

Age-related compensation

Neuromusculoskeletal capacity, reserve & movement objectives

van der Kruk, Eline; Silverman, Anne K.; Koizia, Louis; Reilly, Peter; Fertleman, Michael; Bull, Anthony M.J.

DOI

[10.1016/j.jbiomech.2021.110385](https://doi.org/10.1016/j.jbiomech.2021.110385)

Publication date

2021

Document Version

Final published version

Published in

Journal of Biomechanics

Citation (APA)

van der Kruk, E., Silverman, A. K., Koizia, L., Reilly, P., Fertleman, M., & Bull, A. M. J. (2021). Age-related compensation: Neuromusculoskeletal capacity, reserve & movement objectives. *Journal of Biomechanics*, 122, Article 110385. <https://doi.org/10.1016/j.jbiomech.2021.110385>

Important note

To cite this publication, please use the final published version (if applicable).
Please check the document version above.

Copyright

Other than for strictly personal use, it is not permitted to download, forward or distribute the text or part of it, without the consent of the author(s) and/or copyright holder(s), unless the work is under an open content license such as Creative Commons.

Takedown policy

Please contact us and provide details if you believe this document breaches copyrights.
We will remove access to the work immediately and investigate your claim.



Contents lists available at ScienceDirect

Journal of Biomechanics

journal homepage: www.elsevier.com/locate/jbiomech
www.JBiomech.com

Age-related compensation: Neuromusculoskeletal capacity, reserve & movement objectives

Eline van der Kruk^{a,f,*}, Anne K. Silverman^b, Louis Koizia^c, Peter Reilly^d, Michael Fertleman^e, Anthony M.J. Bull^f^a Department of Biomechanical Engineering, Delft University of Technology, Delft, the Netherlands^b Department of Mechanical Engineering, Colorado School of Mines, Golden, USA^c Department of Medicine, Imperial College Healthcare, London, UK^d Department of Orthopaedics, Imperial College Healthcare, London, UK^e Department of Medicine, Imperial College Healthcare, London, UK^f Department of Bioengineering, Imperial College London, London, UK

ARTICLE INFO

Article history:

Accepted 9 March 2021

Keywords:

Mobility impairments
Neuromusculoskeletal models
Rehabilitation
Optimal control theory
Frailty
Redundancy

ABSTRACT

The prevention, mitigation and treatment of movement impairments, ideally, requires early diagnosis or identification. As the human movement system has physiological and functional redundancy, movement limitations do not promptly arise at the onset of physical decline. A such, prediction of movement limitations is complex: it is unclear how much decline can be tolerated before movement limitations start. Currently, the term 'homeostatic reserve' or 'physiological reserve' is used to refer to the redundancy of the human biological system, but these terms do not describe the redundancy in the muscle architecture of the human body. The result of functional redundancy is compensation. Although compensation is an early predictor of movement limitations, clear definitions are lacking and the topic is underexposed in literature. The aim of this article is to provide a definition of compensation and emphasize its importance. Compensation is defined as an alteration in the movement trajectory and/or altering muscle recruitment to complete a movement task. *Compensation for capacity* is the result of a lack in neuromusculoskeletal reserve, where reserve is defined as the difference between the *capacity* (physiological abilities of the neuromusculoskeletal system) and the task demand. *Compensation for movement objectives* is a result of a shift in weighting of movement objectives, reflecting changing priorities. Studying compensation in biomechanics requires altered protocols in experimental set-ups, musculoskeletal models that are not reliant on prescribed movement, and inclusion of alternative movement objectives in optimal control theory.

© 2021 The Author(s). Published by Elsevier Ltd. This is an open access article under the CC BY license (<http://creativecommons.org/licenses/by/4.0/>).

1. Introduction

By 2050, all regions except for Africa will have at least 25% of their population over 60 years old and the proportion of people aged 80 or over will have tripled by that time (UN 2019). Ageing is often accompanied by a decrease in mobility, which can lead to loss of independence, inability to work, social exclusion, and a reduced quality of life (Gouvernement office for Science 2014).

Ideally, movement limitations would be recognized and prevented at an early stage. Mechanisms that contribute to mobility impairments are therefore major research topics in the fields of

physiology, biomechanics, and motor control. While the fields of biomechanics and motor control seek to understand the mechanisms of age-related mobility decline by understanding dynamics and control of biological systems, the field of physiology focusses on the biological processes. Combining the knowledge from these different fields is necessary to understand age-related movement impairments.

