

BLADDER OUTLET OBSTRUCTION DISRUPTS CIRCADIAN RHYTHMS IN MICE

Hypothesis / aims of study

The circadian clock programs daily rhythms and coordinates multiple behavioral and physiological processes, including micturition. Partial bladder outlet obstruction (pBOO) in mice produces bladder hypertrophy and hyperactive voiding in cystometrograms. However, cystometrograms cannot replicate physiological conditions completely even if performed under conscious conditions. Moreover, long-term effects of pBOO have not sufficiently been clarified. In this study, we investigated the micturition behavior as a circadian rhythm of long-term pBOO in mice.

Study design, materials and methods

Female C57/BL6 mice were used. All mice had free access to food and water, and were kept under a 12 hr light/dark cycle. The proximal urethra was tied as in the procedure for pBOO. Sham surgery was performed. Micturition behavior was evaluated at 1 month, 3 and 6 months after pBOO surgery. We used aVSOP (automated voided stain on paper) method, which is a precise micturition recording system for mice. Urine stains were counted and traced, ranging from 10 to 800 μ l. The parameters evaluated were voided volume and time per void, total urination frequency (daytime and night time) and total urine volume.

Results

There was a tendency for the increase in the body weight of pBOO mice compared to sham-operated mice (27.4g vs. 24.5g in median) at 6 months after pBOO procedure (n=7). The number of micturitions in the pBOO group was significantly increased in 1 month, without affecting the total micturition volume compared to the pre-surgery group. However, 3 and 6 months after surgery, the number of micturitions in the pBOO group was significantly decreased compared to pBOO mice 1 month after operation (p<0.05). Moreover, the increase in daytime micturition frequency and the decrease in average voided volume in daytime were observed compared to sham-operated mice (p<0.05) (circadian rhythm disturbance) (see Figure).

Interpretation of results

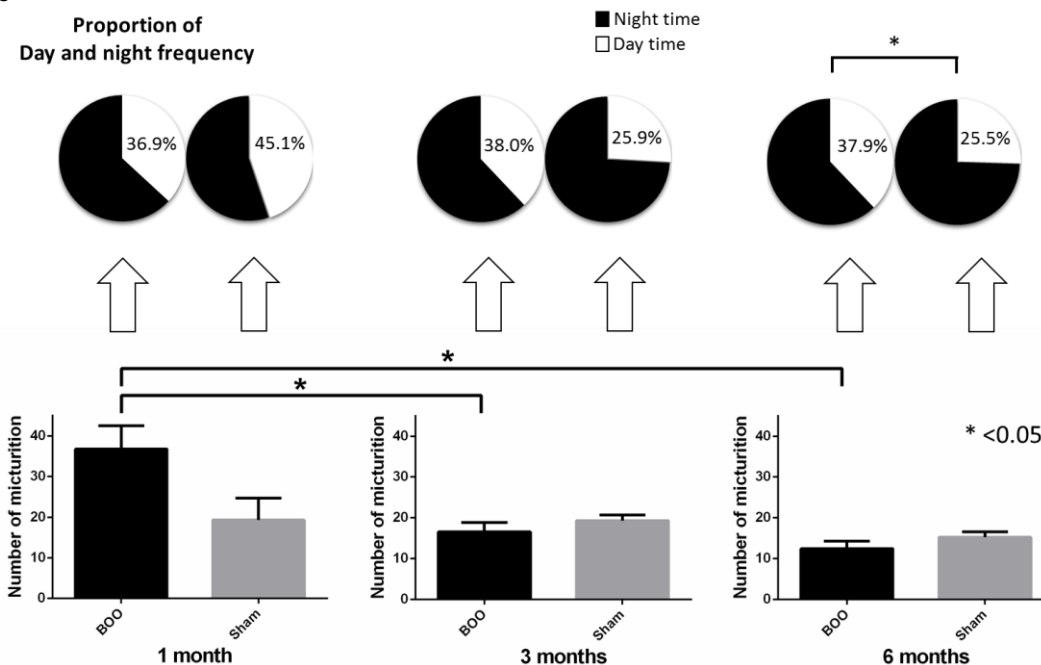
Long-term pBOO leads to disruption of one of the circadian rhythms (the day/night cycle) in mice. Mammals urinate less frequently during the sleep period than the awake period. Mice, which are nocturnal animals, also have a micturition frequency rhythm that is decreased during the day, which is the sleep phase for them.

This mechanism has not been clarified yet. Recently, not only male but also female with LUTS will be overweight and will have features of the MetS. From this perspective, increase in the body weight of pBOO mice could disrupt circadian rhythms. However, this is a kind of chicken or egg question. Further studies are necessary in order to conclude the chicken or the egg.

Concluding message

The current study has found that pBOO leads to disruption of one of the circadian rhythms (the day/night cycle) in mice, similar to those observed in humans as nocturia. Our findings could lead to the establishment of a mouse model of developmental micturition disorders, under non-physiological conditions.

Figure



Disclosures

Funding: None **Clinical Trial:** No **Subjects:** ANIMAL **Species:** Mouse **Ethics Committee:** Ethics Committee of Hokkaido University