

Parkinson's disease Current Awareness Bulletin

August 2022

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1. Parkinson's Disease and SARS-CoV-2 Infection: Particularities of Molecular and Cellular Mechanisms Regarding Pathogenesis and Treatment

Item Type: Journal Article

Authors: Anghelescu, Aurelian; Onose, Gelu; Popescu, Cristina; Baila, Mihai; Stoica, Simona Isabelle; Postoiu, Ruxandra; Bruma, Elena; Petcu, Irina Raluca; Ciobanu, Vlad and Munteanu, Constantin

Publication Date: Apr 26 ,2022

Journal: Biomedicines 10(5)

Abstract: Accumulating data suggest that chronic neuroinflammation-mediated neurodegeneration is a significant contributing factor for progressive neuronal and glial cell death in age-related neurodegenerative pathology. Furthermore, it could be encountered as long-term consequences in some viral infections, including post-COVID-19 Parkinsonism-related chronic sequelae. The current systematic review is focused on a recent question aroused during the pandemic's successive waves: are there post-SARS-CoV-2 immune-mediated reactions responsible for promoting neurodegeneration? Does the host's dysregulated immune counter-offensive contribute to the pathogenesis of neurodegenerative diseases, emerging as Parkinson's disease, in a complex interrelation between genetic and epigenetic risk factors? A synthetic and systematic literature review was accomplished based on the "Preferred Reporting Items for Systematic Principles Reviews and Meta-Analyses" (PRISMA) methodology, including registration on the specific online platform: International prospective register of systematic reviews-PROSPERO, no. 312183. Initially, 1894 articles were detected. After fulfilling the five steps of the selection methodology, 104 papers were selected for this synthetic review. Documentation was enhanced with a supplementary 47 bibliographic resources identified in the literature within a non-standardized search connected to the subject. As a final step of the PRISMA method, we have fulfilled a Population-Intervention-Comparison-Outcome-Time (PICOT)/Population-Intervention-Comparison-Outcome-Study type (PICOS)-based metanalysis of clinical trials identified as connected to our search, targeting the outcomes of rehabilitative kinesitherapeutic interventions compared to clinical approaches lacking such kind of treatment. Accordingly, we identified 10 clinical trials related to our article. The multi/interdisciplinary conventional therapy of Parkinson's disease and non-conventional multitarget approach to an integrative treatment was briefly analyzed. This article synthesizes the current findings on the pathogenic interference between the dysregulated complex mechanisms involved in aging, neuroinflammation, and neurodegeneration, focusing on Parkinson's disease and the acute and chronic repercussions of COVID-19. Time will tell whether COVID-19 neuroinflammatory events could trigger long-term neurodegenerative effects and contribute to the worsening and/or explosion of new cases of PD. The extent of the interrelated neuropathogenic phenomenon remains obscure, so further clinical observations and prospective longitudinal cohort studies are needed.

2. A qualitative examination of apathy and physical activity in Huntington's and Parkinson's disease

Item Type: Journal Article

Authors: Atkins, Kelly J.;Friel, Ciarán P.;Andrews, Sophie C.;Chong, Trevor T. - J;Stout, Julie C. and Quinn, Lori

Publication Date: 2022

Journal: Neurodegenerative Disease Management 12(3), pp. 129-139

Abstract: Aim: In Huntington's disease (HD) and Parkinson's disease (PD), apathy is a frequently cited barrier to participation in physical activity. Current diagnostic criteria emphasize dissociable variants of apathy that differentially affect goal-directed behavior. How these dimensions present and affect physical activity in HD and PD is unknown. Methods: Using a qualitative approach, we examined the experience of apathy and its impact on physical activity in 20 people with early-manifest HD or idiopathic PD. Results: Two major themes emerged: the multidimensionality of apathy, including initiation or goal-identification difficulties, and the interplay of apathy and fatigue; and facilitators of physical activity, including routines, safe environments and education. Conclusion: Physical activity interventions tailored to apathy phenotypes may maximize participant engagement.

3. Bipolar Spectrum disorders in Parkinson's disease: a systematic evaluation

Item Type: Journal Article

Authors: Bacciardi, Silvia;Elefante, Camilla;Brancati, Giulio Emilio;Mazzucchi, Sonia;Del Prete, Eleonora;Frosini, Daniela;Maremmanni, Icro;Lattanzi, Lorenzo;Ceravolo, Roberto;Bonuccelli, Ubaldo and Perugi, Giulio

Publication Date: 2022

Journal: CNS Spectrums: The International Journal of Neuropsychiatric Medicine 27(3), pp. 355-361

Abstract: Objective: Psychiatric disorders are very common in patients affected by Parkinson's disease (PD). However, comorbidity with Bipolar Spectrum disorders is understudied. The aim of this study is to explore the clinical correlates of PD associated with Bipolar Spectrum disorders. Methods: One hundred PD patients were screened for psychiatric comorbidities, cognitive profile, motor, and non-motor symptoms. The sample was divided into three groups: PD-patients with Bipolar Spectrum disorders (bipolar disorder type I, type II, and spontaneous or induced hypomania; N = 32), PD-patients with others psychiatric comorbidities (N = 39), PD-patients without psychiatric comorbidities (N = 29). Clinical features were compared among the groups using analysis of variance and chi-square test. A logistic regression was performed to evaluate the association between Bipolar Spectrum disorders and early onset of PD (≤ 50 years) controlling for lifetime antipsychotic use. Results: In comparison with PD patients with and without other psychiatric comorbidity, subjects affected by Bipolar Spectrum disorders were younger, showed more frequently an early onset PD, reported more involuntary movements and a higher rate of impulse control disorders and compulsive behaviors. No differences were observed in indexes of exposure to dopamine agonist treatments. The early onset of PD was predicted by Bipolar Spectrum comorbidity, independently from lifetime antipsychotic use. Conclusion: Bipolar Spectrum disorders are common in early onset PD. The presence of bipolar comorbidity

could identify a particular subtype of PD, showing higher rates of neurological and psychiatric complications and deserving further investigation.

