

Parkinson's Disease Current Awareness Bulletin January 2023

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

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

Publication Date: 2022

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

Abstract: Background: Tremor is one of the most prevalent symptoms in Parkinson's Disease (PD). The progression and management of tremor in PD can be challenging, as response to dopaminergic agents might be relatively poor, particularly in patients with tremor-dominant PD compared to the akinetic/rigid subtype. In this review, we aim to highlight recent advances in the underlying pathogenesis and treatment modalities for tremor in PD. Methods: A structured literature search through Embase was conducted using the terms "Parkinson's Disease" AND "tremor" OR "etiology" OR "management" OR "drug resistance" OR "therapy" OR "rehabilitation" OR "surgery." After initial screening, eligible articles were selected with a focus on published literature in the last 10 years. Discussion: The underlying pathophysiology of tremor in PD remains complex and incompletely understood. Neurodegeneration of dopaminergic neurons in the retrorubral area, in addition to high-power neural oscillations in the cerebello-thalamo-cortical circuit and the basal ganglia, play a major role. Levodopa is the first-line therapeutic option for all motor symptoms, including tremor. The addition of dopamine agonists or anticholinergics can lead to further tremor reduction. Botulinum toxin injection is an effective alternative for patients with pharmacological-resistant tremor who are not seeking advanced therapies. Deep brain stimulation is the most well-established advanced therapy owing to its long-term efficacy. reversibility, and effectiveness in other motor symptoms and fluctuations. Magnetic resonance-guided focused ultrasound is a promising modality, which has the advantage of being incisionless. Cortical and peripheral electrical stimulation are non-invasive innovatory techniques that have demonstrated good efficacy in suppressing intractable tremor. Copyright: © 2022 The Author(s).

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

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

Publication Date: 2022

Journal: Geriatric Nursing 48, pp. 258-268

Abstract: BACKGROUND: Parkinson's disease (PD) can interfere with individuals' social functioning and lead to social withdrawal. Social withdrawal may result in negative outcomes for persons with PD and their caregivers, such as decreased quality of life. It is necessary to understand the nature of social withdrawal in PD in order to develop strategies to address this issue and prevent negative outcomes. OBJECTIVE: The purpose of this scoping review was to synthesize existing evidence regarding social withdrawal in PD. METHODS: We searched PubMed, CINAHL, and PsycINFO for studies of social withdrawal in individuals living with PD. Findings were organized according to study characteristics, measurement and description of social withdrawal, prevalence, associated factors, and interventions. RESULTS: Fifty-eight studies were included. We found that persons with PD reduced social activities voluntarily and involuntarily, and social withdrawal was related to various factors including physical, cognitive, and psychiatric symptoms and perceived stigma. Community-based social activity programs appeared to improve social participation. Few studies employed longitudinal methods or tested interventions to reduce social withdrawal. CONCLUSIONS: Social withdrawal is associated with various negative outcomes in PD,

though more research is needed to understand the true scope of this problem. Limitations in social withdrawal research include vague conceptualization and methodological limitations (i.e., instrumentation and study design), as well as a paucity of interventional studies. The findings of this review can be used to guide hypothesis generation and future study design, with the ultimate goal of mitigating social withdrawal and improving quality of life for people with PD. Copyright © 2022 The Authors. Published by Elsevier Inc. All rights reserved.

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

Authors: Bashir, Yasir and Khan, Asad U.

Publication Date: 2022

Journal: Frontiers in Neuroscience 16, pp. 1030694

Abstract: What is the effect of our gut microbial flora on brain? Does the gut microbiome have any role in the causation of psychiatric and neurodegenerative diseases? Does the effect of gut microbiota traverse the gut-brain axis? Questions like these have captured the interest and imagination of the scientific community for guite some time now. Research in the guest for answers to these guestions, to unravel the potential role of the microbiota inhabiting the gut in controlling brain functions, has progressed manifold over the last two decades. Although the possibility of microbiome as a key susceptibility factor for neurological disorders viz. Parkinson's disease, Alzheimer's disease, multiple sclerosis, and autism spectrum disorder has bolstered by an increase in the clinical and preclinical evidence, the field is still in its infancy. Given the fact that the diversity of the gut microbiota is affected by various factors including the diet and exercise, the interpretation of such data becomes all the more difficult. Also, such studies have been mostly conducted on animal models, so there is a need for randomized controlled trials in human subjects, corroborated by longitudinal studies, to establish if modulating the gut microbiota can unravel novel therapeutic interventions. Exploring the genomic, metagenomic and metabolomic data from clinical subjects with psychiatric and neurological diseases can prove to be a helpful guide in individual treatment selection. Copyright © 2022 Bashir and Khan.

