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Association between physical activity and cognitive function in post-menopausal women with high parity: the chain-mediating effects of nutritional status and depression

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Abstract

Background It has been reported that the cognitive responses to physical activity (PA) in postmenopausal women vary by parity status, and women with higher parity show a significant association between PA and cognitive function. However, the potential pathways mediating the relationship between PA and cognitive function in women with higher parity remain unclear. The objective of this study was to examine this association in Chinese cohort and further investigate the mediating pathways.

Methods A total of 2296 postmenopausal women were enrolled from the Baoshan District, from April to December 2020. All participant information was collected through interviewer-administered questionnaires or measurements, including personal information, medical history, lifestyle, body mass index (BMI), cognitive function, nutritional status, and depression status. In this cross-sectional study, generalized linear regression models and the chain-mediation analysis were used to examine the relationship between PA and cognitive function and the mediating pathways.

Results There was a significant relationship between PA and cognitive function in the high-parity group (≥ three births). In the fully adjusted generalized linear regression model, PA was significantly associated with cognitive function [β: 0.795, 95% confidence interval (CI): 0.251–1.340, $P < 0.05$]. The chain-mediation analysis showed that depression and nutritional status were two significant mediators, contributing 37.96% of the indirect effect of the overall effect.

Conclusions Our findings suggest that PA is beneficial for women (≥ three births) to maintain cognitive function, and these benefits are mediated by depression and nutritional status.

Keywords Physical activity, Cognitive function, Parity, Depression, Nutritional status

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Background

Physical activity (PA) has been recognized as a promising protector for individual cognitive function and even as a potential prevention for dementia development and progression [1]. Owing to the diverse genetics, socioeconomic status, comorbidity, lifestyle, and sex, the risk and extent of cognitive decline vary between individuals [2]. In particular, women generally have a higher dementia prevalence than men [3], and a growing number of studies have reported that the positive effects of interventions, such as PA, exhibit sex differences [4, 5]. To explain the sex differences in the cognitive benefits of PA, more recent studies have focused on sex-specific biological events, such as pregnancy and fertility history, which are accompanied by long-term dramatic changes in brain function [6], and these changes may lead to different responses to PA. In addition, previous studies have shown that the effects of PA on dementia risk are related to the number of births among women. Notably, using data from the Health, Aging, and Body Composition Study, Barha CK and colleagues first found that the relationship between walking and cognitive function differed by parity status [7]. However, among women with significant relationships, the potential pathways mediating the association between PA and cognitive function were not understood, which would be essential to reflect the beneficial effects of PA on cognitive function and further to guide more precise interventions for women.

A growing body of literature recognizes physical and mental health as two critical channels through which PA exerts its benefits on cognitive function. Controlling body mass index (BMI) is a direct benefit of PA, and decreasing the risk of obesity-related outcomes is meaningful in reducing the morbidity of dementia [8]. A higher BMI usually coincides with a greater risk of diabetes via insulin resistance, which exists both in the periphery and brain. Prior studies have emphasized that PA can reduce brain insulin resistance and improve cognitive function by controlling BMI [9]. Interestingly, in women, the risk of higher BMI and obesity-related outcomes was correlated with parity. A cross-sectional study conducted by Ohashi et al. showed that reproductive history was positively associated with obesity in postmenopausal women [10]. Hypertension has been considered as a common consequence of obesity, and a higher risk of incident hypertension is observed in Iranian women with ≥ three live births/parity than in those with two births [11]. Taken together, these findings provide evidence of the potential indirect effects of BMI on the relationship between PA and cognitive function.

Nutritional status is another important component of physical health and is influenced by PA to some extent. After resistance exercise, enhanced amino acid sensitivity of myofibrillar protein synthesis persisted for up to 24 h [12]. It has been reported that the synergistic effects of nutrition and PA on maintaining skeletal muscle mass and strength are closely related to cognitive function [13]. However, postmenopausal women with lower parity appear to carry lower skeletal muscle mass [14], that is, fewer nutrient reserves [15]. Therefore, in light of skeletal muscle mass, it is necessary to evaluate the indirect effects of nutritional status on cognitive function.

