



ASSOCIATION OF SERUM URIC ACID WITH COGNITION AND CSF PATHOLOGY IN ALZHEIMER'S DISEASE

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Background

- We investigate the correlation between serum uric acid (SUA) levels and cognitive function as well as cerebrospinal fluid (CSF) pathological biomarkers in patients with Alzheimer's disease (AD), and analyze its potential role in the pathophysiological process of AD.

Methods

- A total of 329 AD patients admitted to West China Hospital of Sichuan University from January 2023 to January 2025, who were diagnosed by amyloid PET/CT or CSF pathological biomarkers, were enrolled.
- Patients were divided into high uric acid group (Q4) and low uric acid group (Q1-Q3) according to the quartiles of serum uric acid levels.

Results

- Patient baseline characteristics are shown in Table 1.

Table 1: Baseline Characteristics of Alzheimer's Disease Patients in the High and Low Uric Acid Groups

Variables	Total (n=329)	low uric acid (n=245)	high uric acid (n=84)	P
SUA ($\bar{x} \pm s$, $\mu\text{mol/L}$)	297.47 $\pm$ 82.87	261.51 $\pm$ 51.83	405.77 $\pm$ 61.92	-
Age[M(P ₂₅ -P ₇₅), year]	71.00 (62.00–77.00)	70.00 (61.00–76.00)	71.50 (65.00–78.75)	0.509
BMI ($\bar{x} \pm s$, kg/m ²)	22.12 $\pm$ 3.20	21.87 $\pm$ 3.21	22.90 $\pm$ 3.05	0.018
Education[M(P ₂₅ -P ₇₅), year]	9.00 (8.00–12.00)	9.00 (7.00–12.00)	10.00 (9.00–15.00)	0.140
ACCI [M(P ₂₅ -P ₇₅)]	4.00 (3.00–4.00)	4.00 (3.00–4.00)	4.00 (3.00–4.00)	0.753
MoCA [M(P ₂₅ -P ₇₅)]	14.00 (7.00–19.00)	12.00 (6.00–18.00)	16.00 (11.50–20.00)	<0.001
MMSE [M(P ₂₅ -P ₇₅)]	17.00 (9.00–22.00)	16.00 (9.00–21.50)	18.00 (13.00–23.00)	0.012
FAB [M(P ₂₅ -P ₇₅)]	10.00 (7.00–13.00)	9.00 (6.00–13.00)	11.00 (8.00–14.00)	0.011
IADL [M(P ₂₅ -P ₇₅)]	6.00 (4.00–8.00)	6.00 (4.00–8.00)	5.50 (4.00–8.00)	0.596
Triglyceride [M(P ₂₅ -P ₇₅), mmol/L]	1.10 (0.84–1.53)	1.08 (0.83–1.43)	1.25 (0.90–1.77)	0.025
Cholesterol ($\bar{x} \pm s$, mmol/L)	4.64 $\pm$ 1.15	4.65 $\pm$ 1.17	4.63 $\pm$ 1.11	0.854
Duration [M(P ₂₅ -P ₇₅), year]	2.00 (1.00–4.00)	2.00 (1.00–4.00)	2.00 (1.00–3.00)	<0.001
Sex [n (%)]				<0.001
Man	144 (43.80%)	86 (34.80%)	58 (70.70%)	
Female	185 (56.20%)	160 (65.20%)	25 (29.30%)	
Smoking [n (%)]				0.003
Yes	75 (22.80%)	46 (18.60%)	29 (35.40%)	
No	254 (77.20%)	200 (81.40%)	54 (64.60%)	
Drinking [n (%)]				0.020
Yes	61 (18.50%)	38 (15.40%)	23 (28.00%)	
No	268 (81.50%)	208 (84.60%)	60 (72.00%)	
APOE-ε4 [n (%)]				0.774
Carrier	173 (52.60%)	133 (53.80%)	40 (48.80%)	
Non-carrier	156 (47.40%)	113 (46.20%)	43 (51.20%)	

- Among the 329 AD patients, MMSE, MoCA, and FAB scores in the high uric acid group were significantly higher than those in the low uric acid group (all p<0.05)(fig.1). Correlation analysis showed that SUA levels were positively correlated with MMSE score (r=0.139, p=0.013), MoCA score (r=0.168, p=0.003), and FAB score (r=0.152, p=0.007) in AD patients, and these correlations remained significant after adjusting for sex, age, and education level (all p<0.05). Multiple linear regression analysis further indicated that SUA level was an independent influencing factor for MMSE score (β=0.010, p=0.040) and MoCA score (β=0.012, p=0.009) in AD patients.

