

Association between urinary flow rate and cognition in the elderly: a cross-sectional study

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Background: Urinary abnormalities and cognitive impairment are common in older adults, but their relationship remains incompletely understood. We examined the association between urinary flow rate (UFR) and cognitive performance in this population.

Methods: We analyzed data from 2700 participants aged ≥ 60 years in the 2011–2014 U.S. National Health and Nutrition Examination Survey (NHANES). Cognitive performance was assessed using the Digit Symbol Substitution Test (DSST), Animal Fluency Test (AFT), and the Consortium to Establish a Registry for Alzheimer's Disease (CERAD) immediate- and delayed-recall tests. Multivariable linear regression evaluated associations between UFR and cognitive scores, and segmented regression assessed potential nonlinear threshold effects.

Results: The mean age was 69.58 years, and 51.48% were women. In the fully adjusted model, higher UFR

was associated with higher DSST scores ($\beta = 1.77$, 95% CI: 0.74–2.81; $p = 0.0008$). Participants in the highest UFR tertile had a 2.41-point higher DSST score than those in the lowest tertile ($\beta = 2.41$, 95% CI: 0.90–3.92; $p = 0.0018$; p for trend = 0.0051). Segmented regression identified inflection points of 1.46 mL/min for AFT, 1.30 mL/min for DSST, 0.69 mL/min for CERAD immediate recall, and 0.80 mL/min for CERAD delayed recall. Below these points, higher UFR was significantly associated with better cognitive scores, whereas no significant associations were observed above them. The UFR–DSST association was stronger among participants with BMI ≤ 30 kg/m² (p for interaction = 0.0106).

Conclusions: Lower UFR was associated with poorer cognitive performance in older adults, with a nonlinear pattern. Prospective longitudinal and mechanistic studies are needed to confirm these findings and clarify their clinical relevance.

Key Words: urinary flow rate, cognitive impairment, National Health and Nutrition Examination Survey (NHANES), elderly population

Introduction

The global aging of the population has largely led to an increase in morbidity and disability.¹ Age-related cognitive decline begins in middle age and continues with time.² Elderly cognitive impairment has a great impact on the daily life of patients and their families, increases the mortality of the elderly, and brings a huge burden to society.^{3–5} In view of the occult

incidence of cognitive decline and the slow progression to dementia, and the fact that there is no effective treatment for this disorder at present, it is very important to screen high-risk groups and find early cognitive decline markers for primary prevention.⁶

Urinary flow rate (UFR) represents the amount of urine excreted from the urethra per unit time in a natural state, which is mainly influenced by detrusor contraction strength and bladder outlet resistance.⁷ As a common noninvasive examination, the determination of UFR has the advantages of rapidity, low cost, and high repeatability, which is widely used in the preliminary screening of lower urinary tract symptoms (LUTS). In clinical practice, a reduced urinary flow rate may accompany voiding dysfunction and can be observed in conditions such as detrusor

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underactivity (DU) or bladder outlet obstruction.⁸ According to the definition of the International Continence Society, detrusor underactivity refers to bladder weakness or prolonged bladder emptying time due to decreased contractility.⁹ Many previous studies have shown that poor urination is caused by both myogenic and neurogenic mechanisms.^{10–13} It has been shown that different cortical regions and parts of the frontal lobe, which are involved in cognitive and emotional regulation, are also involved in the processes of bladder control.¹⁴

Previous studies have suggested a close association between urinary dysfunction and impaired cognitive function in older adults, with particularly consistent evidence reported in neurodegenerative diseases such as Parkinson's disease (PD). Gubbiotti et al. reported that lower urinary tract symptoms (LUTS) were highly prevalent among patients with PD, with urgency, increased urinary frequency, and nocturia observed in 92%, 83%, and 77% of patients, respectively; nocturia was also associated with greater motor and non-motor disease severity.¹⁵ More recently, Yang et al. using a large population-based cohort, found that urinary dysfunction was independently associated with an increased risk of incident PD (HR = 1.45, 95% CI: 1.04–2.02), while autonomic dysfunction could be detected years before PD diagnosis and was associated with subsequent PD-related dementia and mortality, suggesting that urinary and other autonomic symptoms may provide clinically relevant information regarding disease risk and prognosis.¹⁶ In addition, Golesorkhi et al. found that greater urinary incontinence severity in patients with PD was significantly associated with poorer cognitive performance measured by the Montreal Cognitive Assessment ($r = -0.52$, $p = 0.046$), further supporting a potential link between urinary symptom burden and cognitive dysfunction in PD.¹⁷ Although urinary dysfunction has been well documented in Parkinson's disease and other neurodegenerative disorders, evidence derived from these disease-specific populations cannot be directly extrapolated to cognitive function in the general older population.^{15–17} Nevertheless, emerging population-based evidence suggests that lower urinary tract symptoms may also be associated with poorer cognitive performance among community-dwelling older adults.¹⁸ While numerous demographic, vascular, metabolic, and lifestyle-related risk factors for cognitive decline have been established, the relationship between objective urinary measures, particularly UFR, and cognitive performance remains insufficiently characterized.³ Therefore, in this study, we aimed to examine the association between UFR and

cognitive performance among older adults using data from the U.S. National Health and Nutrition Examination Survey (NHANES).

