Original Article

The role of dietary fats on cognition and sarcopenia in the elderly

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Background and Objectives: To elucidate the role of dietary fats on the relationship between mild cognitive impairment and sarcopenia and help identifying and preventing the decline of cognitive and muscle function in elderly individuals. **Methods and Study Design:** The study conducted involving a group of 1812 individuals between the ages of 61 and 92. Body composition and BMR were assessed by bioelectrical impedance analysis. Cognitive function and dietary nutrition were evaluated by neuropsychological assessments and questionnaire of food intake frequency. Lipidomics analysis was performed using UHPLC-Qtrap-MS/MS. **Results:** MCI and SA are mutual influencing factors, lower intake of MUFA, PUFA and higher intake of fat was associated with cognitive dysfunction and/or SA ($p < 0.05$). PUFA was important for MCI combined with SA (Compared with Q1, Q4 OR: 0.176, 95%CI: 0.058,0.533). Lipidomics analysis revealed that triacylglycerol (TAG) contain more carbon chains with saturated double bonds may be closely related to cognitive impairment and the progression of SA ($p < 0.05$). While, DAG with carbon chains of unsaturated double bonds is opposite. **Conclusions:** Insufficient intake of unsaturated fatty acids was associated with the development of cognitive decline and the progression of SA. MUFA affecting muscle health, fats and PUFA has a greater impact on MCI combined with SA. Less MUFA intake and increasing saturated double-bonded fatty acid intake might be the key factors on promoting cognitive impairment and SA in the elderly. They have the potential to serve as prospective biomarkers indicating a higher risk of cognitive decline and/or SA in the elderly population.

Key Words: mild cognitive impairment, sarcopenia, dietary fats, lipidomics, the elderly

INTRODUCTION

Cognitive dysfunction and sarcopenia (SA) are prevalent age-related chronic degenerative conditions which can have a considerable impact on the health of the elderly. Mild cognitive impairment (MCI) is considered an early phase of neurodegenerative diseases like Alzheimer's disease (AD).[1] The yearly rate at which individuals with mild cognitive impairment transition to dementia in older adults is approximately 10% to 15%,[2] which is notably higher when compared to the common mass.[3] Study shows that higher risk of falls, disability, weakness, and other unfavorable consequences is linked with SA,[4] which is characterized by the progressive loss of muscle mass and/or strength. Therefore, it is crucial for researchers to continue exploring improved methods for early detection and intervention of MCI and SA in older individuals. So, what are the key factors associated with the occurrence and progression of MCI and SA in the elderly?

Dietary factors significantly contribute to the onset and the development of MCI and SA. Several reports have focused on the role of dietary fat, which is recognised as a key nutrient affecting muscle and brain health.[5-6] Dietary fat is mainly triacylglycerol (TAG), which is composed of glycerol and fatty acids. According to the degree of unsaturation, fatty acids are usually classified as saturated fatty acid (SFA), monounsaturated fatty acid (MUFA), and polyunsaturated fatty acid (PUFA). Fatty acids can be oxidized in the human body to provide energy, metabolized to generate a series of eicosanoid, and also participate in regulating a series of signaling pathways, affecting the body's physiological functions.[7] Higher intake of total fats, SFA, trans fatty acids, cholesterol and its oxidative metabolites are reported as risk factors for cognitive function, while phospholipids, PUFAs, and MUFAs may have protective effects. In addition, saturated fatty acids are considered contributing to obesity, which might be associated with the risk of muscle health.[8] Supplements of unsaturated fatty acids have been shown to counteract many of the catabolic metabolic effects associated with saturated fatty acid intake. For instance, n-3 PUFA has

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been linked to a significant increase in skeletal muscle mass and has beneficial effects on muscle strength and physical function in patients with SA or those at high risk for SA.[9] However, the evidence is always on the only role of cognition or muscle health. It is unknown if they are the main causes of both occurrence of cognitive dysfunction combined with SA.

A research has described that there are differences in phospholipids intake and disturbances in lipid metabolism in individuals with MCI and SA compared to individuals without these conditions.[10] The above indicates the potential role of dietary fats on the occurrence and progression of MCI and SA. In a word, our research focuses on investigating the relationship between dietary fats and cognitive decline and muscle function decrease in the elderly. Specifically, whether dietary fats, as an important dietary factor, are associated with the progression of MCI and SA in the elderly population? Thus, the aim of this study was to clarify the role of different fatty acid types and TAG with different carbon chain structures on MCI and/or SA. To investigate whether they have the potential to be prospective biomarkers for predicting the risk of cognitive decline and/or SA in the elderly population.

