); p. 16-24 **Author(s):** Hirsch ; Standaert, David G.

Abstract: Parkinson's disease is a progressive and debilitating disorder that has so far eluded attempts to develop disease-modifying treatment. Both epidemiological and genetic studies support a role of neuroinflammation in the pathophysiology of Parkinson's disease. Postmortem studies and experimental analyses suggest the involvement of both innate and adaptive immunity in the degenerative process. There is also some circumstantial evidence for effects of immune therapies on the disease. In the present article, we review 10 unanswered questions related to neuroinflammatory processes in Parkinson's disease with the goal of stimulating research in the field and accelerating the clinical development of neuroprotective therapies based on anti-inflammatory strategies. © 2020 International Parkinson and Movement Disorder Society.

Title: Electroconvulsive Therapy for Parkinson's Disease: A Systematic Review and Meta-Analysis.

Citation: Movement Disorders; Jan 2021; vol. 36 (no. 1); p. 50-58

Author(s): Takamiya ; Seki, Morinobu; Kudo, Shun; Yoshizaki, Takahito; Nakahara, Jin; Mimura, Masaru; Kishimoto, Taishiro

Background: Electroconvulsive therapy (ECT) is a well-established treatment for psychiatric disorders, including depression and psychosis. ECT has been reported to be effective in treating such psychiatric symptoms in patients with Parkinson's disease (PD) and has been also reported to be effective in treating motor symptoms. The aim of the study is to summarize previous clinical studies investigating the efficacy of ECT for symptoms in patients with PD.

Methods: A systematic review and meta-analysis of any study designs assessing motor and/or non-motor symptoms in patients with PD before and after ECT. Co-primary outcomes were set as motor manifestations assessed using the Unified Parkinson's Disease Rating Scale or other rating scales, and non-motor symptoms included depression and psychosis. Secondary outcomes were wearing-off phenomenon and cognitive function. The impact of ECT on those symptoms was examined by comparing the severity of the symptoms before and after ECT using a random effect model and was expressed in standardized mean difference.

Results: Of 1219 identified citations, 14 studies (n = 129; 1 randomized controlled study, 9 prospective observational studies, and 4 retrospective studies) were analyzed. The findings were as follows: ECT significantly improved motor manifestations in patients with PD, and the improvement was significant in the subpopulation without psychiatric symptoms; ECT significantly improved depression and psychosis; and ECT significantly relieved wearing-off phenomenon and did not worsen cognitive functioning.

Conclusion: The current meta-analysis suggests the potential benefit of ECT on motor and non-motor symptoms in presumably complicated and difficult-to-treat subgroups. © 2020 International Parkinson and Movement Disorder Society.

Title: Proteotoxicity: A Fatal Consequence of Environmental Pollutants-Induced Impairments in Protein Clearance Machinery.

Citation: Journal of personalized medicine; Jan 2021; vol. 11 (no. 2)

Author(s): Devi, Shweta; Kim, Jong-Joo; Singh, Anand Prakash; Kumar, Surendra; Dubey, Ashish Kant; Singh, Sandeep Kumar; Singh, Ravi Shankar; Kumar, Vijay

Abstract: A tightly regulated protein quality control (PQC) system maintains a healthy balance between correctly folded and misfolded protein species. This PQC system work with the help of a complex network comprised of molecular chaperones and proteostasis. Any intruder, especially environmental pollutants, disrupt the PQC network and lead to PQCs disruption, thus generating damaged and infectious protein. These misfolded/unfolded proteins are linked to several diseases such as Parkinson's disease, Alzheimer's disease, Huntington's disease, and cataracts. Numerous studies on proteins misfolding and disruption of PQCs by environmental pollutants highlight the necessity of detailed knowledge. This review represents the PQCs network and environmental pollutants' impact on the PQC network, especially through the protein clearance system.

Sources Used:

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

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