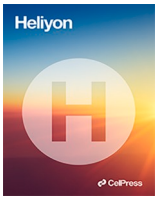
Heliyon 10 (2024) e33832

Contents lists available at ScienceDirect

Heliyon

journal homepage: www.cell.com/heliyon



Research article

Sleep duration and leisure activities are involved in regulating the association of depressive symptoms, muscle strength, physical function and mild cognitive impairment

Linfeng Chen [a,1], Dan Li [b,1], Ke Tang [b], Zhong Li [b,c,d,**], Xiaoyun Huang [a,*]

[a] Department of Neurology, Songshan Lake Central Hospital of Dongguan City, Guangdong Medical University, Dongguan, Guangdong, People's Republic of China
[b] Department of Neurology, The Sixth Affiliated Hospital, Sun Yat-sen University, Guangzhou, GuangDong, People's Republic of China
[c] Shenzhen Research Institute of Sun Yat-Sen University, Shenzhen, Guangdong, People's Republic of China
[d] Guangdong Provincial Key Laboratory of Brain Function and Disease, Guangzhou, GuangDong, People's Republic of China

ARTICLE INFO

Keywords:
Sleep duration
Leisure activity
Depressive symptom
Sarcopenia
MCI

ABSTRACT

Background: In order to lessen the burden of Alzheimer's disease (AD), timely and efficient management and intervention methods for mild cognitive impairment (MCI) are crucial. MCI is seen as a transitional stage between normal aging and dementia. Although sarcopenia is an important risk factor for MCI, it is unclear what factors mediates and regulates the brain-muscle communication. Our objective was to investigate the indirect moderating effects of sleep duration and leisure activity on depressive symptoms, sarcopenia and MCI.

Method: Panel data from the 2015 China Health and Retirement Longitudinal Study (CHARLS) database was used in this investigation. we used Bootstrap sampling to determine the relationship between sleep duration, leisure activity, depressive symptoms, sarcopenia, and MCI in mediation and indirect moderation models. The outcome measurements were odds ratio (OR) and confidence interval (CI).

Result: After adjusting for confounding variables, we discovered that sarcopenia and its traits, such as handgrip strength, gait speed, standing test, and muscle mass, were significantly correlated with MCI. Second, the results implied that depressive symptoms played a role in modulating the link between physical function, muscle strength, and MCI. This moderating effect was impacted by short sleep duration and moderate to high levels of leisure activities.

Conclusion: We discovered that MCI was highly correlated not only with physical function and muscle strength but also with depressed symptoms, which acted as a partially mediating factor in this connection. Handgrip strength, gait speed, and standing test mediated the correction of MCI caused by depression symptoms. Importantly, leisure activities and sleep duration had indirect moderating effects on the above associations, and future management policies should take these factors into account.

* Corresponding author. Department of Neurology, Songshan Lake Central Hospital of Dongguan City, the Third People's Hospital of Dongguan City, Dongguan, Guangdong, People's Republic of China.
** Corresponding author. Department of Neurology, The Sixth Affiliated Hospital, Sun Yat-sen University, Guangzhou, GuangDong, People's Republic of China.
E-mail addresses: lzhong@mail.sysu.edu.cn (Z. Li), hxydg21@163.com (Xiaoyun Huang).
[1] Linfeng Chen & Dan Li are co-first authors.

https://doi.org/10.1016/j.heliyon.2024.e33832
Received 22 February 2024; Received in revised form 11 June 2024; Accepted 27 June 2024
Available online 27 June 2024

1. Introduction

Patients with Alzheimer's disease (AD) usually show memory and cognitive impairment in the early stages, with symptoms worsening over time and eventually loss of self-care and executive function [1]. According to research statistics, the number of AD patients worldwide will reach 150 million by 2050 [2], making early diagnosis and intervention of AD crucial. Mild cognitive impairment (MCI) is considered the symptomatic pre-stage of AD [3], and people with MCI typically exhibit impairment in one or more cognitive domains such as memory, attention, executive functioning, and numeracy, but the ability to perform daily activities is unaffected [4]. Meta-analyses have shown that the global prevalence of MCI among community-dwelling individuals over the age of 50 is more than 15% [5], and that If the risk factors for MCI are not intervened in, then the demographic pressure for dementia will increase significantly in the future [6].

Abbreviations

NC	normal cognitive
MCI	mild cognitive impairment
BMI	Body mass index
CESD-10	Center for Epidemiologic Studies Depression Scale-10
bl_wbc	White Blood Count
bl_crp	C-reactive protein count
FTSST	Five Times Sit to Stand Test
HGS	hand handgrip strength
GS	gait speed
ASMI	appendicular skeletal muscle mass index

The contribution of sarcopenia in MCI has gradually become a hot topic of research in recent years [7–10]. It is a systemic skeletal disorder associated with aging that can manifest as a decline in muscle mass, strength and physical function [11]. Studies have shown that in the early stages of memory loss, people with MCI experience sarcopenia-related manifestations such as poor balance, gait and grip strength [12], which in turn affects activity frequency and increases the risk of falls [13]. At the same time sarcopenia independently increases the risk of MCI, which may be related to chronic inflammation, oxidative stress and low levels of myokine [8–10]. However, so far we do not know the direct signaling molecular mechanisms by which muscles communicate with the brain. In addition, studies have shown that 61.4% of MCI patients exhibit at least one neuropsychiatric symptom, with depression (26.1%) and sleep disturbances (23.6%) being the most common [14], both of which are disease predictors of MCI as well as risk factors for accelerated progression of MCI to AD [15,16]. And both neuropsychiatric symptoms are strongly associated with sarcopenia [17,18]. The homeostatic buffering mechanisms of oxidation and inflammation are dysregulated in depressed individuals [19], and it is possible that it is a mediator in exacerbating the cognitive impairment associated with sarcopenia, but the interrelationships among sarcopenia, depression, and MCI have not yet been elaborated, and searching for the moderating factors may be beneficial to the early diagnosis and intervention of MCI [20].