Depression is a common mental disorder, and older adults with depression have a higher risk of cognitive impairment [16]. Several studies have examined the positive effects of PA on depression via direct and indirect pathways [17, 18]. Previous studies have suggested that parity may be a factor in depression [19, 20], although the relationship between specific births and the risk of depression is inconsistent. Therefore, examining the PA-depression-cognitive function pathway may be helpful in further understanding the varied benefits of PA on cognitive function in women with different parity status.

In conclusion, PA is recommended as a promising strategy for cognitive decline intervention, and there are various cognitive responses to PA among women with different parity status. However, there has been no investigation to examine the underlying mechanisms which could be helpful in identifying the beneficial effects of PA on cognitive function and in providing more precise interventions for women. To address these research gaps, we used data from the Baoshan District to examine the association between PA and cognitive function and its potential underlying pathways in women with low and high parity. The findings of this study provide new evidence for the internal mechanism between PA and cognitive function, and further direct more precise interventions for women.

Methods

Participants

People who were living in Baoshan District and attended in Youyi Road Community Health Service Centre for Baoshan District were invited to participate in this study. Interviewer-administered questionnaires (shown in the Supplementary file) were used to collect participants' personal information, BMI, medical history, lifestyle, cognitive function, nutrition, and depression status. All questionnaires were collected in Youyi Road Community Health Service Centre for Baoshan District. This study

was approved by the Medical Ethics Committee of the Huashan Hospital, Fudan University, Shanghai, China. Written informed consent was obtained from all participants or their legal guardians before data and sample collection. A total of 5482 questionnaires were collected from April to December 2020, of which 4666 were valid for further analysis. This study focused on postmenopausal women over the age of 60 years; 2296 women with no missing values were included.

Measurements

Parity

We defined parity as the number of times a woman has given birth to a live neonate (any gestation) or at 24 weeks or more, regardless of whether the child was viable or non-viable (i.e. stillbirths). A woman who is nulliparous has never previously given birth, and there was no woman surveyed who did not give birth at least once. Thus, in this study, there is no nulliparity group (zero birth), which would be reasonable in the baby boom era in China. Parity was then divided into two groups, including low parity (one or two births) and high parity (≥ three births).

Physical activity

Physical activity was measured by the following question: Have you participated in any of the following physical activities in the last year? The types of physical activity included walking, jogging, riding a bicycle, playing football/basketball/tennis, dancing, swimming, shadowboxing, and other types of exercises identified by the interviewer. The frequency of physical activity was identified by the standard "once a week or more or every day" for more than 20 min. Thus, those who satisfied the frequency and type of PA were classified into the "YES" group, and those who did not were classified in the "NO" group.

Cognitive function

Cognitive function was estimated using the Mini-Mental Status Examination (MMSE), which is widely used to assess cognitive function. There are six domains that measure different cognitive processes: time orientation, place orientation, calculation and attention, immediate recall, delayed verbal recall, language, and others. The maximum score on the MMSE is 30, and a lower score indicates worse cognitive function. This study used the Chinese version of the MMSE, which has been validated for the Chinese population [21].

Body mass index

BMI was calculated as weight in kilograms divided by height in meters squared.

Mini Nutritional Assessment

We used the Mini Nutritional Assessment long form scale (MNA-LF) as a validated tool to assess the nutrition of the elderly. The MNA-LF contains 18 items and assesses four different aspects: anthropometric assessment (BMI, weight loss, and arm and calf circumferences), general assessment (lifestyle, medications taken, mobility, and presence of signs of depression or dementia), short dietary assessment (number of meals, protein and fluid intake, and autonomy of feeding), and subjective assessment (self-perception of health and nutrition, self-assessment of health compared to peers). By adding up the scores, individuals are divided into three groups using threshold values of < 17 for "malnourished," 17–23.5 for "at risk of malnutrition" and ≥ 24 for "normal nutritional status," with a maximum total score of 30 points [22, 23].

Depression

Depression was determined using the 15-item Geriatric Depression Scale (GDS-15), which is a short form of the GDS that is used to screen, diagnose, and evaluate depression in elderly individuals [24]. Higher scores indicated more severe depressive symptoms. Depressive symptoms were defined as a score of five or more.

