Neurourology and Urodynamics 30:183–187 (2011)

The Effect of Acute Increase in Urge to Void on Cognitive Function in Healthy Adults

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Aims: In healthy adults, voluntary inhibition of micturition is associated with an increasing sensation in the urge to void and pain, and acute pain has been associated with transient deterioration in aspects of cognitive function. **Methods:** Eight healthy young adults consumed 250 ml of water every 15 min until they could no longer inhibit voiding. Performance on standardized measures of cognitive function was measured at hourly intervals which were classified as baseline, when individuals reported an increase in the urge to void, a strong increase in the urge to void, an extreme increase in the urge to void and postmicturition. **Results:** Sensations of the urge to void and pain increased with time of inhibition of urge to void and with amount of water consumed. Having an extreme urge to void exerted a large negative effect on attentional and working memory functions (d > 0.8). These cognitive functions returned to normal levels after micturition. **Conclusion:** The magnitude of decline in cognitive function associated with an extreme urge to void was as large and equivalent or greater than the cognitive deterioration observed for conditions known to be associated with increased accident risk. *Neurourol. Urodynam. 30:183–187, 2011.* © 2010 Wiley-Liss, Inc.

Key words: cognition; healthy adult; urology

INTRODUCTION

The neural control of bladder function is complex and involves both spinal and supraspinal inhibitory and excitatory networks.[1,2] Functionally, the urinary system acts in a straightforward manner whereby the bladder fills to a threshold and then an urge to void is initiated with micturition occurring soon thereafter.[1] Although this process occurs automatically in healthy adults, micturition itself is under voluntary control so that it will occur only when deemed appropriate.[3] The voluntary control of micturition means, that in healthy adults, urinary retention can occur beyond the normal threshold for voiding. For example, in some occupational settings, shift and task demands may make it impractical for individuals to void when the bladder is full, requiring active prolongation of the time to micturition.

In healthy adults, the retention of urine is associated with increased bladder pressure that can lead to sensations of pain.[2] There are three distinct sensations associated with bladder filling. First, there is the sensation of filling itself; second, there is an experience of the urge to void; and third, there is a strong urge to void.[2] Sensations of the urge to void and pain abate once voiding has occurred.[4] Prolongation of the time to void beyond these phases gives rise to sensations of pain and increased sensation of urgency to void, however there is individual variation in the magnitude of the sensations and time of urge and the level of pain experienced.[4] If the voluntary prolongation of time to void occurs often, there is an increased risk of developing obstructive uropathy and urinary tract infections.[5] Further, in disorders of the lower urinary tract, sensations of pain and a sudden overpowering urge to void are common symptoms.[6]

It is well recognized that both acute pain and distraction arising from somatic signals can interfere with cognitive function in otherwise healthy adults.[7,8] There is also strong neurobiological evidence implicating common anterior cortical regions in the control of pain and aspects of cognitive function, such as attention and working memory (e.g.[9,10]). Consequently, it is likely that pain and distraction associated with the voluntary retention of urine will also interfere with some aspects of cognitive functions. Pain has the ability to interrupt behavior and to continue to do so until the pain is attended to or removed.[11] This is important as tasks requiring continuous and complex attention such as driving could be negatively affected if the magnitude of any effect on cognitive function from the voluntary inhibition of the urge to void is large. Thus, like low levels of alcohol intoxication or fatigue, inhibiting the urge to void in occupational settings could increase the risk of accidents.

Currently there are no data available on the cognitive effects of voluntary inhibition of the urge to void. Under experimental control and using standardized cognitive tasks, it is possible to examine the effect and magnitude of an increasing sense of urgency to void on cognition. By comparing cognitive outcomes under these conditions with cognitive performance using the same tools under other conditions that are known to increase accident risk, such as an elevated blood alcohol concentration (BAC) or fatigue, the magnitude of the risk can be placed in context. This approach would provide a useful first step in an

Contract grant sponsor: CogState Ltd.
Conflicts of interest: None.
Roger Dmochowski led the review process.
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Received 13 March 2010; Accepted 24 May 2010
Published online 6 November 2010 in Wiley Online Library (wileyonlinelibrary.com).
DOI 10.1002/nau.20963

examination designed to understand the relationship between voluntary urinary retention and accident risk.