Some studies have found that sarcopenia is positively associated with poorer physical activity and sleep quality [21], and that improved exercise and sleep reduces age-related oxidative damage and chronic inflammation, increases autophagy, and improves mitochondrial function, myofactor profiles, and insulin sensitivity [22–24]. Also the management of activity and sleep duration has been recognized as an important factor in improving cognitive performance in older adults [25]. However the exact role of sleep and activity in modulating depressive symptoms, sarcopenia, and the link to MCI is unknown.

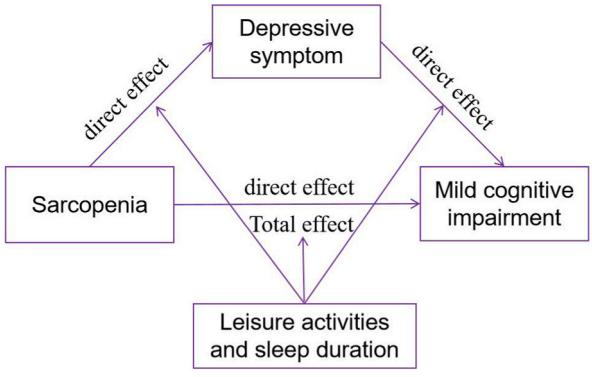


Fig. 1. Hypothetical model.

Therefore, we hypothesize that depressive symptoms mediate the association between sarcopenia and MCI, while sleep duration and leisure activity indirectly modulate this association. In order to realize these hypotheses, we proposed to use the panel data of the 2015 China Health and Retirement Longitudinal Study as the main research object, and sort out the interactions between various factors by building mediation models and indirect moderation models, which will help clinicians better diagnose and manage MCI patients with myasthenia gravis and depressive symptoms. (The hypothesized direct and indirect pathways are shown in Fig. 1).

2. Methods

2.1. Study population

A complete set of high-quality microdata on Chinese families and individuals 45 years of age and older was the aim of the China Health and Retirement Longitudinal Study (CHARLS) [26]. The study's objective was to examine China's problems related to population aging. Probability proportional to Size (PPS) sampling, a multi-stage sampling technique based on population size, was used in this investigation. Four waves of follow-up data had been collected by CHARLS to date, and comprehensive details regarding the CHARLS database had been released and could also be found on the CHARLS website (http://charls.pku.edu.cn/index.htm). To ensure that the data was representative, they included weighted variables. Projects had also been approved by the biomedical ethics council at Beijing University (IRB00001052-11015).

In this study, CHARLS data from 2015 was used. 20967 individuals took part in the baseline survey conducted in 2015. Our inclusion criteria were as follows: (a) age $\geq$ 50 years, gender not limited; (b) complete basic and family information; (c) complete information on health status and function; (d) complete information on physical examination and blood test; (e) complete information on cognitive function. The exclusion criteria were as follows: (a) age $<$ 50 or incomplete data; (b) diagnosed with dementia and stroke; (c) diagnosed with mental abnormality; (d) diagnosed with a tumor or disability. We finally enrolled 2431 eligible participants, and the specific subject selection process could be seen in Fig. 2.

2.2. Assessment of sarcopenia

This study proposed to assess sarcopenia using the diagnostic consensus of the 2019 Asian Working Group for Sarcopenia(AWGS) [27], with diagnostic components including muscle strength, physical performance and muscle mass. Muscle strength was measured by a grip test using WL-1000 hand dynamometer. Participants were asked to squeeze the dynamometer as hard as possible with one hand, testing each hand twice and taking the maximum value. Low grip strength was defined as $<$ 28 kg for males and $<$ 18 kg for females. The appendicular skeletal muscle mass (ASM) in Chinese was calculated based on the body measurements formulae from previous studies [28].

$$ASM = 0.193 \times \text{weight (kg)} + 0.107 \times \text{height (cm)} - 4.157 \times \text{gender} - 0.037 \times \text{age (years)} - 2.631.$$

The SecaTM213 height meter was used to measure height, and the OmronTM HN-286 scale was used to assess weight. Set the gender to 1 if it's male, and to 0 otherwise. Researches showed that the ASM calculated by this formula was in good agreement with dual-energy X-ray absorptiometry (DXA) [28,29]. As with earlier researches [30], the threshold for low muscle mass was based on a height-adjusted, sex-specific minimum of 20% (ASM/height^2); in this study group, the threshold values were $<$ 6.92 kg/m^2 for females and $<$ 8.88 kg/m^2 for males.

By timing how long it took the individual to get up from The Five Times Sit to Stand Test (FTSST), the lower extremity strength of the subject was assessed. The time it took the patient to fold his arms over his chest, stand up straight from a 42-cm-high chair, and then sit down as quickly as possible was recorded. The subject repeated this process five times, without pausing in between or pushing with his arms. The physical performance of the subjects was tested by gait speed (GS). The participant was asked to walk a flat 2.5-m course twice at their usual pace in order to record their fastest gait speed. Low physical function was described by the AWGS 2019 standards as gait speed of less than 1.0 m/s and 5 chair stand tests of less than 12 s [28].

