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Social isolation and cognitive decline among older adults with depressive symptoms: prospective findings from the China Health and Retirement Longitudinal Study

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ABSTRACT

Objectives: : Identifying potentially modifiable risk factors of cognitive decline among people with depressive symptoms could provide insight into strategies for improving treatment effect of depression and prevention of dementia. Quite a few studies have examined the association between social isolation and cognitive function directly among depressed older adults and the results are still mixed. The aim is to examine the association of social isolation and cognitive decline among older adults with depressive symptoms in a non-Western country.
Methods: : This study used data from the China Health and Retirement Longitudinal Study (CHARLS). Depressive symptoms were measured by the Chinese version of the 10-item Center for Epidemiological Studies Depression Scale (CESD-10) (elevated depressive symptom cutoff≥10). Social isolation was assessed based on responses to four items: marital status, residence, contact with children, and social activity. Lagged dependent variable regressions adjusted for confounding factors were used to evaluate the association between baseline social isolation and follow-up cognitive function.
Results: : A number of 2,507 participants [mean age (SD)=61.37 (7.26); male, 41.0%] with increased depressive symptoms were available for the present study. Baseline social isolation was significantly associated with 4-year episodic memory (β=−0.08, $p<0.001$) in depressed women, but not men (β=−0.03, $p=0.350$). No significant association between baseline social isolation and follow-up mental status was found for women (β=−0.04, $p=0.097$) or men (β=0.01, $p=0.741$).
Discussion: : This longitudinal study found that social isolation was significantly associated with memory decline over 4 years among depressed women (but not men) in China.

Introduction

Depression, one of the most common psychiatric disorders among older populations (Lim et al., 2011; Qin, Wang, & Hsieh, 2018), has been linked to an increased risk of morbidity (Frasure-Smith & Lespérance, 2003) and mortality (Blazer, 2003). The prevalence of depression and depressive symptoms has been sharply increasing over the past decades. Globally, more than 264 million people of all ages suffered from depression (James et al., 2018). One study in China using nationally representative samples has found approximately 30% of men and 43% of women aged 45 years and older experiencing depressive symptoms (Lei, Sun, Strauss, Zhang, & Zhao, 2014). Another nationally representative survey also showed that 4.08% of Chinese adults suffered from depression and 37.86% frequently experienced depressive symptoms (Qin et al., 2018).

Although depression is mainly characterized by negative mood, impaired cognition is increasingly acknowledged as a common symptom among depressed people (Baune et al., 2010; Motter et al., 2016). Impaired cognition has been estimated to occur in around two-thirds of depressed older patients (Afridi, Hina, Qureshi, & Hussain, 2011). In addition, cognitive performance in depressed patients is often observed 1-2 standard deviations below the norm (Bortolato, F Carvalho, & S McIntyre, 2014). Poor cognition is associated with poor response to treatment of depression (Cambridge, Knight, Mills, & Baune, 2018).

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Recent studies suggest that maintenance of cognitive dysfunction in the remitted stage presents a barrier to functional recovery in a number of domains (Knight, Air, & Baune, 2018; Rock, Roiser, Riedel, & Blackwell, 2014). Thus, identifying potentially modifiable risk factors of cognitive decline among people with depressive symptoms could provide insight into strategies for improving treatment effect of depression and prevention of dementia.

