J Aging Res & Lifestyle 2023;12:20-22
Published online June 8, 2023, http://dx.doi.org/10.14283/jarlife.2023.5

Editorial

# Physical Activity, Exercise, and Sedentary Time: Insights for Future Research in the Field of Geroscience

*P. de Souto Barreto*[1,2]

1. Gerontopole of Toulouse, Institute of Ageing, Toulouse University Hospital (CHU Toulouse), 31000 Toulouse, France; 2. Maintain Aging Research team, Centre d'Epidémiologie et de Recherche en santé des POPulations (CERPOP), Inserm, Université Paul Sabatier, Toulouse, France.

*Corresponding Author:* Philipe de Souto Barreto, Gérontopôle de Toulouse, Institut du Vieillissement, 37 Allée Jules Guesde, 31000 Toulouse, France, E-mail address: philipebarreto81@yahoo.com.br, Phone number: + 33- 561-145-636

The health benefits of physical activity and exercise and the harmful health effects of sedentary time over the life course are now well-established. Physical activity has been found to reduce the risk of the onset of a myriad of chronic diseases and conditions (1–4), including several types of cancers (5), Alzheimer's disease and other dementias (6, 7), cardiovascular diseases (8), diabetes (9), frailty (10, 11), cognitive decline (12), physical function and even disability (13, 14). Exercise is part of the treatment of most chronic conditions (15), being recommended by the appropriate scientific societies to patients suffering from hypertension, hyperlipidemia, depression, type 2 diabetes, heart diseases, obesity, osteoarthritis (15), and frailty (16) and sarcopenia (17, 18). Conversely, sedentary time is associated with adverse health events on both physical (19, 20) and mental health (21), including an increased risk of diabetes, cardiovascular diseases, and mortality (22, 23). Given the associations of these body movement parameters with such distinct age-related conditions, determined by different pathophysiological cascades, such as cancer and Alzheimer's disease, it is plausible to think that physical activity, exercise, and sedentary time have the potential to modify biological aging progression by either accelerating it or decreasing its speed. This is the central hypothesis giving rise to the recently born research field of Geroscience (24): interventions that act on the main drivers of biological aging will have a final effect on many chronic conditions, such as diseases, geriatric syndromes, and disability.

From a Geroscience perspective, body movement parameters would act as either geroprotectors (elements reducing the speed of biological aging progression: physical activity and exercise) or geroaccelerators (accelerators of biological aging: sedentary time/behavior). The literature on the principal biological drivers of aging (25, 26) supports that physical activity and exercise work as geroprotectors (27–29) by preventing DNA damage, telomere shortening, and adverse epigenetic alterations (30), benefiting the immune system (31), boosting mitochondrial function (32), improving oxidative stress balance (33), gut microbiome (34, 35), chronic inflammation (36, 37) and nutrient sensing (28). The evidence for sedentary time/behavior is less abundant and still unclear, as indicated by a recent review (38). Indeed, some molecular/cellular adaptations due to prolonged sedentary behaviors (e.g., bed rest, limb suspension) seem to promote healthspan, such as a decreased signaling of anabolic pathways, mainly the mammalian target of rapamycin (mTOR). This "sedentary behavior paradox" illustrates the complexity of aging at a biological level and how body movement parameters can act on the main hallmarks of aging: although on the one hand, the reduction of mTOR and other anabolic pathways is a well-established mechanism promoting increased lifespan, on the other hand, such approach is not necessarily advisable for older people since it will lead to muscle atrophy and potentially sarcopenia, with a subsequent cascade of deleterious clinical outcomes, such as falls, fractures, hospitalizations and death (39, 40).

