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Parkinson's Disease Current Awareness Bulletin

June 2023

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1. **Predictors of falls in Parkinson's disease, progressive supranuclear palsy, and multiple system atrophy: a retrospective study.**

Authors: Altmann, C. F.;Koschel, J. and Jost, W. H.

Publication Date: 2023

Journal: Neurologia i Neurochirurgia Polska (pagination), pp. ate of Pubaton: 10 May 2023

Abstract: INTRODUCTION: Recurrent falling is a major clinical milestone in Parkinsonian syndromes. It has a detrimental impact on quality of life, further prognosis, and life expectancy. AIM OF THE STUDY: To improve fall management and prevention, we aimed at identifying clinical parameters predicting fall frequency. To this end, we retrospectively analysed records of fall events of patients with Parkinson's disease (PD), or progressive supranuclear palsy (PSP), or multiple system atrophy (MSA), during their two-week inpatient stay at the Parkinson-Klinik Ortenau, Wolfach, Germany. This data served as an objective proxy for patients' fall frequency and allowed us to estimate the impact of several demographic and clinical variables on the occurrence of falling. MATERIAL AND METHODS: Of 2,111 patients admitted to our hospital, 1,810 presented with PD, 191 with PSP, and 110 with MSA. We employed a multiple (quasi-) poisson regression analysis to model the fall frequency as a function of various demographic variables (age at diagnosis, gender) and clinical variables (disease duration and sub-type, motor and cognitive impairment, autonomic dysfunction). RESULT(S): Statistically significant predictors for falls in PD were cognitive impairment, motor impairment, and autonomic dysfunction. In PSP, significant predictors for falls were motor and autonomic dysfunction, while in MSA only disease duration predicted falls, but with only marginal statistical significance. CONCLUSION(S): Our results stress the importance of different factors in predicting falls in the different types of Parkinsonian syndrome. Preventive interventions should address these disease-specific targets for optimal success.

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2. **Association Between Sleep Factors and Parkinson's Disease: A Prospective Study Based On 409,923 UK Biobank Participants.**

Authors: Chen, Y.;Gao, Y.;Sun, X.;Wang, H.;Qin, L.;Wu, X. Y. and Li, G.

Publication Date: 2023

Journal: Neuroepidemiology , pp. 1

Abstract: INTRODUCTION: Limited evidence indicates an association between sleep factors and the risk of Parkinson's disease (PD). However, large prospective cohort studies including both sexes are needed to verify the association between daytime sleepiness, sleep duration, and PD risk. Furthermore, other sleep factors like chronotype and snoring and their impact on increased PD risk should be explored by simultaneously considering daytime sleepiness and snoring. METHOD(S): This study included 409,923 participants from the UK Biobank. Data on five sleep factors (chronotype, sleep duration, sleeplessness/insomnia, snoring, and daytime sleepiness) were collected using a standard self-administered questionnaire. PD occurrence was identified using linkages with primary care, hospital admission, death register, or self-report. Cox proportional hazard models were used to investigate the association between sleep factors and PD risk. Subgroup (age and sex) and sensitivity analyses were performed. RESULT(S): During a median follow-up of 11.89 years, 2158 incident PD cases were documented. The main association analysis showed that prolonged sleep duration (hazard ratio [HR]: 1.20, 95% confidence interval [CI]: 1.05, 1.37) and occasional daytime sleepiness (HR: 1.15, 95%CI: 1.04, 1.26) increased the PD risk.

Compared to those who self-reported never or rarely having sleeplessness/insomnia, participants who reported usually having sleeplessness/insomnia had a decreased risk of PD (HR: 0.85, 95%CI: 0.75, 0.96). Subgroup analysis revealed that women who self-reported no snoring had a decreased PD risk (HR: 0.84; 95%CI: 0.72, 0.99). Sensitivity analyses indicated that the robustness of the results was affected by potential reverse causation and data completeness. CONCLUSION(S): Long sleep duration increased the PD risk, especially among men and participants >=60 years, while snoring increased the risk of PD in women. Additional studies are needed to i) further consider other sleep traits (e.g., rapid eye movement sleep behaviour disorder and sleep apnoea) that might be related to PD, ii) objectively measure sleep-related exposure, and iii) confirm the effects of snoring on PD risk by considering the impact of obstructive sleep apnoea and investigating its underlying mechanisms.Copyright S. Karger AG, Basel.

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3. **Association Between Sleep Factors and Parkinson's Disease: A Prospective Study Based On 409,923 UK Biobank Participants.**

Authors: Chen, Yancong;Gao, Yinyan;Sun, Xuemei;Wang, Huan;Qin, Lang;Wu, X. Y. and Li, Guowei

