Mutual relationship between grip strength and cognitive function in Chinese older adults over 10 years: a cross-lagged panel analysis **(Supplementary material)**

Measures

Grip strength

Smedley gripometer was used to measure the grip strength. The participants were seated, with their upper arms and elbows close to the body, their forearms straight with the arms positioned at 90 degrees , and their palms facing up. The grip strength of the left and right hands was measured twice each, and the maximum value of the measured results of both hands was obtained, and the average value was calculated as the grip strength (kg) of the participants. After analysis, grip strength ≥ 70 or ≤ 1 kg was rejected as an outlier.

Cognitive function

Cognitive tests included the following four items, (a) Verbal recall (immediate and delayed verbal recall) was used to assess learning ability and memory storage. Participants were told 10 words in succession and repeated three times to strengthen memory. Word recall was repeated 10 minutes later, and 1 point was given for correct recall of a word. The final score was calculated as the average of the four trials (three immediate and one delayed). (b) Verbal fluency was used to assess the ability to retrieve semantic memory information. Participants were asked to say the words (animals) they knew within 1 minute, and one point was scored for correctly saying the name of an animal. (c) Forward digit span was

used to assess attention and immediate memory. Participants were asked to repeat forward several sets of numbers, with the length of the numbers ranging from short to long. (d) Backward digit span was also to assess attention and immediate memory in which participants were asked to repeat backward several sets of numbers. Points were scored for the length of digits that could be correctly repeated, with a maximum of 9 points in order and 8 points in reverse order.

Finally, according to the above seven single cognitive tests, including four verbal recall tests, verbal fluency tests and digit span tests (forward and backward), the total cognitive function score was calculated by factor analysis method, and the original total score was adjusted to the range of 0 to 100, which could assess the overall cognitive function. The higher the total cognitive score, the better the overall cognitive function.

Covariates

Information on sociodemographic characteristics was collected, including age, gender, education level, residence, marital status by questionnaire survey, using standardized questionnaire of SAGE. Comorbidities of chronic diseases were defined as the number of hypertension, diabetes, angina, chronic lung diseases, asthma and arthritis, classified as having 0, 1, 2, 3 or more diseases.

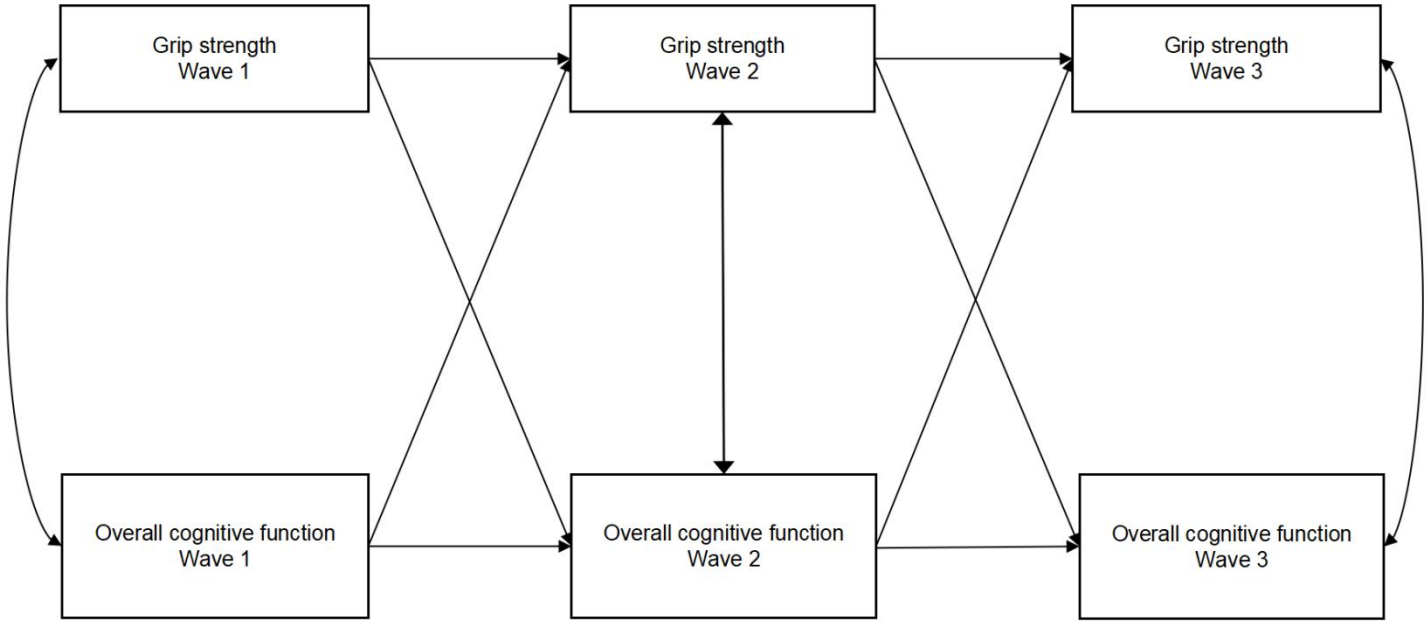
The comorbidities included hypertension, angina, diabetes, chronic lung disease, asthma, and arthritis, each of participants was asked, "Have you

