

Parkinson's Disease Current Awareness Bulletin February 2022

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Title: Are We What We Eat? Impact of Diet on the Gut-Brain Axis in Parkinson's Disease

Citation: Nutrients 14(2), Jan 17 2022, DOI: https://libkey.io/https://dx.doi.org/10.3390/nu14020380 **Authors:** Alfonsetti, Margherita; Castelli, Vanessa and d'Angelo, Michele

Abstract: Parkinson's disease is characterized by motor and non-motor symptoms, such as defects in the gut function, which may occur before the motor symptoms. To date, there are therapies that can improve these symptoms, but there is no cure to avoid the development or exacerbation of this disorder. Dysbiosis of gut microbiota could have a crucial role in the gut-brain axis, which is a bidirectional communication between the central nervous system and the enteric nervous system. Diet can affect the microbiota composition, impacting gut-brain axis functionality. Gut microbiome restoration through probiotics, prebiotics, synbiotics or other dietary means could have the potential to slow PD progression. In this review, we will discuss the influence of diet on the bidirectional communication between gut and brain, thus supporting the hypothesis that this disorder could begin in the gut. We also focus on how food-based therapies might then have an influence on PD and could ameliorate nonmotor as well as motor symptoms.

Title: Multi-omic landscaping of human midbrains identifies disease-relevant molecular targets and pathways in advanced-stage Parkinson's disease.

Citation: Clinical and Translational Medicine 12(1), pp. e692, 2022, DOI: https://libkey.io/https://dx.doi.org/10.1002/ctm2.692

Authors: Caldi Gomes, Lucas; Galhoz, Ana; Jain, Gaurav; Roser, Anna-Elisa; Maass, Fabian; Carboni, Eleonora; Barski, Elisabeth; Lenz, Christof; Lohmann, Katja; Klein, Christine; Bahr, Mathias; Fischer, Andre; Menden, Michael P. and Lingor, Paul

Background: Parkinson's disease (PD) is the second most common neurodegenerative disorder whose prevalence is rapidly increasing worldwide. The molecular mechanisms underpinning the pathophysiology of sporadic PD remain incompletely understood. Therefore, causative therapies are still elusive. To obtain a more integrative view of disease-mediated alterations, we investigated the molecular landscape of PD in human post-mortem midbrains, a region that is highly affected during the disease process.

Methods: Tissue from 19 PD patients and 12 controls were obtained from the Parkinson's UK Brain Bank and subjected to multi-omic analyses: small and total RNA sequencing was performed on an Illumina's HiSeq4000, while proteomics experiments were performed in a hybrid triple quadrupole-time of flight mass spectrometer (TripleTOF5600+) following quantitative sequential window acquisition of all theoretical mass spectra. Differential expression analyses were performed with customized frameworks based on DESeq2 (for RNA sequencing) and with Perseus v.1.5.6.0 (for proteomics). Custom pipelines in R were used for integrative studies.

Results: Our analyses revealed multiple deregulated molecular targets linked to known disease mechanisms in PD as well as to novel processes. We have identified and experimentally validated (quantitative real-time polymerase chain reaction/western blotting) several PD-deregulated molecular candidates, including miR-539-3p, miR-376a-5p, miR-218-5p and miR-369-3p, the valid miRNA-mRNA interacting pairs miR-218-5p/RAB6C and miR-369-3p/GTF2H3, as well as multiple proteins, such as CHI3L1, HSPA1B, FNIP2 and TH. Vertical integration of multi-omic analyses allowed validating disease-mediated alterations across different molecular layers. Next to the identification of individual molecular targets in all explored omics layers, functional annotation of differentially expressed molecules showed an enrichment of pathways related to neuroinflammation, mitochondrial dysfunction and defects in synaptic function.

Conclusions: This comprehensive assessment of PD-affected and control human midbrains revealed multiple molecular targets and networks that are relevant to the disease mechanism of advanced PD. The integrative analyses of multiple omics layers underscore the importance of neuroinflammation, immune response activation, mitochondrial and synaptic dysfunction as putative therapeutic targets for advanced PD. Copyright © 2022 The Authors. Clinical and Translational Medicine published by John Wiley & Sons Australia, Ltd on behalf of Shanghai Institute of Clinical Bioinformatics.

Title: Noninvasive neuromodulation in Parkinson's disease: Neuroplasticity implication and therapeutic perspectives

Citation: Handbook of Clinical Neurology 184, pp. 185-198, 2022, DOI: <u>https://libkey.io/https://dx.doi.org/10.1016/B978-0-12-819410-2.00010-2</u> **Authors:** Cosentino, Giuseppe; Todisco, Massimiliano and Blandini, Fabio

Abstract: Noninvasive brain stimulation techniques can be used to study in vivo the changes of cortical activity and plasticity in subjects with Parkinson's disease (PD). Also, an increasing number of studies have suggested a potential therapeutic effect of these techniques. High-frequency repetitive transcranial magnetic stimulation (rTMS) and anodal transcranial direct current stimulation (tDCS) represent the most used stimulation paradigms to treat motor and nonmotor symptoms of PD. Both techniques can enhance cortical activity, compensating for its reduction related to subcortical dysfunction in PD. However, the use of suboptimal stimulation parameters can lead to therapeutic failure. Clinical studies are warranted to clarify in PD the additional effects of these stimulation techniques on pharmacologic and neurorehabilitation treatments. Copyright © 2022 Elsevier B.V. All rights reserved.

