

## THE ROLE OF NERVE GROWTH FACTOR FOR THE CHANGES OF VOIDING FUNCTION IN THE URINARY BLADDER OF THE RAT ASSOCIATED WITH STREPTOZOTOCIN-INDUCED DIABETES

### Aims of Study

Nerve growth factor (NGF) is a biomolecule, which is produced within the innervated target organs. It participates in the differentiation, induction and maintenance of neural cells. Therefore, the level of NGF in the target organs may induce the adaptation of innervations.

It is confirmed that the level of NGF in the urinary bladder should increase or decrease in various status. However, it is still unclear that the time course of the level of NGF should relate to the changes of voiding function.

Therefore, we investigated the bladder function and the NGF level of bladder in STZ induced diabetic rat with diuresis control group fed 5% sucrose. In addition, using an immunohistochemical technique, the proliferation of bladder smooth muscle was observed.

### Methods

(1) *Materials* Sixty subjects of 7 to 11 week old female Wistar rats were used. They were divided into 30 subjects of the diabetic and 30 subjects of diuresis control group. In the diabetic group, rats were injected STZ (60mg/kg, intraperitoneally) diluted with 0.1 M citrate buffer for one time after fasting for 24 hours. With a blood sugar level over 250 mg/dl, we defined the rat to have diabetes (STZ group).

In the diuresis control group, rats were fed 5% sucrose (SUC) in water. (SUC group)

(2) *Evaluated parameters*

The time course of the tidal voided volume, total voided volume per day and frequency of micturition per day was recorded from induction for 14 days.

The level of NGF in the urinary bladder ([NGF]) was measured on days 2,5,10 and 14.

The proliferation of bladder smooth muscle was elucidated by immunohistochemistry with antibody against the proliferating cell nuclear antigen.

(3) *Statistical analysis* Obtained parameters were evaluated by the Mann-Whitney U test for the difference between the STZ and SUC group. The significance was determined with a p value of less than 0.05

### Results

1. The total voided volume of the SUC group increased immediately after the onset of the hydration with sucrose, whereas the STZ group showed gradual increase after the administration of STZ.

2. The tidal voided volume in both groups increased on day 1 after the treatments. In the SUC group, the increase showed plateau after day 5, whereas in the STZ group the increase persisted until day 10. However, there was no significant difference between the groups on day 14.

3. [NGF] significantly increased on day 2 in the SUC group and on day 5 in the STZ group. The time course of the increase in [NGF] in both groups was parallel to the increase in tidal voided volume and the proliferation of bladder smooth muscle. However, the increase of [NGF] in the STZ group was two times larger than that in the SUC group.

### Conclusions

These findings indicate that [NGF] plays an important role in physiological adaptation to the polyuric state. It is also suggested that there are some other physiological responses aside from polyuria in the STZ group to show the higher level of [NGF].