Publication Date: May 15 ,2023

Journal: Neuroepidemiology 1

Abstract: INTRODUCTION: Limited evidence indicates an association between sleep factors and the risk of Parkinson's disease (PD). However, large prospective cohort studies including both sexes are needed to verify the association between daytime sleepiness, sleep duration, and PD risk. Furthermore, other sleep factors like chronotype and snoring and their impact on increased PD risk should be explored by simultaneously considering daytime sleepiness and snoring. METHODS: This study included 409,923 participants from the UK Biobank. Data on five sleep factors (chronotype, sleep duration, sleeplessness/insomnia, snoring, and daytime sleepiness) were collected using a standard self-administered questionnaire. PD occurrence was identified using linkages with primary care, hospital admission, death register, or self-report. Cox proportional hazard models were used to investigate the association between sleep factors and PD risk. Subgroup (age and sex) and sensitivity analyses were performed. RESULTS: During a median follow-up of 11.89 years, 2158 incident PD cases were documented. The main association analysis showed that prolonged sleep duration (hazard ratio [HR]: 1.20, 95% confidence interval [CI]: 1.05, 1.37) and occasional daytime sleepiness (HR: 1.15, 95%CI: 1.04, 1.26) increased the PD risk. Compared to those who self-reported never or rarely having sleeplessness/insomnia, participants who reported usually having sleeplessness/insomnia had a decreased risk of PD (HR: 0.85, 95%CI: 0.75, 0.96). Subgroup analysis revealed that women who self-reported no snoring had a decreased PD risk (HR: 0.84; 95%CI: 0.72, 0.99). Sensitivity analyses indicated that the robustness of the results was affected by potential reverse causation and data completeness. CONCLUSION: Long sleep duration increased the PD risk, especially among men and participants >=60 years, while snoring increased the risk of PD in women. Additional studies are needed to i) further consider other sleep traits (e.g., rapid eye movement sleep behaviour disorder and sleep apnoea) that might be related to PD, ii) objectively measure sleep-related exposure, and iii) confirm the effects of snoring on PD risk by considering the impact of obstructive sleep apnoea and investigating its underlying mechanisms. Copyright S. Karger AG, Basel.

4. **ID: 221007 Bioelectronic Zeitgebers: Towards Neuromodulation Devices Synchronized to Biological Rhythms**

Authors: Fleming, J., Noone, T., Deli, A., Zamora, M., Zand, A.D., Benjaber, M., Ottaway, J., Gillbe, T., Lamb, G., Campbell, H., Gillbe, I., Green, A. and Denison, T.

Publication Date: 2023

Publication Details: Neuromodulation. Conference: North American Neuromodulation Society 26th Annual Meeting. Las Vegas United States. 26(4 Supplement) (pp S123); Elsevier B.V.,

Abstract: Introduction: Biological rhythms pervade physiology and pathophysiology across multiple timescales. Implantable bioelectronic systems that stimulate the nervous system have been shown as an effective adjunct therapy for medically refractory neurological disorders. However, due to limited sensing and algorithm capabilities of previous device generations, exploring the influence of biological rhythms on therapy efficacy has not been feasible. Devices to date have been limited to running fixed stimulation parameters without consideration of the impact of rhythms on therapy efficacy and therapy's influence on rhythm-related symptoms and physiology. To maximize therapeutic benefits, bioelectronic devices should integrate chronobiology by considering time-related variations in disease symptoms and how to optimally alter therapy output. The aim is to both account for time-based symptom variance, and potentially promote, healthy biological rhythms, using the embedded clocks in bioelectronic systems to provide an additional exogenous "zeitgeber" (time giver). Method(s): To meet these requirements, we developed an implantable bioelectronic device 'Picostim DyNeuMo', a fully implantable, adaptive research stimulator that can titrate stimulation synchronized to biological rhythms1,2. The device integrates digital algorithms that adjust stimulation based on both time and sensor-based physiological biomarkers and is currently being applied in the United Kingdom in investigational studies for Parkinson's Disease, generalized epilepsy, and multiple system atrophy. To illustrate the "bioelectronic zeitgeber" approach, we present preliminary data from two Multiple System Atrophy (MSA) patients implanted in the pedunculopontine nucleus and a single patient implanted in the centromedian nucleus for severe generalized epilepsy. We demonstrate how patient symptoms can be characterized rhythmically, and how these patient-specific chronotypes can then be applied to a feed-forward controller to implement anticipatory, time-based stimulation adjustments. The sensing-based algorithms, such as its motion-adaptive capabilities, can provide acute stimulation adjustments when necessary as an additional feedback mechanism. Result(s): Preliminary evidence from the device's first use in these clinical studies supports its impact on sleep-wake pathology, a common secondary feature of neurological disorders. For the MSA subjects we noted a decrease in excessive daytime sleepiness accompanied by longitudinal modulation of wake-related network oscillations correlated with vigilance. Incorporating night-time settings that did not promote wakefulness produced better sleep, while maintaining daytime therapy efficacy. The device data recording and adaptive algorithm capabilities provides unique insight into rhythmic disease processes, and how bioelectronic zeitgebers might optimize treatment. Conclusion(s): Given the commonality of circadian/diurnal symptom fluctuation in neurological disorders such as epilepsy and chronic pain, we believe the addition of chronotherapy to neuromodulation systems is an opportunity for therapy enhancement. Disclosure: John Fleming, PhD: None, Tara Noone: Bioinduction Ltd: Employee:, Alceste Deli: None, Mayela Zamora: None, Amir Divanbeighi Zand: None, Moaad Benjaber: None, Jon Ottaway: None, Tom Gillbe: Bioinduction Ltd: Employee:, Guy Lamb: Bioinduction Ltd: Employee:, Hannah Campbell: None, Ivor Gillbe: Bioinduction Limited: Ownership Interest: Own Stock, Stock Options, Future Stock Options:, Alexander Green, MD FRCS (SN) BSc MB BS: Abbott: Speakers Bureau: Self, Renishaw plc: Consulting Fee: Self, InBrain: Consulting Fee:, Timothy

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5. **Re-evaluation of Genetic Variants in Parkinson's Disease Using Targeted Panel and Next-Generation Sequencing.**

Authors: Kablan, A.;Silan, F. and Ozdemir, O.

