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THE ANTERIOR CINGULATE GYRUS PLAYS AN IMPORTANT ROLE IN THE CONTROL OF MICTURITION REFLEX IN A RAT MODEL OF PARKINSON'S DISEASE

Hypothesis / aims of study

Micturition reflex is controlled by a complex hierarchy of the central nervous system (CNS). The pontine micturition center and midbrain periaqueductal gray (PAG) integrates bladder sensory information, and control voiding and storage of urine. The anterior cingulate gyrus (ACG) is also thought to participate in the control of micturition and urinary continence, based on the results in recent functional brain imaging studies although its functional role is not fully understood. The present study examined dynamic neural activity changes in the ACG and PAG during the micturition reflex induced by pelvic nerve (PLN) stimulation. (Fig.1)

Study design, materials and methods

Female Sprague-Dawely rats were divided into Parkinson's disease (PD) and sham groups, which were injected with 6-hydroxydopamine and vehicle, respectively, into the substantia nigra pars compacta. Two weeks later, under urethane anesthesia, a tungsten electrode was inserted stereotaxically into the ACG and PAG to record field potentials that were evoked by electrical stimulation of the PLN. The effects of ZM24138 (ZM) (adenosine A_{2A} antagonist) administered intravenously (i.v.) on the PLN-evoked field potentials in the PAG and ACG were examined.

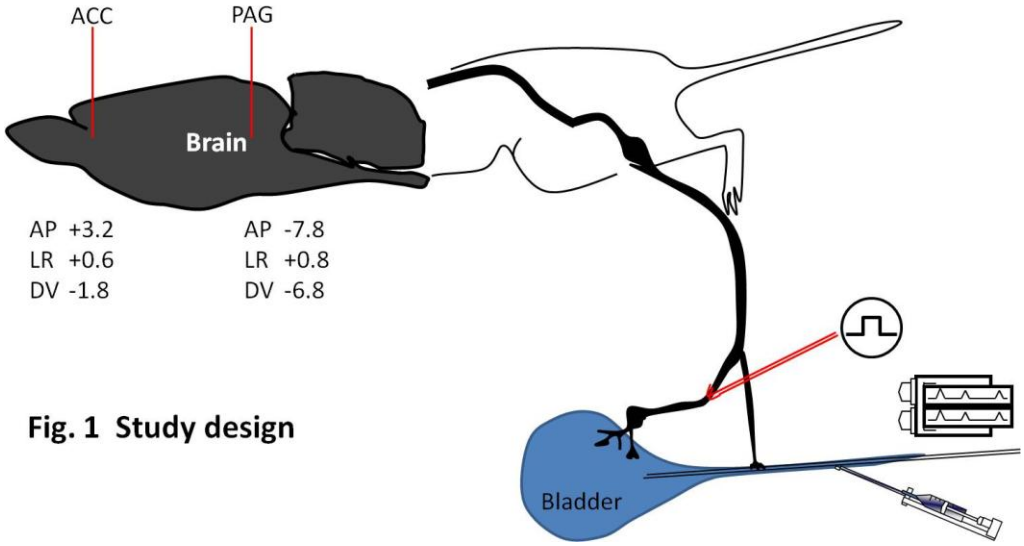

Fig. 1 Study design

Results

PD rats showed bladder overactivity evidenced by a significant decrease in intercontraction intervals (ICI) compared with sham rats. I.v. administration of ZM increased ICI in both PD and sham rats with the inhibitory effects being greater in PD vs. sham rats (Fig.2), and also increased the amplitude of evoked potentials in a dose-dependent manner in the ACG of PD rats. However, no significant changes in ACG evoked potentials were found in sham rats. I.v. administration of ZM reduced the amplitude of evoked potentials in PAG of both PD and sham rats with the inhibitory effects being greater in PD vs. sham rats (Fig.3).

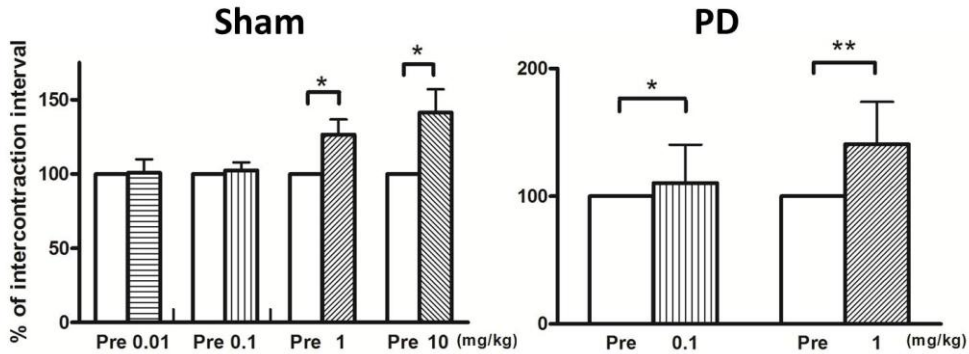

Fig. 2 Effects of i.v. administration of ZM241385 (0.01-10 mg/kg) on intercontraction interval (ICI). Results are expressed as the percentage of change from baseline values after i.v. administration of ZM241385. *P < 0.05, **P < 0.01