Moreover, several methodological aspects must be considered to improve current knowledge about the effects of body movement parameters on the hallmarks of aging. First, research on this area must identify both the conceptual and operational measures of the different parameters: physical activity is the broad term used to designate any movement of a segment of the body performed through muscle contraction and associated energy expenditure (e.g., walking for shopping, or transport, mildly or briskly); exercise is a subtype of physical activity that is planned, purposeful, and repetitive (e.g., brisk walking for 10-to-30min, performed 3-5 times/week, for improving cardiorespiratory fitness and reducing fatigue in sedentary older adults); and sedentary behavior is any waking activity performed in sitting, reclining or lying positions and requiring energy expenditure ≤1.5 metabolic equivalents (METs) (41). All these measures can be operationalized subjectively (e.g., by questionnaires) or objectively (e.g., by accelerometers). Different cut-points can be applied to designate high and low levels of these behaviors. Secondly, the benefits of physical activity and exercise and the deleterious effects of sedentary time are partly independent of each other (42, 43). Indeed, an individual may reach the recommendations of physical activity (44) and spend a large amount of their waking time in sit/lying position

*Received April 20, 2023*
*Accepted for publication April 22, 2023*

doing low energy expenditure activities, being thus exposed to the adverse effects of sedentary behavior. Therefore, any study on this topic must consider the interactions/combinations of these body movement parameters. Thirdly, physical activity is a broad term that involves activities performed at mild, moderate, and vigorous intensities; the benefits of these differences in the hallmarks of aging are probably not the same.

Similarly, sedentary behavior is a broad term that encompasses different patterns: for example, long duration sitting time; several bouts of sedentary time broken by mild physical activity (e.g., breaking sedentary time by taking an upright position regularly); again, the detrimental impact of these different patterns on the main drivers of aging may differ. Fourthly, the links between life course physical activity and the hallmarks of aging are almost unknown. Research in this area has been focused on a single exercise bout (one session of exercise) or small-length exercise trials (often lower than 12 weeks), performed the most often on young adult men, or have used experimental animal study designs. The gaps are still more critical regarding sedentary behavior, for which the evidence is still minimal.

Therefore, although physical activity and exercise may act as geroprotectors and sedentary behavior as a gero-accelerator, the impact of these body movement parameters on the speed of progression of biological aging is a research field still in its infancy. Taking advantage of long-term exercise interventions previously developed and for which a biobank is available, such as LIFE (45), SPRINTT (46), or DO-HEALTH (47), may bring forth essential information about exercise long-time effects under a geroscience perspective. Since those studies are restricted to older adults, their data may be completed by longitudinal observational studies among adults of an extensive age range and with available biobanks and measures of body movement parameters, such as the INSPIRE program (48, 49).

*Conflict of interest:* The author declares no conflict of interest.

