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Factors leading to the trajectory of cognitive decline in middle-aged and older adults using group-based trajectory modeling

A cohort study

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Abstract

Currently, studies exploring factors associated with the cognition at some time point and no study identifying the trajectories of cognitive changes and factors might associate with the trajectories of cognitive changes in people. This study was to identify factors associated with the trend of cognitive decline in middle-aged and older people. In this cohort study, the data of 6954 subjects were collected from China Health and Retirement Longitudinal Survey database. Group-based trajectory modeling was applied for identifying three different trajectories of cognitive function change [high initial level and slow decline group (n = 1024), moderate initial level and moderate decline group (n = 2673) and low initial level and rapid decline (LRD) group (n = 3277)]. Univariate and multivariate logistic regression analysis was conducted to identify variables influencing factors of the trajectories of cognitive function in middle-aged and older people. The follow-up interval was 2 years from 2011 to 2015, and 3 years from 2015 to 2018 via face-to-face interview. High initial level and slow decline group versus LRD group, age (OR = 2.591, 95% CI: 1.962–3.421), gender (OR = 1.398, 95% CI: 1.133–1.725), education (OR = 0.051, 95% CI: 0.039–0.068), place of residence (OR = 2.768, 95% CI: 1.663–4.606), disabled (OR = 1.557, 95% CI: 1.189–2.039), family annual income (OR = 0.757, 95% CI: 0.618–0.929), sleep duration (OR = 1.266, 95% CI: 1.023–1.567), instrumental activity of daily living impairment (OR = 2.513, 95% CI: 1.947–3.245), community activities participation (OR = 0.611, 95% CI: 0.500–0.748), depression (OR = 1.471, 95% CI: 1.185–1.828), and systolic blood pressure (OR = 1.005, 95% CI: 1.001–1.009) were factors influencing the trajectories of cognitive function. Comparing moderate initial level and moderate decline group and LRD group, age (OR = 1.245, 95% CI: 1.052–1.474), gender (OR = 1.244, 95% CI: 1.062–1.458), education (OR = 0.244, 95% CI: 0.190–0.314), marital status (OR = 1.291, 95% CI: 1.079–1.546), place of residence (OR = 1.677, 95% CI: 1.358–2.071), disability (OR = 1.396, 95% CI: 1.180–1.652), smoking (OR = 1.249, 95% CI: 1.071–1.457), family annual income (OR = 0.863, 95% CI: 0.768–0.970), sleep duration (OR = 1.215, 95% CI: 0.973–1.541), instrumental activity of daily living impairment (OR = 1.309, 95% CI: 1.098–1.560), community activities participation (OR = 0.804, 95% CI: 0.718–0.900) and depression (OR = 1.383, 95% CI: 1.217–1.571) were factors associated with the trajectories of cognitive function changes. Middle-aged and older adults who had characteristics associated with increased risk of cognitive decline might be provided with timely interventions.

Abbreviations: BADL = basic activities of daily living, BIC = Bayes criterion, CHARLS = China Health and Retirement Longitudinal Survey, GBTM = group-based trajectory modeling, HSD = high initial level and slow decline, IADL = instrumental activity of daily living, LRD = low initial level and rapid decline, Mean ± SD = Mean ± standard deviation, MMD = moderate initial level and moderate decline, MMSE = mini-mental state examination, SBP = systolic blood pressure.

Keywords: cognitive decline, group-based trajectory modeling, influencing factors, middle-aged and older adults

1. Introduction

Cognitive function is essential for older people, and cognitive impairment decreases the quality of life and results in the inability to live independently of older people.[1] To identify factors leading to the trend of cognitive decline in middle-aged and older people is essential to provide early interventions to those with a high risk of cognitive decline and prevent cognitive decline in those people. Previously, growing numbers of studies have revealed that the change

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of cognitive function was influenced by various factors. Stern believed that more education, higher job attainment, and an active and engaging lifestyle were protective factors of cognitive function.[2] Age, physical activity, metabolic dysregulation and depressive symptoms were also proposed to be factors affecting the cognitive function in older people.[3,4] Another study also indicated that environment especially long- or short-term exposure to different ambient air pollutants might decrease the cognitive function.[5] However, the results from these studies were cross-sectional studies and no follow-up data were analyzed.[6] Follow-up data can provide regular and timely feedback to clinicians to obtain the changes of cognition, which was essential for the timely interventions for decreasing the cognitive decline in people.

Group-based trajectory modeling (GBTM) is a kind of finite mixture model which categorizes individuals into latent groups with similar patterns of a repeated longitudinal measure.[7] GBTM can evaluate the outcomes of diseases over time, which is a method of longitudinal data analysis widely applied in the clinic.[8] Currently, studies exploring factors associated with the cognition at some time point. The follow-up endpoint was only one. However, cognition changes with time goes on, and to explore factors associated with the trajectories of cognitive changes was of more significance. There was no study identifying the trajectories of cognitive changes and factors might associate with the trajectories of cognitive changes in people.

In this study, the cognitive function of the middle-aged and older people was followed up for four times based on the China Health and Retirement Longitudinal Survey (CHARLS) database, and GBTM was used to identify different trajectories of cognitive decline in subjects according to the cognitive function score from the four follow-ups. The influencing factors of the trends of cognitive change in all participants were analyzed via comparing the data in different trajectories.

2. Methods

2.1. Study design and population

In this cohort study, the clinical data of 8752 subjects were collected from CHARLS database, a nationally representative panel survey of Chinese middle-aged and older people involved in 10,257 households in 150 counties/districts and 450 villages or urban communities across 28 provinces.[9] The CHARLS was conducted in 2011, and Wave 2 was conducted in 2013, wave 3 in 2015 and wave 4 in 2018, which collected high-quality nationally representative data.[10] All participants received a face-to-face interview through a structured questionnaire, including the evaluation on social, economic, and health status of all subjects. The baseline data for CHARLS were collected in 2011. 1798 (20.5%) patients were lost follow-up and 6954 participants were followed up to 2018 and finally included in our study. The CHARLS was approved by the Ethical Review Committee of Peking University, and all participants signed an informed consent form before the start of the investigation. According to the Ethics Review Committee of the First Affiliated Hospital of Shenzhen University, retrospective studies using samples from an open database have been exempted from an ethical review. And the Ethics Review Committee of the First Affiliated Hospital of Shenzhen University has waived the requirement of the informed consent for the study.