Title: Gaps and roadmap of novel neuromodulation targets for treatment of gait in Parkinson's disease

Citation: Npj Parkinsons Disease 8(1), pp. 8, Jan 11 2022, DOI: <u>https://libkey.io/https://dx.doi.org/10.1038/s41531-021-00276-6</u> **Authors:** Cury, Rubens Gisbert; Pavese, Nicola; Aziz, Tipu Z.; Krauss, Joachim K.; Moro, Elena and Neuromodulation of Gait Study Group from Movement Disorders Society

Abstract: Gait issues in Parkinson's disease (PD) are common and can be highly disabling. Although levodopa and deep brain stimulation (DBS) of the subthalamic nucleus and the globus pallidus internus have been established therapies for addressing the motor symptoms of PD, their effects on gait are less predictable and not well sustained with disease progression. Given the high prevalence of gait impairment in PD and the limitations in currently approved therapies, there has been considerable interest in alternative neuromodulation targets and techniques. These have included DBS of pedunculopontine nucleus and substantia nigra pars reticulata, spinal cord stimulation, non-invasive modulation of cortical regions and, more recently, vagus nerve stimulation. However, successes and failures have also emerged with these approaches. Current gaps and controversies are related to patient selection, optimal electrode placement within the target, placebo effects and the optimal programming parameters. Additionally, recent advances in pathophysiology of oscillation dynamics have driven new models of closed-loop DBS systems that may or may not be applicable to gait issues. Our aim is to describe approaches, especially neuromodulation procedures, and emerging challenges to address PD gait issues beyond subthalamic nucleus and the globus pallidus internus stimulation. Copyright © 2022. The Author(s).

Title: Is Being Physically Active Enough or Do People with Parkinson's Disease Need Structured Supervised Exercise? Lessons Learned from COVID-19.

Citation: International Journal of Environmental Research & Public Health [Electronic Resource] 19(4), pp. 02 19, 2022, DOI: https://libkey.io/https://dx.doi.org/10.3390/ijerph19042396 **Authors:** Domingos, Josefa; Familia, Carlos; Fernandes, Julio Belo; Dean, John and Godinho, Catarina

Abstract: Social isolation imposed by the COVID-19 pandemic negatively impacted people's lifestyles and daily activities. In this work we compared pre- and post-pandemic clinical outcomes in people with Parkinson's disease, to assess differences according to the type of behaviour and exercise habits adopted by participants. After two months of COVID-19 lockdown, we assessed: changes in exercise behaviour; motor and non-motor aspects of daily life experiences (MDS-UPDRS I & II); activities of daily living (The Schwab & England scale); quality of life (Parkinson Disease Questionnaire); sleep (Parkinson Disease Sleep Scale); falls; and Clinical Global Impression Change. Twenty-seven individuals aged between 57 and 92 years old participated; from these, ten individuals (37%) completely interrupted physical activities, while seventeen (63%) maintained some level of active lifestyle. Regardless of whether they remained active or not, all participants perceived a significant worsening of their clinical condition, reporting an increase in difficulties completing daily activities or chores (37%) and worsening of their health condition (51.8%). The quantifiable influence of exercise habits was borderline for the group who kept active. The active group seem to have a better self-perception of their health condition, although it was not enough to show a clear benefit. People with Parkinson's disease should be informed that being physically active may not be enough and more structured exercise could be needed.

Title: Brain oscillations and Parkinson disease

Citation: Handbook of Clinical Neurology 184, pp. 259-271, 2022, DOI: https://libkey.io/https://dx.doi.org/10.1016/B978-0-12-819410-2.00014-X **Authors:** Foffani, Guglielmo and Alegre, Manuel

Abstract: Brain oscillations have been associated with Parkinson's disease (PD) for a long time mainly due to the fundamental oscillatory nature of parkinsonian rest tremor. Over the years, this association has been extended to frequencies well above that of tremor, largely owing to the opportunities offered by deep brain stimulation (DBS) to record electrical activity directly from the patients' basal ganglia. This chapter reviews the results of research on brain oscillations in PD focusing on theta (4-7Hz), beta (13-35Hz), gamma (70-80Hz) and high-frequency oscillations (200-400Hz). For each of these oscillations, we describe localization and interaction with brain structures and between frequencies, changes due to dopamine intake, task-related modulation, and clinical relevance. The study of brain oscillations will also help to dissect the mechanisms of action of DBS. Overall, the chapter tentatively depicts PD in terms of "oscillopathy." Copyright © 2022 Elsevier B.V. All rights reserved.

Title: Sleep and circadian rhythms in Parkinson's disease and preclinical models

Citation: Molecular Neurodegeneration 17(1), pp. 2, 2022, DOI: https://libkey.io/https://dx.doi.org/10.1186/s13024-021-00504-w **Authors:** Hunt, Jeremy; Coulson, Elizabeth J.; Rajnarayanan, Rajendram; Oster, Henrik; Videnovic, Aleksandar and Rawashdeh, Oliver **Abstract:** The use of animals as models of human physiology is, and has been for many years, an indispensable tool for understanding the mechanisms of human disease. In Parkinson's disease, various mouse models form the cornerstone of these investigations. Early models were developed to reflect the traditional histological features and motor symptoms of Parkinson's disease. However, it is important that models accurately encompass important facets of the disease to allow for comprehensive mechanistic understanding and translational significance. Circadian rhythm and sleep issues are tightly correlated to Parkinson's disease, and often arise prior to the presentation of typical motor deficits. It is essential that models used to understand Parkinson's disease reflect these dysfunctions in circadian rhythms and sleep, both to facilitate investigations into mechanistic interplay between sleep and disease, and to assist in the development of circadian rhythm-facing therapeutic treatments. This review describes the extent to which various genetically-and neurotoxically-induced murine models of Parkinson's reflect the sleep and circadian abnormalities of Parkinson's disease observed in the clinic. Copyright © 2021. The Author(s).

