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Effect of COVID-19 home confinement on sleep monitorization and cardiac autonomic function in people with multiple sclerosis: A prospective cohort study☆,☆☆☆,☆☆

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ABSTRACT

Background: Low sleep quality, cardiac autonomic dysfunction and poor quality of life are some of the most prevalent symptoms in people with Multiple Sclerosis (MS). In addition to the progression of the disease, these symptoms are aggravated by physical inactivity. Therefore, home confinement due to COVID-19 pandemic restrictions could further worsen these symptoms. This study aims to analyze the effect of home confinement on objective and subjective sleep quality, cardiac autonomic control based on heart rate variability (HRV), and health-related quality of life in people with MS.

Methods: Actigraphic and subjective sleep quality (Karolinska Sleep Diary, KSD), HRV (Polar-H7), and quality of life (Multiple Sclerosis Quality of Life-54) were measured before and after 2 months of home confinement in 17 people with MS (7:10 men/women; age: 43.41±10.88 years; body mass index: 24.87±3.31 kg/m^2; Expanded Disability Status Scale: 2.85±1.34 a.u.).

Results: Actigraphic sleep quality (sleep efficiency: ES=1.27, $p = 0.01$, sleep time: ES=0.81, $p = 0.01$) and subjective sleep quality (sleep quality: ES=-0.34, $p = 0.05$), sleep comfort: ES=0.60; $p = 0.03$, ease of falling asleep: ES=0.70; $p = 0.01$, ease of waking up: ES=0.87, $p<0.01$, and having enough sleep: ES=0.87, $p<0.01$) significantly decreased after home confinement. No differences were observed in HRV or quality of life variables ($p \geq 0.13$).

Conclusions: Home confinement has worsened the sleep quality, but not in cardiac autonomic control or quality of life, in people with MS. These data highlight the importance of implementing home physical training programs in this population when situations similar to home confinement occur, thus minimizing the negative effects of physical inactivity and their associated comorbidities.

Introduction

Multiple sclerosis (MS) is a progressive neurological disease with an unknown etiology [1]. Many people with MS have lower quality of life compared to people without pathologies [2], largely as a consequence of poor functional capacity [3,4], high symptomatic fatigue [5] or augmented muscular weakness [4]. In addition to these symptoms, people with MS experience other problems, such as an autonomic dysfunction [6]. This alteration in the sympathetic nervous system (SNS) and parasympathetic nervous system (PNS), both of which form the autonomic nervous system (ANS), affect cardiovascular function [7]. This may be explained by lesions in the areas of the brain related to autonomic control [8], as well as sedentarism, a common behavior in people with MS [9]. A dysfunction in cardiac autonomic control leads to

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an increased risk of sudden death, arrhythmia, left ventricular hypertrophy [10], among others. In order to measure the function of cardiac autonomic control, heart rate variability (HRV) has been used in recent years and is a valid tool to observe modifications in ANS activity [11].

Previous studies have determined that autonomic dysfunction can lead to sleep problems in people with MS [12]. The prevalence of sleep problems is very high in people with MS, reaching almost 62% of the MS population [13–15]. Also, other studies have suggested that low levels of physical activity found in people with MS may explain poor sleep quality [16], and this has been supported by research that has shown an improvement in sleep quality after physical training programs in people with MS [17,18]. Furthermore, sleep quality has been associated with symptomatic fatigue and quality of life in people with MS [19]. This relationship highlights the importance of improving sleep quality in this population, with the aim of attenuating some of the common symptoms of the disease.

Although sleep and exercise are mediated by different physiological mechanisms, there is a large body of evidence that demonstrates that physical exercise directly influences sleep [20]. Atkinson and Davenne [21] have shown that physical exercise improves sleep because of an increase in serotonin levels post-exercise, the thermoregulatory effect of exercise, which could stimulate somnogenic brain areas to initiate sleep, and the reduction in anxiety linked to exercise. Therefore, physical inactivity could further exacerbate sleep-related problems and associated comorbidities, such as sarcopenia [22] or obesity [23]. It has been shown that better sleep quality is related to a decrease in the low frequency (LF) component, a marker of sympathetic modulation, as well as the predominance in the control of the vagal system. Conversely, poor sleep quality is associated with the predominance of the sympathetic system [24,25].

The global emergency caused by COVID-19, a respiratory disease generated by the SARS-CoV-2 [26], has led to an extraordinary situation in which a large part of the world's population has been confined to their homes in an effort to reduce social transmission. In countries, such as Spain, home confinement began in March 2020 and lasted for more than 2 months. This forced, lifestyle change significantly decreased physical activity levels in the general population [27], regardless of age or health status. As a result, the sedentary lifestyle could lead to a dysfunction in the cardiovascular system [28] and, in turn, affect other variables, such as cardiac autonomic control [29] and sleep quality [30]. People with MS are increasingly immersed in physical training programmes, as it is known to be effective in improving sleep and cardiac autonomic control in healthy population and people with pathologies [17,31]. Although there are no specific studies on the impact of covid confinement in this population, it is assumed that this forced confinement has drastically changed their lifestyles (i.e., decreased minutes of daily active living and social contact), like the rest of the adult population without MS [32] It is plausible that sedentarism derived from COVID-19-related home confinement could have worsened two of the common symptoms MS: cardiac autonomic dysfunction and poor sleep quality.

To our knowledge, no studies have analyzed the impact of home confinement due to COVID-19 restrictions on cardiac autonomic control, sleep quality and quality of life in MS people. Therefore, the objective of the study was to analyze the effects of home confinement on objective and subjective sleep quality in people with MS. Secondly, the effect of home confinement was examined on cardiac autonomic control based on HRV and health-related quality of life. Our hypothesis was that both cardiac autonomic control, sleep quality, and quality of life would be impaired after the home confinement period in this population.