Covariates

General information including age, education level (below or above high school), income status (over 50,000 RMB/per year or not), and marital status (living alone or not) were collected in the first part of the questionnaire. Lifestyle (smoking and alcohol consumption) and presence of chronic conditions were collected in the second part of the questionnaire. Smoking was measured by the following question: Do you smoke (smoking means smoking at least one cigarette every day for more than half a year)? Those who never smoked or only occasionally smoked small amount of cigarettes (no more than one per day on average) or quit were classified into "NO" group, otherwise were classified into "YES" group. Alcohol consumption was measured by the following question: Do you drink alcohol at least once a week for at least half a year? Those who never or only occasionally drink alcohol (less than 1 time per week on average) or quit were classified into "NO" group, otherwise were classified into "YES" group. Comorbidities (hypertension, hyperlipidaemia, diabetes, coronary heart disease, nephritis, cancer, gastrointestinal disease, pulmonary disease, and hepatobiliary disease) were considered as confounding factors that may influence both lifestyle factors and cognitive function. We also included medicine intake as a covariate in this study.

Statistical analysis

In this study, medians (interquartile ranges [IQRs]) were presented for variables with non-normal distribution. Comparisons between low- and high-parity groups were tested using the Mann–Whitney U test for continuous variables and chi-square tests for categorical variables. The interaction between parity group and PA was included to test whether the nature of the association between PA and cognitive function depended on parity group. Generalized linear regression models were used to evaluate the relationship between PA and MMSE scores, including crude and adjusted models. Furthermore, mediation analysis was used to investigate the underlying mechanism between PA and cognitive function and to examine the contribution of target variables hypothesized to be on the causal pathway, including BMI, nutritional status, and depression. Based on the significant results of the mediation analysis, we conducted a chain-mediation analysis to explore the interaction between mediators on potential paths. All statistical analyses were performed using R version 4.2.1. For each target mediator, the direct and indirect effects were calculated using the "bruceR" package with bootstrapping confidence intervals. The percentage of indirect effects among the total effects was calculated to indicate the effect size of the mediator on each pathway. The difference was statistically significant ($P < 0.05$).

Results

Demographic characteristics

Table 1 reports the descriptive characteristics of the included 2296 postmenopausal women stratified by parity groups (low and high parity). In general, the high-parity group was older, less educated, and more likely to live alone. Compared with the high-parity group, participants in the low-parity group were more likely to be physically active, showing higher MNA and MMSE scores as well as lower BMI and GDS-15 scores. In addition, there were no significant differences between the two groups in terms of smoking and alcohol consumption. Regarding comorbidities, the distribution of hypertension, diabetes, coronary heart disease, and cancer differed significantly between the two groups.

The association between PA and cognitive function depended on parity group

A significant interaction between PA and parity group was found for MMSE (Table 2), indicating that the nature of the association between PA and cognitive function varied by parity group. The effects of the interaction between PA and cignitive function still significant even after adjusting for all the covariates in Model 4 (β: 1.348, 95% CI: 0.635–2.061, $P < 0.05$).

Generalized linear regression models of the relationship between PA and cognitive function in the low- and high-parity groups

Table 3 presents that the relationship between PA and MMSE varied by parity. There was no significant association between PA and MMSE scores in the low-parity group while the association was significantly positive in the high-parity group. For the high-parity group, in the unadjusted model (Model 1), we found that PA was strongly correlated with higher MMSE scores (β: 3.021, 95% CI: 2.358–3.684, $P < 0.05$). In the minimally adjusted model (Model 2, adjusted for age, education level, income and marital status), the result remained significant though the regression coefficient sharply decreased (β: 1.312, 95% CI: 0.723–1.901, $P < 0.05$), suggesting that covariates in Model 2 were influential in this relationship. In Model 3 (adjusted for the variables in Model 2, also for BMI, nutritional status, and depression), the relationship remained significant (β: 0.794, 95% CI: 0.252–1.335, $P < 0.05$). The regression coefficient in the fully adjusted model (Model 4, adjusted for the variables in Model 3, and also for comorbidities and medicine intake) was similar to that in Model 3 (β: 0.795, 95% CI: 0.251–1.340, $P < 0.05$), indicating that comorbidities and medicine intake may not influence the relationship between PA and MMSE scores.

