

## IDENTIFICATION OF A MICTURITION SUPPRESSING REGION IN THE PERIAQUEDUCTAL GRAY OF THE MESENCEPHALON

### Hypothesis / aims of study

The periaqueductal gray (PAG) of the mesencephalon has been implicated to be involved in the control of micturition [1,2]. We previously showed that electrical and chemical stimulation of the ventrolateral PAG induced micturition in cats [3]. In the present study we investigated the existence of a micturition suppressing region in the PAG.

### Study design, materials and methods

11 decerebrated adult cats were used. A microelectrode was inserted stereotaxically into the PAG and a region was sought where electrical stimulation suppressed isovolumetric bladder contraction. Chemical stimulation with N-methyl-D-aspartate was also applied to the micturition suppressing region. Simultaneous stimulation of the pontine micturition center (PMC) and micturition suppressing region was performed before and after an injection of bicuculline, a GABA<sub>A</sub> blocker, into the PMC. Finally, an antegrade neurotracer, biocytin, was injected into the micturition suppressing region to investigate neural communications with the PMC.

### Results

A micturition suppressing region was found at the dorsolateral margin of the rostral PAG (Fig.1, 2). Chemical stimulation of the region also suppressed bladder contraction. Bladder contraction was not provoked by simultaneous stimulation of the PMC and the micturition suppressing region (Fig.3). However, after bicuculline injection into the PMC, partial bladder contraction was provoked by simultaneous stimulation of the both regions (Fig.3). Biocytin, injected into the unilateral micturition suppressing region, was detected inside the bilateral mesencephalic trigeminal tracts at the tegmental pons, consistent with the location of the PMC.

Fig.1 Electrical stimulation of a micturition suppressing region in the PAG (dark arrows). Bladder contraction was suppressed by electrical stimulation (white arrows). Transient blood pressure increase was synchronized with stimulation. Electromyography (EMG) of the external urethral sphincter did not change significantly.

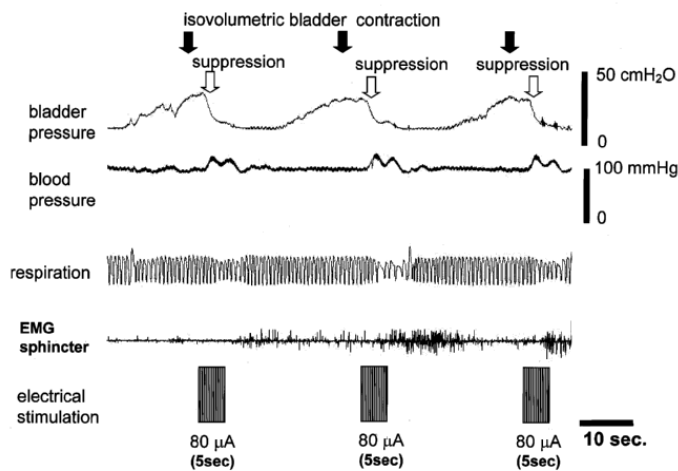


Fig.2 Electrical stimulation sites in the PAG. The stimulation sites were detected by ablation with direct current and electrode scars (arrows). SC; superior colliculus, IC; inferior colliculus.

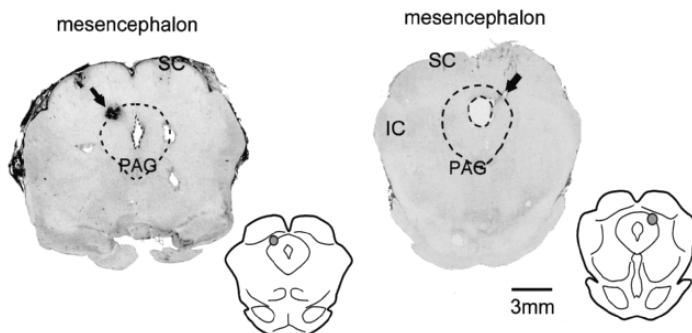
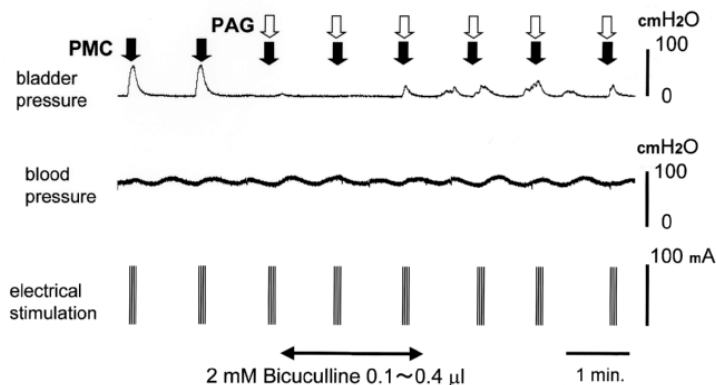


Fig.3 PMC stimulation provoked bladder contraction (dark arrows). Simultaneous stimulation of the PMC and the micturition suppressing region (white arrows) in the PAG did not provoke bladder contraction. After an injection of bicuculline into the PMC, weak bladder contraction was provoked by simultaneous stimulation of the both regions.



#### Interpretation of results

The present study showed the existence of micturition suppressing region in the dorsolateral PAG that inhibited bladder contraction without influencing the activity of the external urethral sphincter. Because the micturition suppressing region was activated by electrical stimulation as well as chemical stimulation with NMDA, it contains nerve cells (soma). In addition, the functional study with a GABA<sub>A</sub> blocker bicuculline and the neurotracer study indicate that the micturition suppressing region in the dorsolateral PAG suppresses the bilateral PMC directly without affecting the pontine storage center and that GABA may be one of the neurotransmitters from the PAG to the PMC. These novel findings contribute to our understanding of the central neurophysiology in the control of micturition.

#### Concluding message

Nerve cells in the dorsolateral PAG have neural communications with the PMC bilaterally and they suppress micturition. GABA is assumed to be one of the neurotransmitters from the micturition suppressing region in the PAG to the PMC.

#### References

- 1 J Urol, **168**: 2035-2039, 2002
- 2 Brain, **124**: 369-377, 2001
3. J Urol, **168**: 1626-1631, 2002

**FUNDING: NONE**

**DISCLOSURES: NONE**

**ANIMAL SUBJECTS:** This study followed the guidelines for care and use of laboratory animals and was approved by ethical use of Asahikawa Medical College