Social isolation is a global public health challenge that influences the health of individuals across the life-course (Cudjoe et al., 2020). There is substantial evidence that social isolation is longitudinally associated with increased rates of cognitive decline in older ages (Evans, Martyr, Collins, Brayne, & Clare, 2019; Yu, Steptoe, Chen, & Jia, 2020). However, most of these studies were conducted in general population. Accumulated evidence has indicated that for those depressed older adults, the same health risk factors may have different effects on health outcomes from those non-depressed ones (Dickinson, Potter, Hybels, McQuoid, & Steffens, 2011; Eslami, Zimmerman, Grewal, Katz, & Lipton, 2016). For example, Dickinson et al. had found the effects of social interaction on cognition varied according to depression status (with vs. without) (Dickinson et al., 2011). Change in social interaction predicted change in cognitive total score among depressed participants rather than non-depressed comparison group. Also, social isolation had been found to be associated with elevated interleukin (IL-6) and C-reactive protein (CRP) levels in depressed men, but not in healthy comparisons (Häfner et al., 2011). Quite a few studies have examined the association between social isolation and cognitive function among depressed older adults directly and the results are still mixed. Using data from the Cognitive Function and Ageing Study–Wales (CFAS-Wales), Evans and his colleagues found a significant cross-sectional association between isolation and poor cognitive function in older people with depressive symptoms (I. E. Evans et al., 2019). In contrast, a study conducted in Duke University Medical Center found that IADL rather than social support predicts cognitive deterioration in late-life depression (Riddle, McQuoid, Potter, Steffens, & Taylor, 2015). Similarly, another recent longitudinal study found no association between social network size and cognitive impairments or decline among depressed older adults (Kuiper et al., 2019). However, some of these studies were limited in cross-sectional design or small sample size. While others were focus on the perceived social support rather than objective social isolation. Further studies are needed to clarify the effects of social isolation on cognitive function among depressed older adults. It is also worth noting that most of these existing studies have focused on Western countries. It remains unclear to what extent the association of social isolation with cognitive function is applied to non-Western populations with depressive symptoms.

In order to examine the association of social isolation and cognitive decline among older adults with depressive symptoms in a non-Western country, the present study was conducted by using data from a nationally representative longitudinal survey of the Chinese older adults. We hypothesized that social isolation would be longitudinally associated with cognitive decline in depressed participants. Regarding previous evidence indicating possible gender differences in the association between social relationship factors and health (Shumaker & Hill, 1991; Shye, Mullooly, Freeborn, & Pope, 1995), we also tested the interaction of gender and social isolation on cognitive function for our sample.

Methods

Participants

Data were obtained from the China Health and Retirement Longitudinal Study (CHARLS), a nationally representative longitudinal survey of the middle-aged and elderly population (45+) in China. The baseline survey was carried out between June 2011 and March 2012 with a response rate of 80.5% (Zhao, Hu, Smith, Strauss, & Yang, 2012). A number of 17,708 respondents were recruited at baseline. In the current study, participants were from two waves of the CHARLS (2011 and 2015) and restricted to those aged 50 and above (n = 13,649) in the baseline. Participants were excluded if they had any missing values on baseline (n = 2,944) or follow-up (n = 1,886) measure of cognitive function, as well as other control variables (n = 1,889). According to the aim of this study, participants free of depressive symptoms (n = 4,423) at baseline were also excluded. Finally, 2,507 participants with increased depressive symptoms were available for the present study [n = 2,507, mean age (SD) = 61.37 (7.26); male, 41.0%]. The process of the analytical sample selection is shown in Figure 1. The ethics application for collecting data on human subjects was approved by Peking University's Institutional Review Board.

Measures

Depressive symptoms

Depressive symptoms were measured by the Chinese version of the 10-item Center for Epidemiological Studies Depression Scale (CESD-10), which had high validity and reliability in the Chinese population (Boey, 1999; Chen & Mui, 2014). Respondents were asked how frequently in the last week they: were bothered by things; had trouble keeping mind on things; felt depressed; felt everything they did require an effort; felt hopeful about the future; felt fearful; had restless sleep; were happy; felt lonely; and could not get going. Each item was rated on a Likert scale ranged from 0 to 3 with answers varying from 'rarely or none of the time (<1 day)' to 'most or all of the time (5-7 days)'. Sum of the scores ranged from 0 to 30, with higher scores indicating an increased level of depressive symptoms. A cut-off point of 10 has been adopted in this study to define elevated depressive symptoms since it has been proven to be highly sensitive and specific by previous studies (Boey, 1999; Lei et al., 2014; X. Yang et al., 2020).