ever been diagnosed with this disease by a doctor?", information was collected by self-reported yes or no. In addition, hypertension was defined as systolic blood pressure ≥ 140 mmHg and/or diastolic blood pressure ≥ 90 mmHg, or self-reported hypertension. The number of chronic diseases was calculated by adding the number of the above 6 diseases, including 0, 1, 2, and ≥ 3 diseases. Body mass index (BMI) was divided into 4 groups, < 18.5 kg/m^2 was defined as low body weight; 18.5-23.9 kg/m^2 was normal; 24.0-27.9 kg/m^2 was overweight; ≥ 28.0 kg/m^2 was obese(20). Use of tobacco was divided into 3 groups, never smoke, not currently smokers and currently smokers. Use of alcohol was divided into 3 groups, life time abstainer, heavy drinker (the number of days with more than 5 standard units of alcohol per day in the past 7 days was 4 or more days) and non-heavy drinkers (other drinkers). Sufficient intake of fruits and vegetables was defined as ≥ 5 servings of vegetables and fruits in 1 day (80 g was 1 servings), otherwise insufficient intake. Physical activity levels were measured based on participant responses to questions drawn from the Global Physical Activity Questionnaire(21). Low, moderate and high physical activity level were calculated and devided from questionnaire items based on the reported time of moderate or vigorous activity at work, during recreation/leisure time, and during transportation.

Statistical Analyses

First, we used t-test and Chi-square tests to compare the differences in the characteristics of the included and excluded participants. We showed different distributions of each variable between males and females in the 3 waves. Then, we presented scores on grip strength and cognitive function in the all, males and females, over the 3 waves, with scores on the four components of cognitive function (word recall, word fluency, digit span, and digit span) in a standardized form by Z-score. After z-score standardization, the score of each group was divided into a standard normal distribution, that is, a mean of 0 and a standard deviation of 1. The line chart shows the trend of their changes visually. Next, we intended to use Random Intercept Cross-Lagged Panel Model to explore the relationship between cognitive function and grip stength. Before that, we conducted bivariate correlation analysis of cognitive function and grip strength in the 3 waves to test whether the premise of cross-lagged study (i.e. stability and synchronization) is valid. With Wave 1, Wave 2, and Wave 3 as three time points, the cross-lagged model analysis as shown in the Supplementary Figure S1 was performed. Covariates adjusted in the cross-lagged analysis are categorized into time-invariant covariates and time-varing covariates. Time-invariant covariates include gender, residence and education. Time-varing covariates include agegroup, marital status, vegetable and fruit intake, physical activity level and chronic diseases. The solid line in indicates that the path of the pointing is statistically significant, and the dashed line indicates no statistical significance. When grip strength was significant for the path pointing to the next period of cognitive function, but path from cognitive function pointing to the grip strength the next period was not significant, we

considered grip strength have an effect on cognitive function, and vice versa. If both paths are significant, then they were supposed to influencing each other. We did Cross-lagged panel analyses in R, and did other statistical analyses in Stata. In terms of $P < 0.05$ was considered statistically significant.



Supplementary Figure S1. Conceptual Model of cross-lagged study between grip strength and cognitive function.