2.2. Variables

All the data of the participants were collected from CHARLS database. The baseline characteristics were collected in 2011 and cognitive function scores (draw a figure, words recall and telephone interview for cognitive status [TICS] score) were collected in the four follow-ups between 2011 to 2018. The variable coding and data missing rates were shown in Table 1. Variables were collected including age (years), gender (males or females), education levels (primary school, junior high school or high school and above), marital status (married/cohabitated

Table 1

The missing value of the variables.

Variable	Coding	Missing value (%)
/	ID	0.00
Age	ba002_1	0.00
Gender	rgender	0.00
Education level	bd001	0.00
Marital status	be001	0.00
Place of residence	bb006	0.00
Disability status	da005_1_-da005_5_	0.00
Physical activities	da053_3_	0.00
Smoking status	da059	0.00
Drinking status	da067	0.00
Family annual income	income_total	0.01
Sleep duration	da049	0.00
Nap time	da050	0.00
Hypertension	da007_1_	0.00
Hyperlipidemia	da007_2_	0.00
Diabetes mellitus	da007_3_	0.00
Number of chronic diseases	da007_4_-da007_14_	0.00
BADL	db010-db020	0.00
Participation in community activities	da056s1-da056s12	0.00
Depression	dc009-dc018	0.00
SBP	qa003 qa007 qa011	0.00
DBP	qa004 qa008 qa012	0.00
Spatial-cognitive ability	dc025	0.00
Recall	dc006s1-dc006s10 dc027s1-dc027s10	0.00
TICS	dc001s1-dc001s3 dc002 dc003 dc019-dc023	0.00

BADL = basic activities of daily living, DBP = diastolic blood pressure, SBP = systolic blood pressure (mm Hg), TICS = telephone interview for cognitive status.

or unmarried/separated), place of residence (urban or rural), disability status, smoking status, drinking status, history of hypertension, hyperlipidemia, and diabetes mellitus, participation in community activities, history of depression, basic activities of daily living (BADL), instrumental activity of daily living (IADL), physical activities, family annual income (yuan), sleep duration (h/d), nap time (h/d), number of chronic diseases, systolic blood pressure (SBP; mm Hg), and diastolic blood pressure (DBP; mm Hg).

2.3. Definition of variables

IADL referred to activities that are necessary to maintain an independent life, including the abilities to do housework, cook, make phone calls, take medicine, shop, and take care of finances etc. BADL referred to the abilities to take a bath, eat, get in and out of bed, dress, use the toilet, and defecate. Each answer was divided into four responses: No, I do not have any difficulty; I have difficulty but still can do it; Yes, I have difficulty and need help; and I cannot do it. In this study, people who completed all items without difficulty were classified as BADL- or IADL-independent; people who reported any difficulty in any item were classified as having BADL or IADL impairment. Urban areas refer to special areas located in cities or suburban areas, towns or suburban areas, or areas where nonagricultural industries account for more than 70%, such as special economic belts and state-owned agricultural enterprises.

2.4. Outcome variable and measurement

Cognitive decline was the primary outcome in the present study. The measurement of cognitive function of participants in CHARLS were conducted based on the Chinese version of the mini-mental state examination (MMSE), which involves in orientation to time (today's date [3 points], day of the week [1 point], and current season [1 point]); recall (immediate recall of a list of 10 words, and delay recall of a list of 10 words; 10 points), calculation (5 points), and construct drawing (1 point).[11] In total, four aspects were included in the test and the total scores ranged from 0 to 21. Lower scores suggested a poorer cognitive function.

2.5. Group-based trajectory modeling

The GBTM was used to identify similar developmental trajectories of cognitive function in all the participants. The survey wave was used as a timescale of trajectories to simulate the cognitive scores in the sample in all waves. First, a base model without covariates was constructed to determine the number of groups and the order of the polynomial functions of the survey wave. The best-fitting model was considered as the trajectory group with the highest probability, which was based on goodness-of-fit statistics via the Bayesian information criterion (BIC) (the one whose absolute value of BIC is closest to zero is selected as the appropriate model).[12] The results of scree test indicated that the trajectories of cognitive function change should be divided into three groups and three different trajectories of cognitive function change were identified based on GBTM. Second, each participant was assigned to the corresponding trajectory group according to the maximum likelihood estimation to estimate the probability of producing variance in cognitive scores. Third, univariate analysis and multivariate logistic regression analysis were applied to explore the influencing factors of cognitive scores at different points.

2.6. Statistical analysis

The measurement data of normal distribution were described as Mean ± standard deviation (Mean ± SD), and analysis of variance was used for comparisons between groups. Non-normal data were described by [M (Q1, Q3)], and Kruskal–Walis H rank sum test was adopted for comparisons between groups. The enumeration data were described by n (%). Chi-square test or Fisher S exact probability method were used for comparison between groups. GBTM was applied to identify the trajectories of cognitive function change and the trajectory group with the highest probability was selected as the best fitting model through the goodness of fit statistics of BIC. The results of scree test indicated that the trajectories of cognitive function change should be divided into three groups and three different trajectories of cognitive function change were identified based on GBTM. Univariate logistic regression analysis was conducted to identify variables with statistical differences among groups followed by the multivariate analysis to explore the influencing factors of the trajectories of cognitive function changes in middle-aged and older people. SAS 9.4 software (SAS Institute Inc., Cary, NC) was used for all statistical analyses in this study and $P < .05$ indicated statistical difference.

3. Results

3.1. The baseline characteristics of all participants

A total of 8752 subjects were included in this study, who were enrolled in 2011 and followed up to 2018, with a loss of follow-up rate of 20.5%. Those who were lost follow-up was excluded (n = 1798). Finally, 6954 subjects were included in the study. Group-based trajectory modeling (GBTM) was applied for identifying three different trajectories of cognitive function change (high initial level and slow decline [HSD] group [n = 1024], moderate initial level and moderate decline [MMD] group [n = 2673] and low initial level and rapid decline [LRD] group [n = 3277]). The detailed screen process was shown in Figure 1.