Title: Gender differences in motor and non-motor symptoms in early Parkinson disease.

Citation: Medicine 101(3), pp. e28643, DOI: https://libkey.io/https://dx.doi.org/10.1097/MD.00000000028643 **Authors:** Kang, Kyung Wook;Choi, Seong-Min and Kim, Byeong C.

Abstract: Gender differences in motor and non-motor symptoms in Parkinson disease (PD) are still controversial. This study aimed to investigate gender differences in clinical characteristics in patients with early PD. This study included 415 PD patients (201 men and 214 women) with modified Hoehn-Yahr stage 1 to 3 and a disease duration of Copyright © 2022 the Author(s). Published by Wolters Kluwer Health, Inc.

Title: MicroRNAs in the pathophysiology of Alzheimer's disease and Parkinson's disease: an overview

Citation: Molecular Neurobiology 59(3), pp. 1589-1603, March 2022, DOI: <u>https://libkey.io/https://dx.doi.org/10.1007/s12035-022-02727-4</u> **Authors:** Khezri, Mohammad Rafi; Yousefi, Keyvan; Zolbanin, Naime Majidi and Ghasemnejad-Berenji, Morteza

Abstract: Neurodegenerative diseases are characterized by a progressive loss of neurons of the central nervous system (CNS) and serve as a major cause of morbidity, mortality and functional dependence especially among the elderly. Despite extensive research and development efforts, the success rate of clinical pipelines has been very limited. However, microRNAs (miRs) have been proved to be of crucial importance in regulating intracellular pathways for various pathologic conditions including those of a neurodegenerative nature. There is ample evidence of altered levels of various miRs in clinical samples of Alzheimer's disease and Parkinson's disease patients with potentially major clinical implications. In the current review, we aim to summarize the relevant literature on the role of miRs in the pathophysiology of Alzheimer's disease (AD) and Parkinson's disease (PD) as the two globally predominant neurodegenerative conditions. Copyright © 2022. The Author(s), under exclusive licence to Springer Science+Business Media, LLC, part of Springer Nature.

Title: Parkinson's disease and diabetes mellitus: common mechanisms and treatment repurposing

Citation: Neural Regeneration Research 17(8), pp. 1652-1658, Aug 2022, DOI: https://libkey.io/https://dx.doi.org/10.4103/1673-5374.332122 **Authors:** Labandeira, Carmen M.; Fraga-Bau, Arturo; Arias Ron, David; Alvarez-Rodriguez, Elena; Vicente-Alba, Pablo; Lago-Garma, Javier and Rodriguez-Perez, Ana I.

Abstract: In the last decade, attention has become greater to the relationship between neurodegeneration and abnormal insulin signaling in the central nervous system, as insulin in the brain is implicated in neuronal survival, plasticity, oxidative stress and neuroinflammation. Diabetes mellitus and Parkinson's disease are both aging-associated diseases that are turning into epidemics worldwide. Diabetes mellitus and insulin resistance not only increase the possibility of developing Parkinson's disease but can also determine the prognosis and progression of Parkinsonian symptoms. Today, there are no available curative or disease modifying treatments for Parkinson's disease, but the role of insulin and antidiabetic medications in neurodegeneration opens a door to treatment repurposing to fight against Parkinson's disease, both in diabetic and nondiabetic Parkinsonian patients. Furthermore, it is essential to comprehend how a frequent and treatable disease such as diabetes can influence the progression of neurodegeneration in a challenging disease such as Parkinson's disease. Here, we review the present evidence on the connection between Parkinson's disease and diabetes and the consequential implications of the existing antidiabetic molecules in the severity and development of Parkinsonism, with a particular focus on glucagon-like peptide-1 receptor agonists.

Title: Constipation and Cigarette Smoking Are Independent Influences for Parkinson's Disease.

Citation: Cureus 14(1), pp. e21689, Jan 2022, DOI: https://libkey.io/https://dx.doi.org/10.7759/cureus.21689 **Authors:** Lehrer, Steven and Rheinstein, Peter H.

Background: Tobacco smokers have reduced Parkinson's disease (PD) risk. Some patients with PD experience constipation long before they develop mobility problems, and constipation is a frequent complaint of people who try to stop smoking. Recently, the gut microbiome has been implicated in PD. Methods In the present study, we analyzed the relationship between smoking and constipation in subjects with PD and controls. We wished to determine whether the effects of smoking and constipation were independent or whether they might be interrelated. To evaluate the relationship, we used a cohort of subjects from the UK Biobank (UKB). Results In 501,174 subjects, the decreased risk of Parkinson's disease with increased smoking was significant (Copyright © 2022, Lehrer et al.)

Title: Artificial intelligence applications and robotic systems in Parkinson's disease (Review)

Citation: Experimental & Therapeutic Medicine 23(2), pp. 153, Feb 2022, DOI: https://libkey.io/https://dx.doi.org/10.3892/etm.2021.11076 **Authors:** Perju-Dumbrava, Lacramioara; Barsan, Maria; Leucuta, Daniel Corneliu; Popa, Luminita C.; Pop, Cristina; Tohanean, Nicoleta and Popa, Stefan L.