Supplementary Table S1. Comparison of characteristics between included and excluded participants

Characteristics	Included participants	Excluded participants	χ2/t	*P*
Age[a]	60.85±0.14	58.63±0.30	6.731	0.000
Gender[b]			0.847	0.358
Male	1665(53.9)	887(55.3)		
Female	1425(46.1)	717(44.7)		
Marital status[b]			2.059	0.357
Unmarried	28(0.9)	20(1.2)		
Currently married	2696(87.3)	1411(87.9)		
Separated/divorced	366(11.8)	175(10.9)		
Education[b]			69.650	0.000
None	626(20.3)	294(22.8)		
Less than primary school	699(22.6)	316(24.5)		
Completed primary school	786(25.4)	379(29.4)		
Completed middle school	602(19.5)	224(17.4)		
Completed high school	300(9.7)	76(5.9)		
Completed 3-year college or above	77(2.5)	2(0.2)		
Residence[b]			40.661	0.000
Urban	1031(33,4)	688(42.8)		
Rural	2059(66.6)	919(57.2)		

Characteristics	Included participants	Excluded participants	χ2/t	*P*
BMI group[b]			4.134	0.247
Low body weight	124(4.0)	67(4.7)		
Normal	1575(51.0)	743(52.7)		
Overweight	1050(34.0)	443(31.4)		
Obesity	341(11.0)	158(11.2)		
Tobacco[b]			3.027	0.220
Never smoke	1901(61.5)	979(63.8)		
Not current smoker	178(5.8)	91(5.9)		
Current smoker	1011(32.7)	465(30.3)		
Alcohol[b]			6.479	0.039
Life time abstainer	2106(68.2)	999(71.7)		
Non-heavy drinker	692(22.3)	287(20.6)		
Heavy drinker	292(9.5)	107(7.7)		
Vegetable and fruit intake[b]			7.488	0.006
Insufficient	904(29.3)	526(35.2)		
Sufficient	2186(70.7)	967(64.8)		
Pysical activity level[b]			37.175	0.000
Low	643(20.8)	417(27.2)		
Moderate	788(25.5)	432(28.1)		
High	1659(53.7)	686(44.7)		

Characteristics	Included participants	Excluded participants	χ2/t	*P*
Comorbidities[b]			52.093	0.000
0	1760(57.0)	863(53.7)		
1	909(29.4)	445(27.7)		
2	314(10.2)	165(10.3)		
≥3	107(3.4)	134(8.3)		
Grip strength[a]	28.50±0.20	29.58±0.33	-3.025	0.001
Cognitive function[a]				
Overall	56.71±0.24	57.44±0.41	-1.531	0.063
Verbal recall	5.55±0.03	5.59±0.05	-0.974	0.165
Verbal fluency	13.10±0.08	12.88±0,13	1.417	0.921
Forward digit span	7.12±0.03	7.09±0.04	0.708	0.760
Backward digit span	3.31±0.023	3.44±0.04	-2.871	0.002

Note: a.T-test was used for comparison between-group comparisons, statistic is t-value. b. Chi-square test were used for between-group comparisons, statistic is χ2.