Methods

Study design

A prospective, observational cohort study was conducted to analyze the effect of COVID-19 home confinement on sleep monitorization and cardiac autonomic function in people with MS. A follow-up was conducted on one cohort. Data collection was carried out immediately before and after home confinement. Pre-confinement measurements were taken during the week of March 1–5, 2020. Post-confinement measurements were conducted in the week of June 8–12, 2020. This study was approved by the Catholic's University of Murcia's Science Ethics Committee according to the Declaration of Helsinki [33]. We want to acknowledge that the baseline measurements were originally meant for an experimental study, which was suspended because of the declaration of the COVID-19 pandemic. Baseline measures were completed just before the National State of Alarm, forcing the whole population to home confinement. When home confinement restrictions ended, it was important for us to follow-up on these study participants.

Setting

The measurements were carried out at the UCAM Sports Center, Murcia, Spain. Participants visited the laboratory twice. In the first visit, they were explained the protocol and were given an accelerometer and asked to fill out questionnaires. After 24 h, participants returned to the laboratory to turn in the completed questionnaires and the accelerometer to the researchers. Actigraphic sleep quality, subjective sleep quality, nocturnal cardiac autonomic activity and quality of life measurements were measured at pre- and post-home confinement. No monitoring was carried out during the weeks of confinement.

Participants

Participants were recruited from the local MS Association. Eighteen people with MS were recruited to participate in this study. A board-certified neurologist had diagnosed these participants with relapsing-remitting MS or primary progressive MS, according to the McDonald criteria [34]. Participants were included if they were in the stable phase of the disease and were capable of walking independently for >10 m. People with MS were excluded if they had presented with one of the following criteria: 1) Expanded Disability Status Scale of <1 or >6, 2) a relapse in the prior 12 months, 3) on corticosteroid treatment in the preceding 2 months, 4) involved in a training program in the prior 4 months and 5) involved in a home-exercise program during home confinement. Before staring the study, all participants read and signed an informed consent document.

Variables

Primary outcome

Actigraphic sleep quality and subjective sleep quality. The actigraphic and subjective sleep quality were measured on the same two nights (1-night pre- and 1-night post-home confinement). The actigraphic sleep quality was recorded using an Actiwatch wGT3X-BT activity monitoring system (Cambridge Neurotechnology, Cambridge, UK), which contained a piezo-electric accelerometer, and was worn on the non-dominant wrist. Eighty counts per epoch was used for the low threshold of actigraphic sensitivity. Actiwatch sleep analysis software was used to analyze the recorded data from nocturnal rest onset (bedtime) until the onset of daytime activity (wake time), where sleep efficiency (%), percentage of time spent asleep, time in bed (min), actual sleep time (min), actual wake time (min), the number of awakenings and average time of each awakening (min) were obtained. Participants also completed the Karolinska Sleep Diary (KSD) [35] to assess subjective sleep quality in the morning soon after waking up. Karolinska Sleep Diary measured the following parameters: sleep quality (1= very poor; 5= very good), sleep comfort (1= very restless; 5= very calm/relax), ease of falling asleep (1= very difficult; 5= very easy), awakening (1= woke up too early; 3= woke up late), ease of waking up (1= very difficult; 5= very easy),

feeling of rest (1= no rest at all; 3= completely rested) and did you have enough sleep (1= no, definitely very poor; 5= Yes, definitely enough).

Secondary outcomes

Heart rate variability analysis. The HRV analysis was performed with a heart rate sensor Polar H7 (Kempele, Finland) to assess the R-R intervals during sleep at pre- and post-home confinement. The analysis of HRV variables was carried out with the Kubios HRV software version 3.0 (Kuopio, Finland). Additionally, if necessary, an artifact correction was performed with this software by applying very low, low or medium threshold filters [36]. Mean R-R interval time (RR; ms), the standard deviation of consecutive R-R intervals (SDNN), the root mean square of successive differences of consecutive R-R intervals (RMSSD) and the percentage of consecutive intervals that differed by more than 50 ms (pNN50) were measured. Furthermore, the Fast Fourier Transform was applied to convert the R-R data into components of the frequency domain as integrals of the respective power spectral density curve. The frequency-domain components were the high-frequency power (HF; 0.15–1.0 Hz), the low-frequency power (LF; 0.04–0.15 Hz), as well as the ratio LF/HF. Additionally, HF was expressed as a natural logarithm-transformed value (HFln). Finally, Poincare plot variables, such as the standard deviation of instantaneous beat-to-beat RR interval variability (SD1) and the standard deviation of continuous long-term R-R interval variability (SD2), were calculated aiming to calculate the stress score (SS; equation 1000 × 1/SD2) and the sympathetic/parasympathetic ratio (S/PS; equation SS/SD1).

Multiple sclerosis quality of life-54. Participants were asked to complete the validated and reliable Spanish version of Multiple Sclerosis Quality of Life-54 (MSQOL-54) questionnaire [37]. MSQOL-54 is a structured, self-report questionnaire that contains 14 sub-scales: physical function, role limitations-physical, role limitations-emotional, pain, emotional well-being, energy, health perceptions, social function, cognitive function, health distress, sexual function, satisfaction with sexual function, change in health and overall quality of life. From the MSQOL-54 questionnaire, 2 summary scores can be derived, which are the physical health composite summary (i.e., the sum of physical function, health perceptions, energy, role limitation-physical, pain, sexual function, social function, and health distress) and the mental health composite summary (i.e., the sum of health distress, overall quality of life, emotional well-being, role limitation-emotional, and cognitive function). Higher scores in each subscale or summary score corresponded to better quality of life.

Bias

Self-selection bias is present in this study. However, as this is a prospective cohort study, self-selection bias cannot be avoided. In addition, confounding bias may have occurred in this study, as the variables analysed in this study may be influenced by other uncontrolled factors (e.g., diet, social contacts). However, these confounding factors are inherent to the exceptional state of home confinement and, therefore, as a whole are the subject of this research.

Statistical methods

Data collection, treatment, and analysis were performed using the SPSS for Windows statistical package (version 20.0; SPSS, Inc., Chicago, IL, USA). Descriptive statistics (mean and SD) were calculated. Before using parametric tests, the assumption of normality was confirmed with the Shapiro-Wilks test. Student's *t*-test for pair samples or the nonparametric equivalent (Wilcoxon test) was used to test if significant changes occurred in differences between pre- and post-home confinement. A level of $p \leq 0.05$ was set to indicate statistical significance. The effect size (ES) was calculated using Cohen's guidelines [38]. Threshold values for ES were ≥0.1 (small), ≥0.3 (moderate), ≥1.2 (large), and ≥2.0 (very large) [39].