In total, there were 2801 (40.28%) subjects aged 45 to 54 years, 2756 (39.63%) aged 55 to 64 years and 1397 (20.09%) aged ≥ 65 years. Among them, 3711 (53.36%) persons were males and 3243 (46.64%) were females. In terms of education levels, 1076 (15.47%) persons were illiterate, 3017 (43.39%) were graduated from primary school, 1888 (27.15%) were graduated from middle school, and 973 (13.99%) were graduated from senior high school or above. There were 873 (12.55%) unmarried/separated subjects. 633 (9.10%) people live in rural areas and 977 (14.34%) people were disabled. 4002 (57.55%) people had a history of smoking and 4773 (64.32%) people had a history of drinking. 1526 (21.94%) people were complicated with hypertension, 645 (9.28%) people had hyperlipidemia and 395 (5.68%) people had diabetes mellitus. 3656 (52.57%) subjects participated in community activities, and 2247 (32.31%) people had depression. 823 (11.83%) participants had BADL impairment and 1038 (14.93%) had IADL impairment. 4523 (65.04%) people exercised 2 hours a day, 3950 (56.80%) people had a family income ≥20,000 yuan, 486 (6.99%) people slept for 9 hours a day, 3180 (45.73%) people did not take a nap, and 2375 (34.15%) people did not have chronic diseases. According to the trajectories of cognitive function, all subjects were divided into three groups: HSD group (n = 1024, 14.73%), moderate initial level and moderate decline (MMD) group (n = 2673, 38.44%) and LRD group (n = 3277, 46.83%) (Table 1).

3.2. Changes in cognitive function and trajectories group of cognitive function

The change trends of cognitive function in middle-aged and older people were displayed in Figure 2, showing that the cognitive function scores decreased gradually with the increase of years, indicating that the cognitive function in middle-aged and older people decreased gradually with the increase of age.

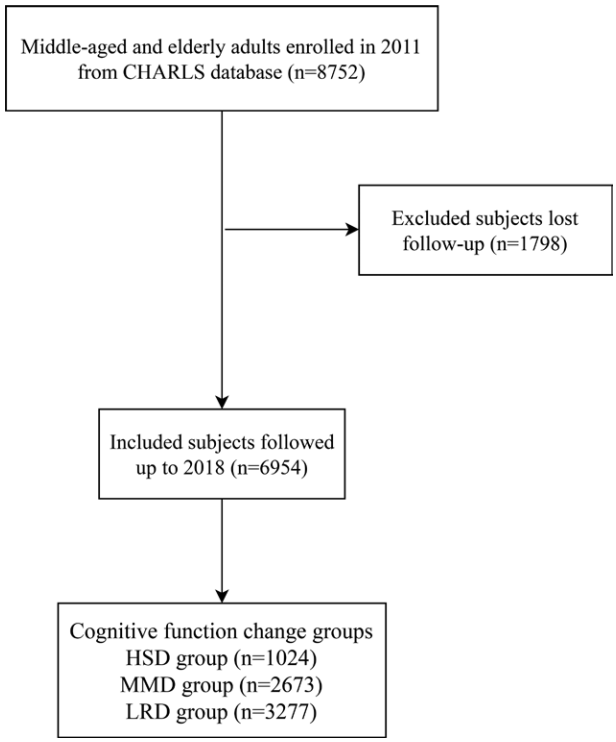

Figure 1. The screen process of participants in this study. CHARLS = China Health and Retirement Longitudinal Survey, HSD = high initial level and slow decline, LRD = low initial level and rapid decline, MMD = moderate initial level and moderate decline, TICS = telephone interview for cognitive status.

Based on GBTM, three different trajectories were determined according to BIC (Fig. 3). As exhibited in Figure 4, In the trajectory 1, the initial cognitive score was high and declined slowly, so it was defined as "high initial level and slow decline group" (HSD group, n = 3257, 46.83%). The initial cognitive score in trajectory 2 was moderate and declined slower than HSD group, so it was defined as "medium initial level and medium decline group" (MMD group, n = 2673, 38.44%). The initial cognitive score in trajectory 3 was low and decreased quickly, so it was defined as "low initial level and rapid decline group" (LRD group, n = 1024, 14.73%).

3.3. Univariate analysis of factors influencing the trajectories of cognitive function changes among different groups

Table 2 showed that the distributions of different age groups ($\chi^2 = 382.744$, $P < .001$), female population (63.28% vs 48.04% vs 40.25%, $\chi^2 = 169.449$, $P < .001$), education level ($\chi^2 = 1780.244$, $P < .001$), the proportion of unmarried/separated subjects (79.39% vs 86.42% vs 90.82%, $\chi^2 = 96.803$, $P < .001$), the proportion of participants in rural areas (2.54% vs 5.72% vs 13.94%, $\chi^2 = 182.278$, $P < .001$), the proportion of disabled subjects (20.41% 16.72% vs 10.47%, $\chi^2 = 82.802$, $P < .001$), the proportion of smokers (68.36% vs 56.23% vs 55.23%, $\chi^2 = 58.030$, $P < .001$), alcohol drinkers (73.73% vs 65.06% vs 60.76%, $\chi^2 = 58.122$, $P < .001$), the proportion of people with hyperlipidemia (5.18% vs 8.12% vs 11.51%, $\chi^2 = 44.096$, $P < .001$), the proportion of people with diabetes mellitus (4.69% vs 5.01% vs 6.54%, $\chi^2 = 8.596$, $P = .014$), the proportion of subjects participating community activities (41.31% vs 49.87% vs 58.24%, $\chi^2 = 103.331$, $P < .001$), the proportion of people with depression (45.41% vs 36.85% vs 24.47%, $\chi^2 = 197.061$, $P < .001$), the proportion of people with BADL impairment (20.02% vs 13.02% vs 8.29%, $\chi^2 = 108.562$, $P < .001$), the proportion of people with IADL impairment (28.91% vs 16.27% vs 9.43%, $\chi^2 = 239.021$, $P < .001$), the proportion of people with family annual income ≥ 20,000 (41.89% vs 53.31% vs 64.35%, $\chi^2 = 181.717$, $P < .001$), sleep duration ($\chi^2 = 65.661$, $P < .001$), nap time ($\chi^2 = 74.270$, $P < .001$) and the average SBP level (134.75 mm Hg vs 129.17 mm Hg vs 128.01 mm Hg, F = 33.538, $P < .001$) were statistically different among HSD group, MMD group and LRD group.