Daily life activities such as walking, standing up from a chair, or ascending stairs are complex motor tasks which involve subtle muscle control and trajectory planning (Harper, Wilken, and Neptune 2018; Caruthers et al. 2016; Winter 1995). Movement limitations do not promptly arise at the onset of physical decline because the human body has redundancy (Lipsitz 2002). The biological redundancy available to compensate for age and disease-related changes has been referred to as the 'homeostatic reserve' or 'physiological reserve' (Clegg et al. 2013). These terms

* Corresponding author.

E-mail addresses: e.vanderkruk@tudelft.nl (E. van der Kruk), asilverm@mines.edu (A.K. Silverman), l.koizia@nhs.net (L. Koizia), p.reilly@imperial.ac.uk (P. Reilly), m.fertleman@imperial.ac.uk (M. Fertleman), a.bull@imperial.ac.uk (A.M.J. Bull).

are also used to indicate frailty or whether a patient is likely to recover from an insult (Rockwood et al. 2005). However, these terms do not incorporate the redundancy in the muscle architecture of the human body, the *functional redundancy*. Terms such as 'physiological capacity' (Oseid 1973), 'musculoskeletal reserve' (Bull, Cleather, and Southgate 2008), and 'musculoskeletal capacity' (Nygård et al. 1987) have been used, but a general understanding and definition of these terms in the fields of biomechanics and motor control is lacking.

Functional redundancy is key in understanding how much decline can be tolerated before movement limitations begin. The result of functional redundancy is what we will refer to as *compensation*. From the onset of physical decline until the moment that movement impairments arise, human movement strategies will include compensation. Compensation is therefore an early indicator of physical decline and as such of importance clinically.

Definitions and terminology on compensation as a result of functional redundancy are lacking and we feel that the topic is underexposed in literature. In this short communication we therefore propose definitions on compensation and emphasize the importance of including compensation in (age-related) biomechanics research.

2. Compensation

We define compensation as an alteration in movement strategy in relation to a baseline (e.g., previous state or a control group). Compensation in movement strategies originates from the redundancy in the muscle architecture of the human body. Humans compensate by altering their movement trajectory and/or altering the muscle recruitment to complete a task:

- **Movement trajectory:** people can complete tasks using a variety of strategies to retain mobility including upper limb to lower limb compensations and postural changes. This form of compensation is a variation in the planned movement trajectory and can be described by kinematics. Examples are using the handrail when climbing stairs, walking with a walking aid, widening the base of support in gait, running with shorter step lengths, or standing up from a chair using the armrests.
- **Muscle recruitment:** this form of compensation engages the altered selection of muscle recruitment. Due to muscle architecture redundancy, compensation by altered muscle recruitment could also occur without a change in trajectory. A possible need of altered recruitment in healthy ageing could be the relative difference in decline of muscle strength between muscle groups (Gross et al. 1998; Abe et al. 2011). An example of this form of compensation is also co-contraction, which is a strategy that can be executed to increase stability (increased co-contraction) or reduce muscle activity (decreased co-contraction) through changes only in muscle recruitment, rather than changes in kinematics.

Apart from the form of compensation, we propose also to distinguish the reasons for compensation. There are two forms:

- **Compensation for Capacity:** We define **neuromusculoskeletal (NMSK) capacity** as the physiological abilities of the neuromusculoskeletal system. With this definition of capacity, we do not directly account for changes in the endocrine, immune, cardiovascular, respiratory, renal, or brain systems. NMSK capacity accumulates due to genetic and/or environmental factors up to a point at which age-related decline sets in (Fig. 1) (Kirkwood 2005). This decline is a result of structural changes of the neural, muscular, and skeletal (including soft tissues) sys-

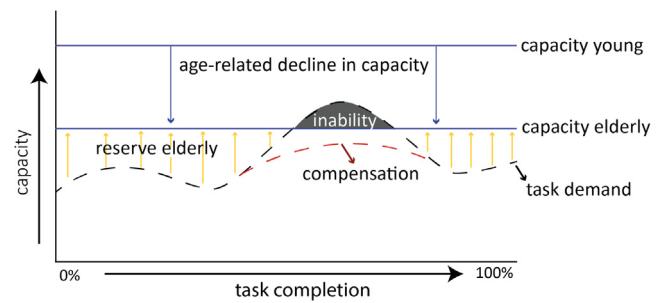


Fig. 1. Reserve is the difference between the capacity and the task demands. Capacity is defined as the physiological abilities of the neuromusculoskeletal system, in this case available for this task. If the reserve cannot meet the task demands, compensation will occur which changes the task demands while achieving the same goal.