Results

At the beginning, 25 participants with MS were consulted to participate in the study. Of these 25 participants, 18 met the inclusion criteria and participated in the study. Finally, 17 people with MS completed the study, since one participant dropped out due to schedule conflicts. Table 1 shows the participant characteristics.

There were no missing data in any of the variables analysed of the 17 study participants. The follow-up visit was conducted at 10 weeks, which was duration of the State of Alarm Decreed of home confinement in Spain (i.e., mid-March to the end of May).

Effects of home confinement on sleep quality

Actigraphic sleep quality significantly decreased with large and moderate effects on sleep efficiency (ES= 1.27, $p = 0.01$) and sleep time (ES= 0.81, $p = 0.01$), respectively, after home confinement (Table 2).

In addition, significant decreases with moderate effects were found on subjective sleep quality (ES= 0.54, $p = 0.05$), sleep comfort (ES= 0.60; $p = 0.03$), ease of falling asleep (ES= 0.79, $p = 0.01$), ease of waking up (ES= 0.87, $p<0.01$), and having enough sleep (ES= 0.87, $p<001$; Table 3).

Effects of home confinement on cardiac autonomic control

Based on the analyzed HRV variables (Table 4), RR showed a tendency to increase with a moderate effect after home confinement (ES= −0.39, $p = 0.14$), indicating a lower heart rate. In addition, there was a trend towards a decrease with a moderate effect in S/PS (ES= 0.38, $p = 0.15$), suggesting a withdrawal of sympathetic activity.

Effect of home confinement on quality of life

There was a trend towards a decrease with moderate effect (ES= 0.39; $p = 0.13$) in the cognitive function subscale. No was no change in the other subscales or summary scores of the MSQOL-54

Discussion

The present study shows that home confinement caused by the restrictions due to the COVID-19 pandemic led to decreased sleep quality in people with MS. However, contrary to what was hypothesized, cardiac autonomic control and quality of life were not affected after this lockdown period.

Table 1
Participant characteristics ($n = 17$).

Characteristics	Mean ± SD
Age (yrs)	43.50 ± 11.23
Sex (men:women)	7:10
EDSS (a.u.)	2.87 ± 1.38
Type of MS (RRMS:SPMS)	15:2
Weight (kg)	70.63 ± 12.34
Height (cm)	167.69 ± 7.18
Lean mass (kg)	51.70 ± 9.56
Fat mass (%)	27.46 ± 9.80
BMI (kg/m^2)	25.01 ± 3.36

Data are presented as mean ± SD.
BMI: Body Mass Index; EDSS: Expanded Disability Status Scale; MS: Multiple Sclerosis; RRMS: Relapsing-Remitting Multiple Sclerosis; SD: Standard Deviation; SPMS: Secondary Progressive Multiple Sclerosis.

Table 2
Pre-post effect on actigraphic sleep quality.

Actigraphic Sleep Quality	Pre(mean±SD)	Post (mean±SD)	Δ± ΔSD	t	p	Effect Size	95% CI for Cohen's d Lower	Upper
*Latency (*min*)*	9.9 ± 4.3	11.3 ± 6.5	0.16±0.42	−1.27	0.22	−0.34	−0.87	0.21
Sleep efficiency (%)	89.4 ± 6.6	84.9 ± 6.9	−0.05±0.04	4.90	0.01*	1.27	0.57	1.94
*Time in bed (*min*)*	451.2 ± 75.6	429.5 ± 75.9	−0.04±0.11	1.65	0.12	0.42	−0.11	0.95
*Actual sleep time (*min*)*	401.8 ± 67.4	364.8 ± 71.5	−0.09±0.12	3.13	0.01*	0.81	0.21	1.39
*Actual wake time (*min*)*	40.1 ± 30.9	44.5 ± 24.1	0.54±1.47	−0.95	0.36	−0.25	−0.76	0.27
Awakenings (n)	11.9 ± 8.4	14.3 ± 6.8	0.53±0.87	−1.43	0.18	−0.37	−0.89	−0.16
*Average time of each awakening (*min*)*	3.7 ± 1.8	3.3 ± 1.4	−0.03±0.32	1.30	0.21	0.33	−0.19	0.85

SD: standard deviation; n: number; CI: Confidence Interval;.
* $p \leq 0.05$ pre-post differences.

Table 3
Pre-post effect on subjective sleep quality.

KSD	Pre(Mean±SD)	Post (Mean±SD)	Δ± ΔSD	t	p	Effect Size	95% CI for Cohen's d Lower	Upper
Sleep quality	3.4 ± 0.9	2.8 ± 1.0	−0.1 ± 0.4	2.18	0.05*	0.54	0.01	1.07
Sleep comfort	3.1 ± 1.4	2.6 ± 1.2	−0.1 ± 0.2	2.41	0.03*	0.60	0.06	1.13
Ease of falling asleep	3.3 ± 1.1	2.6 ± 1.2	−0.2 ± 0.3	3.15	0.01*	0.79	0.21	1.34
Awakening	1.8 ± 0.5	1.6 ± 0.5	−0.1 ± 0.2	1.73	0.10	0.43	−0.09	0.94
Ease of waking up	3.8 ± 0.8	3.1 ± 0.8	−0.2 ± 0.2	3.47	<0.01*	0.87	0.28	1.44
Feeling of rest	2.4 ± 0.5	2.0 ± 0.7	−0.1 ± 0.3	2.09	0.05	0.52	−0.01	1.04
Did you have enough sleep?	3.3 ± 0.8	2.6 ± 0.9	−0.2 ± 0.2	3.47	<0.01*	0.87	0.28	1.43

CI: Confidence Interval; KSD: Karolinska Sleep Diary.
* $p \leq 0.05$ differences pre-post.

Table 4
Pre-post effect on sleeping heart rate variability.

