

## Parkinson's Disease

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## February 2024

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#### 1. Chronobiology of Parkinson's disease: Past, present and future

Authors: Asadpoordezaki, Ziba;Coogan, Andrew N. and Henley, Beverley M.

#### Publication Date: Jan ,2023

#### Journal: European Journal of Neuroscience 57(1), pp. 178-200

**Abstract:** Parkinson's disease is a neurodegenerative disorder predominately affecting midbrain dopaminergic neurons that results in a broad range of motor and non-motor symptoms. Sleep complaints are among the most common non-motor symptoms, even in the prodromal period. Sleep alterations in Parkinson's disease patients may be associated with dysregulation of circadian rhythms, intrinsic 24-h cycles that control essential physiological functions, or with side effects from levodopa medication and physical and mental health challenges. The impact of circadian dysregulation on sleep disturbances in Parkinson's disease is not fully understood; as such, we review the systems, cellular and molecular mechanisms that may underlie circadian perturbations in Parkinson's disease. We also discuss the potential benefits of chronobiology-based personalized medicine in the management of Parkinson's disease both in terms of behavioural and pharmacological interventions. We propose that a fuller understanding of circadian clock function may shed important new light on the aetiology and symptomatology of the disease and may allow for improvements in the quality of life for the millions of people with Parkinson's disease. Copyright © 2022 The Authors. European Journal of Neuroscience published by Federation of European Neuroscience Societies and John Wiley & Sons Ltd.

### 2. Ketogenic interventions in mild cognitive impairment, Alzheimer's disease, and Parkinson's disease: A systematic review and critical appraisal.

Authors: Bohnen, J. L. B.; Albin, R. L. and Bohnen, N. I.

#### Publication Date: 2023

Journal: Frontiers in Neurology 14(pagination), pp. no pagination

Abstract: Background: There is increasing interest in therapeutic ketosis as a potential therapy for neurodegenerative disorders-in particular, mild cognitive impairment (MCI), Alzheimer's disease (AD), and Parkinson's disease (PD)-following a proof-of-concept study in Parkinson's disease published in 2005. Method(s): To provide an objective assessment of emerging clinical evidence and targeted recommendations for future research, we reviewed clinical trials involving ketogenic interventions in mild cognitive impairment, Alzheimer's disease, and Parkinson's disease reported since 2005. Levels of clinical evidence were systematically reviewed using the American Academy of Neurology criteria for rating therapeutic trials. Result(s): 10 AD, 3 MCI, and 5 PD therapeutic ketogenic trials were identified. Respective grades of clinical evidence were objectively assessed using the American Academy of Neurology criteria for rating therapeutic trials. We found class "B" evidence (probably effective) for cognitive improvement in subjects with mild cognitive impairment and subjects with mild-to-moderate Alzheimer's disease negative for the apolipoprotein epsilon4 allele (APOepsilon4-). We found class "U" evidence (unproven) for cognitive stabilization in individuals with mild-to-moderate Alzheimer's disease positive for the apolipoprotein epsilon4 allele (APOepsilon4+). We found class "C" evidence (possibly effective) for improvement of non-motor features and class "U" evidence (unproven) for motor features in individuals with Parkinson's disease. The number of trials in Parkinson's disease is very small with best evidence that acute supplementation holds promise for improving exercise endurance. Conclusion(s): Limitations of the literature to date include the range of ketogenic interventions currently assessed in the literature (i.e., primarily diet or medium-chain triglyceride interventions), with fewer studies using more potent formulations (e.g., exogenous ketone esters). Collectively, the strongest evidence to date exists for cognitive improvement in individuals with mild cognitive impairment and in individuals with mild-to-moderate Alzheimer's disease negative for the apolipoprotein epsilon4 allele. Larger-scale, pivotal trials are justified in these populations. Further research is required to optimize the utilization of ketogenic interventions in differing clinical contexts and to better characterize the response

to therapeutic ketosis in patients who are positive for the apolipoprotein epsilon4 allele, as modified interventions may be necessary.Copyright © 2023 Bohnen, Albin and Bohnen.

### 3. Ketogenic interventions in mild cognitive impairment, Alzheimer's disease, and Parkinson's disease: A systematic review and critical appraisal.

Authors: Bohnen, Jeffrey L. B.; Albin, Roger L. and Bohnen, Nicolaas I.

#### Publication Date: 2023

Journal: Frontiers in Neurology [Electronic Resource]. 14, pp. 1123290

Abstract: Background: There is increasing interest in therapeutic ketosis as a potential therapy for neurodegenerative disorders-in particular, mild cognitive impairment (MCI), Alzheimer's disease (AD), and Parkinson's disease (PD)-following a proof-of-concept study in Parkinson's disease published in 2005. Methods: To provide an objective assessment of emerging clinical evidence and targeted recommendations for future research, we reviewed clinical trials involving ketogenic interventions in mild cognitive impairment, Alzheimer's disease, and Parkinson's disease reported since 2005. Levels of clinical evidence were systematically reviewed using the American Academy of Neurology criteria for rating therapeutic trials. Results: 10 AD, 3 MCI, and 5 PD therapeutic ketogenic trials were identified. Respective grades of clinical evidence were objectively assessed using the American Academy of Neurology criteria for rating therapeutic trials. We found class "B" evidence (probably effective) for cognitive improvement in subjects with mild cognitive impairment and subjects with mild-to-moderate Alzheimer's disease negative for the apolipoprotein epsilon4 allele (APOepsilon4-). We found class "U" evidence (unproven) for cognitive stabilization in individuals with mild-to-moderate Alzheimer's disease positive for the apolipoprotein epsilon4 allele (APOepsilon4+). We found class "C" evidence (possibly effective) for improvement of non-motor features and class "U" evidence (unproven) for motor features in individuals with Parkinson's disease. The number of trials in Parkinson's disease is very small with best evidence that acute supplementation holds promise for improving exercise endurance. Conclusions: Limitations of the literature to date include the range of ketogenic interventions currently assessed in the literature (i.e., primarily diet or medium-chain triglyceride interventions), with fewer studies using more potent formulations (e.g., exogenous ketone esters). Collectively, the strongest evidence to date exists for cognitive improvement in individuals with mild cognitive impairment and in individuals with mild-to-moderate Alzheimer's disease negative for the apolipoprotein epsilon4 allele. Larger-scale, pivotal trials are justified in these populations. Further research is required to optimize the utilization of ketogenic interventions in differing clinical contexts and to better characterize the response to therapeutic ketosis in patients who are positive for the apolipoprotein epsilon4 allele, as modified interventions may be necessary. Copyright © 2023 Bohnen, Albin and Bohnen.

#### 4. Parkinson's disease following COVID-19: six cases report.

Authors: Calculli, A.;Bocci, T.;Porcino, M.;Avenali, M.;Casellato, C.;Arceri, S.;Regalbuto, S.;Priori, A. and Pisani, A.

#### Publication Date: 2023

Journal: European Journal of Neurology (pagination), pp. no pagination

**Abstract:** BACKGROUND: Core clinical manifestation of COVID-19 include flu-like and respiratory symptoms. However, it is now evident that neurological involvement may occur during SARS-CoV-2 infection, covering an extensive spectrum of phenotypical manifestations. A major challenge arising from this pandemic is represented by detecting emerging neurological complications following recovery from SARS-CoV-2 infection. To date, few post-COVID-19 infected subjects diagnosed with Parkinson's Disease (PD) were described, raising the possibility of a connection between the infection and neurodegenerative process. Here, we describe a cases series of six subjects, who developed PD after COVID-19. METHOD(S): Patients were observed at IRCCS Mondino Foundation Hospital, Pavia (Italy),

and San Paolo University Hospital of Milan (Italy) between March 2021 and June 2022. In all subjects, SARS-CoV-2 infection was confirmed by means of a RT-PCR from a nasopharyngeal swab. Subjects underwent an accurate neurological evaluation, and neuroimaging studies were performed. RESULT(S): We describe six subjects, who developed PD with an average time window after SARS-CoV-2 infection of 4-7weeks. Apparently, no relationship with COVID-19 severity emerged, and no overt structural brain abnormalities were found. All subjects experienced unilateral resting tremor at onset and showed a satisfactory response to dopaminergic treatment. CONCLUSION(S): Immune responses to SARS-CoV-2 infection have been shown to shape the individual susceptibility to develop long-term consequences. We hypothesize that, in these subjects, COVID-19 has unmasked a latent neurodegenerative process. Characterization of the neuroinflammatory signatures in larger cohorts is warranted, which might provide novel insights in the pathogenesis of PD.Copyright This article is protected by copyright. All rights reserved.

### 5. Toxin Induced Parkinsonism and Hospitalization Related Adverse Outcome Mitigation for Parkinson's Disease: A Comprehensive Review.

Authors: Dalton, K. R.;Kidd, C. J. and Hack, N.

#### Publication Date: 2023

Journal: Journal of Clinical Medicine 12(3), pp. no pagination

**Abstract:** Patients with Parkinson's disease admitted to the hospital have unique presentations. This unique subset of patients requires a multidisciplinary approach with a knowledge-based care team that can demonstrate awareness of complications specific to Parkinson's disease to reduce critical care admissions, morbidity, and mortality. Early recognition of toxic exposures, medication withdrawals, or medication-induced symptoms can reduce morbidity and mortality. This review can assist in the critical assessment of new or exacerbating Parkinson's disease symptoms.Copyright © 2023 by the authors.

#### 6. Gut bacterial profiles in Parkinson's disease: A systematic review

**Authors:** Li, Zhe;Liang, Hongfeng;Hu, Yingyu;Lu, Lin;Zheng, Chunye;Fan, Yuzhen;Wu, Bin;Zou, Tao;Luo, Xiaodong;Zhang, Xinchun;Zeng, Yan;Liu, Ziyan;Zhou, Zhicheng;Yue, Zhenyu;Ren, Yi;Li, Zhuo;Su, Qiaozhen and Xu, Pingyi

#### Publication Date: Jan ,2023

Journal: CNS Neuroscience & Therapeutics 29(1), pp. 140-157

Abstract: INTRODUCTION: Recent advances have highlighted the relationships between gut dysbiosis and Parkinson's disease (PD). Microbiota transplantation from PD patients to mice can induce increased alpha-synuclein-mediated motor deficits. Human studies have identified differences in the gut microbiota of PD patients compared to healthy controls. We undertook a systematic review to evaluate the available evidence for the involvement of gut bacteria in the etiology of PD. METHODS: The PubMed databank, the China National Knowledge Infrastructure databank, and Wanfang Data were searched from inception until June 2021 to identify human case-control studies that investigated relationships between PD and microbiota quantified from feces. We evaluated the resulting studies focusing on bacterial taxa that were different between PD patients and healthy controls. RESULTS: Twenty-six studies were found in which 53 microbial families and 98 genera exhibited differences between patients with PD and healthy controls. The genera identified by more than two studies as increased in PD were Bifidobacterium, Alistipes, Christensenella, Enterococcus, Oscillospira, Bilophila, Desulfovibrio, Escherichia/Shigella, and Akkermansia, while Prevotella, Blautia, Faecalibacterium, Fusicatenibacter, and Haemophilus had three or more reports of being lower in PD patients. More than one report demonstrated that Bacteroides, Odoribacter, Parabacteroides, Butyricicoccus, Butyrivibrio, Clostridium, Coprococcus, Lachnospira, Lactobacillus, Megasphaera, Phascolarctobacterium, Roseburia, Ruminococcus, Streptococcus, and Klebsiella were altered in both directions.