Social isolation

An index of social isolation was computed by assigning one point if respondents were not married/not living with a partner; had less than weekly contact (by phone, in person, or by e-mail) with children; were living in the rural rather than urban areas; and were not participating in any social activities over the last month (e.g., interacted with friends; played chess or cards; went to a sport, social, or other clubs) (Glei, Goldman, Ryff, Lin, & Weinstein, 2012; Steptoe, Shankar, Demakakos, & Wardle, 2013; Yu, Steptoe, Niu, & Jia, 2020). Inclusion of urban/rural status as one component of social isolation is in consideration of the fact that in China, older adults living in rural areas are lonelier and more isolated than those living in urban areas (Wang et al., 2011; K. Yang & Victor, 2008; Yu, Steptoe, Niu, et al., 2020). Score of isolation ranged 0 to 4 with a higher score indicating a higher level of social isolation.

Cognitive function

CHARLS included similar items for cognitive function as those used in the American Health and Retirement Study (HRS), which were components of the Telephone Interview of Cognitive Status battery (TICS) (Crimmins, Kim, Langa, & Weir, 2011). Following previous studies using HRS and CHARLS data (Glei et al., 2012; Pan, Luo, & Roberts, 2018; Yu, Steptoe, Chen, et al., 2020), we constructed two measures of cognitive function. The first is an episodic memory measurement which was assessed by immediate and delayed recall. Immediate word recall was measured by respondents' capacity to immediately repeat, in any order, 10 Chinese nouns just read to them. After a four-minute measurement of self-rated depression, they are then asked to recall as many of the words as possible (delayed word recall). A single score of memory (ranged from 0 to 10) was calculated by averaging the immediate- and delayed-recall scores. The second cognitive measure is the mental status questions of the Telephone Interview of Cognitive Status (TICS) battery established to capture the intactness or mental status of individuals. TICS questions consist of the following items: serial 7 subtraction from 100 (up to five times); naming today's date (month, day, and year) and the day of the week; and the ability to