Sleeping HRV	Pre(Mean±SD)	Post (Mean±SD)	Δ± ΔSD	t	p	Effect Size	95% CI for Cohen's d Lower	Upper
RR (ms)	893.0 ± 116.0	944.0 ± 118.0	0.07±0.16	−1.56	0.14	−0.39	−0.89	0.12
SDNN (ms)	56.3 ± 34.6	64.3 ± 39.1	0.30±0.82	−1.09	0.29	−0.27	−0.77	0.23
RMSSD (ms)	26.5 ± 17.8	25.3 ± 14.8	−0.01±0.20	1.01	0.32	0.25	−0.25	0.75
pNN50 (%)	7.8 ± 13.9	5.9 ± 8.3	0.48±1.44	1.19	0.25	0.30	−0.21	0.80
HFIn	5.3 ± 0.9	5.2 ± 0.79	−0.01±0.14	0.96	0.35	0.24	−0.26	0.73
LF/HF	2.6 ± 1.7	2.1 ± 1.2	0.14±1.23	1.53	0.15	0.38	−0.13	0.89
SS	18.5 ± 10.5	17.2 ± 10.3	0.02±0.41	0.57	0.57	0.14	−0.35	0.63
S/PS	1.4 ± 1.1	1.2 ± 0.9	0.05±0.46	0.91	0.38	0.23	−0.27	0.72

SD: standard deviation; CI: Confidence Interval; HFIn: Natural Logarithm of High Frequency Power; LF/HF: Low Frequency/High Frequency Ratio; pNN50: Proportion of Pairs of Successive RR Intervals that Differ by More than 50 ms; RMSSD: Root Mean Square of the Successive Differences of RR intervals; RR: Mean Heart Rate; S/PS: Sympathetic/Parasympathetic Ratio; SDNN; Standard Deviation of All Normal N—N Intervals; SS: Stress Score.
*$p \leq 0.05$ differences pre-post.

Table 5
Pre-post effect on quality of life.

MSQOL-54	Pre(Mean±SD)	Post (Mean±SD)	Δ± ΔSD	t	p	Effect Size	95% CI for Cohen's d Lower	Upper
Physical function	57.9 ± 32.7	55.0 ± 32.9	−0.09±0.28	1.16	0.26	0.28	−0.21	0.76
Role limitations-physical	54.4 ± 47.0	47.1 ± 43.2	−0.46±0.46	0.59	0.58	0.14	−0.34	0.61
Role limitations-emotional	66.7 ± 40.8	72.5 ± 39.5	0.13±0.23	−0.90	0.38	−0.22	−0.69	0.27
Pain	68.3 ± 27.2	74.0 ± 25.8	0.15±0.39	−1.18	0.25	−0.29	−0.77	0.20
Emotional well-being	44.9 ± 10.1	44.7 ± 10.9	−0.01±0.13	0.17	0.87	0.04	−0.43	0.52
Energy	45.4 ± 12.0	49.6 ± 19.6	0.11±0.45	−1.01	0.33	−0.25	−0.73	0.24
Health perceptions	37.4 ± 11.7	35.7 ± 10.4	0.01±0.27	0.62	0.54	0.15	−0.33	0.63
Social function	67.6 ± 20.4	68.6 ± 18.5	0.05±0.27	−0.42	0.68	−0.10	−0.58	0.38
Cognitive function	70.9 ± 19.8	66.8 ± 22.3	−0.06±0.18	1.59	0.13	0.39	−0.11	0.88
Health distress	67.4 ± 19.7	66.5 ± 21.3	−0.01±0.18	0.94	0.36	0.23	−0.26	0.71
Sexual function	86.3 ± 17.9	84.3 ± 16.9	0.46±1.95	0.70	0.49	0.17	−0.31	0.65
Change in health	45.6 ± 30.9	42.6 ± 26.2	0.02±0.37	−0.57	0.58	−0.14	−0.61	0.34
Satisfaction sexual	64.7 ± 39.6	67.6 ± 35.1	0.20±0.61	0.49	0.63	0.12	−0.36	0.60
Overall QOL	57.7 ± 15.5	56.2 ± 15.8	0.02±0.28	0.32	0.76	0.08	−0.40	0.55
Physical Health Composite	60.0 ± 15.4	60.1 ± 14.4	0.05±0.36	−0.02	0.99	−0.01	−0.48	0.47
Mental Health Composite	61.4 ± 12.9	61.4 ± 11.4	0.01±0.10	0.08	0.94	0.02	−0.46	0.49

CI: Confidence Interval; MSQOL-54: Multiple Sclerosis Quality of Life-54; QOL: Quality of Life.
*$p \leq 0.05$ differences pre-post.

Sleep quality

To our knowledge, this is the first study to evaluate the impact of forced home confinement on sleep quality in people with MS. Our sample showed a decrease in sleep efficiency and sleep time measured by actigraphy. In addition, significant decreases were found on subjective sleep quality, sleep comfort, ease of falling asleep, ease of waking up, and having enough sleep measured by the KSD questionnaire. Previous research has shown that low levels of physical activity worsen sleep quality in both clinical and general populations [40–42]. This association between physical activity and sleep has also been studied in people with MS, where those who showed higher levels of physical activity had fewer sleep problems [43]. In addition to the sedentary factor, people with MS have greater prevalence of sleep problems than the non-clinical population [13–15]. The pre-confinement sleep efficiency of actigraphic sleep quality in our sample are in line with those found by other authors in people with moderate disability MS [44,45]. However, the post-confinement data are below the usual levels found in the literature for this population (<85% sleep efficiency) [44,45]. Similarly, the KSD data obtained at pre-confinement agree with the values in the literature in adults with occasional sleep disorders [46], while post-confinement data were below the observed literature values in this population.

This decrease shows the great impact that people with MS have experienced on sleep quality produced by almost absolute sedentary lifestyle. Despite the fact that people with MS usually present low levels of physical activity [47], home confinement has forced them to further decrease their levels of daily activity, as different authors have shown recently in other populations [27,48]. The association between sleep quality and physical exercise has been widely studied and is in line with our results [49].