tems (Fig. 2). A higher peak (or plateau) capacity mitigates the effects of decline caused by ageing or age-related diseases and the rate of decline can be adjusted through environmental factors (Warburton, Nicol, and Bredin 2006). Next, we define **NMSK reserve** as task specific and the difference between the capacity and the task demands (Fig. 1). Positive reserve enables the execution of a task. As task requirements vary over the duration of the task, so does reserve. Therefore, inability to achieve the activity may occur for only a portion of the task but still results in task failure. For example, in standing up, the point of lift off from the chair has the highest task demand and the reserve for this part of the task is therefore smallest. It is likely that this part of the task execution will become impaired first. We define **Compensation for capacity** as a changed recruitment of NMSK resources in response to a low reserve (relatively high task demand) in any part (neural, muscular, skeletal) of the NMSK capacity that can occur at any moment during task execution.

- **Compensation for Movement Objectives:** Within the redundancy of capacity and reserve, humans both consciously and unconsciously decide on movement strategies. To achieve a movement goal, there are several feasible strategies within the capacity each with their own task demands. For example, some strategies might demand more from the neural than the muscular system, and some strategies are less stable than others.

Energy-related costs are thought to be the primary driver for cyclic movements like standard gait (Anderson & Pandy, 2001; Cavagna & Franzetti, 1986; Hoyt & Taylor, 1981; Kuo, 2001; Minetti, Ardigo, Reinach, & Saibene, 1999), but there are other drivers (Malatesta et al. 2003; Raynor et al. 2002). The applied motion strategy of humans is probably a consideration of metabolic energy, velocity, stability (safety), and/or pain avoidance; these we jointly refer to as the **movement objectives**. Especially in ageing and neuromuscular deficiencies, it is likely that more emphasis is placed on alternative objectives, such as stability to minimise falling. Therefore, strategy selection is critical in movement impairments, although the specific objectives that are optimised in daily movements are not yet known. **Compensation for movement objectives** manifests as altered movement strategies due to changes in the weighting of movement objectives.

When compensation no longer enables the execution of the task at hand, inability and mobility limitations arise (Fig. 1). Capacity determines whether and which compensation strategies are available. Compensation and capacity are therefore overlapping and interacting. Individuals with greater capacity have more room to deploy effective compensation strategies. But compensation

