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Parkinson's Disease

Current Awareness Bulletin

November 2024

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1. **Daily steps are a predictor of, but perhaps not a modifiable risk factor for Parkinson's Disease: findings from the UK Biobank.**

Authors: Acquah, Aidan;Creagh, Andrew;Hamy, Valentin;Shreves, Alaina;Zisou, Charilaos;Harper, Charlie;Van Duijvenboden, Stefan;Antoniades, Chrystalina;Bennett, Derrick;Clifton, David and Doherty, Aiden

Publication Date: 2024

Journal: MedRxiv : The Preprint Server for Health Sciences

Abstract: Importance: Higher physical activity levels have been suggested as a potential modifiable risk factor for lowering the risk of incident Parkinson's disease (PD). This study uses objective measures of physical activity to investigate the role of reverse causation in the observed association. Objective: To investigate the association between accelerometer-derived daily step count and incident PD, and to assess the impact of reverse causation on this association. Design: This prospective cohort study involved a follow-up period with a median duration of 7.9 years, with participants who wore wrist-worn accelerometers for up to 7 days. Setting: The study was conducted within the UK Biobank, a large, population-based cohort. Participants: The analysis included 94,696 participants aged 43-78 years (56% female) from the UK Biobank who provided valid accelerometer data and did not have prevalent PD. Exposure: Daily step counts were derived using machine learning models to determine the median daily step count over the monitoring period. Main Outcomes and Measures: The primary outcome was incident PD, identified through hospital admission and death records. Cox proportional hazards regression models estimated hazard ratios (HR) and 95% confidence intervals (CI) for the association between daily step count and incident PD, with adjustments for various covariates and evaluation of reverse causation by splitting follow-up periods. Results: During a median follow-up of 7.9 years (IQR: 7.4-8.4), 407 incident PD cases were identified. An inverse linear association was observed between daily step count and incident PD. Participants in the highest quintile of daily steps (>12,369 steps) had an HR of 0.41 (95% CI 0.31-0.54) compared to the lowest quintile (: During a median follow-up of 7.9 years (IQR: 7.4-8.4), 407 incident PD cases were identified. An inverse linear association was observed between daily step count and incident PD. Participants in the highest quintile of daily steps (>12,369 steps) had an HR of 0.41 (95% CI 0.31-0.54) compared to the lowest quintile (Conclusions and Relevance: The observed association between higher daily step count and lower incident PD is likely influenced by reverse causation, suggesting changes in physical activity levels occur years before PD diagnosis. While step counts may serve as a predictor for PD, they may not represent a modifiable risk factor. Further research with extended follow-up periods is warranted to better understand this relationship and account for reverse causation.

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2. **Burden, Anxiety, and Depression Among Caregivers of Parkinson's Disease Patients.**

Authors: Alshimemeri, Sohaila;AlSudais, Hamood;Alamri, Nada K.;Alshoumar, Abdulaziz M.;Bin Dher, Shatha K. and Maashi, Mohammed Hassan

Publication Date: 2024

Journal: Journal of Parkinsons Disease Print 14(7), pp. 1495–1505

Abstract: Background: Parkinson's disease (PD) is a disabling neurodegenerative movement disorder. Most PD patients are looked after by caregivers who are close to them regardless of their relationship. Caregivers may experience a notable impact on their mental health as they dedicate a significant amount of time to the patient while observing the progression of the disease. Objective: The aim of this study was to evaluate the level of burden, depression, anxiety, and stress among caregivers of PD patients. Methods: We conducted a cross-sectional analysis between July and September 2023 among caregivers of PD patients following in the Movement Disorders Clinic at King Khalid University Hospital in Riyadh, Saudi Arabia, and through the Saudi Parkinson's Society. The data collection was done anonymously through an electronic self-administered questionnaire. Caregiver burden was assessed by using the validated Arabic version of the Zarit Burden Interview (ZBI) scale, and the Depression Anxiety Stress Scale (DASS) was used to assess the presence and level of anxiety and depression. Results: There were 118 caregivers (53.39% female, 33.9% aged between 35- 45 years, and 73.73% were sons/daughters) caring for 118 patients (57.63%, male, 38.98% aged between 66- 76). The ZBI score was highest among sibling caregivers. Moreover, burden scores were higher among those who provided care more frequently than others. Conclusions: Our study revealed that PD caregivers face a high risk of care burden, especially those who are siblings and spend longer periods in patient care. Additionally, female caregivers reported higher rates of depression, anxiety, and stress.; plain-language-summary Parkinson's disease (PD) is a serious condition that affects movement, and most PD patients are cared for by someone close to them, such as a family member. This caregiving can significantly impact the mental health of the caregiver, who often spends a lot of time caring for the patient and witnessing the disease's progression. We studied caregivers of PD patients at the Movement Disorders Clinic at King Khalid University Hospital and through the Saudi Parkinson's Society from July to September 2023. Caregivers completed an anonymous electronic questionnaire, and we measured caregiver burden using the Zarit Burden Interview (ZBI) and assessed anxiety and depression using the Depression Anxiety Stress Scale (DASS). Our study included 118 caregivers (53.39% female, most aged 35- 45 years, and 73.73% were sons or daughters) caring for 118 PD patients (57.63% male, most aged 66- 76 years). Caregivers who were siblings or cared for the patient daily had higher burden scores, and female caregivers had higher levels of depression, anxiety, and stress compared to males. Our study revealed that PD caregivers face a high risk of care burden, especially those who are siblings and spend longer periods in patient care, and that female caregivers exhibited an elevated risk of experiencing depression, anxiety, or stress. Language: English

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3. **Eleven Years of Change: Disease Progression in Biomarker-Defined Sporadic Parkinson's Disease.**