Abstract: Parkinson's disease (PD) is the second most frequent neurodegenerative disorder following Alzheimer's disease. Advanced stages of PD, 4 or 5 of the Hoehn and Yahr Scale, are characterized by severe motor complications, limited mobility without assistance, risk of falling, and non-motor complications. The aim of this review was to provide a practical

overview on specific artificial intelligence (AI) systems for the management of advanced stages of PD, as well as relevant technological limitations. The authors conducted a systematic search on PubMed and EMBASE with predefined keywords searching for studies published until December 2020. Full articles that satisfied the inclusion criteria were included in the systematic review. To minimize results bias, the reference list was manually searched for pertinent articles to identify any additional relevant missed publications. Exclusion criteria included the following: Other stages of PD than 4 and 5 of the Hoehn and Yahr Scale, case reports, reviews, practice guidelines, commentaries, opinions, letters, editorials, short surveys, articles in press, conference abstracts, conference papers, and abstracts published without a full article. The search identified 21 studies analyzing AI-based applications and robotic systems used for the management of advanced stages of PD, out of which 6 articles analyzed AI-based applications for autonomous management of pharmacologic therapy, 5 articles analyzed home-based telemedicine systems and 10 articles analysed robot-assisted gait training systems. The authors identified significant evidence demonstrating that current Al-based technologies are feasible for automatic management of patients with advanced stages of PD. Improving the quality of care and reducing the cost for patients and healthcare systems are the most important advantages. Copyright: © Perju-Dumbrava et al.

Title: Systematic review and meta-analysis of clinical effectiveness of selfmanagement interventions in Parkinson's disease.

Citation: BMC Geriatrics 22(1), pp. 45, 2022, DOI: https://libkey.io/https://dx.doi.org/10.1186/s12877-021-02656-2 **Authors:** Pigott, Jennifer S.; Kane, Edward J.; Ambler, Gareth; Walters, Kate and Schrag, Anette

Background: Parkinson's disease is a complex neurodegenerative condition with significant impact on quality of life (QoL), wellbeing and function. The objective of this review is to evaluate the clinical effectiveness of self-management interventions for people with Parkinson's disease, taking a broad view of self-management and considering effects on QoL, wellbeing and function.

Methods: Systematic searches of four databases (MEDLINE, Embase, PsycINFO, Web of Science) were conducted for studies evaluating self-management interventions for people with Parkinson's disease published up to 16th November 2020. Original quantitative studies of adults with idiopathic Parkinson's disease were included, whilst studies of atypical Parkinsonism were excluded. Full-text articles were independently assessed by two reviewers, with data extracted by one reviewer and reliability checked by a second reviewer, then synthesised through a narrative approach and, for sufficiently similar studies, a meta-analysis of effect size was conducted (using a random-effects meta-analysis with restricted maximum likelihood method pooled estimate). Interventions were subdivided into self-management components according to PRISMS Taxonomy. Risk of bias was examined with the Cochrane Risk of Bias 2 (RoB2) tool or ROBIN-I tool as appropriate.

Results: Thirty-six studies were included, evaluating a diverse array of interventions and encompassing a range of study designs (RCT n = 19; non-randomised CT n = five; within subject pre- and post-intervention comparisons n = 12). A total of 2884 participants were assessed in studies across ten countries, with greatest output from North America (14 studies) and UK (six studies). Risk of bias was moderate to high for the majority of studies, mostly due to lack of participant blinding, which is not often practical for interventions of this nature. Only four studies reported statistically significant improvements in QoL, wellbeing or functional outcomes for the intervention compared to controls. These interventions were group-based self-management education and training programmes, either alone, combined with multi-disciplinary rehabilitation, or combined with Cognitive Behaviour Therapy; and a self-guided community-based exercise programme. Four of the RCTs evaluated sufficiently similar interventions and outcomes for meta-analysis: these were studies of selfmanagement education and training programmes evaluating QoL (n = 478). Meta-analysis demonstrated no significant difference between the self-management and the control groups with a standardised mean difference (Hedges g) of - 0.17 (- 0.56, 0.21) p = 0.38. By the GRADE approach, the quality of this evidence was deemed "very low" and the effect of the intervention is therefore uncertain. Components more frequently observed in effective interventions, as per PRISMS taxonomy analysis, were: information about resources; training or rehearsing psychological strategies; social support; and lifestyle advice and support. The applicability of these findings is weakened by the ambiguous and at times overlapping nature of self-management components.

Conclusion: Approaches and outcomes to self-management interventions in Parkinson's disease are heterogenous. There are insufficient high quality RCTs in this field to show effectiveness of self-management interventions in Parkinson's disease. Whilst it is not possible to draw conclusions on specific intervention components that convey effectiveness, there are promising findings from some studies, which could be targeted in future evaluations. Copyright © 2022. The Author(s).

Title: Adaptive deep brain stimulation: Retuning Parkinson's disease

Citation: Handbook of Clinical Neurology 184, pp. 273-284, 2022, DOI: https://libkey.io/https://dx.doi.org/10.1016/B978-0-12-819410-2.00015-1 **Authors:** Pozzi, Nicolo G. and Isaias, Ioannis U.

Abstract: A brain-machine interface represents a promising therapeutic avenue for the treatment of many neurologic conditions. Deep brain stimulation (DBS) is an invasive, neuro-modulatory tool that can improve different neurologic disorders by delivering electric stimulation to selected brain areas. DBS is particularly successful in advanced Parkinson's disease (PD), where it allows sustained improvement of motor symptoms. However, this approach is still poorly standardized, with variable clinical outcomes. To achieve an optimal therapeutic effect, novel adaptive DBS (aDBS) systems are being developed. These devices operate by adapting stimulation parameters in response to an input signal that can represent symptoms, motor activity, or other behavioral features. Emerging evidence suggests greater efficacy with fewer adverse effects during aDBS compared with conventional DBS. We address this topic by discussing the basics principles of aDBS, reviewing current evidence, and tackling the many challenges posed by aDBS for PD. Copyright © 2022 Elsevier B.V. All rights reserved.