This study has been developed as a pilot to measure the effect of an increasing urge to void urine on cognitive function. The first hypothesis was that the self rated level of pain and urge to void would be positively associated as participants drank a volume of water designed to stimulate a need to void. The second hypothesis was that cognitive function would decline as the length of time of voluntary urinary retention and the associated pain increased. The third hypothesis was that cognitive function would return to baseline levels following micturition.

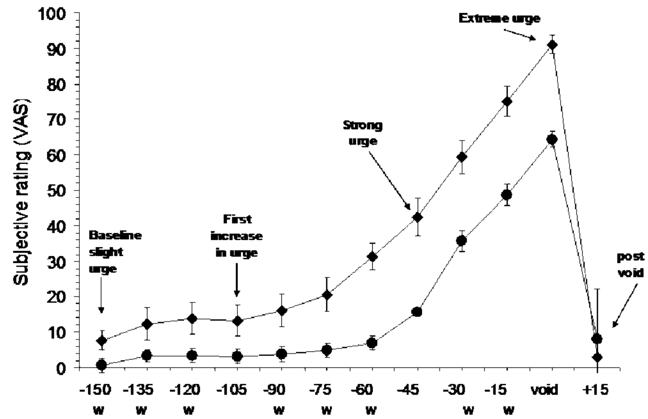

Fig. 1. Time course of change (15 min epochs) in the perception of pain (circles) and the urge to void (diamonds) in healthy adults. All participants performed the cognitive test at the points marked baseline, first increase in urge, strong urge, uncomfortable extreme urge and relief post void. VAS, visual analogue scale. W, 250 ml of water ingested.

METHODS

Participants

Cognitive performance was investigated in eight healthy adults aged between 23 and 45 years (2 females, mean age = 34 years). All had greater than 16 years education and considered themselves to be in good health. None reported any history of urological problems or any neurological or psychiatric illness. All provided written informed consent.

Measures

Subjective ratings of urge to void. Two visual analogue scales (VAS) were used to measure the subjective urge to void. Participants were asked to rate, “How much do you need to void right now?” and “How much pain/discomfort do you feel right now?” Each scale ranged from 0 to 100 with the anchor points for both scales being “not at all” and “the most I have ever felt in my life.”

Cognitive assessments. Three brief computerized tasks were used to measure cognitive function.[12,13] These tasks measured the speed and accuracy of psychomotor function, visual attention, and working memory in the same order at each testing session. All tasks were presented on a computer screen and used playing cards as the stimuli. For each task participants responded “yes” with their dominant hand and “no” with their non-dominant hand. For right-handed participants, the “K” key indicated yes and the “D” key indicated no. The yes and no keys were reversed for left hand dominant participants (n = 2). These tasks demonstrate a negligible practice effect beyond the second presentation to participants.[14] To overcome this we have used a double baseline in this study with the second baseline being treated as the true baseline.

Detection (psychomotor function). A single face down card was presented in the center of the computer screen, and turned face-up at a random inter-stimulus interval varying between 2.5 and3.5 sec. The response requested was to press the “Yes” key as soon as the card turned face-up. Once the participant responded correctly three times consecutively, the instructional cues (on-screen text and keyboard) were hidden (Fig. 1). Participants continued until they made 35 correct responses. This task was repeated at the end of the other tasks making a total of 70 responses.

Identification (visual attention). The same visual instruction and experimental cues were used, with a face-down card turning face-up at similar random intervals as used in the Detection task. The question posed was “Is the face-up card red?” and participants could respond with either the “Yes” or “No” keys. Participants continued until they had made 30 correct responses.

One Back (working memory). The same visual instruction and experimental cues were presented with the instructions asking “Does the face-up card exactly match the one before?” The participant responded with either the “Yes” or “No” keys. This task continued until the participant made 30 correct responses.

Procedure

Participants were instructed to conduct their normal morning activities before arriving at the laboratory before 9 am. After instruction and consent, participants were requested to empty their bladder before the study began. A dual baseline was conducted with cognitive assessments at 10 am and 10:15 am (Assessment 1: Baseline). Starting at 10:15 participants consumed 250 of water every 15 min, defined as an epoch, until they were unable to inhibit the urge to urinate. At the end of each epoch, participants were instructed to rate their subjective desire to void as well as the amount of pain/discomfort they were experiencing on the VAS scales. Cognitive assessments were conducted on each fourth epoch after the subjective ratings had been completed. No water was consumed immediately before cognitive assessment. This procedure was repeated until a participant believed that they could no longer resist the urge to void. At this time, participants completed the cognitive assessment and the subjective rating and emptied their bladder as rapidly and as frequently as they wished. Once participants felt that the need to urinate had passed completely they completed a final assessment and left the laboratory. At all times participants were free to void of their own volition. The procedure was medically supervised by one of the authors (DD). Institutional ethics approval was provided and all subjects gave informed consent.