Authors: Gonzalez-Latapi, Paulina;Gochanour, Caroline;Cho, Hyunkeun;Ho Choi, Seung;Caspell-Garcia, Chelsea;Coffey, Christopher;Brumm, Michael;Lafontant, David-Erick;Xiao, Yuge;Tanner, Caroline;Venuto, Charles S.;Kieburtz, Karl;Chahine, Lana M.;Poston, Kathleen L.;Siderowf, Andrew;Marek, Ken and Simuni, Tanya

Publication Date: 2024

Journal: MedRxiv : The Preprint Server for Health Sciences

Abstract: Long-term longitudinal data on outcomes in sporadic Parkinson's Disease are

limited, especially from cohorts with extensive biological characterization. Recent advances in biomarkers characterization of Parkinson's Disease necessitate an updated examination of long-term progression within contemporary cohorts like the Parkinson's Progression Markers Initiative, which enrolled individuals within 2 years of clinical diagnosis of Parkinson's Disease. Our study leverages the Neuronal Synuclein Disease framework, which defines the disease based on biomarker assessed presence of neuronal alpha-synuclein and dopamine deficit, rather than based on conventional clinical diagnostic criteria. In this study we aimed to provide a comprehensive long-term description of disease progression using the integrated biological and clinical staging system framework. We analyzed data from 344 participants from the sporadic Parkinson's Disease cohort in the Parkinson's Progression Markers Initiative, who met Neuronal Synuclein Disease criteria. We assessed 11-year progression in a spectrum of clinical measures. We used Cox proportional hazards models to assess the association between baseline stage and time to key outcomes, including survival, postural instability (Hoehn & Yahr >= 3), loss of independence (Schwab & England < 80%), cognitive decline, and domain-based milestones such as walking and balance, motor complications, autonomic dysfunction, and activities of daily living. Additional analyses were completed to account for death and participant dropout. Biomarker analysis included dopamine transporter binding measures, as well as serum urate, neurofilament light chain and CSF amyloid-beta, phosphorylated tau and total tau. At baseline, despite the cohort consisting of individuals within 2 years of clinical diagnosis, there was clear separation of participants in Neuronal Synuclein Disease Stages (23% Stage 2b, 67% Stage 3, 10% Stage 4). At 11 years, data were available for 153 participants; 35 participants had died over the follow up period. Of retained participants, 59% presented normal cognition, 24% had evidence of postural instability and mean Schwab & England score was 78.5. Serum neurofilament light chain consistently increased over time. No other biofluids had a consistent change in trajectory. Of importance, baseline Neuronal Synuclein Disease Stage predicted progression to clinically meaningful milestones. This study provides data on longitudinal, 11-year progression in Neuronal Synuclein Disease participants within 2 years of clinical diagnosis. We observed better long-term outcomes in this contemporary observational study cohort. It highlights the heterogeneity in the early Parkinson's Disease population as defined by clinical diagnostic criteria and underscores the importance of shifting from clinical to biologically and functionally based inclusion criteria in the design of new clinical trials.

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4. **Functional movement disorder similar to Parkinson's disease: a case report.**

Authors: Goudarzzadeh, Sarah;Shekarabi, Shayan and Abdi, Mahnaz

Publication Date: Oct 01 ,2024

Journal: Journal of Medical Case Reports [Electronic Resource] 18(1), pp. 453

Abstract: INTRODUCTION: Functional neurological disorder challenges conventional medical understanding, presenting neurological symptoms without organic explanations. This report delves into the intricate interplay between psychological and physical manifestations, emphasizing the importance of timely diagnosis and intervention and its impact on a patient's mental health and quality of life. CASE PRESENTATION: A 40-year-old single Iranian man was admitted for the third time owing to exacerbation of mood symptoms, including depression, irritability, aggression, suicidal ideation, and movement and sensory problems.

The patient's symptoms began with psychological stressors and family conflict, leading to muscle weakness and tremors in the left hand. Over a year, muscle weakness escalated, leading to slow movement, motor impairment in the lower limbs, and reliance on a cane for walking. The patient still exhibited symptoms, such as a mask-like face, stooped walking posture, and a relative improvement of symptoms periodically. At first, the patient was suspected of Parkinson's disease and was placed on levodopa and amantadine. However, the medication was discontinued owing to an unsatisfactory response and the lack of strong evidence in favor of neurological problems on frequent examinations and reviews. Despite multiple hospitalizations, the patient's symptoms remained unresolved. Finally, after years of investigations, based on specialists' recommendations, he was admitted to the psychosomatic ward for diagnostic evaluationele, and he was diagnosed with functional neurological disorder (psychogenic parkinsonism). He underwent pharmacotherapy, electroconvulsive therapy, and psychotherapy. He was discharged with partial improvement of symptoms, but showed periods of relapse and remission during the following years. CONCLUSION: This case study illuminates functional neurological disorder complexities, emphasizing the need for a holistic diagnostic approach. Timely interventions, including psychological support, can alleviate symptoms, reduce healthcare costs, and improve the overall prognosis. The report contributes to evolving functional neurological disorder understanding in psychiatry and neurology. The report underscores early recognition, advocating for comprehensive interventions involving psychiatric support, cognitive-behavioral therapy, and patient psychoeducation.

