Vascular release of catecholamines

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Quantification of the catecholamines in blood is important as a diagnostic procedure and for assessing drug action in both man and animals. It is assumed that there is a relationship between circulating catecholamines and those prevailing in sympathetically innervated tissues. While there is support for this assumption the precise origin of circulating catecholamines has only recently been the subject of investigation. In rats, there is a marked increase in the concentrations of circulating catecholamines (CA) at the time of decapitation (Popper et al 1977; Berkowitz & Head 1978). The origin of the released CAs is thought to be predominately the adrenal glands, a conclusion based on the fact that there is a marked elevation in adrenaline (Ad) concentrations in plasma at the time of decapitation (Berkowitz & Head 1978). The extent to which CAs of extra-adrenal origin contribute to the decapitation-evoked discharge of CAs is not known and the effects of decapitation on the concentrations of NA prevailing in sympathetically innervated tissues have not been determined. We have sought evidence for an extra-adrenal origin of CAs released by decapitation and examined the effects of the procedure on the CA contents of the rat vasculature.

Eight Sprague-Dawley adrenalectomized rats (Zivic Miller Frams, Frederick, Md.), 286 ± 7·2 g, and eight age-matched sham operated controls rats 424 ± 12 g, were used in the first series of experiments. Adrenalectomized rats were housed in cages supplied with tap water and a solution of 0·1% (w/v) NaCl. Rats were decapitated and the blood collected in two fractions from the trunk of the animals in exactly the same manner as described by Berkowitz & Head (1978). The CA content of plasma samples was determined by a modification of the radioenzymatic assay for CAs described by Da Prada & Zürcher (1976). In a second series of experiments segments of vascular tissue were removed from decapitated rats and anaesthetized decapitated rats. Twelve Sprague Dawley rats (Charles River, Wilmington, Mass.), 427 ± 21 g were decapitated and the mesenteric vasculature and heart removed. A further 12 rats, 411 ± 2 g, were anaesthetized with sodium pentobarbitone (50 mg kg^{-1}, i.p.) and then decapitated 15 min later, and the mesenteric vasculature and heart removed. Tissues were washed briefly in ice-chilled saline, blotted on filter paper, weighed and homogenized in perchloric acid (0·4 M) using an all glass homogenizer. The concentrations of CAs in the perchloric acid extracts were determined by the radioenzymatic procedure of Da Prada & Zürcher (1976).

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The results of the experiments in which the changes in CA concentration in plasma accompanying decapitation were determined are summarized in Fig. 1. Decapitation resulted in an increase in the concentrations of Ad and NA in the second fractions of blood from sham operated control rats. The same procedure produced a modest but significant increase in NA in blood from adrenalectomized rats. The failure to detect significant amounts of Ad in adrenalectomized rats confirmed the effectiveness of adrenalectomy. The increase in NA contents of blood in the second fraction of blood collected from adrenalectomized decapitated rats indicates that this release occurred at sites other than the adrenal gland.

The possibility that NA of vascular origin may have contributed to this increase was strongly suspected in view of evidence from this laboratory which suggested that vascular tissue may be a significant source of circulating and urinary NA (Berkowitz & Spector 1976).

To determine whether the discharge of extra-adrenal NA was associated with an alteration in the NA contents of the vasculature, the CA concentrations in the mesenteric artery, mesenteric vein and heart from anaesthetized and non-anaesthetized decapitated rats were measured. Rats were anaesthetized with