Data Analysis

For each participant, data were organized relative to the cognitive assessment conducted immediately before they emptied

TABLE I. The Speed and Accuracy of Performance on the Cognitive Measures at Each Level of Need to Urinate

Assessment	Assessment 1: baseline (slight urge)	Assessment 2: first increase in urge to void	Assessment 3: strong urge to void	Assessment 4: extreme urge to void	Assessment 5: postvoid
Challenge					
Time from baseline (min)	21 (13.4)	50.6 (25.2)	95.6 (25.2)	140 (25.8)	153.6 (25.28)
Water consumed (ml)	350 (223)	843 (421)	1,468 (525)	2,218 (525)	
Visual analogue scales					
Urge to void	8 (2)	13 (16)	59 (13)	91 (7)	3 (6)
Perceived pain	1 (2)	3 (2)	16 (1)	64 (2)	8 (4)
Cognitive assessments					
Detection					
Speed	2.40 (0.05)	2.40 (0.04)	2.41 (0.04)	2.50 (0.09)	2.41 (0.04)
Accuracy	100 (97–100)	100 (96–100)	100 (94–100)	100 (93–100)	100 (97–100)
Identification					
Speed	2.62 (0.06)	2.61 (0.07)	2.60 (0.06)	2.66 (0.07)[a]	2.60 (0.07)
Accuracy	100 (93–100)	100 (91–100)	100 (91–100)	100 (93–100)	100 (97–100)
Working memory					
Speed	2.74 (0.09)	2.75 (0.12)	2.73 (0.12)	2.81 (0.10)[b]	2.72 (0.12)
Accuracy	100 (84–100)	100 (93–100)	100 (84–100)	100 (84–100)	100 (91–100)

Speed = group mean (+SD) log10 transformed RTs, accuracy = group median score (minimum–maximum score).
VAS scores out of 100, higher scores indicate higher amounts.
[a] $P = 0.027$.
[b] $P = 0.008$.

their bladder. To analyze urge to void and perceived pain group means and standard errors of the respective VAS were computed for each assessment. The ratings of both perceived pain and urge to void collected at the time of each cognitive assessment were compared statistically using one-way analysis of variance (ANOVA) with planned comparisons comparing each assessment to the baseline. For each task, the number of errors was automatically computed. Trials on which errors occurred were then removed from the reaction time analyses so that the mean response time could then be computed for correct trials and normalized using a log base 10 transformation. Data from the first baseline test was considered as practice and excluded from the analysis. The mean speed of performance and mean accuracy of performance on each of the cognitive tests was also calculated. The speed of performance on the cognitive measures at each of these time points was compared to baseline using a series of orthogonal planned contrasts (df = 4) set to contrast each assessment to baseline within a one-way repeated measures ANOVA. Because the distributions of accuracy scores violated assumptions of normality, performance at each epoch was compared to baseline using a series of Friedman non-parametric *t*-tests. The magnitude of the difference between conditions for which statistical significance was found was determined using the Dunlap's d measures of effect size.[15] Finally, Pearson correlations were computed between cognitive performance and urge to void and perceived pain.

RESULTS

The average time to reach the point at which participants were unable to resist the urge to void, while consuming the 250 ml of water every 15 min, was 140 mins (range = 105–180, see Table I). In that time, the average amount of water consumed was 2,218 ml (SD = 525 ml). The average time and average volume of water consumed at each assessment is shown on Table I. The effect of epoch was statistically significant for the ratings of urge to void ($F(3,21) = 28.9$; $P < 0.001$) and perceived pain ($F(3,21) = 21.3$; $P < 0.001$) with both increasing over epoch to the point of being unable to resist the urge to void. As expected there was a strong positive association between perceived pain and urge to void ($r = 0.89$; $P < 0.001$). On the basis of the subjective urge to void ratings the research team assigned labels to the times at which cognitive assessments were made: Assessment 1—baseline, Assessment 2—increased urge to void, Assessment 3—strong urge to void, Assessment 4—extreme urge to void, and Assessment 5—postvoid. The data presented in Figure 1 and Table I were organized according to these classifications. For the ratings of urge to void, the planned comparisons indicated that there were significant increases from Assessment 1 in the urge to void to Assessment 2, Assessment 3 and Assessment 4 but that this difference was no longer significant at Assessment 5 after voiding. For perceived pain there were significant increases from Assessment 1 to Assessment 3 and 4 but Assessment 5 conducted after voiding did not show a significant difference. The results for the subjective ratings at each 15 min epoch are shown in Figure 1. When considered across all assessments these data show an exponential increase in the perceptions of pain and urge to void to Assessment 4 when subjects felt an Extreme Urge to Void.