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5. **Grip strength, genetic predisposition, and Incident Parkinson's disease: a prospective cohort study in the UK Biobank.**

Authors: Hu, Wei;Zhao, Chun-Hua;Huang, Yue-Qing;Liu, Bao-Peng and Jia, Cun-Xian

Publication Date: Oct 21 ,2024

Journal: Npj Parkinsons Disease 10(1), pp. 191

Abstract: To examine the association and modifiable risk factors between grip strength (GS) and Parkinson's disease (PD) incidence considering genetic factors, a total of 411,648 individuals without PD at baseline from the UK Biobank were included. GS was measured by a hydraulic dynamometer. The polygenic risk score assessed the genetic predisposition. Multivariable Cox regression models were performed. During a median follow-up of 12.3 years, 2409 individuals developed PD. Compared with those with high GS, low-GS individuals had a 58.5% increased risk of PD (42.7%-76.1%), and 16.3% of this excess risk could be explained by adjusted risk factors. Low GS and high genetic predisposition contribute to the highest PD risk in an additive interaction. We observed that low GS was associated with higher PD incidence, particularly among individuals with high genetic predisposition. In addition to enhancing GS, interventions targeting risk factors (e.g., unhealthy lifestyles) might also reduce the excess risk.

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6. **Health care utilization at the end of life in Parkinson's disease: a population-based register study.**

Authors: Leavy, Breiffni;Akesson, Elisabet;Lokk, Johan;Schultz, Torbjorn;Strang, Peter and

Franzen, Erika

Publication Date: Oct 29 ,2024

Journal: BMC Palliative Care 23(1), pp. 251

Abstract: BACKGROUND: Knowledge of health care utilization at the end of life in Parkinson's disease (PD) is sparse. This study aims to investigate end of life health care utilization, characterized by emergency room (ER) visits, receipt of specialized palliative care (SPC), and acute hospital deaths in a Swedish population-based PD cohort. METHODS: We conducted a retrospective cohort study on deceased patients (>= 18 years) with a PD diagnosis during their last year of life (n = 922), based on health care-provider data from Region Stockholm's data warehouse, for the study period 2015-2021. Univariable and multivariable logistic regression analyses tested associations and adjusted Odds ratios (aORs) were calculated. RESULTS: During the last month of life, approx. half of the cohort had emergency room (ER) visits and risk of frailty (measured by Hospital Frailty Risk Score) significantly predicted these visits (aOR, 3.90 (2.75-5.55)). In total, 120 people (13%) received SPC during their last three months of life, which positively associated with risk for frailty, (aOR, 2.65 (1.43-4.94, p = 0.002). In total, 284 people (31%) died in acute hospital settings. Among community-dwellers, male gender and frailty were strongly associated with acute hospital deaths (aOR, 1.90 (1.15-3.13, p = 0.01) and 3.70 (1.96-6.98, p : During the last month of life, approx. half of the cohort had emergency room (ER) visits and risk of frailty (measured by Hospital Frailty Risk Score) significantly predicted these visits (aOR, 3.90 (2.75-5.55)). In total, 120 people (13%) received SPC during their last three months of life, which positively associated with risk for frailty, (aOR, 2.65 (1.43-4.94, p = 0.002). In total, 284 people (31%) died in acute hospital settings. Among community-dwellers, male gender and frailty were strongly associated with acute hospital deaths (aOR, 1.90 (1.15-3.13, p = 0.01) and 3.70 (1.96-6.98, p CONCLUSIONS: Rates of ER visits at end of life and hospital deaths were relatively high in this population-based cohort. Considering a high disease burden, referral to SPC at end of life was relatively low. Sex-specific disparities in health care utilization are apparent. Identifying people with high risk for frailty could assist the planning of optimal end-of-life care for people with PD. Copyright © 2024. The Author(s).

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7. **The combination of 18F-fluorodeoxyglucose and 18F 9-fluoropropyl-(+)-dihydrotetrabenazine positron emission tomography for distinguishing between early-onset and late-onset idiopathic Parkinson disease and analyzing influencing factors.**

Authors: Li, Shuang;Lu, Weizhao;Yan, Shaozhen;Song, Tianbin;Zhang, Chun;Yang, Chang and Lu, Jie

Publication Date: Oct 01 ,2024

Journal: Quantitative Imaging in Medicine & Surgery 14(10), pp. 7406–7419

Abstract: Background: The classification of Parkinson disease by age of onset has proven to be a valuable method for subtyping, given its practical application in clinical settings. However, the interactions between the metabolic brain changes, dopaminergic dysfunction, and clinical manifestations in patients with early-onset (early-iPD) and late-onset (late-iPD) idiopathic

Parkinson disease have not been adequately evaluated. Therefore, this study aimed to investigate the difference in cerebral metabolism and presynaptic dopaminergic function between patients with early-iPD and those with late-onset disease using 18F-fluorodeoxyglucose (18F-FDG) and [18F] 9-fluoropropyl-(+)-dihydrotetrabenazine (18F-FP-DTBZ) positron emission tomography (PET). Furthermore, the goal was to further explore the correlation between imaging measurements and clinical manifestations in the early and late idiopathic patients with Parkinson disease. Methods: This cross-sectional study included 80 patients with idiopathic Parkinson disease and 29 healthy control participants who underwent 18F-FDG and18F-FP-DTBZ PET imaging at Xuanwu Hospital, Capital Medical University from August 2022 to August 2023. The patients were categorized into early-iPD (n=27) and late-iPD (n=53) groups based on an age threshold of 50 years. The mean standardized uptake value of 18F-FDG and the standardized uptake value ratio (SUVR) of 18F-FP-DTBZ were compared between the early-iPD and late-iPD groups using unpaired Student t-tests. Furthermore, pairwise correlations among cerebral metabolism, dopaminergic function, and corresponding clinical ratings in all patients were conducted using Pearson correlation analysis. Results: Patients with late-iPD exhibited a significant metabolic decrease in the frontal, parietal, and temporal cortex, along with the globus pallidus, putamen, thalamus, and cerebellum, compared to those with early-iPD in 18F-FDG PET imaging (all P values F-FDG PET imaging (all P values 18F-FP-DTBZ binding potential was significantly lower in the contralateral caudate and anterior putamen of patients with late-iPD compared to those with early-iPD (contralateral caudate: 3.16+/-1.2 vs. 2.63+/-0.7, P=0.020; contralateral anterior putamen: 2.49+/-1.2 vs. 2.05+/-0.7, P=0.040). Further analysis of the correlations between imaging clinical features revealed that glucose metabolism increases and dopaminergic function decreases with higher motor ratings. Conclusions: 18F-FDG and 18F-FP-DTBZ PET offer an objective molecular imaging basis for distinguishing between early-onset and late-onset idiopathic with Parkinson disease. Additionally, correlation analysis between imaging and clinical data represents a new approach for exploring the potential applications in future studies involving patients with early-iPD and late-iPD.