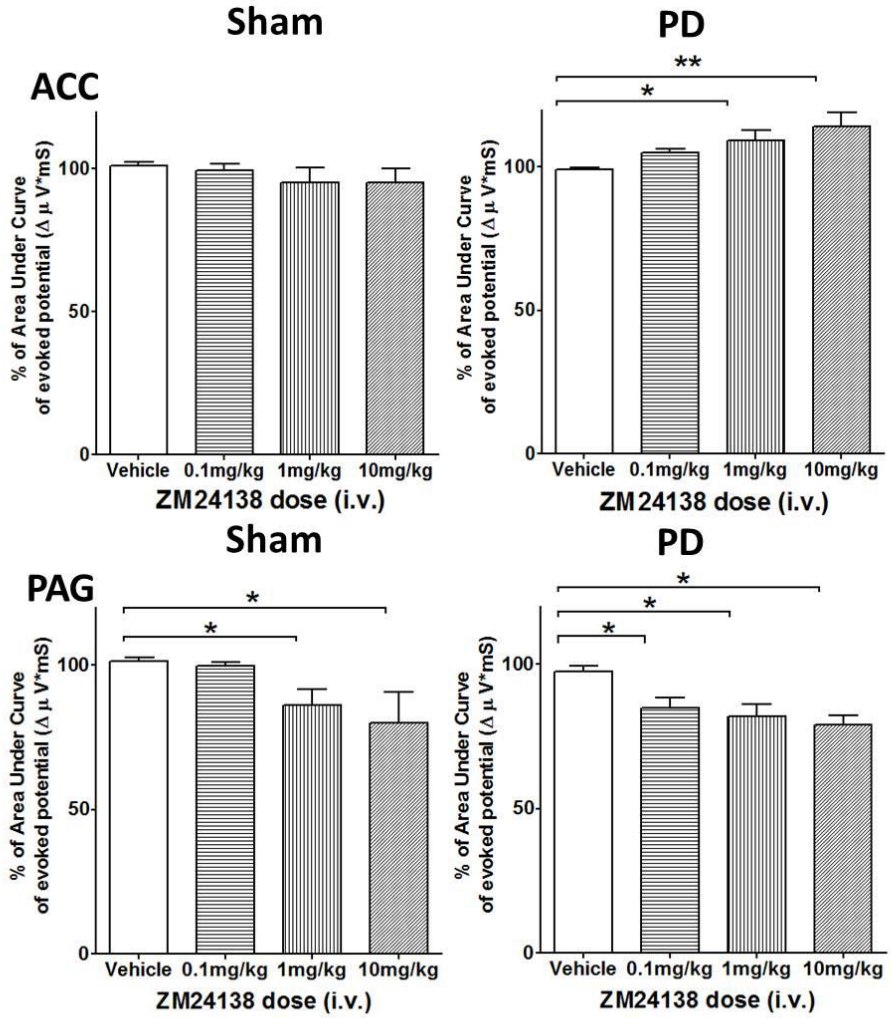

Fig. 3 Evoked potentials in ACC and PAG. Values are shown as mean±SEM. *P<0.05, ** P<0.01 compared to the corresponding Vehicle group.

Interpretation of results

In this study, neural activity in the ACG was significantly increased along with suppression of bladder overactivity after ZM administration only in the PD model, suggesting that ACG neurons have an inhibitory role in the control of bladder activity and that reduced ACG activity due to activation of adenosine A_{2A} receptors may contribute to bladder overactivity in PD. This assumption is supported by previous findings in human functional brain imaging showing increased responses in the ACG during withholding urine. In contrast, a decrease in PAG activity may lead to inhibition of the micturition reflex.

Concluding message

The ACG has an inhibitory role in the micturition control, which seems to be diminished in PD-induced bladder overactivity. Understanding the roles of CNS nuclei including the ACG in the modulation of micturition could provide further insights into the pathophysiology of OAB.

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Is this a clinical trial?	**No**
What were the subjects in the study?	**ANIMAL**
Were guidelines for care and use of laboratory animals followed or ethical committee approval obtained?	**Yes**
Name of ethics committee	**University of Pittsburgh Institutional Animal Care and Use Committee**