The cognitive performance data are presented on Table I. For the speed of performance, statistically significant effects were observed for the Identification task ($F(3,21) = 14.8$; $P < 0.01$) and the One Back task ($F(3,21) = 17.7$; $P < 0.01$) but not for the Detection task ($F(3,21) = 3.2$; $P > 0.05$). The planned contrasts indicated that for both the Identification task and the One Back task there was a significant performance decline at Assessment 4 compared against Assessment 1 (Table I). According to convention,[16] the magnitude of the difference for each of these was moderate to large and increased with task difficulty (Identification $d = 0.98$; One Back $d = 1.30$). When the antilog of the transformed score was calculated, slowing on the Identification task was 40.2 msec (416.9 vs. 457.1 msec) and slowing on the One Back task was 96.1 msec (549.5 vs. 645.7 msec). Performance at Assessment 5 was not statistically different from that at baseline. There were no statistically significant differences observed between assessments for the accuracy measures (Friedman non-parametric test: Detection task (df (3) $\chi^2 = 3.2$; $P > 0.05$), Identification task (df (3) $\chi^2 = 3.2$; $P > 0.05$) One Back task (df (3) $\chi^2 = 3.2$; $P > 0.05$)). Finally, speed of performance on the Identification task was correlated significantly with both urge to void ($r = 0.87$; $P < 0.01$) and perceived pain ($r = 0.76$; $P < 0.01$) and speed of performance on the One Back task was also correlated significantly with both urge to void ($r = 0.76$; $P < 0.01$) and perceived pain ($r = 0.73$; $P < 0.01$). There were no significant correlations between perceived pain and urge to void and the Detection task.

DISCUSSION

In healthy adults, consumption of 250 ml of water at 15-min intervals resulted in time dependent increases in subjective sensations of the urge to void and of perceived pain. On average, the healthy adults experienced an extreme urge to void, where they felt unable to contain the urge to void, after 140 min, by which time they had consumed 2,218 ml of water. The sensation of an extreme urge to void was associated with deterioration in the speed of performance on the measures of attention (Identification task) and working memory (One Back task) but not psychomotor function (Detection task). Having an extreme urge to void did not decrease the accuracy of performance on any test. Thus, the sensation of an extreme urge to void reduced the speed with which healthy adults could make decisions on the basis of available visual information or when information had to be retrieved from working memory. As soon as micturition occurred, cognitive performance returned to baseline levels.

The observed magnitude of the decline in the speed of information processing, associated with an extreme urge to void and high pain, was 0.98 for attentional function and 1.30 for working memory. By convention, these effect sizes are considered to be large in magnitude ($d > 0.8$, e.g.[16]) and expression of the decline in terms of effect sizes allows comparison of the current results to those of previous studies which have used the same tasks to quantify the effects of fatigue due to sustained wakefulness and the effects of low levels of alcohol intoxication in healthy adults.[12] These conditions provide useful benchmarks because both are well known to negatively affect cognition and performance and increase accident risk.[12,17–20] For comparison, the effect sizes of the cognitive impairment due to fatigue after 24 hr of sustained wakefulness, 0.05% BAC (both from Ref.[12]) and an extreme urge to void (from the current study) are presented in Figure 2 for both the attention and working memory tasks. For the measure of attention, the magnitude of deterioration associated with the extreme urge to void was equivalent to that observed after 24 hr of sustained wakefulness and 0.05% BAC. For the measure of working memory, the magnitude of deterioration from baseline associated with an extreme urge to void was greater than that observed after 24 hr of sustained wakefulness or with 0.05% BAC. Thus, this comparison suggests that magnitude of the cognitive decline associated with an extreme urge to void will raise accident risk in a manner similar to that expected with low levels of alcohol intoxication or following 24 hr of sustained wakefulness, and that an extreme urge to void may have a more pronounced effect on working memory. Driving with a %BAC of 0.05 or above is illegal in many jurisdictions and it is a common public policy approach to ensure that drivers and workers understand the deleterious effects of fatigue and alcohol consumption on performance and the associated risk of accident and injury.[21,22] Although only a beginning, the current results suggest that in occupational settings where it is necessary to inhibit the urge to void, risk management approaches that consider the role of an extreme urge to void in preventing work-related accidents may be warranted.