Materials and Methods

Data collection and participant selection

The NHANES study is an ongoing series of cross-sectional surveys conducted by the U.S. National Center for Health Statistics (NCHS) of the Centers for Disease Control and Prevention (CDC). NHANES aimed to assess the health and nutritional status of the U.S. population through interviews and physical examinations, which were performed in specially designed mobile examination centers (MECs). In the process of data acquisition, all interviewers received the training plan and reached the required standards. NHANES uses a complex multistage probability sampling design in 2-year cycles, and survey weights are provided for analyses intended to generate population-representative estimates. The NCHS Research Ethics Review Board approved the NHANES 2011–2012 and 2013–2014 protocols (Protocol #2011-17). Informed consent was provided by all study participants before the data collection and examination procedures. More NHANES data and information are available at <https://www.cdc.gov/nchs/nhanes/index.htm>.

Participants were selected from the NHANES 2011–2012 and 2013–2014 cycles. Individuals were eligible for inclusion if they were aged ≥ 60 years and had complete data for all four cognitive outcomes, including the Animal Fluency Test (AFT), Digit Symbol Substitution Test (DSST), CERAD immediate recall, and CERAD delayed recall, as well as available urinary flow rate (UFR) data. Of the 19,931 participants in NHANES 2011–2014, 16,299 individuals aged < 60 years were excluded, leaving 3632 age-eligible participants. We subsequently excluded 698 participants with incomplete cognitive test data and 166 participants with missing UFR data. In accordance with the prespecified data-processing procedure, 68 participants with UFR values above the 97.5th percentile were further excluded. The final analytic sample comprised 2700 participants (Figure 1).

Because the present study used de-identified, publicly available NHANES data, no additional participant contact, intervention, or informed-consent procedure was performed by the study authors. All experimental methods were performed in accordance with the relevant guidelines and regulations of the CDC.

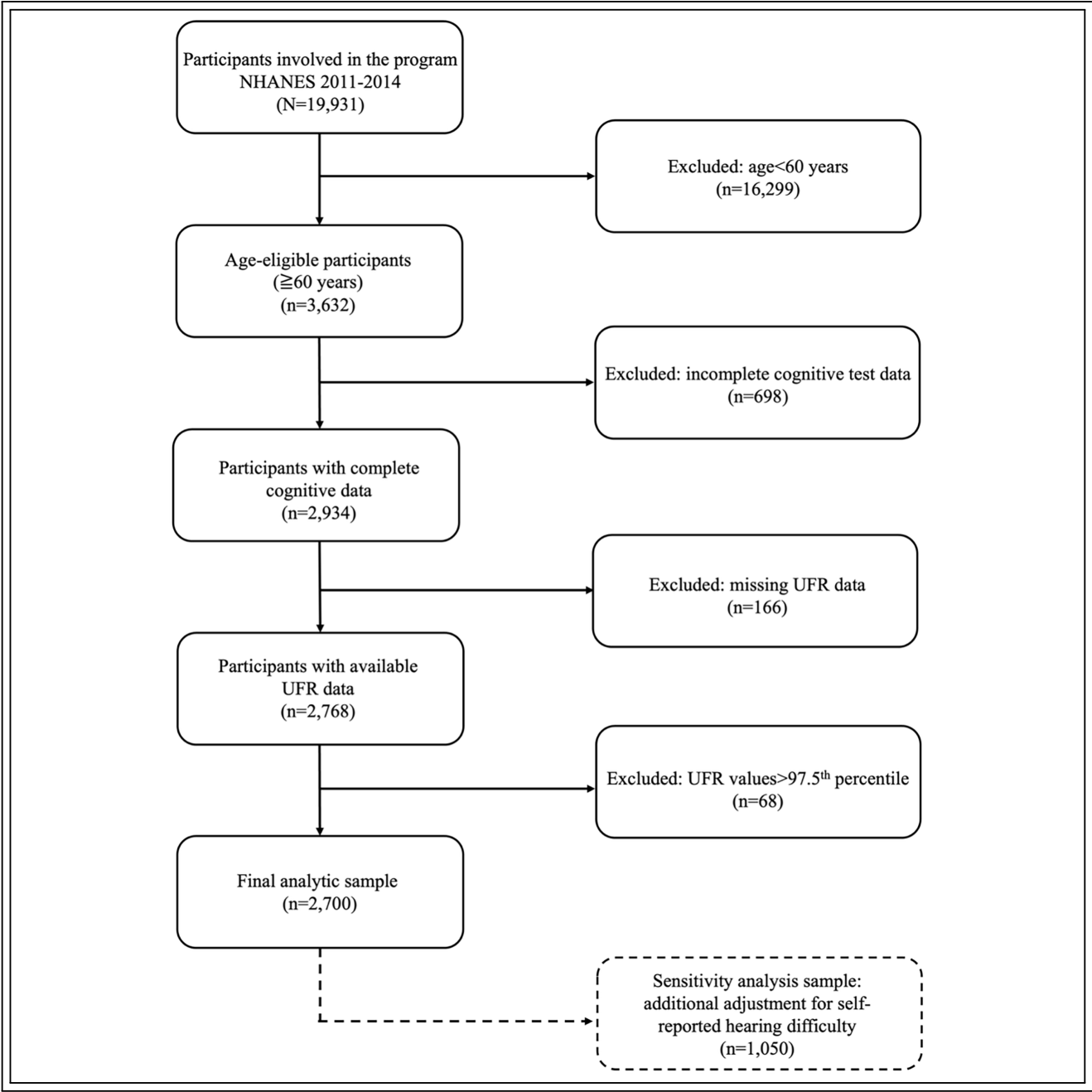


FIGURE 1. Flowchart of participant inclusion and exclusion for analysis

Measurement of urinary flow rate

In NHANES, UFR is a non-invasive quantitative measure of timed urinary excretion and is distinct from clinical uroflowmetry, which measures urinary flow during an observed void and commonly reports maximum and average flow rates. NHANES-derived UFR was determined according to a standardized urine collection protocol.¹⁹ Participants were asked

to record the time of their last urination before urine specimen collection. UFR was calculated as $UFR = V/t$, where V represents the collected urine volume and t represents the time interval between the previous void and the current urine collection; UFR was expressed in mL/min. Because this measure depends on both urine volume and the elapsed inter-void interval, it may be influenced by fluid intake,

hydration status, renal concentrating and water-handling function, and specimen-collection timing, and it should not be interpreted as a direct measure of detrusor contractility or bladder outlet resistance. When multiple urine specimens were collected, up to three measurements were available for each participant, and the composite UFR was calculated using the total urine volume and total time interval covered by the collected specimens. Detailed procedures for urine collection, processing, and handling are provided in the NHANES Laboratory Procedures Manual.²⁰

