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Parkinson's Disease

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February 2025

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1. **Paranoia and unusual sensory experiences in Parkinson's disease.**

Authors: Brown P.;Freeman D.;Loe B.S.;Dow R. and Johns, L.

Publication Date: 2025

Journal: Aging & Mental Health , pp. 1–16

Abstract: OBJECTIVES: There has been limited exploration into the nature and development of psychotic experiences (PEs) in Parkinson's disease (PD). We aimed to comprehensively assess the frequency, severity, and associated distress of paranoia and unusual sensory experiences (USEs) in PD, and to assess what variables are significantly associated with these experiences, focussing on psychological processes central to understanding PEs in non-PD groups. METHOD(S): A questionnaire battery was completed by 369 individuals with PD with a mean age of 66 years and mean time since diagnosis of 5 years. Recruitment was via Parkinson's UK, social media, and local community groups. For a subset of measures, comparisons were made to age-matched controls using pre-existing data. RESULT(S): 182 (49%) participants reported USEs, including almost half of those not taking dopaminergic medication. For 83 (23%), the experience was distressing. Paranoia across the sample was significantly lower than in age-matched controls. However, specific paranoid concerns around abandonment (16%) and spousal betrayal (10%) were reported by some. Depression, anxiety, loneliness, and stigma and desire for support with PEs were high across the sample. Almost all psychological variables were significantly associated with PEs in structural equation models. CONCLUSION(S): PEs in PD are common, even in those not taking dopaminergic medication. For a small subset, these experiences are distressing and not resolved by existing

treatment. Cognitive-affective variables like depression and anxiety could play a maintaining role in PEs in PD thus providing easy avenues for trialling intervention.

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2. **Changes in sensor recorded activity patterns and neuropsychiatric symptoms after deep brain stimulation for Parkinson's disease: 5 case reports.**

Authors: Bruhin, Lena C.;Single, Michael;Naef, Aileen C.;Petermann, Katrin;Sousa, Mario;Castelli, Matilde;Debove, Ines;Maradan-Gachet, Marie E.;Magalhaes, Andreia D.;Diamantaras, Andreas A.;Lachenmayer, M. Lenard;Tinkhauser, Gerd;Waskonig, Julia;El Achkar, Christopher M.;Lemkaddem, Alia;Lemay, Mathieu;Krack, Paul;Nef, Tobias and Amstutz, Deborah

Publication Date: Jan 17 ,2025

Journal: BMC Neurology 25(1), pp. 25

Abstract: BACKGROUND: Effects of subthalamic nucleus deep brain stimulation (STN-DBS) on neuropsychiatric symptoms of Parkinson's disease (PD) remain debated. Sensor technology might help to objectively assess behavioural changes after STN-DBS. CASE PRESENTATION: 5 PD patients were assessed 1 before and 5 months after STN-DBS with the Movement Disorders Society Unified Parkinson's Disease Rating Scale part III in the medication ON (plus postoperatively stimulation ON) condition, the Montreal Cognitive Assessment, the Questionnaire for Impulsive-Compulsive Behaviors in Parkinson's Disease Rating Scale present version, the Hospital Anxiety and Depression Scale and the Starkstein Apathy Scale. Steps taken per hour, nighttime spent in bed and time spent outside were monitored with a smartwatch and ambient sensors placed in patient homes for an average of 20 days pre- and postoperatively. Postoperative improvement in ICDs and concomitant anxious-depressive symptoms was observed in 3 patients and was accompanied by a decrease in steps taken per hour, as well as an increase in nighttime spent in bed. In the two patients without baseline ICDs, mild anxiety and apathy improved postoperatively, and no new neuropsychiatric symptoms occurred. Steps taken per hour did not decrease in these cases and nighttime spent in bed improved in one of the patients, but decreased in the other, who had experienced pain during OFF-phases at night before STN-DBS. CONCLUSION: Changes in neuropsychiatric symptoms are associated with distinct activity patterns after STN-DBS, and wearable and ambient sensors may aid to capture those gradual shifts in behavior.

