Article

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Relationship between Pain and Dementia: The Mediating Effect of Depression among Chinese Elderly

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Abstract

Background: Chronic pain poses a significant problem for older adults and may potentially impact cognitive function. This study aimed to examine the cross-sectional relationship between pain severity and cognitive function in elderly individuals residing in the community. Additionally, this study sought to examine the mediating effect of depression on the relationship between pain and dementia.

Methods: The study sample was derived from the 2018 China Health and Aging Longitudinal Study (CHARLS), comprising cross-sectional data from 4559 community residents aged 65 years or older. The primary outcome assessed was the occurrence of dementia, while the main independent variable was pain severity (none, little, somewhat, quite a bit, very). Depression score served as the mediating factor. Chi-square and binary logistic regression analyses were performed to examine the relationship between depression and the occurrence of pain and dementia. An intermediate model was constructed by stepwise regression.

Results: The study indicates a significant association between cognitive impairment and both chronic pain and depressive symptoms in older adults living in China. Individuals who frequently report experiencing pain exhibit a higher likelihood of developing dementia when compared to those who do not report any pain (odds ratio (OR) = 1.72, $p < 0.001$). Moreover, depressive symptoms significantly mediate the relationship between pain and dementia, with the mediating effect accounting for 65.25%.

Conclusions: Chronic pain not only directly impacts patients' cognitive function but also indirectly exacerbates cognitive impairment through depressive symptoms as a mediating variable. For elderly individuals experiencing depressive symptoms, it is important to provide appropriate psychological treatment in conjunction with pain management strategies.

Keywords

chronic pain; cognitive function; depressive symptoms; elderly

Background

Pain is defined as an unpleasant sensation and emotional response associated with real or potential tissue damage. When pain persists or recurs for more than 3 months, it is characterized as chronic pain [1]. Its occurrence and development involve biological, psychological, and social factors, posing significant challenges to both physical and mental well-being. As individuals age, degenerative changes in various bodily systems and the presence of multiple diseases contribute to a higher prevalence of chronic pain among the elderly [2,3]. According to statistics, chronic pain affects 25%–50% of the global population, with rates as high as 83% among elderly individuals in nursing homes [4].

Chronic pain is characterized by abnormal sensory processes and is closely linked to cognitive, emotional, and social dysfunction [5]. Among older adults, chronic pain interferes with daily functioning and often leads to severe physical disability and impaired mobility. Moreover, chronic pain is documented as one of the primary contributors to disability and medical consultations among the el-

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derly [6–8]. Despite its significant impact, pain in the elderly is often overlooked and underestimated. Alarmingly, more than one-third of patients with persistent pain do not receive analgesic treatment [9], which has a serious impact on their health, daily functioning, and overall quality of life.

Cognitive decline is a neurodegenerative condition that becomes evident as individuals age, with dementia representing the most severe manifestation. The increase in the age and number of populations is expected to increase the prevalence of dementia, exerting significant adverse effects on families, societies, and healthcare systems worldwide [10,11]. Research indicates that interventions targeting modifiable risk factors could potentially reduce dementia incidence by up to 40% [12]. Prior studies have confirmed the association between cognitive impairment and several diseases marked by chronic pain as the predominant symptom, including fibromyalgia (FM), diabetic neuropathy, rheumatoid arthritis, and migraine [13–18]. More than 50% of patients with chronic pain exhibit impaired attention [19,20], particularly notable in those with neuropathic pain and fibromyalgia. These individuals demonstrate lower cognitive screening scores and difficulties with memory and executive function [18,21].

Research has indicated that individuals with chronic pain often experience depression and other negative emotions [22,23]. Furthermore, individuals with chronic pain and concurrent depression tend to experience more significant functional decline, reduced treatment responsiveness, and higher healthcare costs [24]. Several studies have established a notable link between depression and cognitive decline [25,26]. While previous research has clarified the relationship between pain, cognition, and depression, few studies have investigated the potential mediating role of depression in the association between pain and cognitive impairment.