The data obtained through the actigraphy and those obtained through the KSD questionnaire are in the same line, since both show decreases in the main sleep quality variables after home confinement. Although both tools (actigraphy [50] and KSD [51]) have been validated for the measurement of sleep quality, it is suggested that actigraphy underestimates sleep duration and sleep latency and overestimates awakenings and WASO in relation to questionnaires [52,53]. This may be one reason why the results of both questionnaires differ in some variables both at pre- and post-testing.

Sleep is regulated by different neurochemical and biochemical factors, such as pro-inflammatory cytokines, prostaglandins, melatonin, serotonin, cortisol or growth hormone-releasing hormone [54,55]. The levels of these factors regulate sleep-related processes. Al-Sharman et al. [56] concluded that physical exercise impacts the concentrations of these biomarkers, and that changes in their levels result in improvements in sleep quality in people with MS. Thus, forced physical inactivity in the home may have modified the levels of these biomarkers, producing greater sleep problems. In addition, the thermoregulatory effect of exercise and the reduction of parameters such as spasticity or anxiety, both having acute and chronic effects, after physical exercise may explain the diminished quality of sleep found in our sample after home confinement [21].

Improving sleep quality, especially in populations such as MS, should be a major goal for physical therapists and physical-sport educators because of the close relationship between sleep and other comorbidities. Problems with sleep have been associated with abrupt loss of muscle mass (sarcopenia) [22], high fatigue [57], pain [58], or increased psychological problems. Although more research is needed, the relationship between sleep and different processes regulated by the central nervous system, such as pain or fatigue, suggests that there is an important link between these two mechanisms.

It has been widely studied that physical exercise is, along with pharmacological treatment, one of the most used strategies to improve sleep quality in populations with neurological disorders, such as Parkinson [59] and MS [60]. Therefore, if pandemic-induced home confinement were to recur, general strategies would need to be implemented to undertake physical home-training programs for this populations to mitigate the problems associated with sedentary living, as well as to benefit from the physiological and psychological effects of exercise [47,61–63].

Cardiac autonomic control

The HRV values were not modified after forced home confinement in our sample. One study showed that people with MS demonstrated lower HRV compared to a healthy population [64]. The HRV data were also lower in our study compared to the values published in the aforementioned study. A previous study reported that subjects suffered significant reductions in HRV in the general population after 8-weeks confinement in France [29], which contrasts with our lack of change in HRV after 10-weeks home confinement. These differences may be explained by the fact that healthy individuals have higher HRV values to begin with and may have greater possibilities to present with greater cardiac autonomic modulation due to the confinement stress. Since our MS patients showed HRV values in the lower percentiles of normal values [65], this may explain why these values could not decrease further in such a short period of time, even under environmental stressors such as confinement. There are no previous studies that analyzed the effect of home confinement on autonomic modulation in MS patients. However, a recent study, in accordance with our results, followed-up on MS patients during 3 months and did not observe changes in HRV [66]. Thus, it seems necessary longer periods to observe significant changes of HRV in patients with MS.

Therefore, the absence of change in HRV after confinement can be explained by the already existing dysfunction in cardiac autonomic control.

On the other hand, it has been demonstrated that, under normal conditions of daily life, no decrease in RMSSD is observed in periods of 12 to 16 weeks in other pathologies [67,68]. However, RMSSD has been shown to significantly decrease during detraining, that is, if there were previous adaptations achieved after performing physical exercise protocols in people with pathologies. Thus, this could partially explain the reduction of HRV in other studies [64] since it was carried out in people who followed systematic training protocols and suffered from detraining during home confinement. Since our participants did not perform any prior physical conditioning, it is likely that vagal modulation was not lowered by the absence of the detraining process. Likewise, it seems that the stressor of home confinement on autonomic modulation seems to have affected our population with MS to a lesser extent compared to the active population [29].

Quality of life

Quality of life, as measured by the MSQOL-54 questionnaire, did not change significantly in any of the subscales after home confinement in our participants with MS. Although the change was small and not significant, all the variables showed the same trend. The lack of change may be because pre-test values were already low level, so getting substantially worse was probably more difficult to attain. This finding contrasts with other studies that have shown decreases in health-related quality of life after periods of physical inactivity, such as that produced during home confinement related to the COVID-19 pandemic, in non-pathological [32] and clinical populations [69,70]. But, in line with our results, other research did not observe changes in the quality of life after COVID-19 home confinement in populations with neurological disease, such as Alzheimer's [71]. In people with MS, it has been established that quality of life is influenced by a network of variables, of which pain, symptomatic fatigue and sleep quality play an important role [15,72]. In this study, we have found decreases in sleep quality but not in quality of life after home confinement. The absence of change in quality of life after home confinement can be due to a couple of reasons.

First, the scores obtained in the subscales of the questionnaire (i.e. physical function or overall quality of life) were low at pre-home confinement with respect to the one found by other studies in MS populations with moderate disability [73]. Our sample had moderate disability and did not perform physical exercise prior to participation in this study. Thus, the consequences of physical inactivity caused by home confinement on the physical and mental component may have been less accentuated than in a population with a lower level of disability (EDSS<3) that has experienced interruptions in their training programs or physical activity due to home confinement. Second, some of the components assessed in the MSQOL-54, such as sexual function or cognitive function, need longer periods of time to see significant changes in their function. Therefore, studies that have analyzed changes in variables, such as cognitive function, after periods of inactivity [74] or physical training programs [62] have used longer periods of time (>24 weeks).

Limitations

The present study has some limitations. One limitation is the heterogeneity of the sample, since it was composed of participants with different sex (men and women), different subtypes of the disease (relapse-remitting MS and secondary progressive MS) and different disability status (EDSS range: 1–6). Another limitation is that this study only performed measurements at two time points (pre- and post-home confinement). More intermediate measurements would have been interesting to examine the time course of the effects of home confinement. However, due to legal restrictions on mobility during confinement, it was not possible to perform intermediate HRV measurements. Another limitation is that we did not have more socio-demographic information on the participants that would have helped us better interpret and compare our results with those in the literature. Although the sample MS population is within the common characteristics of this group, the results of this study should be taken with caution because the sample is small and heterogeneous, which may affect the external validity of the study.