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3. **Parkinson's disease and deep brain stimulation of the subthalamic nucleus (STN-DBS): long-term disease evaluation and neuropsychological outcomes in a 9-year matched-controlled study.**

Authors: Cabrera-Montes, Jorge;Sanz-Arranz, Alberto;Hernandez-Vicente, Javier and Lara-Almunia, Monica

Publication Date: Jan 23 ,2025

Journal: Neurosurgical Review 48(1), pp. 74

Abstract: Matched-controlled long-term disease evaluation and neuropsychological outcomes derived from deep brain stimulation of the subthalamic nucleus (STN-DBS) in Parkinson's disease (PD) are lacking, with inconsistent results regarding the cognitive impact of this procedure. Here we study the long-term effects associated to DBS comparing outcomes with a matched control group. A prospective observational study of 40 patients with PD with bilateral STN-DBS, with a mean follow-up of 9 (6-12) years was conducted. Disease evaluation was performed using the UPDRS-III, UPDRS-II, Hoehn-Yahr, and Schwab-England scales. Neuropsychological assessments were achieved utilizing the MMSE, DRS, RAVLT, BVRT, Stroop, and verbal fluency tests. A control group was used for comparison. Statistical analysis was performed with SPSSv.26. 40 patients were included, with a mean age of 62.8 +/- 8.5 at the time of intervention. An improvement in motor symptoms of 48.6% (p

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4. **Prodromal Parkinson's disease and subsequent risk of Parkinson's disease and mortality.**

Authors: Chen, Xiao;Li, Yaqi;Shen, Yun;Schwarzschild, Michael A. and Gao, Xiang

Publication Date: Jan 09 ,2025

Journal: Npj Parkinsons Disease 11(1), pp. 14

Abstract: Association of prodromal Parkinson's disease (PD) with risk of PD and risk of mortality in individuals with PD warrant investigation through large-scale prospective study. We included 501,475 participants without PD at baseline. Eight prodromal features were measured. Incident PD cases were identified via hospital admission, death register, and self-report. Cox regression models were used to compute hazard ratios (HRs) and 95% confidence intervals (CIs). Multivariable-adjusted HRs3+vs.0 prodromal PD features and 95%CIs were 3.12 (2.58-3.78) for men and 2.71 (2.11-3.47) for women. Prodromal PD predicted only PD onset occurred during the first 6 years of follow-up (HR3+vs.0 prodromal features = 10.5; 95% CI: 8.60-12.9), but not after 6 years (HR = 1.00; 95%CI: 0.76-1.32). The presence of prodromal PD conferred a higher risk of mortality among participants with PD. Having prodromal PD were associated with higher probability of developing PD in short-term and higher risk of mortality among individuals with PD.

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5. **Is rapid eye movement sleep behavior disorder a marker of Parkinson's disease severity?.**

Authors: de Oliveira P.;Rodolpho Ramalho S.H.;Martins B. and Cardoso, F.

Publication Date: 2025

Journal: Parkinsonism and Related Disorders 131(pagination), pp. Article Number: 107258. Date of Publication: 01 Feb 2025

Abstract: Background: Parkinson's disease (PD) is characterized by motor and non-motor features. There are several proposed clinical markers to define disease severity. However, if

rapid eye movement sleep behavior disorder (RBD) is associated with worse prognosis of both motor and non-motor findings in PD is unknown. Objective(s): To determine whether RBD is a marker of PD clinical severity. Method(s): We cross-sectionally compared patients according to the presence of RBD and used Hoehn Yahr, Schwab and England (ADL), MDS-UPDRS, brain magnetic resonance, polysomnography and autonomic reactivity tests to evaluate PD stage and disability. Pairwise comparisons and regression techniques were used to investigate the association of PD clinical markers with RBD. Result(s): We enrolled 120 PD patients. RBD was present in 46 % (n = 55; median age 65 years; 67 % male), who were compared to PD patients without RBD (n = 65, median age 62 years, 64 % male). There was also a healthy control group comprising 48 subjects (median age 57 years, 54 % male). Comparing PD patients with and without RBD, RBD was associated with higher MDS-UPDRS Part II scores [15(11-21) x 12(7-16), p = 0.02], higher frequency of abnormal gait (43,6 % x 21,5 %; p = 0.01), greater use of walking aids (21,8 % x 4,6 %; p = 0.005), greater dysautonomia (56,4 % x 47,7 %, p = 0.002) and osteoporosis [PR 1,64(1.37-1.96), p Result(s): We enrolled 120 PD patients. RBD was present in 46 % (n = 55; median age 65 years; 67 % male), who were compared to PD patients without RBD (n = 65, median age 62 years, 64 % male). There was also a healthy control group comprising 48 subjects (median age 57 years, 54 % male). Comparing PD patients with and without RBD, RBD was associated with higher MDS-UPDRS Part II scores [15(11-21) x 12(7-16), p = 0.02], higher frequency of abnormal gait (43,6 % x 21,5 %; p = 0.01), greater use of walking aids (21,8 % x 4,6 %; p = 0.005), greater dysautonomia (56,4 % x 47,7 %, p = 0.002) and osteoporosis [PR 1,64(1.37-1.96), p Conclusion(s): The presence of RBD in PD patients was associated with indirect indicators of motor impairment, lower independence in ADL, possibly a higher frequency of dysautonomia and with a higher frequency of osteoporosis.