Chain-mediating effects of BMI, nutritional status, and depression on the relationship between PA and cognitive function

According to the results of generalized linear regression models, we focused on the high-parity group and further explored the mediating effects of BMI, nutritional status, and depression on the relationship between PA and cognitive function. As shown in Fig. 1, nutritional status and depression were two significant mediators of this association, whereas BMI was not, and the mediation proportions were 22.4% and 12.0%, respectively. We further analyzed the chain-mediating effects of the depression and nutritional status, and the results showed that the model fit well, as Fig. 2 shows. There were three indirect paths through which PA affected MMSE scores via depression and nutritional status. Table 4 shows the mediating effects, direct effects, and corresponding effect scales. PA directly affected cognitive function, as defined by the MMSE score, with a direct effect of 0.795 and an effect size of 61.964%. The three indirect paths shown in Table 4 accounted for 37.958% of the total effect size,

Table 1 Participant characteristics, collected from Baoshan district, Shanghai, China, from April to December 2020

	Total (*N* = 2296)	**Low Parity (*N* = 1011)**	**High Parity (*N* = 1285)**	***P***
Age(years)	71.0 (67.0,76.0)	67.0 (66.0,70.0)	74.0 (71.0,79.0)	< 0.0001
Education level (%)				
above high school	551 (24.0%)	268 (26.5%)	283 (22.0%)	0.014
below high school	1745 (76.0%)	743 (73.5%)	1002 (78.0%)	
Income (%)				
< = 50,000 RMB/per year	1901 (82.8%)	841 (83.2%)	1060 (82.5%)	0.702
> 50,000 RMB/per year	395 (17.2%)	170 (16.8%)	225 (17.5%)	
Marital status (%)				
living alone	405 (17.6%)	100 (9.9%)	305 (23.7%)	< 0.0001
not living alone	1891 (82.4%)	911 (90.1%)	980 (76.3%)	
BMI	23.8 (21.8,26.0)	23.8 (21.7,25.6)	24.0 (22.0,26.2)	0.041
MNA	25.5 (24.5,27.0)	26.0 (24.5,27.0)	25.5 (24.0,26.5)	< 0.0001
GDS-15	1.00 (0,2.00)	0 (0,2.00)	1.00 (0,2.00)	< 0.0001
MMSE	27.0 (24.0,28.0)	27.0 (25.0,29.0)	26.0 (22.0,28.0)	< 0.0001
Smoking (%)				
NO	2293 (99.9%)	1010 (99.9%)	1283 (99.8%)	1
YES	3 (0.1%)	1 (0.1%)	2 (0.2%)	
Alcohol (%)				
NO	2283 (99.4%)	1004 (99.3%)	1279 (99.5%)	0.664
YES	13 (0.6%)	7 (0.7%)	6 (0.5%)	
Physical activity (%)				
NO	875 (38.1%)	349 (34.5%)	526 (40.9%)	0.002
YES	1421 (61.9%)	662 (65.5%)	759 (59.1%)	
Hypertension (%)				
NO	1033 (45.0%)	516 (51.0%)	517 (40.2%)	< 0.0001
YES	1263 (55.0%)	495 (49.0%)	768 (59.8%)	
Hyperlipidemia (%)				
NO	2178 (94.9%)	958 (94.8%)	1220 (94.9%)	0.918
YES	118 (5.1%)	53 (5.2%)	65 (5.1%)	
Diabetes (%)				
NO	1886 (82.1%)	867 (85.8%)	1019 (79.3%)	< 0.0001
YES	410 (17.9%)	144 (14.2%)	266 (20.7%)	
Coronary heart disease (%)				
NO	2185 (95.2%)	973 (96.2%)	1212 (94.3%)	0.042
YES	111 (4.8%)	38 (3.8%)	73 (5.7%)	
Nephritis (%)				
NO	2276 (99.1%)	999 (98.8%)	1277 (99.4%)	0.223
YES	20 (0.9%)	12 (1.2%)	8 (0.6%)	
Cancer (%)				
NO	2225 (96.9%)	970 (95.9%)	1255 (97.7%)	0.025
YES	71 (3.1%)	41 (4.1%)	30 (2.3%)	
Gastrointestinal disease (%)				
NO	2241 (97.6%)	986 (97.5%)	1255 (97.7%)	0.938
YES	55 (2.4%)	25 (2.5%)	30 (2.3%)	
Pulmonary disease (%)				
NO	2268 (98.8%)	1001 (99.0%)	1267 (98.6%)	0.484
YES	28 (1.2%)	10 (1.0%)	18 (1.4%)	
Hepatobiliary disease (%)				
NO	2195 (95.6%)	972 (96.1%)	1223 (95.2%)	0.308
YES	101 (4.4%)	39 (3.9%)	62 (4.8%)	
Medicine intake (%)				
NO	770 (33.5%)	394 (39.0%)	376 (29.3%)	< 0.0001
YES	1526 (66.5%)	617 (61.0%)	909 (70.7%)	