Publication Date: 2023

Journal: Twin Research and Human Genetics : The Official Journal of the International Society for Twin Studies , pp. 1-7

Abstract: Parkinson's disease (PD) is a complex disorder with a significant genetic component. Genetic variations associated with PD play a crucial role in the disease's inheritance and prognosis. Currently, 31 genes have been linked to PD in the OMIM database, and the number of genes and genetic variations identified is steadily increasing. To establish a robust correlation between phenotype and genotype, it is essential to compare research findings with existing literature. In this study, we aimed to identify genetic variants associated with PD using a targeted gene panel with next-generation sequencing (NGS) technology. Our objective was also to explore the idea of re-analyzing genetic variants of unknown significance (VUS). We screened 18 genes known to be related to PD using NGS in 43 patients who visited our outpatient clinic between 2018-2019. After 12-24 months, we re-evaluated the detected variants. We found 14 different heterozygous variants classified as pathogenic, likely pathogenic, or VUS in 14 individuals from nonconsanguineous families. We re-evaluated 15 variants and found changes in their interpretation. Targeted gene panel analysis with NGS can help identify genetic variants associated with PD with confidence. Re-analyzing certain variants at specific time intervals can be especially beneficial in selected situations. Our study aims to expand the clinical and genetic understanding of PD and emphasizes the importance of re-analysis.

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6. **Impact of non-motor fluctuations on QOL in patients with Parkinson's disease.**

Authors: Kakimoto, Asako;Kawazoe, Miki;Kurihara, Kanako;Mishima, Takayasu and Tsuboi, Yoshio

Publication Date: 2023

Journal: Frontiers in Neurology [Electronic Resource] 14, pp. 1149615

Abstract: Introduction: Long-term levodopa treatment in patients with Parkinson's disease (PwPD) often causes motor fluctuations, which are known to affect their quality of life (QOL). These motor fluctuations may be accompanied by fluctuations in non-motor symptoms. There is no consensus on how non-motor fluctuations affect QOL. Methods: This was a single-center, retrospective study and included 375 patients with Parkinson's disease (PwPD) who visited the neurology outpatient department of Fukuoka University Hospital between July 2015 and June 2018. All patients were evaluated for age, sex, disease duration, body weight, and motor symptoms by the Movement Disorder Society-Unified Parkinson's Disease Rating Scale part III, depression scale by the Zung self-rating depression scale, apathy scale, and cognitive function by the Japanese version of The Montreal Cognitive Assessment. A nine-item wearing-off questionnaire (WOQ-9) was used to assess the motor and non-motor fluctuations. QOL in PwPD was investigated using the eight-item Parkinson's Disease Questionnaire (PDQ-8). Results: In total, 375 PwPD were

enrolled and classified into three groups according to the presence or absence of motor and non-motor fluctuations. The first group included 98 (26.1%) patients with non-motor fluctuations (NFL group), the second group included 128 (34.1%) patients who presented with only motor fluctuations (MFL group), and the third group included 149 (39.7%) patients without fluctuations in motor or non-motor symptoms (NoFL group). Among them, the PDQ-8 SUM and SI were significantly higher in the NFL group than in the other groups (p p

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7. **A Case Report on Serotonin Syndrome in a Patient With Parkinson's Disease: Diagnostic and Management Challenges**

Authors: Nemet, M., Andrijevic, A., Nedeljkov, D., Andric, V. and Gavrilovic, S.

Publication Date: 2023

Publication Details: United States:

Abstract: Patients with Parkinson's disease are often at risk of polypharmacy, which can lead to serious medication side effects and interactions. Serotonin syndrome (SS) can develop in this patient population due to a possible drug-drug interaction between antidepressants and antiparkinson drugs with serotoninergic activity. On the other hand, these patients are also at risk of malignant syndrome (MS) secondary to dopaminergic medication withdrawal. In this case report, we present a 71-year-old female with Parkinson's disease who developed symptoms suggestive of SS. The patient was admitted to the medical intensive care unit at the Institute for Pulmonary Diseases of Vojvodina in the Republic of Serbia due to impaired consciousness and a previously witnessed cardiorespiratory arrest. Her chronic antiparkinson medication regimen consisted of levodopa, benserazide, entacapone, ropinirole, and rasagiline. Furthermore, she had been prescribed duloxetine for a remote history of depression, which she had only been taking intermittently. Several days before admission, however, the patient started taking duloxetine again due to low mood. Upon admission, laboratory tests revealed leukocytosis with neutrophilia, elevated C-reactive protein, procalcitonin, lactate, urea, and creatinine. Serum creatine kinase (CK) levels were also elevated at 1250 U/L. Six hours after admission to the ICU, the patient developed hyperthermia, hyperreflexia, spontaneous myoclonus, and tremors. Her CK levels continued to rise, reaching 6900 U/L, and her renal function worsened. Due to the possibility of either SS or MS, external cooling measures with frozen gel packs were administered, resulting in the patient's stabilization over a few hours. Further, serotoninergic medication (rasagiline and duloxetine) was discontinued. On the fifth day of hospitalization, a head CT showed signs of cytotoxic edema. On the 11th day, the patient became hemodynamically unstable and passed away despite all adequate resuscitative measures. The purpose of this case report is to raise awareness of possible SS in patients taking monoamine oxidase-B (MAO-B) inhibitors such as rasagiline. Clinicians should have a high index of suspicion for this complication, especially in patients who are treated for comorbid depression with serotoninergic drugs. Furthermore, we emphasize the importance of correctly differentiating SS from MS, which are both risks for patients with Parkinson's disease. A correct approach to these patients is of utmost importance for adequate management and optimal outcomes. Copyright © 2023, Nemet et al.