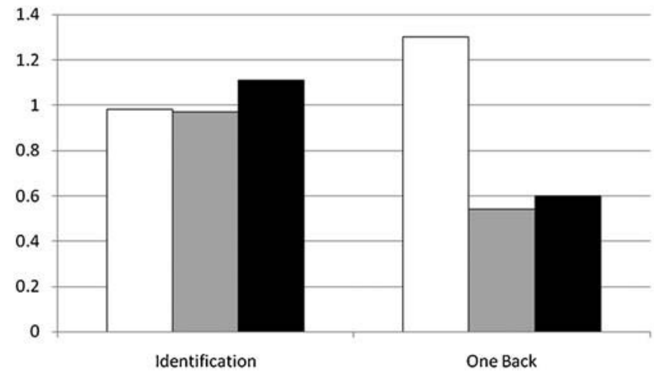

Fig. 2. The magnitude of the effect (Dunlap's d) of cognitive deterioration from baseline for Extreme urge to void (White), 0.05% BAC (Grey), and fatigue associated with 24 hr of sustained wakefulness (Black). NB BAC and fatigue effects sizes are taken from Ref.[12]

The finding that working memory and attention deteriorated only when the urge to void was extreme is consistent with functional neuroanatomical models of bladder control and micturition (e.g.[3,10]). These models revolve around central roles for the periaqueductal gray matter and pontine micturition center and postulate a distributed network involved in the perception of bladder fullness and distinct patterns of activation associated with bladder filling and with the urge to void, or with the inhibition of that urge.[23] As the urge to void increases, there is greater inhibition in cingulate and premotor cortices.[3] In the current group, such inhibition may have interfered with normal attentional and working memory function, as functional neuroimaging studies consistently implicate the cingulate gyrus in the perception of somatic stimulation and pain,[9,24] as well as the control of competing cognitive functions[25] although the regions of the cingulate activated by cognitive interference are generally more anterior than activations associated with pain or visceral stimulation. While this study was not designed to inform neuroscientific models of bladder control,[23] the results are consistent with existing brain-behaviour models outlined here.

Although preliminary, the data presented here demonstrates that an extreme urge to void is associated with impaired cognition in healthy young adults. Importantly, this study was not designed to be a naturalistic observation of normal bladder function and cognition, nor to provide a model of cognition in overactive bladder or urge incontinence; rather it was designed to determine how consumption of an atypically large amount of water would challenge cognitive function. One limitation of this study was that the focus of this work was cognitive function and consequently we did not conduct any urodynamic investigation which would be valuable. A further limitation is that the definitions of need to void are not based on ICS definitions. Therefore, it is unclear how these findings relate to standardized classification of desire to void or to specific urodynamic parameters. The applicability of these findings to populations with a pathological urological condition such as overactive bladder or urge incontinence are unclear however the research model that has been used in this study could be applied in research with groups presenting with lower urinary tract dysfunction given its demonstrated efficacy here and in other research using repeated measures designs with short intervals between assessments.[14]

Although this pilot study was a controlled experimental study with a relatively small sample size, we believe the current results do suggest that further investigation of interactions between the voluntary control of bladder function and cognitive function are warranted. While the presence of impairment in cognitive function itself does not predict that the accident risk will increase under conditions where individuals sense an extreme urge to void, the disruptive nature of the endogenous pain signals being generated by prolonging the time to void may have a deleterious effect on aspects of cognitive function. It is unclear how these results would apply to an older populations experiencing lower urinary tract dysfunction resulting in increased urgency or overactive bladder. More research is needed to replicate results of the current study in larger, more representative samples, with a more complete urodynamic assessment and to evaluate the effect of extreme urge to void on other markers of accident risk, such as in studies of performance in a driving simulator.

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