METHODS

Participants

Between 2020 and 2021, we selected older adults aged 60 or above who have completed a health examination in the study of registered cohort (ChiCTR2100054969). The study followed the same methods and criteria as a previous research.[11-12] This study was a population-based cross-sectional study based on elderly people over 60 years old, and the health examination data of the population were collected and analyzed. This study was conducted with a total of 1812 participants who provided their informed consent. The study adhered to the guidelines outlined in the Declaration of Helsinki and received approval from the Ethics Committee of Capital Medical University (Z2019SY052).

Inclusion criteria: 1. Aged 60 or above; 2. Not diagnosed with Alzheimer's disease; 3. Normal communication and physical activity abilities; 4. No specific medical history, not suffering from major diseases such as malignant tumors.

Exclusion criteria: 1. Patients with a history of cerebrovascular disease, combined with severe cognitive decline due to serious heart, liver, lung, or kidney dysfunction; 2. Patients with cognitive impairment caused by depression, thyroid disease, head trauma, drug or alcohol poisoning; 3. Patients with major diseases such as malignant tumors.

Cognitive assessment

The cognitive function was assessed using the Montreal Cognitive Assessment (MoCA) and Mini-Mental State Examination (MMSE).13 The two-step process for diagnosing patients with MCI is described in our previous studies.[12,14]

Sarcopenia assessment

The assessment of sarcopenia is determined using the criteria established by the Asian Working Group for Sarcopenia (AWGS) in 2019. According to these criteria, individuals with low skeletal muscle mass index (SMI) and low grip strength and/or low physical function are classified as having sarcopenia.[15-20] For further information, please refer to Supplementary Material, “Sarcopenia Assessment” part.

Dietary assessment

We utilized the food frequency questionnaire (FFQ) from the 2002 China National Nutrition and Health Survey (CNHS 2002) to gather data on individuals' dietary information.21 Energy and nutrient intake were determined using the China Food Composition Database (Version 6).[16,20]

Blood sample collection

Collect blood samples from individuals who have not consumed any food since 8 PM the previous night. The enzymatic method was used to measure the levels of total cholesterol (TC), TAG, high-density lipoprotein cholesterol (HDL-C), and low-density lipoprotein cholesterol (LDL-C) in the serum. This measurement was done using an automatic biochemistry analyzer (Olympus AU480, Japan). Non-high density lipoprotein cholesterol (non-HDL-C) is determined by subtracting the HDL-C from the TC. The ratio of LDL-C to HDL-C was also calculated using the measured blood lipids. The clinical reference ranges for TC, TAG, LDL-C, and non-HDL-C are 0-5.20 mmol/L, 0-1.70 mmol/L, 0-3.12 mmol/L, and 0-3.4 mmol/L, respectively. The reference ranges for HDL-C concentration and LDL-C/HDL-C ratio are 1.04-1.7 mmol/L and 1.31-3.19, respectively.

MRM targeted measurement

The experimental method used in this study is the same as in previous study.[21] We used a modified method of lipids extraction and included the details of this method, the Supplementary Material contains details about the reagents, processes, and acquisition software.

Statistical analysis

Continuous variables that did not follow a normal distribution were expressed as medians (P25, P75), while those that did follow a normal distribution were expressed as the mean ± standard deviation (SD). To analyze continuous variables, we employed either analysis of variance (ANOVA) or the Kruskal-Wallis rank test. Categorical variables, on the other hand, were analyzed using MCI chi-squared tests. To examine the relationship of key factors, we used multiple linear regression analysis. After converting dietary factors by quartile grouping into categorical variables, a multivariate logistic regression model was used to investigate the influencing factors of cases. The threshold for statistical significance was established at a two-sided *p*-value less than 0.05. Our statistical analysis was carried out using IBM SPSS Statistics 23.0. We utilized the GraphPad Prism 9.5 software for generating the box and bar plots.

RESULTS

Demographic and clinical characteristics of participants

As shown in Table 1, a total of 1812 subjects (57.9% females) were included in this study, including 705 cases (38.9%) of MCI, 82 cases (4.53%) of SA, and 91 cases (5.02%) of MCI combined with SA. There were notable disparities in the age, body mass index (BMI), and basal metabolic rate (BMR) between the SA group and the control group, as well as between the MCI combined with SA group and the control group. In other words, individuals with SA and with MCI combined with SA were older than controls, and their BMI and BMR were significantly lower than controls. In addition, individuals with SA had a higher likelihood of having a lower education level. As expected, the MoCA scores of all individuals in the MCI, SA, and MCI combined with SA groups were all significantly lower than those in the control group.

Consumption of dietary fats in different groups

According to Table 2, there were significant differences in the composition of dietary fats among the different groups. The intake of total fats was significantly higher in MCI combined with SA individuals compared with control and the only patients of MCI ($p < 0.05$). On the contrary, the PUFA and MUFA were significantly lower in the diets of MCI combined with SA patients compared to other three groups ($p < 0.05$). It was interesting that the intake of energy in MCI combined with SA patients was significantly lower than other groups.

