Physical Activity and Sedentary Behaviour In People With Myasthenia Gravis: A Cross-Sectional Study

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Abstract

Background Despite improvements in the medical management of myasthenia gravis (MG) in recent years, patients continue to report poor health and wellbeing outcomes such as high levels of fatigue, reduced quality of life, walking limitation and reduced balance confidence. Physical activity has been shown to be associated with these outcomes in other populations, however there has been limited research in adults with MG. The primary aim of this study was to describe physical activity and sedentary behaviour in adults with MG and the secondary aim was to explore associations between these behaviours and fatigue, quality of life, balance confidence and walking limitation.

Methods A self-report online survey was used to assess physical activity, sedentary behaviour, fatigue, quality of life, balance confidence and walking limitation in 85 community-dwelling adults with MG. Multiple linear regression was used to examine associations between these variables and descriptive statistics were used to analyse participant characteristics, physical activity and sedentary behaviour.

Results Most participants (n=53, 62.4%) reported sufficient physical activity to meet public health guidelines, however participants also reported an average of 9 h/day of sedentary behaviour (mean 8.9±3.5). Physical activity and fatigue (R^2=0.196), quality of life (R^2=0.330), walking limitation (R^2=0.305) and balance confidence (R^2=0.304) were significantly ($p<0.05$) and positively correlated, with no associations found for sedentary behaviour. When patterns of physical activity and sedentary behaviour were combined, greater fatigue (R^2=0.213), lower quality of life (R^2=0.364), increased walking limitation (R^2=0.341) and lower balance confidence (R^2=0.279) was observed in patients who had greater physical activity levels and lower sedentary time.

Conclusions Physical activity and sedentary behaviour is associated with favorable health and wellbeing outcomes in adults with MG. Findings highlight that physical activity and sedentary behaviour may be possible intervention targets, however longitudinal and intervention studies are needed to determine causality.

Background

Myasthenia gravis (MG) is a chronic autoimmune neuromuscular disease involving dysfunction at the neuromuscular junction resulting in fatigue and muscle weakness. It can present as either one of or a combination of ocular and/or generalised weakness (1). Despite increasing life expectancy and availability of treatments (2), in people with MG, self-reported quality of life remains low (3), fatigue remains high (4) and overall life expectancy is still lower than the general population, however few deaths are directly attributed to the disease itself (5). Due to the pathophysiology of the disease, there has been uncertainty about whether strenuous physical activities will exacerbate weakness and induce exertional fatigue and consequently advice regarding physical activity engagement has historically been conservative (6). More recent evidence has demonstrated that balance (7), strength and aerobic exercises (8, 9) are safe and effective in people with MG and have been shown to positively affect disease

processes (10). Given the established evidence for the positive effect of exercise and physical activity on health outcomes and all-cause mortality in healthy populations (11), physical activity in people with MG warrants further investigation.

Physical activity and time spent sedentary (activities performed while awake in a sitting or lying position with an energy expenditure of < 1.5 METs; metabolic equivalents) (12), are important determinants of health. Evidence supports that higher levels of physical activity and lower time spent sitting is associated with reduced mortality, reduced occurrence of non-communicable diseases and improved quality of life (13). Public health guidelines recommend a minimum of 150 minutes per week of moderate-to-vigorous physical activity with minimising time in prolonged sitting in order to attain health benefits (14). A recent meta-analysis of over 1 million participants has confirmed that the combination of these behaviours are important, demonstrating a dose-response relationship between physical activity and sedentary time, with increasing levels of physical activity mitigating the effects of sedentary behaviour on all-cause mortality (15).

People with diseases that compromise physiological capacity to move (such as in MG) require special consideration as to how best facilitate physical activity and minimise sedentary time. Impairments known to be present in MG such as fatigue, weakness (4, 16–18) and reduced exercise tolerance due to lowered respiratory capacity (19) can reduce movement capacity and subsequently lead to a cycle of deconditioning. As movement becomes more difficult, aversion to movement can increase and in turn physiological effects of inactivity compound, leading to further difficulty with movement (20). This can subsequently increase the risk of non-communicable diseases and premature mortality associated with inactivity (21). This is an important consideration given the lower life expectancy of people with MG compared to the general population, with cause of death often due to factors shown to be modifiable by physical activity (22) such as cancer and cardiovascular disease (23). Concurrently, the pharmaceutical management of individuals with MG places them at risk of further health complications that are also able to be mitigated with exercise, such as osteoporosis (24).