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8. **Polyconnectomic scoring of functional connectivity patterns across eight neuropsychiatric and three neurodegenerative disorders.**

Authors: Libedinsky I.;Helwegen K.;Boonstra J.;Guerrero Simon L.;Gruber M.;Repple J.;Kircher T.;Dannlowski U. and van den Heuvel, M. P.

Publication Date: 2024

Journal: Biological Psychiatry (pagination), pp. Date of Publication: 16 Oct 2024

Abstract: BACKGROUND: Neuropsychiatric and neurodegenerative disorders involve diverse changes in brain functional connectivity. As an alternative to approaches searching for specific mosaic patterns of affected connections and networks, we used polyconnectomic scoring to quantify disorder-related whole-brain connectivity signatures into interpretable, personalized scores. METHOD(S): The polyconnectomic score (PCS) measures the extent to which an individual's functional connectivity (FC) mirrors the whole-brain circuitry characteristics of a trait. We computed PCS for eight neuropsychiatric conditions (attention-deficit/hyperactivity disorder, anxiety-related disorders, autism spectrum disorder, obsessive-compulsive disorder,

bipolar disorder, major depressive disorder, schizoaffective disorder, and schizophrenia) and three neurodegenerative conditions (Alzheimer's disease, frontotemporal dementia, and Parkinson's disease) across 22 datasets with resting-state functional MRI of 10,667 individuals (5,325 patients, 5,342 controls). We further examined PCS in 26,673 individuals from the population-based UK Biobank cohort. RESULT(S): PCS was consistently higher in out-of-sample patients across six of the eight neuropsychiatric and across all three investigated neurodegenerative disorders ([min, max]: AUC = [0.55, 0.73], pFDR = [1.8 x 10-16, 4.5 x 10-2]). Individuals with elevated PCS levels for neuropsychiatric conditions exhibited higher neuroticism (pFDR RESULT(S): PCS was consistently higher in out-of-sample patients across six of the eight neuropsychiatric and across all three investigated neurodegenerative disorders ([min, max]: AUC = [0.55, 0.73], pFDR = [1.8 x 10-16, 4.5 x 10-2]). Individuals with elevated PCS levels for neuropsychiatric conditions exhibited higher neuroticism (pFDR RESULT(S): PCS was consistently higher in out-of-sample patients across six of the eight neuropsychiatric and across all three investigated neurodegenerative disorders ([min, max]: AUC = [0.55, 0.73], pFDR = [1.8 x 10-16, 4.5 x 10-2]). Individuals with elevated PCS levels for neuropsychiatric conditions exhibited higher neuroticism (pFDR RESULT(S): PCS was consistently higher in out-of-sample patients across six of the eight neuropsychiatric and across all three investigated neurodegenerative disorders ([min, max]: AUC = [0.55, 0.73], pFDR = [1.8 x 10-16, 4.5 x 10-2]). Individuals with elevated PCS levels for neuropsychiatric conditions exhibited higher neuroticism (pFDR CONCLUSION(S): Our findings reveal generalizable whole-brain connectivity alterations in brain disorders. PCS effectively aggregates disorder-related signatures across the entire brain into an interpretable, subject-specific metric. A toolbox is provided for PCS computation.Copyright © 2024. Published by Elsevier Inc.

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9. **The effect of two speech and language approaches on speech problems in people with Parkinson's disease: the PD COMM RCT.**

Authors: Sackley, Catherine M.;Rick, Caroline;Brady, Marian C.;Burton, Christopher;Jowett, Sue;Patel, Smitaa;Woolley, Rebecca;Masterson-Algar, Patricia;Nicoll, Avril;Smith, Christina H.;Abdali, Zainab;Ives, Natalie;Beaton, Gillian;Dickson, Sylvia;Ottridge, Ryan;Nankervis, Helen and Clarke, Carl E.

Publication Date: Oc ,2024

Journal: Health Technology Assessment (Winchester, England) 28(58), pp. 1–141

Abstract: Background: Speech impairments are common with Parkinson's disease (reported prevalence 68%), increasing conversational demands, reliance on family and social withdrawal. Objective(s): The PD COMM trial compared the clinical and cost-effectiveness of two speech and language therapy approaches: Lee Silverman Voice Treatment LOUD and National Health Service speech and language therapy for the treatment of speech or voice problems in people with Parkinson's disease to no speech and language therapy (control) and against each other. Design: PD COMM is a phase III, multicentre, three-arm, unblinded, randomised controlled trial. Participants were randomised in a 1 : 1 : 1 ratio to control, National Health Service speech and language therapy or Lee Silverman Voice Treatment LOUD via a central computer-generated programme, using a minimisation procedure with a random element, to ensure allocation concealment. Mixed-methods process and health economic evaluations were conducted. Setting: United Kingdom outpatient and home settings.