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6. **Fast micrographia and frontal lobe dysfunction post-traumatic brain injury: insights into pacing impairment and rehabilitation strategy.**

Authors: Fukui J.;Yamaga T.;Anmoto N. and Inagaki, A.

Publication Date: 2025

Journal: BMJ Case Reports 18(1) (pagination), pp. Article Number: e262065. Date of Publication: 21 Jan 2025

Abstract: Micrographia, characterised by small handwriting, is often linked to Parkinson's disease, but also resulted to injured brain lesions. The left-handed women in her 20s developed 'fast micrographia' after a traumatic brain injury from a traffic accident, showing bilateral subdural haematomas and frontal lobe contusions, but she had no paralysis and extrapyramidal symptoms. Neuropsychological tests showed reduced processing speed and memory deficits, aligning with frontal lobe damage. A 3-month handwriting training programme improved performance with cues, but issues persisted without them. This case highlights the complexity of fast micrographia and the need for targeted rehabilitation strategies and further research.

7. **The Significance of Psychological Support in Managing Depression in Parkinson's Disease: Combining Venlafaxine with Pramipexole and Psychological Care.**

Authors: Huang Z.;Xiao D.;Lao Y.;Lai X.;Huang W. and Zhou, D.

Publication Date: 2025

Journal: Actas Espanolas De Psiquiatria 53(1), pp. 19–25

Abstract: BACKGROUND: Depression is a common comorbidity in patients with Parkinson's disease (PD) and can significantly impact their overall well-being. The combination of venlafaxine and pramipexole is a standard treatment approach for depression in PD. However, the effects of incorporating psychological care into the treatment regimen remain unclear. This study aimed to investigate the impact of psychological intervention in the treatment of depression in Parkinson's disease, using a combination of venlafaxine and pramipexole. METHOD(S): The clinical data of 151 patients with both Parkinson's disease (PD) and depression, treated in Geriatric Hospital of Hainan from May 2021 to May 2023, were analyzed retrospectively. Among the 151 patients, 71 received routine nursing care and were allocated to the control group, while the remaining 80 patients received psychological nursing care based on routine nursing care and were assigned to the study group. The Hamilton Depression Rating Scale (HAMD) and the Hamilton Anxiety Scale (HAMA) were used to evaluate the degree of depression and anxiety in both groups before and after care. The MOS 36-Item Short-Form Health Survey (SF-36) was employed to assess the quality of life of both groups before and after care. The efficacy and adverse reactions in both groups were also analyzed. RESULT(S): Before care, the HAMD and HAMA scores did not significantly differ between the two groups (p > 0.05). However, after care, both groups exhibited a significant reduction in HAMD and HAMA scores (p RESULT(S): Before care, the HAMD and HAMA scores did not significantly differ between the two groups (p > 0.05). However, after care, both groups exhibited a significant reduction in HAMD and HAMA scores (p 0.05). However, following care, the SF-36 scores markedly increased in both groups (p 0.05). However, following care, the SF-36 scores markedly increased in both groups (p 0.05). However, following care, the SF-36 scores markedly increased in both groups (p CONCLUSION(S): Utilizing venlafaxine combined with pramipexole in the treatment of depression in PD, supplemented by psychological nursing care, significantly enhances therapeutic efficacy. This combined approach effectively alleviates symptoms of depression and anxiety in patients without introducing additional side effects. Hence, it emerges as a valuable clinical treatment option.