Low muscular strength or poor physical functioning are indicators of possible sarcopenia. Low muscle mass combined with either low muscle strength or low physical function is known as sarcopenia [27].

2.3. Assessment of cognitive function

We employed the same methods as the American Health and Retirement Study (HRS) [31] to test cognitive performance. Using the phone to access several cognitive state table measures: including self-rated memory, the current season, day of the week, and date; 10 words for recall and delayed recall; and the 100-7 Calculation Series. The total score was 31 points [32]. There was no consensus on diagnostic criteria for MCI. We used age-associated cognitive decline (AACD) [33] in our study to define MCI, which was defined as being at least one standard deviation (SD) below the age norm [34]. All participants over the age of 60 were grouped every 5 years. Participants in each age group who meet AACD criteria would be classified as MCI.

2.4. Assessment of depressive symptom

In this project, depression symptoms were measured using the Center for Epidemiologic Studies Depression Scale-10 (CESD-10) scale, which was adapted from the original 20-item CESD and eliminated items that were excessively redundant. A rating of "how often you have felt this way in the past week" was requested of the respondents. Scores range from 0 to 30 points, a score of 10 or higher

indicates possible depression. The CESD-10 has been thoroughly validated for use in the general population and has shown adequate validity and reliability in the senior Chinese community [35].

2.5. Frequency of leisure activities and sleep duration

The sleep duration was measured by asking participants, "During the past month, how many hours of actual sleep did you get at night (average hours for one night)? (This may be shorter than the number of hours you spend in bed.)". The Frequency of activity was measured by asking participants, "How often in the last month [did/have][you] [do voluntary or charity work/cared for a sick or disabled adult/provided help to family, friends or neighbors/attended an educational or training course/interacted with friends/go to a sport, social or other kind of club/taken part in a community-related organization]? regularly (almost daily, almost every week), or not regularly?" On this basis, we define leisure activity as an ordered categorical variable, where "yes" represnts the presence of leisure activity and "no" represents the absence of leisure activity.

2.6. Potential covariates

Based on a number of previous studies [7,20,36], the covariates in this study consisted mainly of those variables that had an impact on the dependent variable. The following variables were covariates in this study: (1) demographics including age, sex (male or female), location of residence (rural and urban), education level (junior high school through high school, junior college and above, or elementary school or below), marriage status (married or unmarried), and body mass index (BMI); (2) lifestyle behavioral factors, such as drinking status (drinking or not) and smoking status (smoking or not); (3) variables pertaining to the state of chronic illness, such as the presence or absence of hypertension, abnormal blood glucose, dyslipidemia, cardiovascular disease, respiratory disease, rheumatism, liver disease, kidney disease, digestive disease, arthritis, and asthma; (4) Inflammatory indicators: white blood cell count (WBC) and C-reactive protein count (CRP).

2.7. Statistical analysis

SPSS version 26.0 (SPSS Inc., Chicago, Illinois, United States) and version 4.2 of Process (https://processmacro.org/download.html) were used for statistical analysis. Normally distributed measures were expressed as mean ± SD, and independent samples *t*-test was used for comparison between groups; non-normally distributed measures were expressed as median and interquartile spacing, and Mann-Whitney *U* test was used for comparison between groups; and counts were expressed as frequency and percentage, and chi-square test or Fisher exact test was used for comparison between groups. The association between MCI and sarcopenia was determined using logistic regression analysis. Bookstrap sampling method was used to test for mediating effects, which had higher statistical validity compared to other mediating effects testing techniques. When the Bootstrap 95% confidence interval did not include 0,it indicated a mediating effect. Finally, we took a closer look at the conditional mediation effect, which referred to the extent to which the mediation effect (also known as the conditional indirect effect) changed when another moderator variable, Z, took on a different value (usually categorized into low, average, and high levels). If the mediating effect was inconsistent at the three levels, it indicated a conditional mediation effect. The conditional mediation model fit index was interpreted as R-squared (R2), which took values in the range [0,1], with values closer to 1 indicating a better model fit. $P < 0.05$ represented statistical significance.

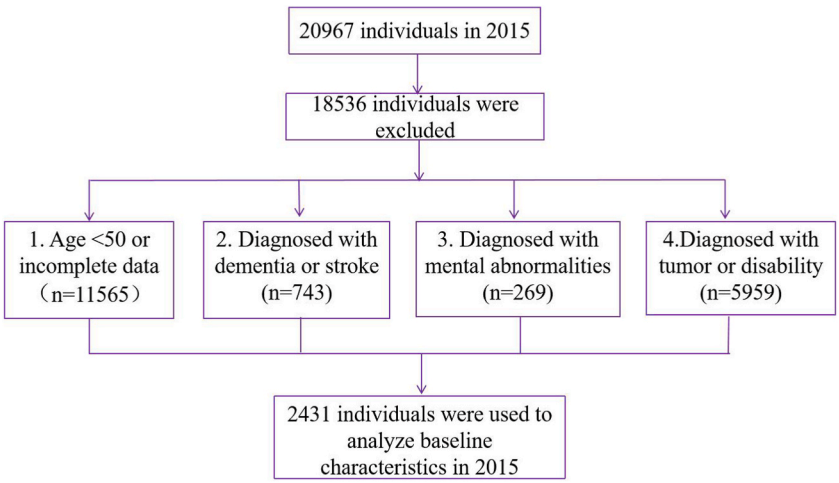


Fig. 2. Flowchart of the sample selection process.