Supplementary Table S2. Characteristics of participants in 3 waves

Characteristics	Wave 1 (baseline)			Wave 2			Wave 3		
	Male n (%) or mean ± SD	Female n (%) or mean ± SD	All n (%) or mean ± SD	Male n (%) or mean ± SD	Female n (%) or mean ± SD	All n (%) or mean ± SD	Male n (%) or mean ± SD	Female n (%) or mean ± SD	All n (%) or mean ± SD
Residence									
Urban	476(28.6)	555(38.9)	1031(33,4)	-	-	-	-	-	-
Rural	1189(71.4)	870(61.1)	2059(66.6)	-	-	-	-	-	-
Education									
None	190(11.4)	436(30.6)	626(20.3)	-	-	-	-	-	-
Less than primary school	384(23.1)	315(22.1)	699(22.6)	-	-	-	-	-	-
Completed primary school	475(28.5)	311(21.8)	786(25.4)	-	-	-	-	-	-
Completed middle school	386(23.2)	216(15.2)	602(19.5)	-	-	-	-	-	-
Completed high school	181(10.9)	119(8.4)	300(9.7)	-	-	-	-	-	-
Completed 3-year college or above	49(2.9)	28(1.9)	77(2.5)	-	-	-	-	-	-
Age	60.99±7.60	60.65±7.48	60.83±7.54	66.51±7.60	66.01±7.64	66.28±7.62	69.76±7.85	69.65±7.85	69.71±7.77
Age group (years)									
50~	829(49.8)	751(52.70)	1580(51.1)	310(18.6)	290(20.4)	600(19.4)	61(3.6)	75(5.3)	136(4.4)
60~	564(33.9)	461(32.3)	1025(33.2)	835(50.1)	709(49.8)	1544(50.0)	852(51.2)	728(51.1)	1580(51.1)
70~	248(14.9)	202(14.2)	450(14.6)	404(24.3)	344(24.1)	748(24.2)	544(32.7)	431(30.2)	975(31.6)
≥80	24(1.4)	11(0.8)	35(2.5)	116(7.0)	82(5.7)	198(6.4)	208(12.5)	191(13.4)	399(12.9)
Marital status									
Unmarried	23(1.4)	5(0.3)	28(0.9)	23(1.4)	5(0.4)	28(0.9)	23(1.4)	4(0.3)	27(0.9)

Characteristics	Wave 1 (baseline)			Wave 2			Wave 3		
	Male n (%) or mean ± SD	Female n (%) or mean ± SD	All n (%) or mean ± SD	Male n (%) or mean ± SD	Female n (%) or mean ± SD	All n (%) or mean ± SD	Male n (%) or mean ± SD	Female n (%) or mean ± SD	All n (%) or mean ± SD
Married/cohabiting	1539(92.4)	1157(81.2)	2696(87.3)	1514(90.9)	1139(79.9)	2653(85.9)	1408(84.5)	1083(76.0)	2491(80.6)
Divorced/separated/widowed	103(6.2)	263(18.5)	366(11.8)	128(7.7)	281(19.7)	409(13.2)	234(14.1)	338(23.7)	572(18.5)
BMI group									
Low body weight	61(3.7)	63(4.4)	124(4.0)	54(3.2)	45(3.2)	99(3.3)	98(5.9)	70(4.9)	168(5.5)
Normal	939(56.4)	636(44.6)	1575(51.0)	886(53.2)	619(43.4)	1505(48.7)	843(50.6)	654(45.9)	1497(48.4)
Overweight	536(32.2)	514(36.1)	1050(34.0)	569(34.2)	520(36.5)	1089(35.2)	562(33.8)	485(34.0)	1047(33.9)
Obesity	129(7.7)	212(14.9)	341(11.0)	156(9.4)	241(16.9)	397(12.8)	162(9.7)	216(15.2)	378(12.2)
Tobacco									
Never smoke	537(32.3)	1364(95.7)	1901(61.5)	444(26.7)	1349(94.7)	1793(58.0)	442(26.5)	1343(94.2)	1785(57.8)
Not current smoker	166(10.0)	12(0.8)	178(5.8)	485(29.1)	44(3.1)	529(17.1)	507(30.5)	45(3.2)	552(17.8)
Current smoker	962(57.8)	49(3.4)	1011(32.7)	736(44.2)	32(2.2)	768(24.9)	716(43.0)	37(2.6)	753(24.4)
Alcohol									
Life time abstainer	795(47.8)	1311(91.9)	2106(68.2)	680(40.8)	1243(87.2)	1923(62.2)	657(39.4)	1216(85.3)	1873(60.6)
Non-heavy drinker	591(35.5)	101(7.1)	692(22.3)	647(38.9)	150(10.5)	797(25.8)	794(47.7)	182(12.8)	976(31.6)
Heavy drinker	278(16.7)	14(1.0)	292(9.5)	338(20.3)	32(2.3)	370(12.0)	214(12.9)	27(1.9)	241(7.8)
Vegetable and fruit intake									
Insufficient	498(29.9)	406(28.5)	904(29.3)	226(13.6)	240(16.8)	466(15.1)	254(15.3)	218(15.3)	472(15.3)
Sufficient	1167(70.1)	1019(71.5)	2186(70.7)	1439(86.4)	1185(83.2)	2624(84.9)	1411(84.7)	1207(84.7)	2618(84.7)

