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Yoshiyama M[1], Roppolo J[2], de Groat W[2]
1. Yamanashi Onsen Hospital, 2. Department of Pharmacology, University of Pittsburgh School of Medicine

EVALUATION OF URETHANE EFFECTS ON THE LOWER URINARY TRACT FUNCTION IN RATS WITH DECEREBRATION, A POSSIBLE METHOD TO EXAMINE THE 'REFLEX' MICTURITION UNDER NO ANESTHESIA

Hypothesis / aims of study

Involuntary 'reflex' voiding is the lower urinary tract dysfunction that one would aim to suppress with drug therapy, and can be revealed, for example, when the inhibitory control from forebrain to pontine micturition center being withdrawn. The 'reflex' micturition is substantially distinct from the voluntary voiding (i.e., 'conscious' micturition). The latter can be influenced by one's consciousness level and thus possibly altered by central nervous system acting drugs, which activate or interfere with neural transmissions in the brain. Hereby, it is difficult to determine whether the effects of such compounds on the lower urinary tract function are exhibited due to affecting consciousness maintaining continence, reflex processing loop or both when evaluating in awake animals. The present study was conducted in unanesthetized rats with decerebration that allowed pharmacological evaluation on the 'reflex' micturition under no anesthesia. The drug examined for the dose-response relations during cystometry was urethane, one of anesthetics generally used for *in vivo* physiological experiments (1), which would affect consciousness and behavior if an awake animal used. Thus, the effects of urethane on the micturition reflex were examined in decerebrate unanesthetized rats.

Study design, materials and methods

Female Sprague-Dawley rats weighing 200-260 g (n=11) were used. All surgical procedures including a precollicular decerebration were performed under halothane anesthesia. A transurethral bladder catheter (PE-50) connected to a pressure transducer was used to record bladder pressure during cystometrograms (CMGs) with single slow infusion (0.04 ml/min, n=6) or continuous fast infusion (0.21 ml/min, n=5) of physiological saline. To examine the external urethral sphincter (EUS) EMG activity, epoxy-coated stainless steel wire (50 µm) electrodes were placed percutaneously in the striated muscle of the EUS/pelvic floor. Three hours after decerebration, experiments were carried out under unanesthetized conditions. Urethane dissolved in sterile water was prepared in concentration of 1.2 g/ml for i.v. injection. Graded doses (0.001-0.3 g/kg for single CMGs or 0.001-0.3, 0.6, 0.9 and 1.2 g/kg for continuous CMGs) of urethane were given to each animal for examining dose-response relations in bladder and EUS EMG activity. All values are expressed as mean +/- S.E.M. Repeated measures one-way ANOVA followed by the Dunnett multiple comparisons test was used for statistical analysis and $P<0.05$ was considered significant.

Results

Baseline values (presented at C, control of each graph in Fig. 1) of cystometric parameters (MP, micturition pressure; PT, pressure threshold for inducing voiding; VT, volume threshold for inducing voiding; VV, voided volume; RV, residual volume; VE, voiding efficiency) were similar to those in the previous study using conscious animals, except for lower PT (2). As shown in Fig. 1, during single slow infusion CMGs, low doses of urethane (0.001-0.01 g/kg i.v.) did not change any parameters. Higher doses (0.03-0.3 g/kg), however, did decrease VV and VE, and increase RV, whereas they yet had no effect on other parameters. During continuous fast infusion CMGs, on the other hand, although 0.001-0.3 g/kg doses had no effect, larger doses 0.6-1.2 g/kg significantly decreased MP and EUS EMG activity (Fig. 2).

Fig. 1 Single infusion CMG

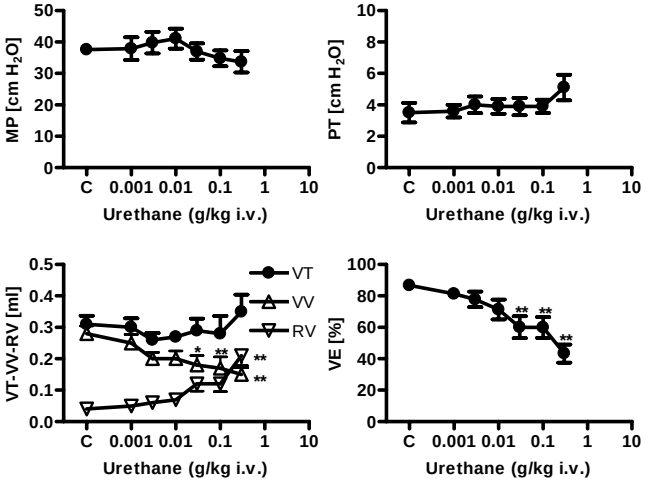
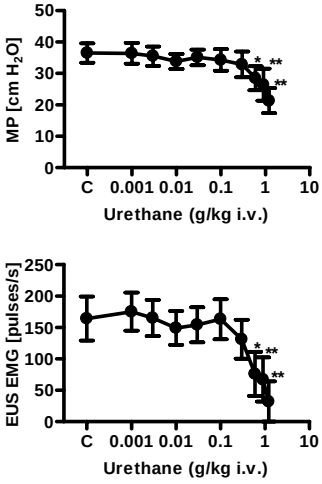


Fig. 2 Continuous infusion CMG



Interpretation of results

Increase of RV and decrease of VE as well as VV during slow infusion CMGs were likely to be due to increase of urethral resistance and/or suppression of EUS oscillatory activity produced by urethane (0.03-0.3 g/kg). Lack of changes in MP, PT and VT implied that urethane doses 0.001-0.3 g/kg had little effect on the descending limb/efferent pathway (for MP) and the afferent pathway (for PT and VT). Furthermore, larger doses (0.6-1.2 g/kg) were required to depress bladder and EUS EMG activity during fast infusion CMGs, and suppression by urethane of EUS activity was more marked than that of bladder contractions.

Concluding message

A precollicular decerebration is the possible method to examine the 'reflex' micturition, which allows conducting *in vivo* experiments under unanesthetized conditions without troubles of animals' conscious change and suffering. This study using decerebrate unanesthetized rats revealed that urethral activity essential for efficient voiding is more sensitive than bladder contractility and afferent signal processing to the inhibitory effect of urethane.

References

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