Studying the impact of pain intensity on cognitive function holds significant potential for risk stratification and informing the development of early interventions for cognitive impairment. Consequently, this study aims to examine the relationship between pain and cognitive function among elderly individuals in the community, aiming to determine whether pain serves as a risk factor for cognitive decline. Additionally, the study will investigate whether depression mediates the relationship between pain and cognitive function in elderly individuals through mediating analysis. Moreover, this research aims to clarify the interrelationships among pain, depression, and cognitive function, aiming to provide a scientific foundation and practical guidance for preventing and intervening in cognitive decline among elderly individuals in community settings. Ultimately, the goal is to reduce cognitive decline and its associated adverse outcomes, thereby improving physical function and quality of life among the elderly.

Materials and Methods

Study Population and Sampling

This study utilized data from the 2018 China Health and Retirement Longitudinal Study (CHARLS https://charls.charlsdata.com/pages/data/111/zh-cn.html). A baseline survey was conducted in 1988, followed by eight subsequent surveys from 2000 to 2018. The study involved individuals aged 65 and older in 22 provinces, municipalities, and autonomous regions across China, using questionnaires and household surveys as the primary data collection methods.

Based on the purpose of this study, the exclusion criteria for the selection of participants are as follows: (1) age <65 years old; (2) no pain and depressive symptoms data; (3) no age, sex, education, marital status, current residence, current smoking, alcohol drinking, or chronic diseases information available for this group of individuals; (4) individuals diagnosed with Alzheimer's Disease.

After applying the aforementioned exclusion criteria, we selected 4559 subjects from the original 17,708 individuals who participated in the fourth wave of the CHARLS for further analytical research.

Measures

Depressive Symptoms

A 10-item scale was developed to measure depressive symptoms and is considered a simplified version of the depression scale developed by Radolff at the National Institute of Mental Health. The scale was developed using the 20 items from the geriatric depression scale, selecting the 10 most relevant items for diagnosing clinical depression [27]. A higher score indicates more severe depressive symptoms. Respondents rate the frequency of their experiences over the past week on a scale of 1 to 4, with questions 5 and 8 designated for "Reverse Scoring". This abbreviated scale is more concise and efficient while maintaining efficacy in depression screening.

Pain Assessment

Pain is an inherently subjective experience that cannot be measured using physiological markers or biometrics. Thus, pain assessment relies heavily on self-reports. Pain characteristics were collected using self-reported questions. In the CHARLS questionnaire, respondents were asked, "Are you often troubled by any bodily pains?" Pain variables were divided into "yes" and "no", with pain severity classified as none, little, somewhat, quite a bit, or very.

Cognitive Status

Patient cognitive status was evaluated using the Mini-Mental State Examination (MMSE) scale. The MMSE is widely used for clinical assessment of patients' cognitive function. It was initially developed by Folstein *et al*. [28] in 1975 and has since undergone several revisions and adaptations. Comprising 30 questions, the scale assesses various cognitive domains including orientation, memory, attention, calculation, recall, language, and visuospatial ability, yielding a total score of 30 [29,30]. Cut-off values for dementia diagnosis on the MMSE were established based on the participants' education levels: scores of $\leq$17 for illiterate individuals, $\leq$20 for those with elementary school education, and $\leq$24 for participants with middle school education and above.

Covariates

The covariates included various sociodemographic characteristics of the respondents, including gender, age, residence area (urban or town, rural), education (Uneducated, primary school, Middle school, college or above), marital status (unmarried, including divorced and widowed), past/current smoking (yes or no), past/current alcohol consumption (yes or no), and chronic diseases such as hypertension, hyperlipidemia, and diabetes.