Characteristics	Wave 1 (baseline)			Wave 2			Wave 3		
	Male n (%) or mean ± SD	Female n (%) or mean ± SD	All n (%) or mean ± SD	Male n (%) or mean ± SD	Female n (%) or mean ± SD	All n (%) or mean ± SD	Male n (%) or mean ± SD	Female n (%) or mean ± SD	All n (%) or mean ± SD
Pysical activity level									
Low	305(18.3)	338(23.7)	643(20.8)	536(32.2)	504(35.4)	1040(33.7)	487(29.3)	451(31.6)	938(30.4)
Moderate	380(22.8)	408(28.6)	788(25.5)	449(27.0)	401(28.1)	850(27.5)	403(24.20)	366(25.7)	769(24.9)
High	980(58.9)	679(47.7)	1659(53.7)	680(40.8)	520(36.5)	1200(38.8)	775(46.5)	608(42.7)	1383(44.8)
Comorbidities									
0	1012(60.8)	748(52.5)	1760(57.0)	942(56.6)	728(51.1)	1670(54.1)	837(50.3)	562(39.4)	1399(45.3)
1	453(27.2)	456(32.0)	909(29.4)	433(26.0)	418(29.3)	851(27.5)	530(31.8)	495(34.7)	1025(33.1)
2	145(8.7)	169(11.9)	314(10.2)	213(12.8)	186(13.1)	399(12.9)	214(12.8)	258(18.1)	472(15.3)
≥3	55(3.3)	52(3.65)	107(3.4)	77(4.6)	93(6.5)	170(5.5)	84(5.1)	110(7.8)	194(6.3)

Supplementary Table S3. cognitive function and grip strength in 3 waves

	Wave 1		Wave 2		Wave 3	
	Original score	Z-score	Original score	Z-score	Original score	Z-score
ALL						
Overall cognitive function[a]	56.71±13.46	-	50.00±15.34	-	49.69±15.44	-
Verbal recall	5.54±1.55	-0.028±0.782	4.82±1.73	-0.086±0.804	4.56±1.70	-0.120±0.857
Verbal fluency	13.10±4.54	0.056±0.909	11.82±4.90	-0.085±0.953	11.12±5.64	-0.014±0.921
Forward digit span	7.12±1.47	0.018±0.927	6.59±1.96	0.053±0.948	6.57±1.75	-0.042±0.982
Backward digit span	3.31±1.30	-0.171±0.876	3.13±1.43	-0.121±0.910	3.25±1.34	-0.177±0.918
Grip strength	28.50±10.97	-	27.81±10.18	-	25.40±8.84	-
Male						
Overall cognitive function[a]	57.44±13.30	-	49,80±14.79	-	49.20±14.86	-
Verbal recall	5.59±1.54	-0.005±0.774	4.75±1.66	-0.117±0.771	4.45±1.64	-0.152±0.828
Verbal fluency	13.61±4.67	0.159±0.936	11.96±4.66	-0.057±0.905	11.03±5.24	-0.031±0.948
Forward digit span	7.24±1.43	0.092±0.904	6.65±1.97	0.082±0.952	6.59±1.74	0.082±0.976
Backward digit span	3.46±1.25	-0.072±0.839	3.28±1.37	-0.025±0.872	3.32±1.42	-0.132±0.910
Grip strength	34.15±9.82	-	33.05±9.27	-	29.00±8.66	
Female						
Overall cognitive function[a]	55.85±13.60	-	50.24±15.97	-	50.25±16.08	-
Verbal recall	5.49±1.57	-0.055±0.792	4.89±1.81	-0.049±0.838	4.64±1.76	-0.081±0.889
Verbal fluency	12.50±4.30	-0.063±0.861	11.66±5.17	-0.117±0.994	11.23±6.08	0.006±0.900

Forward digit span	6.99±1.50	-0.068±0.947	6.52±1.95	0.200±0.944	6.55±1.76	-0.056±0.990
Backward digit span	3.14±1.34	-0.285±0.903	2.96±1.47	-0.232±0.940	3.175±1.35	-0.230±0.925
Grip strength	21.90±8.20	-	21.68±7.40	-	21.19±7.00	-