Measurement of cognitive function

Cognitive performance was assessed using three standardized cognitive instruments, yielding four outcome measures: the Digit Symbol Substitution Test (DSST), the Animal Fluency Test (AFT), and the Consortium to Establish a Registry for Alzheimer's Disease Word Learning Test (CERAD-WL), which provided both immediate- and delayed-recall scores.²¹ The CERAD-WL assesses verbal learning and episodic memory. Participants completed three consecutive learning trials involving 10 unrelated words, with the immediate-recall score calculated as the sum of correctly recalled words across the three trials (range, 0–30). After an interval of approximately 8–10 min, during which the AFT and DSST were administered, participants completed the CERAD delayed-recall task, with scores ranging from 0 to 10.^{21,22} The AFT assesses categorical verbal fluency and executive function; participants were asked to name as many animals as possible within 60 s, and the score was the number of valid animal names generated.²³ The DSST assesses processing speed, sustained attention, and working memory; participants matched symbols to numbers according to a reference key for 120 s, with the score defined as the number of correct matches (range, 0–133).²³ Higher scores on all four measures indicated better cognitive performance. Additional details of test administration are provided in the Supplementary Materials.

Covariates

The multivariate model contains variables that may confound the association between UFR and cognitive function. For covariates, continuous variables included age (years). Categorical variables included: sex (male; female), poverty income ratio (PIR) (<1.3; 1.3–3.5, >3.5), body mass index (BMI) (<25; 25–30; >30), alcohol intake per day (none; moderate; heavy), marital status (married or living with partner; living alone), smoking status (never; former;

current) and comorbidity index (0, 1, 2). BMI values were calculated by dividing participants' weight (in kilograms) by their height (in square meters).²⁴ Alcohol intake was categorized as none (0 g per day), moderate (0.1 to 27.9 g per day for men and 0.1–13.9 g per day for women), and heavy (≥ 28 g per day for men and ≥ 14 g per day for women).²⁵ Diabetes mellitus, congestive heart failure, coronary artery disease, chronic obstructive pulmonary disease (chronic bronchitis and/or emphysema), hypertension, and cancer were comorbid conditions, and the number of subjects reported conditions was then combined to generate an ordinal comorbidity index.²⁶

Statistical analysis

Statistical analyses were conducted using the analytic sample of participants who met the study eligibility criteria. The present analyses were performed without applying NHANES survey weights (<https://wwwn.cdc.gov/nchs/nhanes/tutorials/default.aspx>).

Statistical analyses were conducted using the analytic sample of participants who met the study eligibility criteria. Continuous variables were expressed as mean $\pm$ standard deviation. Categorical variables were expressed as frequency or as a percentage. To investigate whether UFR is correlated with cognitive function in selected participants, our statistical analysis consisted of two main steps.

First, multivariable linear regression models were employed. We estimated three models: model 1, no covariates were adjusted; model 2, only adjusted for sex, age and BMI data; in the final model (model 3), model 2 + other covariates presented in Table 1 (i.e., PIR; marital status; comorbidity index; alcohol intake per day and smoking status). UFR was treated as both a continuous independent variable and a categorical variable (divided into tertiles), with the lowest tertile used as the reference. The linear trend tests were performed by inputting the median value of each UFR category as a continuous variable in the models. Second, we further applied smooth curve fitting and segmented regression models to examine the threshold effect of UFR on cognitive performance. In addition, we also conducted the log-likelihood ratio test and the one-line (non-segmented) model and segmented regression model were compared. In order to explore whether this association was modified by other confounding factors, we conducted interaction analyses and stratified analyses. Moreover, in order to ensure the robustness of the data analysis, we conducted a sensitivity analysis and adjusted for self-reported hearing difficulty.

TABLE 1. Baseline characteristics of participants

Variables	Analytic Sample (N = 2700)
Continuous variables, mean (SD)	
Age, yr, mean $\pm$ SD	69.58 $\pm$ 6.78
UFR	0.84 $\pm$ 0.59
Animal Fluency Test	16.61 $\pm$ 5.47
DSST	45.88 $\pm$ 17.25
CERAD-immediate recall	18.95 $\pm$ 4.62
CERAD-delayed recall	5.93 $\pm$ 2.31
Categorical variables, n (%)	
Sex	
Female	1390 (51.48%)
Male	1310 (48.52%)
Race	
Mexican American	236 (8.74%)
Other Hispanic	277 (10.26%)
Non-Hispanic White	1300 (48.15%)
Non-Hispanic Black	629 (23.30%)
Other Race	258 (9.56%)
PIR	
<1.3	728 (29.49%)
1.3–3.5	960 (38.88%)
>3.5	781 (31.63%)
Educational level	
Less than high school	634 (23.92%)
High school or general educational development	631 (23.81%)
Above high school	1385 (52.26%)
Marital status	
Married or living with partner	1589 (58.94%)
Living alone	1107 (41.06%)
BMI	
<25 kg/m ²	731 (27.46%)
25–30 kg/m ²	949 (35.65%)
>30 kg/m ²	982 (36.89%)
Smoking status	
Never	1337 (49.56%)
Former	1073 (39.77%)
Current	288 (10.67%)
Comorbidity index	
0	743 (27.87%)
1	1232 (46.21%)
2	691 (25.92%)
Alcohol intake per day	
None	1991 (79.23%)
Moderate	216 (8.60%)
Heavy	306 (12.18%)
Self-reported hearing difficulty	
No	790 (62.75%)
Yes	469 (37.25%)

