

# A step towards understanding fatigue and the cost of walking in persons with multiple sclerosis and rheumatoid arthritis

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## Impact

The findings of this dissertation have significant implications for both scientific and societal practices. Our overall aim was to assess whether the self-reported fatigue is accompanied by differences in gait characteristics and the energetic cost of walking in persons with MS and RA. The results suggest that the sensation of fatigue is not associated with changes in cost of walking and gait characteristics in persons with MS and RA. Despite an elevated cost of walking in persons with MS, subjects do not deteriorate in gait characteristics following a 6-minute walk test. Although persons with RA report higher levels of trait fatigue, the comprehensive set of gait parameters and cost of walking show no differences compared to control subjects at imposed walking speeds. However, persons with RA with slower self-selected walking speed were also physically less active in daily life.

The novelty of this dissertation lies in the comprehensive assessment of the energetic cost of walking, gait parameters and self-reported fatigue in persons with MS and RA. Our results which illustrate the cost of walking at various speeds using a polynomial curve, can be valuable for clinical practice by providing guidance for the optimal target speed during gait training. Gait training typically aims to increase the self-selected walking speed whereas the target speed should be within the energetically optimal range rather than simply the speed with the lowest energy cost. While our results primarily focus on identifying the walking speed with the lowest energetic cost, we note that the range of energetically optimal speeds has little variation in energetic cost. Although the clinical significance of this difference remains unknown, the energetic benefit of targeting a speed within an optimal range should be weighed against the participants' ability to increase their walking speed, given factors such as pain. Overall, increasing slow self-selected walking speeds can help reduce energy demand, even if the energetically optimal speed is not achievable for persons with disabilities. Thus, clinicians should focus on increasing walking speed within a range that is feasible and sustainable for the participant, rather than solely aiming for the energetically optimal speed.

Furthermore, clinical practices that commonly use the 6-minute walk test to assess walking ability should consider the elevated cost of walking in persons with MS when comparing reference values to control subjects. Persons with MS require a higher energy demand to walk the same distance as control subjects. When comparing the distance walked between both groups, it is important to note that even though persons with MS may walk at a slower speed, the energy demand could be similar to that of control subjects. As such, a comparison of the 6-minute walk test with control subjects should be interpreted with caution or even avoided. Instead, it might be more useful to monitor within-subject differences in distance walked before and after gait

training or as a structural measure to monitor walking ability for this population. Specifically, since our results did not show any deterioration in gait parameters nor cost of walking due to fatigue one could argue that the 6-minute walk test is not optimal for assessing walking ability.

Our results showing no deterioration in gait parameters are supported by recent literature confirms that the decline in walking speed during the 6-minute walk test is not a reliable indicator of walking fatigability in mildly disabled persons with MS. Instead, for future researchers, it might be more relevant to assess limitations in walking ability that reflect challenges experienced in daily life. Longer walking protocols that induce fatigue as well as real-life walking settings that simulate daily challenges are more reflective to walking limitations experiences in daily life. Walking on unstable terrain, an irregular sidewalk or while performing other tasks like crossing a busy street are less predictive, compared to walking in conventional gait laboratories. This may require other adaptations in gait parameters that limit walking ability, compared to controlled laboratory settings. Although modern technology enables the assessment of daily life walking challenges in controlled laboratory settings, the extent to which this accurately reflects daily life walking remains limited. Future research should first establish daily life walking challenges that explain limitations in walking ability using markerless tracking methods in natural environments. The effect of these limitations on other gait parameters that require measurements in force output or muscle activation could then be tested in a controlled setting. However, when aiming to improve walking ability in a controlled setting, the added benefit of gait training should be measured by settings that reflect daily life walking to the most natural extent possible. Targeting daily life walking challenges during gait training is likely to enhance the value and benefit for persons with limitations in walking ability.

The lack of differences in cost of walking and gait characteristics between persons with RA and control subjects imply that the elevated levels of fatigue in persons with RA are not explained by altered gait. However, the slower self-selected walking speed in persons with RA could also be interpreted as altered gait. Specifically because persons with RA with slower self-selected walking speeds are also physically less active in daily life. Although our results only describe a correlation, future research assessing activity patterns and length of walking bouts might reveal whether this contributes to the elevated levels of fatigue. For example, the initiation of multiple short walking bouts could increase the energetic demand which is not captured in a continuous walking protocol. Investigating daily life activity patterns and their energy demand, combined with our results describing the cost of walking at multiple speeds, could improve our understanding of the elevated levels of fatigue in person with RA beyond walking quality.

For the participants in our studies, our results were disseminated in a brief explanation of their results at the group level. This involvement may motivate subjects to participate in future studies. Additionally, the dataset of Chapter 3 was published as a data in brief and therefore publicly available, allowing for additional analyses and comparative material. This move toward open science contributes to the transparency of research results, encourages collaborations, and promotes new findings that can benefit scientific and social society. With regards to the rehabilitation and medical centres which participated in our study, the results are shared by providing a short presentation. Medical doctors, nurses and physical therapists were informed on the findings which may improve the dissemination of our studies.