4. Prodromal depression and subsequent risk of developing Parkinson's disease: a systematic review with meta-analysis

Item Type: Journal Article

Authors: Bareeqa, Syeda Beenish;Samar, Syeda Sana;Kamal, Sufiyan;Masood, Yasir;Allahyar;Ahmed, Syed Ijlal and Hayat, Ghazala

Publication Date: 2022

Journal: Neurodegenerative Disease Management 12(3), pp. 155-164

Abstract: Aim: Parkinson's disease (PD) is a progressive neurological disorder that predominately affects dopaminergic neurons. We believe that this pooling of data will help to better understand the prodromal nature of depression in PD. Materials & methods: We conducted this study in accordance with PRISMA guidelines 2020. Fifteen eligible articles were shortlisted for final analysis. Risk of bias assessment was also conducted Results: The random-effect model revealed that the risk of subsequent PD in patients with prodromal depression was twice as likely (odds ratio, 2.04; 95% CI, 1.02-4.08) as compared with a healthy population. Conclusion: Our meta-analysis concluded that the subsequent risk of PD is significantly higher in patients with depression as compared with healthy individuals.; plain-language-summary Parkinson's disease (PD) is a nervous system disease that predominantly affects neurons of the brain that controls voluntary movement and behavioral processes such as mood, reward, addiction and stress. There is a wide spectrum of problems that can present in patients with PD, however, there are few that can precede the beginning of the illness. Previous studies have evaluated the relation of psychiatric symptoms with PD. However, many aspects need to be studied to understand this relationship. The main emphasis of this systemic review is to establish the association of prodromal depression before the development of PD. Our study showed that there is a strong association between depression and PD and suggests an increased risk of developing PD in formerly depressed patients. Though, it is still unclear if depression is either an early prodromal symptom of PD or a causative risk factor for PD and warrants further studies to determine the causality relationship between the two. Language: English

5. Association of Motor and Nonmotor Symptoms With Health-Related Quality of Life in a Large Online Cohort of People With Parkinson Disease

Item Type: Journal Article

Authors: Bock, Meredith A.;Brown, Ethan G.;Zhang, Li and Tanner, Caroline

Publication Date: 2022

Journal: Neurology 98(22), pp. e2194-e2203

Abstract: Background and Objectives: There is growing interest in health-related quality of life (HRQOL) as a comprehensive view of the patient's well-being, guiding concept for the treating clinician, and therapeutic trial outcome measure for patients with

Parkinson disease (PwPD). The key determinants of HRQOL have not been investigated in large populations of PwPD. Our objective was to evaluate correlates of HRQOL in a large, online cohort of PwPD. **Methods:** As part of an ongoing online cohort study, we performed a cross-sectional analysis at enrollment of 23,058 PwPD. We conducted univariate and stepwise multivariate linear regression analyses of HRQOL as measured by the EQ-5D-5L tool. In addition, we performed an interaction analysis to evaluate heterogeneity of the effect of motor symptoms on HRQOL and Spearman correlation analysis to evaluate the association of nonmotor symptoms with HRQOL. **Results:** In the multivariate linear regression model, participants with moderate or severe depression, more severe motor symptoms, and a higher burden of medical comorbidities had the most substantially decreased HRQOL as measured by the EQ index (β -0.11, -0.18, -0.02, -0.01, respectively; $p < 0.001$ for all). An interaction analysis showed that more severe motor symptoms had a higher effect on individuals with female sex, lower educational level, lower income, more severe depression, or more severe cognitive impairment ($p \leq 0.01$ for interaction terms). Neuropsychiatric symptoms and falls had the most negative associations with HRQOL (ρ -0.31 to 0.37; $p < 0.0001$). **Discussion:** Potentially treatable motor and nonmotor symptoms, particularly neuropsychiatric symptoms, account for a large amount of the variation in HRQOL in PwPD. Motor symptoms may have differential effects on HRQOL in different demographic and clinical subpopulations, highlighting important areas for future health disparities research. Our findings provide targets for clinician intervention and future research on symptom management to optimize HRQOL in PD. **Classification Of Evidence:** This study provides Class II evidence that motor and neuropsychiatric symptoms are associated with HRQOL in PwPD.

6. A Novel Machine Learning Algorithm Predicts Dementia With Lewy Bodies Versus Parkinson's Disease Dementia Based on Clinical and Neuropsychological Scores

Item Type: Journal Article

Authors: Bougea, Anastasia;Efthymiopoulou, Efthymia;Spanou, Ioanna and Zikos, Panagiotis

Publication Date: 2022

Journal: Journal of Geriatric Psychiatry & Neurology 35(3), pp. 317-320

Abstract: **Objective:** Our aim was to develop a machine learning algorithm based only on non-invasively clinic collectable predictors, for the accurate diagnosis of these disorders. **Methods:** This is an ongoing prospective cohort study (ClinicalTrials.gov identifier NCT number NCT04448340) of 78 PDD and 62 DLB subjects whose diagnostic follow-up is available for at least 3 years after the baseline assessment. We used predictors such as clinico-demographic characteristics, 6 neuropsychological tests (mini mental, PD Cognitive Rating Scale, Brief Visuospatial Memory test, Symbol digit written, Wechsler adult intelligence scale, trail making A and B). We investigated logistic regression, K-Nearest Neighbors (K-NNs) Support Vector Machine (SVM), Naïve Bayes classifier, and Ensemble Model for their ability to predict successfully PDD or DLB diagnosis. **Results:** The K-NN classification model had an accuracy 91.2% of overall cases based on 15 best clinical and cognitive scores achieving 96.42% sensitivity and 81% specificity on discriminating between DLB and PDD. The binomial logistic regression classification model achieved an accuracy of 87.5% based on 15 best features, showing 93.93% sensitivity and 87% specificity. The SVM classification model had an accuracy 84.6% of overall cases based on 15 best features achieving 90.62%

sensitivity and 78.58% specificity. A model created on Naïve Bayes classification had 82.05% accuracy, 93.10% sensitivity and 74.41% specificity. Finally, an Ensemble model, synthesized by the individual ones, achieved 89.74% accuracy, 93.75% sensitivity and 85.73% specificity. Conclusion: Machine learning method predicted with high accuracy, sensitivity and specificity PDD or DLB diagnosis based on non-invasively and easily in-the-clinic and neuropsychological tests.