CONCLUSION: Our review shows that the involvement of the gut microbiome in the etiology of PD may involve alterations of short-chain fatty acids (SCFAs)-producing bacteria and an increase in putative gut pathobionts. SCFAs-producing bacteria may vary above or below an "optimal range," causing imbalances. Considering that Bifidobacterium, Lactobacillus, and Akkermansia are beneficial for human health, increased Bifidobacterium and Lactobacillus in the PD gut microbiome may be associated with PD medications, especially COMT inhibitors, while a high level of Akkermansia may be associated with aging. Copyright © 2022 The Authors. CNS Neuroscience & Therapeutics published by John Wiley & Sons Ltd.

#### 7. Gut-oriented disease modifying therapy for Parkinson's disease

Authors: Lin, Chin-Hsien; Lai, Hsin-Chih and Wu, Ming-Shiang

#### Publication Date: Jan ,2023

Journal: Journal of the Formosan Medical Association 122(1), pp. 9-18

**Abstract:** Neuropathology studies have shown that the pathognomonic feature of Parkinson's disease (PD), one of the most common neurodegenerative disorders, may start from the gut enteric nervous system and then spread to the central dopaminergic neurons through the gut-brain axis. With the advent of metagenomic sequencing and metabolomic analysis, a plethora of evidence has revealed different gut microbiomes and gut metabolites in patients with PD compared with unaffected controls. Currently, although dopaminergic treatments and deep brain stimulation can provide some symptomatic benefits for motor symptoms of the disease, their long-term use is problematic. A mechanism-targeted therapy to halt the neurodegeneration is lacking. The recently observed gut microenvironmental changes in the early stages of the disease play a vital role in the PD pathogenesis. Patients whose disease begins in the gut may benefit most from interventions that target the gut microenvironments. In this review, we will summarize the current studies demonstrating multifunctional roles of gut microbiota in the gut-brain axis of PD and the currently available evidence for targeting the gut microbiota as a novel approach to potential disease-modifying therapy in PD. Copyright © 2022 Formosan Medical Association. Published by Elsevier B.V. All rights reserved.

#### 8. Assessing the risks of treatment in Parkinson disease psychosis: An in-depth analysis.

Authors: Longardner, K.; Wright, B. A.; Alakkas, A.; You, H.; Xu, R.; Liu, L. and Nahab, F. B.

#### Publication Date: 2023

Journal: PLoS ONE 18(1 January), pp. no pagination

Abstract: Background Parkinson disease (PD) psychosis (PDP) is a disabling non-motor symptom. Pharmacologic treatment is limited to pimavanserin, quetiapine, and clozapine, which do not worsen parkinsonism. A Food and Drug Administration black box warning exists for antipsychotics, suggesting increased mortality in elderly patients with dementia. However, the reasons for higher mortality are unknown. Aim Expanding on prior work exploring mortality in treated PDP patients, we conducted a retrospective comparison to understand the links between treatment regimen, clinical characteristics, and negative outcomes. Methods Electronic medical record data extraction included clinically diagnosed PD patients between 4/29/16-4/29/19 and excluded patients with primary psychiatric diagnoses or atypical parkinsonism. Mortality and clinical characteristics during the study period were compared between untreated patients and those receiving pimavanserin, quetiapine, or both agents (combination). Mortality analyses were adjusted for age, sex, levodopa equivalent daily dose (LEDD), and dementia. Results The pimavanserin group (n = 34) had lower mortality than the untreated group (n = 66) (odds ratio = 0.171, 95% confidence interval: 0.025-0.676, p = 0.026). The untreated group had similar mortality compared to the quetiapine (n = 147) and combination (n = 68) groups. All treated groups had a higher LEDD compared to the untreated group, but no other differences in demographics, hospitalizations, medical comorbidities, medications, or laboratory values were found between the

untreated and treated groups. Conclusions PDP patients receiving pimavanserin had lower mortality than untreated patients. We found no other clear differences in clinical characteristics to explain the mortality risk. Prospective randomized trials are needed to definitively identify the optimal PDP treatment regimen and associated risks.Copyright: © 2023 Longardner et al. This is an open access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

#### 9. Barriers to home exercise for patients with Parkinson's disease: a qualitative study.

Authors: Wang, Qiaohong; Chen, Yiping; Li, Linbo; Li, Chao; Li, Li; Cao, Huili and Yang, Hui

Publication Date: 02 08 ,2023

Journal: BMJ Open 13(2), pp. e061932

Abstract: OBJECTIVE: This study aimed to explore the barriers to home exercise for patients with Parkinson's disease (PwPDs) and to provide guidelines for healthcare providers to build and implement home exercise strategies for PwPDs. DESIGN: A qualitative descriptive method was used. Semistructured interviews were conducted and thematic analysis was employed. SETTING: The study was conducted at the Department of Neurology at a grade 3 Class A general hospital in China. PARTICIPANTS: A total of 24 participants were interviewed, including 10 PwPDs, 7 caregivers, 4 nurses, 1head nurse, and 2 Parkinson's clinicians. RESULTS: Five themes were identified in this analysis. (1) Psychosomatic stress and low activity; (2) Lack of early rehabilitation authorisation; (3) Poor 'flow' state of home exercise; (4) ilnaccessibility of continued service; (5) Sociocultural impact on family coping. CONCLUSION: PwPDs, caregivers and specialised medical staff raised the challenges faced by patients' home exercises from different perspectives. We can improve services and integrate resources through the management of multi-disciplinary, early rehabilitation authorisation, exercise experience, continuous service mode, and family coping strategies under different cultures to gradually adjust the home exercise behaviour of PwPDs. Copyright © Author(s) (or their employer(s)) 2023. Reuse permitted under CC BY-NC. No commercial re-use. See rights and permissions. Published by BMJ.

#### 10. Tremor in Parkinson's Disease: From Pathophysiology to Advanced Therapies

Authors: Abusrair, Ali H.; Elsekaily, Walaa and Bohlega, Saeed

#### Publication Date: 2022

Journal: Tremor and Other Hyperkinetic Movements 12, pp. 29

**Abstract:** Background: Tremor is one of the most prevalent symptoms in Parkinson's Disease (PD). The progression and management of tremor in PD can be challenging, as response to dopaminergic agents might be relatively poor, particularly in patients with tremor-dominant PD compared to the akinetic/rigid subtype. In this review, we aim to highlight recent advances in the underlying pathogenesis and treatment modalities for tremor in PD. Methods: A structured literature search through Embase was conducted using the terms "Parkinson's Disease" AND "tremor" OR "etiology" OR "management" OR "drug resistance" OR "therapy" OR "rehabilitation" OR "surgery." After initial screening, eligible articles were selected with a focus on published literature in the last 10 years. Discussion: The underlying pathophysiology of tremor in PD remains complex and incompletely understood. Neurodegeneration of dopaminergic neurons in the retrorubral area, in addition to high-power neural oscillations in the cerebello-thalamo-cortical circuit and the basal ganglia, play a major role. Levodopa is the first-line therapeutic option for all motor symptoms, including tremor. The addition of dopamine agonists or anticholinergics can lead to further tremor reduction. Botulinum toxin injection is an effective alternative for patients with pharmacological-resistant tremor who are not seeking advanced therapies. Deep brain stimulation is the most well-established advanced therapy owing to its

long-term efficacy, reversibility, and effectiveness in other motor symptoms and fluctuations. Magnetic resonance-guided focused ultrasound is a promising modality, which has the advantage of being incisionless. Cortical and peripheral electrical stimulation are non-invasive innovatory techniques that have demonstrated good efficacy in suppressing intractable tremor. Copyright: © 2022 The Author(s).

#### 11. Social withdrawal in Parkinson's disease: A scoping review

Authors: Ahn, Soojung; Springer, Kristen and Gibson, Jessie S.

#### Publication Date: 2022

Journal: Geriatric Nursing 48, pp. 258-268

Abstract: BACKGROUND: Parkinson's disease (PD) can interfere with individuals' social functioning and lead to social withdrawal. Social withdrawal may result in negative outcomes for persons with PD and their caregivers, such as decreased quality of life. It is necessary to understand the nature of social withdrawal in PD in order to develop strategies to address this issue and prevent negative outcomes. OBJECTIVE: The purpose of this scoping review was to synthesize existing evidence regarding social withdrawal in PD. METHODS: We searched PubMed, CINAHL, and PsycINFO for studies of social withdrawal in individuals living with PD. Findings were organized according to study characteristics, measurement and description of social withdrawal, prevalence, associated factors, and interventions. RESULTS: Fifty-eight studies were included. We found that persons with PD reduced social activities voluntarily and involuntarily, and social withdrawal was related to various factors including physical, cognitive, and psychiatric symptoms and perceived stigma. Community-based social activity programs appeared to improve social participation. Few studies employed longitudinal methods or tested interventions to reduce social withdrawal, CONCLUSIONS: Social withdrawal is associated with various negative outcomes in PD, though more research is needed to understand the true scope of this problem. Limitations in social withdrawal research include vague conceptualization and methodological limitations (i.e., instrumentation and study design), as well as a paucity of interventional studies. The findings of this review can be used to guide hypothesis generation and future study design, with the ultimate goal of mitigating social withdrawal and improving quality of life for people with PD. Copyright © 2022 The Authors. Published by Elsevier Inc. All rights reserved.

#### 12. Wrist Rigidity Evaluation in Parkinson's Disease: A Scoping Review

Authors: Alves, Camille Marques;Rezende, Andressa Rastrelo;Marques, Isabela Alves;Mendes, Luanne Cardoso;de Sa, Angela Abreu Rosa;Vieira, Marcus Fraga;Junior, Edgard Afonso Lamounier;Pereira, Adriano Alves;Oliveira, Fabio Henrique Monteiro;de Souza, Luciane Pascucci Sande;Bourhis, Guy;Pino, Pierre;Andrade, Adriano de Oliveira;Morere, Yann and Naves, Eduardo Lazaro Martins

#### Publication Date: Oct 31,2022

#### Journal: Healthcare 10(11)

**Abstract:** (1) Background: One of the main cardinal signs of Parkinson's disease (PD) is rigidity, whose assessment is important for monitoring the patient's recovery. The wrist is one of the joints most affected by this symptom, which has a great impact on activities of daily living and consequently on quality of life. The assessment of rigidity is traditionally made by clinical scales, which have limitations due to their subjectivity and low intra- and inter-examiner reliability. (2) Objectives: To compile the main methods used to assess wrist rigidity in PD and to study their validity and reliability, a scope review was conducted. (3) Methods: PubMed, IEEE/IET Electronic Library, Web of Science, Scopus, Cochrane, Bireme, Google Scholar and Science Direct databases were used. (4) Results: Twenty-eight studies were included. The studies presented several methods for quantitative assessment of rigidity using instruments such as force and inertial sensors. (5) Conclusions: Such methods present good correlation with clinical scales and are useful for detecting and monitoring rigidity. However, the

development of a standard quantitative method for assessing rigidity in clinical practice remains a challenge.

