Trials for Evaluating the Central Actions of Drugs using the Locomotor Activity of SHR Increased by a Novel Circumstances utilizing a Mild Audio Stressor. Katsuhiko Sato, Yasuo Watanabe and Takeshi Shibuya. Department of Pharmacology, Tokyo Medical College, Tokyo 160.

In general, animals show hyperactivity when they are kept under new conditions. The hyperactivity may be related to "fear" conditions, and also to anxiety. It has been reported that spontaneously hypertensive rats (SHR) marked the much increase in locomotor activity in the open field when compared to their normotensive controls (Wistar-Kyoto, WKY). And also it has been well-estimated that this difference in activity can not be correlated with a strain difference in blood pressure.

In this investigation, we examined the hyperactivity of SHR and WKY when they were kept under a novel circumstance with an 85-dB buzzing noise, and measured changes in neuronal Ca^{2+} channel activities in stressed SHR after 10 days repeated administration of Ca antagonist and anti-anxiolytics. The spontaneous locomotor activity (SLMA) of SHR and WKY were measured by Digiscan Animal Activity Monitor when each animal was placed in a transparent polycarbonate cage with a 85-dB buzzing noise at 24 hr after the 10th day administration of either vehicle (5 ml/kg, i.p.), nitrendipine (10 mg/kg, i.p.), tandospirone (10 mg/kg, i.p.) or diazepam (10 mg/kg, i.p.). In the vehicle treated group, SHR demonstrated much hyperactivity than age-matched WKY. The changes in $^{45}\text{Ca}^{2+}$ uptake in crude synaptosomal fractions of frontal cortex and hippocampus under stressed and non-stressed conditions in SHR. In the steady state (5 mM KCl), the values for $^{45}\text{Ca}^{2+}$ in the crude synaptosomal fractions of frontal cortex and hippocampus of non-stressed SHR were 4.76 ± 0.38 and 4.25 ± 0.27 nmol/mg protein, respectively. After depolarization by 70 mM KCl, the value for $^{45}\text{Ca}^{2+}$ in each region was 9.34 ± 0.45 and 9.37 ± 0.57 nmol/mg protein, respectively. In the stressed SHR, the values for $^{45}\text{Ca}^{2+}$ uptake under the steady state did not markedly differ from those of non-stressed SHR. However, the values for $^{45}\text{Ca}^{2+}$ uptake enhanced by 70 mM KCl in both brain regions were about 35% greater than those in non-stressed SHR. In the drug treated groups, the hyperactivity of SHR under the novel condition utilizing the audiogenic stress was significantly inhibited and also the enhanced values for $^{45}\text{Ca}^{2+}$ uptake in stressed SHR brain regions was remarkably diminished.

These results suggest that the hyperactivity of SHR under a novel circumstance using a mild audio stressor is due to the changes in the neuronal Ca^{2+} channel activities, and these evidences obtained by using SHR can be utilized to search the pharmacological properties of central acting drugs.