3.4. Multivariate analysis of factors leading to the trajectories of cognitive function changes

The factors with statistical significance in the univariate analysis and important co-variable including exercise duration were included in the multivariate logistic regression model. The data delineated that HSD group versus LRD group, the risk of being assigned in HSD group was 2.591 times higher in people aged ≥ 65 years old compared with people aged 45 to 54 years old (OR = 2.591, 95% CI: 1.962–3.421). The risk of being assigned in HSD group in women were 1.398 times higher than men (OR = 1.398, 95% CI: 1.133–1.725). Compared to subjects who were illiterate, people with primary school education were associated with a reduced risk of being assigned to HSD group by 0.949 times (OR = 0.051, 95% CI: 0.039–0.068), people with middle school education were associated with a reduced risk of being assigned to HSD group by 0.987 times (OR = 0.013, 95% CI: 0.009–0.019), and subjects with high school or above education was associated with a decreased risk of being assigned into HSD group by 0.994 times (OR = 0.006, 95% CI: 0.003–0.011). The risk of rural subjects being assigned to Group1 was 2.768 times higher than urban/urban subjects (OR = 2.768, 95% CI: 1.663–4.606), and the risk of disabled subjects being assigned to Group1 was increased by 0.557 times compared with non-disabled subjects (OR = 1.557, 95% CI: 1.189–2.039). The risk of participants with family annual income ≥ 20,000 yuan being assigned to Group1 was reduced by 0.243 times compared with family annual income < 20,000 yuan (OR = 0.757, 95% CI: 0.618–0.929). Compared with those who slept 6 to 8 h/d, subjects slept <6 h/d were associated with an increased risk of being assigned to Group1 by 0.266 times (OR = 1.266, 95% CI: 1.023–1.567), and the risk of being assigned to Group1 in subjects who slept >9 h/d were increased by 0.649 times (OR = 1.649, 95% CI: 1.119–2.431). People with IADL impairment were associated with 2.513 times higher risk of being assigned in HSD group (OR = 2.513, 95% CI: 1.947–3.245). People who participated in community activities were linked with a decreased risk of being assigned in HSD group by 0.389 times (OR = 0.611, 95% CI: 0.500–0.748). The risk of depression subjects being assigned to Group1 was increased by 0.471 times (OR = 1.471, 95% CI: 1.185–1.828). For each 1 mm Hg increase in SBP, the risk of subjects assigned to Group1 was increased by 0.005 times (OR = 1.005, 95% CI: 1.001–1.009) (Fig. 5).

According to the results of comparing MMD group and LRD group, participants who aged >65 years old were 1.245 times more likely to be assigned to MMD group than participants who aged 45 to 54 years old (OR = 1.245, 95% CI: 1.052–1.474). The risk of being assigned to MMD group in women were increased by 0.244 times than men (OR = 1.244, 95% CI: 1.062–1.458). Primary school education decreased the risk of being assigned to MMD group by 0.756 times (OR = 0.244, 95% CI: 0.190–0.314), middle school education decreased the risk of being assigned to MMD group by 0.894 times (OR = 0.106, 95% CI: 0.081–0.138), high school or above education reduced the risk of being assigned to MMD group by 0.942 times (OR = 0.058, 95% CI: 0.043–0.078) compared with illiterate subjects. Unmarried/separated subjects had a 1.291 times increased risk of being assigned to MMD group (OR = 1.291, 95% CI: 1.079–1.546), and those living in rural