7. Cost-effectiveness analysis of the Parkinson's KinetiGraph and clinical assessment in the management of Parkinson's disease.

Item Type: Journal Article

Authors: Chaudhuri, K. Ray;Hand, Annette;Obam, Fallon and Belsey, Jonathan

Publication Date: 2022

Journal: Journal of Medical Economics 25(1), pp. 774-782

Abstract: AIMS: The Parkinson's KinetiGraph (PKG) is a wrist-worn movement recording system that collates continuous, objective, data during daily activities in people with Parkinson's disease (PD) providing a report for clinicians. This study explores the cost-effectiveness of adding the PKG to routine PD assessments. METHODS: A de novo Markov model of three health states: uncontrolled, controlled and death compared PKG plus routine assessment by a Movement Disease Specialist (MDS) versus routine assessment. Uncontrolled and controlled states were based on the Movement Disorder Society - Unified Parkinson's Disease Rating Scale (MDS-UPDRS) II and III scores. The transition between health states was dependent on improvement in MDS-UPDRS II and III, and transition to death state on all cause-mortality and PD-specific relative mortality risk. Markov cycle length was yearly beyond year 1 and lifetime horizon 22 years. LIMITATIONS: PKG evidence incorporated in this analysis is based on findings from one clinical trial. Health state utilities were mapped and the probability of patients progressing from uncontrolled to controlled health state at the second visit and beyond was derived from a bootstrap method which assumed a normal distribution for MDS-UPDRS. RESULTS: The addition of the PKG to usual PD assessments is a cost-effective intervention. PKG plus routine assessment is associated with lower total costs compared to routine assessment (141,950 versus 159,312) and improved quality-adjusted life years (7.88 versus 7.61), resulting in an incremental cost-effectiveness ratio of -64,978.99 and a net monetary benefit of 22,706.37 using a 20,000 threshold. Results were robust across sensitivity and scenario analyses. CONCLUSIONS: Management of PD involves monitoring and evaluation of symptoms to assess disease progression and ensure appropriate treatment choices. Adding the PKG to clinical assessment in routine care allows for improved and objective identification of PD motor symptoms which can be used in clinical decision making to improve patient outcomes.; plain-language-summary Hospital doctors caring for people with Parkinson's disease (PwP) regularly monitor and assess their patients' symptoms, relying on patient recall and patient-completed diaries to find out about current symptoms, which can be unreliable. The Parkinson's KinetiGraph (PKG) is a wrist-worn device that collects continuous information on movement in PwP. A report is then provided to the patient's Consultant helping them to understand the PwP's symptoms and make decisions about changing medication to improve symptom control. An economic model compared asking patients to wear a PKG device for 6 days before their check-up appointment with their Consultant with usual check-up without the PKG. Information from a clinical trial exploring the use of PKG provided data on Movement

Disorder Society - Unified Parkinson's Disease Rating Scale (MDS-UPDRS) II and III scores, which were used in the model to predict improvements in quality of life and whether PwP had controlled or uncontrolled disease. The model showed that addition of PKG to usual check-ups is a cost-effective approach. Use of the PKG reduced costs (141,950 versus 159,312 for usual check-ups) and had a positive impact on quality and quantity of life as measured by quality adjusted life years (7.88 versus 7.61). This study shows that adding the PKG to routine check-ups allows Consultants to accurately assess movement (or motor) symptoms in PwP, which can then be used to ensure optimal medication choice and improve patient outcomes. Language: English

8. Acute effect of traditional and adaptive metronomes on gait variability in older individuals with a history of falls

Item Type: Journal Article

Authors: Cronström, Anna; Cole, Michael H.; Chalkley, Daniel; Van Andel, Steven; Pepping, Gert-Jan and Creaby, Mark W.

Publication Date: 2022

Journal: Aging Clinical & Experimental Research 34(6), pp. 1349-1356

Abstract: Background: Metronome cueing has been shown to reduce gait variability and thereby potentially reduce falls risk in individuals with Parkinson's disease. It is unclear however, if metronome cueing has a similar effect in healthy older adults with a history of falls. Aim: To investigate whether a traditional and/or an adaptive metronome, based on an individual's gait pattern, were effective in reducing gait variability in older adults with a history of falls. Methods: Twenty older adults (15 women, 71 ± 4.9 years) with a history of falls were included in this cross-over study. Participants received two types of cueing (adaptive and traditional metronome) 1 week apart. The variability of the participants' stride time, stride length, walking speed and duration of double leg support were recorded during three walking conditions (baseline, during feedback and post-feedback gait). Repeated-measures ANOVA was used to assess the possible effects of the two cueing strategies on gait variables. Results: Compared with the baseline condition, participants had significantly increased stride time variability during feedback ($F(2) = 9.83, p < 0.001$) and decreased double leg support time variability post-feedback ($F(2) 3.69, p = 0.034$). Increased stride time variability was observed with the adaptive metronome in comparison to the traditional metronome. Conclusion: Metronome cueing strategies may reduce double leg support variability in older adults with a history of falls but seem to increase stride time variability. Further studies are needed to investigate if metronome cueing is more beneficial for individuals with greater baseline gait variability than those included in the current study.