Statistical Analysis

The study used IBM SPSS version 25.0 (Chicago, IL, USA) for all statistical analyses. Categorical variables were expressed as frequencies and percentages and analyzed by chi-square analyses, while continuous variables were expressed as mean (M) $\pm$ standard deviation (SD) and analyzed by independent-sample *T*-tests. Logistic regression was used to analyze the odds ratio (OR) and 95% confidence interval (CI) for the cross-sectional associations between pain and dementia at baseline. Specifically, a binary logistic regression analysis was conducted with dementia as the dependent variable and pain severity as the independent variable. The regression models were constructed in a stepwise manner, incorporating various covariates. Initially, Model 1 included pain as the sole predictor. Model 2 incorporated additional covariates such as age, sex, urbanity, education level, marital status, education, smoking, alcohol consumption, and hyperlipemia. Model 3 further included the depression scale. To demonstrate the correlation between pain, depressive symptoms, and cognitive function, a stepwise regression method was used to analyze the intermediary effect. Initially, a linear regression model was established to examine the relationship between pain and cognitive function. Subsequently, depression symptoms were included as mediating variables to assess whether the impact of pain on cognitive function was attenuated or eliminated. If the effect of pain on cognitive function diminishes or disappears in the presence of depressive symptoms, it suggests that depressive symptoms act as a mediator between pain and cognitive function. Statistical significance was considered at $p < 0.05$ for all statistical analyses.

Results

Among the 4559 respondents, the mean age was 71 $\pm$ 5.28 years, with 2373 males (52.1%) and 2186 females (47.9%). A total of 2731 individuals reported experiencing pain, representing 59.9% of the total. Among the 2731 reporting pain, 1531 (56.1%) were women. Additionally, 353 individuals reported frequent pain, representing 7.7% of the total respondents, while 1380 elderly individuals were affected by dementia, accounting for 30.3% of the total. As indicated in Table 1, individuals diagnosed with dementia were significantly older on average ($p < 0.001$), more likely to be female ($p < 0.001$), unmarried ($p < 0.001$), residing in rural areas ($p < 0.001$), had lower levels of education ($p < 0.001$), higher depression scores ($p < 0.001$), and a history of regular alcohol and smoke consumption ($p < 0.001$).

The findings from the binary logistic regression analysis indicated a higher likelihood of dementia development among individuals who frequently reported experiencing pain compared to those who did not report any pain (OR = 1.72, $p < 0.001$). Furthermore, the association between pain and dementia persisted even after controlling for demographic variables, chronic illnesses, and other relevant factors, as shown in Table 2. However, upon inclusion of depression scores in the model, the association between pain and dementia was attenuated and lost statistical significance.

Table 1. Comparison of baseline characteristics in people with or without dementia.

Variable	Normal (n = 3179)	Dementia (n = 1380)	*t* value	χ^2 value	*p* value
Age	70.69 ± 4.98	72.08 ± 5.8	–8.24	-	<0.001
Depression scale	17.66 ± 6.17	19.9 ± 6.69	–11.31		<0.001
Female *n* (%)	1401 (44.1)	785 (56.9)		63.30	<0.001
Urbanity *n* (%)				105.39	<0.001
Town center	764 (24.0)	169 (12.2)			
Rural-urban	225 (7.1)	59 (4.3)			
Rural areas	2190 (68.9)	1152 (83.5)			
Married *n* (%)	2569 (80.8)	984 (71.3)		50.58	<0.001
Pain severity *n* (%)				21.82	<0.001
None	1319 (41.5)	509 (36.9)			
Little	997 (31.4)	427 (30.9)			
Somewhat	332 (10.4)	153 (11.1)			
Quite a bit	319 (10)	150 (10.9)			
Very	212 (6.7)	141 (10.2)			
Education level, *n* (%)				97.16	<0.001
Uneducated	1429 (45)	793 (57.5)			
Primary school	1015 (31.9)	255 (18.5)			
Middle school	677 (21.3)	316 (22.9)			
College and above	58 (1.8)	16 (1.2)			
Smoke *n* (%)	1112 (35)	565 (41)		14.71	<0.001
Drink *n* (%)				29.2	<0.001
Never	872 (27.4)	306 (22.2)			
Occasionally	257 (8.1)	74 (5.4)			
A lot	2050 (64.5)	1000 (72.5)			
Hypertension *n* (%)	380 (11.9)	184 (13.3)		1.31	0.252
Diabetes *n* (%)	189 (5.9)	94 (6.8)		0.98	0.328
Hyperlipemia *n* (%)	353 (11.1)	121 (8.8)		8.22	0.004