## References


1. Arem H, Moore SC, Patel A, Hartge P, Berrington de Gonzalez A, Visvanathan K, et al. Leisure time physical activity and mortality: a detailed pooled analysis of the dose-response relationship. JAMA Intern Med. 2015 Jun;175(6):959–67.
2. de Souto Barreto P, Cesari M, Andrieu S, Vellas B, Rolland Y. Physical Activity and Incident Chronic Diseases: A Longitudinal Observational Study in 16 European Countries. Am J Prev Med. 2017 Mar;52(3):373–8.
3. Moore SC, Patel AV, Matthews CE, Berrington de Gonzalez A, Park Y, Katki HA, et al. Leisure time physical activity of moderate to vigorous intensity and mortality: a large pooled cohort analysis. PLoS Med. 2012;9(11):e1001335.
4. Izquierdo M, Merchant RA, Morley JE, Anker SD, Aprahamian I, Arai H, et al. International Exercise Recommendations in Older Adults (ICFSR): Expert Consensus Guidelines. J Nutr Health Aging. 2021;25(7):824–53.
5. Moore SC, Lee IM, Weiderpass E, Campbell PT, Sampson JN, Kitahara CM, et al. Association of Leisure-Time Physical Activity With Risk of 26 Types of Cancer in 1.44 Million Adults. JAMA Intern Med. 2016 01;176(6):816–25.
6. Iso-Markku P, Kujala UM, Knittle K, Polet J, Vuoksimaa E, Waller K. Physical activity as a protective factor for dementia and Alzheimer's disease: systematic review, meta-analysis and quality assessment of cohort and case-control studies. Br J Sports Med. 2022 Jun;56(12):701–9.
7. Wu W, Ding D, Zhao Q, Xiao Z, Luo J, Ganguli M, et al. Dose-response relationship between late-life physical activity and incident dementia: A pooled analysis of 10 cohort studies of memory in an international consortium. Alzheimers Dement J Alzheimers Assoc. 2023 Jan;19(1):107–22.
8. Paluch AE, Bajpai S, Ballin M, Bassett DR, Buford TW, Carnethon MR, et al. Prospective Association of Daily Steps With Cardiovascular Disease: A Harmonized Meta-Analysis. Circulation. 2023 Jan 10;147(2):122–31.
9. Lee IM, Shiroma EJ, Lobelo F, Puska P, Blair SN, Katzmarzyk PT, et al. Effect of physical inactivity on major non-communicable diseases worldwide: an analysis of burden of disease and life expectancy. Lancet Lond Engl. 2012 Jul 21;380(9838):219–29.
10. Zhao W, Hu P, Sun W, Wu W, Zhang J, Deng H, et al. Effect of physical activity on the risk of frailty: A systematic review and meta-analysis. PloS One. 2022;17(12):e0278226.
11. Liu T, Wang C, Sun J, Chen W, Meng L, Li J, et al. The Effects of an Integrated Exercise Intervention on the Attenuation of Frailty in Elderly Nursing Homes: A Cluster Randomized Controlled Trial. J Nutr Health Aging. 2022;26(3):222–9.
12. Yoneda T, Lewis NA, Knight JE, Rush J, Vendittelli R, Kleineidam L, et al. The Importance of Engaging in Physical Activity in Older Adulthood for Transitions Between Cognitive Status Categories and Death: A Coordinated Analysis of 14 Longitudinal Studies. J Gerontol A Biol Sci Med Sci. 2021 Aug 13;76(9):1661–7.
13. Tak E, Kuiper R, Chorus A, Hopman-Rock M. Prevention of onset and progression of basic ADL disability by physical activity in community dwelling older adults: a meta-analysis. Ageing Res Rev. 2013 Jan;12(1):329–38.
14. Chiba I, Lee S, Bae S, Makino K, Katayama O, Harada K, et al. Association of Daily Physical Activity with Disability in Community-Dwelling Older Adults With/Without Chronic Kidney Disease. J Nutr Health Aging. 2022;26(5):521–8.