Title: New approaches to treatments for sleep, pain and autonomic failure in Parkinson's disease - Pharmacological therapies

Citation: Neuropharmacology 208, pp. 108959, May 01 2022, DOI: https://libkey.io/https://dx.doi.org/10.1016/j.neuropharm.2022.108959 **Authors:** Rukavina, Katarina; Batzu, Lucia; Leta, Valentina and Chaudhuri, K. Ray

Abstract: Non-motor symptoms (NMSs) are highly prevalent throughout the course of Parkinson's disease (PD). Pain, autonomic dysfunction and sleep disturbances remain at the forefront of the most common NMSs; their treatment is challenging and their effect on the quality of life of both patients and caregivers detrimental. Yet, the landscape of clinical trials in PD is still dominated by therapeutic strategies seeking to ameliorate motor symptoms; subsequently, effective strategies to successfully treat NMSs remain a huge unmet need. Wider awareness among industry and researchers is thus essential to give rise to development and delivery of high-quality, large-scale clinical trials in enriched populations of patients with PD-related pain, autonomic dysfunction and sleep. In this review, we discuss recent developments in the field of pharmacological treatment strategies designed or repurposed to target three key NMSs: pain, autonomic dysfunction and sleep disturbances.

We focus on emerging evidence from recent clinical trials and outline some exciting and intriguing findings that call for further investigations. This article is part of the Special Issue on 'New therapeutic approaches to Parkinson's disease'. Copyright © 2022 Elsevier Ltd. All rights reserved.

Title: Gastrointestinal Dysfunction in Parkinson's Disease

Citation: Drugs 82(2), pp. 169-197, Feb 2022, DOI: https://libkey.io/https://dx.doi.org/10.1007/s40265-021-01664-1 **Authors:** Safarpour, Delaram; Sharzehi, Kaveh and Pfeiffer, Ronald F.

Abstract: There has been exponential growth in the awareness and understanding of gastrointestinal (GI) dysfunction in Parkinson's disease (PD) over the past 3 decades. The clinical features of GI dysfunction in PD have been clearly identified and innovative research has demonstrated the presence of pathology within the enteric nervous system (ENS) in individuals with PD, leading to suggestions that the GI system may be ground zero for the genesis and the portal of entry of PD pathology, which then ascends via the vagus nerve to the central nervous system (CNS). This theory, as well as the more recent recognition of the association of PD with dysbiosis within the gut microbiota, has been the object of intense study and scrutiny. Since most PD medications are absorbed through the GI system, the need for better understanding of changes within the GI tract that may potentially affect the pattern of response to medications has become evident. In this review, current knowledge of the pathophysiology of changes within the GI tract and the gut microbiome of individuals with PD, including changes that occur with progression of the disease, will be addressed. We focus on common clinical GI problems in PD that can arise from different segments of the GI tract. Relevant diagnostic evaluations and treatment options for each of these problems will be reviewed. Copyright © 2022. The Author(s), under exclusive licence to Springer Nature Switzerland AG.

Title: The effects of virtual reality training in stroke and Parkinson's disease rehabilitation: a systematic review and a perspective on usability

Citation: European Reviews of Aging & Physical Activity 19(1), pp. 4, Jan 25 2022, DOI: https://libkey.io/https://dx.doi.org/10.1186/s11556-022-00283-3 **Authors:** Sevcenko, Ksenija and Lindgren, Ingrid

Background: Virtual Reality (VR) training is emerging in the neurorehabilitation field. Technological advancement is often faster than clinical implementation. Previous reviews stressed the study design and methodological weaknesses of research in the field of VR for neurorehabilitation. Clinically relevant conclusions on implementation in particular patient groups are needed. The aim was to update the existing knowledge with the recent evidence on the effects of VR training on functional ability of patients with stroke and Parkinson's Disease (PD). Secondary objective was to analyze the aspects of usability of VR intervention in these populations.

Methods: Systematic literature search (via PubMed, CENTRAL) was conducted from inception to February 29, 2020 to identify suitable articles for two population subcategories. Randomized controlled trials published from 2016 to 2020, investigating the effectiveness of VR on a variety of outcomes contributing to the functional independence were included. Critical Appraisal Skills Programme (CASP) checklist was used for a methodological quality assessment of the primary studies. Given the heterogeneity in types of VR intervention and outcomes, a descriptive synthesis was conducted.

Results: A total of 18 randomized controlled trials were included (10 in stroke subcategory, 8 in PD). CASP grading ranged 9-11, suggesting high methodological quality. All studies concluded that overall VR might be as effective as the conventional training, but more

motivating. In some studies, VR was found to have a greater effect, taking the high response to treatment and satisfaction into account.

Conclusions: VR training is suggested as an effective intervention to improve the functional ability in stroke and PD patients. Addition of VR into a rehabilitation program might facilitate patient's motivation, participation and improvement, as this method was generally well accepted, and the results of trials were promising. The consideration of disorder-specific aspects should take place during the decision-making of VR implementation. Copyright © 2022. The Author(s).

Title: Force Platform-Based Intervention Program for Individuals Suffering with Neurodegenerative Diseases like Parkinson.