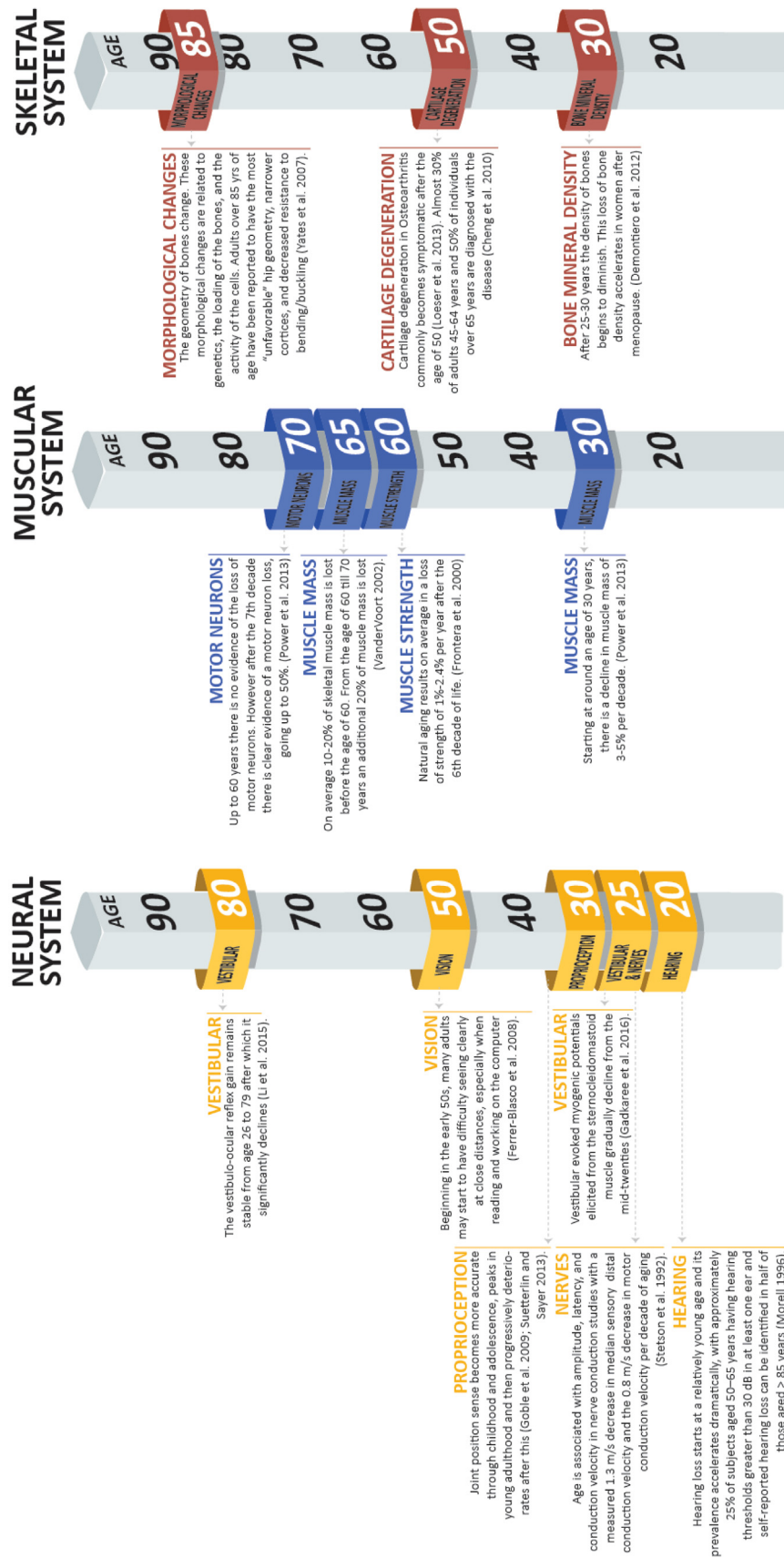


Fig. 2. General onset of decline in the adult neural, muscular and skeletal system (Goble et al. 2009; Suetterlin and Sayer 2013; Gadkaree et al. 2016; Cheng et al. 2010).

strategies can also be detrimental when they result in a habitual over- or underuse of physiological abilities. Elderly people can end up in a negative cycle (cycle of frailty), which accelerates decline of capacity (Xue 2011). A similar mechanism is prevalent in the young after traumatic incidents (Schmitt, Paterno, and Hewett 2012; Barenius et al. 2014; Cinque et al. 2018). The compensation applied after a stressor, for example asymmetry in gait to unload the involved side, can permanently change movement strategies. Such asymmetry could cause underuse of the involved side and overuse of the non-involved side, thereby putting neuromuscular capacity into decline in the long-term.

3. Selection of compensation strategies

Compensation often occurs ahead of when the physical decline results in a lack of reserve. In other words, humans alter their kinematics before this seems physically necessary. Moreover, within the NMSK capacity and reserve there are several feasible movement strategies.

To account for this, the field of biomechanics and motor control mostly assumes that the selection of movement strategies is to occur through a continuous optimization of a cost function (*optimal control theory*) (Todorov and Jordan 2002). In this context, movement objectives and their relative weighting could be considered as a multi-objective function resulting in a weighted average. Often cost functions in this field minimize an energy objective, while there might be alternatives. The shift in weighting factors of multiple movement objectives may explain age-related differences in movement strategies.