Participants: People with idiopathic Parkinson's disease, with self-reported or carer-reported speech or voice problems. We excluded people with dementia, laryngeal pathology and those within 24 months of previous speech and language therapy. Interventions: The Lee Silverman Voice Treatment LOUD intervention included maximum effort drills and high-effort speech production tasks delivered over four 50-minute therapist-led personalised sessions per week, for 4 weeks with prescribed daily home practice. National Health Service speech and language therapy content and dosage reflected local non-Lee Silverman Voice Treatment speech and language therapy practices, usually 1 hour, once weekly, for 6 weeks. Trained, experienced speech and language therapists or assistants provided interventions. The control was no speech and language therapy until the trial was completed. Main outcome measures: Primary outcome: Voice Handicap Index total score at 3 months. Secondary outcomes: Voice Handicap Index subscales, Parkinson's Disease Questionnaire-39; Questionnaire on Acquired Speech Disorders; EuroQol-5D-5L; ICEpop Capabilities Measure for Older Adults; Parkinson's Disease Questionnaire - Carers; resource utilisation; and adverse events. Assessments were completed pre-randomisation and at 3, 6 and 12 months post randomisation. Results: Three hundred and eighty-eight participants were randomised to Lee Silverman Voice Treatment LOUD (n = 130), National Health Service speech and language therapy (n = 129) and control (n = 129). The impact of voice problems at 3 months after randomisation was lower for Lee Silverman Voice Treatment LOUD participants than control [-8.0 (99% confidence interval: -13.3, -2.6); p = 0.001]. There was no evidence of improvement for those with access to National Health Service speech and language therapy when compared to control [1.7 (99% confidence interval: -3.8, 7.1); p = 0.4]. Participants randomised to Lee Silverman Voice Treatment LOUD reported a lower impact of their voice problems than participants randomised to National Health Service speech and language therapy [99% confidence interval: -9.6 (-14.9, -4.4); p Limitations: The number of participants recruited to the trial did not meet the pre-specified power. Conclusions: People that had access to Lee Silverman Voice Treatment LOUD described a significantly greater reduction in the impact of their Parkinson's disease-related speech problems 3 months after randomisation compared to people that had no speech and language therapy. There was no evidence of a difference between National Health Service speech and language therapy and those that received no speech and language therapy. Lee Silverman Voice Treatment LOUD resulted in a significantly lower impact of voice problems compared to National Health Service speech and language therapy 3 months after randomisation which was still present after 12 months; however, Lee Silverman Voice Treatment LOUD was not found to be cost-effective. Future work: Implementing Lee Silverman Voice Treatment LOUD in the National Health Service and identifying alternatives to Lee Silverman Voice Treatment LOUD for those who cannot tolerate it. Investigation of less costly alternative options for Lee Silverman Voice Treatment delivery require investigation, with economic evaluation using a preference-based outcome measure that captures improvement in communication. Study registration: This study is registered as ISRCTN12421382. Funding: This award was funded by the National Institute for Health and Care Research (NIHR) Health Technology Assessment programme (NIHR award ref: 10/135/02) and is published in full in Health Technology Assessment; Vol. 28, No. 58. See the NIHR Funding and Awards website for further award information.; plain-language-summary Most people with Parkinson's disease develop difficulties with their speech and voice. Communicating becomes difficult. This affects their relationships, work, social life and how they feel about themselves. Our PD COMM trial compared two types of speech and language therapy to find out if they helped the speech and voice problems people with Parkinson's have. We measured changes in the way their voice and speech problems affected their lives and how much therapy cost the National Health Service and families. Everyone taking part had speech or voice problems because of their

Parkinson's disease. People could not take part if they had dementia, evidence of laryngeal pathology or previous laryngeal surgery or received speech and therapy for Parkinson's disease in the last 2 years. People who agreed to take part joined one of three groups, which were alike except for the therapy they received. A computer decided which group they joined by chance. National Health Service speech and language therapy Lee Silverman Voice Treatment LOUD No speech and language therapy for 12 months The 388 people who took part came from 41 outpatient clinics in Scotland, England and Wales. Most were older men. The people that received Lee Silverman Voice Treatment LOUD felt better about their speech and voice after 3 months compared to people in the other groups. A year later, they still felt better about it. People that received National Health Service therapy had no benefit compared to people with no access to therapy. Analysis of cost-effectiveness indicated that Lee Silverman Voice Treatment LOUD did not offer value for money and the intervention cost more because more speech and language therapy time was needed to deliver it. Our next question is to ask how we can provide Lee Silverman Voice Treatment LOUD in a way that costs less, for example, using therapy assistants and computer packages or at home. Clear speech and language therapy approaches for people with Parkinson's disease and speech or voice problems should be tested in trials that measure changes in people's lives. Language: English

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10. **Subthalamic Stimulation Improves Short-Term Satisfaction with Life and Treatment in Parkinson's Disease.**

Authors: Sauerbier, Anna;Bachon, Pia;Ambrosio, Leire;Loehrer, Philipp A.;Rizos, Alexandra;Jost, Stefanie T.;Gronostay, Alexandra;Fink, Gereon R.;Ashkan, Keyoumars;Nimsky, Christopher;Visser-Vandewalle, Veerle;Chaudhuri, K. Ray;Timmermann, Lars;Martinez-Martin, Pablo and Dafsari, Haidar S.