Citation: Computational & Mathematical Methods in Medicine 2022, pp. 1636263, 2022, DOI: https://libkey.io/https://dx.doi.org/10.1155/2022/1636263 **Authors:** Ujjan, Javed Ahmed; Morani, William; Memon, Naz; Mohanasundaram, Sugumar; Nuhmani, Shibili and Singh, Bhupesh Kumar

Abstract: The term "neurodegenerative disease" refers to a set of illnesses that primarily affect brain's neurons. Substantia nigra (a midbrain dopaminergic nucleus) with lack of hormone called dopamine causes Parkinson's disease (PD), a neurological disorder. PD leads to tremor, stiffness, impaired posture and balance, and loss of automatic movements. Patient with Parkinson's often develops a parkinsonian gait that includes a tendency to lean forward, small quick steps as if hurrying forward, and reduced swinging of the arms. They also may have trouble initiating or continuing movement. Gait analysis is often used to diagnose neurodegenerative illnesses and determine their stage. In this study, we attempt to investigate postural balance, and of gait signals for Parkinson's patients, also, we incorporate interim rehabilitation technique. We included 25 PD patients who had 2.5 to 3 IV score of Hoehn and Yahr scale. A ten-minute walk test has been performed to observe primary and secondary results of dual task interference on gait velocities, and gait time motion vector for right and left legs was observed. Two experimental ground conditions include three conditions of trunk alignment, that is, erect on a regular basis (RE), trunk dorsiflexion 30degree (TF1), and trunk dorsiflexion 50degree (TF2) were analysed. We identified the walking speed of PD patients was decreased, and trunk dorsiflexion variables influence the gait pattern of Parkinson's disease patients, where higher 95% CI for TF1 condition was reported. The regular erect trunk showed swing time reduction (0.7%) in PD, so the higher unified PD rating scale (UPDRS) values have significant difference in swing phase time in Parkinson's patients. The average Hoehn and Yahr scale (H&Y scale) was 4.3 +/- 2.5 reported in the study participants. In a 10-week follow-up evaluation, the stance duration was shown to be substantial, as was the slower speed gait in the baseline condition. Excessive flexion was discovered in our investigation at the lower limb joints, particularly the knee and ankle. Patients with Parkinson's disease had similar maximum dorsiflexion and minimum plantarflexion values in stance. The trunk fraction conditions were found significant in patients after rehabilitation training. The best response to rehabilitation treatment was seen when the trunk was rotated. When steps and posture distribution analysis performed, we found that the trunk flexure 1 (p p Copyright © 2022 Javed Ahmed Ujjan et al.

Title: Peri-operative management of patients with Parkinson's disease

Citation: Anaesthesia 77(Suppl 1), pp. 123-133, Jan 2022, DOI: <u>https://libkey.io/https://dx.doi.org/10.1111/anae.15617</u> Authors: Yim, R. L. H.;Leung, K. M. M.;Poon, C. C. M. and Irwin, M. G. **Abstract:** Patients with Parkinson's disease are at higher risk of peri-operative medical and surgical complications. Multidisciplinary management, early recognition of potential complications, specialised care of medications and intra-operative protection of the vulnerable brain are all important aspects of the peri-operative management of patients with Parkinson's disease. Advances in continuous dopaminergic treatment, development of a peri-operative Parkinson's disease pathway and application of telemedicine are starting to play a role in improving peri-operative care. Management of patients with advanced Parkinson's disease is also evolving, with potential for incorporation of integrated care and changes in the anaesthetic management for deep brain stimulation surgery. There are new methods for localisation of target nuclei and increasing insight on the effects of anaesthetic drugs on microelectrode recordings and clinical outcomes. Parkinson's disease is a progressive disease, but management is improving with better peri-operative care for patients. Copyright © 2022 Association of Anaesthetists.

Title: Mining imaging and clinical data with machine learning approaches for the diagnosis and early detection of Parkinson's disease

Citation: Npj Parkinsons Disease 8(1), pp. 13, Jan 21 2022, DOI: https://libkey.io/https://dx.doi.org/10.1038/s41531-021-00266-8 Authors: Zhang, Jing

Abstract: Parkinson's disease (PD) is a common, progressive, and currently incurable neurodegenerative movement disorder. The diagnosis of PD is challenging, especially in the differential diagnosis of parkinsonism and in early PD detection. Due to the advantages of machine learning such as learning complex data patterns and making inferences for individuals, machine-learning techniques have been increasingly applied to the diagnosis of PD, and have shown some promising results. Machine-learning-based imaging applications have made it possible to help differentiate parkinsonism and detect PD at early stages automatically in a number of neuroimaging studies. Comparative studies have shown that machine-learning-based SPECT image analysis applications in PD have outperformed conventional semi-quantitative analysis in detecting PD-associated dopaminergic degeneration, performed comparably well as experts' visual inspection, and helped improve PD diagnostic accuracy of radiologists. Using combined multi-modal (imaging and clinical) data in these applications may further enhance PD diagnosis and early detection. To integrate machine-learning-based diagnostic applications into clinical systems, further validation and optimization of these applications are needed to make them accurate and reliable. It is anticipated that machine-learning techniques will further help improve differential diagnosis of parkinsonism and early detection of PD, which may reduce the error rate of PD diagnosis and help detect PD at pre-motor stage to make it possible for early treatments (e.g., neuroprotective treatment) to slow down PD progression, prevent severe motor symptoms from emerging, and relieve patients from suffering. Copyright © 2022. The Author(s).

Title: Healthcare professionals' involvement in breaking bad news to newly diagnosed patients with motor neurodegenerative conditions: a qualitative study.

