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ACUTE DOSE-RELATED DIFFERENTIAL EFFECTS OF METHYLPHENIDATE ON MURINE CYSTOMETRIC PARAMETERS

Hypothesis / aims of study
Methylphenidate is the most widely used central nervous system stimulant in patients with attention deficit hyperactivity disorder. However, few studies have assessed its effects on voiding. Various doses of methylphenidate were investigated for their effects on cystometric parameters in conscious mice.

Study design, materials and methods
Ten male C57BL/6 mice, weighing between 20 and 23 g, were used in this study. To compare the acute drug responses before and after the oral medication was administered in the awake condition, we injected the solution through a catheter inserted into the stomach. Methylphenidate (1.25, 2.5, and 5 mg/kg) in an injection volume of 0.05 mL was administered.

Results
Four mice that received high doses of methylphenidate (2.5 and 5 mg/kg) showed no voiding contraction, with urine leakage. Six mice that received a low dose of methylphenidate (1.25 mg/kg) showed typical micturition cycles before and after administration. The micturition pressure decreased and bladder capacity increased without an increased residual volume after administration (Fig. 1 and 2).

Interpretation of results
A functional role for methylphenidate in the lower urinary tract has not yet been established. The results of the present study showed that methylphenidate in lower doses significantly changes the urodynamic parameters related to the functions of the lower urinary tract, including the bladder and urethra. The pressure parameters decreased as the volume parameters increased, which implies that this drug improves the storage function without a detrimental effect on the voiding function. However, higher doses of this drug showed some unusual urodynamic findings; the peripheral effects seemed to be masked by the central effects.

Concluding message
Methylphenidate has differential, dose-dependent effects on the function of the lower urinary tract, due to the dependent relationship between the brain and lower urinary tract. Especially at higher doses, this drug may interfere with normal micturition. Therefore, more detailed clinical or experimental studies are warranted in the future.

Fig. 1. Representative tracings showing the effects of methylphenidate injected into the gastric tube on cystometric findings. (A) Basic cystometry before methylphenidate administration. (B) Cystometric findings after administration of the lower dose of methylphenidate (1.25 mg/kg). (C) Cystometric findings after administration of the highest dose of methylphenidate (5 mg/kg). The mice that received the highest dose showed no voiding contraction pattern and showed only continuous leakage of a small amount of urine. Pves, vesical pressure.

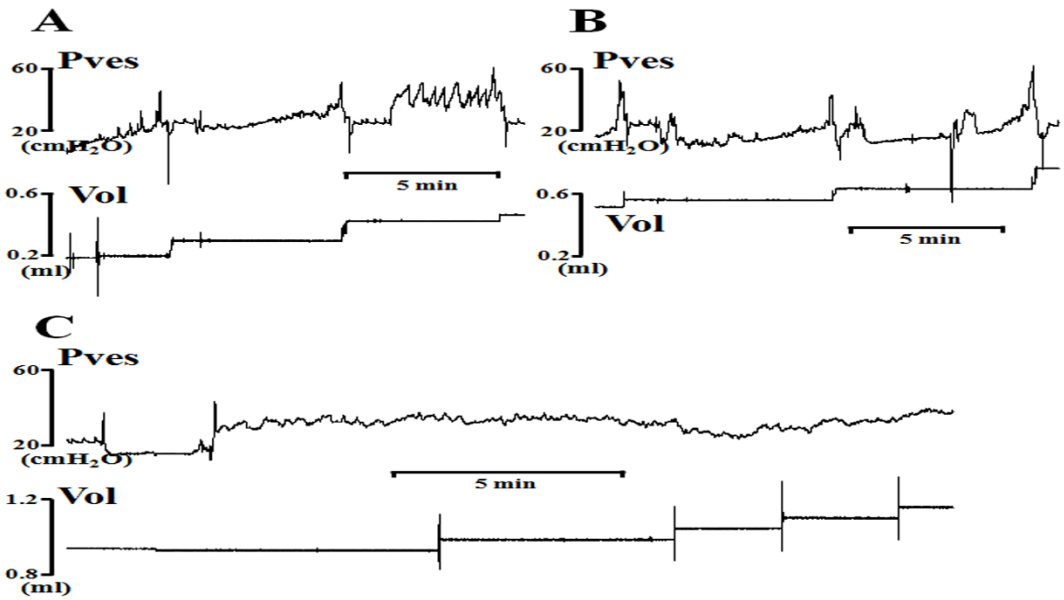
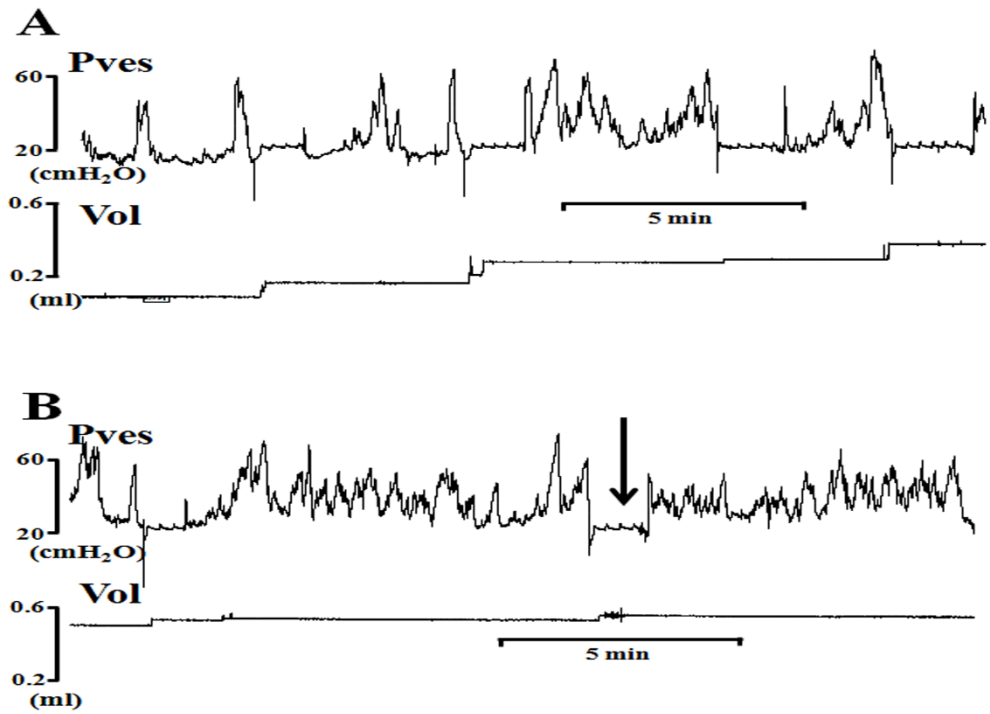


Fig. 2. Representative tracings showing the effects of methylphenidate injected into the gastric tube on cystometric findings. (A) Basic cystometry before methylphenidate admiration. (B) Cystometric findings after administration of the higher dose of methylphenidate (2.5 mg/kg). The mice that received this dose also showed no voiding contraction. There was no residual urine at the time point at which the urine leaked (arrow). Pves, vesical pressure.



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Disclosures
Funding: None **Clinical Trial:** No **Subjects:** ANIMAL **Species:** Mouse **Ethics Committee:** Kangbuk Samsung Hospital Institutional Review Board