Note: Mean $\pm$ SD for continuous variables. Number (%) for categorical variables. UFR, urinary flow rate; DSST, digit symbol substitution test; CERAD, Consortium to Establish a Registry for Alzheimer's Disease; BMI, body mass index; PIR, poverty income ratio; Comorbidity index: diabetes mellitus, congestive heart failure, coronary artery disease, chronic obstructive pulmonary disease (chronic bronchitis and/or emphysema), and hypertension, cancer consisted of comorbid conditions.

Missing covariate data were handled using complete-case analysis for each regression model. Therefore, although the primary analytic cohort included 2700 participants, the effective sample size varied according to covariate availability: $n = 2700$ for Model 1, $n = 2662$ for Model 2, and $n = 2261$ for Model 3. The 439 participants not included in Model 3 had missing data for at least one covariate required in the fully adjusted model. As a sensitivity analysis, self-reported hearing difficulty was additionally included in the fully adjusted model because hearing impairment may influence performance on cognitive testing. Because hearing-difficulty data were incompletely available, this analysis was restricted to participants with complete data for hearing difficulty and all covariates included in Model 3, resulting in a sensitivity-analysis sample of 1050 participants.

All analyses were performed using the statistical software packages R (<http://www.R-project.org>, The R Foundation) and EmpowerStats (<http://www.empowerstats.com>; X&Y Solutions, Inc., Boston, MA, USA). All p values less than 0.05 (two-sided) were considered statistically significant.

Results

Baseline characteristics of the 2700 participants are summarized in Table 1. The mean age was 69.58 ± 6.78 years, and 51.48% of the participants were female. The mean UFR was 0.84 ± 0.59 mL/min. The mean cognitive scores were 16.61 ± 5.47 for the Animal Fluency Test (AFT), 45.88 ± 17.25 for the Digit Symbol Substitution Test (DSST), 18.95 ± 4.62 for CERAD immediate recall, and 5.93 ± 2.31 for CERAD delayed recall. Self-reported hearing difficulty data were available for 1259 participants, of whom 37.25% reported hearing difficulty.

Associations between UFR and cognitive performance are presented in Table 2. In Model 2, after adjustment for sex, age, and BMI, each 1-unit increase in UFR was significantly associated with higher scores on all four cognitive measures: AFT ($\beta = 0.62$, 95% CI: 0.27–0.96; $p = 0.0005$), DSST ($\beta = 3.03$, 95% CI: 1.98–4.09; $p < 0.0001$), CERAD immediate recall ($\beta = 0.32$, 95% CI: 0.04–0.61; $p = 0.0273$), and CERAD delayed recall ($\beta = 0.15$, 95% CI: 0.01–0.29; $p = 0.0372$). After full adjustment in Model 3, the continuous association remained statistically significant for DSST ($\beta = 1.77$, 95% CI: 0.74–2.81; $p = 0.0008$), whereas the continuous associations with AFT and both CERAD measures were no longer statistically significant.

When UFR was analyzed in tertiles, Model 3 showed that, compared with participants in the lowest UFR tertile (T1), those in T2 and T3 had higher AFT scores (T2: $\beta = 0.63$, 95% CI: 0.10–1.16; $p = 0.0209$; T3: $\beta = 0.59$, 95% CI: 0.05–1.13; $p = 0.0317$), although the overall linear trend was not statistically significant (p for trend = 0.0729). For DSST, participants in both T2 and T3 had significantly higher scores than those in T1 (T2: $\beta = 1.97$, 95% CI: 0.48–3.47; $p = 0.0098$; T3: $\beta = 2.41$, 95% CI: 0.90–3.92; $p = 0.0018$), with a significant linear trend (p for trend = 0.0051). No significant tertile associations were observed for CERAD immediate recall. For CERAD delayed recall, T2 was associated with a higher score compared with T1 ($\beta = 0.26$, 95% CI: 0.04–0.48; $p = 0.0214$), whereas the T3 comparison and overall trend were not statistically significant. After full adjustment, smooth curve fitting further suggested nonlinear associations between UFR and cognitive performance (Figure 2).

Smooth curve fitting suggested nonlinear associations between UFR and cognitive performance. Therefore, two piecewise linear regression models were further used to characterize the change in slope and identify the estimated inflection point (K), which are statistical features of this dataset rather than clinical cutoffs or predictors. The results indicated significant positive associations between UFR and cognitive scores below K, whereas the associations were no longer statistically significant above K, suggesting a possible saturation pattern. The estimated K values should be interpreted as data-derived statistical inflection points rather than clinically validated cutoff values. Specifically, the segmented regression showed that the turning point values of UFR were: AFT: $K = 1.46$, DSST: $K = 1.30$, CERAD-immediate recall: $K = 0.69$ and CERAD-delayed recall: $K = 0.80$, respectively. A 1-unit increase in UFR was significantly associated with higher cognitive performance scores by: AFT: 0.85 (95% CI: 0.23, 1.47; $p = 0.0072$), DSST: 3.43 (95% CI: 1.50, 5.35; $p = 0.0005$), CERAD-immediate recall: 1.34 (95% CI: 0.16, 2.52; $p = 0.0267$) and CERAD-delayed recall: 0.55 (95% CI: 0.06, 1.04; $p = 0.0269$) when UFR was lower than the turning point value (K); however, the relationship was not significant when UFR was higher than K ($p > 0.05$). (Log likelihood ratio test: 0.045 (AFT), 0.045 (DSST), 0.036 (CERAD-immediate recall) and 0.040 (CERAD-delayed recall) (Table 3).