Performance of dietary fats on MoCA score and skeletal muscle index

As shown in Table 3, it is important to note that there were strong positive correlations either between consumption of MUFA and MoCA, or between consumption of MUFA and SMI in both unadjusted and adjusted models (adjusted for age, gender, education level, race, BMI; $p<0.001$). Further detection gave the results that when combined with total fat, total fatty acids, SFA, cholesterol and docosahexaenoic acid (DHA), respectively, there was still a strong positive correlation between MUFA and MoCA, as well as between MUFA and SMI in both models ($p < 0.05$).

However, in the adjusted model, when test the MUFA combined with energy or protein, the positive correlation between MUFA and MoCA disappears. On the contrary, the strong positive correlation between MUFA and SMI did not disappear due to combined energy or protein ($p < 0.001$).

Then, we further explored the performance of dietary fats on MoCA score and SMI in depth. Results in Table 4 showed SMI and MUFA were both significantly associated with MoCA score ($p < 0.05$). After adjusted dietary intake of energy and protein, SMI still significantly associated with MoCA score ($p < 0.05$). However, the association of MUFA disappeared instead of an association with protein. Moreover, MoCA score and MUFA were also both significantly associated with SMI ($p < 0.05$). After adjusted dietary intake of energy and protein, the associations of MoCA score, MUFA and SMI did not disappear ($p < 0.05$). Surprisingly, in both models that the higher MoCA score was closely associated with higher SMI, this confirmed that both are mutually influencing factors.

The role of dietary fats on the risk of MCI combined with SA

The results of multiple logistic regression analysis can be found in Table 5. After adjusting for the demographic and clinical parameters, PUFA Q3(OR: 0.250, 95%CI: 0.094,0.664, compared with Q1) and Q4 (OR: 0.176, 95%CI: 0.058,0.533, compared with Q1), as well as lecithin Q3 (OR: 0.421, 95%CI: 0.192,0.921, compared with Q1) and Q4 (OR: 0.385, 95%CI: 0.162,0.913, compared with Q1), are associated with reduced risk of MCI combined with SA ($p < 0.05$).

Targeted lipidomics analysis

Targeted lipidomics analysis was detected by UHPLC-QTRAP®6500+-MS/MS testing the red blood cells of 15 samples in every group. In Figure 1, when comparing with the control group, we observed that TAG (51:1)_FA17:0, TAG (49:1)_FA16:0, and TAG (51:1)_FA18:1 which contained two saturated double bonds fatty acids were upregulated in the MCI combined with SA groups ($p < 0.05$); in the SA group, TAG (40:0)_FA16:0, TAG (51:1)_FA18:0, TAG (58:2)_FA18:1 which contain 1-3 saturated double bonds fatty acids were upregulated; in the MCI group, TAG (49:2)_FA18:2 which contain two saturated double bonds fatty acids were upregulated ($p < 0.05$). Moreover, we found that diglyceride (DAG) (18:2/20:4) was significantly downregulated in the MCI combined with SA groups compared to the control group ($p < 0.05$).

DISCUSSION

MCI and SA are significant health problems among the elderly population, leading to adverse health events such as physical disability, reduced quality of life, and death.[22] Nutrition is considered one of the primary modifiable risk factors.[23] This study aims to explore the role of dietary fats on the risk of MCI and/or SA. Furthermore, targeted lipidomics was used to verify dietary related specific fats as risk markers for MCI combined with SA. Our research indicates that insufficient intake of unsaturated fatty acids, including MUFA and PUFA, as well as excessive intake of fat, are associated with the progression of cognitive dysfunction and SA.

First, demographic and clinical characters gave the evidence that all patients with SA showed older age, lower education, lower BMI and lower BMR than controls and patients only with MCI. Combined with the results of subsequent multiple linear regression analysis, age, education and BMI are the key factors influencing muscle health. On the other hand, obesity and overweight rates were not significantly different between MCI and controls, but were higher in MCI patients compared with patients with SA and patients with MCI combined with SA. This may indicate that the impact of SA on the degree of obesity is greater than MCI. It was worth noting that the MoCA scores of all patients of MCI and/or SA were lower than controls. These results were similar to our previous studies.[10] Studies have shown that the primary factor that determines whether a person has low, nor-

