clear from this study. Presumably all except the lowest levels of auditory transmission in the brainstem were affected because the increase in latency was seen for all peaks except I and II. However, most of the latency increase occurred between peaks III and IV and between peaks VI and VII; this suggests that the intervening processes between those peaks were most susceptible to alcohol.

Alcohol intoxication produces definite and consistent changes in the early auditory evoked potentials from the human brainstem. The value of this observation lies not only in the information it provides concerning the neurological effects of alcohol, but also in the possibility for a functional dissection of brainstem connections in an intact subject. Systematic correlations of the effects of different drugs, with known effects on different central pathways, on the brainstem potentials offers a means of identifying specific transmission or conduction dysfunction.

KENNETH C. SQUIRES
NAI-SHIN CHU
ARNOLD STARR

Department of Neurology, University of California Irvine Medical Center, Orange 92668

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Sympathetic Nervous Control of Cerebrospinal Fluid Production from the Choroid Plexus

Abstract. *The rabbit choroid plexus, responsible for the bulk production of cerebrospinal fluid, is well supplied by sympathetic nerves emanating in the superior cervical ganglia. Electrical stimulation of these nerves markedly reduces production of cerebrospinal fluid, measured by [^{14}C]inulin dilution during ventricular perfusion, whereas sympathetic denervation enhances the rate of formation.*

The mammalian choroid plexus is a highly vascularized villous structure, covered with a single layer of cuboidal epithelial cells. It is present in all four ventricles of the brain and constitutes the major site for the bulk production of cerebrospinal fluid (CSF). The fluid is formed by an active secretory process at a rate that varies considerably from species to species, but that is rather constant when expressed as a fraction of total CSF volume or on the basis of plexus weight—approximately 0.5 percent of total CSF volume is replaced by newly formed fluid every minute (*1*). Little is known about the various physiological factors controlling the rate of CSF formation from the choroid plexus; the possibility of a nervous influence has been suggested on the basis of histological studies, dating back as far as those of Benedikt in 1874, which showed the presence of nerves in the plexuses (*2*). In spite of this, the possibility that the production rate of CSF is influenced by autonomic nerves has not been seriously investigated, probably because of the lack of unequivocal ultrastructural evidence for an innervation of the plexus epithelial cells, apart from the presence of vasomotor nerves (*3*). The present study is part of a series of investigations on the innervation of the mammalian choroid plexus and the effect of autonomic nerves on bulk CSF production as measured quantitatively by the ventriculocisternal perfusion technique according to Pappenheimer and co-workers (*4*).

We used albino and randomly pigmented rabbits (weight, 2 to 3 kg) of either sex that were maintained on stan-

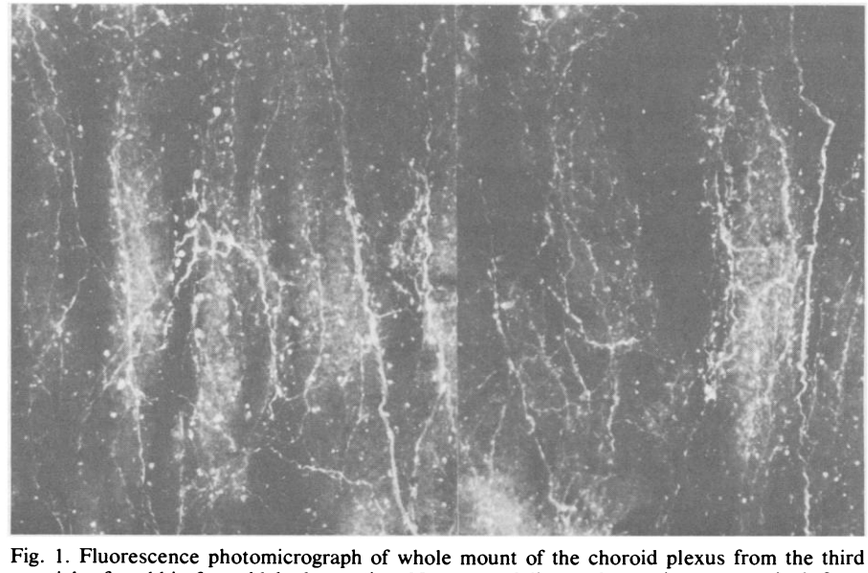

Fig. 1. Fluorescence photomicrograph of whole mount of the choroid plexus from the third ventricle of a rabbit; formaldehyde reaction. Numerous delicate adrenergic axon terminals form a network in the parenchyma among the epithelial cells. Autofluorescent cells and granules are also seen (× 65).