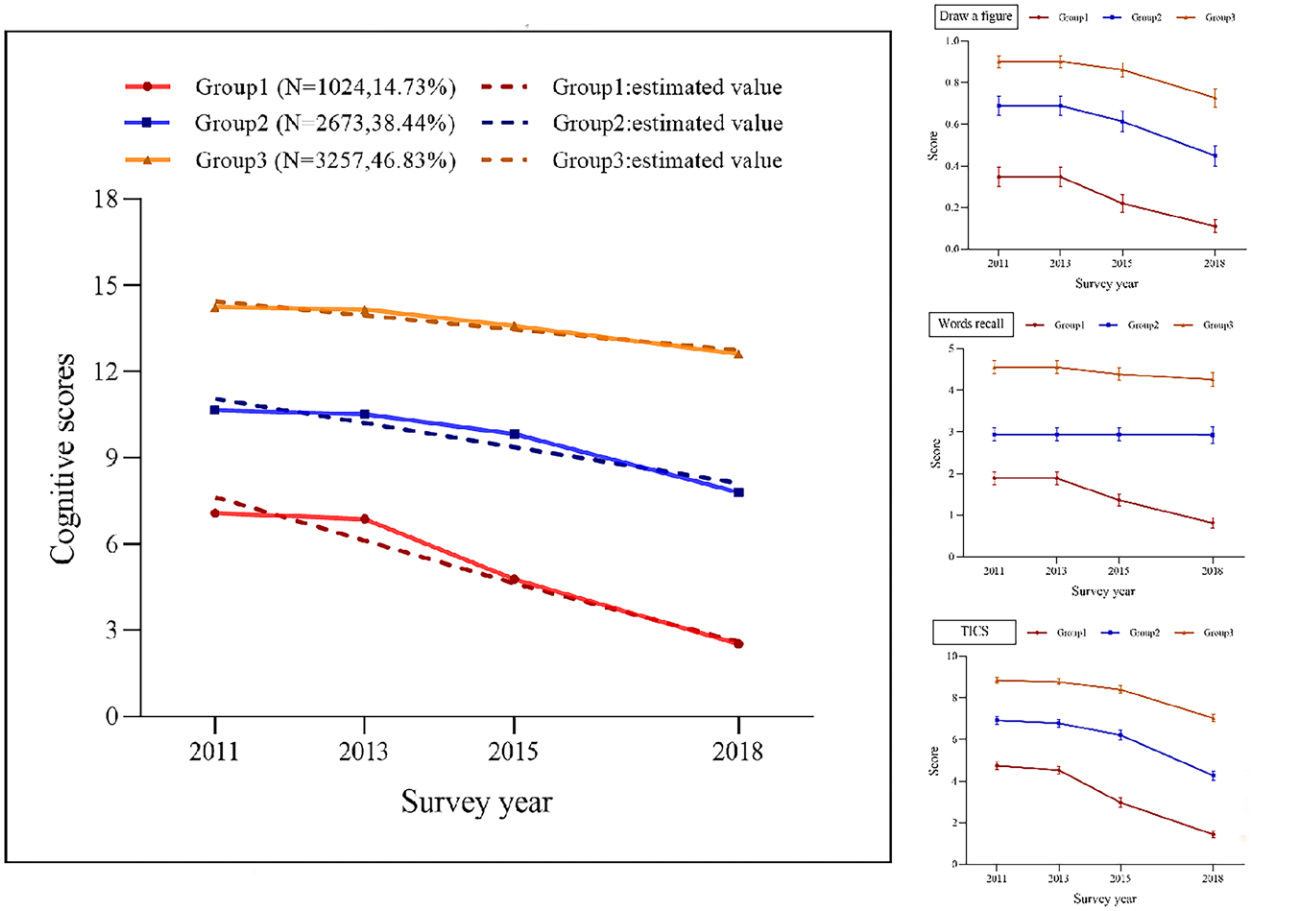

Figure 2. The change trends of cognitive function in middle-aged and older people. TICS = telephone interview for cognitive status.

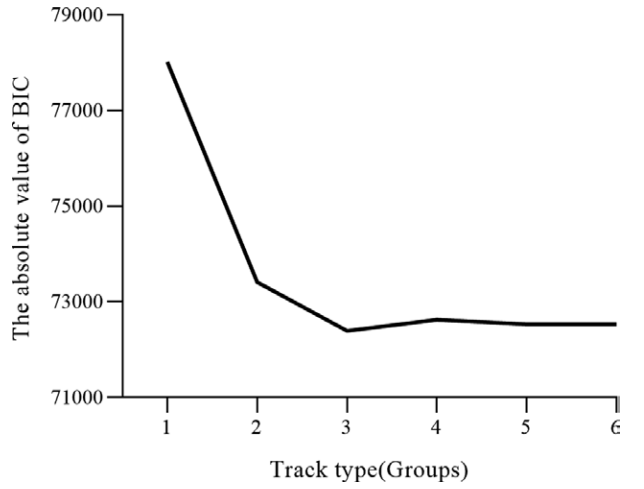

Figure 3. The screen test showing the trajectories of cognitive function changes based on the goodness of fit statistics of BIC. BIC = Bayes criterion.

areas had a 1.677 times higher risk of being assigned to MMD group than those living in urban/urban areas (OR = 1.677, 95% CI: 1.358–2.071). Disabled people increased the risk of being assigned to MMD group by 0.396 times (OR = 1.396, 95% CI: 1.180–1.652), and smoking increased the risk of being assigned to MMD group by 0.249 times (OR = 1.249, 95% CI: 1.071–1.457). The family annual income ≥20,000 yuan reduced the risk of being assigned to MMD group by 0.137 times (OR = 0.863, 95% CI: 0.768–0.970). Compared to those who sleep 6 to 8 h/d, people who slept <6 h had a 1.215 higher risk of being assigned to MMD group (OR = 1.215, 95% CI: 0.973–1.541). Subjects with IADL impairment had a 1.309 higher risk of being assigned to MMD group (OR = 1.309, 95%

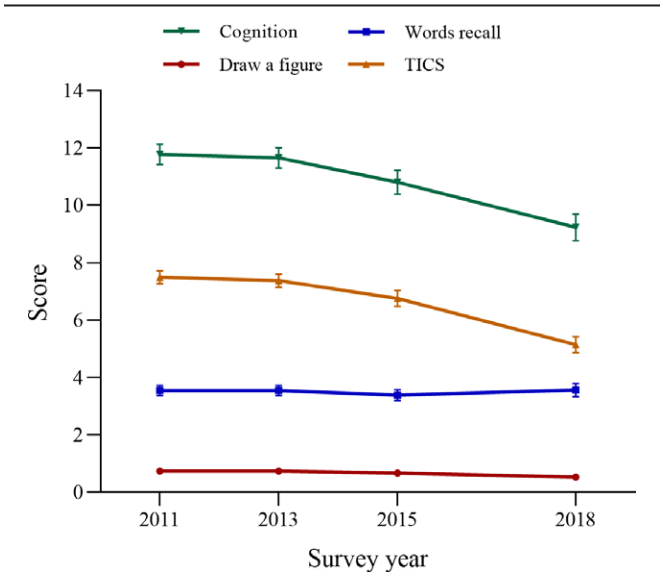

Figure 4. Three different trajectories of cognitive function changes in middle-aged and older people. TICS = telephone interview for cognitive status.

Table 2

Univariate analysis of factors influencing cognitive function changes among different groups.

