transmission scan of 10 minutes was first made for attenuation correction of the emission scans, followed by 3 scanning sessions (6 scans in total). Each scanning session consisted of two measurements, scan-1 in the empty bladder phase and scan-2 in the full bladder, and was repeated three times. Before each scan, 300 MBq of $H_2{}^{15}O$ in saline was intravenously injected. Data acquisition was initiated 40 seconds after the beginning of injection and continued for 90 seconds. To decrease the radiation levels to the background, at least 10 minutes were allowed to elapse between the injections. For filling bladder, distilled water was dripped via the catheter, and the infusion was stopped when the volunteer felt the maximum desire to void. Once a scan-2 was completed, the bladder was emptied again via the catheter for a next scan. The data of each scan were summated and further analyzed using the Statistical Parametric Mapping procedure (SPM95, the Wellcome Department of Cognitive Neurology, London, UK) on a computer. The SPM95 software was used for anatomical realignment, normalization, smoothing and statistical analysis. A corrected P-value less than 0.001 was considered significant.

Results The mean bladder capacity was 400 ml (300-480 ml). During active urine storage, significantly increased blood flow was found in the anterior cingulate gyrus, the thalamus and the upper level of the midbrain, predominantly on the left side. Only the lower part of the midbrain periaqueductal gray showed significant activation on the right side.

Conclusions Our data suggest that the midbrain as well as more rostral regions are involved in the urine storage function in the human brain. Blok et al. previously reported the cortical and pontine micturition sites to be located on the right side [1]. In our PET study, however, significant brain activation associated with urine storage occurs predominantly on the left side.

Reference [1] Brain, 120 (1997) 111-121.

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K. Kaidoh, *H. Takeda, *Y. Yamazaki, *S. Akahane, *H. Miyata, *Y. Ajisawa, Y. Igawa, O. Nishizawa & **K. -E. Andersson

Department of Urology, Shinshu University School of Medicine, Matsumoto, *Central Research Laboratories, Kissei Pharmaceutical Co., Ltd., Hotaka, Japan and **Department of Clinical Pharmacology, Lund University Hospital, Lund, Sweden

EFFECTS OF SELECTIVE β2- AND β3-ADRENOCEPTOR AGONISTS ON DETRUSOR HYPERREFLEXIA IN CEREBRAL-INFARCTED RATS

AIMS OF STUDY It is well known that excitation of the sympathetic nerves during the filling phase, relaxes the bladder via activation of β-adrenoceptors. We have demonstrated using an in vitro functional study that the subtypes of β-adrenoceptor that contribute to the detrusor relaxation in the rat are β2- and β3-adrenoceptors (1).

A rat model of detrusor hyperreflexia associated with cerebral infarction has been recently developed (2). In the present study, we investigated whether selective β2- and β3-adrenoceptor agonists could suppress detrusor hyperreflexia in conscious cerebral-infarcted (CI) rats.

METHODS Female Sprague-Dawley rats weighing 210-260 g (n=132) were used. Under general anesthesia with ketamine and xylazine, a catheter was implanted into the bladder through the dome and a separate catheter into the right jugular vein for drug administration. Three or four days after the operation, cystometric investigations were performed without any anesthesia as a base-line study. Then, the rats were anesthetized again with halothane and the left carotid artery was exposed. The left middle cerebral artery was occluded with a 4-0 monofilament nylon thread introduced from the carotid bifurcation by 17 mm in CI group. In sham-operated animals, the left carotid artery was exposed, but no further procedures were performed. Two hours after the operation, cystometric investigations were repeated without any anesthesia. Then, the effects of intravenous (i.v.) administration of saline (1

ml/kg: vehicle) and CL316243 (0.1-100 μg/kg), a selective β3-adrenoceptor agonist, or procaterol (0.1-100 μg/kg), a selective β2-adrenoceptor agonist on the cystometric parameters were evaluated.