Conclusions

In our sample of people with MS, a worsening in sleep quality variables was observed. These results show the great impact of home confinement and sedentary lifestyle on sleep-related problems in this population. Furthermore, and contrary to the hypothesis, cardiac autonomic control and quality of life were not modified. Even so, these results highlight the need to prescribe home training programs for people with MS if a similar situation were to occur again in order to decrease the consequences of physical inactivity and, therefore, the possible comorbidities associated with sedentary behaviors.

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Nothing to report.

Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

References

[1] J. Kamińska, O.M. Koper, K. Piechal, H. Kemona, Multiple sclerosis - etiology and diagnostic potential, Postepy. Hig. Med. Dosw. 71 (0) (2017) 551–563.
[2] N. Murphy, C. Confavreux, J. Haas, et al., Quality of life in multiple sclerosis in France, Germany, and the United Kingdom, J. Neurol. Neurosurg. Psychiatry 65 (4) (1998) 460–466.
[3] A. Ahmadi, M. Nikbakh, A.A. Arastoo, A.H. Habibi, The effects of a yoga intervention on balance, speed and endurance of walking, fatigue and quality of life in people with multiple sclerosis, J. Hum. Kinet. 23 (2010) 71–78.
[4] P. Aristotelous, M. Stefanakis, M. Pantzaris, C. Pattichis, G.M. Hadjigeorgiou, C. D. Giannaki, Associations between functional capacity, isokinetic leg strength, sleep quality and cognitive function in multiple sclerosis patients: a cross-sectional study, Postgrad. Med. 131 (7) (2019) 453–460.
[5] M.B. Eizaguirre, N. Ciufia, M.S. Roman, et al., Perceived fatigue in multiple sclerosis: the importance of highlighting its impact on quality of life, social network and cognition, Clin. Neurol. Neurosurg. 199 (2020), 106265.
[6] O. Findling, L. Hauer, T. Pezawas, P.S. Rommer, W. Struhal, J. Sellner, Cardiac Autonomic dysfunction in multiple sclerosis: a systematic review of current knowledge and impact of immunotherapies, J. Clin. Med. 9 (2) (2020) 335.
[7] T.B. Kaplan, A.L. Berkowitz, M.A. Samuels, Cardiovascular dysfunction in multiple sclerosis, Neurologist 10 (4) (2015) 364–370.
[8] C. Valencia-Sanchez, B.P. Goodman, J.L. Carter, D.M. Wingerchuk, The spectrum of acute cardiopulmonary events associated with multiple sclerosis exacerbations, Mult. Scler. J. 25 (6) (2019) 758–765.
[9] I. Wens, U. Dalgas, E. Stenager, B.O. Eijnde, Risk factors related to cardiovascular diseases and the metabolic syndrome in multiple sclerosis - a systematic review, Mult. Scler. J. 19 (12) (2013) 1556–1564.
[10] M.J. Shen, D.P. Zipes, Role of the autonomic nervous system in modulating cardiac arrhythmias, Circ. Res. 114 (6) (2014) 1004–1021.
[11] B.L. Thomas, N. Claassen, P. Becker, M. Viljoen, Validity of commonly used heart rate variability markers of autonomic nervous system function, Neuropsychobiology 78 (1) (2019) 14–26.
[12] L. Ferini-Strambi, M. Rovaris, A. Oldani, et al., Cardiac autonomic function during sleep and wakefulness in multiple sclerosis, J. Neurol. 242 (10) (1995) 639–643.
[13] M. Vitkova, Z. Gdovinova, J. Rosenberger, et al., Factors associated with poor sleep quality in patients with multiple sclerosis differ by disease duration, Disabil. Health J. 7 (4) (2014) 466–471.
[14] M. Vitkova, J. Rosenberger, Z. Gdovinova, et al., Poor sleep quality in patients with multiple sclerosis: gender differences, Brain Behav. 6 (11) (2016) e00553.
[15] I.S. Lobentanz, S. Asenbaum, K. Vass, et al., Factors influencing quality of life in multiple sclerosis patients: disability, depressive mood, fatigue and sleep quality, Acta Neurol. Scand. 110 (1) (2004) 6–13.
[16] D.A. Trojan, D. Arnold, J.P. Collet, et al., Fatigue in multiple sclerosis: association with disease-related, behavioural and psychosocial factors, Mult. Scler. 13 (8) (2007) 985–995.
[17] D.S. Bahmani, N. Razazian, V. Farnia, M. Alikhani, F. Tatari, S. Brand, Compared to an active control condition, in persons with multiple sclerosis two different types of exercise training improved sleep and depression, but not fatigue, paresthesia, and intolerance of uncertainty, Mult. Scler. Relat. Disord. 36 (2019), 101356.
[18] C.F. Siengsukon, M. Aldughmi, M. Kahya, et al., Randomized controlled trial of exercise interventions to improve sleep quality and daytime sleepiness in individuals with multiple sclerosis: a pilot study, Mult. Scler. J. Exp. Transl. Clin 2 (2016), 2055217316680639.
[19] S. Kotterba, T. Neusser, C. Norenberg, et al., Sleep quality, daytime sleepiness, fatigue, and quality of life in patients with multiple sclerosis treated with interferon beta-1b: results from a prospective observational cohort study, BMC Neurol. 18 (1) (2018) 123.
[20] M. Banno, Y. Harada, M. Taniguchi, et al., Exercise can improve sleep quality: a systematic review and meta-analysis, PeerJ 6 (2018) e5172.
[21] G. Atkinson, D. Davenne, Relationships between sleep, physical activity and human health, Physiol. Behav. 90 (2–3) (2007) 229–235.
[22] J.Á. Rubio-Arias, R. Rodríguez-Fernández, L. Andreu, L.M. Martínez-Aranda, A. Martínez-Rodriguez, D.J. Ramos-Campo, Effect of sleep quality on the prevalence of sarcopenia in older adults: a systematic review with meta-analysis, J. Clin. Med. 8 (12) (2019) 2156.
[23] W.S. Chan, M.P. Levsen, C.S. McCrae, A meta-analysis of associations between obesity and insomnia diagnosis and symptoms, Sleep Med. Rev. 40 (2018) 170–182.
[24] J.M. Legramante, M.G. Marciani, F. Placidi, et al., Sleep-related changes in baroreflex sensitivity and cardiovascular autonomic modulation, J. Hypertens 21 (8) (2003) 1555–1561.
[25] E. Tobaldini, M. Pecis, N. Montano, Effects of acute and chronic sleep deprivation on cardiovascular regulation, Arch. Ital. Biol. 152 (2–3) (2014) 103–110.
[26] M.A. Shereen, S. Khan, A. Kazmi, N. Bashir, R. Siddique, COVID-19 infection: origin, transmission, and characteristics of human coronaviruses, J. Adv. Res. 24 (2020) 91–98.
[27] C. Zheng, W.Y. Huang, S. Sheridan, C.H.P. Sit, X.K. Chen, S.H.S. Wong, Covid-19 pandemic brings a sedentary lifestyle in young adults: a cross-sectional and longitudinal study, Int. J. Environ. Res. Public Health 17 (17) (2020) 6035.
[28] M. Narici, G. De Vito, M. Franchi, et al., Impact of sedentarism due to the COVID-19 home confinement on neuromuscular, cardiovascular and metabolic health: physiological and pathophysiological implications and recommendations for physical and nutritional countermeasures, Eur. J. Sport Sci. 12 (2020) 1–22.
[29] N. Bourdillon, S. Yazdani, L. Schmitt, G.P. Millet, Effects of COVID-19 lockdown on heart rate variability, PLoS ONE 15 (11) (2020), e0242303.

