Variability in neurosecretory material and responses to reserpine of the pituitary neural lobe in five strains of rat

Brian A. Edwards

Department of Biology, The University of Stirling, Stirling, FK9 4LA, Scotland

Abstract. The levels of vasopressin and neurophysin in the neural lobe of the pituitary were measured in five strains of rat: Wistar, Sprague-Dawley, PVG, Chester Beatty and DA strains. The effect of reserpine administration (5 mg/kg body weight) was determined. There were significant differences in the weight of the neural lobe and the vasopressin and neurophysin contents of this tissue in the various strains. It was possible to show that weight of the neural lobe was not necessarily related to hormone content. The effects of reserpine also varied within the species for, while there was a fall in the vasopressin content in the Wistar and Chester Beatty strains, no change was observed in the Sprague-Dawley, PVG and DA strains. The fall in the vasopressin level in the Wistar animals was not accompanied by a simultaneous fall in the vasopressin-neurophysin content.

The role of noradrenaline in the central control of neurohypophysial hormone release is by no means clearly defined (for reviews see Cross & Dyball 1974; Forsling 1976). The drug reserpine acts by depleting neuronal monoamine transmitter substances (see recent review by Shore & Giachetti 1978) and has therefore been used to study the possible role of noradrenaline in neurohypophysial hormone release.

However, the effects of reserpine have been rather variable. Bridges & Thorn (1970) and Kulshreshta & Dominic (1971) have shown that reserpine inhibited the release of vasopressin and neurosecretory material respectively while an increase in hormone secretion after administration of the drug was shown by Chaudhury et al. (1962), Guzek & Lešnik (1968) and Rechardt & Hervonen (1975). Meanwhile, Dyball (1968) and Guzek et al. (1976) have reported that reserpine had little or no effect on vasopressin release.

Not only have various species been used so far in these studies (rat, guinea pig and musk shrew) but also various strains within one species (Wistar, Sprague-Dawley and unnamed strains of rat).

The effect of reserpine on neurohypophysial hormone levels was therefore investigated simultaneously in a number of strains of rat to see if some of the conflicting reports could be explained.

Materials and Methods

Animals

Five strains of young adult rats (2–3 months old) were used: (a) 52 female Wistar albino rats obtained originally in 1975 from OLAC Ltd., Bicester and weighing 189–301 g; (b) 31 female and 5 male Piebald Virol Glaxo (PVG) hooded rats obtained from Bantin & Kingman Ltd., Aldbrough and weighing 151–228 g; (c) 16 male and 8 female DA agouti rats obtained originally from Professor W. L. Ford, University of Manchester and weighing 166–214 g; (d) 12 female hooded rats obtained originally from the Chester Beatty Research Institute, London and weighing 188–231 g; (e) 7 female and 6 male Sprague-Dawley albino rats obtained from Bantin & Kingman Ltd., Aldbrough and weighing 242–294 g.

All animals were kept at a temperature of 22 ± 2°C with 10 h light per day. Food and water were supplied ad libitum. Animals were killed by cervical dislocation.

Injection of reserpine

Animals were injected ip between 11.00 and 14.00 h once only with 5.0 mg reserpine/kg body weight. The reser-
pine solution was freshly prepared each week by the method of Leyden et al. (1956). Control experiments were carried out by injecting five Wistar rats with the reserpine solvent (vehicle) alone.

Vasopressin and neurophysin content of the pituitary neural lobe

Vasopressin levels were estimated in all five strains of rat by the method of Dekanski (1952) after extraction overnight at 4°C in 0.25% acetic acid. The neurophysin content was measured by polyacrylamide gel electrophoresis in three of the strains using a method similar to Sunde & Sokol (1975) and described in detail by Edwards (1978a).

Results

1. Comparison of control animals of the various strains

Female animals were mainly used in this study. There appeared to be no obvious differences between the two sexes in the vasopressin and neurophysin levels in the neural lobes.

The weight of the neural lobe of each strain of rat is shown in Table 1. The Sprague-Dawley strain had the heaviest neural lobe being significantly greater than that of the Wistar (P<0.01) and DA (P<0.01) strains. The neural lobe of the Chester Beatty strain was also significantly heavier than that of the DA strain (P<0.05).