To gain a deeper understanding of the correlation between pain and dementia, we analyzed the mediating effects of pain, depression, and cognitive function scores (Fig. 1). The results of the linear regression analysis indicated a significant negative correlation between pain scores and cognitive function scores (C = –0.155, $p < 0.001$). Additionally, a notable positive correlation was observed between the pain score and depression score (a = 0.389, $p < 0.001$). When including the depression score into the regression model examining the association between pain score and cognitive function score, the regression coefficient of pain on cognitive function decreased but remained statistically significant (C' = –0.054, $p < 0.001$). Additionally, a significant association was observed between depressive symptom score and frailty score (b = –0.260, $p < 0.001$). After assessing multicollinearity in the aforementioned models, it was determined that the Tolerance values exceeded 0.2 and the Variance Inflation Factor (VIF) remained below 5, suggesting the absence of multicollinearity among the variables in the model. The results indicated that depressive symptoms significantly mediated the relationship between pain and dementia, with the mediating effect accounting for 65.25%.

Discussion

The results of our study indicate a significant association between cognitive impairment and both chronic pain and depressive symptoms in elderly adults in China. Furthermore, it was found that depressive symptoms played a partial mediating role in the relationship between chronic pain and cognitive function.

The study revealed that 59.9% of individuals aged 65 and above have encountered pain, with 7.7% frequently reporting pain. Of note, the prevalence of pain was notably higher among women compared to men, consistent with prior research findings. This gender difference may be attributed to physiological differences, as women tend to exhibit increased pain perception and reaction. Addition-

Table 2. Binary regression analysis of dementia.

Variable	Model 1			Model 2			Model 3		
	β	OR (95% CI)	*p* value	*β*	OR (95% CI)	*p* value	*β*	OR (95% CI)	*p* value
Depression scale	-	-	-	-	-	-	0.05	1.05 (1.03–1.07)	<0.001
Pain severity									
No pain		Reference			Reference			Reference	
Little	0.10	1.11 (0.95–1.29)	0.18	0	1.00 (0.86–1.18)	0.91	0.09	0.91 (0.68–1.21)	0.60
Somewhat	0.18	1.19 (0.96–1.48)	0.10	0.03	1.03 (0.82–1.29)	0.81	0.09	0.91 (0.61–1.37)	0.52
Quite a bit	0.19	1.21 (0.98–1.51)	0.07	0.08	0.92 (0.74–1.17)	0.52	0.34	0.71 (0.45–1.12)	0.66
Very	0.54	1.72 (1.36–2.18)	<0.0001	0.28	1.34 (1.03–1.75)	0.026	0.06	1.06 (0.67–1.68)	0.14

Model 1: Included pain only.

Model 2: Adjusted for age, sex, urbanity, education level, marital status, education, smoking, alcohol drinking, and hyperlipemia.

Model 3: Adjusted for age, sex, urbanity, education level, marital status, education, smoking, alcohol drinking, hyperlipemia, and depression scale.

OR, odds ratio; CI, confidence interval.