9. Recent Trends and Practices Toward Assessment and Rehabilitation of Neurodegenerative Disorders: Insights From Human Gait

Item Type: Journal Article

Authors: Das, Ratan; Paul, Sudip; Mourya, Gajendra Kumar; Kumar, Neelesh and Hussain, Masaraf

Publication Date: 2022

Journal: Frontiers in Neuroscience 16, pp. 859298

Abstract: The study of human movement and biomechanics forms an integral part of various clinical assessments and provides valuable information toward diagnosing neurodegenerative disorders where the motor symptoms predominate. Conventional gait and postural balance analysis techniques like force platforms, motion cameras, etc., are complex, expensive equipment requiring specialist operators, thereby posing a significant challenge toward translation to the clinics. The current manuscript presents an overview and relevant literature summarizing the umbrella of factors associated with neurodegenerative disorder management: from the pathogenesis and motor symptoms of commonly occurring disorders to current alternate practices toward its quantification and mitigation. This article reviews recent advances in technologies and methodologies for managing important neurodegenerative gait and balance disorders, emphasizing assessment and rehabilitation/assistance. The review predominantly focuses on the application of inertial sensors toward various facets of gait analysis, including event detection, spatiotemporal gait parameter measurement, estimation of joint kinematics, and postural balance analysis. In addition, the use of other sensing principles such as foot-force interaction measurement, electromyography techniques, electrogoniometers, force-myography, ultrasonic, piezoelectric, and microphone sensors has also been explored. The review also examined the commercially available wearable gait analysis systems. Additionally, a summary of recent progress in therapeutic approaches, viz., wearables, virtual reality (VR), and phytochemical compounds, has also been presented, explicitly targeting the neuro-motor and functional impairments associated with these disorders. Efforts toward therapeutic and functional rehabilitation through VR, wearables, and different phytochemical compounds are presented using recent examples of research across the commonly occurring neurodegenerative conditions [viz., Parkinson's disease (PD), Alzheimer's disease (AD), multiple sclerosis, Huntington's disease (HD), and amyotrophic lateral sclerosis (ALS)]. Studies exploring the potential role of Phyto compounds in mitigating commonly associated neurodegenerative pathologies such as mitochondrial dysfunction, alpha-synuclein accumulation, imbalance of free radicals, etc., are also discussed in breadth. Parameters such as joint angles, plantar pressure, and muscle force can be measured using portable and wearable sensors like accelerometers, gyroscopes, footswitches, force sensors, etc. Kinetic foot insoles and inertial measurement tools are widely explored for studying kinematic and kinetic parameters associated with gait. With advanced correlation algorithms and extensive RCTs, such measurement techniques can be an effective clinical and home-based monitoring and rehabilitation tool for neuro-impaired gait. As evident from the present literature, although the vast majority of works reported are not clinically and extensively validated to derive a firm conclusion about the effectiveness of such techniques, wearable sensors present a promising impact toward dealing with neurodegenerative motor disorders. Copyright © 2022 Das, Paul, Mourya, Kumar and Hussain.

10. **Non-Invasive Neuromodulation in the Rehabilitation of Pisa Syndrome in Parkinson's Disease: A Randomized Controlled Trial.**

Item Type: Journal Article

Authors: De Icco, Roberto;Putorti, Alessia;Allena, Marta;Avenali, Micol;Dagna, Carlotta;Martinelli, Daniele;Cristina, Silvano;Grillo, Valentina;Fresia, Mauro;Bitetto, Vito;Cosentino, Giuseppe;Valentino, Francesca;Alfonsi, Enrico;Sandrini, Giorgio;Pisani,

Antonio and Tassorelli, Cristina

Publication Date: 2022

Journal: Frontiers in Neurology [Electronic Resource] 13, pp. 849820

Abstract: Background: Pisa syndrome (PS) is a frequent postural complication of Parkinson's disease (PD). PS poorly responds to anti-parkinsonian drugs and the improvement achieved with neurorehabilitation tends to fade in 6 months or less. Transcranial direct current stimulation (t-DCS) is a non-invasive neuromodulation technique that showed promising results in improving specific symptoms in different movement disorders. Objectives: This study aimed to evaluate the role of bi-hemispheric t-DCS as an add-on to a standardized hospital rehabilitation program in the management of PS in PD. Methods: This study included 28 patients with PD and PS (21 men, aged 72.9 +/- 5.1 years) who underwent a 4-week intensive neurorehabilitation treatment and were randomized to receive: i) t-DCS (t-DCS group, n = 13) for 5 daily sessions (20 min-2 mA) with bi-hemispheric stimulation over the primary motor cortex (M1), or ii) sham stimulation (sham group, n = 15) with the same duration and cadence. At baseline (T0), end of rehabilitation (T1), and 6 months later (T2) patients were evaluated with both trunk kinematic analysis and clinical scales, including UPDRS-III, Functional Independence Measure (FIM), and Numerical Rating Scale for lumbar pain. Results: When compared to the sham group, the t-DCS group achieved a more pronounced improvement in several variables: overall posture (p = 0.014), lateral trunk inclination (p = 0.013) during upright standing position, total range of motion of the trunk (p = 0.012), FIM score (p = 0.048), and lumbar pain intensity (p = 0.017). Conclusions: Our data support the use of neuromodulation with t-DCS as an add-on to neurorehabilitation for the treatment of patients affected by PS in PD. Copyright © 2022 De Icco, Putorti, Allena, Avenali, Dagna, Martinelli, Cristina, Grillo, Fresia, Bitetto, Cosentino, Valentino, Alfonsi, Sandrini, Pisani and Tassorelli.