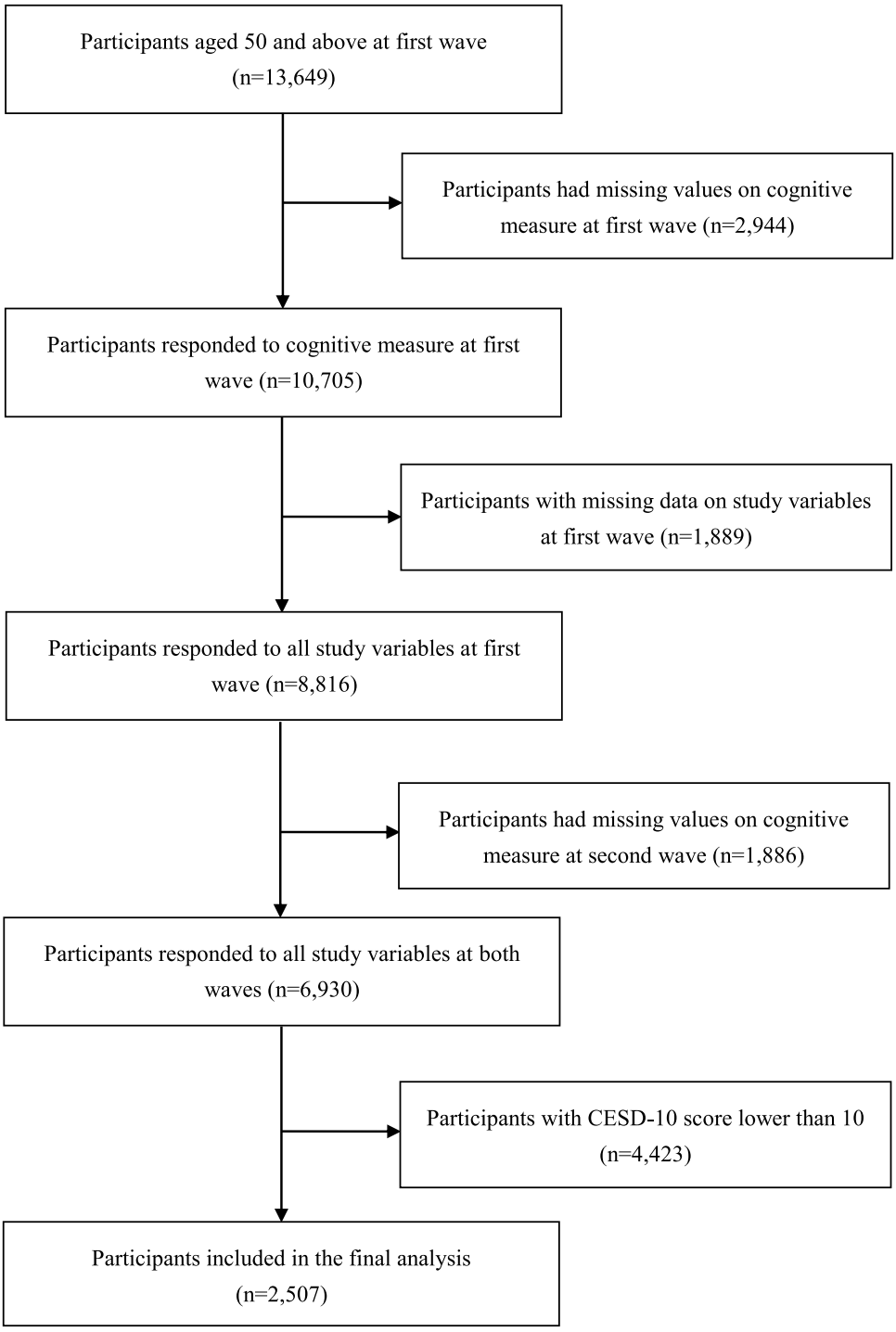

Fig. 1. Flowchart of sample selection

redraw a picture shown to him/her. Scores on these items were aggregated into a single score that ranged from 0 to 10. For all these measurements, higher scores indicated superior cognitive function.

Control variables

Data on all covariates were obtained at baseline. Age, gender, and education were self-reported. Education was dichotomized as lower than secondary school and secondary or above. Chronic diseases including hypertension, diabetes, stroke, and heart diseases were obtained by asking respondents if a physician had ever told them that they had the condition. Body mass index (BMI) was defined as weight in kilograms divided by height squared in meters. Health behaviors including smoking and drinking were collected using a standardized procedure. Respondents were asked whether they were current smokers and whether they consumed alcohol in the past 12 months.

Statistical Analysis

Characteristics of the overall sample at baseline were described using means and standard deviations for continuous data and percentages for categorical data. Chi-square tests or independent sample t-tests were conducted to examine differences for baseline characteristics between participants with no depressive symptoms and elevated depressive

symptoms. To assess the association between social isolation and cognitive function, we used lagged dependent variable regression models with Ordinary Least Squares estimation. Two models were fitted. In model 1, associations between social isolation and cognitive function were adjusted for all control variables including age, gender, education, BMI, chronic diseases, and healthy behaviors. Model 2 additionally included the interaction between isolation and gender. Because significant interaction was found, we reran lagged dependent variable regressions by gender. For all regression analyses, standardized regression coefficients (β) with corresponding robust standard errors were reported. A p-value <0.05 was considered significant. Analyses were carried out using IBM SPSS version 20.0.