Variable	Total (n = 6954)	Trajectories group of cognitive function			Statistical magnitude	*P*
		Group 1 (n = 1024)	Group 2 (n = 2673)	Group 3 (n = 3257)		
Age (yr), n (%)						
45	2801 (40.28)	223 (21.78)	1034 (38.68)	1544 (47.41)	$\chi^2 = 382.744$	<.001
55	2756 (39.63)	398 (38.87)	1099 (41.11)	1259 (38.66)		
≥65	1397 (20.09)	403 (39.36)	540 (20.20)	454 (13.94)		
Gender, n (%)						
Male	3711 (53.36)	376 (36.72)	1389 (51.96)	1946 (59.75)	$\chi^2 = 169.449$	<.001
Female	3243 (46.64)	648 (63.28)	1284 (48.04)	1311 (40.25)		
Education level, n (%)						
Illiteracy	1076 (15.47)	572 (55.86)	420 (15.71)	84 (2.58)	$\chi^2 = 1780.244$	<.001
Primary school education	3017 (43.39)	365 (35.64)	1476 (55.22)	1176 (36.11)		
Middle school education	1888 (27.15)	71 (6.93)	594 (22.22)	1223 (37.55)		
High school education and more	973 (13.99)	16 (1.56)	183 (6.85)	774 (23.76)		
Marital status, n (%)						
Married/cohabiting	6081 (87.45)	813 (79.39)	2310 (86.42)	2958 (90.82)	$\chi^2 = 96.803$	<.001
Unmarried/separated	873 (12.55)	211 (20.61)	363 (13.58)	299 (9.18)		
Place of residence, n (%)						
Urban area	6321 (90.90)	998 (97.46)	2520 (94.28)	2803 (86.06)	$\chi^2 = 182.278$	<.001
Rural area	633 (9.10)	26 (2.54)	153 (5.72)	454 (13.94)		
Disability status, n (%)	997 (14.34)	209 (20.41)	447 (16.72)	341 (10.47)	$\chi^2 = 82.802$	<.001
Smoking status, n (%)	4002 (57.55)	700 (68.36)	1503 (56.23)	1799 (55.23)	$\chi^2 = 58.030$	<.001
Drinking status, n (%)	4473 (64.32)	755 (73.73)	1739 (65.06)	1979 (60.76)	$\chi^2 = 58.122$	<.001
Hypertension, n (%)	1526 (21.94)	242 (23.63)	562 (21.03)	722 (22.17)	$\chi^2 = 3.118$	.210
Hyperlipidemia, n (%)	645 (9.28)	53 (5.18)	217 (8.12)	375 (11.51)	$\chi^2 = 44.096$	<.001
Diabetes mellitus, n (%)	395 (5.68)	48 (4.69)	134 (5.01)	213 (6.54)	$\chi^2 = 8.596$	.014
Participation in community activities, n (%)	3656 (52.57)	423 (41.31)	1333 (49.87)	1900 (58.34)	$\chi^2 = 103.331$	<.001
Depression, n (%)	2247 (32.31)	465 (45.41)	985 (36.85)	797 (24.47)	$\chi^2 = 197.061$	<.001
BADL, n (%)	823 (11.83)	205 (20.02)	348 (13.02)	270 (8.29)	$\chi^2 = 108.562$	<.001
IADL, n (%)	1038 (14.93)	296 (28.91)	435 (16.27)	307 (9.43)	$\chi^2 = 239.021$	<.001
Physical activities (h/d), n (%)						
2	4523 (65.04)	671 (65.53)	1711 (64.01)	2141 (65.74)	$\chi^2 = 4.142$	.126
0	1438 (20.68)	187 (18.26)	543 (20.31)	708 (21.74)		
Never	993 (14.28)	166 (16.21)	419 (15.68)	408 (12.53)		
Family annual income (Yuan), n (%)						
<20,000	3004 (43.20)	595 (58.11)	1248 (46.69)	1161 (35.65)	$\chi^2 = 181.717$	<.001
≥20,000	3950 (56.80)	429 (41.89)	1425 (53.31)	2096 (64.35)		
Sleep duration (h/d), n (%)						
0	3399 (48.88)	546 (53.32)	1403 (52.49)	1450 (44.52)	$\chi^2 = 65.661$	<.001
6	3069 (44.13)	388 (37.89)	1082 (40.48)	1599 (49.09)		
9	486 (6.99)	90 (8.79)	188 (7.03)	208 (6.39)		
Nap time (h/d), n (%)						
Never	3180 (45.73)	559 (54.59)	1288 (48.19)	1333 (40.93)	$\chi^2 = 74.270$	<.001
0	650 (9.35)	89 (8.69)	233 (8.72)	328 (10.07)		
0.5	2341 (33.66)	267 (26.07)	859 (32.14)	1215 (37.30)		
1.5	783 (11.26)	109 (10.64)	293 (10.96)	381 (11.70)		
Number of chronic diseases, n (%)						
0	2375 (34.15)	327 (31.93)	886 (33.15)	1162 (35.68)	$\chi^2 = 6.811$	.033
≥1	4579 (65.85)	697 (68.07)	1787 (66.85)	2095 (64.32)		
SBP (mm Hg), Mean ± SD	129.45 ± 23.17	134.75 ± 28.99	129.17 ± 22.89	128.01 ± 21.00	F = 33.538	<.001
DBP (mm Hg), Mean ± SD	75.96 ± 11.90	75.88 ± 12.24	75.72 ± 12.02	76.19 ± 11.70	F = 1.170	.310

BADL = basic activities of daily living, DBP = diastolic blood pressure, IADL = instrumental activity of daily living, SBP = systolic blood pressure, TICS = telephone interview for cognitive status.

CI: 1.098–1.560), and those who were involved in community activities reduced the risk of being assigned to MMD group by 0.196 times (OR = 0.804, 95% CI: 0.718–0.900). Depression increased the risk of being assigned to MMD group by 0.383 times (OR = 1.383, 95% CI: 1.217–1.571) (Fig. 6).

4. Discussion

Our study assessed the factors influencing the trajectories of cognitive decline function, and the results delineated that based on the GBTM model, three different trajectories of cognitive function was found in all participants and age, female, living in rural areas, low education level, disability, low family annual income, smoking, sleeping duration <6 hours, IADL impairment, depression, no community activities participation and SBP level were risk factors affecting the trajectories of cognitive decline in middle-aged and older adults. The findings of the present study might help identify people with a high risk of cognitive decline and provide timely interventions to prevent or decrease the cognitive decline in those people.

Aging is a natural process associated with cognitive decline. Previous studies have reported that an increased age may be correlated with a decreased cognition.[13] A recent longitudinal study indicated that age was one of the important variable associated with cognitive function.[14] In this study, age was also identified to be a risk factor for cognitive function in middle-aged and older people. This may because increased oxidative stress and neuroinflammation, and reduced neurogenesis and