Citation: Disability and Rehabilitation , pp. 1-14, 2021, DOI: https://libkey.io/https://dx.doi.org/10.1080/09638288.2021.2002436 **Authors:** Anestis, E.; Eccles, F. J. R.; Fletcher, I.; Triliva, S. and Simpson, J.

Purpose: Research on breaking bad news (BBN) in healthcare has mostly focused on the doctor-patient interaction during a single consultation. However, it has been increasingly recognised that BBN is a wider process that also involves other healthcare professionals.

This qualitative study explored non-medical1 healthcare professionals' involvement in BBN to newly diagnosed patients with motor neurodegenerative conditions in the UK.

Materials and Methods: 19 healthcare professionals working with people with motor neurone disease, multiple sclerosis, Parkinson's disease or Huntington's disease took part in individual, semi-structured interviews which were analysed using thematic analysis.

Result(s): Four themes were constructed: dealing with the diagnostic aftermath, unpacking the diagnosis, breaking bad news as a balancing act and empowering patients to regain control over their health and lives. Participants reported being broadly involved in BBN by supporting patients with negative diagnostic experiences, re-iterating diagnostic information and helping patients understand the impact of their condition. The challenges of effectively breaking bad news and how these difficult conversations could help empower patients were also emphasised.

Conclusion(s): BBN was a critical and challenging aspect of healthcare professionals' clinical work with newly diagnosed patients with motor neurodegenerative conditions. Besides providing information, BBN was perceived as a way to educate patients, encourage them to make decisions and prepare for the future.

Implications For Rehabilitation: Breaking bad news is a potentially under-recognised but significant aspect in the neurorehabilitation of neurodegenerative conditions. Listening to patients' stories about a long and occasionally unsatisfactory diagnostic journey and allowing them to express their frustration can be critical in regaining patients' trust and building a relationship with them. Newly diagnosed patients have not always received adequate information about their condition at diagnosis or they might have not understood or retained that information. It is, therefore, essential that patients' understanding of their condition is assessed, misconceptions are cleared and appropriate information about the nature and impact of the diagnosis is provided. Irrespective of the length of experience, breaking bad news was perceived as a multi-faceted, challenging, stressful and emotionally demanding task. Formal support and specialised training on breaking the bad news that addresses the incurable, unpredictable and progressive nature of motor neurodegenerative conditions could help professionals with this challenging task.

Title: High frequency of psychosis in late-stage Parkinsons disease.

Citation: Clinical Parkinsonism & Related Disorders 5, pp. 100119, 2021, DOI: https://libkey.io/https://dx.doi.org/10.1016/j.prdoa.2021.100119 **Authors:** Chendo, Ines; Fabbri, Margherita; Godinho, Catarina; Moiron Simoes, Rita; Severiano Sousa, Catarina; Coelho, Miguel; Voon, Valerie and Ferreira, Joaquim J.

Background: Psychosis is a frequent non-motor symptom in Parkinson's disease (PD). Estimates of the frequency of Parkinsons disease psychosis (PDP) vary widely. Knowledge about the frequency and phenomenology of psychosis in late-stage (LS) PD patients is limited. This study aimed to determine the frequency of psychosis in LSPD patients through clinical diagnostic interview (CDI) (gold standard), according to NINDS/NIMH diagnostic criteria for PDP. The secondary objectives were to characterize the phenomenology, to test selected instruments and assess their adequacy in comparison to CDI, and to assess the psychiatric comorbidities.

Methods: A cross-sectional study including LSPD patients (patients with >= 7 years from symptoms onset and Hoehn and Yahr scale score > 3 or a Schwab and England scale score Copyright © 2021 The Author(s).

Title: Recent advances in preventing neurodegenerative diseases

Citation: Faculty Reviews 10, pp. 81, 2021, DOI: https://libkey.io/https://dx.doi.org/10.12703/r/10-81 **Authors:** Chou, Shih-Ching; Aggarwal, Akanksha; Dawson, Valina L.; Dawson, Ted M. and Kam, Tae-In

Abstract: The worldwide health-care burden of neurodegenerative diseases is on the rise-a crisis created through a combination of increased caseload and lack of effective treatments. The limitations of pharmacotherapy in these disorders have led to an urgent shift toward research and clinical trials for the development of novel compounds, interventions, and methods that target shared features across the spectrum of neurodegenerative diseases. Research targets include neuronal cell death, mitochondrial dysfunction, protein aggregation, and neuroinflammation. In the past few years, there has been a growth in understanding of the pathophysiologic mechanisms of neurodegenerative disorders such as Alzheimer's disease, Parkinson's disease, amyotrophic lateral sclerosis, multiple sclerosis, and Huntington's disease. This increase in knowledge has led to the discovery of numerous novel neuroprotective therapeutic targets. In this context, we reviewed and summarized recent advancements in neuroprotective strategies in neurodegenerative diseases. Copyright: © 2021 Dawson TM et al.

Title: Machine Learning Identifies Six Genetic Variants and Alterations in the Heart Atrial Appendage as Key Contributors to PD Risk Predictivity.

Citation: Frontiers in Genetics 12, pp. 785436, 2021, DOI: https://libkey.io/https://dx.doi.org/10.3389/fgene.2021.785436 **Authors:** Ho, Daniel; Schierding, William; Farrow, Sophie L.; Cooper, Antony A.; Kempa-Liehr, Andreas W. and O'Sullivan, Justin M.