15. de Souto Barreto P. Exercise for Multimorbid Patients in Primary Care: One Prescription for All? Sports Med Auckl NZ. 2017 Nov;47(11):2143–53.
16. Ruiz JG, Dent E, Morley JE, Merchant RA, Beilby J, Beard J, et al. Screening for and Managing the Person with Frailty in Primary Care: ICFSR Consensus Guidelines. J Nutr Health Aging. 2020;24(9):920–7.
17. Daly RM, Iuliano S, Fyfe JJ, Scott D, Kirk B, Thompson MQ, et al. Screening, Diagnosis and Management of Sarcopenia and Frailty in Hospitalized Older Adults: Recommendations from the Australian and New Zealand Society for Sarcopenia and Frailty Research (ANZSSFR) Expert Working Group. J Nutr Health Aging. 2022;26(6):637–51.
18. Park SH, Roh Y. Which intervention is more effective in improving sarcopenia in older adults? A systematic review with meta-analysis of randomized controlled trials. Mech Ageing Dev. 2023 Mar;210:111773.
19. Lf de R, Jp RL, Vk M, O do CL. Sedentary behavior and health outcomes among older adults: a systematic review. BMC Public Health [Internet]. 2014 Sep 4 [cited 2023 Mar 6];14. Available from: http://pubmed.ncbi.nlm.nih.gov/24712381/
20. Chastin SFM, Mandrichenko O, Helbostadt JL, Skelton DA. Associations between objectively-measured sedentary behaviour and physical activity with bone mineral density in adults and older adults, the NHANES study. Bone. 2014 Jul;64:254–62.
21. Teychenne M, Ball K, Salmon J. Sedentary behavior and depression among adults: a review. Int J Behav Med. 2010 Dec;17(4):246–54.
22. Grøntved A, Hu FB. Television viewing and risk of type 2 diabetes, cardiovascular disease, and all-cause mortality: a meta-analysis. JAMA. 2011 Jun 15;305(23):2448–55.
23. Biswas A, Oh PI, Faulkner GE, Bajaj RR, Silver MA, Mitchell MS, et al. Sedentary time and its association with risk for disease incidence, mortality, and hospitalization in adults: a systematic review and meta-analysis. Ann Intern Med. 2015 Jan 20;162(2):123–32.
24. Kennedy BK, Berger SL, Brunet A, Campisi J, Cuervo AM, Epel ES, et al. Geroscience: linking aging to chronic disease. Cell. 2014 Nov 6;159(4):709–13.
25. López-Otín C, Blasco MA, Partridge L, Serrano M, Kroemer G. The hallmarks of aging. Cell. 2013 Jun 6;153(6):1194–217.
26. López-Otín C, Blasco MA, Partridge L, Serrano M, Kroemer G. Hallmarks of aging: An expanding universe. Cell. 2023 Jan 19;186(2):243–78.
27. Garatachea N, Pareja-Galeano H, Sanchis-Gomar F, Santos-Lozano A, Fiuza-Luces C, Morán M, et al. Exercise attenuates the major hallmarks of aging. Rejuvenation Res. 2015 Feb;18(1):57–89.
28. Rebelo-Marques A, De Sousa Lages A, Andrade R, Ribeiro CF, Mota-Pinto A, Carrilho F, et al. Aging Hallmarks: The Benefits of Physical Exercise. Front Endocrinol. 2018;9:258.
29. Carapeto PV, Aguayo-Mazzucato C. Effects of exercise on cellular and tissue aging. Aging. 2021 May 13;13(10):14522–43.
30. Sellami M, Bragazzi N, Prince MS, Denham J, Elrayess M. Regular, Intense Exercise Training as a Healthy Aging Lifestyle Strategy: Preventing DNA Damage, Telomere Shortening and Adverse DNA Methylation Changes Over a Lifetime. Front Genet. 2021;12:652497.
31. Sellami M, Gasmi M, Denham J, Hayes LD, Stratton D, Padulo J, et al. Effects of Acute and Chronic Exercise on Immunological Parameters in the Elderly