Table 1. Demographic and clinical characteristics of subjects

	Total	Categories				*p* value
		Ctrl	MCI	SA	MCI&SA	
Demographic characteristics						
N	1812	934	705	82	91	
Age	70.0 (67.0, 73.0)	70.0 (67.0, 73.0) †,‡	69.0 (67.0, 73.0) §,¶	72.0 (68.0, 75.0) †,§	73.0 (68.0, 77.0) ‡,¶	< 0.001***
Female, n (%)	1049 (57.9)	583 (62.4) †,‡	379 (53.8) †	43 (52.4)	44 (48.4) ‡	< 0.001***
Han Chinese, n (%)	1735 (95.8)	893 (95.6)	675 (95.7)	79 (96.3)	88 (96.7)	0.956
Education						< 0.001***
Illiterate, n (%)	365 (20.1)	250 (26.8) †,‡	67 (9.5) †,§,¶	31 (37.8) ‡,§,††	17 (18.7) ¶,††	
Primary school	600 (33.1)	353 (37.8) †,‡	194 (27.5) †,§	32 (39.0) §,¶	21 (23.1) ‡,¶	
Junior high school, n (%)	682 (37.6)	239 (25.6) †,‡	383 (54.3) †,§	17 (20.7) §,¶	43 (47.3) ‡,¶	
High school and above, n (%)	165 (9.1)	92 (9.9) †	61 (8.7) ‡	2 (2.4) †,‡,§	10 (11.0) §	
BMI (kg/m^2)	26.1 (24.0, 28.6)	26.6 (24.6,29.0) †,‡	26.5 (24.2, 28.8) §,¶	22.5 (20.7,24.5) †,§	22.7 (20.1, 24.3) ‡,¶	< 0.001***
Emaciation n(%)	16 (0.9)	2 (0.2) †	4 (0.6) ‡	1 (1.2) §	9 (9.9) †,‡,§	< 0.001***
Normal n(%)	431 (23.8)	171 (18.3) †,‡	151 (21.4) §,¶	54 (65.9) †,§	55 (60.4) ‡,¶	
Overweight n(%)	801 (44.2)	437 (46.8) †,‡	317 (45.0) §,¶	24 (29.3) †,§	23 (25.3) ‡,¶	
Obesity n(%)	564 (31.1)	324 (34.7) †	233 (33.0) ‡,§	3 (3.7) ‡	4 (4.4) †,§	
BMR (kcal)	1266 (1155, 1402)	1276 (1170, 1408) †,‡	1282 (1168, 1430) §,¶	1101 (1101, 1245) †,§	1130 (1030, 1280) ‡,¶	< 0.001***
MoCA	21 (18, 24)	23 (20, 25) †,‡	19 (16, 22) †,§	22 (18, 24) §,¶	18 (12, 21) ‡,¶	< 0.001***
Serum Cholesterol						
TC (mmol/L)	4.71 (4.01, 5.38)	4.76 (4.01, 5.41)	4.64 (3.97, 5.32)	4.75 (4.09, 5.33)	4.73 (3.87, 5.43)	0.378
TAG (mmol/L)	1.33 (0.97, 1.88)	1.34 (0.99, 1.90)	1.36 (0.97, 1.87)	1.17 (0.82, 1.71)	1.22 (0.90, 1.76)	0.051
HDL-C (mmol/L)	1.27 (1.08, 1.48)	1.28 (1.09, 1.48)	1.25 (1.07, 1.45)	1.30 (1.12, 1.56)	1.22 (0.99, 1.54)	0.151
LCL-C (mmol/L)	2.92 (2.32, 3.52)	2.95 (2.32, 3.51)	2.88 (2.29, 3.50)	2.94 (2.39, 3.65)	2.94 (2.35, 3.68)	0.483
non-HDL-C (mmol/L)	3.39 (2.73, 4.05)	3.44 (2.74, 4.08)	3.31 (2.68, 4.02)	3.36 (2.78, 4.11)	3.39 (2.77, 3.99)	0.570
LDL-C/HDL-C	2.30 (1.75, 2.87)	2.28 (1.77, 2.89)	2.31 (1.73, 2.86)	2.22 (1.69, 2.80)	2.34 (1.85, 2.94)	0.709

MoCA, Montreal cognitive assessment score; TC, total cholesterol; TAG, triglyceride; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol
Categorical and continuous variables were shown as n (%) and medians (P25, P75).
†,‡,§,¶,†† values with the same footnotes indicates a significant difference at $p < 0.05$.
* $p < 0.05$.** $p < 0.01$.*** $p < 0.001$ in all groups.