To date, there has been limited research investigating physical activity and sedentary behaviour in people with MG. One study (n = 27) has explored physical activity, sedentary behaviour and associations with disease severity in MG (25). Using accelerometry, this study found that most participants (n = 13, 78%) with MG met current physical activity recommendations, however they had significantly lower levels of physical activity than age-corresponding healthy individuals (based on World Health Organisation data) and that participants spent an average of 78% of the day sedentary. No associations were found between physical activity and disease severity. However, this study had a small sample size (n = 27) and possible recruitment bias reducing generalisability given the study led into a training intervention. The relationship between physical activity and sedentary behaviour and health and wellbeing outcomes that are commonly reported in individuals with MG, such as higher fatigue (4), reduced quality of life (3), walking limitation (26) and reduced balance confidence (27), are of interest given the demonstrated relationships in other neurological populations; research evidence in other progressive neurological groups have

established positive associations between physical activity and fatigue (28, 29), depression (28) and self-reported quality of life (28, 29).

Therefore, the aim of this cross-sectional study was to describe the patterns of self-reported physical activity and sedentary behaviour in adults with MG and to explore associations between these health-related behaviours and fatigue, quality of life, walking limitation and balance confidence.

Methods

Study design

A cross-sectional design using a self-report electronic survey was used to evaluate physical activity and sedentary behavior in people with MG and the relationship with fatigue, quality of life, walking limitation and balance confidence. Ethical approval was provided by The University of Queensland Human Research Ethics Committee (reference number HREC/2019/000/774).

Participants

To be eligible for the study, participants needed to be aged between 18–80 years, able to provide informed consent, be independently ambulant with or without mobility aids and have stable self-reported MG symptoms for at least four weeks preceding participation. Community-dwelling adults who reported having MG were recruited via convenience sampling using flyers and social media advertising through a disease specific support group. Advertisements included a website link for the electronic online survey. The link first included information about the study, eligibility criteria and contact details of the research team and potential participants were required to indicate that they met eligibility criteria and provide informed consent prior to commencing the survey.

Scales and questionnaires

Participants were asked to report demographic characteristics including age, gender, height, weight, employment, relationship status, disease duration, past medical history, treatments for MG and other medication and comorbidities.

Physical activity was measured using the Active Australia Survey (30), a self-report measure validated in adult populations (31) that asked participants to report the amount of time spent in various types and intensities of activity such as walking (including for recreation and/or transport), gardening and moderate and vigorous-intensity activity in the last week. From these values, an overall MET.min.wk^{-1} score was determined using the following formula: 3.33 METs for brisk walking and moderate-intensity leisure activities and 6.66 METs for vigorous intensity leisure activities (32, 33). Physical activity was then classified into two subcategories: insufficiently active (0 to 499 METmin.wk^{-1}) or sufficiently active according to physical activity guidelines (≥ 500 METminutes.wk^{-1})(34).

Sedentary behaviour was measured using the Past-day Recall of Sedentary Time (PAST) (35), a self-report measure of sedentary behaviour validated in adult populations (35, 36). Participants were asked to report the number of minutes spent sitting or lying in various domains throughout the waking hours of the previous day (such as when working, for transport, while watching television and reading). Total sedentary time was calculated by summing the time reported in each of the domains of sedentary behaviour. The total time was then classified into two categories; <10 and ≥ 10 hours of sedentary time per day, given > 9.5 hours has been reported in the literature as associated with higher risk of early mortality (37) and adverse health outcomes (38).

Fatigue was measured using the Modified Fatigue Impact Scale (MFIS) (39), a 21-item self-report measure used to assess perceived impact of fatigue on quality of life in physical, social and psychosocial domains. There are no reliability or validity studies for this scale in MG specifically, however the measure has been shown to be a reliable and valid measure of fatigue in other neurological populations (40). A higher score indicates a greater impact of fatigue on a persons' daily life.

Quality of life was measured using the Myasthenia Gravis Quality of Life 15-item (MG-QoL-15) (41) a valid survey assessing self-reported impact of disease-specific signs and symptoms on quality of life (42), with a higher score indicating poorer perceived quality of life.

Walking limitation was assessed using the Walk-12G (43), a 12-item survey that assesses self-reported difficulties with walking in everyday life. Validation has occurred in other neurological conditions (43), with a higher score indicating greater limitation of walking.

