Sertoli-cell-only condition. The lumen of many seminiferous tubules were often filled with processes of Sertoli cell cytoplasm (fig. 5).

The present observations are in contrast to previous claims[7] that high doses of TMP (up to 300 mg/kg/week) produce temporary sterility in rats in which the delay in a return to full spermatogenesis function is simply dependent upon the dose. Our studies have demonstrated complete loss of germ cell activity after prolonged doses of TMP. It is clear that the available data do not permit definition of the action of TMP on the function of the testes. Nevertheless, the results emphasize that agents which interfere with fertility by affecting the formation of mature spermatozoa can also disrupt the growth of germ cells, either directly, or indirectly through the Sertoli cells and Leydig cells. The data suggest that the effects of agents on spermatogenesis should be assessed by examination of testicular function as a whole.

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Vasotocin protects rats against convulsions induced by pentylenetetrazol[1]

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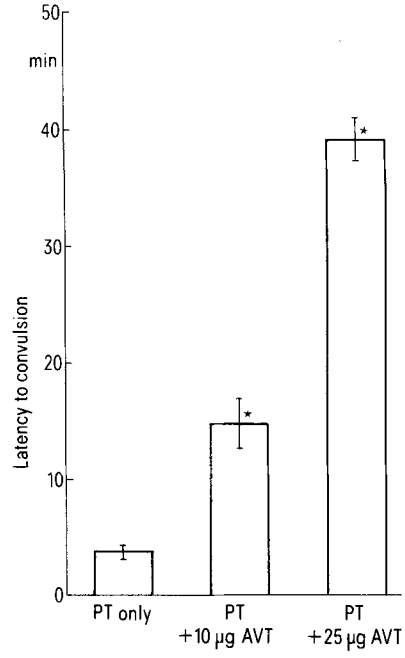
Summary. The AVP analog, vasotocin, administered s.c. effectively antagonized pentylenetetrazol-induced convulsions, supporting the contention that AVP may be a mediator in convulsive disorders.

In recent years, it has been recognized that arginine vasopressin (AVP) may have important functions in the central nervous system (CNS). The many reported behavioral or central physiological effects of AVP provide evidence for a neuromodulator or neurotransmitter role of AVP. Particularly important with regards to this study are the antipyretic effects of AVP when perfused or injected into the septal area of the brain of the sheep and the rat[3-5]. In the former study[4], AVP release in vivo in the septal area of the brain of the sheep was observed during fever. Other studies have observed AVP release into the blood during hyperthermia[6,7]. Interestingly, in contrast to the antipyretic effects of AVP injected directly into the brain tissue of the rat[5], if it is injected as a bolus into the cerebroventricular system, the responses include hypothermia and seizures[8]. This latter effect was dependent on a sensitization process: 1st administration of AVP caused absence-like seizures while subsequent administration caused myoclonic-tonic convulsions even at doses considerably smaller, such as 10 ng. These observations led us to test the hypothesis that AVP might be responsible for febrile convulsions by using a hyperthermia-induced convulsion model in the rat. The results[9], using homozygous Brattleboro rats with genetic absence of AVP, and rats treated with intracerebroventricular anti-AVP antiserum, suggest that AVP may be a mediator of hyperthermia-induced convulsions. Consequently, these experiments were undertaken to determine if an AVP analog, vasocotin (AVT), given parenterally, could influence pentylenetetrazol-induced convulsions. Pentylenetetrazol-induced convulsions are used as an animal model for human convulsive disorders[10,11].

Male, Long-Evans rats of 250–300 g b.wt were used in these experiments. Rats were housed in colony cages with a 12::12 h light-dark cycle at an ambient temperature of 19±0.5 °C. Food and water were available ad libitum. Experiments were performed on 1 rat at a time and each rat was used only once.

Vasotocin (Bachem) (10 µg) was injected s.c. between the shoulder blades of the conscious rat in a volume of 0.5 ml of sterile physiological saline. Pentylenetetrazol-induced convulsions were induced by a s.c. injection of 20 mg of pentylenetetrazol (Sigma) in 0.5 ml sterile physiological saline. This experiment included 3 experimental groups: a) rats which received only pentylenetetrazol, b) rats which received 10 µg of arginine vasotocin (AVT) 10 min before



Pentylenetetrazol-induced convulsions. The bars represent the mean (±SEM) latency to convulsion as assessed by the 1st myoclonic jerk, in response to pentylenetetrazol (20 mg) and arginine vasotocin (10 µg and 25 µg). Each bar represents 5 rats. PT, pentylenetetrazol; AVT, arginine vasotocin. The groups are statistically different from each other by t-test for unpaired samples ($p < 0.01$).

the pentylenetetrazol, c) rats which received 10 µg of AVT 10 min before pentylenetetrazol, then 5 µg AVT at 10-min intervals starting 5 min after pentylenetetrazol (total dose 25 µg AVT). The latency to the 1st myoclonic jerk was recorded. There were 5 rats in each experimental group. Convulsions typically started with a myoclonic jerk of head and forelimbs.