Aged: Can Physical Activity Counteract the Effects of Aging? Front Immunol. 2018;9:2187.
32. Nilsson MI, Tarnopolsky MA. Mitochondria and Aging-The Role of Exercise as a Countermeasure. Biology. 2019 May 11;8(2):40.
33. de Sousa CV, Sales MM, Rosa TS, Lewis JE, de Andrade RV, Simões HG. The Antioxidant Effect of Exercise: A Systematic Review and Meta-Analysis. Sports Med Auckl NZ. 2017 Feb;47(2):277–93.
34. Donati Zeppa S, Agostini D, Ferrini F, Gervasi M, Barbieri E, Bartolacci A, et al. Interventions on Gut Microbiota for Healthy Aging. Cells. 2022 Dec 22;12(1):34.
35. Clark JS, Simpson BS, Murphy KJ. The role of a Mediterranean diet and physical activity in decreasing age-related inflammation through modulation of the gut microbiota composition. Br J Nutr. 2022 Oct 14;128(7):1299–314.
36. Zhao H, He Z, Yun H, Wang R, Liu C. A Meta-Analysis of the Effects of Different Exercise Modes on Inflammatory Response in the Elderly. Int J Environ Res Public Health. 2022 Aug 22;19(16):10451.
37. Kim SD, Yeun YR. Effects of Resistance Training on C-Reactive Protein and Inflammatory Cytokines in Elderly Adults: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. Int J Environ Res Public Health. 2022 Mar 14;19(6):3434.
38. Raffin J, de Souto Barreto P, Le Traon AP, Vellas B, Aubertin-Leheudre M, Rolland Y. Sedentary behavior and the biological hallmarks of aging. Ageing Res Rev. 2023 Jan;83:101807.
39. Kinoshita K, Satake S, Matsui Y, Arai H. Association between Sarcopenia and Fall Risk According to the Muscle Mass Adjustment Method in Japanese Older Outpatients. J Nutr Health Aging. 2021;25(6):762–6.
40. Cruz-Jentoft AJ, Sayer AA. Sarcopenia. Lancet Lond Engl. 2019 Jun 29;393(10191):2636–46.
41. Tremblay MS, Aubert S, Barnes JD, Saunders TJ, Carson V, Latimer-Cheung AE, et al. Sedentary Behavior Research Network (SBRN) – Terminology Consensus Project process and outcome. Int J Behav Nutr Phys Act. 2017 Jun 10;14(1):75.
42. Bankoski A, Harris TB, McClain JJ, Brychta RJ, Caserotti P, Chen KY, et al. Sedentary activity associated with metabolic syndrome independent of physical activity. Diabetes Care. 2011 Feb;34(2):497–503.
43. Ekelund U, Steene-Johannessen J, Brown WJ, Fagerland MW, Owen N, Powell KE, et al. Does physical activity attenuate, or even eliminate, the detrimental association of sitting time with mortality? A harmonised meta-analysis of data from more than 1 million men and women. Lancet Lond Engl. 2016 Sep 24;388(10051):1302–10.
44. World Health Organization. WHO guidelines on physical activity and sedentary behaviour. Geneva: World Health Organization; 2020.
45. Pahor M, Guralnik JM, Ambrosius WT, Blair S, Bonds DE, Church TS, et al. Effect of structured physical activity on prevention of major mobility disability in older adults: the LIFE study randomized clinical trial. JAMA. 2014 Jun 18;311(23):2387–96.
46. Bernabei R, Landi F, Calvani R, Cesari M, Del Signore S, Anker SD, et al. Multicomponent intervention to prevent mobility disability in frail older adults: randomised controlled trial (SPRINTT project). BMJ. 2022 May 11;377:e068788.
47. Bischoff-Ferrari HA, Vellas B, Rizzoli R, Kressig RW, da Silva JAP, Blauth M, et al. Effect of Vitamin D Supplementation, Omega-3 Fatty Acid Supplementation, or a Strength-Training Exercise Program on Clinical Outcomes in Older Adults: The DO-HEALTH Randomized Clinical Trial. JAMA. 2020 Nov 10;324(18):1855–68.
48. de Souto Barreto P, Guyonnet S, Ader I, Andrieu S, Casteilla L, Davezac N, et al. The INSPIRE Research Initiative: A Program for GeroScience and Healthy Aging Research Going from Animal Models to Humans and the Healthcare System. J Frailty Aging. 2021;10(2):86–93.
49. Guyonnet S, Rolland Y, Takeda C, Ousset PJ, Ader I, Davezac N, et al. The INSPIRE Bio-Resource Research Platform for Healthy Aging and Geroscience: Focus on the Human Translational Research Cohort (The INSPIRE-T Cohort). J Frailty Aging. 2021;10(2):110–20.



How to cite this article: P. de Souto Barreto. Editorial: Physical Activity, Exercise, and Sedentary Time: Insights for Future Research in the Field of Geroscience. J Aging Res & Lifestyle 2023;12:20-22, http://dx.doi.org/10.14283/jarlife.2023.5