In the sensitivity analysis with additional adjustment for self-reported hearing difficulty ($n = 1050$), the continuous associations between UFR and the four cognitive outcomes were no longer statistically significant in the fully adjusted model. For AFT, participants in the highest UFR tertile (T3)

TABLE 2. Association between urinary flow rate and cognition among elderly adults in NHANES 2011–2014

Cognitive Assessment	β (95% CI), p Value		β (95% CI), p Value		β (95% CI), p Value	
	Model 1 n = 2700	p Value /	Model 2 n = 2662	p Value /	Model 3 n = 2261	p Value /
Animal fluency test						
Continuous	0.87 (0.52, 1.22)	<0.0001	0.62 (0.27, 0.96)	0.0005	0.34 (−0.03, 0.71)	0.0684
Tertiles						
T1 (n ₁ = 889)	0 (Ref.)	/	0 (Ref.)	/	0 (Ref.)	/
T2 (n ₂ = 911)	1.10 (0.60, 1.61)	<0.0001	0.93 (0.43, 1.43)	0.0003	0.63 (0.10, 1.16)	0.0209
T3 (n ₃ = 900)	1.34 (0.84, 1.84)	<0.0001	0.98 (0.48, 1.48)	0.0001	0.59 (0.05, 1.13)	0.0317
p for trend	/	<0.0001	/	0.0008	/	0.0729
DSST						
Continuous	3.89 (2.79, 4.99)	<0.0001	3.03 (1.98, 4.09)	<0.0001	1.77 (0.74, 2.81)	0.0008
Tertiles						
T1 (n ₁ = 889)	0 (Ref.)	/	0 (Ref.)	/	0 (Ref.)	/
T2 (n ₂ = 911)	4.07 (2.49, 5.66)	<0.0001	3.66 (2.14, 5.18)	<0.0001	1.97 (0.48, 3.47)	0.0098
T3 (n ₃ = 900)	5.31 (3.72, 6.89)	<0.0001	4.14 (2.61, 5.67)	<0.0001	2.41 (0.90, 3.92)	0.0018
p for trend	/	<0.0001	/	<0.0001	/	0.0051
CERAD-immediate						
Continuous	0.54 (0.24, 0.83)	0.0004	0.32 (0.04, 0.61)	0.0273	0.12 (−0.19, 0.42)	0.4514
Tertiles						
T1 (n ₁ = 889)	0 (Ref.)	/	0 (Ref.)	/	0 (Ref.)	/
T2 (n ₂ = 911)	0.61 (0.18, 1.03)	0.0054	0.52 (0.11, 0.93)	0.0127	0.33 (−0.11, 0.77)	0.1382
T3 (n ₃ = 900)	0.81 (0.39, 1.24)	0.0002	0.51 (0.10, 0.92)	0.0148	0.20 (−0.24, 0.64)	0.3773
p for trend	/	0.0005	/	0.0361	/	0.5479
CERAD-delayed						
Continuous	0.27 (0.12, 0.42)	0.0003	0.15 (0.01, 0.29)	0.0372	0.07 (−0.08, 0.22)	0.3818
Tertiles						
T1 (n ₁ = 889)	0 (Ref.)	/	0 (Ref.)	/	0 (Ref.)	/
T2 (n ₂ = 911)	0.40 (0.19, 0.61)	0.0002	0.33 (0.13, 0.53)	0.0016	0.26 (0.04, 0.48)	0.0214
T3 (n ₃ = 900)	0.41 (0.20, 0.63)	0.0002	0.24 (0.04, 0.45)	0.0200	0.12 (−0.10, 0.34)	0.2946
p for trend	/	0.0010	/	0.0696	/	0.5656

Note: 95%CI, 95% Confidence interval. Model 1: no covariates were adjusted. Model 2: adjusted for sex; age; BMI. Model 3: adjusted for sex; age; smoking status; alcohol intake per day; marital status; BMI; poverty income ratio; comorbidity index. UFR tertiles ranges: UFR tertile ranges: T1, 0.01–0.50 mL/min; T2, >0.50–0.91 mL/min; T3, >0.91–3.10 mL/min. T1 was used as the reference group.

had a significantly higher score than those in the lowest tertile (T1) ($\beta = 0.95$, 95% CI: 0.15–1.76; $p = 0.0204$), with a significant trend across UFR tertiles (p for trend = 0.0323). In contrast, the association between continuous UFR and DSST was not statistically significant ($\beta = 1.10$, 95% CI: −0.45–2.66; $p = 0.1652$), nor was the trend across UFR tertiles (p for trend = 0.0805). No significant associations were observed for CERAD immediate or delayed recall in the fully adjusted sensitivity model (Supplementary Table S1).