Balance confidence was assessed using the Activities-specific Balance Confidence Scale (ABC Scale) (44), a 16 item self-reported measure of perceived confidence in balance when mobilising and performing a number of everyday tasks. This scale has been validated in neurological populations (45) with higher scores indicating greater balance confidence.

Data analysis

Statistical analyses were performed using SPSS v25 (IBM Corporation). Data and model residuals were assessed for normality using the Shapiro-Wilk test. Participant characteristics, physical activity ($METmin.wk^{-1}$) and sedentary behaviour (h/day) and clinical characteristics were analysed using descriptive statistics (mean and standard deviation for normally distributed variables, median and interquartile range for non-normally distributed variables and proportions for categorical variables). Associations between study variables (physical activity; sufficiently active (≥ 500METmin.wk-1) and insufficiently active (< 500 MET.min.wk-1) and sedentary behaviour (≥ 10 hours of sitting per day; <10 hours of sitting per day) and fatigue, quality of life, walking limitation and balance confidence were assessed using multiple linear regression. To examine associations between patterns of physical activity and sedentary behaviour and fatigue, quality of life, walking limitation and balance confidence, multiple linear regression was performed using 'sufficient physical activity and < 10 hours/day sitting' as the reference category. All models were adjusted for age, body mass index and disease duration and

unstandardized regression coefficients are presented. Level of significance was set at $p < 0.05$. *Apriori* sample size calculations estimated that a minimum sample size of n = 36 was required based on previously reported correlations between fatigue and physical activity in multiple sclerosis ($r = -0.45$; n = 36) (29).

Results

Participant demographics and clinical characteristics are listed in Table 1. Eighty-five participants with an average age of 48 ± 15.52 completed the survey. Seventy-four percent (n = 63) were female, with most participants reporting generalized (n = 82, 96.5%) versus ocular-only symptoms (n = 3, 3.5%). Over half of the participants (n = 48, 56.5%) reported full or part-time work or study, with 44 (51.8%) participants reporting they had changed their employment and/or study workload as a result of MG. 87% (n = 74) of participants were ambulant without a mobility aid.

Table 1
Participant demographics and clinical characteristics

Measure	Participants (n = 85)
Age, mean ± SD (years)	47.7 ± 15.52
Gender, Female, n (%)	63 (74.1)
Muscle groups affected, n (%)	82 (96.5)
Generalised	3 (3.5)
Ocular only	
Disease duration, median [interquartile range], (years)	3.5 [1.5–10]
Co-morbidities, n (%)	28 (32.9)
0	41 (48.2)
1–3	16 (18.8)
> 4	
Ethnicity, n (%)	69 (81.2)
Caucasian	9 (10.6)
Asian	2 (2.4)
Indigenous Australian	1 (1.2)
African-American	4 (4.7)
Other	
Country of residence, n (%)	
Australia	53 (62.4)
United States of America	24 (28.2)
New Zealand	2 (2.4)
Canada	3 (3.5)
Other	3 (3.5)

Measure	Participants (n = 85)
Treatments for MG, n (%)	36 (42.4)
Thymectomy	14 (16.5)
Plasmapheresis	57 (67.1)
Intravenous immunoglobulin therapy	77 (90.6)
Anticholinesterase medications	70 (82.4)
Immunosuppressive medications	
Employment Status, n (%)	29 (34.1)
Full-time work or study	19 (22.4)
Part-time work or study (< 34 hours)	13 (15.3)
Retired	9 (10.6)
Unemployed	12 (14.1)
Medically retired	3 (3.5)
Home duties	
Change of employment status due to MG, n (%)	44 (51.8)
Highest level of education attained, n (%)	9 (10.6)
Less than grade 12	13 (15.3)
High school graduate	14 (16.5)
Tafe/Vocational training	49 (57.6)
Higher education	
Living situation, n (%)	12 (14.11)
Living alone	73 (85.9)
Living with friends/family	
Ambulant without mobility aid, n (%)	74 (87.1)
Body mass index, median [interquartile range]	26.2 [23.2–32.4]

Results of measures of physical activity, sedentary behaviour, fatigue, quality of life, walking limitation and balance confidence are listed in Table 2. Participants reported a median of 999 MET.min.wk^{-1} of physical activity. Around two-thirds of participants (n = 53, 62.4%) were sufficiently active according to physical activity guidelines. Over half of all participants (n = 46, 54.1%) reported no vigorous physical activity. Participants reported an average of 9 hours per day (mean 8.9 ± 3.5 hours) sedentary, with over a third (n = 36, 42.4%) spending ≥ 10 hours/day sedentary.