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8. **Multimodal Magnetic Resonance Findings in Parkinson's Disease With "Antecedent Essential Tremor": A Case Series of a Large Kindred.**

Authors: Kong, Yu;Yao, Lei;Xiao, Xiangyu;Chen, Anqiang;Wang, Kexin;Yan, Huan;Sun, Ran;Liu, Ruihan and Kong, Qingxia

Publication Date: 2025

Journal: Neuropsychiatric Disease & Treatment 21, pp. 79–92

Abstract: Background: The clinical pictures of essential tremor (ET) and Parkinson's disease (PD) are often quite mimic at the early stage, and longstanding ET may ultimately develop to PD, that is, PD with "antecedent ET". Early diagnosis and differentiation of the two are essential for predicting disease progression and formulating individualized treatment plans. However, current approaches remain challenging. This study aimed at determining the morphological, microstructural and iron-related changes in these patients' brains using multimodal magnetic resonance imaging (MRI). Methods: We reviewed a kindred with ET and PD with "antecedent ET" recruited at our hospital in May 2023. The clinical characteristics, genetic testing and multimodal MRI data of 16 family members were collected. Multimodal MRI analysis included structural MRI, diffusion tensor imaging (DTI) and tractography, and quantitative susceptibility mapping (QSM). Results: Two second-generation family members diagnosed PD had ET history before PD performance appeared, five third-generation family members were diagnosed with ET. Fifteen of the 16 cases had missense mutation in the EIF4G1 gene. Temporal and spatial features of morphology and iron deposition in different brain regions were heterogeneous. DTI showed that the cerebello-thalamo-motor cortical network was involved in both ET and PD cases, and the additional nigrostriatal-thalamo-motor cortical network was involved in PD cases. Conclusion: The combination of morphometric imaging, DTI and QSM could be used as an imaging biomarker for ET and PD diagnosis and could be an effective tool for longitudinal monitoring of disease progression and transformation. Copyright © 2025 Kong et al.

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9. **Detecting freezing of gait: A comprehensive toolkit for enhanced Parkinson's assessment.**

Authors: Phuenpathom W.;Phokaewvarangkul O. and Bhidayasiri, R.

Publication Date: 2025

Journal: Parkinsonism and Related Disorders 132(pagination), pp. Article Number: 107275. Date of Publication: 01 Mar 2025

Abstract: Introduction: Detecting Freezing of Gait (FOG) poses challenges, with the subjective 6-item FOG Questionnaire relying solely on patient perception. We aim to create a holistic FOG Detection Toolkit combining subjective and objective elements (descriptions, images, and videos) to improve FOG detection precision. Method(s): Development of the FOG Detection Toolkit involved a detailed cover sheet on FOG and its triggers, along with video exemplars and a 4-item FOG-specific self-assessment questionnaire, all rigorously validated. The toolkit was administered to 100 eligible consecutive Parkinson's disease (PD) patients at a PD referral clinic in a major public university hospital in Thailand. The FOG Detection Toolkit results are based on the total score from a 4-item FOG-specific self-assessment questionnaire (range: 0-16). Freezers were identified by scores >=6. Result(s): The cover sheet, images, and videos displayed robust content validity and inter-rater reliability. The 4-item questionnaire exhibited high sensitivity (98 %) and specificity (100 %), with a substantial Area Under the Curve (AUC) of 0.990 and satisfactory construct validity (r = 0.68; p = 0.01). Users reported positive pragmatic (1.75) and hedonic (1.34) experiences. Patients with FOG scored significantly higher on the Toolkit and demonstrated distinct gait parameters (p Result(s): The cover sheet, images, and videos displayed robust content validity and inter-rater reliability. The 4-item questionnaire exhibited high sensitivity (98 %) and specificity (100 %), with a substantial

Area Under the Curve (AUC) of 0.990 and satisfactory construct validity (r = 0.68; p = 0.01). Users reported positive pragmatic (1.75) and hedonic (1.34) experiences. Patients with FOG scored significantly higher on the Toolkit and demonstrated distinct gait parameters (p Conclusion(s): The FOG Detection Toolkit showcases strong diagnostic performance, adequate construct validity, and positive user experience, facilitating accurate FOG detection. Its utility extends outside clinical environments, promising broader applicability for FOG management.

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10. **Speech-in-noise hearing impairment is associated with increased risk of Parkinson's: A UK biobank analysis.**

Authors: Readman M.R.;Wang Y.;Wan F.;Fairman I.;Linkenauger S.A.;Crawford T.J. and Plack, C. J.

