THE EFFECT OF CAFFEINE ON MICTURITION BY ENHANCING NEURONAL ACTIVATION AND INCREASING EXPRESSION OF NGF IN NEURONAL MICTURITION CENTERS

Hypothesis / aims of study
It has been suggested that caffeine may promote incontinence through its diuretic effect, especially in people with underlying detrusor overactivity, as well as by increasing muscle contractions of the bladder smooth muscle. Caffeine may also affect bladder function via a central nervous system (CNS) effect; however, the biochemical mechanisms that underlie the molecular and cellular action of caffeine in the brain are diverse. Few studies have investigated whether caffeine is involved in the regulation of voiding behavior. Thus, in the present study, we investigated the direct effects of caffeine on the central micturition reflex by measuring the degree of neuronal activation and quantifying nerve growth factor (NGF) expression in central micturition areas.

Study design, materials and methods
Nine-week-old adult female Sprague-Dawley rats were randomly divided into four groups (n = 8 in each group): a control group, a 10 mg/kg caffeine-consumption group, a 50 mg/kg caffeine-consumption group, and a 100 mg/kg caffeine-consumption group. Caffeine-consumption groups received caffeine orally once a day for 14 consecutive days. An awake urodynamic study was performed to assess bladder function. Immunohistochemical staining for c-Fos and NGF was also performed to detect neuronal activity in central micturition areas (medial preoptic area; MPA, ventrolateral periaqueductal gray; vlPAG, pontine micturition center; PMC).

Results
Ingestion of caffeine increased bladder smooth muscle contraction pressure and frequency as determined by cystometry (P < 0.05). The effect of caffeine on contraction pressure and frequency appeared most potent at the lowest dose of caffeine (10 mg/kg) (P < 0.05). c-Fos and NGF expression in all central micturition areas was significantly enhanced by the administration of caffeine (P < 0.05), and the lowest dose of caffeine enhanced c-Fos and NGF expression to the greatest extent (P < 0.05) (Figure).

Interpretation of results
Our results suggest that caffeine facilitates bladder instability by enhancing neuronal activation and expression of NGF in neuronal micturition centers. Indeed, neuronal activation in the brain micturition center has been shown to potentiate caffeine-induced bladder stimulation.

Concluding message
Most people believe that caffeine has only minor negative health consequences. This is because there is very little evidence that caffeine, in moderation, has any significant negative health effects. Based on the results of the present study, we suggest that caffeine facilitates bladder instability by enhancing neuronal activation and the expression of NGF in neuronal micturition centers. Indeed, neuronal activation in brain micturition centers has been shown to potentiate bladder stimulation by caffeine. Accordingly, caffeine consumption may have a negative effect on voiding symptoms, and caffeine should therefore be considered an aggravating factor when treating patients with LUTS.
References

Disclosures
Funding: None Clinical Trial: No Subjects: ANIMAL Species: Nine-week-old adult female Sprague-Dawley rats Ethics Committee: Kangbuk Samsung Hospital Institutional Review Board