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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 was 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 facilities 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 facilities 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.

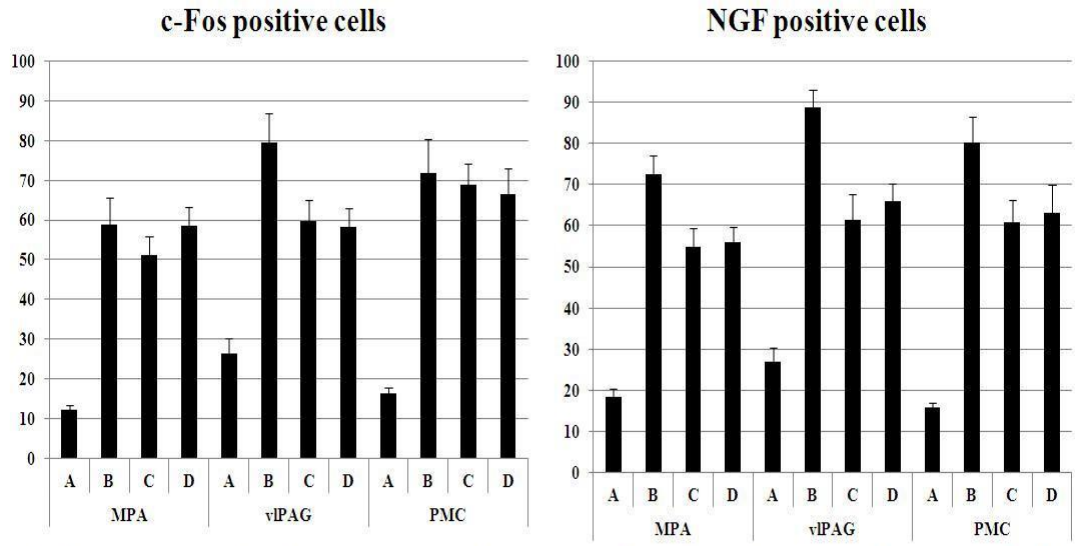

Fig. Effects of caffeine on c-Fos and NGF expression in neuronal micturition areas. The numbers of c-Fos-positive and NGF-positive cells in the MPA, PMC, and vlPAG regions were counted hemilaterally through a light microscope (A: control group, B: 10mg/kg caffeine-treated group, C: 50mg/kg caffeine-treated group, D: 100mg/kg caffeine-treated group). The c-Fos and NGF expression in all central micturition areas was significantly enhanced by the ingestion of caffeine ($P<0.05$). NGF: nerve growth factor, MPA: medial preoptic area, vlPAG: ventrolateral periaqueductal gray, PMC: pontine micturition center.

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Disclosures
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