Table 2
Physical activity, sedentary behaviour, fatigue, quality of life, walking limitation and balance confidence

Measure	n = 85
Physical activity	233.10 [66.6-915.8]
Moderate activity METminutes.wk^{-1}, median [interquartile range]	0.000 [0-799.2]
Vigorous activity METminutes.wk^{-1}, median [interquartile range]	999 [0-11188.8]
Total METminutes.wk^{-1}, median [interquartile range]	
Meeting physical activity guidelines (≥ 500 MET.min.wk-1), n (%)	53 (62.4)
Not meeting physical activity guidelines (≥ 500 MET.min.wk-1), n (%)	32 (37.6)
Sedentary behaviour	
Sedentary behaviour, h/day, mean ± SD	8.98 ± 3.53
Sedentary < 10 h/day, n (%)	49 (57.6)
Sedentary ≥ 10 h/day, n (%)	36 (42.4)
Combined physical activity and sedentary behaviour	
Insufficiently active (< 500 MET.min.wk-1), sedentary ≥ 10 h/day, n (%)	18 (21.2)
Sufficiently active (≥ 500 MET.min.wk-1), sedentary ≥ 10 h/day, n (%)	18 (21.2)
Insufficiently active (< 500 MET.min.wk-1), sedentary < 10 h/day, n (%)	14 (16.5)
Sufficiently active (≥ 500 MET.min.wk-1), sedentary < 10 h/day, n (%)	35 (41.2)

Notes:

MET = metabolic equivalents; SD = standard deviation

*A score out of 84, with higher scores indicating greater impact of fatigue on a person's activities

†A score out of 60, with higher scores indicating poorer perceived quality of life

‡A score out of 42, with higher score indicating greater limitation to walking

§A percentage out of 100 of perceived balance confidence, with a higher score indicating greater confidence in balance

Measure	n = 85
Modified Fatigue Impact Scale*	43.18 ± 20
Total, mean ± SD	23 [14.5–28]
Physical, median [interquartile range]	17.19 ± 9.8
Cognitive, mean ± SD	4 ± 2.5
Psychosocial, mean ± SD	
Myasthenia Gravis Quality of Life 15-Item†, mean ± SD	14.42 ± 7.8
Walk-12G‡, median [interquartile range]	14 [5–26]
Activities-Balance Confidence Scale§, median [range]	73.13 [52.2–94.4]
Notes:	
MET = metabolic equivalents; SD = standard deviation	
*A score out of 84, with higher scores indicating greater impact of fatigue on a person's activities	
†A score out of 60, with higher scores indicating poorer perceived quality of life	
‡A score out of 42, with higher score indicating greater limitation to walking	
§A percentage out of 100 of perceived balance confidence, with a higher score indicating greater confidence in balance	

Associations between physical activity and sedentary behaviour and fatigue, quality of life, walking limitation and balance confidence are presented in Table 3. Physical activity was significantly negatively associated with fatigue, quality of life and walking limitation, with sufficiently active participants reporting reduced fatigue, higher quality of life and better walking compared to their less active counterparts. Being sufficiently active was also significantly positively associated with balance confidence, with sufficiently active participants reporting higher balance confidence. Sedentary behaviour was not significantly associated with any of the outcomes. R^2 values ranged from 0.196–0.330.

Table 3
Multiple linear regression for physical activity and sedentary behaviour

Measures	Physical activity (Sufficiently active compared to insufficiently active)	Sedentary behaviour (< 10 h/day compared to ≥ 10 h/day)	R^2
Fatigue*	-17.65	-0.37	0.196
Unstandardized beta (B)	45.22, 99.32	-8.81, 8.07	
95% Confidence Interval	≤ 0.00	0.931	
P-value			
Quality of life†	-8.83	1.33	0.330
Unstandardized beta (B)	-11.88, -5.79	-1.68, 4.35	
95% Confidence Interval	≤ 0.001	0.380	
P-value			
Walking limitation‡	-11.06	-0.55	0.305
Unstandardized beta (B)	-15.54, -6.57	-5.00, 3.89	
95% Confidence Interval	≤ 0.001	0.805	
P-value			
Balance confidence§	20.70	4.37	0.304
Unstandardized beta (B)	12.28, 29.12	-4.04, 12.79	
95% Confidence Interval	≤ 0.001	0.304	
P-value			

