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Editorial

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

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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

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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.

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