Publication Date: Sep 26 ,2024

Journal: Journal of Personalized Medicine 14(10)

Abstract: The effect of subthalamic stimulation (STN-DBS) on patients' personal satisfaction with life and their Parkinson's disease (PD) treatment is understudied, as is its correlation with quality of life (QoL). Therefore, we tested the hypothesis that STN-DBS for PD enhances satisfaction with life and treatment. In a prospective, multicenter study with a 6-month follow-up involving 121 patients, we measured the main outcomes using the Satisfaction with Life and Treatment Scale (SLTS-7). Secondary outcomes included the eight-item PD Questionnaire (PDQ-8), European QoL Questionnaire (EQ-5D-3L), EQ-Visual Analogue Scale (VAS), Non-Motor Symptom Scale (NMSS), Hospital Anxiety and Depression Scale (HADS), and Unified PD Rating Scale (UPDRS). Longitudinal outcome changes, effect sizes (Cohen's d), and correlations between outcome changes were analyzed. SLTS-7 scores improved at the 6-month follow-up, particularly in the domains of 'satisfaction with physical health' and 'satisfaction with treatment'. Change scores correlated strongly (EQ-VAS), moderately (PDQ-8 SI and HADS), and weakly (UPDRS-activities of daily living and EQ-5D-3L) with other scales. Satisfaction with physical health, psychosocial well-being, or treatment was not related to UPDRS-motor examination. This study provides evidence that STN-DBS enhances patients' personal satisfaction with life and treatment. This satisfaction is associated with improvements in the QoL, daily activities, and neuropsychiatric aspects of PD rather than its motor aspects.

11. **Severe and unclassifiable tremor.**

Authors: Serrano-Duenas, Marcos

Publication Date: Oc ,2024

Journal: Arquivos De Neuro-Psiquiatria 82(10), pp. 1–5

Abstract: BACKGROUND: Patients often exhibit very severe or disabling forms of tremor that cannot be clearly characterized. OBJECTIVE: To present a series of 37 cases of tremor considered unclassifiable. Patients diagnosed with essential tremor according to criteria of the International Parkinson Disease and Movement Disorder Society (IPDMDS), who had been previously studied, were included as controls. All patients underwent a battery of tests between 2019 and 2022, which enabled us to compare them. METHODS: Relevant demographic and clinical information were collected. The following tools were applied: the Mini-Mental State Examination (MMSE); the Hospital Anxiety and Depression Scale (HADS); the Fahn-Tolosa-Marin Tremor Rating Scale (TRS); and the Quality of Life in Essential Tremor (QUEST). A simple brain magnetic resonance imaging (MRI) scan was performed for all patients. The categorical variables were compared using the Chi-squared test and the t-test with Fisher correction if appropriate, and the quantitative variables were compared through the two-tailed Student t-test. Values of p RESULTS: The cases presented higher scores on the anxiety and depression subscales of the HADS than the controls (p p CONCLUSION: There are patients with unclassifiable and extremely disabling tremors who respond poorly to the pharmacological therapy options. Copyright The Author(s). This is an open access article published by Thieme under the terms of the Creative Commons Attribution 4.0 International License, permitting copying and reproduction so long as the original work is given appropriate credit (https://creativecommons.org/licenses/by/4.0/).; Publisher ANTECEDENTES: Os pacientes muitas vezes apresentam formas muito graves ou incapacitantes de tremor que nao podem ser claramente caracterizadas. OBJETIVO: O objetivo deste trabalho foi apresentar uma serie de 37 casos de tremor considerados inclassificaveis. Pacientes diagnosticados com tremor essencial de acordo com os criterios da International Parkinson Disease and Movement Disorder Society (IPDMDS), ja estudados anteriormente, foram incluidos como controles. Todos os pacientes foram submetidos a exames entre 2019 e 2022 para permitir sua comparac ao. MeTODOS: As informac oes demograficas e clinicas relevantes foram coletadas. As seguintes ferramentas foram aplicadas: o Miniexame do Estado Mental (MEEM), a Escala Hospitalar de Ansiedade e Depressao (HADS, do ingles Hospital Anxiety and Depression Scale), a Escala de Avaliac ao de Tremor de Fahn-Tolosa-Marin (TRS, do ingles Fahn-Tolosa-Marin Tremor Rating Scale) e a Qualidade de Vida em Tremor Essencial (QUEST, do ingles Quality of Life in Essential Tremor). Uma ressonancia magnetica simples do cerebro foi realizada em todos os pacientes. As variaveis categoricas foram comparadas pelo teste qui-quadrado e pelo teste t com correc ao de Fisher, se apropriado, enquanto as variaveis quantitativas foram comparadas por meio do teste t de Student bicaudal. Valores de p p p <= 0,000). A atrofia cerebelar foi apresentada por todos os pacientes do grupo de casos e em 24 individuos do grupo de controle. A distonia foi observada em sete individuos do grupo de casos e em nenhum dos pacientes do grupo controle. CONCLUSaO: Ha pacientes com tremores inclassificaveis e extremamente incapacitantes que respondem mal as opc oes terapeuticas farmacologicas. Language: Portuguese

12. **Gut-Brain Nexus: Mapping Multi-Modal Links to Neurodegeneration at Biobank Scale.**

Authors: Shafieinouri, Mohammad;Hong, Samantha;Schuh, Artur;Makarious, Mary B.;Sandon, Rodrigo;Lee, Paul Suhwan;Simmonds, Emily;Iwaki, Hirotaka;Hill, Gracelyn;Blauwendraat, Cornelis;Escott-Price, Valentina;Qi, Yue A.;Noyce, Alastair J.;Reyes-Palomares, Armando;Leonard, Hampton L.;Tansey, Malu;Dadu, Anant;Faghri, Faraz;Singleton, Andrew;Nalls, Mike A., et al