Table 2. Consumption of dietary fats in different groups

	Total	Ctrl	MCI	SA	MCI&SA	*p* value
N	1812	934	705	82	91	
Energy (kcal/d)	1766 (1453, 2150)	1794 (1490, 2192) [†]	1753 (1438, 2132)	1799 (1388, 2107)	1629 (1292, 2031) [†]	0.025*
Protein (g/d)	57.6 (45.9, 72.5)	59.5 (47.9, 74.9) [†,‡]	56.6 (45.0, 70.9) [†,§]	54.6 (44.2, 74.8)	50.3 (37.4, 64,3) [‡,§]	<0.001***
Fat (g/d)	117 (71.0, 197)	118 (71.7, 200) [†]	111 (70.3, 182.9) [‡]	135 (68.0, 217)	165 (98.2, 227) [†,‡]	0.001**
CHO (g/d)	125 (78.7, 200)	128 (78.6, 203) [†]	135 (80.9, 205) [‡]	111 (80.0, 169) [§]	89.9 (62.2, 115) [†,‡,§]	< 0.001***
Cholesterol (mg/d)	343 (253, 401)	348 (263, 403) [†]	340 (245, 399)	344 (274, 394)	312 (170, 381) [†]	0.025*
Lecithin (mg/d)	88.1 (68.8, 109)	90.2 (71.4, 111) [†]	87.2 (68.8, 109) [‡]	86.5 (71.8, 102)	73.0 (53.4, 96.2) [†,‡]	< 0.001***
Total fatty acids (g/d)	69.3 (54.6, 90.3)	69.6 (55.0, 90.4)	69.2 (54.7, 90.2)	68.8 (54.1, 93.2)	65.6 (52.0, 86.7)	0.573
SFA (g/d)	19.0 (14.3, 25.0)	19.2 (14.6, 25.3)	19.0 (14.2, 25.0)	18.4 (13.2, 26.2)	17.2 (12.7, 23.4)	0.077
MUFA (g/d)	20.5 (13.3, 29.8)	20.9 (13.8, 30.2) [†]	21.1 (13.4, 30.9) [‡]	18.3 (11.4, 25.8) [§]	13.0 (8.17, 20.7) [†,‡,§]	< 0.001***
PUFA (g/d)	12.8 (4.99, 20.6)	13.1 (5.37, 20.8) [†]	14.0 (5.22, 21.4) [‡]	9.75 (4.38, 16.7) [§]	4.70 (2.60, 11.7) [†,‡,§]	< 0.001***
LA (mg/d)	13.5 (7.96, 21.8)	13.4 (8.06, 21.6)	12.6 (7.85, 21.5) [†]	15.3 (7.43, 25.5)	17.8 (10.6, 24.3) [†]	0.046*
ALA (mg/d)	1.15 (0.565, 1.83)	1.13 (0.542, 1.87)	1.10 (0.576, 1.74)	1.35 (0.504, 2.17)	1.43 (0.826, 2.14)	0.058
EPA (mg/d)	0.108 (0.072, 0.162)	0.106 (0.072, 0.157)	0.107 (0.070, 0.162)	0.118 (0.071, 0.189)	0.111 (0.084, 0.163)	0.182
DHA (mg/d)	< 0.001 (< 0.001, 0.001)	< 0.001 (< 0.001, 0.001)	< 0.001 (< 0.001, 0.001)	< 0.001 (< 0.001, 0.002)	0.001 (< 0.001, 0.001)	0.307

CHO, carbohydrate; SFA, saturated fatty acid

Continuous variables were shown as medians (P25, P75) or mean ± standard deviation

[†,‡,§] values with the same footnotes indicates a significant difference at $p < 0.05$.

* $p < 0.05$.** $p < 0.01$.*** $p < 0.001$ in all groups

Table 3. Performance of dietary fats on MoCA score and SMI

	Unadjusted Model				Adjusted Model †			
	MoCA		SMI		MoCA		SMI	
	B	*p* value	B	*p* value	B	*p* calue	B	*p* value
MUFA (g/d)	0.036	< 0.001***	0.018	< 0.001***	0.017	0.003**	0.012	< 0.001***
MUFA (g/d)	0.037	< 0.001***	0.024	< 0.001***	0.020	0.013*	0.018	< 0.001***
SFA (g/d)	-0.002	0.929	-0.015	< 0.001***	-0.009	0.579	-0.017	< 0.001***
MUFA (g/d)	0.061	< 0.001***	0.033	< 0.001***	0.040	< 0.001***	0.027	< 0.001***
Total fatty acids (g/d)	-0.014	0.003**	-0.009	< 0.001***	-0.013	0.002**	-0.008	< 0.001***
MUFA (g/d)	0.030	< 0.001***	0.013	< 0.001***	0.017	0.004**	0.012	< 0.001**
BMR (kcal)	0.006	< 0.001***	0.005	< 0.001***	0.004	< 0.001***	0.003	< 0.001**
MUFA (g/d)	0.024	0.001**	0.015	< 0.001***	0.009	0.141	0.013	< 0.001***
Energy (kcal/d)	0.001	< 0.001**	0.000	< 0.001***	0.001	0.008**	< 0.001	0.362
MUFA (g/d)	0.023	0.001**	0.016	< 0.001***	0.007	0.268	0.012	< 0.001***
Protein (g/d)	0.022	< 0.001***	0.004	0.001**	0.018	< 0.001***	0.001	0.458
MUFA (g/d)	0.037	< 0.001***	0.017	< 0.001***	0.019	0.001**	0.010	< 0.001***
Fat (g/d)	0.001	0.543	-0.002	< 0.001***	0.002	0.142	-0.002	< 0.001***
MUFA (g/d)	0.030	< 0.001***	0.017	< 0.001***	0.013	0.027*	0.012	< 0.001***
Cholesterol (mg/d)	0.002	0.003**	0.000	0.019*	0.002	0.023*	< 0.001	0.431
MUFA (g/d)	0.038	< 0.001***	0.018	< 0.001***	0.018	0.002**	0.012	< 0.001***
DHA (mg/d)	110	0.005**	-6.44	0.467	61.5	0.073	-27.9	< 0.001***