3. Results

3.1. Baseline characteristics

As shown in Fig. 2, 2431 people were ultimately included in this study for analysis. 1331 were male, and 1100 were female. Regarding demographics, the factors that accounted for a higher percentage of participants in the MCI group were female, poor educational attainment, rural location, and unmarried status. Notably, Table 1 also showed that individuals in the MCI group had lower depression scores and body mass index, shorter sleep duration, less activities, poorer muscular strength and physical performance, and a higher prevalence of sarcopenia ($P < 0.001$) in terms of health-related parameters.

3.2. Association of MCI with sarcopenia, depressive symptoms, sleep duration and activities

After adjusting for confounding variables like age, sex, place of residence, education level, marital status, smoking, alcohol consumption, hypertension, dyslipidemia, abnormal blood sugar, heart disease, kidney disease, respiratory disease, arthritis, and asthma, the logistic regression model revealed that the odds ratios (OR) of possible sarcopenia were 0.718 [95% confidence interval (CI): 0.555–0.928, $P = 0.012$] and 1.357 (95% CI: 1.031–1.787, $P = 0.029$) for the group with sarcopenia compared to the non-muscle-

Table 1
Baseline characteristics of participants based on cognitive state.

Variables	NC(n = 1992)	MCI(n = 439)	P
Age	66.61(52–89)	67.10(57–85)	0.133
Sex			<0.001
Male	1172(58.84 %)	159(36.22 %)	
female	820(41.16 %)	280(63.78 %)	
Education			<0.001
Primary school and below	1408(70.68 %)	423(96.36 %)	
Junior and Senior High School	550(27.61 %)	15(3.42 %)	
College and above	34(1.71 %)	1(0.23 %)	
Residence			<0.001
City	481(24.15 %)	28(6.38 %)	
Village	1511(75.85 %)	411(93.62 %)	
Marital status			0.0015
married	1777(89.21 %)	368(83.83 %)	
unmarried	215(10.79 %)	71(16.17 %)	
Smoking status			<0.001
Yes	962(48.29 %)	159(36.22 %)	
No	1030(51.71 %)	280(63.78 %)	
Drinking status			<0.001
Yes	776(38.96 %)	121(27.56 %)	
No	1216(61.04 %)	318(72.44 %)	
BMI	23.55(16–38)	22.65(15–33)	<0.001
Hypertension	500(25.10 %)	101(23.01 %)	0.358
Dyslipidemia	213(10.69 %)	22(5.01 %)	<0.001
Dysglycemia	135(6.78 %)	19(4.33 %)	0.057
Chronic lung diseases	215(10.79 %)	46(10.48 %)	0.847
Liverdisease	65(3.26 %)	15(3.42 %)	0.870
Heart problems	226(11.35 %)	34(7.74 %)	0.027
Kidney diease	126(6.33 %)	21(4.78 %)	0.220
Digestive disease	440(22.09 %)	92(20.96 %)	0.604
Rheumatism	656(32.93 %)	165(37.59 %)	0.062
Asthma	83(4.17 %)	12(2.73 %)	0.161
CESD-10	5(0–24)	6(0–22)	<0.001
Depressive symptoms	310(15.56)	119(27.12)	<0.001
Sleep duartion(h)			<0.001
≤4	276(13.86 %)	109(24.83 %)	
4–8	1108(55.62 %)	172(39.18 %)	
≥8	608(30.52 %)	158(35.99 %)	
Leisure activities			0.009
Yes	1107(55.57 %)	214(48.75 %)	
No	885(44.43 %)	225(51.25 %)	
bl_wbc	5.97(2.5–13.75)	5.9(2.75–10.9)	0.336
bl_crp	2.71(0.1–80.3)	2.38(0.1–19)	0.249
HGS	31.83(7–58)	27.25(9.5–47.2)	<0.001
GS	1668(83.73 %)	402(91.57 %)	<0.001
FTSST	9.02(0.09–26.31)	9.81(5–20)	<0.001
ASMI	8.34(6–12)	8.58(6–11)	<0.001
Possible sarcopenia	395(19.83 %)	123(28.02 %)	<0.001
Sarcopenia	326(16.37 %)	107(24.71 %)	<0.001

reducing group. There was a strong correlation between MCI and the diagnostic markers of sarcopenia, including handgrip strength, gait speed, FTSST, and appendicular skeletal muscle mass index (ASMI). Furthermore, we discovered a substantial correlation between MCI in older persons with depressive symptoms (OR = 0.956, 95% CI = 0.937–0.976). Further analysis revealed a significant nonlinear regression association between MCI and leisure activities (P = 0.000). Table 2 below also revealed the non-linear association between sleep duration and the risk of cognitive impairment (P < 0.001). Specifically, we identified a significant U-shaped link between sleep duration and MCI in the fully adjusted model (OR = 1.781, 95 % CI = 1.331–2.385; OR = 1.446, 95 % CI = 1.123–1.861).

