Intracranial pressure in conscious rabbits after intraventricular reserpine

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Ventricular fluid pressure was measured continuously for 50 hours in conscious rabbits via a cannula implanted into the left lateral ventricle. Intraventricular injection of 25 μg reserpine (in a volume of 10 μl) resulted in increased pressure compared to that in non-injected controls during the first 7 to 10 hours. This was interpreted as depletion of noradrenaline in intracranial sympathetic nerves leading to increased cerebral blood volume and increased cerebrospinal fluid production. During the remainder of the experiment, the ventricular fluid pressure was reduced, probably due to a predominance of the central depressant effects of reserpine.

Key Words: cerebrospinal fluid · ventricular fluid pressure · intraventricular reserpine · amine depletion

The ventricular fluid pressure (VFP) is primarily maintained and influenced through a combination of changes in the cerebral blood volume and in the cerebrospinal fluid (CSF) dynamics. Fluorescence histochemistry has shown that intracranial vessels are supplied by numerous adrenergic nerve terminals that innervate the pial vascular bed, particularly the carotid system, as well as intracerebral arterioles. Denervation of the intracranial vessels by excision of the superior cervical sympathetic ganglia has been shown to influence the cerebral blood volume and has confirmed the fact that these nerves act as vasoconstrictors. The choroid plexuses also receive adrenergic nerves that arise in the same ganglia and form a plexus closely related both to blood vessels and epithelial cells in the plexus tufts. The effects of sympathectomy on carbonic anhydrase activity indicate that these adrenergic nerves inhibit cerebrospinal fluid production in the choroid plexuses.

To allow an experimental analysis of how these factors influence the VFP, a technique was devised for continuous recording of the pressure in conscious rabbits over a period of up to 80 hours. This method has been used to demonstrate a sympathetic neural influence on the VFP by recording the effects of pre- or postganglionic cranial sympathectomy in normal animals or in animals in which the CSF outflow pathways have been blocked by intracisternal kaolin. The experiments indicate that sympathetic denervation produces an increase in VFP and markedly modifies the intracranial hypertension induced by blockade of CSF outflow.
Our study was undertaken to compare the effects of cranial sympathectomy and administration of the amine-depleting agent reserpine on the VFP. We attempted to minimize the extracranial effects by injecting small amounts into the ventricular system.

**Methods**

We used 17 adult rabbits of both sexes, weighing between 2.3 and 3.0 kg, fed freely during the entire experimental period with standard pellets,* turnips, and tap water.

The animals were conscious during the entire procedure. Under local anesthesia (3 ml of 2% lidocain), a pressure cannula was inserted into the left lateral ventricle of the brain through a burr hole placed in the frontoparietal region according to the procedure previously described. The subsequent recordings of the VFP were performed in a Grass Model 7 polygraph via a Statham Model P23AC transducer. A second burr hole was placed in the corresponding region of the contralateral side in seven animals. Between 2 and 5 hours after the operation, a small injection needle (gauge No. 20) was inserted into the right lateral ventricle, through the second burr hole. The right position of the needle tip was checked by gentle aspiration of CSF which was re-injected together with 10 μl (25 μg) of reserpine† or the corresponding amount of solvent (supplied by Ciba). A small catheter was inserted into an ear artery, and its tip was directed down into the carotis externa for measurement of the blood pressure during the experiment.

Differences between the mean values of the control group and the reserpine-treated group of animals, were analyzed by student’s t-test.

**Results**

The implantation of the pressure cannula was in itself enough to produce an increase in the VFP (Fig. 1a) due to a local traumatic brain edema; these alterations in the VFP constitute a methodological base curve derived from the control animals. The control curve allows correction for the curves obtained from the reserpine experiments (Fig. 1b) to give the true reserpine-induced changes in VFP (the net VFP). The correction was made by subtracting each mean pressure in the control group from the corresponding time-related sequence of mean pressure levels in the reserpine-treated animals. The time-course of alterations in VFP after intraventricular injection of reserpine is illustrated in Fig. 1c.

The mean pressure measured immediately after introducing the cannula was 7 mm physiological saline (Fig. 1b). After 1 hour there was already a fairly rapid increase in pressure (Fig. 1a and b) corresponding to the injury caused by the pressure cannula. The introduction of the 20-gauge needle and injection of the 10 μl of fluid did not overtly influence VFP.

During 7 to 10 hours after the reserpine injection (i.e., 3 to 12 hours after implantation of the cannula), the net VFP (Fig. 1c) increased to a maximum of 25 mm saline, which is significantly different (p < 0.001) from the pressure in the time-matched controls (Fig. 1a). The VFP then fell lower than that in the controls; at the end of the experiment this difference was as much as 50 mm saline.

The arterial blood pressure did not change during the experiments and did not differ in the two groups of animals.

**Discussion**

The primary pharmacological action of reserpine is exerted through its blockade of the amine storage mechanism, leading to a depletion of the amine from both central and peripheral neurons. Injection of reserpine in a dose of as little as 10 μg in the lateral ventricles of cats results in, for example, relaxation of the nictitating membrane and narrowing of the palpebral fissure; the effects have been seen to occur first on the side of the injection. These findings, and the observations that reserpine-induced symptoms may set in before any decrease in peripheral adrenergic function is evident, show that reserpine depresses

*Standard pellets made by SAN-bolagen, Celsiusgatan 35, Malmö 1, Sweden.
†Xylocain made by Astra Läkemedel AB, Kranbergagatan 16, S-151 85 Södertälje, Sweden.
‡Serpa$ made by Ciba-Geigy AG, Basel, Switzerland.
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**Fig. 1.** a. Mean VFP from recordings on 10 untreated control rabbits. The curve represents the methodological base curve. b. Changes in actual mean VFP after intraventricular injection of 25 μg reserpine. c. Net VFP (= true changes in VFP after reserpine injection) obtained by subtracting the values at each time interval in the methodological base curve (a) from the corresponding (time-matched) actual values (b). Solid line = mean; broken line = ± standard error of the mean.
aminergic nervous activity by combined central and peripheral effects.

The increased VFP recorded during the first hours after intraventricular reserpine injection corresponds well to the depletion of noradrenaline from the intracranial sympathetic nerves which produces increased cerebral blood volume and enhanced CSF production in the same manner as after postganglionic sympathectomy. The remainder of the pressure changes do not resemble those seen after transmitter loss following surgical sympathectomy. This agrees with the findings that reserpinization does not produce cocaine-like supersensitivity of the receptors to noradrenaline since the intraneural inactivation of circulating amines remains unimpaired. The lowering of the VFP could instead have resulted from the central and peripheral depressant action of reserpine, including tranquility, hypothermia, and hypotension.

References


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