[30] J. Pinto, M. van Zeller, P. Amorim, et al., Sleep quality in times of Covid-19 pandemic, Sleep Med. 74 (2020) 81–85.
[31] B.B. Gambassi, B. Rodrigues, D.J. Feriani, et al., Effects of resistance training of moderate intensity on heart rate variability, body composition, and muscle strength in healthy elderly women, Sport Sci. Health 12 (2016) 389–395.
[32] M. Qi, P. Li, W. Moyle, B. Weeks, C. Jones, Physical activity, health-related quality of life, and stress among the chinese adult population during the COVID-19 pandemic, Int. J. Environ. Res. Public Health 17 (8) (2020) 6494.
[33] World Medical Association, Declaration of helsinki - ethical principles for medical research involving human subjects (2000), Bull. World Heal. Organ. 79 (2001) 373–374.
[34] A.J. Thompson, B.L. Banwell, F. Barkhof, W.M. Carroll, T. Coetzee, Diagnosis of multiple sclerosis: 2017 revisions of the McDonald criteria, Lancet Neurol. 17 (2018) 162–173.
[35] T. Akerstedt, K. Hume, D. Minors, J. Waterhouse, The subjective meaning of good sleep, an intraindividual approach using the Karolinska Sleep Diary, Percept. Mot. Skills 79 (1) (1994) 287–296.
[36] C. Aranda, La De, B. Cruz, J. Naranjo, Effects of different automatic filters on the analysis of heart rate variability with kubios HRV software, Arch. Med. del. Deport. 34 (4) (2017) 196–200.
[37] M. Aymerich, I. Guillamón, H. Perkal, et al., Spanish adaptation of the disease-specific questionnaire MSQOL-54 in multiple sclerosis patients, Neurologia 21 (4) (2006) 181–187.
[38] J. Cohen, Statistical Power Analysis for the Behavioral Sciences, 2013.
[39] W.G. Hopkins, S.W. Marshall, A.M. Batterham, J. Hanin, Progressive statistics for studies in sports medicine and exercise science, Med. Sci. Sports. Exerc. 41 (1) (2009) 3–13.
[40] A.D. Christie, E. Seery, J.A. Kent, Physical activity, sleep quality, and self-reported fatigue across the adult lifespan, Exp. Gerontol. 77 (2016) 7–11.
[41] X. Wu, S. Tao, Y. Zhang, S. Zhang, F. Tao, Low physical activity and high screen time can increase the risks of mental health problems and poor sleep quality among Chinese college students, PLoS ONE 10 (3) (2015), e0119607.
[42] A.D. Orsey, D.B. Wakefield, M.M. Cloutier, Physical activity (PA) and sleep among children and adolescents with cancer, Pediatr. Blood Cancer 60 (11) (2013) 1908–1913.
[43] A. Aburub, H. Khalil, A. Al-Sharman, M. Alomari, O. Khabour, The association between physical activity and sleep characteristics in people with multiple sclerosis, Mult. Scler. Relat. Disord. 12 (2017) 29–33.
[44] L. Mendozzi, F. Tronci, M. Garegnani, L. Pugnetti, Sleep disturbance and fatigue in mild relapsing remitting multiple sclerosis patients on chronic immunomodulant therapy: an actigraphic study, Mult. Scler 16 (2) (2010) 238–247.
[45] M. Aldughmi, J. Huisinga, S.G. Lynch, C.F. Siengsukon, The relationship between fatigability and sleep quality in people with multiple sclerosis, Mult. Scler. J. Exp. Transl. Clin. 2 (2016), 2055217316682774.
[46] R.P. Rosenberg, S.G. Hull, D.A. Lankford, et al., A randomized, double-blind, single-dose, placebo-controlled, multicenter, polysomnographic study of gabapentin in transient insomnia induced by sleep phase advance, J. Clin. Sleep Med. 15 (10) (2014) 1093–1100.
[47] R.W. Motl, E. McAuley, E.M. Snook, Physical activity and multiple sclerosis: a meta-analysis, Mult. Scler. 11 (4) (2005) 459–463.
[48] E. Robinson, E. Boyland, A. Chisholm, et al., Obesity, eating behavior and physical activity during COVID-19 lockdown: a study of UK adults, Appetite 156 (1) (2020), 104853.
[49] B. Holfeld, J.C. Ruthig, A longitudinal examination of sleep quality and physical activity in older adults, J. Appl. Gerontol. 33 (7) (2014) 791–807.
[50] C.M. Depner, P.C. Cheng, J.K. Devine, et al., Wearable technologies for developing sleep and circadian biomarkers: a summary of workshop discussions, Sleep 43 (2) (2020) zsz254.
[51] K. Aili, S. Åström-Paulsson, U. Stoetzer, M. Svartengren, L. Hillert, Reliability of actigraphy and subjective sleep measurements in adults: the design of sleep assessments, J. Clin. Sleep Med. 13 (1) (2017) 39–47.
[52] S. Ancoli-Israel, J.L. Martin, T. Blackwell, L. Buenaver, L. Liu, L.J. Meltzer, et al., The SBSM guide to actigraphy monitoring: clinical and research applications, Behav. Sleep. Med. 14 (1) (2015) 4–38.