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8. **The gait parameters in patients with Parkinson's Disease under STN-DBS therapy and associated clinical features.**

Authors: Onder, H.;Dinc, E.;Yucesan, K. and Comoglu, S.

Publication Date: 2023

Journal: Neurological Research (pagination), pp. ate of Pubaton: 2023

Abstract: Objective: We aimed to investigate the gait parameters in patients with subthalamic nucleus deep brain stimulation (STN-DBS) therapy using quantitative gait analyses and reveal the associated clinical features. Method(s): Parkinson's disease (PD) subjects with STN-DBS who applied to our movement disorders outpatient clinics between December/2021 and March/2022 were enrolled. In addition to the evaluation of the demographic data and the clinical features; clinical scales measuring the freezing of gait (FOG), falls and quality of life were performed. A gait analyzer program was used to perform gait analysis. Result(s): Thirty patients with a mean age of 59.4 +/- 8.3 (F/M = 7/23) were enrolled. The comparative analyses between the tremor-dominant and akinetic-rigid (AR) subtype patients showed that the step time asymmetry measures were higher in the AR group. The comparative analyses according to the symptom onset side showed that the step length was smaller in those with left-side symptom onset. The correlation analyses showed that there were correlations between the quality-of-life indexes and FOG questionnaire and falls efficacy scale (FES) scores. Finally, the correlation analyses between clinical scales and gait parameters revealed that there were significant correlations between the FES scores and the step length asymmetry (SLA). Conclusion(s): We found a strong relationship between falls and quality of life indexes of our patients under STN-DBS therapy. In this patient group, particular evaluation of fallings and the follow-up of SLA in gait analysis may constitute important points during the evaluation of patients in routine clinical practice.

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9. **Hospitalization and the Risk of Initiation of Antipsychotics in Persons With Parkinson's Disease.**

Authors: Pirttila, A.;Tiihonen, M.;Paakinaho, A.;Hartikainen, S. and Tolppanen, A. M.

Publication Date: 2023

Journal: Journal of the American Medical Directors Association (pagination), pp. ate of Pubaton: 20 May 2023

Abstract: OBJECTIVES: The use of antipsychotics in persons with Parkinson's disease (PD) is common, although their use may aggravate the symptoms of PD. Clozapine and quetiapine are the only antipsychotics recommended in PD treatment guidelines. Information on factors associated with initiation of antipsychotics is needed. We investigated whether recent hospitalization is associated with initiation of antipsychotics in persons with PD, and whether discharge diagnoses differ between those who had antipsychotics initiated and those who did not. DESIGN: Nested case-control study in the nationwide register-based Finnish Study on Parkinson's disease (FINPARK). SETTING AND PARTICIPANTS: The FINPARK study includes 22,189 persons who received an incident, clinically verified PD diagnosed during 1996-2015 and were community-dwelling at the time of diagnosis. The cases were 5088 persons who had antipsychotics initiated after PD diagnosis, identified with 1-year washout. The controls were 5088 age-, sex-, and time from PD diagnosis-matched persons who did not use antipsychotics on the matching date (antipsychotic purchase date). Recent hospitalization was defined as discharge in the 2-week period preceding the matching date. METHOD(S): Associations were investigated with conditional logistic regression. RESULT(S): Quetiapine was the most commonly initiated antipsychotic (72.0% of cases), followed by risperidone (15.0%). Clozapine was initiated rarely (1.1%). Recent hospitalization associated strongly with antipsychotic initiation [61.2% of cases and 14.9% of controls, odds ratio (OR) 9.42, 95% CI 8.33-10.65], and longer hospitalizations were more

common among cases. PD was the most common discharge diagnosis category (51.2% of hospitalized cases and 33.0% controls), followed by mental and behavioral disorders (9.3%) and dementia (9.0%) among cases. Antidementia and other psychotropic medication use were more common among cases. CONCLUSIONS AND IMPLICATIONS: These results suggest that antipsychotics were initiated because of neuropsychiatric symptoms or aggravation of those symptoms. Antipsychotics should be prescribed after careful consideration to avoid adverse effects in persons with Parkinson's disease.

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10. **Scoring festination and gait freezing in people with Parkinson's: The freezing of gait severity tool-revised.**

Authors: Scully, A. E.;Tan, D.;Oliveira, B. I. R.;Hill, K. D.;Clark, R. and Pua, Y. H.