As an example, the relationship between oxygen consumption per unit distance and gait speed has a minimum which matches the preferred walking speed in adults ("optimal walking speed") (Pearce et al. 1983; di Prampero 1986). In older adults, however, preferred walking speed declines and energy expenditure per unit distance increases (Malatesta et al. 2003). Part of this can be explained by biological changes (objectively lower efficiency), but part of this is due to the selection of a slower walking speed. Selecting a lower walking speed suggests a shift in the weighting of the movement objectives that results in a less energetically economic movement pattern (Malatesta et al. 2003). This has been postulated as the minimisation of muscular fatigue rather than the minimisation of metabolic cost of transport (Song and Geyer 2018). However, there is no study to date that has explored possible psychological reasons for this, such as an increased emphasis on stability or pain avoidance. Humans likely make comparative assessments of movement objectives based on the task goal, their capacity, and psychological reasons related to a fear of falling, pain, or an unknown environment (Papa and Cappelz 2000); the emphasis on energy-cost alone is inadequate to characterize movement, particularly in an ageing population.

4. Compensation in biomechanics research

To summarize, NMSK capacity declines with healthy ageing. This decline is apparent in the neural, muscular, and skeletal systems and each influence the execution of complex motor tasks. For a specific task, humans have NMSK reserve, so that, if NMSK capacity reduces, the task can still be achieved. Humans compensate by altering their movement trajectory and/or altering the muscle recruitment to complete a task. Compensation can be a result of a lack of reserve, when capacity does not meet the task demands, or due to a shift in weighting of movement objectives, reflecting changing priorities.

Experimental design plays an important role in facilitating or constraining compensation strategies. Many studies impose stan-

dardisations on protocol, so the possibility of compensation is restricted. For example, most studies on sit-to-stand do not permit the participants to compensate using their arms, thus limiting their translation to characterising mobility of the elderly in their homes, communities, and clinic (van der Kruk et al., 2021). They therefore also do not provide insight into how much decline can be tolerated before movement limitations in daily life arise nor how humans select compensatory movement strategies for a task.

Musculoskeletal models and simulations are useful tools for estimating variables in human movement that are difficult to measure directly in human subjects. Models allow for simulations that cannot be performed with human subjects, such as studying site specific muscle weakness (e.g. Smith, Reilly, and Bull 2019). The conventional method in these modelling approaches, however, uses prescribed (measured) kinematics. Therefore, these simulations do not incorporate compensation. If wanting to model compensation, kinematics should be generated *de novo* (without tracking experimental data) using predictive simulations (Ong et al. 2017; Geijtenbeek 2019; Falisse et al. 2019). However, current state-of-the-state predictive models are too limited to simulate compensation strategies in daily life activities, as they have been simplified to upper or lower limb separately, mostly in two dimensions (Ong et al. 2017; Falisse et al. 2019; Song and Geyer 2018). In reality, people often use out-of-plane, asymmetric, and upper-lower-limb compensation strategies, like arm support in standing up or stair walking. These models therefore need further development before providing valid insights into compensation strategies of humans.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements

This study was supported by NWO-ENW Rubicon under Grant 019.173EN.023, 2018;

References

- Abe, Takashi, Sakamaki, Mikako, Yasuda, Tomohiro, Bembem, Michael G, Kondo, Masakatsu, Kawakami, Yasuo, Fukunaga, Tetsuo, 2011. Age-Related, Site-Specific Muscle Loss in 1507 Japanese Men and Women Aged 20 to 95 Years. *J. Sports Sci. Med.* 10 (1), 145.
- Anderson, Frank C, Pandey, Marcus G, 2001. Dynamic Optimization of Human Walking. *J. Biomech. Eng.* 123 (5), 381–390.
- Barenius, Björn, Ponzer, Sari, Shalabi, Adel, Bujak, Robert, Norlén, Louise, Eriksson, Karl, 2014. Increased Risk of Osteoarthritis after Anterior Cruciate Ligament Reconstruction: A 14-Year Follow-up Study of a Randomized Controlled Trial. *Am. J. Sports Med.* 42 (5), 1049–1057.
- Bull, A.M.J., Cleather, D., Southgate, D., 2008. Musculoskeletal Reserve: A Tool to Quantify Frailty in Ageing. In: *Bioengineering 08 London*, 49.
- Caruthers, Elena J, Thompson, Julie A, Chaudhari, Ajit M W, Schmitt, Laura C, Best, Thomas M, Saul, Katherine R, Siston, Robert A, 2016. Muscle Forces and Their Contributions to Vertical and Horizontal Acceleration of the Center of Mass during Sit-to-Stand Transfer in Young, Healthy Adults. *J. Appl. Biomech.* 32 (5), 487–503.
- Cavagna, G.A., Franzetti, P., 1986. The Determinants of the Step Frequency in Walking in Humans. *J. Physiol.* 373 (1), 235–242.
- Cheng, Y.J., Hootman, J.M., Murphy, L.B., Langmaid, G.A., Helmich, C.G., 2010. Prevalence of Doctor-Diagnosed Arthritis and Arthritis-Attributable Activity Limitation—United States, 2007–2009. *Morb. Mortal. Wkly Rep.* 59 (39), 1261–1265.
- Cinque, Mark E, Dornan, Grant J, Chahla, Jorge, Moatshe, Gilbert, LaPrade, Robert F, 2018. High Rates of Osteoarthritis Develop after Anterior Cruciate Ligament Surgery: An Analysis of 4108 Patients. *Am. J. Sports Med.* 46 (8), 2011–2019.
- Clegg, Andrew, Young, John, Iliffe, Steve, Rikkert, Marcel Olde, Rockwood, Kenneth, 2013. Frailty in Elderly People. *The Lancet* 381 (9868), 752–762.
- Falisse, Antoine, Serranoli, Gil, Dembia, Christopher L, Gillis, Joris, Jonkers, Ilse, De Groote, Friedl, 2019. Rapid Predictive Simulations with Complex