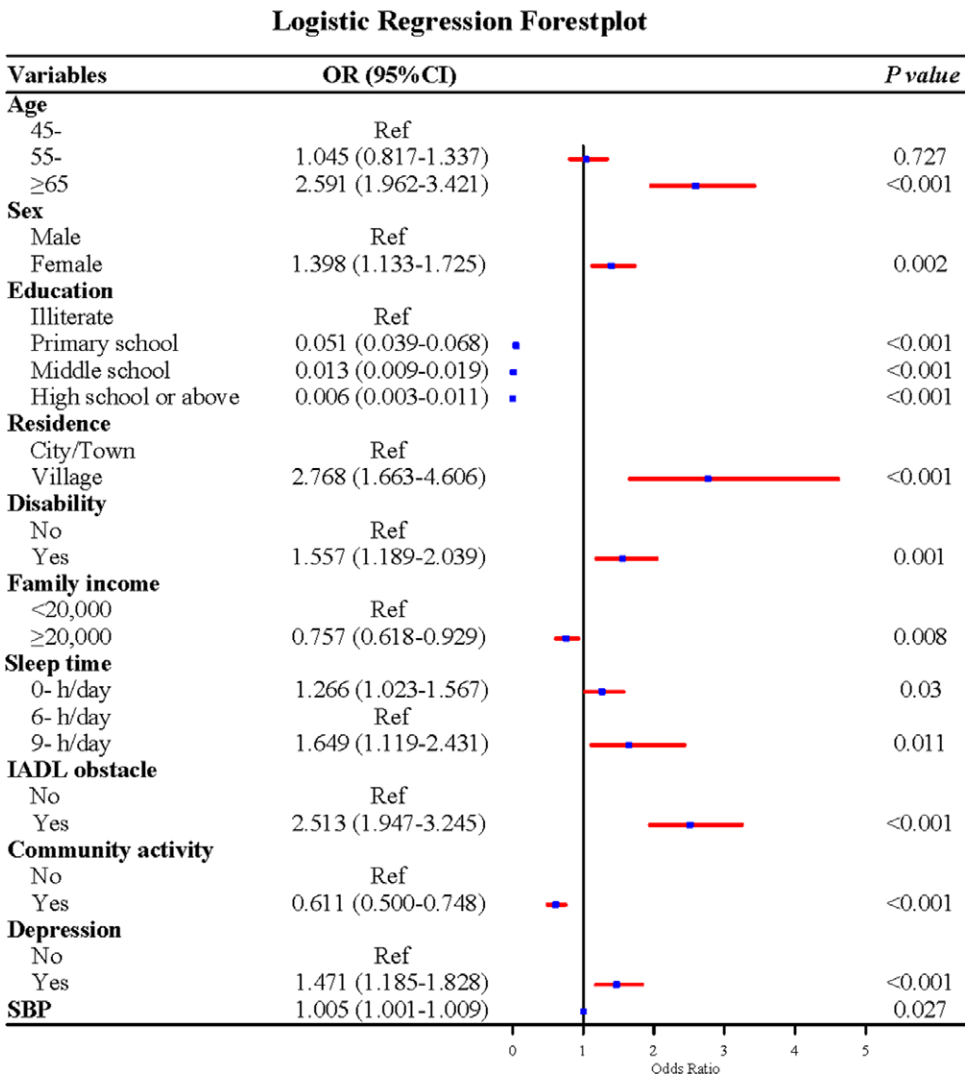

Figure 5. The forest plot of multivariate analysis of factors leading to of the trajectories of cognitive function changes by comparing HSD group and LRD group. HSD = high initial level and slow decline, IADL = instrumental activity of daily living, LRD = low initial level and rapid decline, SBP = systolic blood pressure.

synaptic plasticity influenced the hippocampus in old people and decreased the ability in learning and memory consolidation, which may lead to a decreased cognition.[15] A study from Li et al[16] indicated that females had a higher risk of cognitive decline than men in older people in Taiwan. This supported the findings of our study, showing females were more likely to suffer cognitive decline than men. Education level was reported to have a positive association with cognition.[17] This was allied with the results in our study. In the present study, we identified that people with a higher education was associated with a lower risk of cognitive decline. Education can provide improved cognitive reserve and access to more socioeconomic resources to people, which may help reduce the decline of cognitive function.[18] A study investigating the association of place of residence and cognitive function among the adult population in India revealed that people living in urban areas were associated with better cognitive function.[19] Here in, participants from rural areas showed a higher risk of cognitive decline than those from urban areas. Disabled older people have reduced mobility, less physical exercise, decreased social engagement, and less brain activity, which may result in a lower cognitive function.[20] This gave support to the results of our study, demonstrating that disabled middle aged and older people were linked with a higher risk of cognitive decline. A collaboration network in Latin American evaluated the socioeconomic status of 1175 participants, which uncovered that subjects with a lower income were more related to cognition decline.[21] In the present paper, we also found that in middle aged and older people, a lower income may lead to a decreased cognitive function. People with improved sleep duration may have a better cognitive function,[22] but a cohort study in the Doetinchem also revealed that middle-aged people who had too long sleep duration may also result in a lower cognitive function.[23] This was allied with the data in this study, people slept <6 or >9 h/d were associated with a higher risk of cognitive decline compared with people slept 6 to 8 h/d. Sleep duration should be control for middle-aged and older adults to reduce the risk of cognition decline. For those who with sleep disorders, sleep monitoring should be performed and appropriate interventions or medicines helping sleep may be adopted.

Previously. Zhang et al[4] provided evidence that the total score of IADL was a predictor of cognitive function, and a higher IADL score predicted a better cognitive function. In the current study, IADL impairment was also a risk factor for cognitive function in middle age and older people. Middle aged and older adults are recommended to do more instrumental activity to prevent the cognitive decline. Additionally, people engaged in more leisure activities or social activities were reported to have a low risk of cognitive decline because of enhanced cognitive reserve capacity.[24,25] Poor social networks were found to have longitudinal association with higher risk of cognitive decline,

