Parkinson's Disease
Current Awareness Bulletin
February 2023

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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. 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.

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3. **Gut-oriented disease modifying therapy for Parkinson's disease**

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

Publication Date: Jan ,2023

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.

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4. **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

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.

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5. **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

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.

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6. **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

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).

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7. **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.

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.

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8. **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

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.

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

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

Abstract: PURPOSE OF REVIEW: Neurogenic dysphagia worsens quality 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.

10. **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.

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11. **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.

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12. 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

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.

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13. Sleep Disturbances in Neurological Disease: A Target for Intervention

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

Publication Date: Oct ,2022

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.

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14. 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.

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15. 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.

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16. 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.

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17. 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 1.24% in MCs, and the rate of implant-related complications is 5.09% 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.

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18. **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

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).

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19. **Neurologic Music Therapy in Geriatric Rehabilitation: A Systematic Review**

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

Publication Date: Oct 31 ,2022

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.

20. 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

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.

21. 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

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).

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

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

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.

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

Authors: Zhang, Shuo and Ma, Yan

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 long-term 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.

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24. 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).

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25. 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 drug regimens was: rotigotine, levodopa, cabergoline, 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 & Medline.

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