SFA, saturated fatty acid; MoCA, Montreal cognitive assessment score; SMI, skeletal muscle index.
†Adjusted Model adjusted for age, sex, education, ethnicity, and BMI.
* $p < 0.05$.** $p < 0.01$.*** $p < 0.001$ in all groups.

Table 4. Performance of dietary fats on MoCA score and SMI

	Unadjusted Model				Adjusted Model †			
	MoCA		SMI		MoCA		SMI	
	B	*p* value	B	*p* value	B	*p* value	B	*p* value
MUFA (g/d)	0.021	0.001**	-	-	0.013	0.036*	-	-
SMI (kg)	0.834	< 0.001***	-	-	0.370	0.010*	-	-
MUFA (g/d)	0.012	0.109	-	-	0.004	0.505	-	-
SMI (kg)	0.811	< 0.001***	-	-	0.348	0.015*	-	-
Energy (kcal/d)	0.000	0.346	-	-	0.000	0.230	-	-
Protein (g/d)	0.027	0.004**	-	-	0.026	0.002**	-	-
MUFA (g/d)	-	-	0.017	< 0.001***	-	-	0.012	< 0.001***
MoCA	-	-	0.042	< 0.001***	-	-	0.010	0.010*
MUFA (g/d)	-	-	0.014	< 0.001***	-	-	0.013	< 0.001***
MoCA	-	-	0.041	< 0.001***	-	-	0.009	0.015*
Energy (kcal/d)	-	-	0.000	< 0.001***	-	-	0.000	0.005**
Protein (g/d)	-	-	-0.003	0.101	-	-	0.004	0.009**

SMI, skeletal muscle index; MoCA, Montreal cognitive assessment score.
†Adjusted Model adjusted for age, sex, education, ethnicity, and BMI.
* $p < 0.05$.** $p < 0.01$.*** $p < 0.001$ in all groups..

Table 5. The role of dietary fats on the risk of MCI combined with SA

	Q1	Q2		Q3		Q4		*p* for trend
		OR (95%CI)	*p* value	OR (95%CI)	*p* value	OR (95%CI)	*p* value	
MCI and SA vs. Ctrl†								
PUFA (g/d)	Ref	0.582 (0.301, 1.125)	0.108	0.250 (0.094, 0.664)	0.005**	0.176 (0.058, 0.533)	0.002*	0.001**
Lecithin (mg/d)	Ref	0.545 (0.281, 1.056)	0.072	0.421 (0.192, 0.921)	0.030*	0.385 (0.162, 0.913)	0.030*	0.012*

†Adjusted for age, sex, education, ethnicity, BMR and BMI.
* $p < 0.05$.** $p < 0.01$.