Publication Date: 2024

Journal: MedRxiv : The Preprint Server for Health Sciences

Abstract: Alzheimer's disease (AD) and Parkinson's disease (PD) are influenced by genetic and environmental factors. Using data from UK Biobank, SAIL Biobank, and FinnGen, we conducted an unbiased, population-scale study to: 1) Investigate how 155 endocrine, nutritional, metabolic, and digestive system disorders are associated with AD and PD risk prior to their diagnosis, considering known genetic influences; 2) Assess plasma biomarkers' specificity for AD or PD in individuals with these conditions; 3) Develop a multi-modal classification model integrating genetics, proteomics, and clinical data relevant to conditions affecting the gut-brain axis. Our findings show that certain disorders elevate AD and PD risk before AD and PD diagnosis including: insulin and non-insulin dependent diabetes mellitus, noninfective gastro-enteritis and colitis, functional intestinal disorders, and bacterial intestinal infections, among others. Polygenic risk scores revealed lower genetic predisposition to AD and PD in individuals with co-occurring disorders in the study categories, underscoring the importance of regulating the gut-brain axis to potentially prevent or delay the onset of neurodegenerative diseases. The proteomic profile of AD/PD cases was influenced by comorbid endocrine, nutritional, metabolic, and digestive systems conditions. Importantly, we developed multi-modal prediction models integrating clinical, genetic, proteomic and demographic data, the combination of which performs better than any single paradigm approach in disease classification. This work aims to illuminate the intricate interplay between various physiological factors involved in the gut-brain axis and the development of AD and PD, providing a multifactorial systemic understanding that goes beyond traditional approaches.

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13. **Association of Baseline Depression and Anxiety with Longitudinal Health Outcomes in Parkinson's Disease.**

Authors: Shi, Yiwen;Dobkin, Roseanne;Weintraub, Daniel;Cho, Hyunkeun R.;Caspell-Garcia, Chelsea;Bock, Meredith;Brown, Ethan;Aarsland, Dag and Dahodwala, Nabila

Publication Date: Se ,2024

Journal: Movement Disorders Clinical Practice 11(9), pp. 1103–1112

Abstract: BACKGROUND: Anxiety and depression are common non-motor symptoms in Parkinson's disease (PD) but remain under-recognized and under-treated. OBJECTIVES: To evaluate functional outcomes associated with baseline anxiety or depression and effects related to the initiation of new psychiatric treatment. METHODS: We analyzed 7 years of data

from patients with de novo PD enrolled in the Parkinson's Progression Markers Initiative. Longitudinal regression models evaluated the association between baseline anxiety and depression with Schwab and England (SE) and MDS-UPDRS total scores over time. Cox proportional hazard models assessed effects of baseline anxiety and depression on time to initiation of dopaminergic therapy. Piecewise linear regression models examined the association of treatment initiation for anxiety and depression with SE and MDS-UPDRS. RESULTS: 490 participants with baseline depression and anxiety data were included. Anxiety and depression were associated with lower SE (anxiety: beta = -1.31, P = 0.038, depression: beta = -1.96, P = 0.012, co-morbid: beta = -2.70, P = 0.003) and higher MDS-UPDRS scores (anxiety: beta = 5.37, P : 490 participants with baseline depression and anxiety data were included. Anxiety and depression were associated with lower SE (anxiety: beta = -1.31, P = 0.038, depression: beta = -1.96, P = 0.012, co-morbid: beta = -2.70, P = 0.003) and higher MDS-UPDRS scores (anxiety: beta = 5.37, P : 490 participants with baseline depression and anxiety data were included. Anxiety and depression were associated with lower SE (anxiety: beta = -1.31, P = 0.038, depression: beta = -1.96, P = 0.012, co-morbid: beta = -2.70, P = 0.003) and higher MDS-UPDRS scores (anxiety: beta = 5.37, P : 490 participants with baseline depression and anxiety data were included. Anxiety and depression were associated with lower SE (anxiety: beta = -1.31, P = 0.038, depression: beta = -1.96, P = 0.012, co-morbid: beta = -2.70, P = 0.003) and higher MDS-UPDRS scores (anxiety: beta = 5.37, P : 490 participants with baseline depression and anxiety data were included. Anxiety and depression were associated with lower SE (anxiety: beta = -1.31, P = 0.038, depression: beta = -1.96, P = 0.012, co-morbid: beta = -2.70, P = 0.003) and higher MDS-UPDRS scores (anxiety: beta = 5.37, P CONCLUSIONS: Anxiety and depression at PD onset are associated with multiple negative longitudinal trajectories. However, preliminary findings suggest that anxiety and depression treatment may be linked with improved motor and non-motor outcomes.

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14. **Parkinson's families project: a UK-wide study of early onset and familial Parkinson's disease.**

Authors: Towns, Clodagh;Fang, Zih-Hua;Tan, Manuela M. X.;Jasaityte, Simona;Schmaderer, Theresa M.;Stafford, Eleanor J.;Pollard, Miriam;Tilney, Russel;Hodgson, Megan;Wu, Lesley;Labrum, Robyn;Hehir, Jason;Polke, James;Lange, Lara M.;Schapira, Anthony H. V.;Bhatia, Kailash P.;Singleton, Andrew B.;Blauwendraat, Cornelis;Klein, Christine;Houlden, Henry, et al

Publication Date: Oct 17 ,2024

Journal: Npj Parkinsons Disease 10(1), pp. 188

Abstract: The Parkinson's Families Project is a UK-wide study aimed at identifying genetic variation associated with familial and early-onset Parkinson's disease (PD). We recruited individuals with a clinical diagnosis of PD and age at motor symptom onset

15. **Prospective study of bipolar disorder and neurodegenerative diseases.**

Authors: Xu, Xinming;Li, Yaqi;Lu, Hanyu;Wang, Han;Guo, Yi;Dregan, Alexandru;Sun, Liang;Shen, Yun;Geng, Tingting and Gao, Xiang

Publication Date: Oct 03 ,2024

Journal: Npj Parkinsons Disease 10(1), pp. 184

Abstract: Bipolar disorder (BD) is linked to an increased risk of neurodegenerative diseases such as dementia and Parkinson disease (PD), yet several uncertainties still remain and the extent to which the associations could be explained by BD-related medications (antipsychotics, lithium, and antiepileptics) was unknown. This study included 501,233 UK Biobank participants (mean [standard deviation] age, 56.5 [8.10] years; 54.4% women), free of dementia and PD at baseline. After a median 13.8 year follow-up, 9422 cases of dementia and 3457 PD cases were identified. Participants with BD had a significantly higher risk of dementia (adjusted hazard ratio [HR] 2.52, 95% CI 2.00-3.19) and PD (adjusted HR 2.88, 95% CI 2.03-4.08). Findings suggest that up to two-thirds of the association of neurodegenerative diseases with BD may be mediated by BD-related medications. Further research is needed to confirm these findings and explore the underlying mechanisms. Copyright © 2024. The Author(s).

