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Sedentary behaviour in people with multiple sclerosis: Is it time to stand up against MS?

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Abstract

Historically, people with multiple sclerosis (MS) have been considered sedentary, although the actual scientific study of sedentary behaviour in MS did not originate until 2011. Sedentary behaviour, which is conceptually distinct from physical inactivity, is defined as any waking activity characterised by an energy expenditure ≤ 1.5 metabolic equivalents *and* in a sitting or reclining posture. In the general population, the volume of sitting time is associated with increased risks of morbidity and mortality, independent of physical activity, and has been suggested to carry a greater risk of mortality than smoking behaviour. There are many symptoms of MS (e.g. mobility disability, fatigue) that could increase the prevalence of sedentary behaviour, and sedentary behaviour may have considerable implications for the development of comorbid conditions prevalent in MS. This review provides a summary of the rates, correlates, and consequences of, and interventions attempting to reduce sedentary behaviour in MS. We provide a research agenda that guides future research on sedentary behaviour in MS. This paper provides a clarion call that it is time to “stand-up against MS.”

Sedentary behaviour: The new public health enemy

Sedentary behaviour has been suggested to result in more deaths than smoking behaviour¹. This is based on more people in industrialised countries leading a sedentary lifestyle which has unique health risks. Adults from the general population spend on average between 7.3 and 9.3 hours per day sitting² and this is often accumulated during the course of a working day. Large epidemiological studies have indicated that the volume of sitting time is associated with increased risk of morbidity and mortality, independent of levels of physical activity.³ Moreover, the adverse health consequences of high levels of sitting seemingly exceed the well-known public health problems of physical inactivity, obesity, and smoking among adults from the general population.⁴ This has prompted considerable investment in the development of behaviour interventions targeting the reduction of sedentary behaviour in the general population.

Much less is known about sedentary behaviour in clinical populations living with chronic conditions such as multiple sclerosis (MS). This is in stark contrast with the knowledge on physical activity behaviour in people with MS.⁵ Indeed, there is substantial evidence that people with MS are less physically active than the general population or even persons with other chronic diseases,⁶ despite the substantial benefits of physical activity demonstrated in over 50 clinical trials.⁵ By comparison, people with MS are often assumed to lead a sedentary lifestyle, yet this has not been systematically studied.

Why is sedentary behaviour important in MS? One reason is that the manifestations of MS (e.g., fatigue, depression, or pain) might predispose sedentary behaviour among those with MS. The mobility disabling consequences of MS might additionally result in increased rates of time spent sedentary in this clinical population. We further note that comorbidity (e.g., depression, anxiety, hypertension, hypercholesterolemia, obesity and chronic lung disease) is exceedingly prevalent and burdensome in MS,⁷⁻⁹ and comorbidity could be associated with rates of sedentary behaviour in this disease condition. To that end, we believe that an agenda should be built which focuses on sedentary behaviour in MS.

This topical review defines sedentary behaviour and systematically reviews the existing research on rates, correlates, consequences, and interventions for changing this behaviour in people with MS. We lastly provide directions for future research, and hope that this agenda will help others recognise the potential importance of “standing-up against MS”.

What is sedentary behaviour?

Sedentary behaviour is sometimes erroneously defined as the lack of meeting recommendations for physical activity or the absence of physical activity behaviour. Sedentary behaviour and physical activity are typically weakly correlated in bivariate analysis,¹⁰ and, even among adults who participate in more than 1 hour of moderate-to-vigorous physical activity (MVPA) per week, the volume of sedentary behaviour was associated with a more than 1.5-fold increase in risks of all-cause and cardiovascular mortality.¹¹ These findings might be explained by the distinct physiological characteristics of sedentary behaviour and physical activity,¹² as illustrated by the example of lipoprotein lipase activity, for which it has been shown that the response to sedentary behaviour is not merely the inverse of the response to exercise training as a form of physical activity.¹² Therefore, the Sedentary Behaviour Research Network has recommended that sedentary behaviour should be defined as ‘any waking behaviour characterised by an energy expenditure ≤ 1.5 METs while in a sitting or reclining posture’.¹³ We endorse this definition throughout our topical review.