Pentylenetetrazol-induced convulsions were markedly affected by AVT (fig.). Pentylenetetrazol alone caused myoclonic convulsions within a mean latency of 3.8 ± 0.4 min. Prophylactic AVT (10 µg) significantly increased the latency to convulsions to a mean of 14.8 ± 2.1 min and continued AVT treatment could further delay the convulsions to a mean of 39.3 ± 3.4 min. Indeed, when convulsions finally did occur, they were of a milder degree and shorter duration than untreated pentylenetetrazol convulsions. Rats generally laid quietly with deep breathing after AVT administration but whether this is important in protection against convulsions cannot be answered from these experiments.

Whether the AVP analog, AVT, is effective because it acts as an antagonist at the AVP receptor in the CNS, by a negative feedback mechanism on AVP in the brain or by some mechanism unrelated to AVP cannot be determined by these experiments.

The antagonistic effects of AVT on the convulsive state induced by pentylenetetrazol, suggest that the AVP analog, AVT, or other AVP analogs may be effective in the treatment of convulsive disorders.

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Spontaneously (genetic) hypertensive rats: Naloxone-reversible and propranolol-reversible decrease in pain sensitivity

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Summary. Adult spontaneously hypertensive rats (SHR) are less sensitive to painful stimuli than their normotensive controls, Wistar-Kyoto (WKY) rats. This difference can be eliminated by the specific opiate antagonist, naloxone, and by the β-adrenergic blocking agent, propranol.

Anatomical, biochemical, physiological, pharmacological and pathophysiological evidence suggests that the central regulatory mechanisms for control of pain and blood pressure are closely associated. A number of specific brain stem areas are involved in the regulation of both blood pressure and pain[2,3]. Electrical stimulation of discrete brain sites often results in coincidental changes in pain sensitivity and blood pressure[2]. Experimental evidence strongly suggests that central catecholamines are involved in blood pressure control as well as in the central regulation of pain sensitivity[2,4]. Both catecholamines and enkephalins are present in the same discrete areas involved in the integration of the central regulation of cardiovascular function[5,6]. Pharmacological manipulations of central monoamines affect the blood pressure control as well as the sensitivity to pain[7]. A decreased sensitivity to pain occurs in experimentally hypertensive rats[8].

We wish to report that spontaneously hypertensive rats (SHR)[9] are less sensitive to painful stimuli than their normotensive controls, the Wistar-Kyoto (WKY) rats, and that this difference can be eliminated by pretreatment of the animals with the specific opiate antagonist, naloxone, as well as with the β-adrenergic blocking agent, 1-propranolol.

Methods. The degree of analgesia was measured by determination of the latency time of the tail withdrawal reflex when a painful stimulus, warm water at 50 ± 1 °C, was applied to the tail of the animals (tail-flick test)[10-12]. Adult male SHR and WKY rats, 12 weeks old, were obtained from Taconic Farms (Germantown, N.Y.) and kept for 1 week under a 12-h light-dark cycle, with lights off from 18.00 to 06.00 h, before testing. Naloxone (2 mg/kg) was dissolved in saline and injected i.p. 30 min before testing. Propranolol (1 mg/kg) and clonidine (0.25 and 2.5 mg/kg) were dissolved in saline and injected i.p.; rats were tested 15 and 30 min after administration of the drugs. Control groups received saline only. Data were analyzed by a 2-way analysis of variance, and a Student Newman-Keuls test was used for comparisons of individual means[13].

Results and discussion. The SHR were significantly less responsive to the thermal stimulus than the normotensive control rats, since the latency time for the tail withdrawal reflex was increased in SHR by 145% when compared with control WKY rats (fig.).

The specific opiate antagonist naloxone produced a non-significant 28% increase in pain sensitivity of control WKY rats, but a significant, 56% increase in pain sensitivity in SHR (fig.). After naloxone treatment, hypertensive and normotensive rats no longer differed in their latency time for the tail withdrawal effect (fig.). The β-adrenergic blocking drug, 1-propanolol, produced no change in pain sensi-