In the stratified analyses, significant interactions with BMI were observed for DSST (p for interaction = 0.0106), CERAD immediate recall (p for interaction = 0.0370), and CERAD delayed recall (p for interaction = 0.0144), whereas no significant BMI interaction was observed for AFT. For DSST, each 1-unit increase in UFR was significantly associated with a 3.54-point higher score among participants with BMI < 25 kg/m² ($\beta = 3.54$, 95% CI: 1.56–5.53; $p = 0.0005$) and a 2.58-point higher score among those with BMI 25 to 30 kg/m² ($\beta = 2.58$, 95% CI: 0.82–4.35; $p = 0.0042$), whereas no significant association was observed among participants with BMI ≥ 30 kg/m².

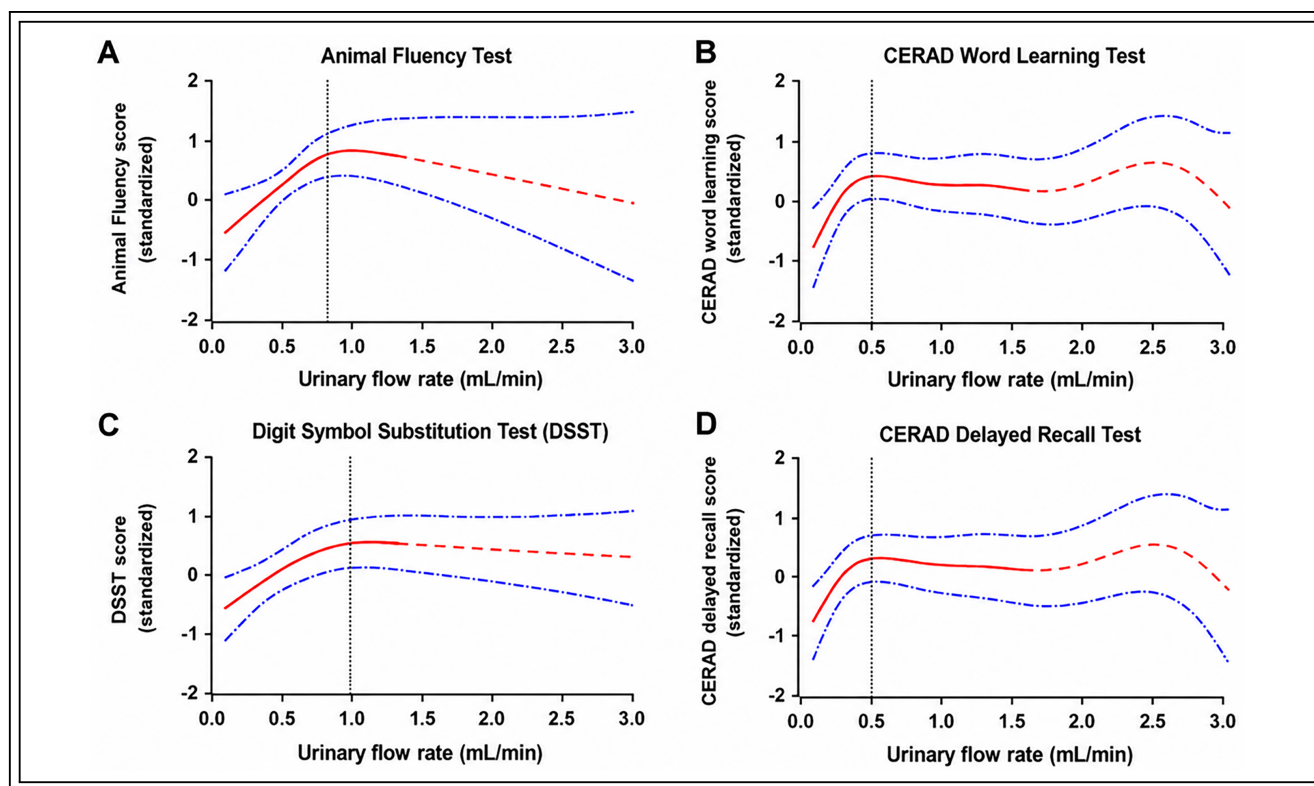


FIGURE 2. Association between urinary flow rate and cognition among elderly adults in NHANES 2011–2014. (A) Animal Fluency Test; (B) CERAD Word Learning Test; (C) Digit Symbol Substitution Test (DSST); (D) CERAD Delayed Recall Test. The x-axis represents urinary flow rate measured in mL/min. The black vertical dashed line marks the estimated inflection point (K) identified by segmented regression. Red solid line indicates the fitted smooth curve before the inflection point (p for non-linearity < 0.05); red dashed line indicates the fitted smooth curve after the inflection point (not significant); blue dash-dot lines indicate 95% confidence intervals

Although significant interactions with BMI were also identified for CERAD immediate and delayed recall, the corresponding within-BMI subgroup associations did not individually reach statistical significance in the fully adjusted model (Supplementary Table S2).

Discussion

Among older adults included in the NHANES 2011–2014 analytic sample, lower UFR levels were associated with poorer cognitive performance, with the most consistent association observed for DSST. Sex-stratified analyses showed a significant positive association between UFR and DSST performance in women, while a similar positive tendency was observed in men. Smooth curve fitting and segmented regression further showed nonlinear associations, with positive associations below the estimated inflection points and attenuation above

them. These findings are cross-sectional and do not establish whether lower UFR precedes poorer cognition, whether cognitive status influences urinary behavior, or whether shared physiological factors contribute to both. One possible explanation for the observed saturation pattern is that NHANES-derived UFR partly reflects fluid intake, hydration status, and renal water handling.²⁷ Previous studies have reported nonlinear relationships between hydration status and cognitive performance, particularly DSST performance in older women, suggesting that the cross-sectional association may differ across physiological ranges rather than increase continuously with greater urinary excretion.²⁸ Further prospective and mechanistic studies are needed to evaluate this hypothesis.