#### 13. Assessment Tasks and Virtual Exergames for Remote Monitoring of Parkinson's Disease: An Integrated Approach Based on Azure Kinect.

**Authors:** Amprimo, Gianluca;Masi, Giulia;Priano, Lorenzo;Azzaro, Corrado;Galli, Federica;Pettiti, Giuseppe;Mauro, Alessandro and Ferraris, Claudia

#### Publication Date: Oct 25,2022

#### Journal: Sensors 22(21)

Abstract: Motor impairments are among the most relevant, evident, and disabling symptoms of Parkinson's disease that adversely affect quality of life, resulting in limited autonomy, independence, and safety. Recent studies have demonstrated the benefits of physiotherapy and rehabilitation programs specifically targeted to the needs of Parkinsonian patients in supporting drug treatments and improving motor control and coordination. However, due to the expected increase in patients in the coming years, traditional rehabilitation pathways in healthcare facilities could become unsustainable. Consequently, new strategies are needed, in which technologies play a key role in enabling more frequent, comprehensive, and out-of-hospital follow-up. The paper proposes a vision-based solution using the new Azure Kinect DK sensor to implement an integrated approach for remote assessment, monitoring, and rehabilitation of Parkinsonian patients, exploiting non-invasive 3D tracking of body movements to objectively and automatically characterize both standard evaluative motor tasks and virtual exergames. An experimental test involving 20 parkinsonian subjects and 15 healthy controls was organized. Preliminary results show the system's ability to quantify specific and statistically significant (p < 0.05) features of motor performance, easily monitor changes as the disease progresses over time, and at the same time permit the use of exergames in virtual reality both for training and as a support for motor condition assessment (for example, detecting an average reduction in arm swing asymmetry of about 14% after arm training). The main innovation relies precisely on the integration of evaluative and rehabilitative aspects, which could be used as a closed loop to design new protocols for remote management of patients tailored to their actual conditions.

### 14. The interplay between the gut-brain axis and the microbiome: A perspective on psychiatric and neurodegenerative disorders

Authors: Bashir, Yasir and Khan, Asad U.

#### Publication Date: 2022

#### Journal: Frontiers in Neuroscience 16, pp. 1030694

**Abstract:** What is the effect of our gut microbial flora on brain? Does the gut microbiome have any role in the causation of psychiatric and neurodegenerative diseases? Does the effect of gut microbiota traverse the gut-brain axis? Questions like these have captured the interest and imagination of the scientific community for quite some time now. Research in the quest for answers to these questions, to unravel the potential role of the microbiota inhabiting the gut in controlling brain functions, has progressed manifold over the last two decades. Although the possibility of microbiome as a key susceptibility factor for neurological disorders viz. Parkinson's disease, Alzheimer's disease, multiple sclerosis, and autism spectrum disorder has bolstered by an increase in the clinical and preclinical evidence, the field is still in its infancy. Given the fact that the diversity of the gut microbiota is affected by various factors including the diet and exercise, the interpretation of such data becomes all the more difficult. Also, such studies have been mostly conducted on animal models, so there is a need for randomized controlled trials in human subjects, corroborated by longitudinal studies, to establish if modulating the gut microbiota can unravel novel therapeutic interventions. Exploring the genomic,

metagenomic and metabolomic data from clinical subjects with psychiatric and neurological diseases can prove to be a helpful guide in individual treatment selection. Copyright © 2022 Bashir and Khan.

#### 15. Association Between Antiepileptic Drugs and Incident Parkinson Disease in the UK Biobank.

Authors: Belete, Daniel;Jacobs, Benjamin M.;Simonet, Cristina;Bestwick, Jonathan P.;Waters, Sheena;Marshall, Charles R.;Dobson, Ruth and Noyce, Alastair J.

#### Publication Date: 2022

#### Journal: JAMA Neurology

Abstract: Importance: Recent studies have highlighted an association between epilepsy and Parkinson disease (PD). The role of antiepileptic drugs (AEDs) has not been explored. Objective: To investigate the association between AEDs and incident PD. Design, Setting, and Participants: This nested case-control study started collecting data from the UK Biobank (UKB) in 2006, and data were extracted on June 30, 2021. Individuals with linked primary care prescription data were included. Cases were defined as individuals with a Hospital Episode Statistics (HES)-coded diagnosis of PD. Controls were matched 6:1 for age, sex, race and ethnicity, and socioeconomic status. Prescription records were searched for AEDs prescribed prior to diagnosis of PD. The UKB is a longitudinal cohort study with more than 500000 participants; 45% of individuals in the UKB have linked primary care prescription data. Participants living in the UK aged between 40 and 69 years were recruited to the UKB between 2006 and 2010. All participants with UKB-linked primary care prescription data (n = 222106) were eligible for enrollment in the study. Individuals with only a self-reported PD diagnosis or missing data for the matching variables were excluded. In total, 1477 individuals were excluded; 49 were excluded due to having only self-reported PD, and 1428 were excluded due to missing data. Exposures: Exposure to AEDs (carbamazepine, lamotrigine, levetiracetam, and sodium valproate) was defined using routinely collected prescription data derived from primary care. Main Outcomes and Measures: Odd ratios and 95% CIs were calculated using adjusted logistic regression models for individuals prescribed AEDs before the first date of HES-coded diagnosis of PD. Results: In this casecontrol study, there were 1433 individuals with an HES-coded PD diagnosis (cases) and 8598 controls in the analysis. Of the 1433 individuals, 873 (60.9%) were male, 1397 (97.5%) had their race and ethnicity recorded as White, and their median age was 71 years (IQR, 65-75 years). An association was found between AED prescriptions and incident PD (odds ratio, 1.80; 95% CI, 1.35-2.40). There was a trend for a greater number of prescription issues and multiple AEDs being associated with a greater risk of PD. Conclusions and Relevance: This study, the first to systematically look at PD risk in individuals prescribed the most common AEDs, to our knowledge, found evidence of an association between AEDs and incident PD. With the recent literature demonstrating an association between epilepsy and PD, this study provides further insights.

#### 16. Cannabidiol for neurodegenerative disorders: A comprehensive review

Authors: Bhunia, Sukanya;Kolishetti, Nagesh;Arias, Adriana Yndart;Vashist, Arti and Nair, Madhavan

#### Publication Date: 2022

#### Journal: Frontiers in Pharmacology 13, pp. 989717

**Abstract:** Despite the significant advances in neurology, the cure for neurodegenerative conditions remains a formidable task to date. Among various factors arising from the complex etiology of neurodegenerative diseases, neuroinflammation and oxidative stress play a major role in pathogenesis. To this end, some phytocannabinoids isolated from Cannabis sativa (widely known as marijuana) have attracted significant attention as potential neurotherapeutics. The profound effect of 9-tetrahydrocannabinoid system as a molecular target in the central nervous system (CNS). Cannabidiol (CBD), the major non-psychoactive component of cannabis, has recently emerged as a potential

prototype for neuroprotective drug development due to its antioxidant and anti-inflammatory properties and its well-tolerated pharmacological behavior. This review briefly discusses the role of inflammation and oxidative stress in neurodegeneration and demonstrates the neuroprotective effect of cannabidiol, highlighting its general mechanism of action and disease-specific pathways in Parkinson's disease (PD) and Alzheimer's disease (AD). Furthermore, we have summarized the preclinical and clinical findings on the therapeutic promise of CBD in PD and AD, shed light on the importance of determining its therapeutic window, and provide insights into identifying promising new research directions. Copyright © 2022 Bhunia, Kolishetti, Arias, Vashist and Nair.

### 17. Developments in the mechanistic understanding and clinical application of deep brain stimulation for Parkinson's disease

Authors: Bove, Francesco; Genovese, Danilo and Moro, Elena

#### Publication Date: 2022

Journal: Expert Review of Neurotherapeutics 22(9), pp. 789-803

**Abstract:** INTRODUCTION: Deep brain stimulation (DBS) is a life-changing treatment for patients with Parkinson's disease (PD) and gives the unique opportunity to directly explore how basal ganglia work. Despite the rapid technological innovation of the last years, the untapped potential of DBS is still high. AREAS COVERED: This review summarizes the developments in the mechanistic understanding of DBS and the potential clinical applications of cutting-edge technological advances. Rather than a univocal local mechanism, DBS exerts its therapeutic effects through several multimodal mechanisms and involving both local and network-wide structures, although crucial questions remain unexplained. Nonetheless, new insights in mechanistic understanding of DBS in PD have provided solid bases for advances in preoperative selection phase, prediction of motor and non-motor outcomes, leads placement and postoperative stimulation programming. EXPERT OPINION: DBS has not only strong evidence of clinical effectiveness in PD treatment but technological advancements are revamping its role of neuromodulation of brain circuits and key to better understanding PD pathophysiology. In the next few years, the worldwide use of new technologies in clinical practice will provide large data to elucidate their role and to expand their applications for PD patients, providing useful insights to personalize DBS treatment and follow-up.

#### 18. Remote programming for subthalamic deep brain stimulation in Parkinson's disease.

Authors: Chen, Si;Xu, Shu-Jun;Li, Wei-Guo;Chen, Teng;Li, Chao;Xu, Shuo;Yang, Ning and Liu, Yi-Ming

#### Publication Date: 2022

Journal: Frontiers in Neurology [Electronic Resource] 13, pp. 1061274

**Abstract:** Introduction: Deep brain stimulation (DBS) of the subthalamic nucleus (STN) is effective for the treatment of Parkinson's disease (PD). Moreover, remote programming is widely used in Mainland China. This necessitates evaluating the ability of remote programming to achieve the ideal postoperative effect. Therefore, we aimed to retrospectively evaluate the effects of different programming modes on the effectiveness of STN-DBS 12 months postoperatively in patients with PD. Methods: Clinical data were collected retrospectively, before and 12 months after surgery, in 83 patients with PD. Based on the programming modes voluntarily selected by the patients during 12 months postoperatively, they were divided into three groups, namely remote programming alone, hospital programming alone, and hospital + remote programming. We compared the programming data and the effects of different programming methods on STN-DBS-related improvements 12 months postoperatively among these groups. Furthermore, we analyzed STN-DBS was not influenced by the three programming modes. The postoperative Movement Disorder Society Unified Parkinson's

Disease Rating Scale scores did not reveal statistically significant differences between the remote alone and hospital alone programming groups, except for motor examination. The postoperative decline in the levodopa equivalent daily dose was most apparent in the hospital programming alone group. The programming frequency of the hospital + remote programming group was considerably higher than that of the remaining groups. Seventy-six patients with PD displayed good STN-DBS surgical efficacy. Conclusion: Programming modes do not influence the short-term efficacy of STN-DBS, and remote programming can yield a satisfactory surgical effect. Copyright © 2022 Chen, Xu, Li, Chen, Li, Xu, Yang and Liu.

### 19. Association of circadian rhythms with brain disorder incidents: a prospective cohort study of 72242 participants.