Note: a, adjusted original score to the range of 0 to 100 by using factor analysis; ***$P < 0.001$ **$P < 0.01$ *$P < 0.05$

Supplementary Table S4. Correlation between cognitive function and grip strength

	1	2	3	4	5	6
1. Cognitive function at Wave 1	1					
2. Cognitive function at Wave 2	0.318***	1				
3. Cognitive function at Wave 3	0.322***	0.395***	1			
4. Grip strength Wave 1	0.127***	0.051**	0.098***	1		
5. Grip strength Wave 2	0.131***	0.211***	0.135**	0.513***	1	
6. Grip strength Wave 3	0.138***	0.064***	0.205***	0.466***	0.481***	1

Note: ***$P < 0.001$ **$P < 0.01$ * $P < 0.05$.

Supplementary Table S5. Correlation between verbal recall and grip strength

	1	2	3	4	5	6
1. Verball recall at Wave 1	1					
2. Verball recall at Wave 2	0.290***	1				
3. Verball recall at Wave 3	0.285***	0.351***	1			
4. Grip strength Wave 1	0.107***	0.028	0.092***	1		
5. Grip strength Wave 2	0.128***	0.189***	0.128***	0.513***	1	
6. Grip strength Wave 3	0.112***	0.036*	0.177***	0.466***	0.481***	1

Note: ***$P < 0.001$ **$P < 0.01$ * $P < 0.05$

Supplementary Table S6. Correlation between verbal fluency and grip strength

	1	2	3	4	5	6
1. Verball fluency at Wave 1	1					
2. Verball fluency at Wave 2	0.236***	1				
3. Verball fluency at Wave 3	0.180***	0.233***	1			
4. Grip strength Wave 1	0.095***	0.071***	-0.006	1		
5. Grip strength Wave 2	0.056**	0.138***	0.012	0.513***	1	
6. Grip strength Wave 3	0.123***	0.113***	0.094***	0.466***	0.481***	1

Note: ***$P < 0.001$ **$P < 0.01$ * $P < 0.05$

Supplementary Table S7. Correlation between forward digit span and grip strength

	1	2	3	4	5	6
1. Forward digit span at Wave 1	1					
2. Forward digit span at Wave 2	0.206***	1				
3. Forward digit span at Wave 3	0.245***	0.308***	1			
4. Grip strength Wave 1	0.156***	0.058**	0.130***	1		
5. Grip strength Wave 2	0.036*	0.170***	0.099***	0.513***	1	
6. Grip strength Wave 3	0.156***	0.080***	0.227***	0.466***	0.481***	1

Note: ***$P < 0.001$ **$P < 0.01$ * $P < 0.05$

Supplementary Table S8. Correlation between backward digit span and grip strength

	1	2	3	4	5	6
1. Back digit span at Wave 1	1					
2. Back digit span at Wave 2	0.338***	1				
3. Back digit span at Wave 3	0.207***	0.262***	1			
4. Grip strength Wave 1	0.135***	0.173***	0.094***	1		
5. Grip strength Wave 2	0.171***	0.200***	0.150***	0.513***	1	
6. Grip strength Wave 3	0.135***	0.142***	0.194***	0.466***	0.481***	1

Note: ***$P < 0.001$ **$P < 0.01$ * $P < 0.05$

Supplementary Table S9. Fit indices of cross-lagged model

	grip strength with overall cognitive function	grip strength with verbal recall	grip strength with verbal fluency	grip strength with forward digit span	grip strength with backward digit span
x2(df)	819.785(97)	780.870(97)	855.485(97)	860.204(97)	729.790(97)
p-value	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001
CFI	0.906	0.904	0.882	0.886	0.905
TLI	0.845	0.843	0.807	0.814	0.845
RMSEA	0.049	0.048	0.050	0.050	0.046
SRMR	0.019	0.019	0.020	0.021	0.019

Note: CFI, Comparative Fit Index. TLI, Tucker-Lewis index. RMSEA, Root Mean Square Error of Approximation, SRMR Standardized Root Mean Square Residual.