Recent evidence indicates that lower urinary tract dysfunction is common in several neurodegenerative disorders, including PD, AD, DLB, and MSA.¹⁴ In

TABLE 3. Threshold effect analysis for the relationship between urinary flow rate and cognition among elderly adults in NHANES 2011–2014

Models ^a	β (95% CI)	Animal Fluency Test	p-Value
Linear Model (One-line)			
One-line slope	0.34 (–0.03, 0.71)		0.0684
Segmented Model (Two-line)			
Turning point (K = 1.46 mL/min)			
<1.46	0.85 (0.23, 1.47)		0.0072
>1.46	–0.57 (–1.54, 0.40)		0.2493
Slope 2 – Slope 1	–1.42 (–2.82, –0.03)		0.0459
Predicted at	17.97 (17.43, 18.51)		/
Log-likelihood ratio test	/		0.045 ^b
Models	β (95%CI)	DSST	p-Value
Linear Model (One-line)			
One-line slope	1.77 (0.74, 2.81)		0.0008
Segmented Model (Two-line)			
Turning point (K = 1.30 mL/min)			
<1.30	3.43 (1.50, 5.35)		0.0005
>1.30	–0.35 (–2.67, 1.98)		0.7694
Slope 2 – Slope 1	–3.78 (–7.48, –0.07)		0.0459
Predicted at	50.41 (48.86, 51.96)		/
Log-likelihood ratio test	/		0.045 ^b
Models	β (95%CI)	CERAD-immediate recall	p-Value
Linear Model (One-line)			
One-line slope	0.12 (–0.19, 0.42)		0.4514
Segmented Model (Two-line)			
Turning point (K = 0.69 mL/min)			
<0.69	1.34 (0.16, 2.52)		0.0267
>0.69	–0.17 (–0.58, 0.23)		0.4070
Slope 2 – Slope 1	–1.51 (–2.92, –0.10)		0.0363
Predicted at	19.37 (19.06, 19.68)		/
Log-likelihood ratio test	/		0.036 ^b
Models	β (95%CI)	CERAD-delayed recall	p-Value
Linear Model (One-line)			
One-line slope	0.07 (–0.08, 0.22)		0.3818
Segmented Model (Two-line)			
Turning point (K = 0.80 mL/min)			
<0.80	0.55 (0.06, 1.04)		0.0269
>0.80	–0.10 (–0.32, 0.12)		0.3765
Slope 2 – Slope 1	–0.65 (–1.27, –0.03)		0.0412
Predicted at	6.17 (6.01, 6.34)		/
Log likelihood ratio test	/		0.040 ^b

Note: Log-likelihood ratio test: p -value < 0.05 means **the segmented model** is significantly different from **the linear model**, which indicates a non-linear relationship. Predicted at K: the estimated cognitive score (95% CI) at the corresponding inflection point (K) derived from the segmented regression model. ^aadjusted for sex; age; smoking status; alcohol intake per day; marital status; BMI; poverty income ratio; comorbidity index. ^bindicates that the **Segmented Model** is significantly different from the **Linear Model**; Sample sizes varied across models because each adjusted analysis was restricted to participants with complete data for all covariates included in the corresponding model.

PD, recent clinical and systematic studies have documented frequent storage and voiding symptoms and abnormalities in urodynamic parameters.^{15,29} MSA, a progressive α -synucleinopathy characterized by prominent autonomic failure, is particularly associated with impaired bladder emptying and urinary retention.^{30,31} Recent urodynamic studies have further demonstrated abnormalities in detrusor contractility and voiding efficiency in patients with MSA.³² These findings highlight the close coexistence of neurological and urinary dysfunction in aging-related neurodegenerative disorders.

The UFR measure used in NHANES should be distinguished from clinical uroflowmetry. NHANES-derived UFR represents timed urinary excretion based on collected urine volume and the elapsed interval between voids, whereas clinical uroflowmetry characterizes flow during a monitored void and is used to assess lower urinary tract function. Consequently, the NHANES measure may vary with fluid intake, hydration status, renal concentrating ability, renal water handling, and collection timing independently of bladder contractility or outlet resistance. These same systemic factors may also be related to cognitive performance. Recent studies have shown that hydration status is associated with cognitive performance in middle-aged and older adults, particularly executive function and processing speed, and that these relationships may be nonlinear, with poorer cognitive performance observed at suboptimal hydration levels.^{33,34} Prospective evidence has also suggested that poorer physiological hydration status is associated with greater deterioration in global cognitive performance over time.³⁵ These findings provide a plausible physiological context for the association observed in the present study.

In addition, the relationship between UFR and cognition may partly reflect shared aging-related systemic pathways. Kidney dysfunction has been associated with cognitive impairment, supporting the concept of a brain–kidney axis in which vascular, metabolic, and inflammatory abnormalities may affect both organs.³⁶ Vascular aging, particularly arterial stiffness and microvascular dysfunction, may impair cerebral blood flow, endothelial function, and cerebrovascular reserve, thereby contributing to poorer cognitive performance in older adults.³⁷ Chronic low-grade systemic inflammation may further promote endothelial and microcirculatory dysfunction and has increasingly been implicated in age-related cognitive impairment.³⁸ These overlapping processes suggest that lower UFR and poorer cognitive performance may coexist as manifestations of a broader age-related

physiological milieu rather than through a direct neuro-urological pathway.