Publication Date: 2023

Journal: Physiotherapy Research International : The Journal for Researchers and Clinicians in Physical Therapy , pp. e2016

Abstract: BACKGROUND AND PURPOSE: To improve existing clinical assessments for freezing of gait (FOG) severity, a new clinician-rated tool which integrates the varied types of freezing (FOG Severity Tool-Revised) was developed. This cross-sectional study investigated its validity and reliability. METHOD(S): People with Parkinson's disease who were able to independently ambulate eight-metres and understand study instructions were consecutively recruited from outpatient clinics of a tertiary hospital. Those with co-morbidities severely affecting gait were excluded. Participants were assessed with the FOG Severity Tool-Revised, three functional performance tests, the FOG Questionnaire, and outcomes measuring anxiety, cognition, and disability. The FOG Severity Tool-Revised was repeated for test-retest reliability. Exploratory factor analysis and Cronbach's alpha were computed for structural validity and internal consistency. Reliability and measurement error were estimated with ICC (two-way, random), standard error of measurement, and smallest detectable change (SDC95). Criterion-related and construct validity were calculated with Spearman's correlations. RESULT(S): Thirty-nine participants were enrolled [79.5% (n = 31) male; Median (IQR): age-73.0 (9.0) years; disease duration-4.0 (5.8) years], with fifteen (38.5%) who reported no medication state change contributing a second assessment for reliability estimation. The FOG Severity Tool-Revised demonstrated sufficient structural validity and internal consistency (alpha = 0.89-0.93), and adequate criterion-related validity compared to the FOG Questionnaire (rho = 0.73, 95% CI 0.54-0.85). Test-retest reliability (ICC = 0.96, 95%CI 0.86-0.99) and random measurement error (%SDC95 = 10.4%) was acceptable in this limited sample. DISCUSSION AND CONCLUSION(S): The FOG Severity Tool-Revised appeared valid in this initial sample of people with Parkinson's. While its psychometric properties remain to be confirmed in a larger sample, it may be considered for use in the clinical setting.

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11. **Scoring festination and gait freezing in people with Parkinson's: The freezing of gait severity tool-revised.**

Authors: Scully, Aileen E.;Tan, Dawn;Oliveira, Beatriz Ito Ramos de;Hill, Keith D.;Clark, Ross and Pua, Yong Hao

Publication Date: May 18 ,2023

Journal: Physiotherapy Research International e2016

Abstract: BACKGROUND AND PURPOSE: To improve existing clinical assessments for freezing of gait (FOG) severity, a new clinician-rated tool which integrates the varied types of freezing (FOG Severity Tool-Revised) was developed. This cross-sectional study investigated its validity and reliability. METHODS: People with Parkinson's disease who were able to independently ambulate eight-metres and understand study instructions were consecutively recruited from outpatient clinics of a tertiary hospital. Those with co-morbidities severely affecting gait were excluded. Participants were assessed with the FOG Severity Tool-Revised, three functional performance tests, the FOG Questionnaire, and outcomes measuring anxiety, cognition, and disability. The FOG Severity Tool-Revised was repeated for test-retest reliability. Exploratory factor analysis and Cronbach's alpha were computed for structural validity and internal consistency. Reliability and measurement error were estimated with ICC (two-way, random), standard error of measurement, and smallest detectable change (SDC95). Criterion-related and construct validity were calculated with Spearman's correlations. RESULTS: Thirty-nine participants were enrolled [79.5% (n = 31) male; Median (IQR): age-73.0 (9.0) years; disease duration-4.0 (5.8) years], with fifteen (38.5%) who reported no medication state change contributing a second assessment for reliability estimation. The FOG Severity Tool-Revised demonstrated sufficient structural validity and internal consistency (alpha = 0.89-0.93), and adequate criterion-related validity compared to the FOG Questionnaire (rho = 0.73, 95% CI 0.54-0.85). Test-retest reliability (ICC = 0.96, 95%CI 0.86-0.99) and random measurement error (%SDC95 = 10.4%) was acceptable in this limited sample. DISCUSSION AND CONCLUSIONS: The FOG Severity Tool-Revised appeared valid in this initial sample of people with Parkinson's. While its psychometric properties remain to be confirmed in a larger sample, it may be considered for use in the clinical setting.

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12. **SARS-CoV-2 susceptibility and COVID-19 illness course and outcome in people with pre-existing neurodegenerative disorders: systematic review with frequentist and Bayesian meta-analyses**

Authors: Smadi, Muhannad;Kaburis, Melina;Schnapper, Youval;Reina, Gabriel;Molero, Patricio and Molendijk, Marc L.

Publication Date: May 15 ,2023

Journal: British Journal of Psychiatry 1-14

Abstract: BACKGROUND: People with neurodegenerative disease and mild cognitive impairment (MCI) may have an elevated risk of acquiring severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and may be disproportionally affected by coronavirus disease 2019 (COVID-19) once infected. AIMS: To review all eligible studies and quantify the strength of associations between various pre-existing neurodegenerative disorders and both SARS-CoV-2 susceptibility and COVID-19 illness course and outcome. METHOD: Pre-registered systematic review with frequentist and Bayesian meta-analyses. Systematic searches were executed in PubMed, Web of Science and preprint servers. The final search date was 9 January 2023. Odds ratios (ORs) were used as measures of effect. RESULTS: In total, 136 primary studies (total sample size n = 97 643 494), reporting on 268 effect-size estimates, met the inclusion criteria. The odds for a positive SARS-CoV-2 test result were increased for people with pre-existing dementia (OR = 1.83, 95% CI 1.16-2.87), Alzheimer's disease (OR = 2.86, 95% CI 1.44-5.66) and Parkinson's disease (OR = 1.65, 95% CI 1.34-2.04). People with pre-existing dementia were more likely to experience a relatively severe