3.3. Reciprocal mediation of MCI-related depressive symptoms, muscle strength, physical performance, and possible sarcopenia

Fig. 3 (A), (B), (C), and (D) below illustrated how we constructed the mediating role model using MCI as the dependent variable, depressive symptoms as the mediating variable, and sarcopenia and associated parameters as independent variables. The findings revealed that the relationship between handgrip strength, gait speed, standing tests, and possible sarcopenia with MCI was partially mediated by depressed symptoms (indirect size = −0.001, Boot SE = 0.006, 95% boot CI = −0.029 ~ −0.003, R2 = 0.100; indirect size = −0.005, Boot SE = 0.002, 95% boot CI = −0.01 ~ −0.001, R2 = 0.097; indirect size = 0.001, Boot SE = 0.004, 95% boot CI = 0.003 ~ 0.020, R2 = 0.099; indirect size = 0.008, Boot SE = 0.004, 95% boot CI = 0.003 ~ 0.017, R2 = 0.097). In turn, as shown in Fig. 4 (E), (F), (G), and (H), we constructed the mediation model using MCI as the dependent variable, depressive symptoms as the independent variable, and muscle strength and physical function as the mediating factors. The findings indicated that the relationship between depressive symptoms and MCI was partially mediated by handgrip strength, gait speed, standing tests, and possible sarcopenia (indirect size = 0.001, Boot SE = 0.003, 95% boot CI = 0.004 ~ 0.016, R2 = 0.100; indirect size = 0.000, Boot SE = 0.001, 95% boot CI = −0.000 ~ 0.005, R2 = 0.097; indirect size = 0.000, Boot SE = 0.002, 95% boot CI = 0.001 ~ 0.013, R2 = 0.099; indirect size = 0.000, Boot SE = 0.002, 95% boot CI = −0.001 ~ 0.01, R2 = 0.097). Simultaneously, we discovered a noteworthy association (c = 0.006, P < 0.001) between depressed symptoms and MCI.

3.4. Leisure activities were involved in regulating the association of depressive symptoms, muscle strength, physical function and MCI

With the goal of better managing patients with MCI who also experienced depressive symptoms, we investigated the moderating effect of leisure activity frequency further, taking into account the mediating effect of depressive symptoms as the core. With activity frequency serving as the indirect moderator variable, we built the indirect moderation model based on three routes of independent, dependent, and mediating variables. The findings demonstrated that the mediating effects of depressive symptoms on physical function, muscle strength, and potential sarcopenia and MCI were inconsistent at different activity frequency levels, suggesting the possibility of conditioned mediating effects of activity frequency. Specifically, gait speed, standing tests, handgrip strength, and potential sarcopenia linked to MCI were all moderated by moderate to high level leisure activities. However, neither ASMI nor sarcopenia were regulated by it. The details were shown in Table 3 below.

3.5. Sleep duration was involved in regulating the association of depressive symptoms, muscle strength, physical function, and MCI

Sleep duration was also confirmed as a regulating variable in this study because it was strongly linked to mood, cognitive state, and muscle function. The findings suggested that short sleep duration was involved in the indirect modulatory effects of depressive symptoms on muscle strength, physical function, and MCI. Specifically, the results showed changes in depressive symptoms mediating handgrip strength, gait speed, standing tests, and possible sarcopenia with MCI at sleep duration of 6 h or less. However, sleep duration had no effect on ASMI and sarcopenia. The details were shown in Table 4 below.

Table 2
Findings from a logistic regression analysis of several variables related to MCI.

Variables	crude model OR(95%CI)	*P*-value	Adjusted model OR(95%CI)	*P*-value
HGS	1.07(1.056–1.084)	<0.001	1.047(1.028–1.066)	<0.001
GS	2.11(1.477–3.016)	<0.001	1.571(1.076–2.291)	<0.001
FTSST	0.918(0.888–0.949)	<0.001	0.946(0.912–0.982)	<0.01
ASMI	0.845(0.775–0.922)	<0.001	1.405(1.171–1.687)	<0.001
Possible sarcopenia	0.635(0.502–0.804)	<0.001	0.718(0.555–0.928)	0.012
Sarcopenia	1.647(1.285–2.111)	<0.001	1.357(1.031–1.787)	0.029
Depressive symptom	0.940(0.922–0.957)	<0.001	0.956(0.937–0.976)	<0.001
Sleep duration(≤4h)	2.544(1.935–3.345)	<0.001	1.781(1.331–2.385)	<0.001
Sleep duration(≥8h)	1.674(1.320–2.123)	<0.001	1.446(1.123–1.861)	0.004
Leisure activities	0.760(0.618–0.935)	<0.01	0.814(0.653–1.016)	0.065

Adjusted model: age, sex, place of residence, education level, marital status, smoking, alcohol consumption, BMI, hypertension, dyslipidemia, abnormal blood sugar, heart disease, kidney disease, respiratory disease, liver disease, arthritis, asthma. FTSST: Five Times Sit to Stand Test; HGS: hand handgrip strength; GS: gait speed; ASMI: appendicular skeletal muscle mass index.