Publication Date: 2025

Journal: Parkinsonism and Related Disorders 131(pagination), pp. Article Number: 107219. Date of Publication: 01 Feb 2025

Abstract: Background: Hearing impairment is implicated as a risk factor for Parkinson's disease (Parkinson's) incidence, with evidence suggesting that clinically diagnosed hearing loss increases Parkinson's risk 1.5-1.6 fold over 2-5 years follow up. However, the evidence is not unanimous with additional studies observing that self-reported hearing capabilities do not significantly influence Parkinson's incidence. Thus, additional cohort analyses that draw on alternative auditory measures are required to further corroborate the link between Parkinson's and hearing impairment. Objective(s): To determine whether hearing impairment, estimated using a speech-in-noise test (the Digit Triplet Test, DTT), is a risk factor for Parkinson's incidence. Method(s): This was a pre-registered prospective cohort study using data from the UK Biobank. Data pertaining to 159,395 individuals, who underwent DTT testing and were free from Parkinson's at the point of assessment, were analysed. A Cox Proportional Hazard model, controlling for age, sex and educational attainment was conducted. Result(s): During a median follow up of 14.24 years, 810 cases of probable Parkinson's were observed. The risk of incident Parkinson's increased with baseline hearing impairment [hazard ratio: 1.57 (95%CI: 1.018, 2.435; P = .041)], indicating 57 % increase in risk for every 10 dB increase in speech-reception threshold (SRT). However, when hearing impairment was categorised in accordance with UK Biobank SRT norms neither 'Insufficient' nor 'Poor' hearing significantly influenced Parkinson's risk compared to 'Normal' hearing. Conclusion(s): The congruence of these findings with prior research further supports the existence of a relationship between hearing impairment and Parkinson's incidence.

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11. **Cognitive impairment in PSP compared with PD: assessment by clinical subtype and longitudinal change.**

Authors: Tsuboi, Takeharu;Tatsumi, Hiroshi;Kobayasi, Kosuke;Hashimoto, Rina and Aiba, Ikuko

Publication Date: 2025

Journal: BMJ Neurology Open 7(1), pp. e000946

Abstract: Background: Longitudinal studies investigating cognitive function changes in patients with progressive supranuclear palsy (PSP) are limited. The variability of cognitive impairment across clinical subtypes of PSP remains unclear. Objective: This study aimed to compare the longitudinal changes in cognitive function between patients with PSP and Parkinson's disease (PD) and to assess differences in cognitive impairment among PSP subtypes. Methods: A retrospective observational study was conducted using neuropsychological testing data from patients with PSP and PD admitted to our hospital. Results: The study included 38 patients with PD and 41 patients with PSP (23 PSP-Richardson's syndrome, 14 PSP-progressive gait freezing (PSP-PGF), 3 PSP-Parkinsonism and 1 PSP-predominant corticobasal syndrome). At baseline, cognitive function was significantly lower in the PSP group than in the PD group. Over 12 months, patients with PSP exhibited significant declines in multiple cognitive domains, whereas no significant changes were observed in the PD group. Among PSP subtypes, PSP-RS showed a faster rate of cognitive decline than PD, while PSP-PGF demonstrated a lower progression than PSP-RS. Conclusion: PSP is associated with progressive cognitive impairment, with rates of decline varying by subtype. PSP-PGF exhibited a slower progression than PSP-RS. Clinical management should consider subtype-specific differences in cognitive prognosis to tailor treatment and care.

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12. **Chronic Musculoskeletal Pain and Risk of Incident Parkinson's Disease: A 13-Year Longitudinal Study.**

Authors: Vazirian F.;Tian J.;Jane A.;Aitken D.;Callisaya M.L.;Cicuttini F.;Jones G. and Pan, F.

Publication Date: 2025

Journal: Movement Disorders 40(1), pp. 87–96

Abstract: Background: Chronic musculoskeletal pain often co-occurs with Parkinson's disease (PD); however, whether individuals with chronic pain have a higher risk of developing PD is unclear. Objective(s): To investigate the associations between chronic pain and incident risk of three neurodegenerative parkinsonism categories including PD, multiple system atrophy (MSA), and progressive supranuclear palsy (PSP). Method(s): This study included 355,890 participants (mean [standard deviation] age, 56.51 [8.07] years, 48.40% male) who did not have parkinsonism at baseline from a population-based cohort. Musculoskeletal pain in the hip, neck/shoulder, back, knee, or "all over the body" was assessed. Chronic pain was defined if pain lasted >=3 months. Participants were categorized into four groups: no chronic pain, having one or two, three or four sites, and pain "all over the body." The diagnosis of PD, MSA, and PSP used self-reports, hospital records, and death registries. Multivariable-adjusted Cox regression was performed for the analyses. Result(s): Over a median follow-up of 13.0 years, 2044 participants developed PD, 77 participants developed MSA, and 126 participants developed PSP. In multivariable analyses, there was a dose-response relationship between number of chronic pain sites and incident risk of PD (hazard ratio, 1.15; 95% confidence interval, 1.07-1.23). Participants with one or two pain sites and three or four pain sites had an 11% and 49% increased risk of developing PD, respectively. There were no associations

between chronic pain and MSA or PSP. Conclusion(s): Chronic musculoskeletal pain was independently associated with PD, suggesting that chronic pain could be used to identify individuals at risk of developing PD. © 2024 International Parkinson and Movement Disorder Society.

