Sex-specific and Obesity-specific Association of Serum Uric Acid with Cognitive Function in Older Adults

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BACKGROUND

- Uric acid is an antioxidant that accounts for over half of the free radical scavenging activity in humans.[1]
- Lower serum uric acid concentrations (SUA) have been linked to cognitive dysfunction.[1]
- Higher SUA concentrations have been associated with slower progression of several neurodegenerative diseases.[2]
- On the other hand, elevated SUA concentrations have also been associated with poorer processing speed and executive functioning and greater white matter atrophy.[1,3]

METHODS

- **Study population**: Adults 65 to 79 years old who are beginning to experience mild cognitive decline, but are generally healthy, were enrolled in this study.
- **Blood biomarkers:** Serum lipid profiles, glucose, creatinine, and SUA were analyzed in fasting blood with an automated enzymatic procedure.
- **Inclusion criteria**: Daily fruit/vegetable intake < 5 servings; not diagnosed with dementia or Alzheimer's disease, central nervous system disorders, psychiatric disorders, gastrointestinal/digestive problems, or diabetes; body mass index (BMI) < 34.9 lbs./in^2; not taking certain prescription drugs; and right-handed
- **Statistical analysis**: Analyses were carried out using SAS version 9.3 (SAS Institute, Cary, NC, USA).
- **Cognitive function**: Cognitive function was assessed using the Montreal Cognitive Assessment (MoCA, **Fig 1**), and the Spatial Working Memory (**Fig 2)** and Rapid Visual Information Processing (**Fig 3)** tests from the Cambridge Neuropsychological Test Automated Battery (CANTAB).

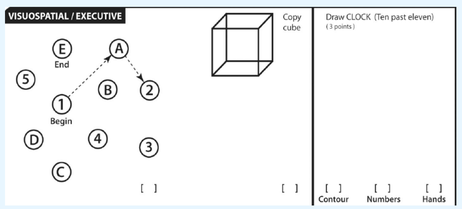


Fig 1. The Montreal Cognitive Assessment (MoCA) was designed as a rapid screening instrument for mild cognitive decline. It assesses different cognitive domains: attention and concentration, executive functions, memory, language, visuoconstructional skills, conceptual thinking, calculations, and orientation. Time to administer the MoCA is approximately 10 minutes.

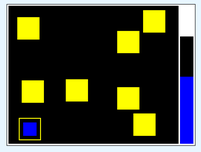


Fig 2. Spatial Working Memory (SWM): Participants search for blue tokens. They must remember where they have already found a blue token so as not to search there again. They search for 4, 6, and 8 tokens.

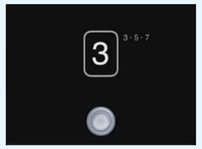


Fig 3. Rapid Visual Information Processing (RVP): Participants are asked to detect target sequences of digits (for example, 2-4-6, 3-5-7, 4-6-8) and to register responses using the press pad.

AIM

- To explore the relation between uric acid concentrations and cognitive function in a population of older adults with mild cognitive decline using biomarkers, cognitive testing, and demographics.

RESULTS

- Mean concentrations of SUA in 107 individuals (mean age = 72.7 ± 4.3 years) were 5.9 ± 2.3 mg/dL.
- Males had significantly higher SUA concentrations (6.2 ± 1.1 mg/dL) compared to females (5.9 ± 2.3 mg/dL) (p<0.0001) (**Fig 4A**).
- Hyperuricemia (in males, SUA > 7mg/dL and in females, SUA > 6mg/dL) was present in 24% of the individuals (**Fig 4B**).
- SUA concentrations were higher (6.2 ± 1.1 mg/dL) in obese as compared to overweight (6.0 ± 1.1 mg/dL) and normal weight individuals (5.1 ± 1.2mg/dL) (p<0.001) (**Fig 5A**).
- The prevalence of hyperuricemia was higher in obese and overweight than normal weight individuals (p<0.01) (**Fig 5B**).
- Compared with normouricemic individuals, hyperuricemic had significantly (p<0.05) elevated serum triglycerides levels (122.1 ± 67.0 vs 184.5 ± 152 mg/dL) and higher waist circumference (WC) (39.3 ± 4.0 vs. 41.1 ± 3.0 in).

