

CARDIOVASCULAR EFFECTS OF TRH I.C.V. IN CONSCIOUS RATS

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INTRODUCTION

In addition to the endocrine effects, the thyrotropin releasing hormone (TRH) is known to induce dose-dependent increases in blood pressure and heart rate after intracerebroventricular (i.c.v.) administration in urethane-anaesthetised rats (1, 2). The aim of the present study was to investigate whether TRH has similar effects in conscious rats of various strains i.e. spontaneously hypertensive rats (SHR), normotensive Wistar-Kyoto (WKY) and Wistar (NR) rats.

MATERIALS AND METHODS

Male rats of three different strains were used. Spontaneously hypertensive rats of Okamoto-Aoki strain (270-330 g, 12-15 weeks of age) and normotensive Wistar-Kyoto rats (270-300 g, 13-16 weeks of age) were purchased from Moellegaards Avlslaboratorier, Denmark. Age-matched Wistar rats (280-400 g) were also used. The rats were accommodated to standard ambient conditions for at least one week before the surgery.

One week before the experiments the rats were anaesthetised with ketamine (30-40 mg/rat i.p.) and xylazine (2 mg/rat i.m.). A polyethylene catheter was introduced into the aorta through the left carotid artery. The catheter was exteriorised at the nape of the neck and sealed until use. The right lateral ventricle of the brain was cannulated with a PE-20 polyethylene cannula. The coordinates were relative to the bregma, L=1.0, AP=-3.0 and from the skull surface V= 6.0mm. After insertion of two stainless steel anchoring screws, dental cement was applied to secure the cannula in place. The intracerebroventricular injections were