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13. **Establishing a robust triangulation framework to explore the relationship between hearing loss and Parkinson's disease.**

Authors: Zhang, Hao;Chen, Keying;Gao, Tongyu;Yan, Yu;Liu, Ying;Liu, Yuxin;Zhu, Kexuan;Qi, Jike;Zheng, Chu;Wang, Ting and Zeng, Ping

Publication Date: Jan 03 ,2025

Journal: Npj Parkinsons Disease 11(1), pp. 5

Abstract: The relationship between hearing loss (HL) and Parkinson's disease (PD) remains unclear. Using individual-level and summary-level data from the UK Biobank and the largest genome-wide association studies, we examined this link through observational, Mendelian randomization and genetic pleiotropy analyses. Among 158,229 participants, PD risk rose with HL severity especially in elder and males, and hearing aids significantly reduced PD risk in males. Although our results did not support a causal association, genetic correlation analysis suggested a localized genetic overlap (17q21.31). We identified 1545 SNPs and 63 genes with pleiotropic effects on HL and PD, including 79 novel SNPs across 6 loci, with 3 showing strong co-localization. These loci were enriched in key tissues like brain, heart, liver and pancreas, linked to the dihydrolipoyl dehydrogenase complex pathway, and targeted by drugs such as Warfarin and Phenprocoumon. Overall, this study reveals the risk association, genetic basis, and pleiotropic loci connecting HL and PD. Copyright © 2025. The Author(s).

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

Authors: Alshimemeri S.;Alsudais H.;Alamri N.K.;Alshoumar A.M.;Bin Dher S.K. and Maashi, M. H.

Publication Date: 2024

Journal: Journal of Parkinson's Disease 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(s): The aim of this study was to evaluate the level of burden, depression, anxiety, and stress among caregivers of PD patients. Method(s): 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. Result(s): 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. Conclusion(s): 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.

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15. **Machine learning analysis of population-wide plasma proteins identifies hormonal biomarkers of Parkinson's Disease.**

Authors: Chaudhry, Fayzan;Kim, Tae Wan;Elemento, Olivier and Betel, Doron

Publication Date: 2024

Journal: MedRxiv : The Preprint Server for Health Sciences

Abstract: As the number of Parkinson's patients is expected to increase with the growth of the aging population there is a growing need to identify new diagnostic markers that can be used cheaply and routinely to monitor the population, stratify patients towards treatment paths and provide new therapeutic leads. Genetic predisposition and familial forms account for only around 10% of PD cases [1] leaving a large fraction of the population with minimal effective markers for identifying high risk individuals. The establishment of population-wide omics and longitudinal health monitoring studies provides an opportunity to apply machine learning approaches on these unbiased cohorts to identify novel PD markers. Here we present the application of three machine learning models to identify protein plasma biomarkers of PD using plasma proteomics measurements from 43,408 UK Biobank subjects as the training and test set and an additional 103 samples from Parkinson's Progression Markers Initiative (PPMI) as external validation. We identified a group of highly predictive plasma protein markers including known markers such as DDC and CALB2 as well as new markers involved in the JAK-STAT, PI3K-AKT pathways and hormonal signaling. We further demonstrate that these features are well correlated with UPDRS severity scores and stratify these to protective and adversarial features that potentially contribute to the pathogenesis of PD.