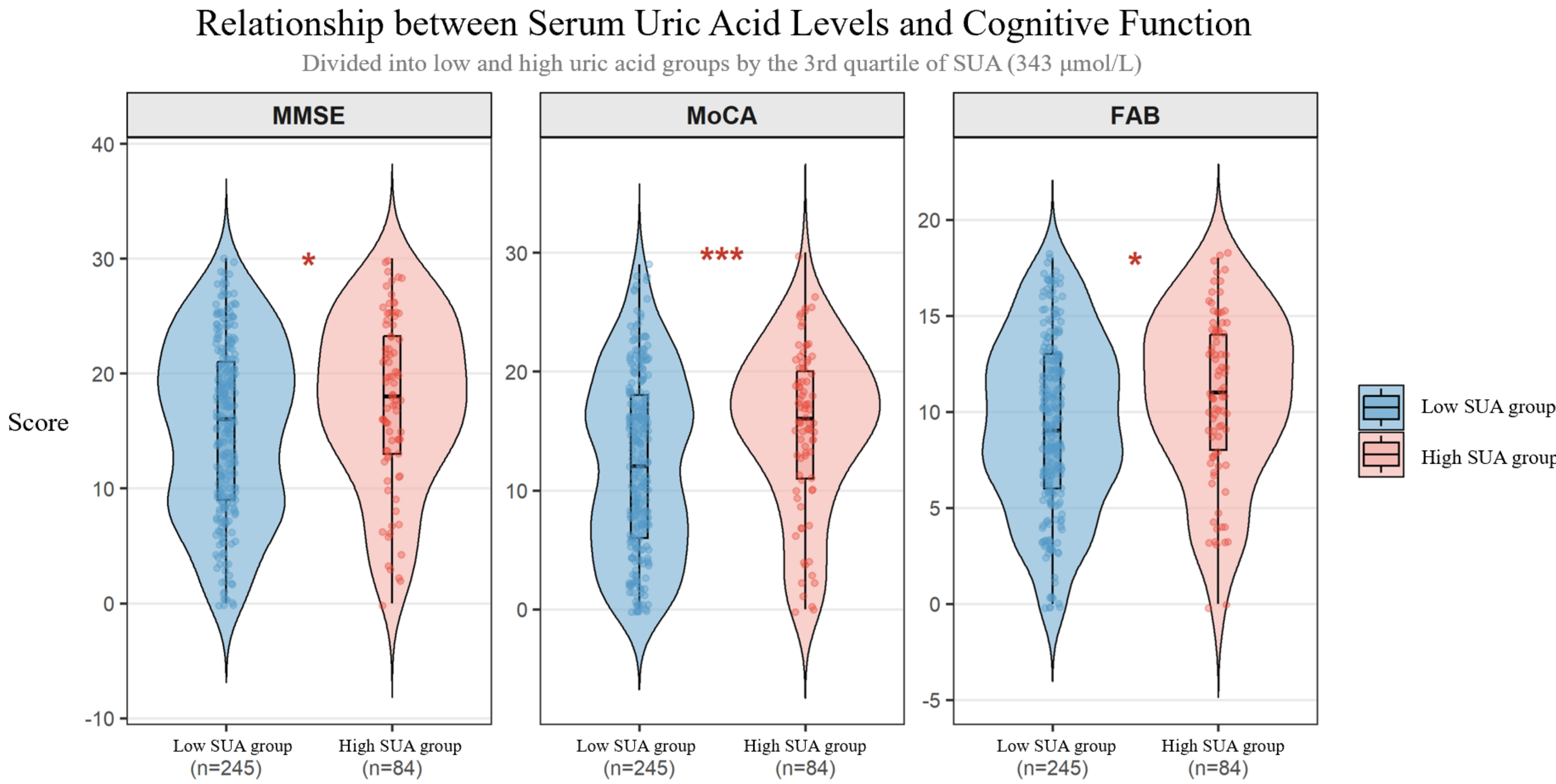


Figure 1. Comparison of cognitive scores between high and low uric acid groups * p<0.05, *** p<0.01

- A total of 149 AD patients had data on CSF core pathological biomarkers. Among these patients, ln(Aβ42) levels in the high uric acid group were significantly lower than those in the low uric acid group (adjusted mean difference=−0.061, 95% CI: −0.116 to −0.007, p=0.028).
- Partial correlation analysis showed that, after adjusting for age, sex, years of education, and APOE ε4 status, SUA was negatively correlated with ln(Aβ42) (p<0.05).
- Multiple linear regression further revealed that with FAB included as an independent variable for cognitive assessment, serum uric acid independently influenced ln(Aβ42) (β = −0.188, p = 0.045). By contrast, when MMSE or MoCA was employed as the cognitive assessment variable, serum uric acid merely exhibited a negative trend with ln(Aβ42) (MMSE: β = −0.172, p = 0.063; MoCA: β = −0.176, p = 0.057).
- Exploratory analysis revealed no significant interaction or mediation effects among blood uric acid, ln(Aβ42), and cognitive scores.

Conclusions

Higher SUA levels are associated with better cognitive performance in AD patients and are independently correlated with lower CSF ln(Aβ42) levels, suggesting that SUA may participate in the pathological process of AD by influencing cerebral Aβ metabolism, thereby providing new clues for potential intervention targets. However, interaction and mediation effect analyses showed no significant interaction or mediation effects among SUA, ln(Aβ42), and cognitive scores, indicating that the association between SUA and cognitive function is neither mediated by Aβ42 levels nor modulated by Aβ42 levels.