Notes:

All models were adjusted for age, disease duration and body mass index

*Assessed using the Modified Fatigue Impact Scale, scored out of 84 with a higher score indicating greater impact of fatigue on a person's daily life

Measures	Physical activity (Sufficiently active compared to insufficiently active)	Sedentary behaviour (< 10 h/day compared to ≥ 10 h/day)	R^2
[†]Assessed using the Myasthenia Gravis Quality of Life 15-Item, scored out of 60 with a higher score indicating poorer perceived quality of life			
[‡]Assessed using the Walk-12G, scored out of 42 with a higher score indicating greater limitation to walking			
[§]Assessed using the Activities-Balance Confidence Scale, scored as a percentage out of 100 of perceived balance confidence, with a higher score indicating greater confidence in balance			

Associations between patterns of both physical activity and sedentary behaviour and fatigue, quality of life, walking limitation and balance confidence are reported in Table 4. Compared with the reference group (those who were sufficiently active and spent < 10 h/day sitting), fatigue was significantly higher in the insufficiently active groups for both < 10 hours and ≥ 10 hours sitting. Quality of life was significantly lower across all groups compared to the reference group and in the sufficiently active and ≥ 10 h/day sitting group, as was walking limitation. Balance confidence was reduced among those in the insufficiently active and ≥ 10 hours sitting group only when compared to the reference group. Generally, beta-coefficients were larger in those who were inactive and sat more compared to those that were inactive and sat less, indicating that sedentary behaviour alone may have an important effect on these outcomes irrespective of physical activity.

Table 4
Multiple regression for patterns of physical activity and sedentary behaviour and fatigue, quality of life, walking limitation and balance confidence

Measures	Sufficiently active, < 10 hours sitting	Sufficiently active, ≥ 10 hours sitting	Insufficiently active, < 10 hours sitting	Insufficiently active, ≥ 10 hours sitting	R^2
Fatigue*	Reference category	-4.15	12.41	19.42	0.213
Unstandardized beta (B)		-15.01, 6.70	0.79, 24.03	8.67, 30.16	
95% Confidence Interval		0.448	0.037	≤ 0.001	
P-value					
Quality of life†	Reference category	-3.80	5.96	8.26	0.364
Unstandardized beta (B)		-7.64, 0.01	1.87, 10.06	4.48, 12.05 ≤ 0.001	
95% Confidence Interval		0.0051	0.005		
P-value					
Walking limitation‡	Reference category	-3.15	6.76	12.76	0.341
Unstandardized beta (B)		-8.78, 2.48	0.73, 12.80	7.18, 18.33 ≤ 0.001	
95% Confidence Interval		0.0269	0.028		
P-value					

Notes:

All models were adjusted for age, disease duration and body mass index

*Assessed using the Modified Fatigue Impact Scale, scored out of 84 with a higher score indicating greater impact of fatigue on a person's daily life

†Assessed using the Myasthenia Gravis Quality of Life 15-Item, scored out of 60 with a higher score indicating poorer perceived quality of life

‡Assessed using the Walk-12G, scored out of 42 with a higher score indicating greater limitation to walking

§Assessed using the Activities-Balance Confidence Scale, scored as a percentage out of 100 of perceived balance confidence, with a higher score indicating greater confidence in balance

Measures	Sufficiently active, < 10 hours sitting	Sufficiently active, ≥ 10 hours sitting	Insufficiently active, < 10 hours sitting	Insufficiently active, ≥ 10 hours sitting	R^2
Balance confidence[§] Unstandardized beta (B) 95% Confidence Interval P-value	Reference category	1.54 -11.62, 14.70 0.816	-10.68 -24.77, 3.41 0.135	-21.81 -34.84, -8.78 ≤ 0.001	0.279
Notes:					
All models were adjusted for age, disease duration and body mass index					
[*]Assessed using the Modified Fatigue Impact Scale, scored out of 84 with a higher score indicating greater impact of fatigue on a person's daily life					
[†]Assessed using the Myasthenia Gravis Quality of Life 15-Item, scored out of 60 with a higher score indicating poorer perceived quality of life					
[‡]Assessed using the Walk-12G, scored out of 42 with a higher score indicating greater limitation to walking					
[§]Assessed using the Activities-Balance Confidence Scale, scored as a percentage out of 100 of perceived balance confidence, with a higher score indicating greater confidence in balance					

