Effect of baroreceptor deafferentation on central catecholamines in the rat

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Summary
1. Sinoaortic deafferentation in the rat leads to increased blood pressure and heart rate.
2. Early increases in tyrosine hydroxylase activity both in brain stem and hypothalamus suggest that increased noradrenaline synthesis may contribute to the development of neurogenic hypertension.
3. After 4 weeks, phenylethanolamine-N-methyltransferase activity was reduced in the hypothalamus.
4. Noradrenaline- and adrenaline, but not dopamine-containing neurones may participate in regulation of sympathetic efferent activity.

Key words: baroreceptors, blood pressure, brain catecholamines.

Abbreviation: PNMT, phenylethanolamine-N-methyltransferase.

Introduction
Deafferentation of the carotid sinus and aortic arch baroreceptors removes a major inhibitory input to the central nervous system. This results in an increase in peripheral sympathetic activity, often manifested by a rise in blood pressure and heart rate (neurogenic hypertension). Previous studies have demonstrated central catecholaminergic involvement in arterial baroreceptor reflexes and neurogenic hypertension either directly or as modulators (Chalmers & Wurtman, 1971; Chalmers & Reid, 1972; Haeusler & Lewis, 1975; Reis, Doba, Snyder & Nathan, 1977) but they do not permit a distinction between the role of different catecholamines. In this study, a microdissection technique together with sensitive radiometric assays have been used to investigate the changes in adrenaline, noradrenaline and dopamine in brain areas after baroreceptor denervation in the rat.

Method
Male Wistar rats weighing 200–250 g were anaesthetized with chloral hydrate and lignocaine was infiltrated subcutaneously in the midline of the neck. The carotid sinus and aortic arch baroreceptors were denervated bilaterally through a midline incision by a procedure based on the technique of Kreiger (1964). Sham operations, carried out in litter mates, involved the same procedure for general and local anaesthesia but, after exposing the neurovascular sheath on both sides of the neck, no attempt was made to dissect out the carotid bifurcation or any of the baroreceptor afferents.

Systolic blood pressure was measured at various intervals in the 28 days after operation by tail plethysmography (Narco Biosystems, Houston, Texas). Heart rate was obtained by counting from the arterial pressure record.

Groups of eight rats were killed by decapitation 7 and 28 days after operation and the brains rapidly removed and dissected over ice. The hypothalamus was divided into anterior and posterior regions. The hind brain was frozen with solid carbon dioxide, from which brain-stem nuclei and portions of cerebellar cortex were removed from 300 μm-thick frozen sections (Palkovits, 1973). The noradrenaline (Petty & Reid, 1977), adrenaline and dopamine concentrations (Da Prada & Zürcher, 1976), tyrosine hydroxylase and phenylethanolamine-N-methyltransferase activities (Petty
Results

Systolic blood pressure increased significantly in the denervated animals from 149 mmHg at 2 days to 169 mmHg at 28 days, compared with 122 mmHg before operation. The increase in pressure was maintained unabated at the end of the 28 day period. Heart rate was also significantly increased in these animals, being 453 beats/min at 7 days compared with 385 beats/min in the sham-operated rats. Twenty-eight days after operation these values were 432 and 364 beats/min respectively.

In the sham-operated group noradrenalin concentrations ranged from 2.8 ng/mg of protein in cerebellar cortex to 23.3 ng/mg of protein in locus coeruleus. Seven days after operation the concentration was significantly elevated in the lateral reticular nucleus, parahypoglossal nucleus and cerebellar cortex of the denervated animals (158, 167 and 171% of control respectively). In both the anterior and posterior hypothalamus values were significantly reduced to 65% and 72% of control respectively. At 28 days after operation these differences were no longer evident.

Seven days after operation no change was apparent in either adrenaline or dopamine concentration, although at 28 days the adrenaline concentration of the anterior hypothalamus was raised to 247% of that of sham-operated rats. In order to relate changes in endogenous catecholamines to neuronal activity, the activity of the synthetic enzymes was measured. Table 1 shows the activity of both tyrosine hydroxylase and phenylethanolamine-N-methyltransferase (PNMT) in sham-operated and denervated animals. An elevation in the former activity occurred 7 days after operation; this was no longer evident at 28 days. Conversely, PNMT activity was reduced in the posterior hypothalamus at 7 days and at 28 days in both the anterior and posterior hypothalamus.

Discussion

Systolic blood pressure and heart rate measured indirectly by the tail-cuff method in conscious rats was significantly elevated after denervation of the carotid sinus and aortic arch.

In the present experiment tyrosine hydroxylase activity appears to reflect changes in noradrenergic neurones, since the changes both in noradrenaline concentration and activity of the enzyme were only evident 7 days after operation. The direction of change in these central noradrenergic neurones would support an increase in synthesis of noradrenaline and thus an increase in turnover, which may be involved in the initiation of the neurogenic hypertension.

Central adrenergic neurones appear to play a more important role in the long-term response to baroreceptor denervation. The time course of changes in PNMT activity is slower and delayed, suggesting that central adrenergic neurones may have a role in the maintenance of experimental hypertension.

Changes in adrenaline formation, as assessed by PNMT activity, have been previously reported in established doca/salt hypertensive rats (Saavedra, Grobecker & Axelrod, 1976), renovascular hypertensive rats (Petty & Reid, 1979) and also during the development of spontaneous hypertension in the rat (Saavedra, Grobecker & Axelrod, 1977; Nakamura & Nakamura, 1978). In all these cases PNMT activity was increased, particularly in brain-stem areas. After baroreceptor denervation in the present series of experiments

Table 1. Tyrosine hydroxylase (after 7 days) and phenylethanolamine-N-methyltransferase (after 4 weeks) in rat-brain areas

<table>
<thead>
<tr>
<th>Area</th>
<th>Tyrosine hydroxylase activity (nmol h$^{-1}$ mg$^{-1}$ of protein)</th>
<th>Phenylethanolamine-N-methyltransferase activity (pmol h$^{-1}$ mg$^{-1}$ of protein)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Sham-operated</td>
<td>Denervated</td>
</tr>
<tr>
<td>Lateral reticular nucleus</td>
<td>21.37 ± 3.39</td>
<td>28.35 ± 3.84</td>
</tr>
<tr>
<td>Parahypoglossal nucleus</td>
<td>12.23 ± 2.12</td>
<td>31.03 ± 4.21**</td>
</tr>
<tr>
<td>Locus coeruleus</td>
<td>87.05 ± 19.59</td>
<td>165.97 ± 16.48**</td>
</tr>
<tr>
<td>Cerebellar cortex</td>
<td>8.43 ± 2.31</td>
<td>14.1 ± 2.17</td>
</tr>
<tr>
<td>Anterior hypothalamus</td>
<td>18.98 ± 3.53</td>
<td>20.67 ± 4.18</td>
</tr>
<tr>
<td>Posterior hypothalamus</td>
<td>6.56 ± 1.42</td>
<td>14.78 ± 2.76*</td>
</tr>
</tbody>
</table>
Baroreceptor denervation and brain catecholamines

PNMT activity was decreased. This change may reflect the marked difference in baroreceptor afferent input after denervation compared with other models of experimental hypertension.

The early changes in tyrosine hydroxylase were also in the opposite direction to those reported at early times during the development of renovascular hypertension (Petty & Reid, 1979), which makes it possible that early changes in the latter are a secondary result of baroreceptor activation.

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References


