

Editorial

Special Issue: Non-Pharmacological Interventions for People with Parkinson's Disease: Are We Entering a New Era?

E. Kalbe^{a,*}, B.R. Bloem^b, L.V. Kalia^c and A. Nieuwboer^d

^a*Medical Psychology | Neuropsychology and Gender Studies & Center for Neuropsychological Diagnostics and Intervention (CeNDI), University Hospital Cologne and Medical Faculty of the University of Cologne, Cologne, Germany*

^b*Radboud University Medical Centre, Donders Institute for Brain, Cognition and Behaviour, Department of Neurology, Centre of Expertise for Parkinson and Movement Disorders, Nijmegen, The Netherlands*

^c*Krembil Research Institute, Edmond J. Safra Program in Parkinson's Disease and the Morton and Gloria Shulman Movement Disorders Clinic, Toronto Western Hospital, University Health Network, Toronto, Canada*

^d*Department of Rehabilitation Sciences, Research Group for Neurorehabilitation (eNRGy), KU Leuven, Leuven, Belgium*

Pre-press 6 August 2024

Published 13 August 2024

Non-pharmacological interventions for people with Parkinson's disease (PwPD) have traditionally been regarded as supportive or “add-on” measures to primarily alleviate motor symptoms. While physiotherapy, speech-language, and occupational therapy have gradually become an integral part of the overall management of Parkinson's disease (PD) [1], other non-pharmacological interventions like cognitive training, cognitive behavioral therapy, and art or light therapy have remained rather “exotic” and are just beginning to be included in therapy guidelines [2]. But times are changing, driven by complimentary forces: the empirical observations of clinicians who continually face the limitations of pharmacotherapy; the wishes and desires of PwPD, most of whom consistently ask for a more holistic approach to their disease; and importantly, the growing support of evi-

dence that comes from adequately designed research studies.

Recently, non-pharmacological approaches for PwPD have made substantial steps forward, many of which are highlighted in this special issue. Developments include, among others: (i) expansion of the types of interventions, (ii) standardization of intervention protocols [3], (iii) development of digital forms of interventions [4, 5] (iv), scientific evaluation of the feasibility and effects of the interventions [6], (v) understanding of underlying mechanisms of therapy-induced plasticity processes [7], (vi) integration of non-pharmacological interventions in patient care concepts [8], and (vii) transition from merely symptomatic to preventive therapies [9]. Last but not least, the voice of PwPD, who are the real experts of the disease, is getting louder in all this work. In fact, we are increasingly witnessing participatory research approaches in which patients are involved in designing novel treatment programs, preparing consensus statements on the delivery of multidisciplinary care, and in defining outcome measures [10, 11]. Taken

*Correspondence to: E. Kalbe, Medical Psychology | Neuropsychology and Gender Studies & Center for Neuropsychological Diagnostics and Intervention (CeNDI), University Hospital Cologne and Medical Faculty of the University of Cologne, Cologne, Germany. E-mail: elke.kalbe@uk-koeln.de.

together, these developments yield a much wider perspective on patient care than hitherto endorsed.

This *special issue on non-pharmacological treatment for patients with Parkinson's Disease* is set right in the middle of this rich and exciting current. It captures a wealth of novel topics addressing three main themes: (1) physical perspectives, (2) mental perspectives, and (3) perspectives on access to care. What these sections have in common is that both research and clinical application of this wide array of topics are presented by leading experts in the field. Not surprisingly, they also point towards the important research gaps that are still on the agenda, while delineating various directions for future research.

PHYSICAL PERSPECTIVES

In this section, the importance of early delivery of physical training is emphasized in line with the recently published consensus statement by the Parkinson's Foundation task force [11]. However, several papers in this issue suggest to go one step further. Indeed, a number of promising proactive lifestyle interventions are presented for application in the early phase of clinically manifest PD, and even in the prodromal disease phase; the proposed interventions include dietary mediation therapy in conjunction with physical training. There is also wide acknowledgement for the need to validate accurate instruments to detect subtle motor and non-motor changes and for incorporating the cost-effectiveness of such preventative programs.

Patient compliance is always a central theme in training-based interventions, and in particular the long-term compliance which will be required if non-pharmacological interventions are truly to achieve secondary or tertiary disease prevention in the prodromal phase or clinically manifest phase of PD, respectively. Hence, this section also provides a much-needed and in-depth insight in how to deal with the day-to-day struggles to gain patients' engagement in exercise therapy. Innovative approaches are suggested by involving patients in training without actual physical effort and to enrich the training experience through action observation and motor imagery techniques.