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dard pellet food and tap water, given without restriction. Thirty-six animals, all killed by intravenous injection of air, were used for studies on the plexus innervation. Eighteen of these animals were sympathectomized 1 week beforehand by bilateral excision of the superior cervical ganglia under light Nembutal–ethyl ether anesthesia. The adrenergic nerve supply was studied by fluorescence microscopy according to the Falck-Hillarp formaldehyde technique, in which separate whole mounts from all four ventricles were used, and the concentration of norepinephrine was measured fluorometrically in samples consisting of plexuses pooled from three animals and homogenized in ice-cold 0.4*N* perchloric acid (*5*).

Fluorescence microscopy showed the presence in all plexuses of catecholamine-containing nerve terminals with a characteristic beaded appearance. Some of the fibers formed networks around small vessels belonging to both the arterial and venous systems, whereas others appeared isolated in between blood vessels and epithelium in the plexus parenchyma (Fig. 1). The supply of fluorescent nerves was best developed in the plexus of the third ventricle, followed in order by the plexuses of the lateral and fourth ventricles. The density of innervation in the plexuses corresponded well to the presence of 0.4 μg of norepinephrine per gram of tissue, wet weight (Fig. 2a). A similar distribution of adrenergic nerves has been found in choroid plexuses from numerous other animals, including monkeys, and it corresponds to an equally well developed cholinergic nerve supply of the plexuses (*6*). Within 1 week after bilateral cervical sympathectomy the fluorescent adrenergic nerves had disappeared completely from the choroid plexuses of the lateral and third ventricles, whereas a small number of fibers were still visible in the plexus of the fourth ventricle, showing that a few of the sympathetic nerves in this region originate from sources other than the superior cervical ganglia. These findings agree with the presence of only small amounts of norepinephrine in the entire choroid plexus tissue after ganglionectomy (Fig. 2a).

In electron microscopic studies, we have recently shown that the autonomic axon terminals in the choroid plexus have a close relation not only with the smooth muscle wall of small arterioles but also with the epithelial cells (*7*) to which the terminals reach as close as 20 nm from the membrane, suggesting a true innervation of the cell. The endings either are located contiguous to the base