The control levels of vasopressin in the five strains of rat are also shown in Table 1. The Chester Beatty strain had the largest amount of vasopressin (when expressed as mU/100 g body weight) and this was significantly greater than the levels in the PVG (P<0.01), Sprague-Dawley (P<0.001) and Wistar (P<0.001) strains. The DA strain had the second highest vasopressin level, being significantly higher than the Sprague-Dawley (P<0.02) and Wistar (P<0.01) strains. The differences between the strains were substantially the same when the results were expressed as mU/gland or mU/mg wet neural lobe tissue.

The level of neurophysin A (vasopressin-neurophysin) in the Wistar and PVG strains was significantly higher than that of the DA strain (P<0.02, P<0.001 respectively). The content of neurophysin B (oxytocin-neurophysin) was higher in the PVG animals than in the Wistar and DA strains (P<0.05, P<0.01 respectively). Neurophysin C was present in greater amounts in the

<table>
<thead>
<tr>
<th>Strain</th>
<th>Weight of neural lobe (mg/100 g body weight)</th>
<th>Neural lobe vasopressin content</th>
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<tbody>
<tr>
<td></td>
<td></td>
<td>Control</td>
</tr>
<tr>
<td></td>
<td></td>
<td>mU/gland</td>
</tr>
<tr>
<td></td>
<td></td>
<td>mU/gland</td>
</tr>
<tr>
<td>Wistar</td>
<td>0.483 ± 0.025 (6)</td>
<td>513.9 ± 44.4 (6)</td>
</tr>
<tr>
<td>Sprague-Dawley</td>
<td>0.617 ± 0.032 (7)</td>
<td>620.6 ± 54.5 (7)</td>
</tr>
<tr>
<td>Chester Beatty</td>
<td>0.542 ± 0.014 (6)</td>
<td>705.0 ± 23.2 (6)</td>
</tr>
<tr>
<td>PVG</td>
<td>0.569 ± 0.039 (6)</td>
<td>468.8 ± 30.7 (6)</td>
</tr>
<tr>
<td>DA</td>
<td>0.463 ± 0.026 (6)</td>
<td>582.0 ± 31.4 (6)</td>
</tr>
</tbody>
</table>

Reserpine-treated animals were given 5 mg reserpine/kg body weight by ip injection. Results are shown as mean ± sem. Number of animals given in parentheses.
Table 2.
The neural lobe neurophysin A, B & C content in three strains of control and reserpine-treated rats.

<table>
<thead>
<tr>
<th>Control</th>
<th>Wistar strain</th>
<th></th>
<th>PVG strain</th>
<th></th>
<th>DA strain</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>A</td>
<td>B</td>
<td>C</td>
<td>A</td>
<td>B</td>
<td>C</td>
</tr>
<tr>
<td>Control</td>
<td>25.4±1.9</td>
<td>14.6±1.3</td>
<td>13.7±1.1</td>
<td>30.9±1.7</td>
<td>21.2±2.1</td>
<td>16.2±2.0</td>
</tr>
<tr>
<td>24 h after reserpine</td>
<td>24.0±2.4</td>
<td>12.2±1.1</td>
<td>12.9±1.1</td>
<td>39.3±2.2</td>
<td>23.2±2.1</td>
<td>20.9±1.6</td>
</tr>
</tbody>
</table>

Neurophysin levels are expressed in arbitrary units/100 g initial body weight. 50 arbitrary units are equivalent to 3.9 μg bovine serum albumin fraction V (Sigma London, Poole). Results are given as mean ± SEM with number of animals in parentheses. Reserpine-treated animals received 5 mg reserpine/kg body weight.

Wistar and PVG strains when compared to the DA strain (both P<0.02) (Table 2).