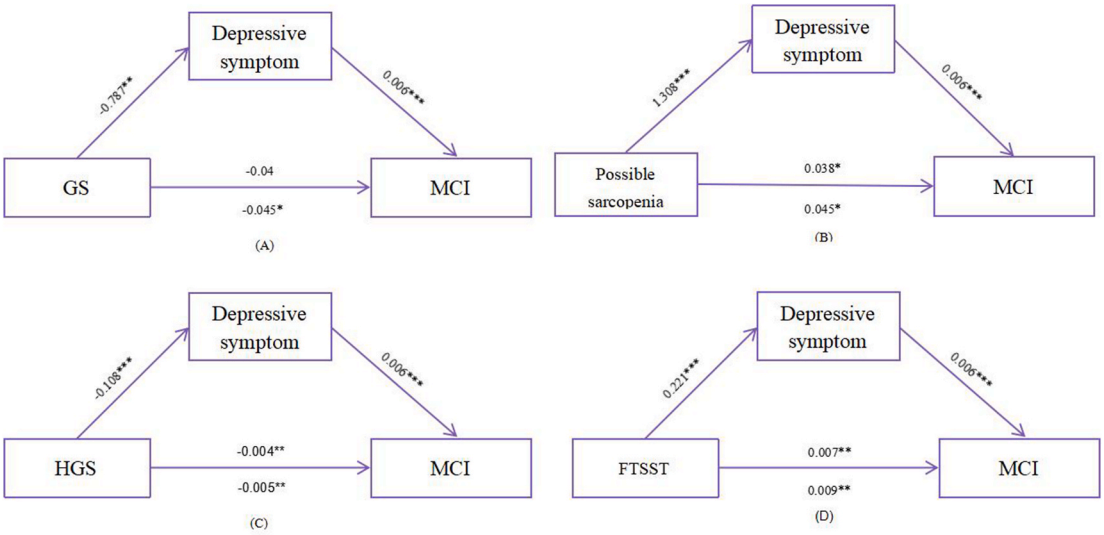


Fig. 3. Diagram of mediator model centered on depressive symptoms.
Note: * p<0.05 **p<0.01 ***p<0.001. Figures (A), (B), (C), and (D) represent depressive symptoms partially mediating the associations of gait speed, handgrip strength, five-time-sit-to-stand test, and possible sarcopenia and MCI, respectively. HGS: handgrip strength; GS: Gait speed; FTSST: five-time-sit-to-stand test; MCI: mild cognitive impairment.

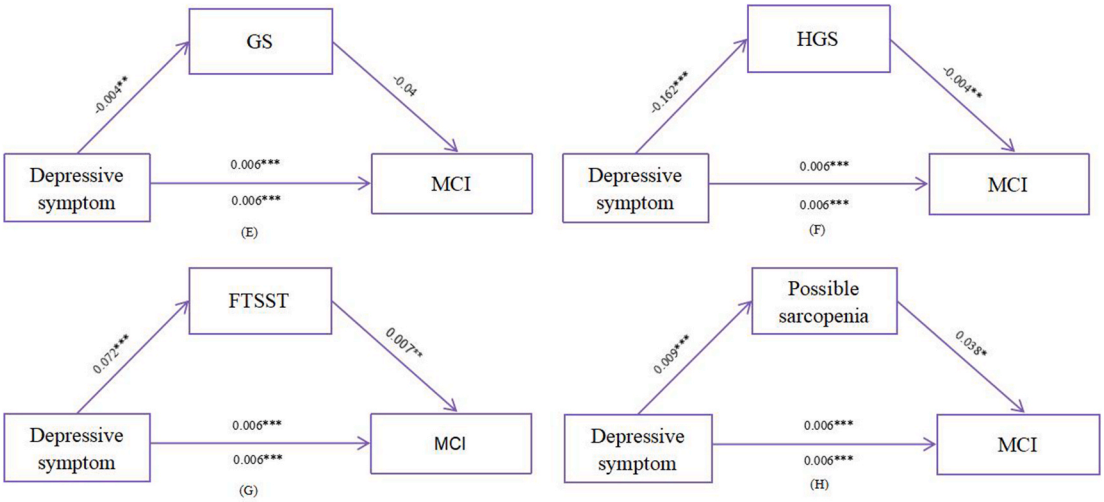


Fig. 4. Diagram of mediated modeling centered on muscle strength and somatic functioning.
Note: *p < 0.05 **p < 0.01 ***p < 0.001. Figures (E), (F), (G), and (H) represent gait speed, handgrip strength, five-time-sit-to-stand test, and possible sarcopenia partially mediating the association between depressive symptoms and MCI, respectively. HGS: handgrip strength; GS: Gait speed; FTSST: five-time-sit-to-stand test; MCI: mild cognitive impairment.

4. Discussion

We aimed to investigate the associations and mediating pathways of sarcopenia, including its various components (muscle mass, muscle strength, and physical fitness), and depressive symptoms with the MCI, as well as the mediating role of indirect regulation of sleep duration and leisure activities. The findings indicated that depressive symptoms acted as a partial mediating factor in the relationship between potential sarcopenia, muscular strength, physical function, and MCI. Conversely, the relationship between depressive symptoms and MCI was partially mediated by muscular strength and physical performance. In addition, the relationship between sarcopenia, depressive symptoms, and MCI might be regulated by moderate to low levels of sleep duration and moderate to high levels of leisure activities.

According to this study, 18.1% of patients over 50 had MCI, which was comparable to the findings of other sizable cross-sectional studies conducted in China [37]. Furthermore, a significant number of studies [38–40] supported our findings that sarcopenia and its

Table 3
Indirect moderating effects of activities frequency.