Authors: Chen, Si-Jia;Deng, Yue-Ting;Li, Yu-Zhu;Zhang, Ya-Ru;Zhang, Wei;Chen, Shi-Dong;Wu, Bang-Sheng;Yang, Liu;Dong, Qiang;Feng, Jianfeng;Cheng, Wei and Yu, Jin-Tai

#### Publication Date: Dec 14,2022

Journal: Transl Psychiatry Psychiatry 12(1), pp. 514

Abstract: Circadian rhythm disruption (CRD) is a shared characteristic of various brain disorders, such as Alzheimer's disease (AD), Parkinson's disease (PD), and major depression disorder (MDD). Disruption of circadian rhythm might be a risk factor for brain disorder incidents. From 7-day accelerometry data of 72,242 participants in UK Biobank, we derived a circadian relative amplitude variable, which to some extent reflected the degree of circadian rhythm disruption. Records of brain disorder incidents were obtained from a wide range of health outcomes across self-report, primary care, hospital inpatient data, and death data. Using multivariate Cox proportional hazard ratio regression, we created two models adjusting for different covariates. Then, linear correlations between relative amplitude and several brain morphometric measures were examined in participants with brain MRI data. After a median follow-up of around 6.1 years, 72,242 participants were included in the current study (female 54.9%; mean age 62.1 years). Individuals with reduced relative amplitude had increasing risk of all-cause dementia (Hazard ratio 1.23 [95% CI 1.15 to 1.31]), PD (1.33 [1.25 to 1.41]), stroke (1.13 [1.06 to 1.22]), MDD (1.18 [1.13 to 1.23]), and anxiety disorder (1.14 [1.09 to 1.20]) in fully adjusted models. Additionally, significant correlations were found between several cortical regions and white matter tracts and relative amplitude that have been linked to dementia and psychiatric disorders. We confirm CRD to be a risk factor for various brain disorders. Interventions for regulating circadian rhythm may have clinical relevance to reducing the risk of various brain disorders. Copyright © 2022. The Author(s).

### 20. High frequency of Depressive Disorders and Suicidal Phenomena in Late-Stage Parkinson's Disease - A Cross-Sectional Study.

**Authors:** Chendo, Ines;Fabbri, Margherita;Godinho, Catarina;Simoes, Rita Moiron;Sousa, Catarina Severiano;Coelho, Miguel;Voon, Valerie and Ferreira, Joaquim J.

Publication Date: Oct 22 ,2022

Journal: Journal of Geriatric Psychiatry & Neurology 8919887221135556

**Abstract:** BACKGROUND: Depressive disorders (DD) are widely recognized as one of the most frequent neuropsychiatric disorders in Parkinson's disease. Patients with late-stage Parkinson's disease (LSPD) continue to be a neglected population, and little is known about DD frequency in LSPD. OBJECTIVES: To determine the frequency of DD in LSPD patients through a clinical diagnostic interview (CDI) and according to diagnostic DSM- 5 criteria. Secondary objectives were to determine the predictive ability of depressive scales to detect DD, to identify potential predictors of DD in LSPD and, to evaluate suicidal phenomena in LSPD. METHODS: A cross-sectional study including LSPD patients (>=7 years from symptom onset and Hoehn and Yahr scale score >3 or a Schwab and

England scale score <50% in the ON condition) was conducted. Patients were subjected to psychiatric, neurological, and neuropsychological evaluations. Six depression scales were applied. RESULTS: 92 LSPD patients were included. 59.78% of LSPD patients had a current diagnosis of DD according to CDI, 38.04% patients had a diagnosis of major depressive disorder, and 21.72% non-major depressive disorder. Suicidal ideation was present in 36.96% of patients. All applied scales were able to detect depressive disorders. CONCLUSIONS: More than half of LSPD patients met DD diagnostic criteria and over one-third were diagnosed with major depressive disorder. Overall, the LSPD population seem to have a unique clinical phenotype regarding the frequency and features of DD, whose early identification and treatment could improve the quality of life of patients and caregivers.

### 21. Approaching the Gut and Nasal Microbiota in Parkinson's Disease in the Era of the Seed Amplification Assays

Authors: Consonni, Alessandra; Miglietti, Martina; De Luca, Chiara Maria Giulia; Cazzaniga, Federico Angelo; Ciullini, Arianna; Dellarole, Ilaria Linda; Bufano, Giuseppe; Di Fonzo, Alessio; Giaccone, Giorgio; Baggi, Fulvio and Moda, Fabio

#### Publication Date: Nov 19,2022

#### Journal: Brain Sciences 12(11)

**Abstract:** Parkinson's disease (PD) is a neurodegenerative disorder often associated with pre-motor symptoms involving both gastrointestinal and olfactory tissues. PD patients frequently suffer from hyposmia, hyposalivation, dysphagia and gastrointestinal dysfunctions. During the last few years it has been speculated that microbial agents could play a crucial role in PD. In particular, alterations of the microbiota composition (dysbiosis) might contribute to the formation of misfolded alpha-synuclein, which is believed to be the leading cause of PD. However, while several findings confirmed that there might be an important link between intestinal microbiota alterations and PD onset, little is known about the potential contribution of the nasal microbiota. Here, we describe the latest findings on this topic by considering that more than 80% of patients with PD develop remarkable olfactory deficits in their prodromal disease stage. Therefore, the nasal microbiota might contribute to PD, eventually boosting the gut microbiota in promoting disease onset. Finally, we present the applications of the seed amplification assays to the study of the gut and olfactory mucosa of PD patients, and how they could be exploited to investigate whether pathogenic bacteria present in the gut and the nose might promote alpha-synuclein misfolding and aggregation.

#### 22. Neuropathic Pain in Parkinson's Disease

**Authors:** Cortes-Altamirano, Jose Luis;Reyes-Long, Samuel;Bandala, Cindy;Morraz-Varela, Abril;Bonilla-Jaime, Herlinda and Alfaro-Rodriguez, Alfonso

#### Publication Date: 2022

#### Journal: Neurology India 70(5), pp. 1879-1886

**Abstract:** Pain is a well-recognized and important non-motor manifestation in Parkinson disease (PD). Painful or unpleasant sensations in PD can be classified as musculoskeletal, dystonia, akathisia, radicular, and central or primary pain; the last two are associated with neuropathic pain. Particularly, neuropathic pain in PD has not been fully clarified; therefore, it goes somewhat unnoticed, and the affected patients do not receive adequate pain treatment. The main purpose of this literature review was to identify the incidence of neuropathic pain in PD and the involvement of dopamine of this type of pain by the integration of different lines of investigation. In this review, a search was conducted using PubMed, ProQuest, EBSCO, Medline, EMBASE, and the Science Citation index for studies evaluating pain in patients with PD. The inclusion criteria were as follows: original articles that evaluated incidence and possible mechanism of neuropathic, central, and radicular pain in PD. Nine studies related to the incidence of neuropathic, central, and radicular pain in PD. Nine studies related to the incidence of neuropathic pain in PD suggest the activation of cerebral areas, such as the cortex,

striatum, amygdala, thalamus, raphe nuclei, and locus coeruleus. Neuropathic pain is related to altered levels of dopamine, serotonin, and norepinephrine; these neurotransmitters are related to the sensitive and emotional dimensions of pain. Dopamine could cause hypersensitivity to pain, either indirectly through modulatory effects on affective pain processing and/or directly by affecting the neural activity in key areas of the brain that modulate pain. A considerable proportion of patients with PD suffer neuropathic pain; however, it has been disregarded, this has led to an inability to achieve an adequate treatment and a decrease in pain to improve the quality of life of these patients. We consider that neuropathic pain in PD is possibly induced by neurophysiological changes due to the degradation of dopaminergic neurons.

#### 23. Assessment and treatment of neurogenic dysphagia in stroke and Parkinson's disease

Authors: Cosentino, Giuseppe;Todisco, Massimiliano;Giudice, Carla;Tassorelli, Cristina and Alfonsi, Enrico

#### Publication Date: Dec 01 ,2022

#### Journal: Current Opinion in Neurology 35(6), pp. 741-752

Abstract: PURPOSE OF REVIEW: Neurogenic dysphagia worsens guality of life and prognosis of patients with different neurological disorders. Management of neurogenic dysphagia can be challenging. This review provides a comprehensive overview of current evidence on screening, diagnosis, and treatment of neurogenic dysphagia in stroke and Parkinson's disease, suggesting clues for clinical practice. RECENT FINDINGS: The pros and cons of diagnostic techniques are discussed in the light of updated evidence. Findings from recent meta-analyses of different treatment approaches, including traditional dysphagia therapy, peripheral and central neurostimulation techniques, and treatment with botulinum toxin, are critically discussed, emphasizing inconsistencies and controversial issues. SUMMARY: Screening tests and clinical swallow examination should be routinely performed in neurological patients at risk for dysphagia. In patients testing positive for dysphagia, first-line instrumental investigations, represented by fiberoptic endoscopic evaluation of swallowing or videofluoroscopic swallow study, should be performed to confirm the presence of dysphagia, to assess its severity, and to inform the treatment. Second-line and third-line instrumental methods can be used in selected patients to clarify specific pathophysiological aspects of oropharyngeal dysphagia. Treatment strategies should be personalized, and combination of traditional dysphagia therapy with innovative treatment approaches may increase the chance of restoring effective and safe swallowing. Copyright © 2022 Wolters Kluwer Health, Inc. All rights reserved.

### 24. Impact of Off-Time on Quality of Life in Parkinson's Patients and Their Caregivers: Insights from Social Media.

**Authors:** Damier, Philippe;Henderson, Emily J.;Romero-Imbroda, Jesus;Galimam, Laura;Kronfeld, Nick and Warnecke, Tobias

#### Publication Date: 2022

Journal: Parkinsons Disease 2022, pp. 1800567

**Abstract:** Introduction: In Parkinson's disease (PD), the quality of life of both patients and caregivers is affected. While key issues relating to quality of life may not emerge in conversations with healthcare professionals (HCPs), unguarded social media conversations can provide insight into how people with Parkinson's disease (PwPD) and their caregivers are affected. We conducted a qualitative and quantitative netnographic study of PD conversations posted on social media sites over a 12-month period. Objective: To identify key themes and issues for PwPD. Methods: Using predefined and piloted search terms, we identified 392,962 social media posts (between March 31, 2020, and March 31, 2021, for the UK and France, and between September 30, 2019, and March 31, 2021, for Italy, Spain, and Germany). A random sample of these posts was then analyzed using natural language processing

(NLP), and quantitative, qualitative, in-depth contextual analysis was also performed. Results: Key themes that emerged in the PD conversation related to the changing experience of symptoms over time are the physical, emotional, and cognitive impact of symptoms, the management and treatment of PD, disease awareness among the general public, and the caregiver burden. The emotional impact of motor symptoms on PwPD is significant, particularly when symptoms increase and PwPD lose their independence, which may exacerbate existing anxiety and depression. Nonmotor symptoms can also compound the difficulties with managing the physical impact of motor symptoms. The burden of nonmotor symptoms is felt by both PwPD and their caregivers, with the impact of nonmotor symptoms on cognitive processes particularly frustrating for caregivers. The experience of off-time was also featured in the online conversation. Some PwPD believe there is a lack of adequate management from healthcare professionals, who may not appreciate their concerns or take sufficient time to discuss their needs. Conclusion: This study identified key themes that PwPD and their caregivers discuss online. These findings help signpost issues of importance to PwPD and areas in which their care may be improved. Copyright © 2022 Philippe Damier et al.

