339

Kitta T[1], Tanaka H[1], Mitsui T[1], Kanno Y[1], Moriya K[1], Nonomura K[1], Yoshimura N[2]
1. *Hokkaido University, Department of urology,* ***2.*** *Department of Urology, University of Pittsburgh School of Medicine*

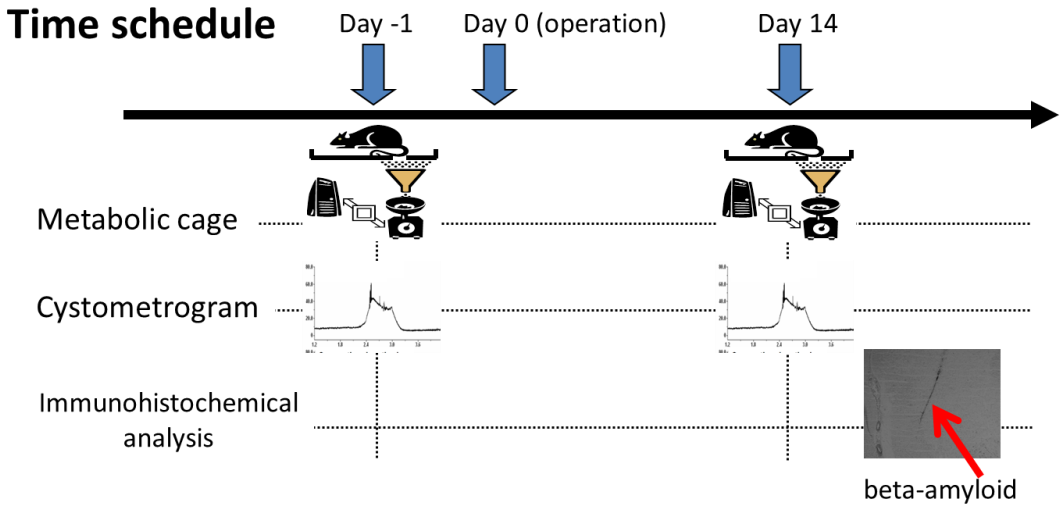
BLADDER DYSFUNCTION IN AN EXPERIMENTAL RAT MODEL OF ALZHEIMER'S DISEASE

Hypothesis / aims of study

Alzheimer's disease (AD) is one of the most common neurodegenerative diseases, and most prevalent form of dementia. Moreover, occurrence of detrusor overactivity (DO) has been reported in 40% of AD patients. AD is thought to attributable to pathologic changes in the beta-amyloid deposition in the frontal cortex and cause a decline in the cholinergic system of basal forebrain, which projects to the cerebral cortex and participates in the control of micturition reflex. Also, chronic infusion of beta-amyloid in animals can lead to a reduction in the levels of selected neuropeptides resembling the pattern seen in AD patients. We therefore evaluated the changes in bladder function using a rat model of AD induced by beta-amyloid injection into the brain.

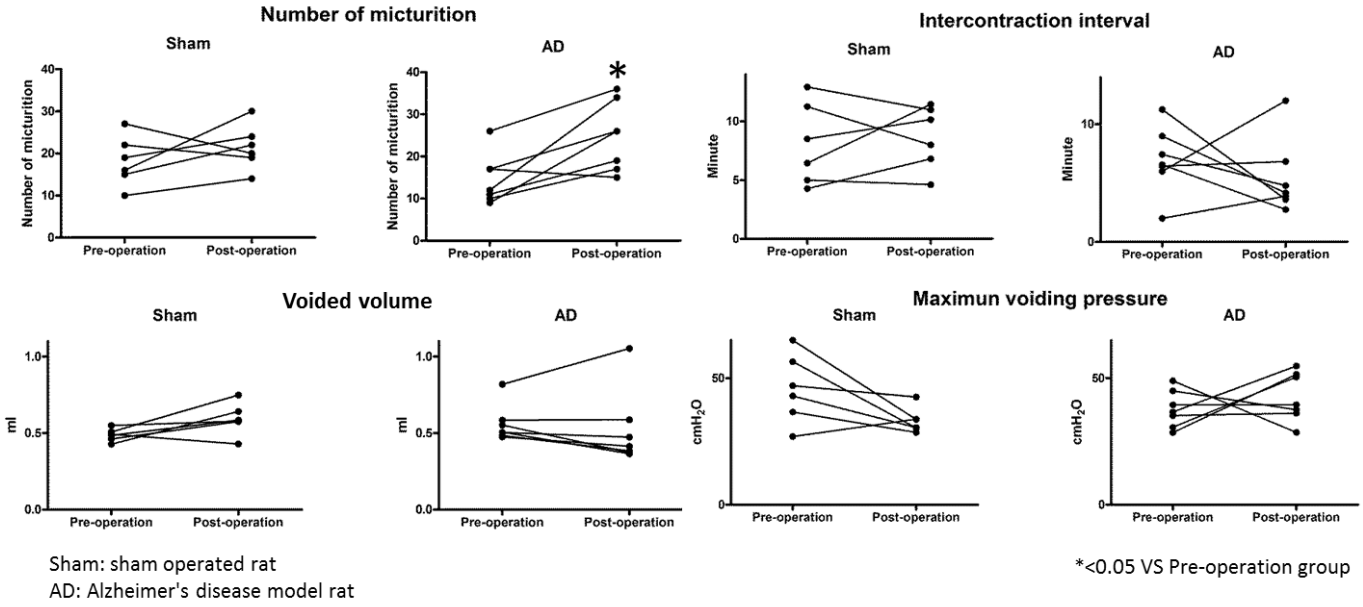
Study design, materials and methods

Female Sprague-Dawley rats were used. A cannula attached to an osmotic mini-pump was implanted into the rat right cerebral ventricle (A: −0.3 mm, L: 1.2 mm, V: 4.5 mm from the bregma) and either beta-amyloid (5 micro g/hr) or vehicle was continuously infused for 14 days. Thereafter, rats were placed in a metabolic cage, and the number of micturition per day and voided volume per micturition were recorded continuously for 48 h. Continuous cystometrograms were then recorded under urethane anesthesia. Bladder function was evaluated by measuring intercontraction interval (ICI) and maximal voiding pressure (MVP). After experimentation, rats were subjected to immunohistochemical analysis using antibodies for beta-amyloid.



Results

No difference in body weight was seen between sham and AD rats. In metabolic cage studies, the number of micturition averaged 24.7 ± 3.1 / 24hrs (mean ± SE) in AD rats, which was significantly higher ($P<0.05$) than that in sham rats (21.5 ± 2.2 / 24hrs). There was also a tendency for a reduction in voided volume per micturition in AD rats compared to sham rats (0.52 ± 0.09ml vs. 0.59 ± 0.10ml) although the difference was not significant. No significant changes were found in ICI or MVP between sham and AD rats under urethane anesthesia (figure 1). Beta-amyloid deposition in the brain was found in AD rats.



Interpretation of results

In this study, AD rats showed bladder overactivity shown by frequent voiding in an awake condition, which was not detected in cystometrogram under anesthesia. This discrepancy could be due to the effects of urethane, which suppresses activity of the central nervous system to mask bladder overactivity.

Concluding message

Rats with beta-amyloyd injection represent a promising model for studying neurogenic bladder dysfunction of AD.

Disclosures

Funding: NIH DK57267, DK88836 and DOD SC100134 **Clinical Trial:** No **Subjects:** ANIMAL **Species:** Rat **Ethics Committee:** University of Pittsburgh Institutional Animal Care and Use Committee