[53] N.P. Walsh, S.L. Halson, C. Sargent, et al., Sleep and the athlete: narrative review and 2021 expert consensus recommendations, Br. J. Sports Med. (2020), 102025.
[54] A.A. Prather, A.L. Marsland, M. Hall, S.A. Neumann, M.F. Muldoon, S.B. Manuck, Normative variation in self-reported sleep quality and sleep debt is associated with stimulated pro-inflammatory cytokine production, Biol. Psychol. 82 (1) (2009) 12–17.
[55] N. Buscemi, B. Vandermeer, R. Pandya, et al., Melatonin for treatment of sleep disorders, Evid. Rep. Technol. Assess. 108 (2004) 1–7.
[56] A. Al-Sharman, H. Khalil, K. El-Salem, M. Aldughmi, A. Aburub, The effects of aerobic exercise on sleep quality measures and sleep-related biomarkers in individuals with Multiple Sclerosis: a pilot randomised controlled trial, NeuroRehabilitation 45 (2019) 107–115.
[57] M. Paucke, S. Kern, T. Ziemssen, Fatigue and sleep in multiple sclerosis patients: a comparison of self-report and performance-based measures, Front. Neurol. 8 (2018) 703.
[58] M. Haack, N. Simpson, N. Sethna, S. Kaur, J. Mullington, Sleep deficiency and chronic pain: potential underlying mechanisms and clinical implications, Neuropsychopharmacology 45 (1) (2020) 205–216.
[59] M.E. Cusso, K.J. Donald, T.K. Khoo, The impact of physical activity on non-motor symptoms in Parkinson's disease: a systematic review, Front. Med. 3 (2016) 35.
[60] C.F. Siengsukon, M. Aldughmi, M. Kahya, et al., Randomized controlled trial of exercise interventions to improve sleep quality and daytime sleepiness in individuals with multiple sclerosis: a pilot study, Mult. Scler. J. Exp. Transl. Clin. 2 (2016), 2055217316680639.
[61] B.M. Sandroff, R.W. Motl, M.R. Scudder, DeLuca J. Systematic, Evidence-based review of exercise, physical activity, and physical fitness effects on cognition in persons with multiple sclerosis, Neuropsychol. Rev. 26 (3) (2016) 271–294.
[62] T. Kjølhede, S. Siemonsen, D. Wenzel, et al., Can resistance training impact MRI outcomes in relapsing-remitting multiple sclerosis? Mult. Scler. J. 24 (10) (2018) 1356–1365.
[63] U. Dalgas, E. Stenager, T. Ingemann-Hansen, Multiple sclerosis and physical exercise: recommendations for the application of resistance-, endurance- and combined training, Mult. Scler. 14 (1) (2008) 35–53.
[64] O. Damla, C. Altug, K.K. Pinar, K. Alper, I.G. Dilek, A. Kadriye, Heart rate variability analysis in patients with multiple sclerosis, Mult. Scler. Relat. Disord. 24 (2018) 64–68.
[65] M.M. Corrales, B. de la Cruz Torres, A.G. Esquivel, M.A.G. Salazar, J.N Orellana, Normal values of heart rate variability at rest in a young, healthy and active Mexican population, Health 4 (2012) 377.
[66] T. Reynders, Y. Gidron, J. De Ville, M. Bjerke, I. Weets, A. Van Remoortel, et al., Relation between heart rate variability and disease course in multiple sclerosis, J. Clin. Med. 9 (2020) 3.
[67] B. Gutin, P. Barbeau, M.S. Litaker, M. Ferguson, S. Owens, Heart rate variability in obese children: relations to total body and visceral adiposity, and changes with physical training and detraining, Obes. Res. 8 (2000) 12–19.
[68] A.D. Reis, J.B.S. Garcia, R.R. Diniz, et al., Effect of exercise training and detraining in autonomic modulation and cardiorespiratory fitness in breast cancer survivors, J. Sport Med. Phys. Fit. 57 (2017) 1062–1068.
[69] N. Kumar, R. Gupta, H. Kumar, et al., Impact of home confinement during COVID-19 pandemic on Parkinson's disease, Parkinsonism. Relat. Disord. 77 (2020) 15–22.
[70] D. Guo, B. Han, Y. Lu, et al., Influence of the COVID-19 pandemic on quality of life of patients with Parkinson's disease, Park. Dis 2020 (2020) 1–7.
[71] B. Lara, A. Carnes, F. Dakterzada, I. Benitez, G. Piñol-Ripoll, Neuropsychiatric symptoms and quality of life in Spanish patients with Alzheimer's disease during the COVID-19 lockdown, Eur. J. Neurol. 27 (9) (2020) 1744–1747.
[72] P.K. Newland, R.T. Naismith, M. Ullione, The impact of pain and other symptoms on quality of life in women with relapsing-remitting multiple sclerosis, J. Neurosci. Nurs. 41 (6) (2009) 322–328.
[73] A. Romberg, A. Virtanen, R. Ruutiainen, Long-term exercise improves functional impairment but not quality of life in multiple sclerosis, J. Neurol. 252 (7) (2005) 839–845.
[74] M.C. Aichberger, M.A. Busch, F.M. Reischies, A. Ströhle, A. Heinz, M.A. Rapp, Effect of Physical Inactivity on Cognitive Performance after 2.5 Years of Follow-Up, GeroPsych (Bern) 23 (1) (2010) 7–15.