11. Personalized Care in Late-Stage Parkinson's Disease: Challenges and Opportunities

Item Type: Journal Article

Authors: Fabbri, Margherita;Coelho, Miguel;Garon, Michela;Biundo, Roberta;Mestre, Tiago A.;Antonini, Angelo and On Behalf Of iCARE-Pd Consortium

Publication Date: May 18 ,2022

Journal: Journal of Personalized Medicine 12(5)

Abstract: Late-stage Parkinson's disease (LSPD) patients are highly dependent on activities of daily living and require significant medical needs. In LSPD, there is a significant caregiver burden and greater health economic impact compared to earlier PD stages. The clinical presentation in LSPD is dominated by motor and non-motor symptoms (NMS) that most of the time have a sub-optimal to no response to dopaminergic treatment, especially when dementia is present. Non-pharmacological interventions, including physiotherapy, cognitive stimulation, speech, occupational therapy, and a specialized PD nurse, assume a key role in LSPD to mitigate the impact of disease milestones or prevent acute clinical worsening and optimize the management of troublesome NMS. However, the feasibility of these approaches is limited by patients' cognitive impairment and the difficulty in delivering care at home. The present care challenge for LSPD is the ability to offer a person-centered, home-delivered palliative

care model based on Advanced Care Planning. An ongoing European multicentric project, PD_Pal, aims to address this challenge.

12. Dysregulated miRNAs as Biomarkers and Therapeutical Targets in Neurodegenerative Diseases

Item Type: Journal Article

Authors: Gentile, Giulia;Morello, Giovanna;La Cognata, Valentina;Guarnaccia, Maria;Conforti, Francesca Luisa and Cavallaro, Sebastiano

Publication Date: May 10 ,2022

Journal: Journal of Personalized Medicine 12(5)

Abstract: Alzheimer's disease (AD), Parkinson's disease (PD), and Amyotrophic Lateral Sclerosis (ALS) are representative neurodegenerative diseases (NDs) characterized by degeneration of selective neurons, as well as the lack of effective biomarkers and therapeutic treatments. In the last decade, microRNAs (miRNAs) have gained considerable interest in diagnostics and therapy of NDs, owing to their aberrant expression and their ability to target multiple molecules and pathways. Here, we provide an overview of dysregulated miRNAs in fluids (blood or cerebrospinal fluid) and nervous tissue of AD, PD, and ALS patients. By emphasizing those that are commonly dysregulated in these NDs, we highlight their potential role as biomarkers or therapeutical targets and describe the use of antisense oligonucleotides as miRNA therapies.

13. Brain-Derived Neurotrophic Factor in Neurodegenerative Disorders

Item Type: Journal Article

Authors: Ibrahim, Abdallah Mohammad;Chauhan, Lalita;Bhardwaj, Aditi;Sharma, Anjali;Fayaz, Faizana;Kumar, Bhumi;Alhashmi, Mohamed;AlHajri, Noora;Alam, Md Sabir and Pottou, Faheem Hyder

Publication Date: May 16 ,2022

Journal: Biomedicines 10(5)

Abstract: Globally, neurodegenerative diseases cause a significant degree of disability and distress. Brain-derived neurotrophic factor (BDNF), primarily found in the brain, has a substantial role in the development and maintenance of various nerve roles and is associated with the family of neurotrophins, including neuronal growth factor (NGF), neurotrophin-3 (NT-3) and neurotrophin-4/5 (NT-4/5). BDNF has affinity with tropomyosin receptor kinase B (TrkB), which is found in the brain in large amounts and is expressed in several cells. Several studies have shown that decrease in BDNF causes an imbalance in neuronal functioning and survival. Moreover, BDNF has several important roles, such as improving synaptic plasticity and contributing to long-lasting memory formation. BDNF has been linked to the pathology of the most common neurodegenerative disorders, such as Alzheimer's and Parkinson's disease. This review aims to describe recent efforts to understand the connection between the level of BDNF and neurodegenerative diseases. Several studies have shown that a high level of BDNF is associated with a lower risk for developing a neurodegenerative disease.

14. Effect of Exercise and Rehabilitation Therapy on Risk of Hospitalization in Parkinson's Disease.

Item Type: Journal Article

Authors: Kannarkat, George T.;Rafferty, Miriam R.;Luo, Sheng;Liu, Hongliang and Mills, Kelly A.

Publication Date: May ,2022

Journal: Movement Disorders Clinical Practice 9(4), pp. 494-500

Abstract: Background: Exercise and physical therapy (PT) can improve motor function and quality of life in individuals with Parkinson's disease (PD), but their role in hospitalization avoidance is not well-studied. Objectives: To determine the longitudinal and temporal association of exercise and PT use with hospital encounter. Methods: Longitudinal regression and chi2 analyses were performed on Parkinson's Foundation Parkinson's Outcome Project exercise and PT use data from 4674 and 9259 persons with PD, respectively. Results: Greater exercise duration and intensity were associated with reduced odds of hospital encounter, whereas both PT and occupational therapy use were associated with increased odds. In the 2 years before a hospital encounter, there was an increased frequency of PT use, but not reductions in exercise. Conclusions: Consistent exercise may reduce hospitalization risk whereas PT referral may identify at-risk individuals without preventing this outcome. Further work to incentivize consistent exercise in PD may reduce healthcare use. Copyright © 2022 International Parkinson and Movement Disorder Society.

15. Associations of Sleep Disorders With Depressive Symptoms in Early and Prodromal Parkinson's Disease

Item Type: Journal Article

Authors: Ma, Jiangnan;Dou, Kaixin;Liu, Ruize;Liao, Yajin;Yuan, Zengqiang and Xie, Anmu

