Supraspinal Origin of Abnormal Hindquarter Vasoconstrictor Tone in Spontaneously Hypertensive Rats

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Iriuchijima, J. Supraspinal Origin of Abnormal Hindquarter Vasoconstrictor Tone in Spontaneously Hypertensive Rats. Tohoku J. Exp. Med., 1992, 167 (2), 115-119 — The object of this study was to determine whether the abnormal hindquarter tone in spontaneously hypertensive rats (SHR) is of spinal origin or not. SHR were implanted with a catheter in the left common carotid and an electromagnetic flow probe around the terminal aorta. About three days after implantation, the spinal cord was transected at Th 1 under ether anesthesia. One hour later, when the rat restored consciousness and the arterial pressure recovered partially to a new plateau level which was significantly higher than that in similarly treated normal rats, ganglionic blockade with hexamethonium did not significantly decrease hindquarter (terminal aortic) resistance, calculated as arterial pressure divided by hindquarter flow. It was concluded that there was no appreciable sympathetic vasoconstrictor tone in the hindquarters of SHR after spinal transection and that the origin of the abnormal tone was at the supraspinal level.

The important role played by the sympathetic nerves in spontaneously hypertensive rats (SHR), (Okamoto and Aoki 1963) was first reported by Okamoto et al. (1967) and later confirmed (Iriuchijima 1973; Judy et al. 1976). However, these studies were for the most part on anesthetised rats with blood pressure as the main hemodynamic variable observed.

Recently, we have been studying regional sympathetic vasoconstrictor tone in resistance vessels in normal and hypertensive rats in the conscious state (Iriuchijima 1985, Iriuchijima and Sakata 1985). Our criterion for the presence of tone is whether or not peripheral resistance is significantly decreased on ganglionic blockade with hexamethonium bromide (C6) (25 mg/kg, i.v.). Peripheral resistance is calculated by dividing mean arterial pressure by mean regional blood flow. Arterial pressure is recorded with an indwelling catheter and blood flow with an implanted electromagnetic flow probe.

According to the criterion stated above, in normal Wistar rats, the tone was present in the carotid and renal areas but not in the superior mesenteric and...
hindquarter (terminal aortic) areas (Iriuchijima and Sakata 1985). However, in all kinds of hypertensive rats so far tested, an additional or abnormal tone was found in the hindquarter area (Iriuchijima 1985, 1988).

The tone present in the carotid and renal areas in normal rats seems to be spinal in origin because it was still present after high spinal transection (Iriuchijima 1990). The present study was undertaken whether the abnormal tone in the hindquarters in SHR similarly survives spinal transection. The observed results pointed to the converse, its supraspinal origin.

METHODS

Implantation of flow probes and catheters

In 5 male SHR 19±2 (mean ± s.d.) weeks of age weighing 290±28 g, an electromagnetic flow probe type FC, with an internal diameter of 1.5 or 2 mm (Nikon Kohden, Tokyo) was implanted around the terminal aorta under anesthesia with thiamylal sodium (50 mg/kg, i.p.). The technical details are described elsewhere (Kawaue and Iriuchijima 1984). A polyethylene catheter for arterial pressure measurement was inserted into the right common carotid artery. Another catheter for injection of drugs was inserted into the right external jugular vein.

Spinal cord transection

After implantation, the rat was kept separately in a polyethylene cage containing wood chips. Three or 4 days later, flow and pressure were measured in the conscious, resting state in the home cage and then the rat was anesthetised with ether. In the rat, placed on the abdomen, a midline skin incision was made in the dorsal neck. The spinous process of the vertebra prominens (2nd dorsal in the rat) was cut and removed. Through the space thus formed the spinal cord was transected above the vertebra prominens with an ophthalmological scalpel under visual control.

A local anesthetic xylocaine jelly was applied to the wound made for transection and the skin was sutured. The ether was removed, the rat was released and returned to the home cage. Throughout these procedures and thereafter, flow and pressure were being recorded continuously.

Ganglionic blockade

One hour after transection, when the rat restored consciousness and the arterial pressure recovered partially and reached a new plateau level (Iriuchijima and Numao 1977), C6 (2.5% solution) was infused at a rate of 0.8 mg/min for a total dose of 25 mg/kg.

Statistical treatment

The paired t-test was used to determine the significance of change of a variable on spinal transection and on subsequent ganglionic blockade.

RESULTS

Fig. 1 shows one example of simultaneous recording of arterial pressure and hindquarter blood flow in a spontaneously hypertensive rat, whose spinal cord had been transected at Th 1 one hour before, when C6 was infused for the underlined period. Pressure and flow decreased similarly, with hindquarter resistance, calculated as arterial pressure divided by hindquarter flow, remaining almost un-
In Fig. 2 are presented the mean ± s.e. of arterial pressure, hindquarter flow and hindquarter resistance from the 5 SHR in the intact resting state, one hour after spinal transection and after subsequent ganglionic blockade. By the paired t-test, the decrease in hindquarter resistance after spinal transection was significant at \( p < 0.05 \) but that after C6 was not significant.

**DISCUSSION**

After spinal transection, ganglionic blockade with C6 did not significantly decrease hindquarter resistance in SHR (Figs. 1 and 2). This was entirely different from what was observed in intact SHR, in which the resistance decreased significantly on blockade (Iriuchijima 1985, 1988), and similar to what was observed in intact or acute spinal normal rats (Iriuchijima 1990). These findings indicate that the abnormal hindquarter tone in SHR originates at the supraspinal level. Although spinal transection was performed at Th 1 and not between the brain and the spinal cord, it is unlikely that the origin of the tone is present in the part of the spinal cord left above transection, i.e., the cervical cord.

Previously, we concluded the presence of abnormal sympathetic vasoconstrictor tone in the hindquarters of SHR from the experimental fact that ganglionic blockade decreased hindquarter resistance significantly in SHR, but not in normal rats (Iriuchijima 1985, 1988). One objection to this would be the possibility of the presence of an abnormal autoregulatory function in the hindquarters in SHR, instead of an abnormal sympathetic tone. The decrease in hindquarter resistance, which was observed when arterial pressure decreased on ganglionic blockade, might be accounted for by either mechanism. However, if autoregulation were the case, hindquarter resistance should have decreased on ganglionic blockade even after spinal transection. This is against what was actually observed in the present study. In other words, the present study denied autoregulation.
One might argue that, one hour after spinal transection, the spinal tone generator, if there were such a thing for the abnormal hindquarter tone in SHR, would not have recovered from spinal shock. However, arterial pressure in SHR one hour after spinal transection was already significantly higher than in normal rats similarly treated (Iriuchijima and Numao 1977). Furthermore, in the carotid and renal areas of normal rats, sizable spinal tone was present already one hour after transection (Iriuchijima 1990).

In summary, hindquarter resistance in SHR was not decreased by ganglionic blockade after spinal transection, indicating a supraspinal origin of the abnormal hindquarter tone in them.

**Fig. 2.** Arterial pressure (AP), hindquarter flow (HF) and hindquarter resistance (HR) from 5 SHR before and one hour after spinal transection (CS) and after subsequent ganglionic blockade with hexamethonium bromide (C6). Data are mean ± S.E. *Significantly different from the preceding value by the paired t-test at p < 0.05; **p < 0.025; ***p < 0.01; n.s., not significant. The insignificant change in HR on ganglionic blockade indicates that there was no appreciable sympathetic tone in resistance vessels in the hindquarters after transection.
Hindquarter Tone in Hypertensive Rats

References