# Selective depletion of spinal noradrenaline inhibits post-decapitation convulsions in rats

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*Summary.* Local administration of 6-hydroxydopamine in the subarachnoidal space of the spinal cord in rats resulted in a selective long-lasting depletion of spinal noradrenaline, but not of dopamine, and prevented the occurrence of post-decapitation convulsions.

Decapitation of rats and mice in the cervical region is followed by clonic flexor-extensor reflexes (called convulsions). Central administration of catecholamine depleting agents strongly suppresses these reflexes[3-5]. This report concerns the effect of selective depletion of spinal noradrenaline on them.

*Methods.* Male albino rats (Wistar, WU, obtained from CPB-TNO, Zeist) weighing 200-240 g were used as experimental animals. The subarachnoidal space of the spinal cord was cannulated under ether anesthesia through a small incision in the atlanto-occipital membrane as described by Yaksh and Rudy[6]. 6-Hydroxydopamine (6-OHDA) was injected over a 30-sec period at the level of $T_5$-$T_6$ at a dose of 250 µg in a volume of 5 µl vehicle (0.9% NaCl solution containing 1 mg/ml ascorbic acid). After injection the cannula was left in position for 1-2 min. Control animals received vehicle only. The rats were decapitated 7, 31 and 42 days after 6-OHDA administration and the presence or absence of clonic convulsions was recorded for each animal; the rats were observed for 2 min. The thoraco-lumbar region of the spinal cord and the brain were quickly removed and the medulla oblongata/pons, cortex cerebri and, in 1 experiment, the hypothalamus were dissected. Noradrenaline (NA) and dopamine (DA) levels were determined fluoriphotometrically[7,8]. In 1 experiment a combined radiochemical assay for NA and DA was used as described by van der Gugten et al.[9]. The catecholamine measurements were corrected for recoveries and calculated on the basis of wet tissue weight. Student's t-test was used for statistical evaluation of differences.

*Results.* The decapitation of control animals was always followed within 3-5 sec by clonic convulsions lasting 20-30 sec. The convulsions were completely absent at 7, 31 and 42 days after 6-OHDA pretreatment. The table shows catecholamine levels in various parts of the central nervous system at various times after 6-OHDA administration. NA in the spinal cord fell to a very low level, without statistically significant changes in NA content of cortex and hypothalamus. NA levels in the medulla oblongata were slightly depressed at 31 days, but not at 7 and 42 days after treatment. DA levels were moderately affected only in the spinal cord at 7 days, but not at 31 and 42 days after 6-OHDA administration.

*Discussion.* Post-decapitation convulsions have been suggested to be a phenomenon resulting from the disappearance of the tonic inhibition of spinal interneurons mediated by bulbospinal NA neurons[5,10,11]. In a recent study Suenaga et al.[10] could not rule out the possibility that cortical or hypothalamic NA was involved in these convulsions, since they administered 6-OHDA intracerebroventricularly and consequently depleted NA not only in the spinal cord but also in these brain regions. In the present report we have shown that selective depletion by 6-OHDA of spinal NA but not DA fully prevented the occurrence of post-decapitation convulsions. Serotonin depletion by centrally administered 5,6-dihydroxytryptamine enhanced these convulsions[12]. There is as yet no evidence for the involvement of other transmitter systems in the post-decapitation convulsions. From the results of the present study we conclude that intact spinal NA transmission is essential for the phenomenon of post-decapitation convulsions.

Noradrenaline and dopamine concentrations in several regions of the central nervous system at various times after spinal administration of 6-hydroxydopamine (6-OHDA)

| Time after treatment | Regions | Noradrenaline (µg/g tissue) Control | 6-OHDA | Dopamine (µg/g tissue) Control | 6-OHDA |
|---|---|---|---|---|---|
| 7 days | Cortex cerebri | 0.514±0.037 (8) | 0.444±0.041 (4) | 0.217±0.037 (8) | 0.168±0.017 (4) |
| | Medulla oblongata/pons | 0.730±0.054 (8) | 0.564±0.048 (4) | 0.205±0.030 (8) | 0.233±0.025 (4) |
| | Spinal cord | 0.638±0.016 (8) | 0.027±0.008$^c$ (4) | 0.112±0.011 (8) | 0.057±0.010$^b$ (4) |
| 31 days | Cortex cerebri | 0.390±0.036 (9) | 0.340±0.042 (10) | 0.211±0.035 (9) | 0.206±0.024 (10) |
| | Medulla oblongata/pons | 1.220±0.138 (8) | 0.850±0.067$^a$ (10) | 0.380±0.118 (7) | 0.430±0.142 (10) |
| | Spinal cord | 0.390±0.067 (9) | 0.004±0.003$^c$ (10) | 0.080±0.014 (9) | 0.050±0.019 (10) |
| | Hypothalamus | 2.570±0.229 (9) | 2.210±0.321 (10) | 0.360±0.047 (9) | 0.360±0.048 (10) |
| 42 days | Cortex cerebri | 0.502±0.068 (7) | 0.546±0.046 (9) | 0.236±0.040 (7) | 0.303±0.051 (9) |
| | Medulla oblongata/pons | 0.804±0.076 (7) | 0.770±0.122 (9) | not measured | not measured |
| | Spinal cord | 0.438±0.042 (7) | 0.014±0.004$^c$ (9) | 0.099±0.006 (7) | 0.089±0.009 (9) |

Data are expressed as mean±SEM; the number of animals per group is given in brackets. Catecholamines were assayed using a fluorimetric method (7 and 42 days) or a radiometric method (31 days). $^a p<0.05$; $^b p<0.01$; $^c p<0.001$, for differences between 6-OHDA-treated rats and controls (Student's t-test; 2-tailed).

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