0014-4754/94/020105-02$1.50 + 0.20 © Birkhäuser Verlag Basel, 1994

Hydrocortisone administration enhances vessel contractility in Koltushi low-, and Koltushi high-avoidance rats

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Received 9 September 1993; accepted 30 September 1993

Abstract. The contractility of tail artery rings was investigated in rats psychogenetically selected for rapid (KHA) and slow (KLA) acquisition of an avoidance response in the shuttle box. The vessel contractility was greater in the KHA rats. Hydrocortisone administration enhanced vessel contractility in both strains.
Key words. Genetics of behavior; corticosteroids; arterial contractility; rat.

Cardiovascular function is strongly influenced by the hypothalamo-pituitary-adrenal axis. Thus, hydrocortisone enhances the contractility of the portal vein in vitro[1]. Cardiovascular reactivity, like other components of the stress response, depends on the genetic background of the animal[2,3]. Roman high-avoidance (RHA) and low-avoidance (RLA) rats have been selectively bred for rapid acquisition of a conditioned avoidance response in a two-way shuttle box (RHA), or the failure to acquire this response (RLA)[4]. Cardiovascular reactivity[5] as well as plasma corticosterone and ACTH levels have been found to differ in RHA and RLA rats[6]. In the present study, we used the Koltushi high-avoidance (KHA) and Koltushi low-avoidance (KLA) rat strains. These strains have been selected according to the same behavioral parameter, i.e. divergent performance in the shuttle box avoidance procedure[7,8]. Thus, KLA rats may be compared to the RLA rats and, similarly, KHA to RHA rats.

The main aim of this study was to extend the exploration of cardiovascular reactivity in these genetic models by investigating blood vessel contractility. Another goal was to determine whether the difference, if any, is due to a different amount of glucocorticoids in blood.

Methods

Male KHA and KLA rats, weighing 180–250 g, and bred at the Pavlov Institute of Physiology, were maintained under standard laboratory conditions and a 12 h light:12 h darkness cycle (lights off at 17.00), with free access to food and water.

Hydrocortisone acetate (Richter, Hungary) at the dose of 50 mg/kg b.wt was administered i.p. in 1 ml of 0.9% NaCl between 9.00 and 10.00 a.m. Subjects were decapitated between 4.00 and 5.00 p.m. on the third day of injection. The number of rats was: KHA non-treated, 7; hydrocortisone-treated, 6; KLA non-treated, 6; hydrocortisone-treated, 5.

A 1 cm long segment of the tail artery was isolated from the base of the tail of each of the subjects. From each segment, a ring about 1.2 mm long was cut and put on 2 tungsten needles (70 μm diam.), one of which was connected to a force transducer, and another to a displacement device. Each ring was placed in a tissue bath, where it was allowed to equilibrate for 30 min. In pilot experiments the maximal response of a ring has been found when the internal circumference is about 600 μm we stretched all rings till this value was obtained. The internal circumference of a ring was calculated according to a formula used by Mulvany and Halpern[9]. The bath was supplied with a continuous flow of fresh Krebs bicarbonate solution at 37 °C and a rate of 5 ml/min. This solution was bubbled with a mixture of 95% oxygen:5% carbon dioxide. Mean distance between the inner edges of the needles was adjusted by a micrometer and determined by means of a microscope using a micrometer eyepiece. To stimulate a ring electrically, an electric impulse (60 V, 3 msec duration) was passed through 2 platinum electrodes. It is known[10] that impulses of such duration stimulate the nerves and not the smooth muscles. Noradrenaline (Serva, Sweden) solution at a concentration of 1 nM was poured into a second bath, heated to 37 °C, and the ring mounted in it. This concentration was chosen because it is within the range found in rats, according to available data[11]. After recording a response, the ring was placed back in the first bath. The order of rings from different groups was randomized. The output of the force transducer was connected to a chart recorder. For the statistical evaluation of data the ANOVAs were determined by Tukey's test. Rats not treated with hydrocortisone were included in the analysis, when a comparison between KHA and KLA rats was carried out.