The nonlinear association observed in the present study may also be compatible with this interpretation. Within the lower UFR range, higher urinary excretion may partly correspond to more favorable hydration and physiological homeostasis, whereas once an adequate physiological range is reached, further increases in UFR may not be accompanied by additional cognitive benefit, resulting in an apparent plateau. This explanation remains hypothetical and should be investigated in studies incorporating direct measures of hydration and renal function. Given the cross-sectional design of the present study, UFR cannot be considered an early predictor of subsequent cognitive decline; rather, our findings suggest that UFR may warrant further investigation as a potential physiological marker associated with cognitive performance in older adults.

The sensitivity analysis additionally adjusting for self-reported hearing difficulty provided further information on the robustness of the primary findings. After additional adjustment, the continuous associations between UFR and the four cognitive outcomes were no longer statistically significant, although the association with AFT remained significant when UFR was analyzed in tertiles. This suggests that hearing difficulty may partly influence cognitive test performance and the observed associations. However, the sensitivity analysis was based on a smaller complete-case sample of 1050 participants, which reduced statistical power. In addition, restricting the analysis to participants with complete hearing and covariate data may have introduced selection bias if these participants differed systematically from those excluded because of missing data. Therefore, the sensitivity findings should be interpreted as complementary to, rather than inconsistent with, the primary analysis.

This study has several strengths. To our knowledge, it is among the first studies to systematically examine the association between NHANES-derived UFR and cognitive performance in older adults. Unlike studies relying primarily on self-reported urinary symptoms, the present study used an objective quantitative measure of timed urinary excretion, providing a complementary perspective on the relationship between urinary physiology and cognitive health. Cognitive performance was comprehensively evaluated across multiple domains using three standardized instruments yielding four cognitive outcomes, including processing speed, executive/verbal fluency, and immediate and delayed memory. In addition to conventional

Multivariable linear regression, UFR was analyzed both continuously and in tertiles, and smooth curve fitting with segmented regression was further applied to characterize potential nonlinear and threshold associations. The robustness of the findings was additionally explored through stratified analyses and sensitivity analyses incorporating self-reported hearing difficulty. Moreover, the relatively large, ethnically diverse, community-based NHANES sample and standardized data-collection protocols provided a valuable setting in which to investigate these associations. Collectively, these methodological features strengthen the internal consistency of the findings and provide a useful foundation for future prospective longitudinal studies and mechanistic investigations to clarify the biological basis and potential clinical relevance of the relationship between UFR and cognitive performance.

This study has several limitations. First, the cross-sectional design precludes determination of temporal or causal relationships between UFR and cognitive performance, and a single UFR assessment may not fully capture intraindividual variation over time. Second, although multiple cognitive domains were assessed, the available tests did not provide a comprehensive neuropsychological evaluation. In addition, NHANES-derived UFR represents timed urinary excretion rather than clinical uroflowmetry and may be influenced by fluid intake, hydration status, renal water handling, and other physiological factors; therefore, it cannot directly characterize bladder contractility or lower urinary tract function. Third, residual confounding and selection bias cannot be completely excluded. In particular, educational attainment was described in [Table 1](#) but was not included in the original multivariable adjustment models, and several potentially relevant urological factors were also unavailable or not included. Moreover, substantial missing data reduced the sensitivity-analysis sample to 1050 participants, corresponding to 38.9% of the primary analytic cohort, which may have introduced additional selection bias and reduced statistical precision. Because the analyses were unweighted, the findings should be interpreted within the present analytic sample rather than as nationally representative estimates. Future prospective cohorts with repeated assessments and mechanistic studies are warranted to clarify the temporal and biological basis of the observed association and to evaluate its potential clinical relevance.

Conclusion

Among older adults included in NHANES 2011–2014, lower UFR levels were associated with poorer cognitive performance, particularly within the lower UFR range below the estimated inflection points. The nonlinear pattern observed in this study suggests that UFR-related urinary excretion characteristics may provide additional physiological information relevant to cognitive health in older adults. Further prospective longitudinal studies and mechanistic investigations are needed to validate these findings, clarify their temporal and biological basis, and determine the potential clinical relevance of UFR in the integrated assessment of urinary and cognitive health.

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Author Contributions

The authors confirm contribution to the paper as follows: Conceptualization, Jiandong Liu and Yifan Li; methodology, Jiandong Liu; software, Yifan Li; validation, Jiandong Liu; formal analysis, Jiandong Liu; investigation and data curation, Yifan Li; writing—original draft preparation, Jiandong Liu; writing—review and editing, Jiandong Liu and Yifan Li; visualization, Yifan Li; supervision and project administration, Dan Xia; funding acquisition, Dan Xia. All authors reviewed and approved the final version of the manuscript.

Availability of Data and Materials

The data sets generated and/or analyzed during the current study are available from the NHANES

repository, <https://www.cdc.gov/nchs/nhanes/index.htm>.

Ethics Approval

The NHANES 2011–2012 and 2013–2014 protocols were approved by the NCHS Research Ethics Review Board (Protocol #2011-17), and all informed consents had been obtained from the eligible subjects before initiating data collection and NHANES health examinations. (<https://www.cdc.gov/nchs/nhanes/irba98.htm>). The present study was a secondary analysis of publicly available, de-identified NHANES data; therefore, no additional ethical approval or informed consent was required for the present study. All authors confirmed that all methods were carried out in accordance with relevant NHANES Analytic Guidelines. (<https://www.cdc.gov/nchs/nhanes/analyticguidelines.aspx#analytic-guidelines>).

Conflicts of Interest

The authors declare no conflicts of interest.

Supplementary Materials

The supplementary material is available online at <https://www.techscience.com/doi/10.32604/cju.2026.087823/s1>.

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