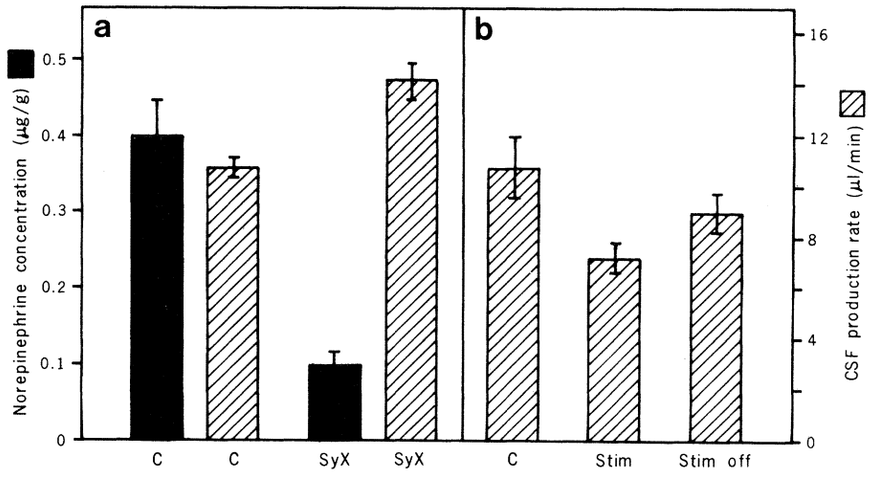

Fig. 2. (a) Denervation: One week following sympathetic denervation (*SyX*) of the rabbit choroid plexus there is a marked reduction in the norepinephrine concentration concomitant with a highly significant increase in the rate of CSF production compared with unoperated controls (*C*). Differences between mean values (± S.E.M.) according to Student's *t*-test: $P < .001$ in both groups. (b) Stimulation: Production rate of CSF before (*C*) and during (*Stim*) bilateral electrical stimulation of the superior cervical ganglia, which markedly reduces the rate of production (the difference, based on paired observations, was of highest significance: $P < .001$). After finishing stimulation (*Stim off*) there is a tendency to normalization of the production rate (*Stim* versus *Stim off*: $P = .01$). Bars indicate mean ± S.E.M.

of the cells or cell processes or are found between adjacent cells or within cellular invaginations (*7*). More functional evidence for a relation between sympathetic axons and the secretory epithelium of the plexus comes from studies showing that cervical sympathectomy or treatment with reserpine (which abolishes norepinephrine from sympathetic nerves) significantly increases the activity of carbonic anhydrase (*7*), an important enzyme involved in the process of CSF production.

A direct measure of the influence of sympathetic nerves on the rate of CSF production was obtained by ventriculocisternal perfusion of radioactive inulin in another 26 rabbits. The principles of the Pappenheimer technique (*4*) were followed—the animals were sedated with Nembutal, tracheotomized, and then anesthetized with halothane and a mixture of N_2O and O_2 in an open system during artificial ventilation. They were placed in a prone position with the head fixed in a metal frame. Artificial CSF (*8*), that contained inulin labeled with [^{14}C]carboxylic acid (1 μCi/100 ml) and that had been warmed to 38°C, was infused at a constant rate of 30 μl/min through an inflow probe into the right lateral ventricle during continuous recording of infusion pressure by a Statham transducer, model P23AC. The fluid was drained at the same rate by means of a needle placed in the cisterna magna, and the outflow (150 μl) was collected at 5-minute intervals. Blood gases were frequently measured throughout the experiment in an Astrup system (Radiometer, Copenhagen), and systemic blood pressure was monitored continuously. Attempts were made to maintain blood gases constant within narrow limits throughout the experiments by small adjustments in the respiratory rate, giving the following mean values [± standard error of the mean (S.E.M.)]: P_{a,CO_2}, 31.7 ± 0.4 mm-Hg; P_{a,O_2}, 117 ± 1 mm-Hg; and *p*H 7.41 ± 0.01 (*9*). Radioactivity was measured by liquid scintillation counting, quench corrections being obtained according to the conventional principles. A plateau in the radioactivity of the effluent was found to be reached after infusion for about 2 hours, and once this steady state had been obtained samples were collected over a further period of 2 to 3 hours.

Since diffusion of inulin from the ventricular system is negligible, it follows that any dilution of inulin during passage through the ventricles results from newly formed, inulin-free fluid at a rate equal to the rate of inflow times the difference between the inulin concentrations in the inflow and outflow, divided by the concentration in the outflow (*4*). The mean bulk production of CSF in the untreated rabbit was found to be 10.8 μl/min (Fig. 2), which is in good agreement with previously published figures (*1*).

Bilateral excision of the superior cervical ganglia (ten animals), which produced an almost complete sympathetic denervation of the choroid plexuses within a week (Fig. 2a) and which significantly enhances carbonic anhydrase activity in the tissue (*7*), resulted in a 33 percent increase in the rate of bulk CSF

production (Fig. 2a) compared with the intact controls (ten animals).