COVID-19 course, once infected (OR = 1.43, 95% CI 1.00-2.03). People with pre-existing dementia or Alzheimer's disease were at increased risk for COVID-19-related hospital admission (pooled OR range: 1.60-3.72). Intensive care unit admission rates were relatively low for people with dementia (OR = 0.54, 95% CI 0.40-0.74). All neurodegenerative disorders, including MCI, were at higher risk for COVID-19-related mortality (pooled OR range: 1.56-2.27). CONCLUSIONS: Our findings confirm that, in general, people with neurodegenerative disease and MCI are at a disproportionally high risk of contracting COVID-19 and have a poor outcome once infected.

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13. **Clinical features and outcomes of hospitalised patients with COVID-19 and Parkinsonian disorders: a multicentre UK-based study.**

Authors: Sorrell, L.;Leta, V.;Barnett, A.;Stevens, K.;King, A.;Inches, J.;Kobylecki, C.;Walker, R.;Chaudhuri, K. R.;Martin, H.;Rideout, J.;Sneyd, J. R.;Campbell, S. and Carroll, C.

Publication Date: 2023

Journal: medRxiv (pagination), pp. ate of Pubaton: 25 Ar 2023

Abstract: Background: Parkinson's disease has been identified as a risk factor for severe Coronavirus disease 2019 (COVID-19) outcomes. However, whether the significant high risk of death from COVID-19 in people with Parkinson's disease is specific to the disease itself or driven by other concomitant and known risk factors such as comorbidities, age, and frailty remains unclear. Objective(s): To investigate clinical profiles and outcomes of people with Parkinson's disease and atypical parkinsonian syndromes who tested positive for COVID-19 in the hospital setting in a multicentre UK-based study. Method(s): A retrospective cohort study of Parkinson's disease patients with a positive COVID-19 test admitted to hospital between February 2020 and July 2021. An online survey was used to collect data from clinical care records, recording patient, Parkinson's disease and COVID-19 characteristics. Associations with time-to-mortality and severe outcomes were analysed using either the Cox proportional hazards model or logistic regression models, as appropriate. Result(s): Data from 552 admissions were collected: 365 (66%) male; median (inter-quartile range) age 80 (74-85) years. The 34-day mortality rate was 38.4%; male sex, increased age and frailty, Parkinson's dementia syndrome, requirement for respiratory support and no vaccination were associated with increased mortality risk. Community-acquired COVID-19 and co-morbid chronic neurological disorder were associated with increased odds of requiring respiratory support. Hospital-acquired COVID-19 and delirium were associated with requiring an increase in care level post-discharge. Conclusion(s): This first, multicentre, UK-based study on people with Parkinson's disease or atypical parkinsonian syndromes, hospitalised with COVID-19, adds and expands previous findings on clinical profiles and outcomes in this population.

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14. **Antiparkinsonian Medication Reconciliation as a Strategy to Improve Safety by Preventing Medication Errors.**

Authors: ViudezMartinez, A.;RamirezLopez, A.;LopezNieto, J.;ClimentGrana, E. and Riera, G.

Publication Date: 2023

Journal: Movement Disorders Clinical Practice (pagination), pp. ate of Pubaton: 2023

Abstract: Background: About 70% of neurologists report that PD patients do not get their medication properly when hospitalized, and 33% are prescribed contraindicated drugs. Objective(s): To execute medication reconciliation (MedRec) focused on antiparkinsonian drugs to identify, characterize and, eventually, prevent medication errors, thus promoting therapeutic quality and safety in daily practice. Method(s): An interventional, single-center, 1 year, prospective study. All the patients who were hospitalized and had, at least, one active prescription containing an antiparkinsonian drug at hospital admission were included. MedRec was performed by following a three-phased check: inpatient electronic prescription validation after assessing the outpatient medication schedule, review of the latest clinical report emitted by the Neurology Department/General Practitioner, and pharmacist-driven interview of the patient and/or caregiver to confirm the information regarding medication gathered. Result(s): A total of 171 admission episodes from 132 patients were registered (February 1, 2021, and January 31, 2022). Of 224 prescription lines involving antiparkinsonian drugs, 179 contained, at least, one medication error (59.8%). Commission errors (91.62%) were more frequent than omitted drugs (8.38%). The most common medication errors were related to timing (41.90%), frequency (21.23%), and dosing (19.55%). The implementation of this program prevented the erroneous administration of 2716 antiparkinsonian doses, 60% of the total number of doses prescribed. Interestingly, a significant relationship between the number of medication errors and having levodopa prescribed was evidenced (P Result(s): A total of 171 admission episodes from 132 patients were registered (February 1, 2021, and January 31, 2022). Of 224 prescription lines involving antiparkinsonian drugs, 179 contained, at least, one medication error (59.8%). Commission errors (91.62%) were more frequent than omitted drugs (8.38%). The most common medication errors were related to timing (41.90%), frequency (21.23%), and dosing (19.55%). The implementation of this program prevented the erroneous administration of 2716 antiparkinsonian doses, 60% of the total number of doses prescribed. Interestingly, a significant relationship between the number of medication errors and having levodopa prescribed was evidenced (P Conclusion(s): Clinical pharmacists' implementation of an antiparkinsonians reconciliation program sharply reduced medication errors and prescription of contraindicated drugs.