Results

The results of the experiment are shown in the figure. The active force of the stimulated rings, i.e. the force developed by the artery ring in noradrenaline solution (1 nM), was greater in the KHA rats than in the KLA rats ($F(1,41) = 4.41$, $p = 0.042$) but ANOVA revealed a

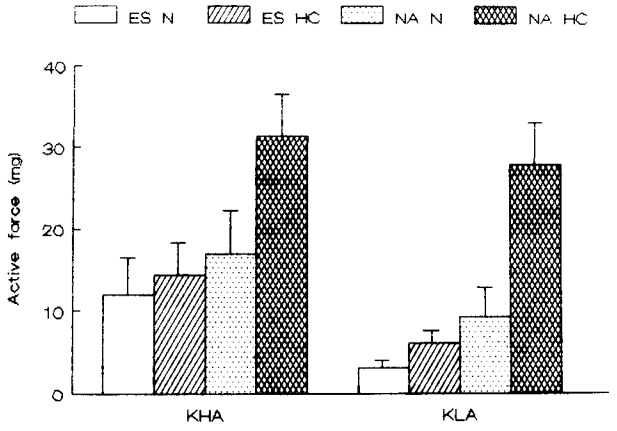

Figure. Active force produced by the tail artery of Koltushi high-avoidance (KHA) and Koltushi low-avoidance (KLA) rats when the rings were stimulated by electric current (open bars: without treatment; hatched bars: hydrocortisone-treated) or 1 nM noradrenaline (dotted bars: without treatment; crosshatched bars: hydrocortisone-treated). Data are means and SE of 5-7 rings.

significant difference between strains only when rings were stimulated by electric current ($F(1,21) = 6.51$, $p = 0.019$), and not by noradrenaline ($F(1,18) = 1.29$, $p = 0.27$). On the other hand, the effect of treatment with hydrocortisone was significant in the groups stimulated by noradrenaline only ($F(1,18) = 9.11$, $p = 0.0074$), but not by electric current ($F(1,21) = 2.17$, $p = 0.16$), and this was in accordance with an interaction revealed between treatment and mode of stimulation ($F(2,39) = 5.83$, $p = 0.02$).

Discussion

The present results show that, in general, the vessels of the KHA rats are more reactive than those of the KLA strain. It may be that the hormonal status of the rats causes this difference. The effects of various hormones, for instance hydrocortisone, on a vessel's reaction to vasoconstrictors are well known[12,13]. It is still unclear whether the effect found in the present study is solely due to exogenous hydrocortisone, as suppression of endogenous corticosterone production following such treatment has been shown[14].

In the present experiments the vessel rings of hydrocortisone-treated rats showed a greater response to noradrenaline in rats of both strains. Nevertheless, the difference between strains in this response was insignificant ($p = 0.27$). The main cause of the difference was a higher reactivity of vessels from KHA rats to electric stimulation. If, as suggested above, this was not due to a difference in hormonal status, then it may be explained by greater excitability of the nervous system of the KHA rats, perhaps due to the number of nervous fibers or amount/activity of transmitter released. The influence of hormones cannot be excluded in this case, but the latter possibility is more likely to be the main cause of greater vessel responses of the KHA rats. This suggestion is supported by the proven existence of a sympathetic hyperreactivity in rats with high levels of behavioural activity[15]. According to several studies[9,16,17], vessels of hypertensive rats have greater contractility in comparison with normotensive ones. Taking this into account, it may be reasoned that KHA rats are more susceptible to hypertension development than rats of the KLA line. This suggestion is supported by the marginally higher blood pressure found in RHA as compared to RLA rats[18].

In conclusion, the present study has demonstrated strain differences in vessel contractility between KHA and KLA rats, i.e. animals selectively bred for behavioral differences. Vessels from the KHA rats show a greater response to electrostimulation than vessels from the KLA rats, and this is not connected to differences in hydrocortisone levels in the blood. These findings lend further support to the linkage of genetically-determined behavioral and physiological characteristics[3].

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