Norepinephrine Sensitivity, Reactivity and Neuronal Uptake in the Isolated Vas Deferens from SHRSP and WKY.

Atsuko Niwa, Noriko Murakami, Takashi Miyazato and Aritomo Suzuki.
Departments of Parasitology and Pharmacology, Kinki University School of Medicine, Osaka-fu 589.

It has been shown alterations in the norepinephrine-induced responses in the sympathetically innervated smooth muscle from SHRSP. One of several factors for modulation is related to an efficiency of norepinephrine inactivation, being predominantly neuronal uptake in such vas deferens that possess dense adrenergic innervation and a narrow synaptic cleft. The purpose of this study was to compare the effects of cocaine, an inhibitor of neuronal uptake and to assess the ability of neuronal uptake pump on contractile responses in the isolated vasa deferentia from SHRSP and WKY.

Male SHRSP and WKY at 6 months old were used. The isolated vas deferens was divided into three and the medial portion was discarded. The epididymal (EE) and prostatic (PE) ends were suspended in organ baths containing Locke solution, maintained at 30 ŽC and bubbled with a gas mixture of 95 % O2 and 5 % CO2. The preparation was preloaded with 1 g and the change in tension was recorded isometrically. The agonists were exogenously applied and the dose-response curves were stepwise performed in the absence and presence of cocaine.

The order of the mean pD2 values for norepinephrine was: SHRSP EE>WKY EE>SHRSP PE>WKY PE. The maximal tension for norepinephrine was higher in the epididymal end from SHRSP and those were almost the same in the other portions. The order of the mean pD2 values for methoxamine, which is not a substrate for neuronal uptake, was: SHRSP EE>WKY EE>WKY PE>SHRSP PE. The maximal responses for methoxamine were comparable to those obtained by norepinephrine in the epididymal ends from both SHRSP and WKY. While methoxamine in the both prostatic ends produced small contractions.

Cocaine produced shifts to the left of the dose-response curves to norepinephrine without an increase in the maximal response in all the portions. The degree of this supersensitivity was: WKY PE>WKY EE>SHRSP EE>SHRSP PE. In consequence, in the presence of cocaine the order of norepinephrine potency was changed to: SHRSP EE>WKY EE>WKY PE>SHRSP PE.

On the other hand, cocaine produced a shift to the left of the dose-response curve to methoxamine in the epididymal end from SHRSP but had no effect in the other portions. This supersensitivity to methoxamine was blocked by calcium flux inhibitor diltiazem. Cocaine also produced a shift to the left of the dose-response curve for KCl in the presence of alpha-adrenoceptor antagonist prazosin in the epididymal end from SHRSP. Therefore, the increase in sensitivity to norepinephrine in the presence of cocaine in the epididymal end from SHRSP may involve the enhancement of Ca influx across the cell membrane. While those in the other portions are due to blockade of neuronal uptake.

These results suggest that the neuronal uptake ability in the vas deferens from WKY is more efficient than that from SHRSP. However, the difference in the sensitivity and reactivity to norepinephrine between SHRSP and WKY is not entirely responsible for neuronal uptake mechanism, being rather the nature of smooth muscle in each vas deferens. Because, the response to norepinephrine in the presence of cocaine as well as that to methoxamine were greater in SHRSP than in WKY. The regional differences between the epididymal and the prostatic end from both rats are also likely to depend on the postsynaptic nature.