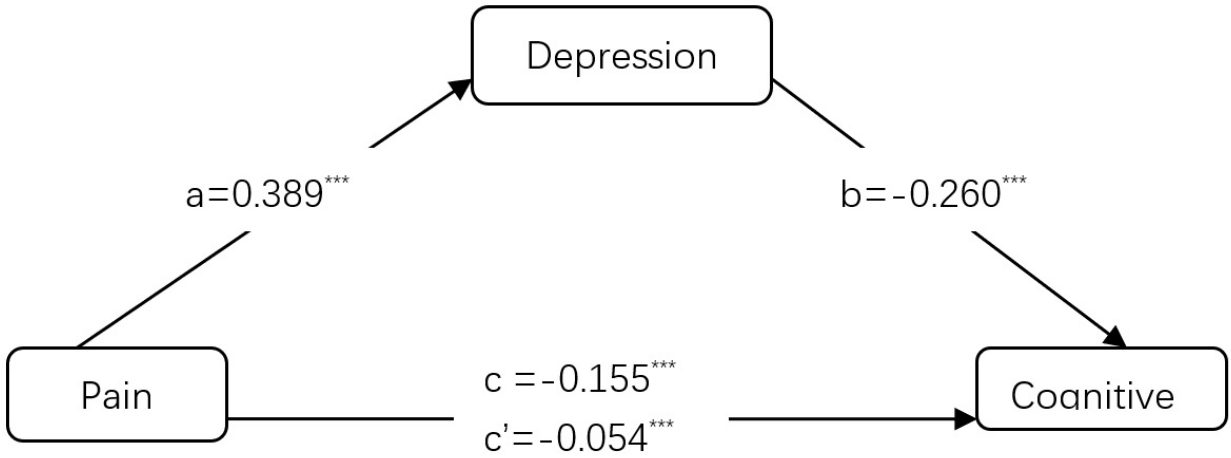

Fig. 1. Intermediate analysis path diagram. Note: Path coefficients were shown in the standardized regression coefficient. *** $p <$ 0.001. Mediation models of pain, depressive symptoms, and cognitive function in Chinese elderly adults. Represents the potential mediating effect of depressive symptoms on the association between pain and cognitive function. The effects of each variable relationship are shown alongside their respective arrows.

ally, women may also experience unique types of pain, such as menstrual pain, childbirth, and breastfeeding. Moreover, women's heightened susceptibility to emotional factors may exacerbate or trigger chronic pain compared to men [31,32]. Despite the evident prevalence of pain among the elderly community, there has been insufficient focus on the diagnosis and treatment of pain [9], leading to its frequent neglect or delayed management.

Previous research, both cross-sectional and longitudinal studies, has demonstrated an association between chronic pain and cognitive function. In a longitudinal study tracking cognitive trajectories among individuals in American neighborhoods, participants experiencing persistent pain exhibited a 9.2% decline in memory scores over time, with a corresponding 7.7% higher dementia prevalence compared to those without such pain [33]. Similarly, a study in Taiwan found that individuals aged 50 and above experiencing pain had an increased risk of dementia compared to those without pain (adjusted hazard ratio [AHR]: 1.21; 95% confidence interval [CI]: 1.15–1.26) [34]. The findings of our study align with previous research, revealing elevated pain levels among older adults with dementia compared to cognitively normal older adults. Further analysis revealed a notable association between pain and cognitive function, indicating lower cognitive function scores in elderly adults experiencing pain. Chronic pain has been identified as a risk factor for cognitive decline; however,

the biological mechanism through which pain induces cognitive impairment remains unclear. Prior studies suggest a potential link between cognitive decline in individuals with chronic pain and alterations in the volume of gray matter in the brain [35]. Individuals enduring chronic pain exhibit diminished cortical gray matter in the bilateral dorsolateral prefrontal cortex (DLPFC), thalamus, brainstem, primary somatosensory cortex (S1), and posterior parietal cortex, alongside atypical brain functional patterns associated with cognitive functions [36]. These changes result in a decrease in cognitive function. However, pain treatment can lead to a significant increase in cortical thickness in affected regions and a return to baseline levels of functional brain activities [37]. Moreover, chronic pain-induced dysfunction of the LC-NE system can result in cognitive and emotional behavioral abnormalities [38]. Additionally, chronic pain can elevate microglia activation and neuroinflammation, which is considered contributing factors to Alzheimer's disease pathogenesis [39,40].