Prevalent and impactful non-motor symptoms, such as pain [12], but also orthostatic hypotension and urinary incontinence, are often overlooked in standard patient care, and thus remain undertreated,

leading to avoidable disability. Yet, various behavioral and other physiotherapeutical interventions, that are delivered by allied health professionals for conditions other than PD, may incur transferable effects. Therefore, it is inspirational to observe the scientific interest and the widening of the scope of physical interventions for PD in this issue.

MENTAL PERSPECTIVES

The high prevalence of cognitive impairment [13] and affective disorders in PwPD [14] has a great impact on quality of life and caregiver burden [15]. Pharmacotherapy often has only a limited effect for these symptoms, while it may be associated with adverse effects on cognition or alertness. Therefore, it is encouraging to see that non-pharmacological interventions are receiving much more attention to alleviate these non-motor symptoms, in the hope that these may play a pivotal role in their future treatment. While there is no doubt that physical exercise improves physical outcomes in PwPD [6], its impact on brain health is manifold and may also beneficially affect mental health problems, including cognition and affect [16, 17]. These multifaceted effects of exercise are considered extensively in this issue. Also, to treat affective disorders further, next to cognitive behavioral therapy, which is well-known to be effective yet rarely prescribed for PwPD, novel experimental interventions are being discussed, including non-invasive brain stimulation, electroconvulsive therapy, light therapy, and art interventions. As demonstrated in this issue, much research is needed to fully understand the mechanisms and the potential of these interventions for treating mental symptoms and to promote mental health in PwPD. What should be kept in mind is that many of these treatments could be delivered digitally. While digital health technology for PwPD is developing rapidly [18] (e.g. in the context of telehealth, deep brain stimulation, wearable sensors, and smartphone applications), health literacy may be lagging behind, yet is indispensable for adherence. This said, the insufficiency in digital skills as well as the inequities in access to digital health technologies in certain populations still constitute a major challenge for PwPD to benefit from this therapeutic avenue. Therefore, it will not only be important to develop and optimize new technologies, but also ways to enhance digital health literacy in PwPD regardless of their back-

ground. Only if patients are empowered and learn self-management strategies that are tailored to their specific wishes and needs will they be able to play a key role as managers of their disease to improve their care and quality of life. Concepts to achieve this important role are also reviewed in this issue.

PERSPECTIVES ON ACCESS

Access to patient-centered care is a key issue for PwPD, not only requiring sufficient allied health resources but also a different way of thinking about the organization of care management [19]. This section addresses several facets of the diversity of access to adequate multidisciplinary expertise, as well as a balanced view on its benefits and drawbacks. As the communication between expert team members is vital for the success of integrated care models, it is espoused that the Parkinson nurse specialist is ideally placed for care titration, referral to allied health professionals, and fulfillment of many other roles in the holistic care of PwPD.

Obtaining mere access to allied health professionals can be surprisingly disappointing even in developed countries [20]. However, the current challenges faced by the African continent afford a special consideration in this issue. A possible solution is offered by enhancing remote access through the development of telehealth platforms, thereby avoiding expensive travelling in underserved areas. Remote allied health platforms have grown spectacularly in the last five years, now covering speech therapy, exercise interventions, occupational therapy, and multidisciplinary management. While online-management reduces healthcare cost, a more thorough understanding of the pros and cons of remote service delivery is warranted and also tackled in this issue.

CONCLUSION

In conclusion, it is gratifying to witness that non-pharmacological interventions are subject to critical thinking, continuous updating of knowledge, and scientific scrutiny. As editors of this special issue, we are happy to present this exciting work, while concluding that the field of non-pharmacological therapy is clearly reaching clinical and scientific maturity and has the potential to substantially improve patient care in the future.