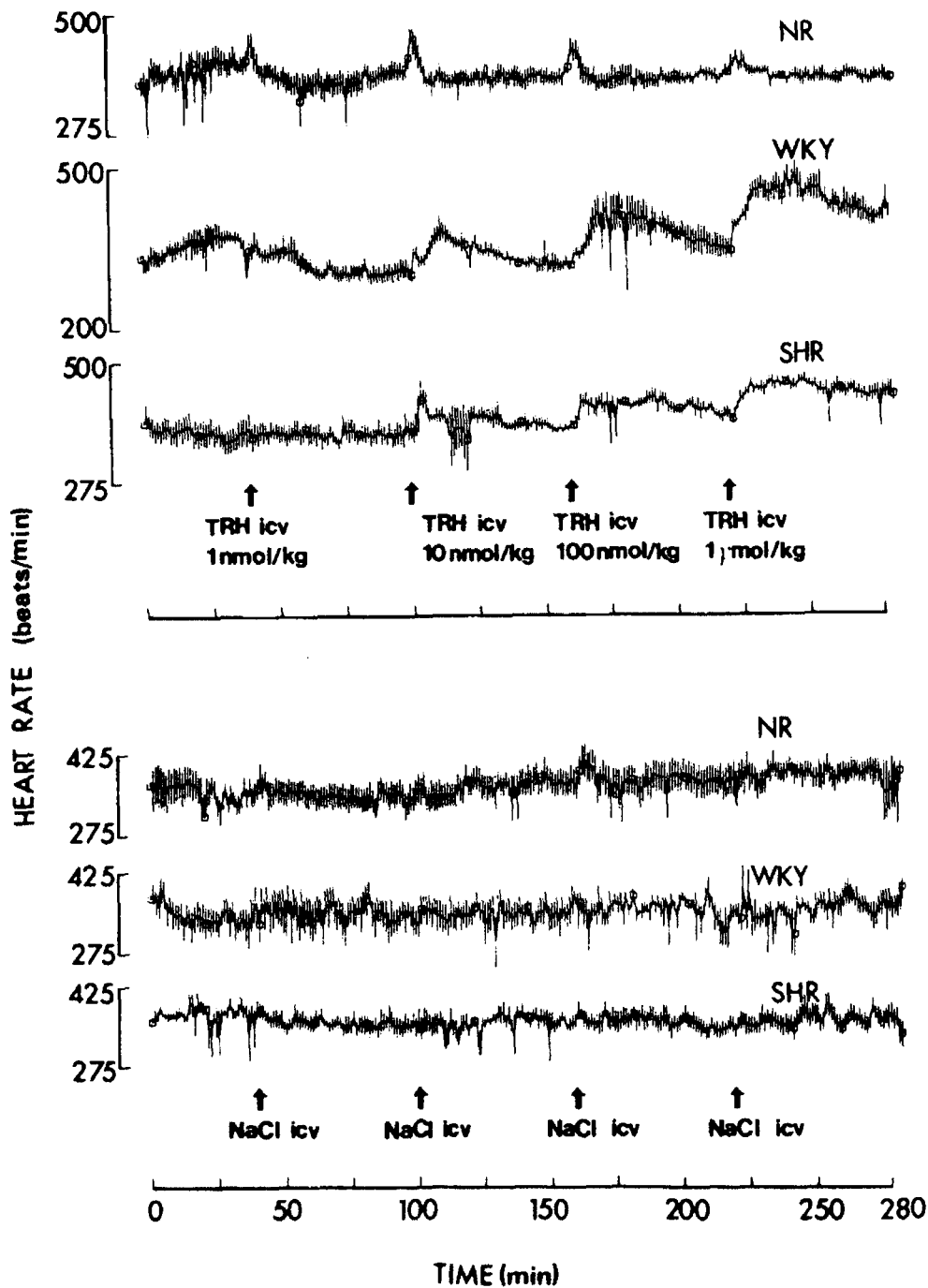


FIGURE 1. Effect of TRH i.c.v. on heart rate in conscious rats. Each graph represents mean \pm SEM. The differences between the groups were significant at the $p < 0.001$ level. As compared to the control group, the TRH-induced tachycardia was significant at the dose of 100 nmol/kg in NR ($p < 0.01$) and at the three highest doses in WKY ($p < 0.05-0.001$) and in SHR ($p < 0.05$). Numbers of rats were: $n=5$ WKY-TRH, $n=6$ NR-TRH, WKY-NaCl, SHR-TRH, $n=7$ NR-NaCl and in SHR-NaCl.