Although the limitations of our study precluded confirmation of the aforementioned potential biological mechanisms, our mediating analysis revealed that depressive symptoms partially mediate the link between pain and cognition. This finding offers an alternative perspective on how pain contributes to cognitive impairment. Previous research suggests that individuals experiencing pain are more likely to develop depression or anxiety disorders [22]. Furthermore, the quantity of pain sites, pain severity, and pain frequency have emerged as the most reliable indicators of depression in elderly adults within the general population [41,42]. Psychological and epidemiological studies have also established a correlation between the exacerbation of depressive symptoms in elderly adults and the deterioration of cognitive function. Depressive symptoms are recognized as a risk factor for the progression of mild cognitive impairment to dementia. Additionally, negative emotions, sleep disorders are also considered to be precursors of cognitive function decline [42–44]. This observation aligns with our research results. In conclusion, it can be inferred that persistent chronic pain may result in depression and contribute to cognitive deterioration in the elderly population.

This study elucidated the correlation between pain, depressive symptoms, and cognitive function in elderly Chinese adults. This discovery holds significant implications for both public health policy and clinical practice.

Assessing and managing pain in community residents is a complex undertaking that necessitates the use of more comprehensive and reliable tools for accurately identifying pain. Additionally, it requires a multidimensional approach to pain management. The effective management of pain should be considered an essential component of both preventive and interventional strategies for addressing cognitive impairment in the elderly. Particularly for older individuals exhibiting symptoms of depression, it is essential to implement appropriate psychological treatment measures alongside pain management.

The study's strength lies in its substantial sample size and strong representativeness. However, the study is still subject to certain limitations. Due to the cross-sectional study design, this investigation was unable to establish a causal relationship between the different variables. Future longitudinal studies are necessary to verify the association more comprehensively between pain and cognitive impairment, and to elucidate its underlying mechanism. Furthermore, the present study did not evaluate the specific pain location, pain duration, or the type of pain relief treatment received by the elderly. Subsequent research endeavors could incorporate these factors to enhance comprehension of the association between pain and cognitive impairment.

Conclusions

In this study, we identified a significant negative correlation between pain severity in elderly adults and their current cognitive function. After adjusting for confounding variables, we observed a notable increase in the risk of cognitive impairment among elderly individuals experiencing frequent pain. Furthermore, our findings reveal that depression, often comorbid in older adults, is more prevalent among those who frequently experience pain, further exacerbating the risk of cognitive impairment. Additionally, depression partially mediates the relationship between pain and cognitive impairment. There is a necessity to advocate for regular pain assessment and prompt implementation of pain management and psychological interventions. These measures could potentially delay cognitive decline and support the process of healthy aging.

Availability of Data and Materials

The raw data used in this study are freely available from the China Health and Retirement Longitudinal Study (CHARLS; https://charls.charlsdata.com/pages/data/111/zh-cn.html), a nationally representative longitudinal survey of the population in China organized by Peking University National School of Development.

Author Contributions

BRD: Conceptualization, writing—review and editing; WRD: acquiring the data, conducting the formal analysis, and writing the original draft; JH and QLH provided significant help and advice on data processing and analysis, ensuring the accuracy and integrity of data interpretation. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

This study used the free data from the China Health and Retirement Longitudinal Study (CHARLS). The CHARLS was conducted following The Code of Ethics of the World Medical Association (World Medical Association Declaration of Helsinki) for experiments involving humans. Ethical approval was granted from the Biomedical Ethics Review Committee of Peking University (approval id. IRB00001052–11015), and all participants provided informed consent.

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Conflict of Interest

The authors declare no conflict of interest.

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