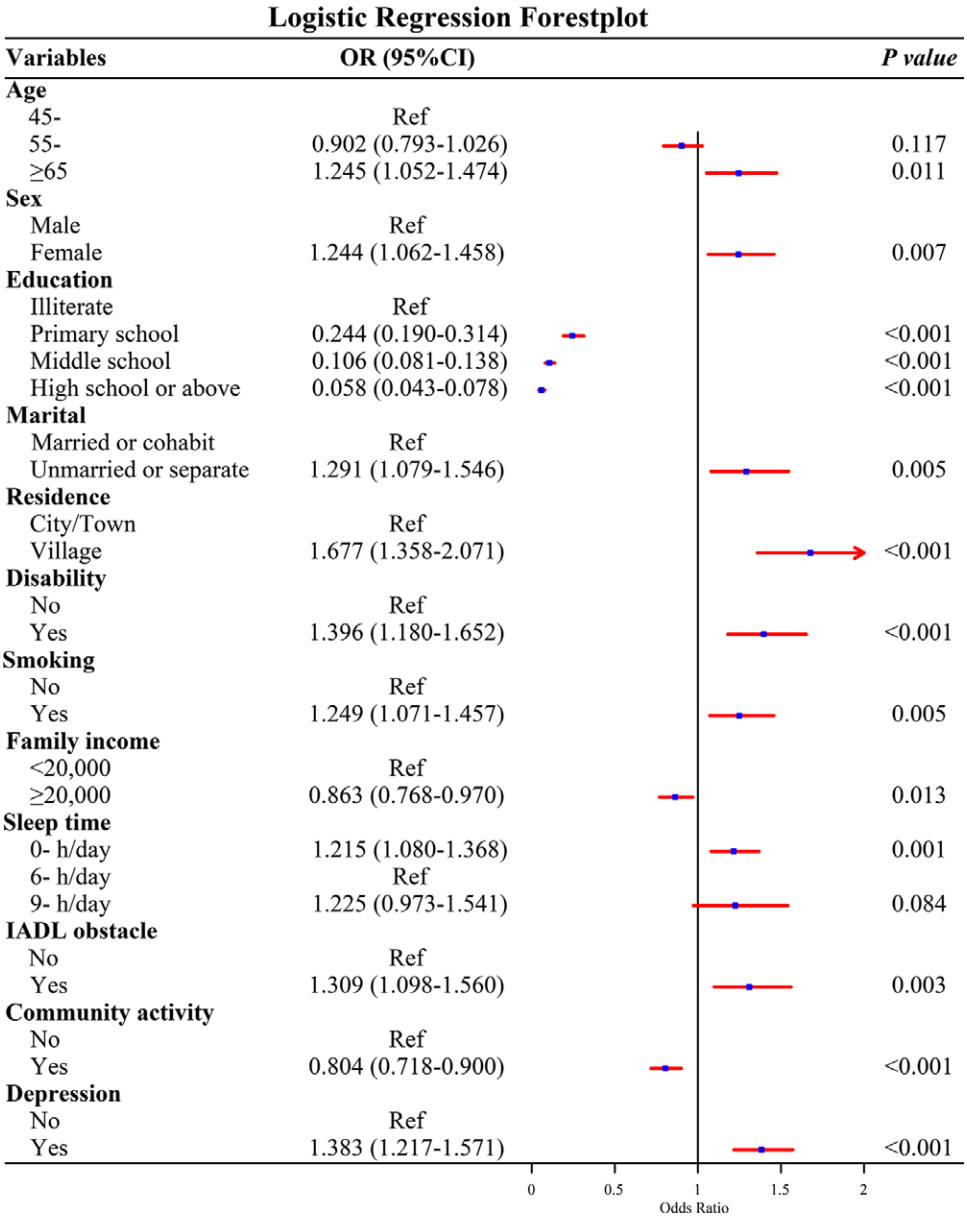

Figure 6. The forest plot of multivariate analysis of factors leading to the trajectories of cognitive function changes by comparing MMD group and LRD group. IADL = instrumental activity of daily living, LRD = low initial level and rapid decline, MMD = moderate initial level and moderate decline.

dementia, and other adverse health outcomes in later life.[26] According to the results in our study, middle-aged and older people with more community activity were less likely to suffer cognitive decline. Thus, middle aged and older people should be more active to take part in leisure or social activities. Here in, unmarried/separated middle aged and older people also have a higher risk of cognition decline, which was evidenced by previous studies, showing that widowed or divorced people were also correlated with a poor cognitive function.[27,28] In a previous study, the data revealed that smoking history was associated with the cognitive function of patients with multiple sclerosis.[29] In our study, smoking was reported to be a risk factor for cognition decline, and this reminded middle aged and older people to quit smoking. Higher SBP was also identified to decrease the cognitive function in middle aged and older people, which was allied with a previous systematic review and meta-analysis, delineating that lowering blood pressure was benefit for the prevention of cognitive impairments.[30] Patients with hypertension should be caution with the blood pressure and effective control of the blood pressure should be performed. Depressive symptoms were associated with worse cognitive function in US adults.[31] This gave support to the results of our study, showing depression was a risk factor for cognition decline and patients with depressive symptoms should receive timely interventions to prevent the occurrence of cognition decline.

The present study evaluated the factors influencing the trajectories of cognitive function in middle aged and older population based on GBTM. Previously, studies were mainly focused on exploring the factors affecting cognitive function,[6,32,33] but they neglected that cognitive function changes over time. GBTMs are widely applied for identifying the developmental course of symptoms and evaluate the heterogeneity in response to clinical interventions in clinical researches.[8] In our study, GBTMs could clearly observe the trajectories of cognitive function at different time points. The factors associated with the trajectories of cognitive function were identify rather than the factors influencing the cognitive function at some point in time. The data delineated that participants in the trajectory 1 showed a higher initial cognitive score and the cognitive function declined slower. For people who already had these risk factors, early interventions

such as taking part in more community activities especially in males should be provided and should pay attention on the cognitive function changes over time. For the government, organizing more various communities attracting more old adults to join is of great significance. Governments should also ensure the basic insurance for common people. Depression screening was also important, and ear identify those who depression and offer proper anti-depression treatment might help decrease the risk of cognitive decline. People especially females should get enough sleep, for those without 6 to 8 h/d, a nap was recommended. There were several limitations in this study. Firstly, the lost follow-up rate was as high as 20.5%, which might influence the reliability of results in our study. Secondly, variables such as community activities participation and sleep duration were self-rating, which might have recall bias. In the future, prospective randomized controlled trial with large sample size were required to verify the findings of our study.

5. Conclusions

Age, gender, place of residence, education level, disability, family annual income, smoking, sleeping duration, IADL impairment, depression, community activities participation and SBP were factors influencing the trajectories of cognitive decline in middle-aged and older adults. The findings of our study might also provide a reference for the government to organize more community activities and ensure the coverage of basic insurance of comment people.

Author contributions

Study design and manuscript writing: Jun Su.
Data collection, analysis and interpretation: Xiaohua Xiao.
Manuscript review and editing: Jun Su.

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