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15. **Subcutaneous infusion of apomorphine: Recommendations for health care providers for installation in hospitals or at home.**

Authors: Zagnoli, F.;Verin, M.;Tirel, A.;Tir, M.;OryMagne, F.;Marques, A.;Maltete, D.;Frismand, S.;Fluchere, F.;Drapier, S.;Defebvre, L.;Decombe, R.;Bereau, M. and Bannier, S.

Publication Date: 2023

Journal: Pratique Neurologique - FMC (pagination), pp. ate of Pubaton: 2023

Abstract: Subcutaneous apomorphine by continuous infusion is increasingly used in the management of motor complications of Parkinson's disease when fluctuations become troublesome. Until now, it has been administered in hospital, usually in an expert centre, which in some regions could limit its accessibility. A better mastery of this treatment by practitioners, the increased involvement of service providers offering this type of service and the improvement of devices are contributing to greater accessibility of this therapy, to the point of allowing its implementation at home in certain cases. However, this prescription must comply with a certain number of rules. Thus, to enable all eligible patients to benefit from this treatment under good conditions, recommendations are proposed detailing the role

of the various health actors and the prescription methods.

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16. **Neuropsychiatric features of Parkinson's disease in the era prior to the use of dopaminergic therapies.**

Authors: Zhang, Chengyu;Reeves, Suzanne;David, Anthony S.;Costello, Harry and Rogers, Jonathan

Publication Date: May 12 ,2023

Journal: Cognitive Neuropsychiatry 1-10

Abstract: BACKGROUND: Psychosis in Parkinson's disease includes hallucinations and delusions. Other non-psychotic neuropsychiatric features include depression, anxiety and apathy. There is currently controversy over whether psychosis in Parkinson's is an intrinsic part of the disorder or the result of dopaminergic medications. This study aimed to examine a historical cohort of individuals with Parkinson's prior to the use of dopaminergic therapy to assess the prevalence of psychotic and other neuropsychiatric features. METHODS: The case notes of patients with Parkinson's disease admitted to the National Hospital for Neurology and Neurosurgery, London between 1924 and 1946 were examined. Demographic and clinical variables were extracted along with any neuropsychiatric features. Cases meeting criteria for encephalitis lethargica were excluded. RESULTS: 115 cases of individuals with Parkinson's disease were identified. 58 (41.7%) were female. Mean age was 54.0 (SD 9.6) years and mean time since Parkinson's diagnosis was 5.3 (SD 5.7) years. No individuals met criteria for encephalitis lethargica. No cases of hallucinations or delusions were reported. There was one case of an illusion in a patient who was using anticholinergic medication. Other neuropsychiatric features reported were sleep disorder (present in 10, 8.7%), depression (8, 7.0%), memory impairment (5, 4.3%), impulsivity (4, 3.5%), bradyphrenia (4, 3.5%), impaired attention (3, 2.6%), anxiety (1, 0.9%), fatigue (1, 0.9%) and apathy (1, 0.9%). CONCLUSIONS: Prior to the use of dopaminergic therapies, patients with Parkinson's disease admitted to hospital rarely, if ever, reported psychotic symptoms, although other neuropsychiatric symptoms were more prevalent. The main limitation is that a lack of systematic enquiry about psychotic symptoms may have resulted in underreporting.

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17. **Physical Frailty, Genetic Predisposition, and Incident Parkinson Disease.**

Authors: Zheng, Z.;Lv, Y.;Rong, S.;Sun, T. and Chen, L.

Publication Date: 2023

Journal: JAMA Neurology 80(5) (pagination), pp. Arte Number: no230006. ate of Pubaton: 08 May 2023

Abstract: IMPORTANCE Cross-sectional evidence implicates high prevalent frailty in patients with Parkinson disease (PD), whereas the longitudinal association remains unknown. OBJECTIVES To examine the longitudinal association of the frailty phenotype with the development of PD and to explore the modification role of genetic risk of PD in such an association. DESIGN, SETTING, AND PARTICIPANTS This prospective cohort study launched in 2006 to 2010 with a follow-up of 12 years. Data were analyzed from March 2022 to December 2022. The UK Biobank recruited over 500 000 middle-aged and older adults from 22 assessment centers across the United Kingdom. Participants who were younger than 40 years (n = 101), diagnosed with dementia or PD at baseline, and developed