Fig 4A. SUA stratified by gender

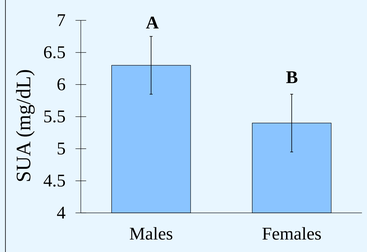


Fig 4B. Frequency of participants with hyperuricemia

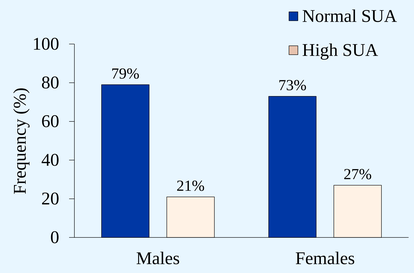


Fig 5A. SUA stratified by BMI

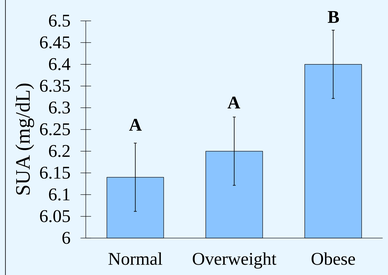
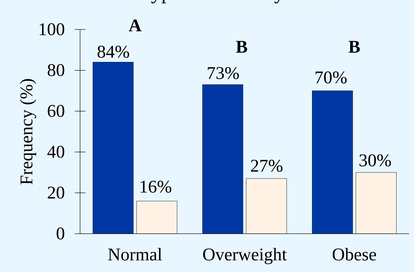


Fig 5B. Frequency of participants with hyperuricemia by BMI



RESULTS

- SUA was significantly correlated with BMI, WC, serum creatinine, glucose, triglycerides, and HDL-C (**Table 1**).
- Pearson's correlation coefficient test showed that SUA was negatively associated with MoCA scores (r^2= -0.23, p<0.05) (**Table 2**).
- SUA was positively associated with errors made on the CANTAB spatial working memory task (t=2.6, p<0.01) in men but not in women.
- SUA was positively associated with spatial working memory errors (t=2.9, p<0.01) and rapid visual processing errors (t=3.0, p<0.01) from the CANTAB in obese individuals but not in normal or overweight individuals.

Table 1–Pearson's correlation coefficients for SUA with urine and serum profiles.

			Urine		Serum						
	Age	**BMI**	**UACreat Ratio**	**FEUA**	**Creat**	**Gluc**	**Chol**	**Trig**	**HDL-C**	**LDL-C**	**Non HDL-C**
Total (n=107)	0.03	**0.38****	-0.08	**-0.45****	**0.45****	**0.27***	-0.09	**0.31***	**-0.43****	-0.02	0.09
Males (n=47)	-0.1	0.11	0.24	-0.18	**0.34***	-0.05	0.1	**0.30***	-0.19	0.1	0.14
Females (n=60)	0.11	**0.51****	-0.03	**-0.55****	**0.30***	**0.45***	-0.01	**0.42***	**-0.42***	-0.01	0.21

Pearson's correlation coefficients *p<0.05; **p<0.001

Table 2 – Pearson's correlation coefficients for SUA with cognitive scores.

		Spatial Working Memory		Rapid Visual Information Processing
	MoCA	**Between errors z-score**	**Within errors z-score**	**Total hits z-score**
Total (n=107)	**-0.23***	-0.02	0.05	-0.08
Males (n=47)	-0.14	-0.11	0.16	-0.08
Females (n=60)	-0.19	0.11	-0.03	0.09

Pearson's correlation coefficients *p<0.05

DISCUSSION AND CONCLUSION

- Among older adults, higher serum uric acid concentrations were linked to poorer cognitive function in all individuals, poorer spatial working memory in men and obese individuals, and poorer processing in obese individuals compared to other groups.
- These findings indicate serum uric acid concentrations may impact the neurological processes involved in cognitive functions in older adults.

References

1. Vannorsdall, T.D., Kueider, A.M., Carlson, M.C., Schretlen, D.J. (2014). Higher baseline serum uric acid is associated with poorer cognition but not rates of cognitive decline in women. *Experimental Gerontology*, 60:136-139. PMCID: PMC4272197.
2. Schretlen, D.J., Inscore, A.B., Jinnah, H.A., Rao, V., Gordon, B., Pearlson, G.D. (2007). Serum uric acid and cognitive function in community-dwelling older adults. *Neuropsychology*, 21(1):136-40. doi: 10.1037/0894-4105.21.1.136.
3. Cicero, A.F., Desideri, G., Grossi, G., Urso, R., Rosticci, M., D'Addato, S., Borghi, C. (2015). Serum uric acid and impaired cognitive function in a cohort of healthy young elderly: data from the Brisighella Study. *Internal and Emergency Medicine*, 10(1):25-31. PMID 24986078.

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