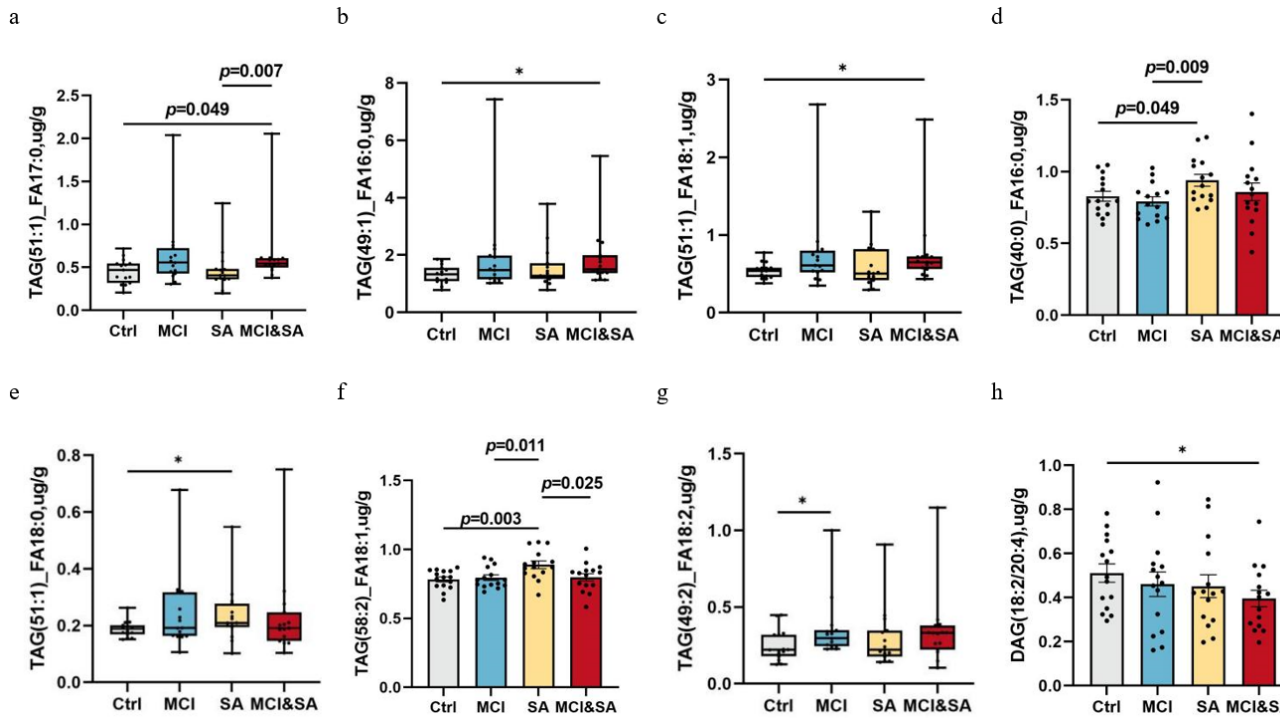

Figure 1. The comparisons for the content of TAG and DAG based on targeted lipidomic analysis

mal, or high concentrations of serum cholesterol is genetic. The effect of dietary fats on any individual's serum cholesterol is superimposed on the genetically determined concentration of serum cholesterol.[24] In short, dietary factors cannot replace genetic factors in determining an individual's serum cholesterol levels. So this may explain why the intake of fat, PUFA, and MUFA were different among the four groups, however there was no significant difference in serum cholesterol levels among the groups. Research findings have shown that patients with AD and MCI exhibit notable irregularities in lipid metabolism.[25] Meanwhile, there is a positive correlation between lipid metabolism abnormalities in older individuals and the risk of sarcopenia.[26] These results imply that metabolism dysfunction of fats is an important factor on brain and muscle health, but may have specific roles in cognitive dysfunction and SA.

In this study, the patients of MCI combined with SA had higher intake of total fat but lower intake of MUFA, PUFA, lecithin. Our previous research results show that compared to the control group and the pure MCI group, although there was no significant difference in fat intake in SA group and MCI combined with SA group, there was an increasing trend[10]. However, a cross-sectional study based on The Helsinki Businessmen Study (HBS) showed that SA was associated with lower total fat (p=0.015).[27] The appearance of such conflicting conclusions may be attributed to the race of the subjects, as well as their dietary structure and habits. Therefore, the clear correlation between fat and MCI and/or SA still needs further confirmation. There is strong evidence that greater intake of MUFA and PUFA related to better cognitive function in the Italian Longitudinal Study on Aging after an 8.5-year follow-up.[28] Our previous study showed that inadequate dietary intake and lower concentrations of the erythrocyte lipid profile of phospholipids and unsaturated fatty acids might be the key points that lead to progress in MCI and SA, as well as in their link.[10] These features could be recognized not only for the powerful dietary biomarkers of lipid metabolism disorders, but also could be used as the prospective biomarkers for the higher risk of cognitive decline and/or SA in elderly population.[29] Given that there is limited research on the relationship between dietary fats and MCI combined with SA at present, we will further investigate the role of dietary fats in the occurrence and progression of comorbidity in the following.

The more effective roles were shown on MUFA and PUFA in all patients with SA. Multiple linear regression gave very strong evidence that MUFA is higher related with MoCA score and SMI. This aligns with a systematic review results that demonstrate a correlation between a decreased consumption of MUFA and a higher risk of muscle loss.[30] A cross-sectional analysis of Macronutrient composition and sarcopenia in the oldest-old men also showed that unsaturated fat intake (both MUFA and PUFA) were inversely associated with SA.[27] Interestingly, the association between MUFA and MoCA score could be affected by dietary intake of energy and protein. However, the association between MUFA and SMI is so strong that it could not be disturbed by dietary factors such as energy and protein. This might imply that MUFA might be the key marker in the relation of MCI and SA, which have more power on muscle health. The results of a cross-sectional study could partially support our research finding, which explore the relationship between dietary macronutrients and cognitive impairment in 278 elderly individuals aged 65-84 who do not have dementia. The study found that the odds ratios for cognitive decline decreased significantly as the intake of MUFA increased, even after accounting for educational level. Age, as a confounding factor in the context of “MUFA education”, is

