Results: Bladder capacity become significantly smaller than before IA injection. Seven to 10 days after IA injection, bladder capacity was approximately 43% of SO rats. CAT activity in the frontal cortices was reduced in BF rats. Oxotremorine M increased bladder capacity in BF rats, while decreased in SO rats. Pirensepine significantly increased bladder capacity both in BF and SO rats, and antagonised the effect of oxotremorine M. Direct injection of oxotremorine M into the PMC decreased bladder capacity in BF and SO rats, while injection of pirensepine had no effects on CMG.

Conclusions

These results indicate that M1 muscarinic system in the cerebral cortex has inhibitory influence to micturition reflex pathway. Down-regulation of this inhibitory mechanism plays an important role on overactive bladder in Alzheimer type dementia. M2 muscarinic system in the brainstem is likely to have excitatory influence on micturition reflex pathway.

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Title (type in CAPITAL LETTERS, leave one blank line before the text):

**AN EFECT OF L-DOPA ON MICTURITION DISTURBANCE IN PATIENTS WITH PARKINSON'S DISEASE; A COMPARISON OF 'ON' AND 'OFF' PERIODS**

**Background** Recently dopaminergic drugs are the main therapy for patients with Parkinson's disease (PD). However, exact effects of L-dopa on micturition are not ascertained. Animal experiments showed the fact that selective D2 receptor agonist quinpirole reduced bladder volume threshold for the micturition reflex in MPTP lesioned parkinsonian monkeys. We evaluated that an effect of L-dopa (D1/D2 receptor agonist) on micturition disturbance in patients with PD by using urodynamic studies.

**Methods** We recruited 10 patients with PD (including 5 men, 5 women), mean age 64 years. All patients have been taking dopaminergic drugs including only L-dopa / carbidopa in 3 and L-dopa / carbidopa with other antiparkinsonian drugs in 7. All patients showed marked 'on' (alleviation) and 'off' (worsening of motor performance) phenomenon in a day depending on the time of L-dopa medication. We performed detailed questionnaire of urinary symptoms and urodynamic assessments before ('off' period) and one hour after taking 100 mg of L-dopa / carbidopa ('on' period). No patient had apparent prostate hypertrophy on rectal examination and ultrasonography.

**Results** Comparing the 'on' period to the 'off' period, three complained exacerbation in urinary urgency in filling phase, however seven noticed improvement of voiding difficulty. Urodynamic study in the 'off' period showed that seven had detrusor hyperreflexia (DH) and none had detrusor sphincter dyssynergia (DSD). In the 'on' period, DH did not disappeared in any patients, but bladder capacity was decreased in 9 (-15 %) and increased in 1 patient. Bladder capacity of all three patients without DH was also decreased. Maximum value of watts factor (WFmax) was increased in all patients (+8.4 %). Residual urine volume (RV) was decreased in 5 (-85 %), unchanged in 4 and increased in 1 patient. All cases with unchanged RV had originally little residual urine volume (0-20 ml). DSD did not appeared in any patients, however maximum flow rate (Qmax) was decreased in 6, unchanged in 3 and increased in 1 patient and AG number (Pdet at Qmax – 2Qmax) was increased in 7, unchanged in 1 and decreased in 2 patients. Maximum urethral closure pressure (UPmax) was measured in 2 patients, and both patients showed UPmax was increased.

**Conclusion** Comparing urinary function in the 'on' and 'off' periods of L-dopa treatment, the results showed that L-dopa decreased bladder capacity in most of our patients, even without DH. In the voiding phase, L-dopa augmented detrusor contractility but also L-dopa increased urethra obstruction, and overall lessened post-micturition residuals in most patients. These findings may reflect central and peripheral dopaminergic action of L-dopa or its metabolite.