BMI body mass index, *MNA* Mini Nutritional Assessment, *GDS-15* 15-item Geriatric Depression Scale, *MMSE* Mini-Mental Status Examination

Table 2 The effects of the interaction between physical activity and parity group on cognitive function

All (*N* = 2296)			
	β	**95% CI**	***P***
Model 1	2.607	1.760, 3.454	< 0.0001
Model 2	1.622	0.857, 2.387	< 0.0001
Model 3	1.316	0.603, 2.029	0.0003
Model 4	1.348	0.635, 2.061	0.0002

Model 1: physical activity, parity group, physical activity*parity group

Model 2: adjusted for age, education level, income, and marital status

Model 3: adjusted for age, education level, income, marital status, body mass index, nutritional status, depression

Model 4: adjusted for variables in Model 3, and also for comorbidities (hypertension, hyperlipidaemia, diabetes, coronary heart disease, nephritis, cancer, gastrointestinal disease, pulmonary disease, hepatobiliary disease) and medicine intake

CI confidence interval

consisting of Path a (effect size: 11.224%), Path b (effect size: 20.031%), and Path c (effect size: 6.703%).

Discussion

Based on cross-sectional data from the Youyi Road Community Health Service Centre, this study showed that the association between PA and cognitive function in postmenopausal women varied by parity status, which was consistent with a previous study [7]. Furthermore, we investigated the direct and underlying indirect effects of PA on cognitive function, and the results of the chain-mediation analysis showed that depression status and nutritional status were two significant mediators, contributing 37.96% of the indirect effect of the overall effect.

Compared to the low-parity group (one or two births), there was a stronger association between PA and cognitive function in the high-parity group (≥ three births). Previous studies have reported that higher parity is related to an increased risk of developing Alzheimer's disease (AD), AD-related pathology, and even decreased longevity [25], indicating that women with higher parity are more vulnerable to cognitive decline and ageing. The results from recent studies support that multiple estrogen fluctuations during multiparous processes contribute to an increased risk of cognitive impairment. During pregnancy, blood estradiol levels are > 10 times higher than peak menstrual cycle levels for several months [26], which may have a detrimental effect on cognitive function [27]. In addition, there are reports of estrogen withdrawal after hormone-simulated pregnancy suppressing hippocampal cell proliferation and glucocorticoid upregulation inducing neuronal loss in the hippocampus [28]. Because of an abrupt postpartum withdrawal of estrogen and upregulation of cortisol induced by delivery, multiple parity may have compounding effects that decrease brain and cognitive reserves in women [29]. Together, multiple parity has a repeated dramatic estrogen fluctuation and further affects brain plasticity [30] which is likely related to the varied cognitive responsivity to PA.

This study confirmed that nutritional status mediates the relationship between PA and cognitive function. A randomized controlled trial conducted by Fiorilli G and colleagues found that participants showed improved nutritional status after a 24-month period of moderate-to-high-intensity PA programs, indicating a positive association between PA and nutritional status [31]. Similarly, nutrition risk was less likely to occur among those with a healthy physical performance, but more often occur among those with sedentarism [32]. In addition, robust evidence supports the positive link between nutritional status and cognitive function, providing a solid foundation for the mediating effects of nutritional status [33, 34].