Publication Date: 2022

Journal: Frontiers in Aging Neuroscience 14, pp. 1-13

Abstract: Background: Non-motor symptoms, including sleep disorders and depression, are common in Parkinson's disease (PD). The purpose of our study is to explore the effect of sleep disorders, including the probable rapid eye movement (REM) sleep behavior disorder (pRBD) and the daytime sleepiness, on depressive symptoms in patients with early and prodromal PD. Methods: A total of 683 participants who obtained from the Parkinson Progression Markers Initiative (PPMI) were included, consisting of 423 individuals with early PD, 64 individuals with prodromal PD, and 196 healthy controls (HCs), who were followed up to 5 years from baseline. Multiple linear regression models and linear mixed-effects models were conducted to explore the relationship between sleep disorders and depression at baseline and longitudinally,

respectively. Multiple linear regression models were used to further investigate the association between the change rates of daytime sleepiness score and depression-related score. Mediation analyses were also performed. Results: At baseline analysis, individuals with early and prodromal PD, who had higher RBD screening questionnaire (RBDSQ) score, or who were considered as pRBD, or who manifested specific behaviors of RBD (things falling down when sleep or disturbance of sleep), showed significantly the higher score of depression-related questionnaires. Our 5-year follow-up study showed that sleep disorders, including pRBD and daytime sleepiness, were associated with the increased depressive-related score in individuals with early and prodromal PD. Interestingly, we also found that the increased possibilities of daytime sleepiness were associated with depressive-related score. Finally, mediation analysis demonstrated that the relationship between RBD and depressive symptoms was partially mediated by autonomic symptoms, such as postural hypertension, salivation, dysphagia, and constipation. Conclusion: Our study shows that sleep disorders, including pRBD and daytime sleepiness, are associated with depression at baseline and longitudinally, which is partially mediated by the autonomic dysfunction in early and prodromal PD, with an implication that sleep management is of great value for disease surveillance.

16. Neuropsychiatric Symptoms in Clinically Defined Parkinson's Disease: An Updated Review of Literature

Item Type: Journal Article

Authors: Macias-Garcia, Paloma; Rashid-Lopez, Raul; Cruz-Gomez, Alvaro J.; Lozano-Soto, Elena; Sanmartino, Florencia; Espinosa-Rosso, Raul and Gonzalez-Rosa, Javier J.

Publication Date: 2022

Journal: Behavioural Neurology 2022, pp. 1213393

Abstract: Background: Neuropsychiatric symptoms (NPS) are a common and potentially serious manifestation of Parkinson's disease (PD) but are frequently overlooked in favor of a focus on motor symptomatology. Here, we conducted a literature review of the prevalence and type of NPS experienced by PD patients with a clinically defined course of their illness. Methods: We identified reports of NPS in patients with PD and mean disease duration over 3 years. Three databases-PubMed, Scopus, and Dialnet-were searched for relevant literature published between 2010 and 2020. Predefined exclusion criteria were applied prior to a descriptive analysis of the literature base. Results: In all, 87 unique reports were identified and 30 met inclusion and exclusion criteria. These included 7142 patients with PD (male: 67.3%; mean age: 66.2 years; mean disease duration: 6.7 years). The most frequent NPS were mood disorders (apathy, depression, and anxiety), psychosis, and impulse control disorders (ICD). Treatment with dopamine agonists was identified as an important risk factor for ICD. Co-occurrence of NPS and cognitive dysfunction was also evidenced in a number of studies. Patients with more significant cognitive deficits and higher levels of NPS appeared to be of older age with a longer disease duration and to have more severe motor symptoms. Conclusions: NPS, most commonly mood disorders (apathy, depression, and anxiety), psychosis, and ICDs are frequent manifestations of PD. The results of this review reflect the need to develop unified validated assessment protocols for NPS in PD, as well as to improve their management in clinical practice. Copyright © 2022 Paloma Macias-Garcia et al.

17. Parkinson's Disease Drug Therapies in the Clinical Trial Pipeline: 2022 Update

Item Type: Journal Article

Authors: McFarthing, Kevin;Rafaloff, Gary;Baptista, Marco;Mursaleen, Leah;Fuest, Rosie;Wyse, Richard K. and Stott, Simon R. W.

Publication Date: 2022

Journal: Journal of Parkinsons Disease Print 12(4), pp. 1073-1082

Abstract: BACKGROUND: As the international community dealt with the ongoing COVID-19 pandemic, important progress continued to be made in the development of new drug-based therapies for the neurodegenerative condition of Parkinson's disease (PD) in 2021. This progress included both "symptomatic treatments" (ST - improves/reduces symptoms of the condition) and "disease modifying treatments" (DMT - attempts to delay/slow progression by addressing the underlying biology of PD), which can be categorised further based on their mechanisms of action and class of drug. OBJECTIVE: This report continues previous efforts to provide an overview of the pharmacological therapies - both ST and DMT - in clinical trials for PD during 2021-2022, with the aim of creating greater awareness and involvement in the clinical trial process. We also hope to stimulate collaboration amongst all stakeholders, including industry, academia, advocacy organizations, and most importantly patient community. METHODS: We conducted a review of clinical trials of drug therapies for PD using trial data obtained from the ClinicalTrials.gov and World Health Organisation (WHO) registries, and performed a breakdown analysis of studies that were active as of January 31st 2022. We also assessed active drug development projects that had completed one clinical phase but were yet to start the next. RESULTS: There was a total of 147 clinical trials registered on the ClinicalTrials.gov website as active during the period of analysis. Of these trials, 91 (62%)were investigating STs, while 56 (38%)focused on DMTs. Approximately 1/3 of the studies (34.7%; 51 trials) were in Phase 1, while over half of the trials were in Phase 2 (50.3%; 74 trials). Only 15% (22 trials) of the studies were in Phase 3, of which only 3 trials were evaluating DMTs. Novel therapeutics (42%)were the most common type of agents being tested across all phases of testing, followed by repurposed agents (34%)and reformulations (20%). CONCLUSION: Despite significant global health constraints, the development of new drug-based therapies for PD continued in 2021. Hopefully with a shift towards a post-pandemic world in which COVID-19 is better managed, we will see an increase in the number of clinical trials focused on drug development for PD. The need for more Phase 3 studies for DMTs remains acute.

18. Role of SARS-CoV-2 in Modifying Neurodegenerative Processes in Parkinson's Disease: A Narrative Review

Item Type: Journal Article

Authors: Morowitz, Jeremy M.;Pogson, Kaylyn B.;Roque, Daniel A. and Church, Frank C.