Fig.1

| CASE | Motor states | Hoehn &Yahr | During UDS Urinary urgency | During UDS Voiding difficulty | DH | DSD | Bladder capasity (ml) | WFmax | Redidual urine (ml) | Qmax | AG number | UPmax (static) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | off | 4 | + | + | + | - | 210 | 6.31 | 20 | 8 | 22 | - |
| | on | 3 | + | « | + | - | 260 | 7.03 | 50 | 4 « | 49 a | - |
| 2 | off | 3 | ± | + | + | - | 450 | 4.47 | 140 | 3 | 32 | - |
| | on | 2 | ± | « | + | - | 400 « | 4.5 a | 60 « | 3 | 32 | - |
| 3 | off | 5 | + | + | - | - | 280 | 7.81 | 20 | 19 | -18 | - |
| | on | 3 | a | « | - | - | 210 « | 8.1 a | 10 « | 16 | -21 | - |
| 4 | off | 5 | + | + | + | - | 270 | 7.01 | 120 | 8 | 25 | - |
| | on | 3 | " | « | + | - | 230 « | 7.96 | 35 « | 13 | 18 | - |
| 5 | off | 4 | + | + | - | - | 410 | 6.2 | 10 | 10 | 12 | - |
| | on | 3 | a | « | - | - | 310 « | 7.26 | 0 « | 9 « | 20 a | - |
| 6 | off | 4 | + | - | + | - | 170 | 7.41 | 10 | 15 | -3 | - |
| | on | 3 | " | - | + | - | 150 « | 8.76 | 15 | 12 | 11 a | - |
| 7 | off | 2 | + | - | + | - | 600 | 8.82 | 65 | 22 | -31 | - |
| | on | 1 | + | - | + | - | 550 « | 9.02 | 0 « | 6 « | 75 a | - |
| 8 | off | 3 | + | + | + | - | 570 | 7.62 | 250 | 16 | -10 | 47 |
| | on | 2 | + | « | + | - | 500 « | 8.55 | 10 « | 14 | 16 a | 60 a |
| 9 | off | 3 | + | - | ± | - | 450 | 8.27 | 0 | 23 | -23 | 60 |
| | on | 2 | a | - | + | - | 380 « | 8.45 | 0 | 20 | 0 a | 79 a |
| 10 | off | 4 | - | + | - | - | 600 | 8.53 | 80 | 13 | 37 | - |
| | on | 3 | - | « | - | - | 590 « | 8.75 | 0 « | 10 | 50 a | - |

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**HYPOGASTRIC NERVE BLADDER AFFERENTS ARE INVOLVED IN FACILITATING AFFERENT EFFECTS OF CHEMICAL BLADDER IRRITATION ON MICTURITION REFLEX AND SPINAL C-FOS EXPRESSION**

**AIMS OF STUDY:**

The hypogastric plexus(HGP) innervates the pelvic viscera via hypogastric nerves(HGN) and is implicated in the pelvic visceral pain[1]. A previous study has demonstrated that the bursting activation of bladder chemo-receptive afferent nerves in HGN rather than pelvic nerve (PLN) can signal noxious stimulation of bladder[2]. Since chemical irritation of the bladder is known to facilitate micturition reflex and spinal c-fos expression which is a functional marker for nociceptive neural activity[3,4], the present study was undertaken to evaluate the influence of HGN transection on the facilitating effects of chemical bladder irritation.

**METHODS:**

**[continuous cystometry]** Female Wistar rats were used and divided into 3 groups; (1)control(n=7), (2)capsaicin desensitization(n=6): capsaicin (75 mg/kg, subcutaneously) was administered 4 days before experiment, (3)HGP-transection(n=8): HGP was removed transabdominally under anesthesia with pentobarbital (40mg/kg, intraperitoneally[i.p]) 7 days before experiment. A polyethylene catheter(PE-60) was inserted into the bladder through the dome. Five days after catheter insertion, continuous cystometry was performed without anesthesia under a constant infusion of normal saline and then 0.1% acetic acid at the rate of 0.1 ml/min. After a 60-min stabilization period, intercontraction interval(ICI) and maximal voiding pressure(MVP) were compared in each group.