Discussion

The aims of this study were to describe the patterns of self-reported physical activity and sedentary behaviour in people with MG and to explore associations between these health-related behaviours and fatigue, quality of life, walking limitation and balance confidence. The findings of this study indicate that despite over two-thirds of the participants meeting physical activity guidelines, over a quarter also spend over 10 hours sitting per day. Further, participants largely met guidelines through accruing moderate-intensity physical activity, with less than half of all participants engaging in any vigorous activity at all. There were significant associations found between meeting physical activity guidelines and less fatigue, greater quality of life, less walking limitation and greater balance confidence, while conversely no associations were found between these variables and sedentary behaviour alone. However there were also significant dose-response relationships between patterns of physical activity and sedentary behaviour, with those that were inactive but accruing < 10 h/day of sedentary time significantly associated with less fatigue, greater quality of life, less walking limitation and greater balance confidence compared to those that are inactive but reported sitting ≥ 10 h/day.

The Australian Physical Activity Guidelines recommend 150 minutes per week of moderate-vigorous physical activity in order to attain significant health benefits (46), which equates to 500 METminutes.wk^{-1}. Two-thirds of the participants in our study were classified as sufficiently active, however less than half of this sufficiently active group engaged in any vigorous physical activity. This is slightly lower than a previous study investigating physical activity and sedentary behaviour in 27 adults with MG (mean age 62 ± 16 years), which reported that 78% of participants reached physical activity guidelines, however only 11% engaged in ≥ 20 min/day of vigorous activity for a minimum of three days per week (25). It is important to note that this previous study used device-based measures of physical activity, whereas the current student utilised self-report which typically results in higher estimates of physical activity (47). There is a possible recruitment bias as the cross-sectional study was a part of a larger study that included a training opportunity for participants. Subsequently, those recruited may have had an interest in physical activity that influenced the cross-sectional data. Given the additional health benefits of vigorous physical activity (48), further investigation into the barriers to vigorous activity in this population is warranted.

Regarding sedentary behaviour, similar findings were reported in both our own and the aforementioned study, with high levels of sedentary behaviour in both (25). Our findings indicate the median daily sedentary time among participants was approximately 9 h/day (8.98 ± 3.53), 2.5 hours more than found in the general adult population in one study (n = 3,699), where average self-report sedentary behaviour was 6.5 h/day (95% CI 6.2–6.7)(49). This is also higher than findings in other neurological populations; one study in adults with multiple sclerosis reported average self-report sedentary time of 7.5 ± 3.7 h/day (n = 1081) (50). The medical advice and benefits of exercises in multiple sclerosis has evolved greatly over the past two decades and the overall lower sedentary time for this group may be reflective of this. Given the evidence for higher sedentary time and poor health outcomes including increased mortality (51), further interventional research to reduce sedentary time in people with MG is needed to reduce these risks.

In the present study, significant associations were found between physical activity and fatigue, quality of life, walking limitation and balance confidence. This is the first study, to our knowledge, that has explored this in people with MG. In other populations physical activity interventions have shown positive effects on fatigue (52–54), quality of life (55), walking ability (55, 56) and balance (56). Pathologies associated with impaired movement such as in MG may result in reduced capacity for physical activity and more sedentary behaviour, thereby risking physiological effects from disuse. The positive benefits in the above studies may be a direct consequence of breaking this disuse cycle, restoring the physiological deficits from disuse and/or having an impact on the primary symptoms of the pathologies (20). At this stage for people with MG it is unclear whether the participants who engage in more physical activity, do because they are less fatigued, have better quality of life, less walking limitation and/or greater balance confidence and thus able to break this disuse cycle, or the other way around. Longitudinal research is warranted to investigate these relationships further and determine direction of associations and treatment impacts. Nonetheless, these preliminary findings are of important clinical consideration given

the historical concerns of increased activity leading to provocation of symptoms in this population. Overall, our findings support the growing body or literature that higher levels of exercise and physical activity do not appear to be associated with negative outcomes in people with MG and may in fact have similar positive outcomes as seen in healthy populations. However, despite the statistical significance, R^2 values in our study are low and so our findings should be interpreted with caution.