Moderator variable	variable	Level	Level value	Effect	BootSE	BootLLCI	BootULCI
		Low level (-1SD)	1.045	−0.000	0.000	−0.001	0.000
	HGS*	Average	1.543	−0.001	0.000	−0.001	−0.000
		high level (+1SD)	2.042	−0.001	0.000	−0.001	−0.000
		Low level (-1SD)	1.045	−0.004	0.003	−0.008	0.001
	GS*	Average	1.543	−0.005	0.002	−0.009	−0.001
		high level (+1SD)	2.042	−0.006	0.004	−0.017	−0.002
		Low level (-1SD)	1.045	0.001	0.001	−0.000	0.002
Leisure activity	FTSST*	Average	1.543	0.001	0.001	0.000	0.002
		high level (+1SD)	2.042	0.001	0.001	0.000	0.003
		Low level (-1SD)	1.045	0.007	0.004	−0.002	0.014
	Possible Sarcopenia*	Average	1.543	0.008	0.003	0.002	0.013
		high level (+1SD)	2.042	0.008	0.004	−0.000	0.016
		Low level (-1SD)	1.045	−0.001	0.002	−0.007	0.002
	Sarcopenia	Average	1.543	−0.000	0.002	−0.004	0.004
		high level (+1SD)	2.042	0.001	0.004	−0.006	0.010
		Low level (-1SD)	1.045	0.005	0.008	−0.002	0.024
	ASMI	Average	1.543	0.005	0.010	−0.003	0.031
		high level (+1SD)	2.042	0.006	0.013	−0.005	0.040

Note: * represents a positive result. The moderator variable was activities frequency,"Level"represents the mean minus one standard deviation, the mean and the mean plus one standard deviation of the moderator variable. If the mediation of the independent variable is not consistent at the three levels, it indicates a moderating mediation effect. The"level value"represents different levels of activities frequency. ASMI: appendicular skeletal muscle mass index; HGS: handhandgrip strength; GS: Grit speed; FTSST: five-time-sit-to-stand test.

Table 4
Indirect moderating effects of sleep duration.

Moderator variable	variable	Level	Level value	Effect	BootSE	BootLLCI	BootULCI
		Low level (-1SD)	4.400	−0.001	0.000	−0.001	−0.000
	HGS*	Average	6.373	−0.000	0.000	−0.001	−0.000
		high level (+1SD)	8.345	−0.000	0.000	−0.001	0.000
		Low level (-1SD)	4.400	−0.006	0.005	−0.017	0.001
	GS*	Average	6.373	−0.004	0.002	−0.007	−0.000
		high level (+1SD)	8.345	−0.001	0.003	−0.008	0.003
		Low level (-1SD)	4.400	0.002	0.001	0.001	0.004
	FTSST*	Average	6.373	0.001	0.000	0.000	0.002
Sleep duration		high level (+1SD)	8.345	0.000	0.001	−0.001	0.001
		Low level (-1SD)	4.400	0.011	0.005	0.003	0.022
	Possible Sarcopenia*	Average	6.373	0.006	0.003	0.002	0.011
		high level (+1SD)	8.345	0.002	0.004	−0.006	0.010
		Low level (-1SD)	4.400	−0.003	0.004	−0.011	0.003
	Sarcopenia	Average	6.373	−0.000	0.002	−0.004	0.004
		high level (+1SD)	8.345	0.000	0.002	−0.002	0.004
		Low level (-1SD)	4.400	0.008	0.013	−0.003	0.042
	ASMI	Average	6.373	0.005	0.008	−0.002	0.027
		high level (+1SD)	8.345	0.002	0.006	−0.008	0.021

Note: * represents a positive result. The moderator variable was sleep duration,"Level"represents the mean minus one standard deviation, the mean and the mean plus one standard deviation of the moderator variable. If the mediation of the independent variable is not consistent at the three levels, it indicates a moderating mediation effect. The"level value"represents different levels of sleep duration. ASMI: appendicular skeletal muscle mass index; HGS: handhandgrip strength; GS: Grit speed; FTSST: five-time-sit-to-stand test.

defining characteristics, such as handgrip strength, gait speed, chair standing time, and ASMI, were significantly associated with MCI. The incidence of MCI was 19.83% and 24.71% for possible sarcopenia and sarcopenia groups, with a significantly statistical difference, which was also supported by a relative part of studies. For instance, a meta-analysis involving 27428 patients from 13 studies [8] revealed that patients with muscle sarcopenia had a combined prevalence of MCI of 20.5% (95% CI: 0.140–0.269). The first longitudinal research data from CHARLS [7] revealed a causal relationship between sarcopenia and MCI, with the incidence of MCI in the possible sarcopenia and sarcopenia groups being 16.5% and 24.2%, respectively. Some researches [41,42], on the other hand, contended that there was no connection between the onset of cognitive impairment or cognitive domains and sarcopenia or muscle mass. In addition, our research showed a connection between MCI and depressed symptoms. Crucially, the association between MCI and handgrip strength, gait speed, chair standing time, and depressive symptoms was mediated by each other. This result suggested that MCI, sarcopenia and depressive symptoms were all mutually reinforcing, and that interventions for MCI patients must consider both depressive symptoms and physical function. This outcome will facilitate the formulation of more individualized treatment plans and management techniques. However, the present study found that depressive symptoms only played a partial mediating role was a side effect of the fact that there were still other possible risk factors that played a role between sarcopenia and MCI, such as physical

activity, basal metabolic rate, atherosclerosis, and so on [43–45]. Furthermore, we did not find that muscle mass and defined sarcopenia were involved in the mediating associations described above, probably because we obtained the data by calculating formulas, which was still a far cry from objective measurements, and this needs to be further explored, but their own associations with MCI are significantly present, which does not contradict other studies [7,9,10,40].