Sedentary behaviour is often expressed as a total daily volume (e.g., minutes/day of sedentary behaviour such as sitting), but its pattern and distribution throughout the day are important too. For example, the number of sedentary breaks during a day and the duration of uninterrupted sitting time have been associated with health outcomes such as physical function¹⁴ and physical independence.¹⁵ Collectively, sedentary behaviour should be examined based on its pattern of accumulation as well as the total volume throughout the day. A complete list of outcomes for defining and objectively measuring sedentary behavior in MS has been provided Ezeugwu and colleagues¹⁶.

Literature review

Rates of sedentary behaviour in people with MS

Our literature review identified 11 articles that quantified the rates of sedentary behaviour in MS¹⁶⁻²⁶ (see Table 1). All studies included people with MS who were able to walk with or without assistive devices, which is reflected by relatively mild to moderate mobility disability. The reports of sedentary time ranged between 7 and 10 hours per day, and represented between 47 and 85% of the waking hours of the day. The variability could be due to different methods used to quantify sedentary behaviour. For example, overall sitting time was lower when self-report measures were used compared with objective assessments. It has also been suggested that four to six days of monitoring are necessary to obtain a reliable assessment of sedentary behaviour in people with MS.²⁶ Persons with MS had higher rates of sedentary time when compared against controls without MS based on accelerometry over several days,^{20,23} but not when measured using a questionnaire¹⁷ or an activity monitor worn for 48 hrs.²²

There is further evidence on the pattern of sitting time during the day. Overall static activity, which includes standing, sitting and lying, was higher in the afternoon in people with MS compared to control participants, which was attributed to people with MS spending more time lying down.²² Sitting activity was higher in the afternoon and evening compared to the morning among both people with MS and control participants.²⁷ The pattern of sedentary behaviour can further be assessed by exploring uninterrupted sedentary bouts. The only study to examine sedentary bouts revealed that sedentary time in people with MS was accumulated in longer rather than shorter bouts compared with control participants,²³ yet the overall number of breaks and mean sedentary bout duration did not differ between MS and controls.²³ Collectively, the initial efforts on quantifying sedentary behaviour in MS suggest that the volume of this behaviour is of problematic levels and might be more prevalent in MS

than in controls. The pattern further suggests that people with MS tend to accumulate sedentary time in longer rather than shorter bouts.

Correlates of sedentary behaviour in people with MS

We located four studies that examined putative correlates of sedentary behaviour in MS.^{16-18,24} Disease severity, measured by Expanded Disability Severity Scale (EDSS) or Patient Determined Disease Steps (PDDS), was most consistently associated with sedentary behaviour in ambulatory people with MS.^{16-18,24} Even though different cut off points have been used, comparisons between those with high and those with low disease severity reliably show that sedentary behaviour is more prevalent in those with more severe disease severity. Time spent in inactivity was significantly greater in ambulatory people with EDSS scores > 4.5 (85% of time spent in inactivity) compared to those with milder disease severity (76% spent in inactivity) but similar with regards to age and disease duration.²⁴ Similarly, the average daily volume of sedentary time was significantly higher in people with mobility disability (PDSS \geq 3) compared to those without mobility disability (533 versus 505 min/day, respectively), and sedentary time was accumulated using a greater number of sedentary bouts of 30 minutes or longer after adjustment for group differences in age and disease duration.¹⁶ In line with these objective assessments of sedentary time, people with moderate to severe ambulatory impairment (PDDS \geq 5) reported spending more than 2 hours longer per day in sedentary behaviours compared to those without ambulatory impairment.¹⁷ Correlational analyses support these findings, with self-reported disease severity significantly associated with objectively assessed¹⁸ and subjectively assessed¹⁷ sedentary behaviour. Using multiple linear regression analyses revealed that disease severity was associated with sedentary time, even when correcting for physical activity, marital status, employment status, and educational level.¹⁷