- Musculoskeletal Models Suggest That Diverse Healthy and Pathological Human Gaits Can Emerge from Similar Control Strategies. *J. R. Soc. Interf.* 16 (157), 20190402.
- Gadkaree, Shekhar K., Sun, Daniel Q., Li, Carol, Lin, Frank R., Ferrucci, Luigi, Simonsick, Eleanor M., Agrawal, Yuri, 2016. Does Sensory Function Decline Independently or Concomitantly with Age? Data from the Baltimore Longitudinal Study of Aging. *J. Aging Res.* 2016.
- Geijtenbeek, Thomas, 2019. SCONE: Open Source Software for Predictive Simulation of Biological Motion. *J. Open Source Softw.* 4, 1421.
- Goble, Daniel J., Coxon, James P., Wenderoth, Nicole, Van Impe, Annouchka, Swinnen, Stephan P., 2009. Proprioceptive Sensibility in the Elderly: Degeneration, Functional Consequences and Plastic-Adaptive Processes. *Neurosci. Biobehav. Rev.* 33 (3), 271–278.
- Government office for Science, UK, 2014. Future of an Ageing Population. https://Assets.Publishing.Service.Gov.Uk/Government/Uploads/System/Uploads/Attachment_data/File/816458/Future-of-an-Ageing-Population.Pdf, 2014.
- Gross, M.M., Stevenson, P.J., Charette, S.L., Pyka, G., Marcus, R., 1998. Effect of Muscle Strength and Movement Speed on the Biomechanics of Rising from a Chair in Healthy Elderly and Young Women. *Gait Posture* 8, 175–185.
- Harper, Nicole G., Wilken, Jason M., Neptune, Richard R., 2018. Muscle Function and Coordination of Stair Ascent. *J. Biomech. Eng.* 140 (1).
- Hoyt, Donald F., Richard Taylor, C., 1981. Gait and the Energetics of Locomotion in Horses. *Nature* 292 (5820), 239–240.
- Kirkwood, Thomas B.L., 2005. Understanding the odd science of aging. *Cell* 120 (4), 437–447.
- Kuo, Arthur D., 2001. A Simple Model of Bipedal Walking Predicts the Preferred Speed-Step Length Relationship. *J. Biomech. Eng.* 123 (3), 264–269.
- Lipsitz, Lewis A., 2002. Dynamics of Stability: The Physiologic Basis of Functional Health and Frailty. *J. Gerontol. Ser. A: Biol. Sci. Med. Sci.* 57 (3), B115–B125.
- Malatesta, Davide, Simar, David, Dauvilliers, Yves, Candau, Robin, Borrani, Fabio, Préfaut, Christian, Caillaud, Corinne, 2003. Energy Cost of Walking and Gait Instability in Healthy 65-and 80-Yr-Olds. *J. Appl. Physiol.* 95 (6), 2248–2256.
- Minetti, A.E., Ardigo, L.P., Reinach, E., Saibene, F., 1999. The Relationship between Mechanical Work and Energy Expenditure of Locomotion in Horses. *J. Exp. Biol.* 202 (17), 2329–2338.
- Nygård, C.-H., Luopajarvi, T., Cedercreutz, G., Ilmarinen, J., 1987. Musculoskeletal Capacity of Employees Aged 44 to 58 Years in Physical, Mental and Mixed Types of Work. *Eur. J. Appl. Physiol.* 56 (5), 555–561.
- Ong, Carmichael F., Geijtenbeek, Thomas, Hicks, Jennifer L., Delp, Scott L., 2017. Predictive Simulations of Human Walking Produce Realistic Cost of Transport at a Range of Speeds. In: *Proceedings of the 16th International Symposium on Computer Simulation in Biomechanics*, pp. 19–20.