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

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

Publication Date: 2022

Journal: JAMA Neurology

Abstract: Importance: Recent studies have highlighted an association between epilepsy and Parkinson disease (PD). The role of antiepileptic drugs (AEDs) has not been explored. Objective: To investigate the association between AEDs and incident PD. Design, Setting, and Participants: This nested case-control study started collecting data from the UK Biobank (UKB) in 2006, and data were extracted on June 30, 2021. Individuals with linked primary care prescription data were included. Cases were defined as individuals with a Hospital Episode Statistics (HES)-coded diagnosis of PD. Controls were matched 6:1 for age, sex, race and ethnicity, and socioeconomic status. Prescription records were searched for AEDs prescribed prior to diagnosis of PD. The UKB is a longitudinal cohort study with more than

500000 participants: 45% of individuals in the UKB have linked primary care prescription data. Participants living in the UK aged between 40 and 69 years were recruited to the UKB between 2006 and 2010. All participants with UKB-linked primary care prescription data (n = 222106) were eligible for enrollment in the study. Individuals with only a self-reported PD diagnosis or missing data for the matching variables were excluded. In total, 1477 individuals were excluded; 49 were excluded due to having only self-reported PD, and 1428 were excluded due to missing data. Exposures: Exposure to AEDs (carbamazepine, lamotrigine, levetiracetam, and sodium valproate) was defined using routinely collected prescription data derived from primary care. Main Outcomes and Measures: Odd ratios and 95% CIs were calculated using adjusted logistic regression models for individuals prescribed AEDs before the first date of HES-coded diagnosis of PD. Results: In this case-control study, there were 1433 individuals with an HES-coded PD diagnosis (cases) and 8598 controls in the analysis. Of the 1433 individuals, 873 (60.9%) were male, 1397 (97.5%) had their race and ethnicity recorded as White, and their median age was 71 years (IQR, 65-75 years). An association was found between AED prescriptions and incident PD (odds ratio, 1.80; 95% CI, 1.35-2.40). There was a trend for a greater number of prescription issues and multiple AEDs being associated with a greater risk of PD. Conclusions and Relevance: This study, the first to systematically look at PD risk in individuals prescribed the most common AEDs, to our knowledge, found evidence of an association between AEDs and incident PD. With the recent literature demonstrating an association between epilepsy and PD, this study provides further insights.

5. Cannabidiol for neurodegenerative disorders: A comprehensive review

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

Publication Date: 2022

Journal: Frontiers in Pharmacology 13, pp. 989717

Abstract: Despite the significant advances in neurology, the cure for neurodegenerative conditions remains a formidable task to date. Among various factors arising from the complex etiology of neurodegenerative diseases, neuroinflammation and oxidative stress play a major role in pathogenesis. To this end, some phytocannabinoids isolated from Cannabis sativa (widely known as marijuana) have attracted significant attention as potential neurotherapeutics. The profound effect of 9-tetrahydrocannabinol (THC), the major psychoactive component of cannabis, has led to the discovery of the endocannabinoid system as a molecular target in the central nervous system (CNS). Cannabidiol (CBD), the major non-psychoactive component of cannabis, has recently emerged as a potential prototype for neuroprotective drug development due to its antioxidant and anti-inflammatory properties and its well-tolerated pharmacological behavior. This review briefly discusses the role of inflammation and oxidative stress in neurodegeneration and demonstrates the neuroprotective effect of cannabidiol, highlighting its general mechanism of action and disease-specific pathways in Parkinson's disease (PD) and Alzheimer's disease (AD). Furthermore, we have summarized the preclinical and clinical findings on the therapeutic promise of CBD in PD and AD, shed light on the importance of determining its therapeutic window, and provide insights into identifying promising new research directions. Copyright © 2022 Bhunia, Kolishetti, Arias, Vashist and Nair.

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

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

Publication Date: 2022

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

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

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

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

Publication Date: 2022

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

Abstract: Introduction: Deep brain stimulation (DBS) of the subthalamic nucleus (STN) is effective for the treatment of Parkinson's disease (PD). Moreover, remote programming is widely used in Mainland China. This necessitates evaluating the ability of remote programming to achieve the ideal postoperative effect. Therefore, we aimed to retrospectively evaluate the effects of different programming modes on the effectiveness of STN-DBS 12 months postoperatively in patients with PD. Methods: Clinical data were collected retrospectively, before and 12 months after surgery, in 83 patients with PD. Based on the programming modes voluntarily selected by the patients during 12 months postoperatively, they were divided into three groups, namely remote programming alone, hospital programming alone, and hospital + remote programming. We compared the programming data and the effects of different programming methods on STN-DBS-related improvements 12 months postoperatively among these groups. Furthermore, we analyzed STN-DBS-related improvements at 12 months postoperatively in 76 patients. Results: The effectiveness of STN-DBS was not influenced by the three programming modes. The postoperative Movement Disorder Society Unified Parkinson's Disease Rating Scale scores did not reveal statistically significant differences between the remote alone and hospital alone programming groups, except for motor examination. The postoperative decline in the