### 25. APDM gait and balance measures fail to predict symptom progression rate in Parkinson's disease.

**Authors:** Dewey, D. Campbell;Chitnis, Shilpa;McCreary, Morgan C.;Gerald, Ashley;Dewey, Chadrick H.;Pantelyat, Alexander;Dawson, Ted M.;Rosenthal, Liana S. and Dewey, Richard B. Jr

#### Publication Date: 2022

#### Journal: Frontiers in Neurology [Electronic Resource] 13, pp. 1041014

Abstract: Parkinson's disease (PD) results in progressively worsening gait and balance dysfunction that can be measured using computerized devices. We utilized the longitudinal database of the Parkinson's Disease Biomarker Program to determine if baseline gait and balance measures predict future rates of symptom progression. We included 230, 222, 164, and 177 PD subjects with 6, 12, 18, and 24 months of follow-up, respectively, and we defined progression as worsening of the following clinical parameters: MDS-UPDRS total score, Montreal Cognitive Assessment, PDQ-39 mobility subscale, levodopa equivalent daily dose, Schwab and England score, and global composite outcome. We developed ridge regression models to independently estimate how each gait or balance measure, or combination of measures, predicted progression. The accuracy of each ridge regression model was calculated by cross-validation in which 90% of the data were used to estimate the ridge regression model which was then tested on the 10% of data left out. While the models modestly predicted change in outcomes at the 6-month follow-up visit (accuracy in the range of 66-71%) there was no change in the outcome variables during this short follow-up (median change in MDS-UPDRS total score = 0 and change in LEDD = 0). At follow-up periods of 12, 18, and 24 months, the models failed to predict change (accuracy in the held-out sets ranged from 42 to 60%). We conclude that this set of computerized gait and balance measures performed at baseline is unlikely to help predict future disease progression in PD. Research scientists must continue to search for progression predictors to enhance the performance of disease modifying clinical trials. Copyright © 2022 Dewey, Chitnis, McCreary, Gerald, Dewey, Pantelyat, Dawson, Rosenthal and Dewey.

#### 26. Genetic architecture of Parkinson's disease subtypes - Review of the literature

Authors: Dulski, Jaroslaw; Uitti, Ryan J.; Ross, Owen A. and Wszolek, Zbigniew K.

#### Publication Date: 2022

Journal: Frontiers in Aging Neuroscience 14, pp. 1023574

**Abstract:** The heterogeneity of Parkinson's disease (PD) has been recognized since its description by James Parkinson over 200 years ago. The complexity of motor and non-motor PD manifestations has led to many attempts of PD subtyping with different prognostic outcomes; however, the

pathophysiological foundations of PD heterogeneity remain elusive. Genetic contributions to PD may be informative in understanding the underpinnings of PD subtypes. As such, recognizing genotypephenotype associations may be crucial for successful gene therapy. We review the state of knowledge on the genetic architecture underlying PD subtypes, discussing the monogenic forms, as well as oligoand polygenic risk factors associated with various PD subtypes. Based on our review, we argue for the unification of PD subtyping classifications, the dichotomy of studies on genetic factors and genetic modifiers of PD, and replication of results from previous studies. Copyright © 2022 Dulski, Uitti, Ross and Wszolek.

#### 27. Prevalence and outcomes of Covid-19 in Parkinson's disease: Acute settings and hospital.

Authors: Fearon, Conor and Fasano, Alfonso

#### Publication Date: 2022

Journal: International Review of Neurobiology 165, pp. 35-62

**Abstract:** The global explosion of COVID-19 necessitated the rapid dissemination of information regarding SARS-CoV-2. Hence, COVID-19 prevalence and outcome data in Parkinson's disease patients were disseminated at a time when we only had part of the picture. In this chapter we firstly discuss the current literature on the prevalence of COVID-19 in people with PD. We then discuss outcomes from COVID-19 in people with PD, specifically risk of hospitalization and mortality. Finally, we discuss specific contributing and confounding factors which may put PD patients at higher or lower risk from COVID-19. Copyright © 2022 Elsevier Inc. All rights reserved.

### 28. Assistive Devices for Personal Mobility in Parkinson's Disease: A Systematic Review of the Literature

**Authors:** Garcia-Bustillo, Alvaro; Valinas-Sieiro, Florita; Allende-Rio, Marta; Gonzalez-Santos, Josefa; Cubo, Esther and and the Multidisciplinary Telemedicine Group

#### Publication Date: Nov ,2022

Journal: Movement Disorders Clinical Practice 9(8), pp. 1040-1046

Abstract: Background: Gait abnormalities are a hallmark of Parkinson's disease and contribute to falling risk. As disease symptoms progress, assistive devices are often prescribed. However, there are no guidelines for choosing appropriate ambulatory devices for gait impairment. Objective: To review the scientific evidence on assistive devices for gait impairment in Parkinson's disease. Methods: We performed a systematic literature review for articles relating to parkinsonian gait impairment and assistive devices. We assessed the studies' methodological quality and risk of bias using the PEDro scale. Results: Seventeen articles were reviewed. Four articles (23.53%) showed that canes and standard and two-wheeled walkers without visual cues decreased gait speed and stride length, with no significant effects on freezing of gait or falls. Instead, improvements were observed with the use of visual [seven articles (41.18%)] and auditory cues [three articles (17.65%)], including decreased number of freezing episodes and increased stride length. Conclusions: Although assistive devices seem to improve confidence, there is still limited information about the efficacy of assistive devices on gait parameters and functional disability in Parkinson's disease. Further, longitudinal, multicenter, randomized, blinded, and controlled studies using assistive devices in a free-living context are required to provide the best scientific evidence. Copyright © 2022 The Authors. Movement Disorders Clinical Practice published by Wiley Periodicals LLC on behalf of International Parkinson and Movement Disorder Society.

#### 29. The association of comorbidity with Parkinson's disease-related hospitalizations.

Authors: Hommel, Adrianus L. A. J.; Krijthe, Jesse H.; Darweesh, Sirwan and Bloem, Bastiaan R.

#### Publication Date: Nov ,2022

Journal: Parkinsonism & Related Disorders 104, pp. 123-128

**Abstract:** INTRODUCTION: Unplanned hospital admissions associated with Parkinson's disease could be partly attributable to comorbidities. METHODS: We studied nationwide claims databases and registries. Persons with newly diagnosed Parkinson's disease were identified based on the first Parkinson's disease-related reimbursement claim by a medical specialist. Comorbidities were classified based on the Charlson Comorbidity Index. We studied hospitalization admissions because of falls, psychiatric diseases, pneumonia and urinary tract infections, PD-related hospitalizations-not otherwise specified. The association between comorbidities and time-to-hospitalization was estimated using Cox proportional hazard modelling. To better understand pathways leading to hospitalizations, we performed multiple analyses on causes for hospitalizations. RESULTS: We identified 18 586 people with newly diagnosed Parkinson's disease. The hazard of hospitalization was increased in persons with peptic ulcer disease (HR 2.20, p = 0.009), chronic obstructive pulmonary disease (HR 1.61, p Copyright © 2022 The Authors. Published by Elsevier Ltd.. All rights reserved.

#### 30. Sleep Disturbances in Neurological Disease: A Target for Intervention

Authors: Khambadkone, Seva G. and Benjamin, Sara E.

#### Publication Date: Oct ,2022

Journal: Seminars in Neurology 42(5), pp. 639-657

**Abstract:** Sleep is a biological function required for neurological and general health, but a significant and under-recognized proportion of the population has disturbed sleep. Here, we briefly overview the biology of sleep, sleep requirements over the lifespan, and common sleep disorders. We then turn our attention to five neurological diseases that significantly contribute to global disease burden and neurology practice makeup: epilepsy, headache, ischemic stroke, Parkinson's disease, and Alzheimer's disease. For each disease, we review evidence that sleep disturbances contribute to disease risk and severity and discuss existing data that addressing sleep disturbances may have disease-modifying effects. We provide recommendations derived from the literature and existing clinical guidelines to facilitate the evaluation and management of sleep disturbances within the context of each neurological disease. Finally, we synthesize identified needs and commonalities into future directions for the field and practical sleep-related recommendations for physicians caring for patients at risk for or currently suffering from neurological disease. Copyright Thieme. All rights reserved.

### 31. Effectiveness of electrical vestibular nerve stimulation on the range of motion in patients with Parkinson's disease.

**Authors:** Kumar Goothy, Sai Sailesh;Gawarikar, Sudhir;Choudhary, Anita;Govind, Potey Gajanan;Purohit, Manju;Pathak, Ashish;Chouhan, Rohit Singh;Ali, Zaki;Tiwari, Mini and Khanderao, Mahadik Vijay

#### Publication Date: 2022

Journal: Journal of Basic & Clinical Physiology & Pharmacology

**Abstract:** OBJECTIVES: The present study was undertaken to observe the effectiveness of electrical vestibular stimulation on the range of motion (ROM) in patients with Parkinson's disease (PD). METHODS: The present study was a randomized controlled trial (ClinicalTrials.gov Identifier:

NCT04450550). The study participants were assessed at three points of time. After recording baseline cognitive functions, electrical vestibular nerve stimulation was administered to the intervention group and placebo stimulation was administered to the control group for 12 weeks. Post-intervention parameters were recorded after 6 weeks and after 12 weeks after the intervention in both control and intervention groups. A total of 30 cases of PD, including both males and females were recruited in the study by convenient sampling after obtaining written informed consent. All ROM and flexibility measurements were recorded using a universal goniometer and standard protocol with help of an experienced physiotherapist at our hospital. RESULTS: There was a significant improvement in the hip internal and external rotation right and left sides. There was a significant improvement in the hip extension right and left. There was a significant improvement in the ankle plantarflexion left and ankle dorsiflexion right and left followed by the intervention. There was a significant decline in the hip internal rotation on right and left sides. There was a significant decline in the hip extension and ankle dorsiflexion on the left side. CONCLUSIONS: The study results confirm the improvement of motor activities of patients with PD followed by vestibular stimulation. Further detailed studies are recommended to support the application of vestibular stimulation as an alternative therapy in the management of motor functions in patients with PD. Copyright © 2022 Walter de Gruyter GmbH, Berlin/Boston.