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16. **Lifetime brain atrophy estimated from a single MRI: measurement characteristics and genome-wide correlates.**

Authors: Furtjes A.E.;Foote I.F.;Xia C.;Davies G.;Moodie J.;Taylor A.;Liewald D.C.;Redmond P.;Corley J.;McIntosh A.M.;Whalley H.C.;Maniega S.M.;Hernandez M.V.;Backhouse E.;Ferguson K.;Bastin M.E.;Wardlaw J.;de la Fuente J.;Grotzinger A.D.;Luciano M., et al

Publication Date: 2024

Journal: bioRxiv (pagination), pp. Date of Publication: 07 Nov 2024

Abstract: A measure of lifetime brain atrophy (LBA) obtained from a single magnetic resonance imaging (MRI) scan could be an attractive candidate to boost statistical power in uncovering novel genetic signals and mechanisms of neurodegeneration. We analysed data from five young and old adult cohorts (MRi-Share, Human Connectome Project, UK Biobank, Generation Scotland Subsample, and Lothian Birth Cohort 1936 [LBC1936]) to test the validity and utility of LBA inferred from cross-sectional MRI data, i.e., a single MRI scan per participant. LBA was simply calculated based on the relationship between total brain volume (TBV) and intracranial volume (ICV), using three computationally distinct approaches: the difference (ICV-TBV), ratio (TBV/ICV), and regression-residual method (TBV~ICV). LBA derived with all three methods were substantially correlated with well-validated neuroradiological atrophy rating scales (r = 0.37-0.44). Compared with the difference or ratio method, LBA computed with the residual method most strongly captured phenotypic variance associated with cognitive decline (r = 0.36), frailty (r = 0.24), age-moderated brain shrinkage (r = 0.45), and longitudinally-measured atrophic changes (r = 0.36). LBA computed using a difference score was strongly correlated with baseline (i.e., ICV; r = 0.81) and yielded GWAS signal similar to ICV (rg = 0.75). We performed the largest genetic study of LBA to date (N = 43,110), which was highly heritable (h2 SNP GCTA = 41% [95% CI = 38-43%]) and had strong polygenic signal (LDSC h2 = 26%; mean chi2 = 1.23). The strongest association in our genome-wide association study (GWAS) implicated WNT16, a gene previously linked with neurodegenerative diseases such as Alzheimer, and Parkinson disease, and amyotrophic lateral sclerosis. This study is the first side-by-side evaluation of different computational approaches to estimate lifetime brain changes and their measurement characteristics. Careful assessment of methods for LBA computation had important implications for the interpretation of existing phenotypic and genetic results, and showed that relying on the residual method to estimate LBA from a single MRI scan captured brain shrinkage rather than current brain size. This makes this computationally-simple definition of LBA a strong candidate for more powerful analyses, promising accelerated genetic discoveries by maximising the use of available cross-sectional data.

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17. **Motor response in patients with Parkinson's disease underwent unilateral posteroventral pallidotomy.**

Authors: Gonzalez Gonzalez Y.;Trinchet Soler R.M.;Ramos Pupo C. and Gonzalez Gonzalez, A.

Publication Date: 2024

Journal: Revista Habanera De Ciencias Medicas 23(pagination), pp. Date of Publication: 01 Jan 2024

Abstract: Introduction: Unilateral posteroventral pallidotomy reduces dyskinesia and motor disability in Parkinson's disease. Objective(s): To identify the characteristics of postoperative motor response in patients who underwent unilateral posteroventral pallidotomy. Material(s) and Method(s): A quasi-experimental retrospective-prospective study was conducted in 13 patients with advanced Parkinson's disease who underwent unilateral posteroventral pallidotomy procedures at the Clinical Surgical Hospital of Holguin between November 2016

and March 2018 and completed a two-year postoperative followup during this period. All patients gave informed consent, met the inclusion criteria and had no postoperative motor complications. Age and sex were determined. Preoperative and postoperative values of the variables: bradykinesia, tremor, gait and dyskinesia were evaluated with the MDS-UPDRS (Movement Disorders Society-Unified Parkinson's Disease Rating Scale). Postoperative motor status was determined by the physical examination, the value of variables and the performance of daily activities. The differences in motor status were evaluated by means of the statistical Wilcoxon signed-rank test with alpha=0.05. The p-value (p Material(s) and Method(s): A quasi-experimental retrospective-prospective study was conducted in 13 patients with advanced Parkinson's disease who underwent unilateral posteroventral pallidotomy procedures at the Clinical Surgical Hospital of Holguin between November 2016 and March 2018 and completed a two-year postoperative followup during this period. All patients gave informed consent, met the inclusion criteria and had no postoperative motor complications. Age and sex were determined. Preoperative and postoperative values of the variables: bradykinesia, tremor, gait and dyskinesia were evaluated with the MDS-UPDRS (Movement Disorders Society-Unified Parkinson's Disease Rating Scale). Postoperative motor status was determined by the physical examination, the value of variables and the performance of daily activities. The differences in motor status were evaluated by means of the statistical Wilcoxon signed-rank test with alpha=0.05. The p-value (p Result(s): The Wilcoxon test showed statistically significant differences between preoperative values (3-4) and postoperative values (0-1) of dyskinesia, bradykinesia and gait. In addition, 68 % of patients showed a better motor status in the Wilcoxon test with improvement of dyskinesias, sustained benefits in disability, and lower values of the variables considered in this study. Conclusion(s): It is concluded that 68 % of patients had a strong motor response to unilateral posteroventral pallidotomy.