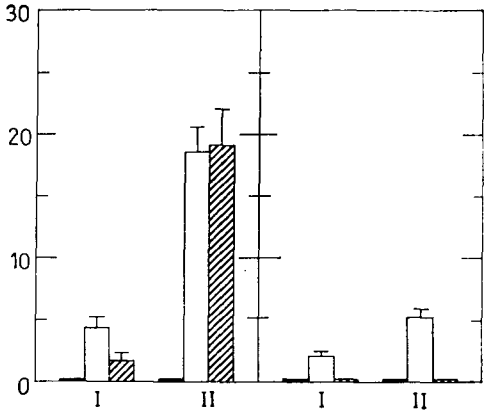

FIG. 1. Changes in circulating concentrations of dopamine (solid columns) noradrenaline (open columns) and adrenaline (hatched columns) (ng ml^{-1}) accompanying decapitation of adrenalectomized rats (right-hand panel) and sham operated control rats (left-hand panel). Shown are the mean catecholamine contents in plasma obtained from the first 1·0 ml (I) and a subsequent 5·0 ml (II) sample of blood collected from the trunk of decapitated adrenalectomized rats (n = 8) and sham operated control rats (n = 8). Vertical lines show the s.e. of the means. Ordinate: concentration of plasma catecholamines (ng ml^{-1}).

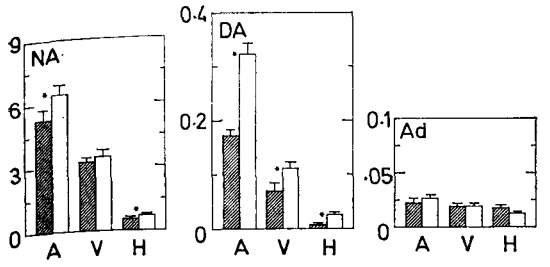

FIG. 2. The effects of pentobarbitone anaesthesia on the noradrenaline (NA), dopamine (DA) and adrenaline (Ad) contents ($\mu g\ g^{-1}$) of the rat mesenteric artery (A), vein (V) and heart (H), removed from decapitated rats. Shown are the mean catecholamine contents of tissues from 12 decapitated rats (hatched columns) and 12 anaesthetized decapitated rats (open columns). The vertical lines show the s.e. of the means and * denotes a significant difference ($P<0.05$, Student's unpaired t-test) between observations. Ordinates: $\mu g\ g^{-1}$.

pentobarbitone before decapitation. The results of these experiments are summarized in Fig. 2 where it can be seen that the NA and dopamine (DA) contents of the vasculature in anaesthetized decapitated rats are greater than in those rats decapitated without anaesthesia. In view of evidence that pentobarbitone anaesthesia in the rat depresses sympathetic neuronal discharge of CAs (Roizen et al 1978), our results are interpreted as reflecting a decapitation-evoked discharge of NA from the sympathetic nerve endings in the vasculature in the non-anaesthetized rat. This conclusion is entirely consistent with the extra-adrenal origin of part of the decapitation-evoked release of NA into plasma demonstrated in the preceding experiments and entirely in accord with the findings of Berkowitz & Spector (1976) suggesting that CAs of vascular origin may contribute to the circulating concentrations of CAs in the rat.

The marked decreases in the DA contents of the vasculature accompanying decapitation may reflect either release of DA from CA-containing storage sites in the tissues or a rapid depletion of neuronal cytoplasmic DA as a result of a rapid conversion of DA to NA accompanying sympathetic neuronal discharge of NA. Although a decapitation-evoked increase in DA concentrations in blood from decapitated adrenalectomized rats was not observed, in consideration of the extremely small concentrations of DA in blood from rats, both of the above explanations should be considered. The failure to see a difference in Ad concentrations in vasculature from anaesthetized and non-anaesthetized decapitated rats suggests that the small Ad contents in the vasculature are not directly influenced by the sympathetic neuronal response to decapitation.

In summary it is concluded that the changes in CA disposition accompanying decapitation are not due selectively to an adrenal medullary release of CAs but include a discharge of CAs from extra-adrenal tissue sites including the vasculature. The significance of these findings is twofold. Firstly, the proportion of NA of extra-adrenal origin in blood collected from decapitated rats is much smaller than that of adrenal origin and furthermore these small amounts of extra-adrenal NA reflect the activity of the sympathetic nervous system in a response to decapitation. Thus it is extremely unlikely that basal values of NA released from the sympathetic nervous system can be determined in blood collected after decapitation. Secondly, it is very probable that sympathetically innervated tissues removed from decapitated rats have undergone a considerable sympathetic neuronal discharge before their removal from the animal. The latter aspect may be of importance in experiments in which the action of pharmacological agents or the effects of disease on the concentration of CAs prevailing in sympathetically innervated tissues are determined.

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