The ratio of the control levels of vasopressin: neurophysin A in the neural lobe was also calculated in three of the strains by random association of the vasopressin content (in mU/100 g body weight) of six animals with the neurophysin A content (in arbitrary units/100 g body weight) of six different animals of the same strain. The ratios for the Wistar (8.75 ± 0.77, n = 6) and PVG (8.28 ± 0.79, n = 6) strains were not significantly different but they were both smaller than that of the DA strain (18.26±2.03 mU/arbitrary unit, n = 6) (both P<0.01).

2. The effects of reserpine on:

(a) Vasopressin content of the neural lobe

There was a significant fall in the vasopressin content of the Wistar (P<0.01) and Chester Beatty (P<0.05) strains 24 h after reserpine injection (Table 1) but no change was observed in the PVG, Sprague-Dawley and DA strains (results expressed in terms of body weight). In the Wistar strain the decrease was not shown 12 or 48 h after injection, nor after the injection of the vehicle alone (results not shown).

When the vasopressin results were expressed as mU/gland a significant fall was found in the Chester Beatty strain from 705.0±23.2 to 582.6±22.2 (P<0.01) while a significant rise from 468.8±30.7 to 576.6±33.6 was found in the PVG strain (P<0.05). No significant changes occurred in the Wistar, Sprague-Dawley and DA strains.

The only significant change found when the results were expressed as mU/mg wet neural lobe tissue was the fall from 624.2±29.5 to 512.2±15.2 in the Chester Beatty strain after reserpine injection (P<0.01). No changes were observed in the other four strains.

The vasopressin levels which did not alter when expressed per gland or fresh neural lobe weight have been omitted for brevity.

(b) Neurophysin content of the neural lobe

There was a significant increase in the level of neurophysin A in the PVG strain (P<0.02) but the levels of this protein were unchanged in the Wistar and DA strain (results expressed in terms of body weight). No changes were observed in neurophysins B and C in all three strains investigated (Table 2).

There were no significant alterations in any of the neurophysins in all three strains when the levels were expressed per gland or per mg fresh weight of neural lobe. The results are not shown.

Discussion

There were significant differences between the various strains studied in the fresh weight of the neural lobes and the vasopressin and neurophysin contents of this tissue in control animals. The Sprague-Dawley strain was found to have the heaviest neural lobe while the vasopressin content was actually lower than that of a number of the strains. This demonstrates a danger in using the
weight of the neural lobe as an index of storage potential or ability to sustain a maximum antidiuresis for a certain length of time.

Ames & van Dyke (1950) reported that the vasopressin content of the neural lobe of Long-Evans rats was 110 mU/100 g body weight while Jones & Pickering (1969) found a much higher level (260 mU/100 g body weight) in Wistar rats of the Porton substrain. This latter value is somewhat higher than that found for Wistar rats in this laboratory (218 mU/100 g body weight). North et al. (1977) have shown significant differences in the neurophysin levels of Long-Evans, Wistar, Sprague-Dawley and Holtzman strains of rat. The extent of the differences found are similar to those reported here. These authors also observed seasonal differences in the neurophysin levels between animals sampled in the summer (July/August) and winter (January/February). The vasopressin and neurophysin determinations in this laboratory were all made during the autumn and winter (October to February) so that a seasonal variation is less likely.

There was actually more than twice as much vasopressin in the DA strain than in the Wistar and PVG strains for the same amount of neurophysin A (as indicated earlier by the ratios of hormone to carrier protein). However, it is rather difficult to comment further until the arbitrary units in which the neurophysin levels were calculated can be expressed on a molar basis.

The reaction of the various strains to reserpine was also varied for, while a fall in vasopressin was seen in the Wistar and Chester Beatty animals, no change as observed in the Sprague-Dawley, PVG and DA strains (when the levels were expressed on a body weight basis). However a significant rise in neural lobe vasopressin was seen in the PVG strain when the levels were expressed per gland. Thus the complex picture described in the Introduction is repeated here in this simultaneous study of five strains of one species.

Although there was a fall in the vasopressin content of the Wistar animals there was not a coincident fall in the level of neurophysin A. A similar situation was also seen in the golden hamster after two weeks cold exposure (Edwards 1978b). Such results might indicate the existence of other mechanisms of hormone release in addition to exocytosis.

References


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