associated with further increases in cognitive impairment or cognitive decline.[31] Multiple logistic regression gives the evidence that high-dose intake of PUFA and lecithin are associated with a reduced risk of MCI combined with SA. This is consistent with the results that high PUFA intake can protect against the development of cognitive impairment and muscle loss.[32-33] These results remind that elderly individuals who have inadequate intake of unsaturated fatty acids are at a higher risk of developing MCI and/or SA, highlighting the important role of fatty acid carbon chain type from diet.

To further validate the above findings, we conducted targeted lipidomics analysis on the subjects' red blood cells, which could reflect long-term dietary intake of fats. As triglycerides are glycerol esters formed by esterification of three hydroxyl groups of glycerol with three fatty acid molecules. The TAG (51:1)_FA17:0, TAG (49:1)_FA16:0, and TAG (51:1)_FA18:1 could be classified into lipids containing 2 saturated double bonds fatty acids, which were upregulated in the patients of MCI combined with SA. Similarly, the TAG (40:0)_FA16:0, TAG (51:1)_FA18:0, TAG(58:2)_FA18:1 which contain 1-3 saturated double bonds fatty acids were upregulated in SA patients. TAG (49:2)_FA18:2 which contain 2 saturated double bonds fatty acids were upregulated in the individuals of MCI. This result consisted with the dietary results in Table 2 that MCI combined with SA patients had a higher intake of fat. In Table 2, although no difference in SFA was observed among the groups, SA group and MCI combined with SA group still showed a downward trend, especially in MCI combined with SA group. This also echoes our result in targeted lipidomics analysis. We believe that exploring the association between dietary fats on cognition and sarcopenia in the elderly from the perspective of TAG is fresh, which can provide better evidence support for our research.

On the other hand, we observed a significant downregulation of DAG (18:2/20:4) in MCI combined with SA patients compared to controls. DAG has been found to have the ability to reduce the buildup of body fat and lower triglyceride levels in the blood after eating. Additionally, it has been shown to increase the density of bone minerals and enhance the structure of bones.[34] It might be a new lipid marker for preventing MCI and SA. However, further evidence is needed to support the hypothesis.

Finally, surprisingly, we found a positive association between MoCA and SMI in Multiple linear regression, and the association remains unaffected by dietary factors such as MUFA and other confounding factors. This evidence is in line with the results from a meta-analysis, which demonstrated that cognitive impairment was significantly higher prevalent in participants with sarcopenia compared with those without sarcopenia, furthermore this positive association was independent of confounders such as age, sex, depression, education level, physical performance, and common comorbidities.[35] Recently Yang et al further observed that the prevalence of MCI is relatively high in patients with sarcopenia, and put forward that sarcopenia may be a risk factor for MCI.[36] This proves that SA has the potential to promote the development of MCI. Conversely, a study revealed a high prevalence rate of sarcopenia in subjects with AD, even in the early stages of AD. Lower cognitive function were associated with sarcopenia in the AD patients.[36] This indicates that as the earliest stage of developing clinical symptoms in the progression of AD, MCI also plays a promoting role in the occurrence of SA. The mutual influence MCI and SA has been further substantiated in current research, the involvement of dietary factors in this association and its role in it still needs further exploration.

This study had some limitations. First, the subjects of this study were less representative due to the geographical limitation. In addition, it is easy to produce information bias when conducting retrospective investigation. We will strive to minimize the interference of the above-mentioned issues on the research results as much as possible in future research.

Conclusion

In summary, there is mutual influence between MCI and SA. Insufficient intake of unsaturated fatty acids including MUFA and PUFA is the key factor in the progress of cognitive dysfunction and SA. MUFA potentially has a greater association with muscle health. The intake of dietary fats and PUFA has a more significant association with MCI combined with SA. Less consumption of MUFA and higher intake of fats with saturated double bonds fatty acids might be of critical importance promoting cognitive dysfunction and SA in the elderly population. They have the potential to serve as prospective biomarkers indicating a higher risk of cognitive decline and/or SA in the elderly population.

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CONFLICT OF INTEREST AND FUNDING DISCLOSURES

The authors declare no conflict of interest. The work described has not been published previously, and the publication is approved by all authors. Informed consent was obtained from all subjects involved in the study. The funders had no role in the design of the study; in the collection, analyses, or interpretation of data; in the writing of the manuscript, or in the decision to publish the results.

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