#### 32. Clinical applications of exercise in Parkinson's disease: what we need to know?

**Authors:** Machado, Sergio;Teixeira, Diogo;Monteiro, Diogo;Imperatori, Claudio;Murillo-Rodriguez, Eric;da Silva Rocha, Fernanda Pereira;Yamamoto, Tetsuya;Amatriain-Fernandez, Sandra;Budde, Henning;Carta, Mauro Giovanni;Caixeta, Leonardo and de Sa Filho, Alberto Souza

#### Publication Date: 2022

Journal: Expert Review of Neurotherapeutics 22(9), pp. 771-780

**Abstract:** INTRODUCTION: Exploring the potential of exercise in the rehabilitation process of patients with Parkinson's (PD) may be an interesting treatment perspective. Exercise-induced responses derived from neurotrophic elements appear to ameliorate the decline in neurodegeneration. Despite this understanding, the literature needs to be updated. AREAS COVERED: Our review focuses on: a) the key mechanisms of exercise on PD, highlighting mainly the responses related to neuroplasticity; b) the effects induced by different traditional types of exercise, also highlighting the effects of complementary therapies related to movement; c) the volume of exercise required to support efficient results are explored in the context of PD. Additionally, the proposition of new clinical application strategies in the context of PD will also be determined. EXPERT OPINION: It is suggested that different intensities of aerobic exercise be explored for the treatment of PD. The results associated with high intensity seem promising for performance, physiological and clinical parameters, such as BDNF production and cognition. On the other hand, the diversification of tasks and repetition of motor gestures appear as consistent arguments to exercise prescription. Finally, for future investigations, the neuromodulation strategy in association with aerobic exercise appears as a potential inducer of benefits on gait and cognitive function.

#### 33. Computerized analysis of speech and voice for Parkinson's disease: A systematic review

Authors: Ngo, Quoc Cuong;Motin, Mohammod Abdul;Pah, Nemuel Daniel;Drotar, Peter;Kempster, Peter and Kumar, Dinesh

#### Publication Date: Nov ,2022

Journal: Computer Methods & Programs in Biomedicine 226, pp. 107133

**Abstract:** BACKGROUND AND OBJECTIVE: Speech impairment is an early symptom of Parkinson's disease (PD). This study has summarized the literature related to speech and voice in detecting PD and assessing its severity. METHODS: A systematic review of the literature from 2010 to 2021 to

investigate analysis methods and signal features. The keywords "Automatic analysis" in conjunction with "PD speech" or "PD voice" were used, and the PubMed and ScienceDirect databases were searched. A total of 838 papers were found on the first run, of which 189 were selected. One hundred and forty-seven were found to be suitable for the review. The different datasets, recording protocols, signal analysis methods and features that were reported are listed. Values of the features that separate PD patients from healthy controls were tabulated. Finally, the barriers that limit the wide use of computerized speech analysis are discussed. RESULTS: Speech and voice may be valuable markers for PD. However, large differences between the datasets make it difficult to compare different studies. In addition, speech analytic methods that are not informed by physiological understanding may alienate clinicians. CONCLUSIONS: The potential usefulness of speech and voice for the detection and assessment of PD is confirmed by evidence from the classification and correlation results. Copyright © 2022. Published by Elsevier B.V.

#### 34. Parkinson's Disease: Risk Factor Modification and Prevention

Authors: Rajan, Suraj and Kaas, Bonnie

#### Publication Date: Oct ,2022

#### Journal: Seminars in Neurology 42(5), pp. 626-638

**Abstract:** The global burden of Parkinson's disease (PD) has increased from 2.5 to 6.1 million since the 1990s. This is expected to rise as the world population ages and lives longer. With the current consensus on the existence of a prediagnostic phase of PD, which can be divided into a preclinical stage and a prodromal stage, we can better define the risk markers and prodromal markers of PD in the broader context of PD pathogenesis. Here, we review this pathogenetic process, and discuss the evidence behind various heritability factors, exposure to pesticides and farming, high dairy consumption, and traumatic brain injuries that have been known to raise PD risk. Physical activity, early active lifestyle, high serum uric acid, caffeine consumption, exposure to tobacco, nonsteroidal anti-inflammatory drugs, and calcium channel blockers, as well as the Mediterranean and the MIND diets are observed to lower PD risk. This knowledge, when combined with ways to identify at-risk populations and early prodromal PD patients, can help the clinician make practical recommendations. Most importantly, it helps us set the parameters for epidemiological studies and create the paradigms for clinical trials. Copyright Thieme. All rights reserved.

### 35. A Computerized Analysis with Machine Learning Techniques for the Diagnosis of Parkinson's Disease: Past Studies and Future Perspectives

Authors: Rana, Arti; Dumka, Ankur; Singh, Rajesh; Panda, Manoj Kumar and Priyadarshi, Neeraj

#### Publication Date: Nov 05, 2022

#### **Journal:** Diagnostics 12(11)

**Abstract:** According to the World Health Organization (WHO), Parkinson's disease (PD) is a neurodegenerative disease of the brain that causes motor symptoms including slower movement, rigidity, tremor, and imbalance in addition to other problems like Alzheimer's disease (AD), psychiatric problems, insomnia, anxiety, and sensory abnormalities. Techniques including artificial intelligence (AI), machine learning (ML), and deep learning (DL) have been established for the classification of PD and normal controls (NC) with similar therapeutic appearances in order to address these problems and improve the diagnostic procedure for PD. In this article, we examine a literature survey of research articles published up to September 2022 in order to present an in-depth analysis of the use of datasets, various modalities, experimental setups, and architectures that have been applied in the diagnosis of subjective disease. This analysis includes a total of 217 research publications with a list of the various datasets, methodologies, and features. These findings suggest that ML/DL methods and novel biomarkers hold promising results for application in medical decision-making, leading to a more

methodical and thorough detection of PD. Finally, we highlight the challenges and provide appropriate recommendations on selecting approaches that might be used for subgrouping and connection analysis with structural magnetic resonance imaging (sMRI), DaTSCAN, and single-photon emission computerized tomography (SPECT) data for future Parkinson's research.

#### 36. The impact of Parkinson's disease on results of primary total knee arthroplasty

Authors: Rodriguez-Merchan, E. Carlos and Kalbakdij-Sanchez, Carlos

#### Publication Date: Oct 26 ,2022

Journal: EFORT Open Reviews 7(10), pp. 701-709

**Abstract:** Parkinson's disease (PD) is a common neurodegenerative disorder. When patients with PD undergo total knee arthroplasty (TKA) for knee osteoarthritis, poorer knee function and poorer quality of life are obtained than in matched cohorts (MCs). However, the degree of patient satisfaction is usually high. The mean length of stay is 6.5% longer in patients with PD than in MCs. Compared with MCs, patients with PD undergoing TKA have a 44% higher risk of complications. In patients with PD, the overall complication rate is 26.3% compared with 10.5% in MCs; the periprosthetic joint infection rate is 6.5% in patients with PD vs 1.7% in MCs; and the periprosthetic fracture rate is 2.1% in patients with PD vs 1.7% in MCs. The 90-day readmission rate is 16.29% in patients with PD vs 12.66% in MCs. More flexion contractures occur in patients with PD. The rate of medical complications is 4.21% in patients with PD vs 3.15% in MCs. At 5.3 years' mean follow-up, the need for revision surgery is 23.6%. The 10-year implant survival, taking revision of any of the components as an endpoint, is 89.7% in patients with PD vs 98.3% in MCs.

#### 37. Parkinson's disease and palliative care: a quality of care Delphi study.

Authors: Rogers, Alice; Richfield, Edward William; Thomas, Sue; Wee, Bee and Trotter, Sophie Anne

#### Publication Date: 2022

#### Journal: BMJ Supportive & Palliative Care

Abstract: OBJECTIVES: Extending palliative care services to those with long-term neurological conditions is a current aim of UK health policy. Lack of holistic guidelines for palliative and end-of-life care, and differing models of service provision, has resulted in heterogeneity in care access and quality. There is a need for evidence-based standards of care to audit Parkinson's services and drive improvements. METHODS: A two-stage Delphi process was used to achieve consensus on statements that define quality standards in palliative care for patients with Parkinson's disease (PD). An expert panel was selected to comprise healthcare professionals, patients and carers based in the UK; this panel evaluated the statements via a Delphi survey. Quantitative and qualitative analysis of the results informed modifications between the Delphi rounds. RESULTS: A final set of 16 statements was produced, reflecting aspirational standards of palliative care in PD. These statements, split into four domains ('Structures and processes of care', 'Preparing for the end of life', ' Care in the last weeks of life' and 'Care in the last days of life') underline the importance of joint working between generalist and specialist services, individualised care and early and regular advance care planning. CONCLUSIONS: The Delphi process has established a set of standards which can be integrated within and guide services, helping to improve the guality and equality of care. Further work remains to establish the effectiveness of different models of service provision, including the implementation of keyworkers and telemedicine. Copyright © Author(s) (or their employer(s)) 2022. No commercial re-use. See rights and permissions. Published by BMJ.

# 38. Levelling the Playing Field: The Role of Workshops to Explore How People With Parkinson's Use Music for Mood and Movement Management as Part of a Patient and Public Involvement Strategy.

Authors: Rose, Dawn C.;Poliakoff, Ellen;Hadley, Rebecca;Guerin, Segolene M. R.;Phillips, Michelle and Young, William R.

#### Publication Date: 2022

Journal: Frontiers in Rehabilitation Sciences 3, pp. 873216

Abstract: From a humanistic perspective, participatory processes in research find support on both ethical and moral grounds. In practical terms however, it is often difficult to establish protocols that best honour (i.e., elicit, capture, and integrate) the opinions of individuals and groups that represent the various specific stakeholders (e.g., from allied health, scientific, and academic disciplines) needed to investigate complex phenomena. Here, we describe a consultation process (funded by Parkinson's UK) devised to explore use of music among people with Parkinson's in relation to potential applications to enhance guality of life. People with Parkinson's were paired with researchers in order to discuss music on an equal footing so as to enable participant empowerment. We describe outcomes that demonstrate avenues of success as a result of this approach and additional insights gained through these processes in the hope of informing future practise. It has been our experience that researchers must establish a balance between (a) ensuring methodological rigour within an appropriate framework, and (b) facilitating informal "playtime" that develops connectivity between participants and enables both creative thinking and reflexive practise amongst stakeholders. We encourage researchers not to underestimate "playtime" as an important vehicle to foster this social interactivity and fuel the good will required to conduct inclusive and relevant research. Copyright © 2022 Rose, Poliakoff, Hadley, Guerin, Phillips and Young.

#### 39. Why do 'OFF' periods still occur during continuous drug delivery in Parkinson's disease?

Authors: Rota, Silvia;Urso, Daniele;van Wamelen, Daniel J.;Leta, Valentina;Boura, Iro;Odin, Per;Espay, Alberto J.;Jenner, Peter and Chaudhuri, K. Ray

#### Publication Date: 10 13 ,2022

Journal: Translational Neurodegeneration 11(1), pp. 43

**Abstract:** Continuous drug delivery (CDD) is used in moderately advanced and late-stage Parkinson's disease (PD) to control motor and non-motor fluctuations ('OFF' periods). Transdermal rotigotine is indicated for early fluctuations, while subcutaneous apomorphine infusion and levodopa-carbidopa intestinal gel are utilised in advanced PD. All three strategies are considered examples of continuous dopaminergic stimulation achieved through CDD. A central premise of the CDD is to achieve stable control of the parkinsonian motor and non-motor states and avoid emergence of 'OFF' periods. However, data suggest that despite their efficacy in reducing the number and duration of 'OFF' periods, these strategies still do not prevent 'OFF' periods in the middle to late stages of PD, thus contradicting the widely held concepts of continuous drug delivery and continuous dopaminergic stimulation. Why these emergent 'OFF' periods still occur is unknown. In this review, we analyse the potential reasons for their persistence. The contribution of drug- and device-related involvement, and the problems related to site-specific drug delivery are analysed. We propose that changes in dopaminergic and non-dopaminergic mechanisms in the basal ganglia might render these persistent 'OFF' periods unresponsive to dopaminergic therapy delivered via CDD. Copyright © 2022. The Author(s).