Results

In total, 2,507 participants with elevated depressive symptoms were included in the final analysis [mean age (SD) = 61.37 (7.26); male, 41.0%]. Table 1 shows the characteristics of all the available participants at baseline. Compared to those whose CESD score < 10 (n = 4,423), participants with elevated depressive symptoms (n = 2,507) were older, more likely to be women, and had a lower level of education (all p<0.001). The depressed participants were more likely to have hypertension, diabetes, heart disease and stroke (all p<0.01), but less likely to be a smoker or an alcohol consumer (all p<0.001). Additionally, individuals who had elevated depressive symptoms had a higher level of isolation (mean score: 1.55 vs 1.26; p<0.001). Their episodic memory (mean score: 3.08 vs 3.66; p<0.001) and mental status (mean score: 5.73 vs 6.93; p<0.001) were worse than those who did not have depressive symptoms.

Table 2 lists the results of lagged dependent variable regressions for the cognitive function at follow-up in all participants with elevated depressive symptoms. Social isolation was significantly associated with follow-up episodic memory (β = −0.06, p < 0.001) when all control variables including age, gender, education, BMI, chronic diseases, healthy behaviors, CESD-10 score and baseline episodic memory score were adjusted (model 1). However, no significant association was observed between baseline social isolation and follow-up mental status (β = −0.02, p = 0.254) (model 1). In model 2, we additionally added the interaction term between isolation and gender on model 1. Significant interaction was found for mental status (β = −0.12, p = 0.047), but not episodic memory (β = −0.13, p = 0.059).

Simple effect analysis was then conducted to explore the pattern of the interaction between isolation and gender. The results were shown in Table 3. Baseline social isolation was significantly associated with 4-years episodic memory (β = −0.08, p < 0.001) in depressed women, but not men (β = −0.03, p = 0.350). No significant association between baseline social isolation and follow-up mental status was found for women (β = −0.04, p = 0.097) or men (β = 0.01, p = 0.741).

Table 1
Baseline characteristics of the available participants

Characteristic	All (n=6,930)	CES-D < 10 (n=4,423)	CES-D≥10 (n=2,507)	p-value
Age, M(SD), years	60.97 (7.25)	60.75 (7.23)	61.37 (7.26)	.001
Gender (male, %)	50.5	56.0	41.0	<.001
Education level, (Less than lower secondary education, %)	89.8	87.2	94.4	<.001
BMI, M (SD), kg/m^2	23.45 (3.90)	23.65 (3.83)	23.10 (4.00)	<.001
Hypertension, %	28.0	26.3	31.1	<.001
Diabetes, %	6.9	6.2	8.0	.004
Heart disease, %	13.5	11.3	17.4	<.001
Stroke, %	2.4	1.7	3.5	<.001
Smoking, %	33.0	34.9	29.6	<.001
Drinking, %	33.9	37.1	28.3	<.001
CESD-10, M (SD)	8.35 (6.30)	4.42 (2.77)	15.30 (4.53)	<.001
Baseline Episodic memory, M (SD)	3.45 (1.62)	3.66 (1.67)	3.08 (1.48)	<.001
Baseline Mental Status, M (SD)	6.50 (2.83)	6.93 (2.73)	5.73 (2.84)	<.001
Social isolation, M (SD)	1.37 (0.84)	1.26 (0.84)	1.55 (0.81)	<.001
Not married, %	11.7	9.5	15.7	<.001
Less than weekly contact with children, %	8.3	7.2	10.3	<.001
Live in the rural area, %	64.6	60.6	71.6	<.001
Not participate in social activities, %	52.4	49.3	57.8	<.001

M, mean; SD, standard deviation; BMI, body mass index; CESD, Center for Epidemiologic Studies Depression scale.

Discussion

In this study, a large representative sample of Chinese older adults with depressive symptoms was selected to examine the associations of social isolation with cognitive decline over a 4-year follow-up period. Overall, a higher level of social isolation was found to be significantly associated with decreases in episodic memory over time for older adults with depressive symptoms. Further analyses indicated that this association was limited to depressed women. For depressed men, neither episodic memory nor mental status was found to be associated with social isolation. To our best knowledge, this is the first large investigation of cognitive function in relation to social isolation for older adults with depressive symptoms in China using longitudinal data.