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16. **Association between neutrophil-to-lymphocyte ratio and motor subtypes in idiopathic Parkinson's disease: a prospective observational study.**

Authors: Yi, Hongyan;Liang, Xiaojing;Xu, Fugui;Li, Tiantian;Yang, Xiu;Wei, Ming;Ou, Zhou;Wang, Lijun and Tong, Qiang

Publication Date: Oct 08 ,2024

Journal: BMC Neurology 24(1), pp. 379

Abstract: BACKGROUND: Peripheral immunity and neuroinflammation interact with each other and they play important roles in the pathophysiology of idiopathic Parkinson's disease (IPD). There have been very few real-world reports on the relationship between peripheral immune inflammation and motor phenotypes of IPD. This study aimed to investigate the potential correlation between peripheral inflammatory indicators and motor subtypes in patients with IPD. METHODS: This observational, prospective case-control study examined patients with IPD and healthy controls (HC) matched for age and sex between September 2021 and July 2023 at the Affiliated Huaian No. 1 People's Hospital of Nanjing Medical University. The levels of peripheral inflammatory indicators were collected from each patient with IPD and HCs. Differences in the levels of peripheral inflammatory indicators among groups were compared. Binary logistic regression analysis was used to explore the inflammatory mechanism underlying the motor subtype of IPD. RESULTS: A total number of 94 patients with IPD were recruited at the Affiliated Huaian No. 1 People's Hospital of Nanjing Medical University between September 2021 and July 2023, including 49 males and 45 females, and 37 healthy volunteers matched for age and sex were also enrolled as the control group. Of the 94 patients with IPD, 42.6% performed as the TD motor subtype and 57.4% performed as the AR motor subtype. NLR and the plasma levels of IL-1betaand TNF-alpha in

the IPD group were higher than those in the HC group (P : A total number of 94 patients with IPD were recruited at the Affiliated Huaian No. 1 People's Hospital of Nanjing Medical University between September 2021 and July 2023, including 49 males and 45 females, and 37 healthy volunteers matched for age and sex were also enrolled as the control group. Of the 94 patients with IPD, 42.6% performed as the TD motor subtype and 57.4% performed as the AR motor subtype. NLR and the plasma levels of IL-1betaand TNF-alpha in the IPD group were higher than those in the HC group (P : A total number of 94 patients with IPD were recruited at the Affiliated Huaian No. 1 People's Hospital of Nanjing Medical University between September 2021 and July 2023, including 49 males and 45 females, and 37 healthy volunteers matched for age and sex were also enrolled as the control group. Of the 94 patients with IPD, 42.6% performed as the TD motor subtype and 57.4% performed as the AR motor subtype. NLR and the plasma levels of IL-1betaand TNF-alpha in the IPD group were higher than those in the HC group (P CONCLUSION: NLR is strongly associated with the AR motor subtype in IPD, and peripheral immunity is probably involved in the pathogenesis of AR motor subtype in IPD. Copyright © 2024. The Author(s).

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17. **Deep brain stimulation for Parkinson's disease: bibliometric analysis of the top 100 cited literature**

Authors: Zhao, Weijie;Shao, Xinxin;Wang, Ziyue;Mi, Chuanhao;Wang, Yu;Qi, Xianghua and Ding, Xiao

Publication Date: 2024

Journal: Frontiers in Aging Neuroscience 16, pp. 1413074

Abstract: Background: Deep Brain Stimulation (DBS) has been widely applied and accepted in the treatment of neurological and psychiatric disorders. Despite numerous studies exploring the effects of DBS on the progression of neurodegenerative diseases and the treatment of advanced Parkinson's disease (PD), there is a limited number of articles summarizing this research. The purpose of this study is to investigate the current trends, hot topics, and potential in research surrounding DBS therapy for PD, as well as to anticipate the challenges of such research. Methods: We searched the Web of Science Core Collection database (WoSCC) for DBS research literature related to PD published from January 2014 to January 2024, utilized CiteSpace, VOS viewer, the bibliometric online analysis platform, Scimago Graphica, Microsoft Excel 2021, and R software version 4.2.3 for data analysis. And we conducted quantitative research on publications, citations, journals, authors, countries, institutions, keywords, and references, visualized the results in network graphs. Results: From 2014 to 2024, papers from 39 journals from 11 countries were among the top 100 cited. Most papers were published in Neurology, with the highest average citations per paper in Nature Neuroscience. The United States (US) contributed the most publications, followed by the United Kingdom (UK) and Germany. In terms of total publications, University College London (UCL) contributed the most papers. The primary classifications of articles were Clinical Neurology, Neurosciences, and Surgery. The top five keywords were subthalamic nucleus, DBS, PD, medical therapy, and basal ganglia. Cluster analysis indicates that DBS research focus on improving quality of life and applying computational models. Conclusion: Through bibliometric analysis, researchers could quickly and clearly understand the hotspots and boundaries of their research field, thus guiding their research direction and scope to improve

research efficiency and the quality of outcomes. Although studies indicate that DBS is currently a crucial method for treating advanced PD, in the long run, creating a personalized, low-cost treatment regimen with precise targeting and long-term efficacy poses a challenge.

Sources Used:

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

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