RESULTS In the CI animals, a significant ($p<0.01$) decrease in the bladder capacity and a significant ($p<0.01$) increase in the amplitude of voiding contractions were observed after the occulusion of the middle cerebral artery. On the other hand, the sham-operated animals did not show any changes of cystometric parameters after the operation (Fig. 1A, 1B). I.v. administration of saline (vehicle) did not affect any cystometric parameters in the CI or sham-operated group. In the CI group, CL 316243 (0.1-100 μg/kg given i.v.) increased the bladder capacity in a dose-dependent manner (Fig. 2A) without affecting the amplitude of voiding contractions and residual volumes. In the sham-operated group, no significant changes were observed after i.v. administration of CL316243 (0.1-100 μg/kg: Fig. 2A). Procaterol, administered i.v. at 10 μg/kg, significantly ($p<0.01$) increased the bladder capacity in the CI group (Fig. 2B). Procaterol at 10 and 100 μg/kg also tended to increase residual volumes in the CI group, but the increase was not statistically significant. In the sham-operated group, no significant changes in the cystometric parameters were observed after i.v. administration of procaterol (0.1-100 μg/kg: Fig. 2B).

CONCLUSIONS Although neither β2- nor β3-adrenoceptor agonists affected micturition in neurologically intact rats, both th selective agonists for β2- and β3-adrenoceptor, CL316243 and procaterol, could suppress detrusor hyperreflexia without affectin voiding efficacy in rats with cerebral infarction. Thus, selective agonists for β2- or β3-adrenoceptor might be promising drugs in th treatment of detrusor hyperreflexia associated with cerebral infarction.

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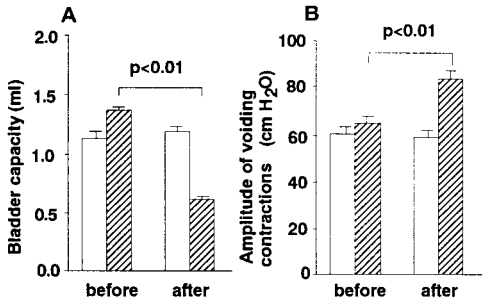

Fig. 1. Bladder capacity (A) and amplitude of voiding contractions (B) obtained before or after operation. Open bars and slashed bars represent the sham-operated group and cerebral-infarcted group, respectively.
Each bar represents the mean ± S.E. of 66 animals.

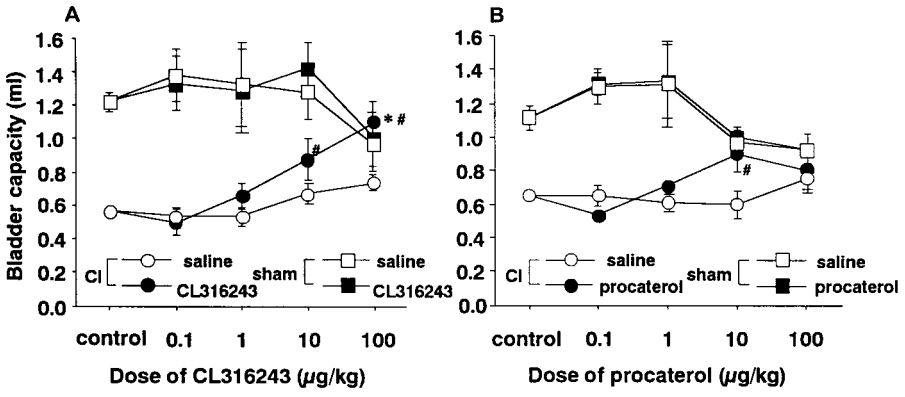

Fig. 2. Effects of CL316243 (A) and procaterol (B) on bladder capacity in cerebral-infarcted (CI) and sham-operated rats. Each point represents the mean ± S.E. of 6 animals
*; $p<0.05$ significantly different from that with saline. #; $p<0.01$ signicantly different from control.