- Oseid, S., 1973. Physical Work Capacity in Puberty, Physiological Capacity, Sex Differences and Possibilities of Influence. *Tidsskrift for Den Norske Laegeforening: Tidsskrift for Praktisk Medicin, Ny Raekke* 93 (14), 1007–1011.
- Papa, Elisabetta, Cappozzo, Aurelio, 2000. Sit-to-Stand Motor Strategies Investigated in Able-Bodied Young and Elderly Subjects. *J. Biomech.* 33 (9), 1113–1122. [https://doi.org/10.1016/S0021-9290\(00\)00046-4](https://doi.org/10.1016/S0021-9290(00)00046-4).
- Pearce, M.E., Cunningham, D.A., Donner, A.P., Rechner, P.A., Fullerton, G.M., Howard, J.H., 1983. Energy Cost of Treadmill and Floor Walking at Self-Selected Paces. *Eur. J. Appl. Physiol.* 52 (1), 115–119.
- di Prampero, P.E., 1986. The Energy Cost of Human Locomotion on Land and in Water. *Int. J. Sports Med.* 7, 55–72.
- Raynor, Annette J., Yi, Chow Jia, Abernethy, Bruce, Jong, Quek Jin, 2002. Are Transitions in Human Gait Determined by Mechanical, Kinetic or Energetic Factors? *Hum. Mov. Sci.* 21 (5–6), 785–805.
- Rockwood, Kenneth, Song, Xiaowei, MacKnight, Chris, Bergman, Howard, Hogan, David B., McDowell, Ian, Mitnitski, Arnold, 2005. A Global Clinical Measure of Fitness and Frailty in Elderly People. *CMAJ* 173 (5), 489–495.
- Schmitt, Laura C., Paterno, Mark V., Hewett, Timothy E., 2012. The Impact of Quadriceps Femoris Strength Asymmetry on Functional Performance at Return to Sport Following Anterior Cruciate Ligament Reconstruction. *J. Orthop. Sports Phys. Ther.* 42 (9), 750–759.
- Smith, S.H.L., Reilly, P., Bull, A.M.J., 2019. Serratus Anterior Weakness Is a Key Determinant of Arm-Assisted Standing Difficulties. *Medical Engineering and Physics*.
- Song, Seungmoon, Geyer, Hartmut, 2018. Predictive Neuromechanical Simulations Indicate Why Walking Performance Declines with Ageing. *J. Physiol.* 596 (7), 1199–1210.
- Sueterlin, Karen Joan, Sayer, Avan Aihie, 2013. Proprioception: Where Are We Now? A Commentary on Clinical Assessment, Changes across the Life Course, Functional Implications and Future Interventions. *Age Ageing* 43 (3), 313–318.
- Todorov, Emanuel, Jordan, Michael I., 2002. Optimal Feedback Control as a Theory of Motor Coordination. *Nat. Neurosci.* 5 (11), 1226–1235.
- UN, 2019. United Nations. 2019.
- van der Kruk, Eline, Silverman K., Anne, Reilly, Peter, Bull M.J., Anthony, 2021. Compensation due to age-related decline in sit-to-stand and sit-to-walk. *J. Biomech.* <https://doi.org/10.1016/j.jbiomech.2021.110411>. In this issue.
- Warburton, Darren E R, Nicol, Crystal Whitney, Bredin, Shannon S D, 2006. Health Benefits of Physical Activity: The Evidence. *CMAJ* 174 (6), 801–809.
- Winter, David A., 1995. Human Balance and Posture Control during Standing and Walking. *Gait Posture* 3 (4), 193–214.
- Xue, Qian-Li, 2011. The Frailty Syndrome: Definition and Natural History. *Clin. Geriatr. Med.* 27 (1), 1–15.