We have found a significant association between isolation and 4-year cognitive decline in depressed older adults, which is in contrast to some previous studies that did not detect similar association in depressed samples (Dickinson, Potter, Hybels, McQuoid, & Steffens, 2011; Kuiper et al., 2019; Riddle et al., 2015). Kuiper et al. found that social network size was not related with cognitive performance after 2 years (Kuiper et al., 2019). A study conducted with 299 cognitively intact depressed older adults found that disability rather than social support predicts cognitive decline (Riddle et al., 2015). In a longitudinal study, social support did not predict cognitive decline in 112 depressed older adults while a decrease in the frequency of social interaction was associated with a subsequent decrease in global cognitive performance and Digit Span Forward scores specifically (Dickinson et al., 2011). However, using social isolation index assessed by the Lubben Social Network Scale–6 (LSNS-6), Evans et al. found social isolation was significantly associated with poor cognitive function among older people with depression (I. E. Evans et al., 2019). One possible reason for these discrepancies could be different measurements of social isolation used by different studies. It might be some specific element of social isolation that play a role in cognitive decline among depressed older adults. According to our findings with evidence from previous studies, compare to social network size, frequency of social interaction might be more important in predicting cognitive decline in depressed older adults (Kuiper et al., 2019).

Several pathways may explain the association of social isolation with episodic memory in depressed older adults. First, as a potent factor that can induce stress, social isolation is thought to cause cognitive impairments through decreased connectivity and plasticity of the prefrontal cortex, resulting in impairments in working memory especially (Bruce S. McEwen & Morrison, 2013). Second, social isolation and depressive symptoms may have a synergistic effect on the increased release of glucocorticoids (Dickinson et al., 2011; B. S. McEwen, 2000). Cumulative exposure to glucocorticoids, in turn, could result in neurodegeneration of the hippocampus which is related to memory. No significant association was observed between social isolation and mental status in depressed older adults in the present study. However, previous studies conducted in general populations have found that social isolation was significantly associated with both mental status and episodic memory (Shankar, Hamer, McMunn, & Steptoe, 2013; Yu, Steptoe,

Table 2
Associations between baseline social isolation and subsequent episodic memory and mental status (n=2,507)

	Episodic Memory						Mental status					
	Model 1			Model 2			Model 1			Model 2		
	β	RSE	p	β	RSE	p	β	RSE	p	β	RSE	p
Age	−0.21	0.00	<.001	−0.21	0.00	<.001	−0.12	0.01	<.001	−0.12	0.01	<.001
Gender	−0.02	0.08	0.400	0.05	0.15	0.272	−0.13	0.13	<.001	−0.07	0.23	0.080
Education	0.08	0.13	<.001	0.08	0.13	<.001	0.07	0.22	<.001	0.07	0.21	<.001
BMI	0.04	0.01	0.020	0.04	0.01	0.024	0.04	0.01	0.015	0.04	0.01	0.017
Hypertension	−0.03	0.07	0.180	-0.03	0.07	0.184	0.02	0.11	0.192	0.02	0.11	0.188
Diabetes	0.03	0.12	0.173	0.02	0.12	0.195	0.01	0.19	0.677	0.01	0.19	0.721
Heart diseases	0.07	0.08	<.001	0.07	0.08	<.001	0.03	0.13	0.086	0.03	0.13	0.095
Stroke	−0.03	0.16	0.110	−0.03	0.16	0.098	−0.02	0.26	0.272	−0.02	0.26	0.248
Smoking	−0.04	0.08	0.060	−0.04	0.08	0.057	−0.03	0.13	0.114	−0.03	0.13	0.109
Drinking	0.02	0.07	0.327	0.02	0.07	0.318	0.02	0.12	0.167	0.02	0.12	0.161
Baseline EM	0.31	0.02	<.001	0.30	0.02	<.001	-	-	-	-	-	-
Baseline MS	-	-	-	-	-	-	0.50	0.02	<.001	0.49	0.02	<.001
CESD-10	−0.01	0.01	0.521	−0.01	0.01	0.496	-0.00	0.01	0.940	-0.00	0.01	0.915
Social isolation	**−0.06**	**0.04**	**<.001**	0.05	0.13	0.442	−0.02	0.06	0.254	0.08	0.20	0.129
Isolation*gender	-	-	-	−0.13	0.08	0.059	-	-	-	**−0.12**	**0.12**	**0.047**