It is noteworthy that, we also discovered a relationship between the presence of leisure activities, sleep duration and MCI, which has not been further investigated in previous researches. In older adults with MCI and dementia, physical activity—such as multicomponent exercise, high-intensity progressive resistance training, or aerobic activity—has a positive effect on cognitive function [46–48]. Conversely, physical inactivity is a major contributing factor to the majority of chronic diseases [49]. However, high-intensity exercise may put older people at greater risk for falls and balance issues [50], therefore leisure activities appear to be a better fit for older people's exercise demands. Therefore, we further explored the mediating impact of leisure activity and sleep duration in MCI in individuals with depressive symptoms and sarcopenia. The results implied that moderate to high levels of activity and short sleep duration ($\leq$ 6 h) supported the mediation function of depression symptoms. Although the precise process is unknown, sleep deprivation and inactivity are major risk factors for a number of diseases. For instance, lack of sleep caused a decrease in CSF/blood clearance of these biomarkers and an increase in Tau phosphorylation and Aβ deposition in CSF, which accelerated the onset of cognitive impairment [51,52]. According to the findings of a recent large cohort study, individuals who slept less than 5 h per night were linked to a 2.6-fold increased risk of depression in comparison to those who slept between five and 9 h [53]. Effective sleep management may improve depressive symptoms and cognitive function. Insufficient sleep also has an impact on physical activity performance and level as well. These two factors frequently interact and can lead to a number of unfavorable health consequences, including cancer, cardiovascular disease, MCI, and all-cause mortality [54–56]. In this study, we first showed that the relationship between depressive symptoms, physical function, and cognitive impairment was regulated by moderate to high levels of leisure activity. According to a recent long-term study that includes a 10-year follow-up [57], maintaining a healthy lifestyle that includes a balanced diet, frequent exercise, wholesome social connections, and mental stimulation can stall memory loss. Actually, social contact and cognitive tasks form the core of the leisure activities in this study. This result broadens the scope and significance of recreational activities' function in mental, physical, and cognitive disorders from a side perspective, and it provides a path forward.

This study has several strengths. First, this study included a large nationally representative sample size, thus allowing our findings to be widely generalized to the Chinese middle-aged and elderly population. Second, we revealed potential mediating associations of depressive symptoms, sarcopenia, and MCI, as well as indirect moderating effects of moderate to high levels of leisure activities and insufficient sleep duration, which have not been combined and elaborated in other studies.

However, this study has some shortcomings. First, because this study was cross-sectional, it was not possible to determine a causal relationship between MCI, muscle strength, physical performance, and depressive symptoms. Therefore, longer-term longitudinal studies are needed. Second, due to limitations in the questionnaire design of the CHARLS database and the fact that diagnoses of illnesses in CHARLS are self-reported physician diagnoses, memory bias is unavoidable; and third, the present study used observational data, which may have biased the observed relationships through the introduction of confounders. To minimize this bias, we considered as many relevant factors as possible in our analyses. However, other potential confounders cannot be ruled out; fourth, more discussion of the precise frequency of leisure activities is necessary because the frequency of activities was not grouped in detail in this study. In addition, we only discussed the duration of sleep, and further research is needed on other aspects of sleep, including sleep efficiency, quality, and the relationship with daytime dysfunction. There is also the fact that we do not know whether the effects of sleep duration and leisure activities on outcomes are positively or negatively moderated, so there is still a lot of room for subsequent work on this topic. Fifth, this study did not find that depressive symptoms mediated the association between ASMI and the identified sarcopenia and MCI. This result may be due to the relative lack of objectivity in the ASMI calculation formula. Future clinical studies should use bioelectrical impedance techniques (BIA) or dual-energy X-ray absorptiometry (DXA) for reliable assessment of ASMI [27].

In conclusion, the present study confirms that depressive symptoms and muscle strength and physical performance mutually mediate each other's association with MCI, while moderate to low levels of sleep duration and presence of leisure activities indirectly moderated their interactions, and subsequent preventive measures and health management regarding patients with MCI should comprehensively take into account the effects of these factors, future studies should further investigate the facilitating and inhibiting effects of sleep duration and activity on MCI-related risk factors.

Ethics statement

This study did not include any animal or human experiments. Projects have been approved by the biomedical ethics council at Beijing University. The IRB approval number for the main household survey, including anthropometrics, is IRB00001052-11015; the IRB approval number for biomarker collection, was IRB00001052-11014.

Funding

This research was supported by the Dongguan Social Science and Technology Development Project (No: 20211800904952), the Key Project of Guangzhou Science and Technology Program, China (No: 202206010142)×, and the Guangdong Basic and Applied Basic Research Foundation (No: 2021B1515140026).

Data availability statement

Data relevant to this study can be obtained free of charge by contacting the authors of the paper or The China Health and Retirement Longitudinal Study database.

CRediT authorship contribution statement

Linfeng Chen: Writing – review & editing, Writing – original draft, Visualization, Supervision, Software, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Dan Li:** Writing – review & editing, Writing – original draft, Formal analysis, Data curation, Conceptualization. **Ke Tang:** Writing – review & editing, Writing – original draft, Software, Formal analysis, Data curation, Conceptualization. **Zhong Li:** Writing – review & editing, Writing – original draft, Visualization, Methodology, Funding acquisition, Conceptualization. **Xiaoyun Huang:** Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Resources, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation.

Declaration of competing interest

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

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