Publication Date: Apr 22 ,2022

Journal: Brain Sciences 12(5)

Abstract: The COVID-19 pandemic, caused by SARS-CoV-2, continues to impact global health regarding both morbidity and mortality. Although SARS-CoV-2 primarily causes acute respiratory distress syndrome (ARDS), the virus interacts with and influences other organs and tissues, including blood vessel endothelium, heart, gastrointestinal tract, and brain. We are learning much about the pathophysiology of SARS-CoV-2 infection; however, we are just beginning to study and understand the long-term and chronic health consequences. Since the pandemic's beginning in late 2019, older adults, those with pre-existing illnesses, or both, have an increased risk of contracting COVID-19 and developing severe COVID-19. Furthermore, older adults are also more likely to develop the neurodegenerative disorder Parkinson's disease (PD), with advanced age as the most significant risk factor. Thus, does SARS-CoV-2 potentially influence, promote, or accelerate the development of PD in older adults? Our initial focus was aimed at understanding SARS-CoV-2 pathophysiology and the connection to neurodegenerative disorders. We then completed a literature review to assess the relationship between PD and COVID-19. We described potential molecular and cellular pathways that indicate dopaminergic neurons are susceptible, both directly and indirectly, to SARS-CoV-2 infection. We concluded that under certain pathological circumstances, in vulnerable persons-with-Parkinson's disease (PwP), SARS-CoV-2 acts as a neurodegenerative enhancer to potentially support the development or progression of PD and its related motor and non-motor symptoms.

19. Novel Non-invasive Transcranial Electrical Stimulation for Parkinson's Disease

Item Type: Journal Article

Authors: Ni, Rui;Yuan, Ye;Yang, Li;Meng, Qiujian;Zhu, Ying;Zhong, Yiya;Cao, Zhenqian;Zhang, Shengzhao;Yao, Wenjun;Lv, Daping;Chen, Xin;Chen, Xianwen and Bu, Junjie

Publication Date: 2022

Journal: Frontiers in Aging Neuroscience 14, pp. 880897

Abstract: Conventional transcranial electrical stimulation (tES) is a non-invasive method to modulate brain activity and has been extensively used in the treatment of Parkinson's disease (PD). Despite promising prospects, the efficacy of conventional tES in PD treatment is highly variable across different studies. Therefore, many have tried to optimize tES for an improved therapeutic efficacy by developing novel tES intervention strategies. Until now, these novel clinical interventions have not been discussed or reviewed in the context of PD therapy. In this review, we focused on the efficacy of these novel strategies in PD mitigation, classified them into three categories based on their distinct technical approach to circumvent conventional tES problems. The first category has novel stimulation modes to target different modulating mechanisms, expanding the rang of stimulation choices hence enabling the ability to modulate complex brain circuit or functional networks. The second category applies tES as a supplementary intervention for PD hence amplifies neurological or behavioral improvements. Lastly, the closed loop tES stimulation can provide self-adaptive individualized stimulation, which enables a more specialized intervention. In summary, these novel tES have validated potential in both alleviating PD symptoms and improving understanding of the pathophysiological mechanisms of PD. However, to assure wide

clinical used of tES therapy for PD patients, further large-scale trials are required.
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20. Characterizing Quality of Life in Caregivers of People with Parkinson's Disease and Dysphagia

Item Type: Journal Article

Authors: Perry, Sarah E.;Borders, James C.;Dakin, Avery E. and Troche, Michelle S.

Publication Date: 2022

Journal: Dysphagia (0179051X) 37(3), pp. 523-532

21. Communication strategies used by Parkinson's nurse specialists during healthcare interactions: A qualitative descriptive study

Item Type: Journal Article

Authors: Pitts, Emilie;Wylie, Karen;Loftus, Andrea M. and Cocks, Naomi

Publication Date: 2022

Journal: Journal of Advanced Nursing (John Wiley & Sons, Inc.) 78(6), pp. 1773-1786

Abstract: Aim: To explore the range and use of communication strategies by Parkinson's nurse specialists, and describe key communication strategies, to support health professionals in their healthcare interactions with people with Parkinson's. Design: A qualitative descriptive study. Methods: Due to the COVID-19 pandemic, the study took place in an online setting. Online semi-structured interviews were conducted with eight Australian Parkinson's nurse specialists and one UK Parkinson's nurse between August and October of 2020. Interviews explored healthcare communication, specifically (1) ways Parkinson's nurse specialists support communication during healthcare interactions, (2) factors influencing the use of communication strategies, and (3) how the nurses learned to communicate effectively with people with Parkinson's disease. Reflexive thematic analysis was used to analyse the data. Results: Parkinson's nurse specialists described the importance of establishing strong therapeutic relationships, the key role of the communication partner, adapting communication to reduce cognitive load, ensuring two-way understanding, and enabling expressive communication for people with Parkinson's. Knowing the person and family, knowing the disease and understanding the symptoms appeared to influence the choice of communication strategies in healthcare interactions. Learning through others, learning through experience and learning through education and research were considered important parts of becoming a skilled healthcare communicator when working with people with Parkinson's. Conclusion: Knowledge and use of effective communication strategies to support people with Parkinson's is crucial for all health professionals working with this population, in order to reduce the occurrence of poor healthcare outcomes. A deep understanding of how Parkinson's disease affects communication and experience in implementing communication strategies were reported as contributing to the success of Parkinson's nurses in communicating with their patients. Impact This

study provides a description of the key, translational communication strategies that can be used by all health professionals to support healthcare interactions with people with Parkinson's.