β = standardized regression coefficient; RSE = robust standard error.
EM, episodic memory; MS, mental status; BMI, body mass index; CESD, Center for Epidemiologic Studies Depression scale.

Table 3
Associations between baseline social isolation and subsequent cognitive function by gender

	Episodic Memory			Mental status		
Gender	β	RSE	p	β	RSE	p
Women [a] (n=1,480)	**−0.08**	**0.05**	**<.001**	−0.04	0.08	0.097
Men [a] (n=1,027)	−0.03	0.06	0.350	0.01	0.09	0.741

β = standardized regression coefficient; RSE = robust standard error.
[a] : adjusted for age, education, BMI, hypertension, diabetes, heart disease, stroke, smoking, drinking, CESD-10, and baseline episodic memory or mental status.

Chen, et al., 2020). Further studies are warranted to clarify how social isolation affects domain-specific cognitive capacity among people with depressive symptoms.

As expected, we have found a significant interaction between gender and social isolation for predicting episodic memory, and further analysis revealed that depressed women are more vulnerable to the impact of social isolation on cognitive impairment than depressed men. This gender difference may be explained in several ways. First, women are more sensitive to the interpersonal context and prefer greater interpersonal connectedness than do men (Ahmadi, 2015; Timmers, Fischer, & Manstead, 1998). Second explanation is related with stress-buffering theory, which proposed that social relationships are beneficial in stressful situations (Fratiglioni, Paillard-Borg, & Winblad, 2004). Stress has been associated with cognitive decline due to structural changes in the hippocampus (Wilson et al., 2003). Accumulated evidence has shown that social support was negatively related to stress in women but not men (Beehr, Farmer, Glazer, Gudanowski, & Nair, 2003; Zhang, Zhang, Zhang, Zhang, & Feng, 2018). Thus, compared with men, women who had experienced social isolation may have a higher risk of memory decline.

Major strengths of our study include the large sample size. Cognitive function was assessed with a series of objective tests. However, there are also limitations to acknowledge. First, depressive symptoms were assessed by CESD-10. Despite wide use in the literature and good reliability and validity for Chinese older population (Boey, 1999; Chen & Mui, 2014), this measure is less reliable than a clinical diagnosis. Second, some potential confounders, such as stroke, heart disease, hypertension, and diabetes at baseline were ascertained by self-reported doctor diagnosis. This may lead to unavoidable misclassification due to misreporting of these chronic diseases. Finally, this is an observational study, and causal conclusions cannot be drawn. Although we took multiple covariates into account, there may be other unmeasured factors responsible for the associations recorded here.

Conclusion

In this longitudinal study, a high level of social isolation was significantly associated with cognitive decline among Chinese older adults with depressive symptoms. Further analysis revealed that this association was limited to episodic memory of depressed women. These findings expand our knowledge about the association of social isolation with cognitive function in non-Western depressed populations.

Authors' contribution

Lizhi Guo made substantial contributions to the design of the work, drafted the manuscript as well as analyzed and interpreted data of the work. Fengping Luo and Ningcan Gao edited and revised the manuscript critically for important intellectual content. Bin Yu contributed to the study design, data analysis and critical revision of the article for important intellectual content. All authors gave final approval of the version to be published.

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Declaration of Competing Interest

None.

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