Abstract: Parkinson's disease (PD) is a complex neurodegenerative disease with a range of causes and clinical presentations. Over 76 genetic loci (comprising 90 SNPs) have been associated with PD by the most recent GWAS meta-analysis. Most of these PD-associated variants are located in non-coding regions of the genome and it is difficult to understand what they are doing and how they contribute to the aetiology of PD. We hypothesised that PD-associated genetic variants modulate disease risk through tissue-specific expression quantitative trait loci (eQTL) effects. We developed and validated a machine learning approach that integrated tissue-specific eQTL data on known PD-associated genetic variants with PD case and control genotypes from the Wellcome Trust Case Control Consortium. In so doing, our analysis ranked the tissue-specific transcription effects for PD-associated genetic variants and estimated their relative contributions to PD risk. We identified roles for SNPs that are connected with INPP5P, CNTN1, GBA and SNCA in PD. Ranking the variants and tissue-specific eQTL effects contributing most to the machine learning model suggested a key role in the risk of developing PD for two variants (rs7617877 and rs6808178) and eQTL associated transcriptional changes of EAF1-AS1 within the heart atrial appendage. Similarly, effects associated with eQTLs located within the Brain Cerebellum were also recognized to confer major PD risk. These findings were replicated in two additional. independent cohorts (the UK Biobank, and NeuroX) and thus warrant further mechanistic investigations to determine if these transcriptional changes could act as early contributors to PD risk and disease development. Copyright © 2022 Ho, Schierding, Farrow, Cooper, Kempa-Liehr and O'Sullivan.

Title: The Gut-Brain Axis and Its Relation to Parkinson's Disease: A Review

Citation: Frontiers in Aging Neuroscience 13, pp. 782082, 2021, DOI: https://libkey.io/https://dx.doi.org/10.3389/fnagi.2021.782082 **Authors:** Klann, Emily M.; Dissanayake, Upuli; Gurrala, Anjela; Farrer, Matthew; Shukla, Aparna Wagle; Ramirez-Zamora, Adolfo;Mai, Volker and Vedam-Mai, Vinata **Abstract:** Parkinson's disease is a chronic neurodegenerative disease characterized by the accumulation of misfolded alpha-synuclein protein (Lewy bodies) in dopaminergic neurons of the substantia nigra and other related circuitry, which contribute to the development of both motor (bradykinesia, tremors, stiffness, abnormal gait) and non-motor symptoms (gastrointestinal issues, urinogenital complications, olfaction dysfunction, cognitive impairment). Despite tremendous progress in the field, the exact pathways and mechanisms responsible for the initiation and progression of this disease remain unclear. However, recent research suggests a potential relationship between the commensal gut bacteria and the brain capable of influencing neurodevelopment, brain function and health. This bidirectional communication is often referred to as the microbiome-gut-brain axis. Accumulating evidence suggests that the onset of non-motor symptoms, such as gastrointestinal manifestations, often precede the onset of motor symptoms and disease diagnosis, lending support to the potential role that the microbiome-gut-brain axis might play in the underlying pathological mechanisms of Parkinson's disease. This review will provide an overview of and critically discuss the current knowledge of the relationship between the gut microbiota and Parkinson's disease. We will discuss the role of alpha-synuclein in non-motor disease pathology, proposed pathways constituting the connection between the gut microbiome and the brain, existing evidence related to pre- and probiotic interventions. Finally, we will highlight the potential opportunity for the development of novel preventative measures and therapeutic options that could target the microbiome-gut-brain axis in the context of Parkinson's disease. Copyright © 2022 Klann, Dissanayake, Gurrala, Farrer, Shukla, Ramirez-Zamora, Mai and Vedam-Mai.

Title: Systematic Review on Parkinson's Disease Medications, Emphasizing on Three Recently Approved Drugs to Control Parkinson's Symptoms

Citation: International Journal of Environmental Research & Public Health,19(1), pp. 12 30, 2021, DOI: https://libkey.io/https://dx.doi.org/10.3390/ijerph19010364 **Authors:** Sivanandy, Palanisamy; Leey, Tan Choo; Xiang, Tan Chi; Ling, Tan Chi; Wey Han, Sean Ang; Semilan, Samantha Lia Anak and Hong, Phoon Kok

Abstract: Parkinson's Disease (PD) is a disease that involves neurodegeneration and is characterised by the motor symptoms which include muscle rigidity, tremor, and bradykinesia. Other non-motor symptoms include pain, depression, anxiety, and psychosis. This disease affects up to ten million people worldwide. The pathophysiology behind PD is due to the neurodegeneration of the nigrostriatal pathway. There are many conventional drugs used in the treatment of PD. However, there are limitations associated with conventional drugs. For instance, levodopa is associated with the on-off phenomenon, and it may induce wearing off as time progresses. Therefore, this review aimed to analyze the newly approved drugs by the United States-Food and Drug Administration (US-FDA) from 2016-2019 as the adjuvant therapy for the treatment of PD symptoms in terms of efficacy and safety. The new drugs include safinamide, istradefylline and pimavanserin. From this review, safinamide is considered to be more efficacious and safer as the adjunct therapy to levodopa as compared to istradefylline in controlling the motor symptoms. In Study 016, both safinamide 50 mg (p = 0.0138) and 100 mg (p = 0.0006) have improved the Unified Parkinson's Disease Rating Scale (UPDRS) part III score as compared to placebo. Improvement in Clinical Global Impression-Change (CGI-C), Clinical Global Impression-Severity of Illness (CGI-S) and off time were also seen in both groups of patients following the morning levodopa dose. Pimavanserin also showed favorable effects in ameliorating the symptoms of Parkinson's Disease Psychosis (PDP). A combination of conventional therapy and non-pharmacological treatment is warranted to enhance the well-being of PD patients.

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

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