Best Basic Science Abstract

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THE ROLE OF SEROTONERGIC MECHANISM IN THE RAT PREFRONTAL CORTEX FOR CONTROLLING THE MICTURITION REFLEX: AN IN VIVO MICRODIALYSIS STUDY

Hypothesis / aims of study

The prefrontal cortex (PFC) is considered to be the critical region of the neural control system of micturition reflex[1)]. Although human functional brain imaging revealed the importance of the PFC in micturition reflex, there is few basic research regarding the PFC. We investigated the role of the PFC in micturition reflex using an in vivo microdialysis study.

Study design, materials and methods

Adult female Sprague-Dawley rats were used in this study. Following anesthesia with urethane, a guide cannula and a polyethylene catheter were implanted into the PFC and the bladder, respectively. All experiments were conducted 7 days after the surgery under consciousness and free movement.

Experiment 1: Samples including extracellular neurotransmitters (serotonin, dopamine, and glutamate) were collected by microdyalysis and analyzed by high performance liquid chromatography. At the same time, physiological saline was infused into the bladder, and intercontraction interval (ICI) and maximum voiding pressure (MVP) were measured.

Experiment 2: SSRI (citalopram, 1 μM) was administered into the PFC, and microdyalysis and cystometrography (CMG) were performed simultaneously.

Experiment 3: Following SSRI administration, 5-HT1A agonist (8-OH-DPAT, 300 μM), which has effect of decreasing serotonin level in the PFC, was administered into the PFC, and microdyalysis and CMG were performed simultaneously.

Results

Experiment 1: Extracellular level of serotonin in the PFC significantly increased during micturition reflex (Fig.1, $p<0.05$), whereas levels of glutamate or dopamine was not significantly changed. Experiment 2: Local administration of SSRI in the PFC increased the level of serotonin up to about 500% of basal level. It also significantly increased ICI ($p<0.05$), whereas no significant change was found in MVP (Fig.2). Experiment 3: The extracellular level of serotonin gradually decreased after local administration of 5-HT1A agonist, thereby ICI significantly decreased (Fig.3, $p<0.05$).

Interpretation of results

An examination of neurotransmitters in the PFC during the micturition reflex revealed dynamic changes in the extracellular levels of 5-HT, which significantly increased during the micturition reflex, but not in those of dopamine or glutamate. The local administration of SSRI (citalopram) into the PFC, which induced an increase in 5-HT levels in the PFC, significantly increased ICI in CMG. These results suggest that the PFC has suppressive effect on neural control of micturition reflex via serotonin. According to the previous behavioural studies[2), 3)], the PFC is an important structure for performing executive functions including working memory, temporal processing, planning, flexibility, rule learning, inhibitory control, and decision-making. The prefrontal 5-HT is involved in these executive functions. Especially, “inhibitory control” of the PFC may be associate with controlling the micturition reflex. According to the working model[1)], the periaqueductal grey (PAG) has a pivotal role in the voluntary control of micturition. The PAG receives and passes bladder afferents to higher brain areas and controls inputs to the pontine micturition center (PMC) during the filling phase. The PFC has direct or indirect connections with the PAG, and suppresses voiding until a socially appropriate timing(Fig.4). Serotonin in the PFC is one of the key neurotransmitters that affects the PAG in the control of the micturition reflex.

Concluding message

Investigations on the neural mechanism in the PFC affecting the micturition reflex contribute to the development of new treatments for OAB and urinary incontinence.

Fig.1

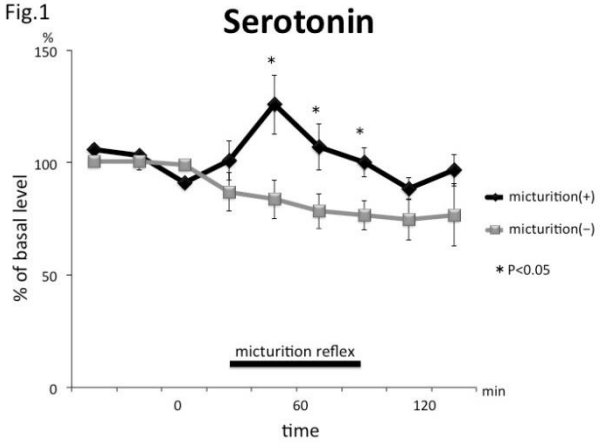


Fig.2

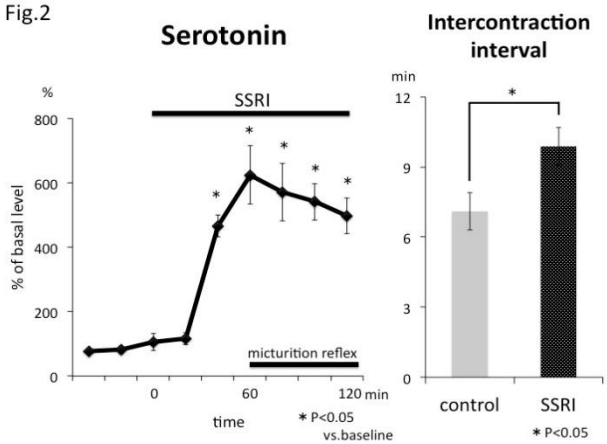


Fig.3

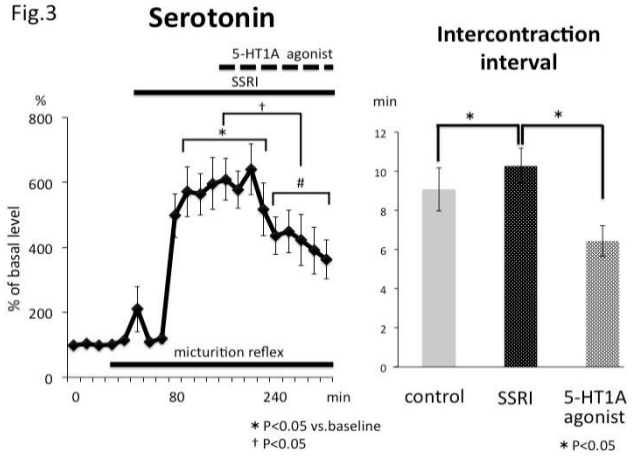
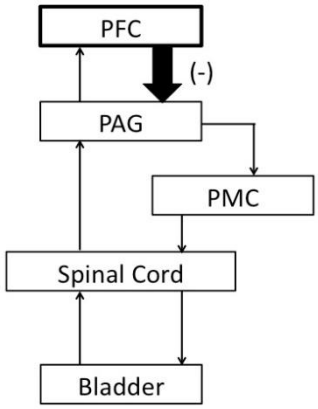


Fig.4



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Disclosures

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