However, it is not just disability status which has been explored with regards to sedentary time. Disease duration was not related to sedentary behaviour, but the type of MS did correlate with this

behaviour; those with progressive MS were more sedentary than those with relapsing remitting MS.¹⁷

One recent paper indicated that age was associated with objective assessment of sedentary time in a large group of people with MS. Older people with MS (≥ 60 years) were significantly more sedentary compared to middle-aged people with MS (40-59 years), who, in turn, were more sedentary compared to younger people with MS (20-39 years).²⁵ However, the age groups differed with regards to disability status and type of MS, and it remains possible that these factors contributed the differences in sedentary time. Collectively, mobility disability was the most consistently reported correlate of sedentary behaviour in people with MS. It should be acknowledged that these studies on putative correlates of sedentary behaviour have only considered non-modifiable, disease-based correlates of MS, and have not focused on behavioural or motivation-related, modifiable variables that might serve as targets for behaviour interventions.

Consequences of sedentary behaviour in people with MS

The putative consequences of sedentary behaviour in people with MS have been examined in five studies.^{17,18,20,21,24} Such research indicates that greater sedentary time was related to both lower walking endurance and slower walking speed,¹⁸ as well as various indicators of physical activity.^{17,24} For example, the percentage of the day spent in inactivity was negatively correlated with average daily step count and average number of minutes spend being active.²⁴ As reported above, self-reported physical activity was related to sedentary time independently of other consequences and correlates.¹⁷ No associations were apparent between sedentary time and fatigue,²⁴ muscle recovery from exhaustive exercise,²⁰ brain structure based on MRI,²¹ or cognitive function.¹⁸ One unpublished study has indicated that self-reported sedentary behaviour was associated with higher blood pressure in persons with MS, but not controls. (Hubbard et al, personal communication) Of note, the samples sizes in the studies with non-significant results were relatively small yielding low statistical power for assessing the putative consequences of sedentary behaviour, and the influence of disease severity is not always taken into

account. We are surprised by the lack of research examining consequences of sedentary behaviour for comorbid conditions in particular, and this will be important for future research given the extent and consequences of comorbidity in MS.⁷⁻⁹

Interventions to change sedentary behaviour in MS

We located only one study that examined the effects of a behavioural intervention on sedentary behaviour in people with MS.¹⁹ The 24-week Internet-delivered behavioural intervention was based on social cognitive theory and consisted of a website and one-on-one video coaching sessions. The website presented information on self-efficacy, outcome expectations, goal setting, and facilitators and barriers for changing behaviour. All participants further had weekly video chat sessions with a behavioural coach that reinforced the content from the website and provided dialogue on behaviour change.¹⁹ The intervention reduced self-reported daily sitting time by 99 min/day compared with the control condition, but the health benefits of this reduction were not considered.¹⁹ One explanation for the success of this intervention could be that it provided suitable support for the participants to reallocate sedentary behaviour to physical activity (e.g., sitting less and moving more). This provides hope for designing behavioural interventions for reducing sedentary behaviour in MS and examining secondary effects on comorbidity and other outcomes.

Future research

Overall, our understanding of sedentary behaviour in MS is emerging from a stage of infancy, and our knowledge of sedentary behaviour and its measurement, rates, correlates, consequences, and interventions should be expanded considerably. Herein, we provide an agenda for advancing our understanding of sedentary behaviour in MS.