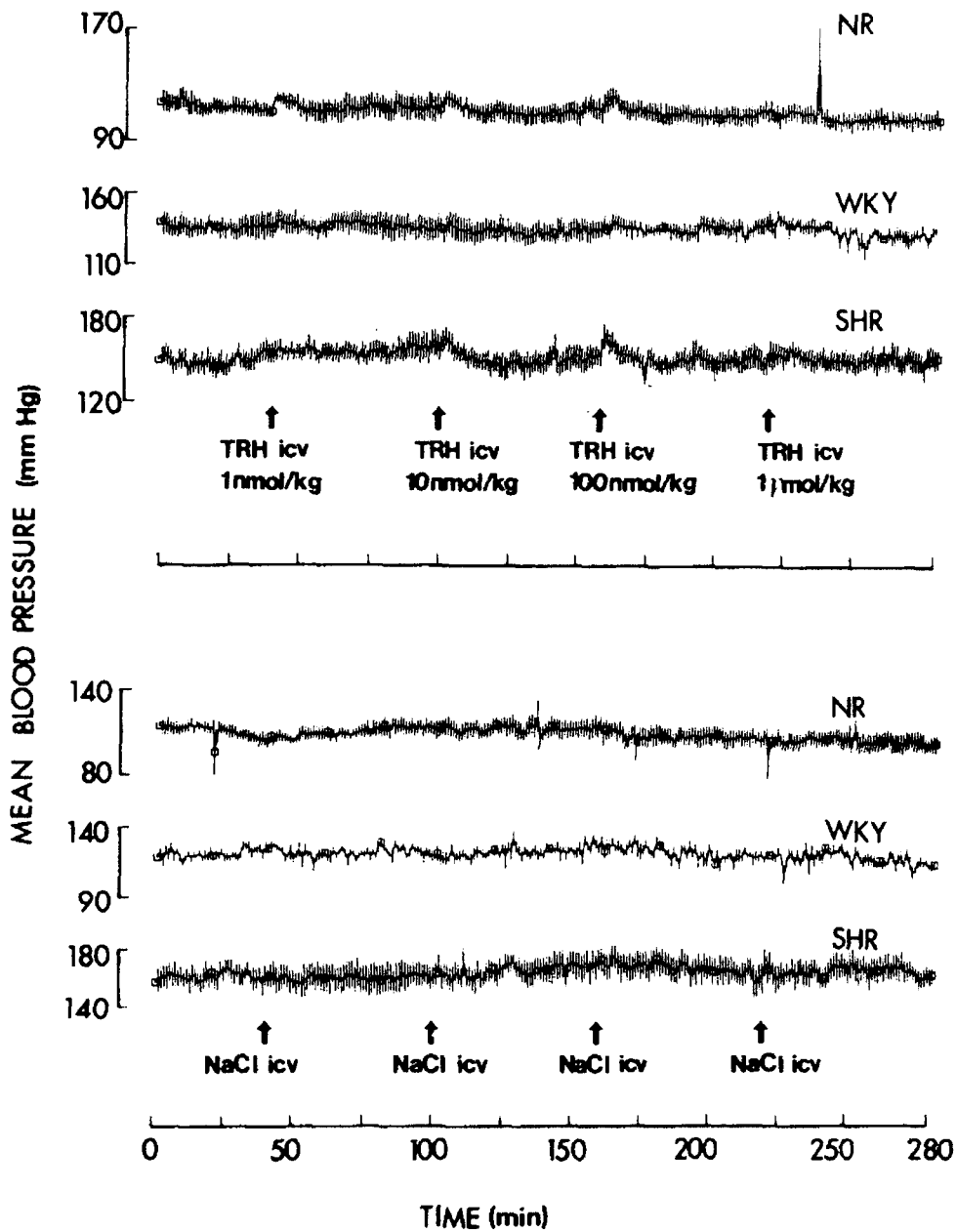


FIGURE 2. Effect of TRH i.c.v. on mean arterial blood pressure in conscious rats. Each graph represents mean \pm SEM. The differences between the groups were not statistically significant. Numbers of rats were: n=5 WKY-TRH, n=6 NR-TRH, WKY-NaCl, SHR-TRH, n=7 NR-NaCl and in SHR-NaCl.

performed by the following way: A 26 ga needle was attached to a PE-50 polyethylene catheter and the whole system was filled with the drug or control solution to be infused. The needle was then adhered to the i.c.v. cannula and the desired amount of the solution (15 microliters) was allowed to flow slowly by virtue of the hydrostatic pressure. The blood pressure and heart rate were continuously monitored while the rats were conscious and unrestrained in plastic cages (26x20x13 cm). The analysis and the follow-up of the experiment were carried out by a laboratory computer (PDP 11/23 Digital Equipment Corp.). For further details on the computerized recording system see Paakkari (3). The proper position of the i.c.v. cannulae was ascertained after each experiment by an injection of dye into the cerebral ventricles.

TRH (Sigma Chemical Co.) was dissolved in saline (0.9% NaCl w/v). Increasing doses of TRH (1-1000 nanomoles/kg) or saline were administered i.c.v. at 60 min intervals.

Analysis of variance with repeated measures followed by the Bonferroni test for multiple comparisons was used for the statistical evaluation of the data.

RESULTS

In conscious unrestrained rats TRH, 1-1000 nanomoles/kg i.c.v., induced tachycardia (FIG 1.). The maximal increase in heart rate was about 140 beats/min in WKY, 80 beats/min in SHR and 60 beats/min in NR. In WKY and SHR TRH induced a long-lasting tachycardic response which reached its maximum in 5-15 min. In NR the TRH-induced increases in heart rate were very brief with a maximum in about 2 min after the infusion.

TRH (1-1000 nanomoles/kg i.c.v.) failed to affect significantly the blood pressure in NR, WKY or SHR (FIG 2.).

DISCUSSION

The i.c.v. administration of increasing doses of TRH induced tachycardia in conscious NR, WKY and SHR. The cardioacceleratory effect of TRH was most prominent in WKY. Only in NR the TRH-induced tachycardia was accompanied by a slight but not dose-dependent increase in blood pressure. In agreement with our results it has been reported recently that an injection of a single dose of 10 micrograms/rat (about 28 nmol/rat) of TRH i.c.v. induced rises of heart rate and blood pressure in conscious Sprague-Dawley rats (2). However, the strong hypertensive response to i.c.v. administered TRH reported in urethane-anaesthetised rats (1, 2) was not observed in the present study. This may be due to the anaesthesia-induced absence of the reflectory counterregulation to the hypertensive effect of TRH. The presence of tachycardia both in anaesthetised and in conscious state suggests that TRH

influences the heart activity via a mechanism, at least partly, different from that mediating its hypertensive response.

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