REFERENCES

- [1] Fox SH, Katzenschlager R, Lim SY, Barton B, de Bie RMA, Seppi K, Coelho M, Sampaio C (2018) Movement Disorder Society Evidence-Based Medicine Committee. International Parkinson and movement disorder society evidence-based medicine review: Update on treatments for the motor symptoms of Parkinson's disease. *Mov Disord* **33**, 1248-1266.
- [2] Deutsche Gesellschaft für Neurologie e.V. (DGN) (2023) S-2k-Leitlinie Parkinson-Krankheit. Version 8.1. <https://register.awmf.org/de/leitlinien/detail/030-010>. Accessed 30 April 2024
- [3] Eldemir S, Eldemir K, Saygili F, Ozkul C, Yilmaz R, Akbostancı MC, Guclu-Gunduz A (2024) The effects of standard and modified LSVT BIG therapy protocols on balance and gait in Parkinson's disease: A randomized controlled trial. *Brain Behav* **14**, e3458.
- [4] Canning CG, Allen NE, Nackaerts E, Paul SS, Nieuwboer A, Gilat M (2020) Virtual reality in research and rehabilitation of gait and balance in Parkinson disease. *Nat Rev Neurol* **16**, 409-425.
- [5] Ellis TD, Earhart GM (2021) Digital Therapeutics in Parkinson's Disease: Practical Applications and Future Potential. *J Parkinsons Dis* **11**, 95-101.
- [6] Ernst M, Folkerts AK, Gollan R, Lieker E, Caro-Valenzuela J, Adams A, Cryns N, Monsef I, Dresen A, Roheger M, Eggers C, Skoetz N, Kalbe E (2024) Physical exercise for people with Parkinson's disease: A systematic review and network meta-analysis. *Cochrane Database Syst Rev* **4**, CD013856.
- [7] Johansson ME, Cameron IGM, Van der Kolk NM, de Vries NM, Klimars E, Toni I, Bloem BR, Helmich RC (2022) Aerobic Exercise Alters Brain Function and Structure in Parkinson's Disease: A Randomized Controlled Trial. *Ann Neurol* **91**, 203-216.
- [8] Weintraub D, Aarsland D, Biundo R, Dobkin R, Goldman J, Lewis S (2022) Management of psychiatric and cognitive complications in Parkinson's disease. *BMJ* **379**, e068718.
- [9] Janssen Daalen JM, Schootemeijer S, Richard E, Darweesh SKL, Bloem BR (2022) Lifestyle Interventions for the Prevention of Parkinson Disease: A Recipe for Action. *Neurology* **99**, 42-51.
- [10] Hanff AM, Pauly C, Pauly L, Rauschenberger A, Leist AK, Krüger R, Zeegers MP, McCrum C (2024) NCER-PD consortium. Determinants of patient-reported functional mobility in people with Parkinson's disease: A systematic review. *Gait Posture* **108**, 97-109.
- [11] Goldman JG, Volpe D, Ellis TD, Hirsch MA, Johnson J, Wood J, Aragon A, Biundo R, Di Rocco A, Kasman GS, Ianssek R, Miyasaki J, McConvey VM, Munneke M, Pinto S, St Clair KA, Toledo S, York MK, Todaro R, Yarab N, Wallock K (2024) Delivering Multidisciplinary Rehabilitation Care in Parkinson's Disease: An International Consensus Statement. *J Parkinsons Dis* **14**, 135-166.
- [12] Lei J, Tang LL, You HJ (2024) Pathological pain: Non-motor manifestations in Parkinson disease and its treatment. *Neurosci Biobehav Rev* **1**, 105646.
- [13] Aarsland D, Batzu L, Halliday GM, Geurtsen GJ, Ballard C, Chudhuri KR, Weintraub D (2021), Parkinson disease-associated cognitive impairment. *Nat Rev Dis Primers* **7**, 47.
- [14] Macias-Garcia P, Rashid-López R, Cruz-Gómez AJ, Lozano-Soto E, Sanmartino F, Espinosa-Rosso R,

- González-Rosa JJ (2022), Neuropsychiatric Symptoms in Clinically Defined Parkinson's Disease: An Updated Review of Literature. *Behavioural Neurology* **2022**, 1213393.
- [15] Duncan GW, Khoo TK, Yarnall AJ, O'Brien JT, Coleman SY, Brooks DJ, Barker RA, Burn DJ (2013), Health-related quality of life in early Parkinson's disease: The impact of nonmotor symptoms. *Movement Disorders* **29**, 195-202.
- [16] Petzinger GM, Fisher BE, McEwen S, Beeler JA, Walsh JP, Jakowec MW (2013) Exercise-enhanced neuroplasticity targeting motor and cognitive circuitry in Parkinson's disease. *Lancet Neurol* **12**, 716-26.
- [17] Almikhlafi MA (2023). The role of exercise in Parkinson's Disease. *Neurosciences* **28**, 4-12.
- [18] Esper CD, Valdovinos BY, Schneider RB (2024) The Importance of Digital Health Literacy in an Evolving Parkinson's Disease Care System. *J Parkinsons Dis* doi: 10.3233/JPD-230229
- [19] Radder DLM, Nonnekes J, van Nimwegen M, Eggers C, Abbruzzese G, Alves G, Browner N, Chaudhuri KR, Ebersbach G, Ferreira JJ, Fleisher JE, Fletcher P, Frazzitta G, Giladi N, Guttman M, Iannsek R, Khandhar S, Klucken J, Lafontaine AL, Marras C, Nutt J, Okun MS, Parashos SA, Munneke M, Bloem BR (2020) Recommendations for the Organization of Multidisciplinary Clinical Care Teams in Parkinson's Disease. *J Parkinsons Dis* **3**, 1087-1098.
- [20] Dibble LE, Ellis TD (2021) The sobering and puzzling reality of rehabilitation referrals for Parkinson disease. *Parkinsonism Relat Disord* **83**, 113-114.