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18. **Living with pain and Parkinson's developing an understanding of the impact, trajectory and pain management needs: a qualitative interview study protocol.**

Authors: Naisby J.;Avery L.;Baker K.;Parkinson M.;Hand A.;Rochester L.;Yarnall A.;Walker R.;Flynn D.;Ryan C. and Finch, T.

Publication Date: 2024

Journal: BMJ Open 14(12) (pagination), pp. Article Number: e078754. Date of Publication: 26 Dec 2024

Abstract: Introduction Pain is reported as one of the most troubling symptoms for people with Parkinson's (PwP); however, the literature exploring their lived experience of pain and how to manage it is limited. Pain affects PwP at all stages of their condition and can fluctuate and change over time. Therefore, it is pertinent to speak to PwP to understand their experiences of pain to inform the development of tailored behavioural interventions to manage pain. How pain interacts with other Parkinson's symptoms lacks consensus. Gaining a better understanding of this from the perspective of PwP is important to inform interventions. Exploring the behavioural determinants, including the barriers and enablers to pain management from the perspective of PwP, the role of healthcare professionals and impact of other symptoms alongside pain will inform the development of a fit for purpose, pain management toolkit for PwP. Methods and analysis A longitudinal qualitative study using semi structured interviews at two time points

within an 18-month period will be conducted. PwP living with pain will be purposefully sampled from four NHS sites in the North of England. Data will be thematically analysed with reference to the Theoretical Domains Framework. Ethics and dissemination A favourable ethical opinion has been granted by the National Health Service East Midlands-Derby Research Ethics Committee (22/EM/0176) and the NHS Health Research Authority (IRAS ID 316403). Findings will be disseminated via scientific conferences, academic journals, lay summaries and public engagement events.

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19. **Satisfaction and Preferences for Infusion Therapies in Advanced Parkinson's Disease-Patient Perspective.**

Authors: Wegrzynek-Gallina, Julia;Chmiela, Tomasz;Boronczyk, Michal;Buczek, Aleksandra;Hudzinska, Patrycja;Bigajski, Hubert;Waksmundzki, Damian;Gawryluk, Justyna and Siuda, Joanna

Publication Date: 2024

Journal: Medicina (Kaunas, Lithuania)

Abstract: Background and Objectives: The rapid growth of the number of advanced Parkinson's disease (PD) patients has caused a significant increase in the use of device-aided therapies (DATs), including levodopa-carbidopa intestinal gel (LCIG) and continuous subcutaneous apomorphine infusion (CSAI). The objective of this study was to evaluate patients' satisfaction and the factors influencing preferences for CSAI and LCIG. Materials and Methods: The research focused on individuals diagnosed with advanced PD undergoing DAT at the Neurology Department of the University Hospital in Katowice. A telephone survey conducted between June and July 2024 evaluated the experiences of patients with LCIG and CSAI. The Parkinson's Disease Questionnaire (PDQ-8) and the Stress Scale for Family Caregivers (BSFC-s) were applied. Based on medical record data comprising reasons for the exclusion of individuals, disease-related and treatment data were collected. Results: Among the original cohort of 64 patients, 50 completed the survey, including 31 who might choose between infusion therapies. The average patient ages were 70.6 +/- 4.7 (CSAI) and 71.2 +/- 7.2 years (LCIG), with disease durations of 15 (IQR: 12-19) and 18 (IQR: 13-19) years, respectively. LCIG patients presented higher PDQ-8 scores (20 (IQR: 13-27) vs. 13 (IQR: 6-19), p = 0.008), and higher BSFC-s scores (19 (IQR: 12-21) vs. 9 (IQR: 2.5-13), p = 0.011). Furthermore, significant factors influencing patient preferences included fear of surgery (75% vs. 36.8%, p = 0.043) and concerns about DAT safety (83.3% vs. 47.4%, p = 0.049). Conclusions: LCIG and CSAI therapies offer benefits and disadvantages, with safety concerns and fear of surgery seeming to be decisive in the decision-making process.

Sources Used:

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

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