levodopa equivalent daily dose was most apparent in the hospital programming alone group. The programming frequency of the hospital + remote programming group was considerably higher than that of the remaining groups. Seventy-six patients with PD displayed good STN-DBS surgical efficacy. Conclusion: Programming modes do not influence the short-term efficacy of STN-DBS, and remote programming can yield a satisfactory surgical effect. Copyright © 2022 Chen, Xu, Li, Chen, Li, Xu, Yang and Liu.

8. Neuropathic Pain in Parkinson's Disease

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

Publication Date: 2022

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

Abstract: Pain is a well-recognized and important non-motor manifestation in Parkinson disease (PD). Painful or unpleasant sensations in PD can be classified as musculoskeletal, dystonia, akathisia, radicular, and central or primary pain; the last two are associated with neuropathic pain. Particularly, neuropathic pain in PD has not been fully clarified; therefore, it goes somewhat unnoticed, and the affected patients do not receive adequate pain treatment. The main purpose of this literature review was to identify the incidence of neuropathic pain in PD and the involvement of dopamine of this type of pain by the integration of different lines of investigation. In this review, a search was conducted using PubMed, ProQuest, EBSCO, Medline, EMBASE, and the Science Citation index for studies evaluating pain in patients with PD. The inclusion criteria were as follows: original articles that evaluated incidence and possible mechanism of neuropathic, central, and radicular pain in PD. Nine studies related to the incidence of neuropathic pain in PD suggest the activation of cerebral areas, such as the cortex, striatum, amygdala, thalamus, raphe nuclei, and locus coeruleus. Neuropathic pain is related to altered levels of dopamine, serotonin, and norepinephrine; these neurotransmitters are related to the sensitive and emotional dimensions of pain. Dopamine could cause hypersensitivity to pain, either indirectly through modulatory effects on affective pain processing and/or directly by affecting the neural activity in key areas of the brain that modulate pain. A considerable proportion of patients with PD suffer neuropathic pain; however, it has been disregarded, this has led to an inability to achieve an adequate treatment and a decrease in pain to improve the quality of life of these patients. We consider that neuropathic pain in PD is possibly induced by neurophysiological changes due to the degradation of dopaminergic neurons.

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

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

Publication Date: 2022

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

Abstract: Parkinson's disease (PD) results in progressively worsening gait and balance dysfunction that can be measured using computerized devices. We utilized the longitudinal

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

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

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

Publication Date: 2022

Journal: Frontiers in Aging Neuroscience 14, pp. 1023574

Abstract: The heterogeneity of Parkinson's disease (PD) has been recognized since its description by James Parkinson over 200 years ago. The complexity of motor and non-motor PD manifestations has led to many attempts of PD subtyping with different prognostic outcomes; however, the pathophysiological foundations of PD heterogeneity remain elusive. Genetic contributions to PD may be informative in understanding the underpinnings of PD subtypes. As such, recognizing genotype-phenotype associations may be crucial for successful gene therapy. We review the state of knowledge on the genetic architecture underlying PD subtypes, discussing the monogenic forms, as well as oligo- and polygenic risk factors associated with various PD subtypes. Based on our review, we argue for the unification of PD subtyping classifications, the dichotomy of studies on genetic factors and genetic modifiers of PD, and replication of results from previous studies. Copyright © 2022 Dulski, Uitti, Ross and Wszolek.

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

Authors: Fearon, Conor and Fasano, Alfonso

Publication Date: 2022

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

Abstract: The global explosion of COVID-19 necessitated the rapid dissemination of information regarding SARS-CoV-2. Hence, COVID-19 prevalence and outcome data in Parkinson's disease patients were disseminated at a time when we only had part of the

picture. In this chapter we firstly discuss the current literature on the prevalence of COVID-19 in people with PD. We then discuss outcomes from COVID-19 in people with PD, specifically risk of hospitalization and mortality. Finally, we discuss specific contributing and confounding factors which may put PD patients at higher or lower risk from COVID-19. Copyright © 2022 Elsevier Inc. All rights reserved.