dementia, PD, or died within 2 years from baseline were excluded (n = 4050). Participants who had no genetic data or mismatch between genetic sex and reported gender (n = 15 350), were not of self-reported British White descent (n = 27 850), and had no data for frailty assessment (n = 100 450) or any covariates were also excluded (n = 39 706). The final analysis included 314 998 participants. EXPOSURES The physical frailty was assessed by the Fried criteria's frailty phenotype through 5 domains, ie, weight loss, exhaustion, low physical activity, slow walking speed, and low grip strength. The polygenic risk score (PRS) for PD comprised 44 single-nucleotide variants. MAIN OUTCOMES AND MEASURES New-onset PD was identified through the hospital admission electronic health records and death register. RESULTS Among 314 998 participants (mean age, 56.1 years; 49.1% male), 1916 new-onset PD cases were documented. Compared with nonfrailty, the hazard ratio (HR) of incident PD in prefrailty and frailty was 1.26 (95% CI, 1.15-1.39) and 1.87 (95% CI, 1.53-2.28), respectively, and the absolute rate difference per 100 000 person-years was 1.6 (95% CI, 1.0-2.3) for prefrailty and 5.1 (95% CI, 2.9-7.3) for frailty. Exhaustion (HR, 1.41; 95% CI, 1.22-1.62), slow gait speed (HR, 1.32; 95% CI, 1.13-1.54), low grip strength (HR, 1.27; 95% CI, 1.13-1.43), and low physical activity (HR, 1.12; 95% CI, 1.00-1.25) were associated with incident PD. A significant interaction between frailty and PRS on PD was found and the highest hazard was observed in participants with frailty and high genetic risk. CONCLUSIONS AND RELEVANCE Physical prefrailty and frailty were associated with incident PD independent of sociodemographic factors, lifestyles, multiple morbidities, and genetic background. These findings may have implications for the assessment and management of frailty for PD prevention.

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18. **Coronavirus disease 2019 and neurodegenerative disease: what will the future bring?.**

Authors: McAlpine, L. S.;FesharakiZadeh, A. and Spudich, S.

Publication Date: 2021

Journal: Current Opinion in Psychiatry 34(2), pp. 177-185

Abstract: Purpose of reviewOver 70 million people worldwide, including those with neurodegenerative disease (NDD), have been diagnosed with coronavirus disease 2019 (COVID-19) to date. We review outcomes in patients with NDD and COVID-19 and discuss the hypothesis that due to putative commonalities of neuropathogenesis, COVID-19 may unmask or trigger NDD in vulnerable individuals.Recent findingsBased on a systematic review of published literature, patients with NDD, including dementia, Parkinson's disease, and multiple sclerosis (MS) make up a significant portion of hospitalized COVID-19 patients. Such patients are likely to present with altered mental status or worsening of their preexisting neurological symptoms. Patients with NDD and poor outcomes often have high-risk comorbid conditions, including advanced age, hypertension, diabetes, obesity, and heart/lung disease. Patients with dementia including Alzheimer's disease are at higher risk for hospitalization and death, whereas those with preexisting Parkinson's disease are not. MS patients have good outcomes and disease modifying therapies do not increase the risk for severe disease. Viral infections and attendant neuroinflammation have been associated with the pathogenesis of Alzheimer's disease, Parkinson's disease, and MS, suggesting that COVID-19 may have the potential to incite or accelerate neurodegeneration.SummarySince patients with Alzheimer's disease are at higher risk for hospitalization and death in the setting of COVID-19, additional precautions and protective measures should be put in place to prevent infections and optimize management of comorbidities in this vulnerable population. Further studies are needed to determine whether COVID-19 may lead to an increased risk of developing NDD in susceptible individuals.

19. **Content and impact of pharmacy services for patients with Parkinson's disease: A systematic review and meta-analysis.**

Authors: Yi, Z. M.;Li, T. T.;Tang, Q. Y.;Zhang, Y.;Willis, S. and Zhai, S. D.

Publication Date: 2020

Journal: Medicine (United States) 99(27), pp. E20758

Abstract: Background:Medicines optimisation is important for the management of Parkinson's disease (PD). As many patients with PD have other long-term conditions, treatment is complex and risk of adverse events for these patients is high. Objective(s):To explore the role of pharmacists and impact of pharmacy interventions for PD patients. Method(s):We comprehensively searched PubMed, Embase, the Cochrane Library and Chinese databases Sinomed, China National Knowledge Infrastructure to identify studies reporting pharmacist interventions and pharmacy services for PD patients using a predefined search strategy. The search period was from inception to March 2019. We also manually searched the reference list of included studies and ClinicalTrials.gov. We conducted meta-analyses to synthesize the evidence quantitatively. Result(s):A total of 1607 studies were identified by applying the search criteria. After screening, 19 cross-sectional and case-controlled studies with 1458 PD patients from 9 countries were included. Pharmacist interventions for PD patients most commonly related to adverse drug reactions (ADRs) (13 studies), adherence assessment (12 studies), medication review (12 studies), identification of drug interactions (11 studies), monitoring response to medication therapy (11 studies), identification of inappropriate medication (11 studies), and patient education (10 studies). Most pharmacy services were provided in outpatient settings (13 studies). Reported impact measures included adherence (8 studies), quality of life (7 studies), and identification of drug-related problems (6 studies) such as ADRs (393 times out of 1760 times, 22.33%, 6 studies), inappropriate drug choice (349 times, 19.83%, 6 studies), inappropriate dosage (335 times, 19.03%, 6 studies), inappropriate drug use (257 times, 14.60%, 3 studies) and drug-drug interactions (146 times, 8.3%, 4 studies). Pooled results from 3 studies indicated no statistically significant impact of pharmacy services on all subscales of PD Questionnaire-39. Conclusion(s):ADRs were the most widely reported drug-related problems for PD patients; pharmacy services may have a role to play in medication adherence but were not found to impact on quality of life. Copyright © 2020 the Author(s).

Sources Used:

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

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