Rates of sedentary behaviour in MS

The current review provides ample evidence that people with MS are sedentary, nevertheless there is variability across the reported rates. This variability is most likely due to the different methods of

assessment of sedentary time. Therefore, it is important to validate existing objective and subjective measures for capturing sedentary behaviour and to develop a clear consensus on how to report the rates of sedentary behaviour. This consensus should, for example, include advice regarding adjustment for wear time of the accelerometer and number of days of monitoring to obtain a reliable assessment of sedentary behaviour.²⁶ More information is needed regarding the pattern of sedentary time throughout the day, as this has been related to health consequences in the general population.²⁸ Preliminary data suggest that daily patterns of physical activity differ in people with MS compared to healthy control participants,²³ and it is likely that sedentary behaviour has a distinct pattern in people with MS. We further require a large, population-based study for characterising the rate and distribution of sedentary behaviour in MS for a precise estimate and generation of normative values.

Correlates of sedentary behaviour in MS

There is very little known about correlates of sedentary behaviour in MS, and such inquiry is important for designing behavioural interventions. To date, mobility disability is the most consistently reported correlate of sedentary behaviour in ambulatory people with MS, and this informs researchers that interventions should target this segment of the MS population. However, no information is available about other potential correlates of sedentary behaviour that can inform the design of behaviour interventions in MS. The only study with a sufficient sample size to conduct regression analyses, revealed that physical activity, marital status, employment status and educational level were related to self-reported sedentary time independently from mobility disability. Given the consistent association between disease severity and sedentary time, more work is needed to explore other correlates while correcting for mobility disability. For example, it would be interesting to examine if the reported differences in sedentary behaviour between MS type¹⁷ and age²⁵ remain when participants are matched for disease severity. Further, no information is available about modifiable behavioural factors related to sedentary and this warrants further investigation. Such inquiry might consider adopting qualitative

methodology for “exploring” opportunities for behaviour change in MS, or adopt known theories of behaviour change (e.g., social cognitive theory, self-determination theory) for explaining sedentary behaviour using cross-sectional or longitudinal designs.

Consequences of sedentary behaviour in MS

There are likely to be significant consequences of sedentary behaviour in MS that are independent of physical activity, but this has not been a focal area of research. For example, there is evidence from the general population that sedentary behaviour based on volume (i.e., min/day) has been associated with cardiovascular disease, cancer and diabetes.³ Such associations have been independent of physical activity levels. There is further evidence that patterns of sedentary behaviour (e.g., long, continuous bouts of sitting) have distinct outcomes in the general population. We seek similar evidence in MS. For example, do the rates and/or patterns of sitting time as a sedentary behaviour predict comorbidity in MS? This is likely given the rates of sedentary behaviour and comorbidity in those with MS. Do the rates and/or patterns of sedentary behaviour explain outcomes such as immune function, neural integrity, functions such as fitness, symptoms, walking and cognition, and quality of life in MS, over and above the influence of disease severity. Such evidence should be collected with cross-sectional and longitudinal designs, and will inform outcome selection and design of behavioural interventions. For example, should interventions target total volume of sedentary time or the pattern of sedentary behaviour for improving outcomes in people with MS?

Interventions to reduce sedentary behaviour in MS

We located only one sedentary behaviour intervention in people with MS, and the intervention included elements of sedentary and physical activity behaviour change.^{19,29} Unfortunately, the health benefits of this intervention have not been described. This observation is not restricted to people with MS, as surprisingly little is known about the consequences of sedentary behaviour interventions in the general population.^{30,31} It has been suggested that particularly in people with low levels of fitness, like MS,

reducing sedentary time and increasing light physical activity can have substantial health benefits.³² Indeed, reallocating sedentary time to light physical activity has improved health outcomes (e.g., biomarkers for cardiovascular disease),³³ even in the absence of MVPA.³⁴ Reallocating sitting time to physical activity is likely to be feasible even for those with more severe mobility disability, given that the provision of bilateral walking support was related to increased levels of physical activity.¹⁶ Moreover, reducing sedentary behaviour in this group of people with MS could have even have greater impact on health as mobility disability is consistently associated with greater levels of sedentary behaviour. Therefore, future research should explore the health benefits of changing sedentary behaviour in people with MS with different levels of mobility disability.