Although there were no associations found between sedentary behaviour alone and the outcomes assessed in this study, there were significant associations with these variables when patterns of sedentary behaviour were analysed in combination with sufficient versus insufficient physical activity. Our findings indicate that even in those who are inactive, lower levels of sedentary time (< 10 h/day) are associated with less fatigue, higher quality of life, less walking limitation and greater balance confidence compared to those with higher sedentary time (≥ 10 h/day). This is a promising finding, potentially suggesting that sedentary behaviour may be an appropriate intervention target even when physical activity levels are low. The potential protective effect of physical activity against the detriments of sedentary behaviour is another consideration in this population. A recent meta-analysis found that the increased mortality risk associated with high sedentary time appears to be mitigated with increasing physical activity levels and even reversed in those who are in the highest quartile for physical activity (> 2130 METminutes.wk^{-1}) (15). These findings indicate that changing sedentary time has a positive effect on mortality irrespective of physical activity levels, and so warrants further investigation as to a potential target intervention for people with MG, given that the findings of our study indicate high levels of sedentary behaviour in this population. As these benefits are most impactful when combined with higher levels of physical activity, interventions targeting whole of day activity and thus incorporating both physical activity and sedentary behaviour may be of benefit in improving health and well-being outcomes in adults with MG.

The findings of this study should be considered in light of a number of limitations. The cross-sectional design gives insight into these behaviours at only one point in time and therefore limits the ability to determine causality. Further longitudinal and/or interventional research is needed to determine direction of associations and efficacy, respectively. Most of our participants reported generalised (n = 92, 96.5%) compared with ocular-only symptoms (n = 3, 3.5%); an underrepresentation of people with symptoms limited to the ocular muscles. Ocular-only MG is estimated to occur in approximately 17% of MG cases and around half will then progress to generalised symptoms (57). Despite symptoms only affecting the ocular muscles, associated symptoms such as diplopia are common in this type of MG (3) and can impact on function in daily tasks (58), and as such we opted to include both ocular and generalised in the analysis.

Self-report measures were utilised for both physical activity and sedentary behaviour, which can lead to over-reporting by participants (47) and be inaccurate when compared with objective device-based monitoring (59). Additionally, these measures were not specific to MG as no such MG specific measures of physical activity or sedentary behaviour are currently available. Despite limitations in the use of self-report measures, a strength of this type of measure is the ease of distribution which facilitated a larger

sample size for our study (n = 85) than what has been used in prior related research (n = 27) (25). Given the low incidence of MG and subsequent recruitment difficulties, using an electronic self-report survey enabled recruitment across a larger geographical area. This method, however, limited our capacity to classify disease severity amongst participants given the lack of face to face clinical assessment and absence of a single universally acceptable classification of severity in this population (60). Prior research, although limited, suggests there is no relationship between disease severity and physical activity in this population (25), however further high-quality evidence is required to investigate this further. Finally, the R^2 values of our models was generally low, indicating that there may be a number of other variables contributing to these relationships.

Conclusions

Although physical activity guidelines were met by most participants with MG in our study, a large proportion of participants also reported high levels of sedentary behaviour. Our findings provide preliminary evidence that physical activity and sedentary behaviour may be potential intervention targets given our findings of associations between higher physical activity levels and lower sedentary time and less fatigue, higher quality of life, lower walking limitation and higher balance confidence. There is a need for high quality, large sample size studies in individuals with MG that can further investigate and confirm the direction of the relationship between these variables.

Abbreviations

ABC Scale
Activities-Balance Confidence Scale
MET
Metabolic equivalent of task
MFIS
Modified-Fatigue Impact Scale
Mg-QoL-15
Myasthenia Gravis Quality of Life 15-Item
MG
myasthenia gravis
PA
physical activity
PAST
Past-day Recall of Sedentary Time
SB
sedentary behaviour

Declarations

Ethics approval and consent to participate

Ethical approval was provided by The University of Queensland Human Research Ethics Committee (reference number HREC/2019/000/774).

Consent for publication

Not applicable

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors contributions

All authors contributed to the study conception and design. Material preparation and data collection was performed by Tahlia Alsop, and analysis were performed by all authors. The first draft of the manuscript was written by Tahlia Alsop and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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