#### 40. Neurologic Music Therapy in Geriatric Rehabilitation: A Systematic Review

Authors: Rusowicz, Jagoda;Szczepanska-Gieracha, Joanna and Kiper, Pawel

#### Publication Date: Oct 31,2022

#### **Journal:** Healthcare 10(11)

**Abstract:** (1) Introduction: Neurologic music therapy (NMT) is a non-pharmacological approach of interaction through the therapeutic use of music in motor, sensory and cognitive dysfunctions caused by damage or diseases of the nervous system. (2) Objective: This study aimed to critically appraise the available literature on the application of particular NMT techniques in the rehabilitation of geriatric disorders. (3) Methods: PubMed, ScienceDirect and EBSCOhost databases were searched. We considered randomized controlled trials (RCTs) from the last 12 years using at least one of the NMT techniques from the sensorimotor, speech/language and cognitive domains in the therapy of patients over 60 years old and with psychogeriatric disorders. (4) Results: Of the 255 articles, 8 met the inclusion criteria. All papers in the final phase concerned the use of rhythmic auditory stimulation (RAS) (sensorimotor technique) in the rehabilitation of both Parkinson's disease (PD) patients (six studies) and stroke patients (SPs) (two studies). (5) Conclusion: All reports suggest that the RAS technique has a significant effect on the improvement of gait parameters and the balance of PD patients and SPs, as well as the risk of falls in PD patients.

### 41. Exacerbation of Pre-existing Neurological Symptoms With COVID-19 in Patients With Chronic Neurological Diseases: An Updated Systematic Review

**Authors:** Sakibuzzaman, Md;Hassan, Anid;Hayee, Samira;Haque, Fariah Asha;Bushra, Sumaita Sadida;Maliha, Maisha;Tania, Maksuda Khan;Sadat, Anahita;Akter, Fahima;Mazumder, Tanusree;Razzaque, Joyeta;Kapuria, Progga;Jalal, Ishra and Shah-Riar, Prince

#### Publication Date: Sep ,2022

#### Journal: Cureus 14(9), pp. e29297

**Abstract:** The neurotropism of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) can potentially explain the worsening of symptoms in patients with a history of neurological conditions such as stroke, Parkinson's disease, Alzheimer's, and epilepsy. Several studies have reported that these pre-existing conditions may worsen with a higher frequency of flare-ups, thus resulting in a more significant risk of patient mortality. In this review, we sought to provide an overview of the relationship between pre-existing neurological disorders and COVID-19, focusing on whether the initial infection directly influenced the severity of symptoms. We systematically searched the electronic database PubMed (MEDLINE) and used specific keywords related to our aims from January 2020 to July 2022. All articles published on COVID-19 with keywords pertaining to pre-existing neurological diseases were retrieved and subsequently analyzed. After independent review, the data from 107 articles were selected and evaluated. After analyzing the data from selected articles reviewing the effect of COVID-19 on neurological conditions, we have documented the relationship between said pre-existing neurological diseases, showing an increased risk of hospitalization, admission length, worsening of symptoms, and even mortality in COVID-19 patients. Copyright © 2022, Sakibuzzaman et al.

#### 42. Universal clinical Parkinson's disease axes identify a major influence of neuroinflammation.

**Authors:** Sandor, Cynthia;Millin, Stephanie;Dahl, Andrew;Schalkamp, Ann-Kathrin;Lawton, Michael;Hubbard, Leon;Rahman, Nabila;Williams, Nigel;Ben-Shlomo, Yoav;Grosset, Donald G.;Hu, Michele T.;Marchini, Jonathan and Webber, Caleb

#### Publication Date: Nov 16,2022

Journal: Genome Medicine 14(1), pp. 129

**Abstract:** BACKGROUND: There is large individual variation in both clinical presentation and progression between Parkinson's disease patients. Generation of deeply and longitudinally phenotyped

patient cohorts has enormous potential to identify disease subtypes for prognosis and therapeutic targeting. METHODS: Replicating across three large Parkinson's cohorts (Oxford Discovery cohort (n = 842)/Tracking UK Parkinson's study (n = 1807) and Parkinson's Progression Markers Initiative (n = 472)) with clinical observational measures collected longitudinally over 5-10 years, we developed a Bayesian multiple phenotypes mixed model incorporating genetic relationships between individuals able to explain many diverse clinical measurements as a smaller number of continuous underlying factors ("phenotypic axes"). RESULTS: When applied to disease severity at diagnosis, the most influential of three phenotypic axes "Axis 1" was characterised by severe non-tremor motor phenotype. anxiety and depression at diagnosis, accompanied by faster progression in cognitive function measures. Axis 1 was associated with increased genetic risk of Alzheimer's disease and reduced CSF Abeta1-42 levels. As observed previously for Alzheimer's disease genetic risk, and in contrast to Parkinson's disease genetic risk, the loci influencing Axis 1 were associated with microglia-expressed genes implicating neuroinflammation. When applied to measures of disease progression for each individual, integration of Alzheimer's disease genetic loci haplotypes improved the accuracy of progression modelling, while integrating Parkinson's disease genetics did not. CONCLUSIONS: We identify universal axes of Parkinson's disease phenotypic variation which reveal that Parkinson's patients with high concomitant genetic risk for Alzheimer's disease are more likely to present with severe motor and non-motor features at baseline and progress more rapidly to early dementia. Copyright © 2022. The Author(s).

### 43. An update on advanced therapies for Parkinson's disease: From gene therapy to neuromodulation

Authors: Serva, Stephanie N.;Bernstein, Jacob;Thompson, John A.;Kern, Drew S. and Ojemann, Steven G.

#### Publication Date: 2022

#### Journal: Frontiers in Surgery 9, pp. 863921

**Abstract:** Advanced Parkinson's disease (PD) is characterized by increasingly debilitating impaired movements that include motor fluctuations and dyskinesias. At this stage of the disease, pharmacological management can result in unsatisfactory clinical benefits and increase the occurrence of adverse effects, leading to the consideration of advanced therapies. The scope of this review is to provide an overview of currently available therapies for advanced PD, specifically levodopa-carbidopa intestinal gel, continuous subcutaneous apomorphine infusion, radiofrequency ablation, stereotactic radiosurgery, MRI-guided focused ultrasound, and deep brain stimulation. Therapies in clinical trials are also discussed, including novel formulations of subcutaneous carbidopa/levodopa, gene-implantation therapies, and cell-based therapies. This review focuses on the clinical outcomes and adverse effects of the various therapies and also considers patient-specific characteristics that may influence treatment choice. This review can equip providers with updated information on advanced therapies in PD to better counsel patients on the available options. Copyright © 2022 Serva, Bernstein, Thompson, Kern and Ojemann.

#### 44. Cerebellar deep brain stimulation for movement disorders

Authors: Tai, Chun-Hwei and Tseng, Sheng-Hong

#### Publication Date: 2022

Journal: Neurobiology of Disease 175, pp. 105899

**Abstract:** Deep brain stimulation (DBS) conventionally target at basal ganglia or thalamic structures, modulating nodal points in the cortico-basal ganglia circuit, in order to effectively treat various movement disorders, including Parkinson's disease, tremor and dystonia (especially mobile type dystonia). However, there are still some other movement disorders, such as dystonia (especially fixed

type dystonia), ataxia and freezing of gait, which are not responding well to the current DBS therapy. Cerebellum, similar to basal ganglia, also plays a critical role in the pathophysiology of movement disorders. Deep cerebellar structures, such as dentate nucleus or superior cerebellar peduncle, are noticed for their potential role as treatment targets in movement disorders in recent years. With increasing evidences of animal DBS experiments, recent clinical human subject studies reported that some movement disorders patients not responding to DBS with conventional targets, may benefit significantly from cerebellar DBS. These pioneer study results are invaluable for understanding the clinical use of cerebellar DBS for treatment of movement disorders. We review the recent data of cerebellar DBS performed by different groups and summarize the indications, surgical targets, programming details and outcomes in these clinical reports. We then synthesize the current pathophysiological study of cerebellar DBS. In addition to basal ganglia, it is important to study new DBS targets in the cerebellum for more comprehensive treatment of movement disorders. Copyright © 2022 The Authors. Published by Elsevier Inc. All rights reserved.

### 45. Nomogram to Predict the Probability of Functional Dependence in Early Parkinson's Disease.

**Authors:** Valent, Dora;Krismer, Florian;Grossauer, Anna;Peball, Marina;Heim, Beatrice;Mahlknecht, Phillipp;Djamshidian, Atbin;Poewe, Werner and Seppi, Klaus

#### Publication Date: 2022

#### Journal: Journal of Parkinsons Disease Print

Abstract: BACKGROUND: Early identification of Parkinson's disease (PD) patients at risk for becoming functionally dependent is important for patient counseling. Several models describing the relationship between predictors and outcome have been reported, however, most of these require computer software for practical use. OBJECTIVE: Here we report the development of a risk nomogram allowing an approximate graphical computation of the risk of becoming functionally dependent in early PD. METHODS: We analyzed data form the Parkinson's Progression Markers Initiative cohort of newly diagnosed PD patients from baseline through the first 5 years of follow-up. Functional dependence was defined as a score < 80 on the Schwab & England Activities of Daily Living scale. A binary logistic model was developed to estimate the risk of functional dependence and based on the results, a nomogram for the prediction of functional dependence was drawn in order to provide an easy-to-use tool in clinical and academic settings as a part of personalized medicine approach to PD treatment. RESULTS: At baseline, three patients and over the five-year follow-up, 85 (22%) out of 395 patients were functionally dependent as scored by the Schwab & England Activities of Daily Living rating scale. The binary logistic model showed that clinical parameters such as MDS-UPDRS I (rater part), MDS-UPDRS II, and MDS-UPDRS axial motor score were significant predictors for functional dependence within 5 years. CONCLUSION: We here provide an easy-to-use tool to estimate the risk of functional dependence in PD patients based on the MDS-UPDRS part I, II and axial motor score.

#### 46. Interactions between gut microbiota and Parkinson's disease: The role of microbiotaderived amino acid metabolism

**Authors:** Wang, Wang;Jiang, Shujun;Xu, Chengcheng;Tang, Lili;Liang, Yan;Zhao, Yang and Zhu, Guoxue

#### Publication Date: 2022

Journal: Frontiers in Aging Neuroscience 14, pp. 976316

**Abstract:** Non-motor symptoms (NMS) of Parkinson's disease (PD), such as constipation, sleep disorders, and olfactory deficits, may emerge up to 20 years earlier than motor symptoms. A series of evidence indicates that the pathology of PD may occur from the gastrointestinal tract to the brain.