22. Age-Related Midbrain Inflammation and Senescence in Parkinson's Disease

Item Type: Journal Article

Authors: Russo, Taylor and Riessland, Markus

Publication Date: 2022

Journal: Frontiers in Aging Neuroscience 14, pp. 1-7

Abstract: Immune responses are arising as a common feature of several neurodegenerative diseases, such as Parkinson's disease (PD), Alzheimer's disease (AD), and Amyotrophic Lateral Sclerosis (ALS), but their role as either causative or consequential remains debated. It is evident that there is local inflammation in the midbrain in PD patients even before symptom onset, but the underlying mechanisms remain elusive. In this mini-review, we discuss this midbrain inflammation in the context of PD and argue that cellular senescence may be the cause for this immune response. We postulate that to unravel the relationship between inflammation and senescence in PD, it is crucial to first understand the potential causative roles of various cell types of the midbrain and determine how the possible paracrine spreading of senescence between them may lead to observed local immune responses. We hypothesize that secretion of pro-inflammatory factors by senescent cells in the midbrain triggers neuroinflammation resulting in immune cell-mediated killing of midbrain dopaminergic (DA) neurons in PD.

23. Clinical Aspects of the Differential Diagnosis of Parkinson's Disease and Parkinsonism

Item Type: Journal Article

Authors: Shin, Hae-Won;Hong, Sang-Wook and Youn, Young Chul

Publication Date: May ,2022

Journal: Journal of Clinical Neurology 18(3), pp. 259-270

Abstract: Parkinsonism is a clinical syndrome presenting with bradykinesia, tremor, rigidity, and postural instability. Nonmotor symptoms have recently been included in the parkinsonian syndrome, which was traditionally associated with motor symptoms only. Various pathologically distinct and unrelated diseases have the same clinical manifestations as parkinsonism or parkinsonian syndrome. The etiologies of parkinsonism are classified as neurodegenerative diseases related to the accumulation of toxic protein molecules or diseases that are not neurodegenerative. The former class includes Parkinson's disease (PD), multiple-system atrophy, progressive supranuclear palsy, and corticobasal degeneration. Over the past decade, clinical diagnostic criteria have been validated and updated to improve the accuracy of diagnosing these diseases. The latter class of disorders unrelated to neurodegenerative diseases are

classified as secondary parkinsonism, and include drug-induced parkinsonism (DIP), vascular parkinsonism, and idiopathic normal-pressure hydrocephalus (iNPH). DIP and iNPH are regarded as reversible and treatable forms of parkinsonism. However, studies have suggested that the absence of protein accumulation in the nervous system as well as managing the underlying causes do not guarantee recovery. Here we review the differential diagnosis of PD and parkinsonism, mainly focusing on the clinical aspects. In addition, we describe recent updates to the clinical criteria of various disorders sharing clinical symptoms with parkinsonism. Copyright © 2022 Korean Neurological Association.

24. Antioxidant and Neuroprotective Effects of Carnosine: Therapeutic Implications in Neurodegenerative Diseases

Item Type: Journal Article

Authors: Solana-Manrique, Cristina;Sanz, Francisco Jose;Martinez-Carrion, Guillermo and Paricio, Nuria

Publication Date: Apr 26 ,2022

Journal: Antioxidants 11(5)

Abstract: Neurodegenerative diseases (NDs) constitute a global challenge to human health and an important social and economic burden worldwide, mainly due to their growing prevalence in an aging population and to their associated disabilities. Despite their differences at the clinical level, NDs share fundamental pathological mechanisms such as abnormal protein deposition, intracellular Ca²⁺ overload, mitochondrial dysfunction, redox homeostasis imbalance and neuroinflammation. Although important progress is being made in deciphering the mechanisms underlying NDs, the availability of effective therapies is still scarce. Carnosine is a natural endogenous molecule that has been extensively studied during the last years due to its promising beneficial effects for human health. It presents multimodal mechanisms of action, being able to exert antioxidant, anti-inflammatory and anti-aggregate activities, among others. Interestingly, most NDs exhibit oxidative and nitrosative stress, protein aggregation and inflammation as molecular hallmarks. In this review, we discuss the neuroprotective functions of carnosine and its implications as a therapeutic strategy in different NDs. We summarize the existing works that study alterations in carnosine metabolism in Alzheimer's disease and Parkinson's disease, the two most common NDs. In addition, we review the beneficial effect that carnosine supplementation presents in models of such diseases as well as in aging-related neurodegeneration.

25. Apathy as a Within-Person Mediator of Depressive Symptoms and Cognition in Parkinson's Disease: Longitudinal Mediation Analyses

Item Type: Journal Article

Authors: Szymkowicz, Sarah M.;Jones, Jacob D.;Timblin, Holly;Ryczek, Cameron A.;Taylor, Warren D. and May, Pamela E.

Publication Date: 2022

Journal: American Journal of Geriatric Psychiatry 30(6), pp. 664-674

Abstract: Objective: Greater depressive symptoms are associated with worse cognitive functions in Parkinson's disease (PD); however, it is unclear what underlying factors drive this association. Apathy commonly develops in PD and may be a pathway through which depressive symptoms negatively influence cognition. Prior research examining depressive symptoms, apathy, and cognition in PD is limited by being predominantly cross-sectional. This study examined the role of apathy as a within- and between-person mediator for the longitudinal relationships between depression severity and cognitive functioning in patients with early PD. Methods: Participants included 487 individuals newly diagnosed with PD followed annually for up to 5 years by the Parkinson's Progression Marker Initiative. At each visit, participants completed depressive symptom measures, apathy ratings, and cognitive tests. Multi-level structural equation models examined both the within- and between-person effects of depressive symptoms on cognition through apathy, controlling for demographics and motor severity. Results: At the within-person level, apathy mediated the association between depressive symptoms and select cognitive functions (global cognition, attention/working memory, visuospatial functions, and immediate verbal memory; indirect effects, bootstrap p's <0.05). Significant between-person direct effects were found for depressive symptoms predicting apathy (bootstrap p <0.001) and lower scores on most cognitive tests (bootstrap p's <0.05). However, the indirect effects did not reach significance, suggesting between-person mediation did not occur. Conclusion: Findings suggest worsening of depressive symptoms over time in patients with PD may be a risk factor for increased apathy and subsequent decline in specific cognitive functions.

Sources Used:

The following databases are used in the creation of this bulletin: CINAHL, Medline, BNI.

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