Interventions should focus on sedentary time and the way sedentary behaviour is accumulated throughout the day and the variation between days. Breaking up sedentary time has been related to less mobility disability in people with MS¹⁶ as well as better physical function¹⁴ in elderly people. These improvements in function could be due to more frequent muscular contractions needed to stand up.¹² Experimental studies revealed that breaking up prolonged sitting with 2-minute bouts of physical activity induced several acute physiological changes, such as muscle gene expression³⁵ and decreases in blood pressure³⁶ and inflammation³⁷ compared to uninterrupted prolonged sitting, and in some cases, breaking up sedentary time with light physical activity resulted in similar benefits as MVPA.^{36,37} Such findings point to the potential of increasing light physical activity to induce health benefits, which importantly is feasible for ambulatory people with MS even with more severe mobility disability.

Conclusion

This is a clarion call that we must stand together and consider sedentary lifestyle as a new target for managing MS and improving the lives of people with this chronic condition. We know very little about sedentary behaviour in MS, but we believe that this represents a new target of importance for disease and self-management. People with MS spend considerably more time in sedentary behaviour than

physical activity, and this represents a substantially larger pool for health behaviour change. Such a large pool affords many opportunities for a meaningful impact on those living with MS. We believe that the research agenda suggested in this review will help to provide clear evidence for researchers, clinicians and practitioners that it is time to stand-up against sedentary behaviour in people with MS.

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Table 1. Summary of demographics, sedentary behaviour measurement and sedentary data reported in the studies reviewed.

Reference	N	Study design	EDSS*	MS type	Sedentary Behavior			
					Measure	Criteria	Time (mins)	Time (%)
Cavanaugh et al 2011²⁴	21	cross-sectional	3.5-7.5 (range)	NR	Step activity monitor	0 steps/min		76-85
Ickmans et al 2014²⁰	18	case-control	1.6, 1.0 (mean, SD)	NR	Actical accelerometer	NR		47
Klaren et al 2014¹⁹	70	intervention	2.0, 3.0 INT 3.0, 3.0 CON (PDDS)	RR/SP/PP	IPAQ	time sitting	412-550	
Rietberg et al 2014²²	43	case-control	3.5, 2.5	RR/SP/PP	Vitaport activity monitor	time sitting	478	
Blikman et al 2015²³	23	case-control	2.0, 3.0	RR/SP	ActiGraph GT3X+ accelerometer	≤150 counts/min		63.2
Ezeugwu et al 2015¹⁶	439	cross-sectional	0-6 (range)	RR/SP/PP	ActiGraph 7164 accelerometer	<100 counts/min	505-533	
Hubbard et al 2015¹⁷	1081	case-control	2.0 (mean PDDS)	RR/SP/PP	IPAQ	time sitting	451	
Hubbard & Motl 2015¹⁸	82	cross-sectional	3.5, 4.5	RR/SP/PP	ActiGraph GT3X Accelerometer	<100 counts/min	582	

Klaren et al 2015²¹	39	cross-sectional	4.5, 2.5	RR/SP/PP	ActiGraph GT3X Accelerometer	<100 counts/min	594	
Klaren et al in press²⁵	963	Cross-sectional	1.0, 2.0, 3.0	RR/SP/PP	ActiGraph 7164 accelerometer	<100 counts/min	510, 533, 554	
Klaren et al in press²⁶	442	Cross-sectional	2.0 (4.0)	RR/SP/PP	ActiGraph 7164 accelerometer	<100 counts/min	532	

NOTE: CON= control; PDDS= Patient Determined Disease Steps; INT= intervention; IPAQ= International Physical Activity Questionnaire; NR= not reported; SR-EDSS= self-reported Expanded Disability Status Scale. *Values are mdn, IQR unless otherwise noted.