Numerous studies support that the gut microbiota communicates with the brain through the immune system, special amino acid metabolism, and the nervous system in PD. Recently, there is growing recognition that the gut microbiota plays a vital role in the modulation of multiple neurochemical pathways via the "gut microbiota-brain axis" (GMBA). Many gut microbiota metabolites, such as fatty acids, amino acids, and bile acids, convey signaling functions as they mediate the crosstalk between gut microbiota and host physiology. Amino acids' abundance and species alteration, including glutamate and tryptophan, may disturb the signaling transmission between nerve cells and disrupt the normal basal ganglia function in PD. Specific amino acids and their receptors are considered new potential targets for ameliorating PD. The present study aimed to systematically summarize all available evidence on the gut microbiota-derived amino acid metabolism alterations associated with PD. Copyright © 2022 Wang, Jiang, Xu, Tang, Liang, Zhao and Zhu.

#### 47. Management of psychiatric and cognitive complications in Parkinson's disease

Authors: Weintraub, Daniel; Aarsland, Dag; Biundo, Roberta; Dobkin, Roseanne; Goldman, Jennifer and Lewis, Simon

#### Publication Date: 10 24 ,2022

#### Journal: Bmj 379, pp. e068718

**Abstract:** Neuropsychiatric symptoms (NPSs) such as affective disorders, psychosis, behavioral changes, and cognitive impairment are common in Parkinson's disease (PD). However, NPSs remain under-recognized and under-treated, often leading to adverse outcomes. Their epidemiology, presentation, risk factors, neural substrate, and management strategies are incompletely understood. While psychological and psychosocial factors may contribute, hallmark PD neuropathophysiological changes, plus the associations between exposure to dopaminergic medications and occurrence of some symptoms, suggest a neurobiological basis for many NPSs. A range of psychotropic medications, psychotherapeutic techniques, stimulation therapies, and other non-pharmacological treatments have been studied, are used clinically, and are beneficial for managing NPSs in PD. Appropriate management of NPSs is critical for comprehensive PD care, from recognizing their presentations and timing throughout the disease course, to the incorporation of different therapeutic strategies (ie, pharmacological and non-pharmacological) that utilize a multidisciplinary approach. Copyright Published by the BMJ Publishing Group Limited. For permission to use (where not already granted under a licence) please go to http://group.bmj.com/group/rights-licensing/permissions.

#### 48. The mechanism of exercise for pain management in Parkinson's disease

Authors: Yu, Wen-Ye; Yang, Qi-Hao and Wang, Xue-Qiang

#### Publication Date: 2022

Journal: Frontiers in Molecular Neuroscience 15, pp. 1039302

**Abstract:** The research and clinical applications of exercise therapy to the treatment of Parkinson's disease (PD) are increasing. Pain is among the important symptoms affecting the daily motor function and quality of life of PD patients. This paper reviewed the progress of research on different exercise therapies for the management of pain caused by PD and described the role and mechanism of exercise therapy for pain relief. Aerobic exercise, strength exercise, and mind-body exercise play an effective role in pain management in PD patients. The pain suffered by PD patients is divided into central neuropathic, peripheral neuropathic, and nociceptive pain. Different types of pain may coexist with different mechanistic backgrounds and treatments. The analgesic mechanisms of exercise intervention in PD-induced pain include altered cortical excitability and synaptic plasticity, the attenuation of neuronal apoptosis, and dopaminergic and non-dopaminergic analgesic pathways, as well as the inhibition of oxidative stress. Current studies related to exercise interventions for PD-induced pain suffer from small sample sizes and inadequate research of analgesic mechanisms. The

neurophysiological effects of exercise, such as neuroplasticity, attenuation of neuronal apoptosis, and dopaminergic analgesic pathway provide a sound biological mechanism for using exercise in pain management. However, large, well-designed randomized controlled trials with improved methods and reporting are needed to evaluate the long-term efficacy and cost-effectiveness of exercise therapy for PD pain. Copyright © 2022 Yu, Yang and Wang.

### 49. Emerging role of psychosis in Parkinson's disease: From clinical relevance to molecular mechanisms

Authors: Zhang, Shuo and Ma, Yan

#### Publication Date: Sep 19,2022

Journal: World Journal of Psychiatry 12(9), pp. 1127-1140

Abstract: Parkinson's disease (PD) is the second most common neurodegenerative disease. Psychosis is one of the common psychiatric presentations in the natural course of PD. PD psychosis is an important non-motor symptom, which is strongly correlated with a poor prognosis. Increasing attention is being given to PD psychosis. In this opinion review, we summarized and analyzed the identification, screening, epidemiology, mechanisms, risk factors, and therapeutic approaches of PD psychosis based on the current clinical evidence. PD psychosis tends to have a negative effect on patients' quality of life and increases the burden of family caregiving. Screening and identification in the early stage of disease is crucial for establishing tailored therapeutic strategies and predicting the longterm outcome. Development of PD psychosis is believed to involve a combination of exogenous and endogenous mechanisms including imbalance of neurotransmitters, structural and network changes, genetic profiles, cognitive impairment, and antiparkinsonian medications. The therapeutic strategy for PD psychosis includes reducing or ceasing the use of dopaminergic drug, antipsychotics, cholinesterase inhibitors, and non-pharmacological interventions. Ongoing clinical trials are expected to provide new insights for tailoring therapy for PD psychosis. Future research based on novel biomarkers and genetic factors may help inform individualized therapeutic strategies. Copyright @The Author(s) 2022. Published by Baishideng Publishing Group Inc. All rights reserved.

### 50. Single- and dual-task gait performance and their diagnostic value in early-stage Parkinson's disease.

Authors: Zhang, Xiaodan; Fan, Weinv; Yu, Hu; Li, Li; Chen, Zhaoying and Guan, Qiongfeng

#### Publication Date: 2022

Journal: Frontiers in Neurology [Electronic Resource] 13, pp. 974985

**Abstract:** Background: Gait parameters are considered potential diagnostic markers of Parkinson's disease (PD). We aimed to 1) assess the gait impairment in early-stage PD and its related factors in the single-task (ST) and dual-task (DT) walking tests and 2) evaluate and compare the diagnostic value of gait parameters for early-stage PD under ST and DT conditions. Methods: A total of 97 early-stage PD patients and 41 healthy controls (HC) were enrolled at Hwa Mei hospital. Gait parameters were gathered and compared between the two groups in the ST and DT walking test, controlling for covariates. Utilizing the receiver operating characteristic curve, diagnostic parameters were investigated. Results: In the ST walking test, significantly altered gait patterns could be observed in early-stage PD patients in all domains of gait, except for asymmetry (P P P P P P P.0.05). Combining all gait parameters with diagnostic values under ST and DT walking test, the predictive power significantly increased with an AUC of 0.924 (sensitivity, 85.4%; specificity, 92.7%; P Copyright © 2022 Zhang, Fan, Yu, Li, Chen and Guan.

### 51. A systematic review and meta-analysis on effects of aerobic exercise in people with Parkinson's disease

Authors: Zhen, Kai; Zhang, Shiyan; Tao, Xifeng; Li, Gen; Lv, Yuanyuan and Yu, Laikang

Publication Date: Oct 31,2022

Journal: Npj Parkinsons Disease 8(1), pp. 146

**Abstract:** Previous studies have shown that aerobic exercise is an effective way to improve symptoms of Parkinson's disease (PD). The aim of this study [PROSPERO CRD42022340730] was to explore the effects of aerobic exercises on balance, gait, motor function, and quality of life in PD patients. Searches were performed in PubMed, Web of Science, and EBSCO electronic databases. The Cochrane risk assessment tool was used to evaluate the methodological quality of the included literature. From 1287 search records initially identified, 20 studies were considered eligible for systematic review and meta-analysis. There was a significant effect of aerobic exercise on improving timed up and go test [standardized mean difference (SMD), -0.41 (95% CI, -0.61 to -0.22), p Copyright © 2022. The Author(s).

### 52. Aberrant gray matter volume and functional connectivity in Parkinson's disease with minor hallucination.

**Authors:** Zhong, Min;Li, Chenglin;Lu, Hongquan;Xue, Donghui;Wang, Yaxi;Jiang, Yinyin;Zhu, Sha;Gu, Ruxin;Jiang, Xu;Shen, Bo;Zhu, Jun;Zhang, Wenbin;Pan, Yang;Yan, Jun and Zhang, Li

#### Publication Date: 2022

Journal: Frontiers in Aging Neuroscience 14, pp. 923560

**Abstract:** Background: Minor hallucination (MH) is the most common psychotic symptom in Parkinson's disease (PD); it can develop into well-structured visual hallucination (VH), suggesting that MH may be a staccato form of well-structured VH. However, it remains unclear whether the pathogenesis is the same. Therefore, the aim of this study was to investigate the altered gray matter volume (GMV) and functional connectivity (FC) of MH in PD to further understand the complex mechanisms. Materials and methods: We included 67 PD patients who attended the outpatient clinic of Nanjing Medical University Affiliated Brain Hospital and recruited 31 healthy controls (HC). Demographic data and clinical characteristics of all subjects were recorded, and cranial structural magnetic resonance imaging (MRI) and resting-state functional MRI data were acquired. Patients were classified into the PD with MH (PD-MH) group and PD without hallucinations or delusions (PD-NH) group. Voxel-based morphometry was used to analyze the differences in GMV in the structural pattern. Seed-based FC was used to analyze the functional pattern. Gaussian random field correction was used, with voxel level P P Copyright © 2022 Zhong, Li, Lu, Xue, Wang, Jiang, Zhu, Gu, Jiang, Shen, Zhu, Zhang, Pan, Yan and Zhang.

### 53. Effects of Anti-Parkinsonian Drugs on Verbal Fluency in Patients with Parkinson's Disease: A Network Meta-Analysis

Authors: Zhu, Yuxia;Li, Sichen;Lai, Hongyu;Mo, Lijuan;Tan, Changhong;Liu, Xi;Deng, Fen and Chen, Lifen

Publication Date: Nov 04 ,2022

Journal: Brain Sciences 12(11)

**Abstract:** Verbal fluency impairment is common in patients with Parkinson's disease (PD), but the effect of drugs on verbal fluency in PD patients has not been comprehensively evaluated. We

conducted a network meta-analysis based on four online databases to compare the effect of drugs on verbal fluency in PD patients. This study was performed and reported according to PRISMA-NMA guidelines. In total, 6 out of 3707 articles (three RCTS and three cross-sectional studies) covering eight drug regimens were included (five for letter fluency, five for semantic fluency). In terms of letter fluency, the ranking of the overall efficacy of included drug regimens was: levodopa, levodopa combined with pramipexole, rotigotine, cabergoline, pramipexole, pergolide, but no drug regimen presented a significant advantage over the others. In terms of semantic fluency, the ranking of the overall efficacy of included according, cabergoline, pergolide, pergolide, pramipexole, among which, levodopa alone (SMD = 0.93, 95%CI: 0.28-1.59) and rotigotine alone (SMD = 1.18, 95%CI: 0.28-2.09) were statistically superior to pramipexole, while no significant difference was identified between all the other drug regimens. Levodopa and rotigotine seem to be more appropriate choices for PD patients with verbal fluency impairment. Further study is needed to illustrate the efficacy of drugs on verbal fluency in PD patients.

#### Sources Used:

The following databases are used in the creation of this bulletin: EMBASE and Medline.

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