Table 3 Generalized linear regression models of the relationship between physical activity and cognitive function in the low- and high- parity group

	Low Parity			**High Parity**		
	(*N* = 1011)			**(*N* = 1285)**		
	β	95% CI	*P*	β	95% CI	*P*
Model1	0.414	−0.011, 0.838	0.056	3.021	2.358, 3.684	< 0.0001
Model2	0.247	−0.167, 0.660	0.247	1.312	0.723, 1.901	< 0.0001
Model3	0.133	−0.279, 0.545	0.527	0.794	0.252, 1.335	0.004
Model4	0.121	−0.294, 0.537	0.567	0.795	0.251, 1.340	0.004

Model 1: unadjusted

Model 2: adjusted for age, education level, income, and marital status

Model 3: adjusted for age, education level, income, marital status, body mass index, nutritional status, depression

Model 4: adjusted for variables in Model 3, and also for comorbidities (hypertension, hyperlipidaemia, diabetes, coronary heart disease, nephritis, cancer, gastrointestinal disease, pulmonary disease, hepatobiliary disease) and medicine intake

CI confidence interval

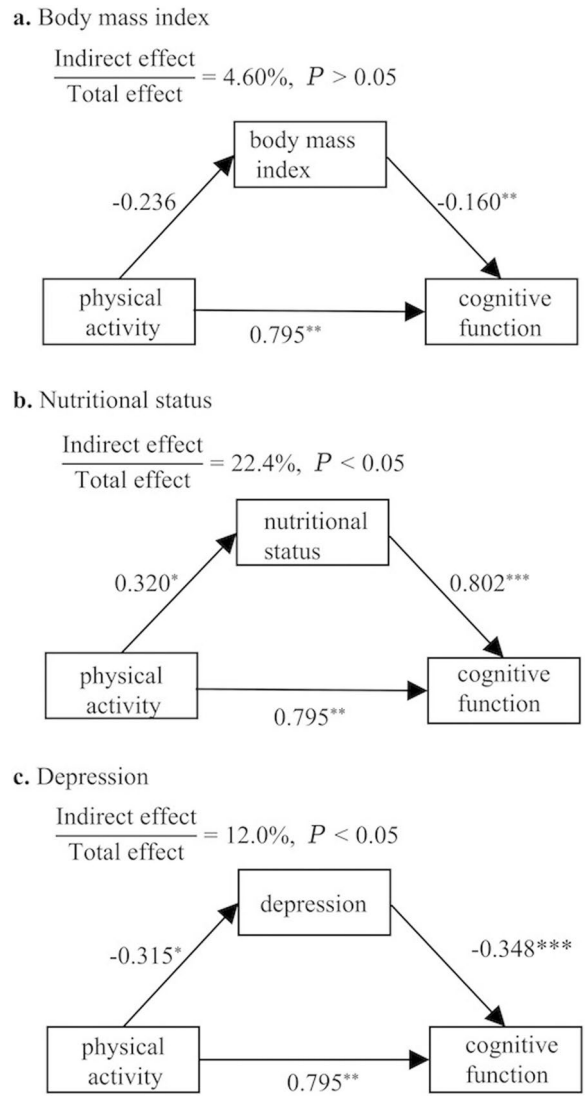

Fig. 1 The mediating effects of body mass index, depression, and nutritional status on the association between physical activity and cognitive function. $^{*}P<0.05$, $^{**}P<0.01$, $^{***}P<0.001$

Depression status was another significant mediator in this study. Depression risk for women changes across the life span, with a higher risk corresponding to life stages in which ovarian hormones fluctuate across the monthly menstrual cycle and reproductive events, such as parturition and menopause. Previous studies in the Chinese population have found that the number of births has a great effect on women's mental health status, especially their depression status [35, 36]. Basic and clinical studies have demonstrated that depression is associated with reduced size of brain regions that regulate mood and cognitive function, including the prefrontal cortex and hippocampus, and decreased neuronal synapses in these areas [37]. Nevertheless, it has been well established that PA has great potential to decrease the risk of depression [38] and may be an effective treatment for depression in the elderly [39]. In addition, we found a chain link between depression status and nutritional status, which is consistent with a previous study. Bailly et al. demonstrated that lack of pleasure, as a symptom of depression, could lead to poor food intake and further affect nutritional status [40]. Although BMI was commonly identified as a significant response to PA, it was not significantly associated with PA in this study after adjusting for possible covariates.

This study has several limitations that must be considered. This was a cross-sectional study; therefore, we could not determine the causal relationship between PA and cognitive function. Except for parity and menopause status, other information on reproductive history was unavailable, including age at menopause, menarche age, age at first birth, breastfeeding history; accordingly, we could not carry out subgroup analyses to further identify the relationship. Additionally, the APOE genotype could cause some bias in the different cognitive responses to PA between the low- and high-parity groups, which we cannot control in this study. Moreover, our results would be more convincing if combined with analysis of the nulliparity group.