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

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

Publication Date: 2022

Journal: Journal of Basic & Clinical Physiology & Pharmacology

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

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

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

Publication Date: 2022

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

Abstract: INTRODUCTION: Exploring the potential of exercise in the rehabilitation process of patients with Parkinson's (PD) may be an interesting treatment perspective. Exercise-

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

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

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

Publication Date: 2022

Journal: BMJ Supportive & Palliative Care

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

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

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

Publication Date: 2022

Journal: Frontiers in Rehabilitation Sciences 3, pp. 873216

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

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

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

Publication Date: 2022

Journal: Frontiers in Surgery 9, pp. 863921

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

17. Cerebellar deep brain stimulation for movement disorders

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

Publication Date: 2022

Journal: Neurobiology of Disease 175, pp. 105899

Abstract: Deep brain stimulation (DBS) conventionally target at basal ganglia or thalamic structures, modulating nodal points in the cortico-basal ganglia circuit, in order to effectively treat various movement disorders, including Parkinson's disease, tremor and dystonia (especially mobile type dystonia). However, there are still some other movement disorders, such as dystonia (especially fixed type dystonia), ataxia and freezing of gait, which are not responding well to the current DBS therapy. Cerebellum, similar to basal ganglia, also plays a critical role in the pathophysiology of movement disorders. Deep cerebellar structures, such as dentate nucleus or superior cerebellar peduncle, are noticed for their potential role as treatment targets in movement disorders in recent years. With increasing evidences of animal DBS experiments, recent clinical human subject studies reported that some movement disorders patients not responding to DBS with conventional targets, may benefit significantly from cerebellar DBS. These pioneer study results are invaluable for understanding the clinical use of cerebellar DBS for treatment of movement disorders. We review the recent data of cerebellar DBS performed by different groups and summarize the indications, surgical targets, programming details and outcomes in these clinical reports. We then synthesize the current pathophysiological study of cerebellum on different movement disorders and discuss the potential mechanism of action of cerebellar DBS. In addition to basal ganglia, it is important to study new DBS targets in the cerebellum for more comprehensive treatment of movement disorders. Copyright © 2022 The Authors. Published by Elsevier Inc. All rights reserved.

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

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

Publication Date: 2022

Journal: Journal of Parkinsons Disease Print

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

19. Interactions between gut microbiota and Parkinson's disease: The role of microbiota-derived amino acid metabolism

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

Publication Date: 2022

Journal: Frontiers in Aging Neuroscience 14, pp. 976316

Abstract: Non-motor symptoms (NMS) of Parkinson's disease (PD), such as constipation. sleep disorders, and olfactory deficits, may emerge up to 20 years earlier than motor symptoms. A series of evidence indicates that the pathology of PD may occur from the gastrointestinal tract to the brain. Numerous studies support that the gut microbiota communicates with the brain through the immune system, special amino acid metabolism, and the nervous system in PD. Recently, there is growing recognition that the gut microbiota plays a vital role in the modulation of multiple neurochemical pathways via the "gut microbiota-brain axis" (GMBA). Many gut microbiota metabolites, such as fatty acids, amino acids, and bile acids, convey signaling functions as they mediate the crosstalk between gut microbiota and host physiology. Amino acids' abundance and species alteration, including glutamate and tryptophan, may disturb the signaling transmission between nerve cells and disrupt the normal basal ganglia function in PD. Specific amino acids and their receptors are considered new potential targets for ameliorating PD. The present study aimed to systematically summarize all available evidence on the gut microbiota-derived amino acid metabolism alterations associated with PD. Copyright © 2022 Wang, Jiang, Xu, Tang, Liang, Zhao and Zhu.

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

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

Publication Date: 2022

Journal: Frontiers in Molecular Neuroscience 15, pp. 1039302

Abstract: The research and clinical applications of exercise therapy to the treatment of Parkinson's disease (PD) are increasing. Pain is among the important symptoms affecting the daily motor function and quality of life of PD patients. This paper reviewed the progress of research on different exercise therapies for the management of pain caused by PD and described the role and mechanism of exercise therapy for pain relief. Aerobic exercise, strength exercise, and mind-body exercise play an effective role in pain management in PD patients. The pain suffered by PD patients is divided into central neuropathic, peripheral neuropathic, and nociceptive pain. Different types of pain may coexist with different mechanistic backgrounds and treatments. The analgesic mechanisms of exercise intervention in PD-induced pain include altered cortical excitability and synaptic plasticity, the attenuation of neuronal apoptosis, and dopaminergic and non-dopaminergic analgesic pathways, as well as the inhibition of oxidative stress. Current studies related to exercise interventions for PD-induced pain suffer from small sample sizes and inadequate research of analgesic mechanisms. The neurophysiological effects of exercise, such as neuroplasticity, attenuation of neuronal apoptosis, and dopaminergic analgesic pathway provide a sound biological mechanism for using exercise in pain management. However, large, well-designed randomized controlled trials with improved methods and reporting are needed to evaluate the long-term efficacy and cost-effectiveness of exercise therapy for PD pain. Copyright © 2022 Yu, Yang and Wang.

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

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

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

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

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

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

Sources Used:

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