In another series of experiments on six animals, the sympathetic trunks in the neck were stimulated electrically on both sides by two pairs of platinum wire electrodes that were fixed with an uninsulated loop around the nerve trunks immediately below the superior cervical ganglia. After reaching the steady state in perfusion required to calculate normal flow, the cervical sympathetics were stimulated intermittently (stimulation on 30 seconds, off 30 seconds) during 1 to 2 hours with monopolar square waves (3 to 10 V; pulse duration, 2 msec; frequency, 15 Hz). The sympathetic activation produced a reduction in the rate of CSF formation by a mean of 32 percent compared with the control situation before stimulation (Fig. 2b). After cessation of the stimulation, the radioactivity in the effluent adjusted to a new plateau level from which it could be calculated that the CSF flow rate returned approximately halfway (49 percent) toward normal during the 1-hour period after stimulation (Fig. 2b). Each train of 30-second stimulation sometimes caused a transient insignificant reduction in systemic blood pressure (by, at most, 10 mm-Hg), probably due to inadvertent stimulation of the vagus nerve or nerves. During the entire stimulation period there was usually a progressive slight fall in the infusion pressure (which, under the condition of the constant inflow and outflow rates, reflects intraventricular pressure) by a maximum of 25 mm-H_2O.

The studies have shown that the rabbit choroid plexus receives a well-developed adrenergic nerve supply originating almost entirely from the superior cervical sympathetic ganglia. The nerves appear to have an inhibitory effect on bulk CSF production, a situation thus resembling the sympathetic inhibition of the aqueous humor formation from the ciliary body (*10*). This is consistent with the observation that cervical sympathectomy (or intraventricular administration of reserpine) markedly increases ventricular fluid pressure to a level that is even lethal if CSF outflow pathways have been blocked by cisternal injection of kaolin (*11*). Since the sympathetic nerve terminals in the plexuses innervate both the local vascular bed and the secretory epithelium, the effect on CSF production may have been mediated through changes in plexus blood flow as well as through direct effects on the secretory cells. It is unlikely that a primary action on plexus blood flow would account for the very marked changes in CSF production observed, and there is also experimental evidence that the marked increase in cerebral blood flow associated with moderate hypercapnia does not enhance the rate of CSF production (*12*). Moreover, the increase in carbonic anhydrase activity of the plexus epithelium found after sympathetic denervation (*7*) favors a prominent direct effect of adrenergic nerves on the plexus epithelium and its secretory functions.

It is concluded that the sympathetic nerves in the choroid plexus have an inhibitory function on bulk CSF production by a control exerted primarily on the plexus epithelium.

MARIA LINDVALL
LARS EDVINSSON
CHRISTER OWMAN

Department of Histology,
University of Lund,
S-223 62 Lund, Sweden

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A Fertility Reaction to a Historical Event: Southern White Birthrates and the 1954 Desegregation Ruling

Abstract. *On 17 May 1954 the Supreme Court, in its decision in* Brown v. Board of Education, *declared de jure segregation of the public schools to be unconstitutional. It is argued here that a consequence of that decision was a decline in childbearing among white Southerners. In the nation as a whole, period fertility rates increased between 1954 and 1955, but in 9 of the 11 former Confederate states they decreased. Further analysis shows that these Southern fertility decreases began about 12 months after the Supreme Court decision. This variation in behavior in reaction to a historical event has important implications for the explanation and prediction of fertility.*

At a time in the 1950's when the overall U.S. birthrate was increasing sharply, the states of the South (*1*) displayed a markedly lower increase, thereby closing, even reversing, a longstanding regional difference in fertility (*2*). The most marked convergence between the entire South and the remainder of the country occurred between 1954 and 1955 (Fig. 1). This one sharp shift is the subject of this report; the long-range change also seen in Fig. 1 is discussed elsewhere (*2*).

Because these fertility rates were computed from sample data from the 1960 and 1970 censuses, the shift in 1954–55 was originally dismissed as being due to random variation. However, further inspection revealed that the same pattern exists in the total number of births actually registered. We examined reported vital registration data for whites and blacks. In the South the number of white births increased faster than in the nation as a whole between 1953 and 1954 (2.2 percent in the South, 0.8 percent nationally) but declined by 0.7 percent between 1954 and 1955, while the national figure was increasing by 1.9 percent. Between 1955 and 1956 the number of white births increased again in the South (by 2.2 percent), but more slowly than in the nation as a whole (the national increase was 2.6 percent). In 1955, 23 of the 32 non-Southern states had more white births than in 1954, whereas only 4 of the 16 Southern states did. The year before, 28 of the non-Southern states and 14 of the Southern states had shown increases.

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