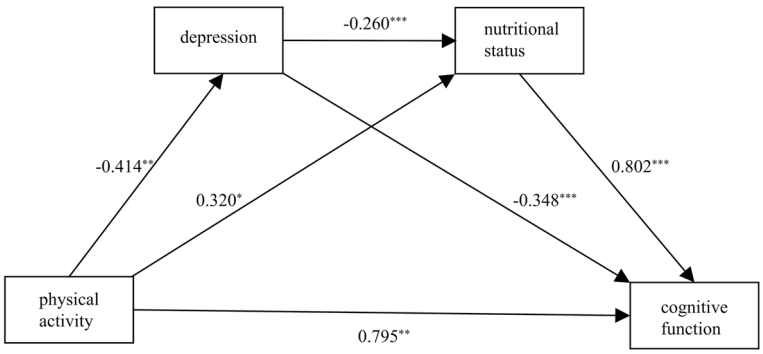

Fig. 2 The chain-mediating effects of depression and nutritional status on the association between physical activity and cognitive function. $^{*}P<0.05$, $^{**}P<0.01$, $^{***}P<0.001$

Table 4 Chain mediating effects of depression and nutritional status on the relationship between physical activity and cognitive function

	Path	Effect	SE	P	95% CI	effect size (%)
Direct effect	Physical activity → cognitive function	0.795	0.278	0.004	0.249, 1.322	61.964
Mediating effect	Path a: Physical activity → depression → cognitive function	0.144	0.061	0.017	0.047, 0.281	11.224
	Path b: Physical activity → nutritional status → cognitive function	0.257	0.103	0.013	0.071, 0.475	20.031
	Path c: Physical activity → depression → nutritional status → cognitive function	0.086	0.031	0.005	0.032, 0.149	6.703
Total indirect effect		0.487	0.134	< 0.001	0.243, 0.759	37.958
Total effect		1.283	0.3	< 0.001	0.732, 1.848	

SE standard error, *CI* confidence interval, *effect size (%)* the ratio of indirect effect to total effect

Conclusions

In conclusion, the results of this study are consistent with the hypothesis that there are different cognitive responses to PA between the low- and high-parity groups, and further provide evidence of the chain-mediating effects of depression and nutritional status on the relationship between PA and cognitive function.

Abbreviations

PA	Physical activity
BMI	Body mass index
MMSE	Mini-Mental Status Examination
MNA	Mini Nutritional Assessment
GDS-15	15-Item Geriatric Depression Scale
AD	Alzheimer's disease

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12905-025-03548-y.

Supplementary Material 1

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Authors' contributions

Xiaotong Chen conceived and designed the study, performed the analyses, wrote the first draft of the manuscript, contributed to the interpretation of the results and critically revised the manuscript. Kai Wei participated in data collection, co-wrote the first draft of the manuscript with xiaotong Chen, contributed to the interpretation of the results and critically revised the manuscript. Shanshan Peng contributed to the interpretation of the results and critically revised the manuscript. Na Liu contributed to the interpretation of the results and critically revised the manuscript. Leqi He contributed to the interpretation of the results and critically revised the manuscript. Biying Wu contributed to the interpretation of the results and critically revised the manuscript. Meifang Shi conceived and designed the study, contributed to the interpretation of the results and critically revised the manuscript. Yong Lin conceived and designed the study, contributed to the interpretation of the results, and critically revised the manuscript.

Kai Wei participated in data collection, co-wrote the first draft of the manuscript with xiaotong Chen, contributed to the interpretation of the results and critically revised the manuscript.

Shanshan Peng contributed to the interpretation of the results and critically revised the manuscript.

Na Liu contributed to the interpretation of the results and critically revised the manuscript.

Leqi He contributed to the interpretation of the results and critically revised the manuscript.

Biying Wu contributed to the interpretation of the results and critically revised the manuscript.

Meifang Shi conceived and designed the study, contributed to the interpretation of the results and critically revised the manuscript.

Yong Lin conceived and designed the study, contributed to the interpretation of the results, and critically revised the manuscript.

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Data availability

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

Declarations

Ethics approval and consent to participate

This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by Huashan Hospital Institutional Review Board (N0.KY2020-004). All participants provided informed written consent prior to their participation.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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