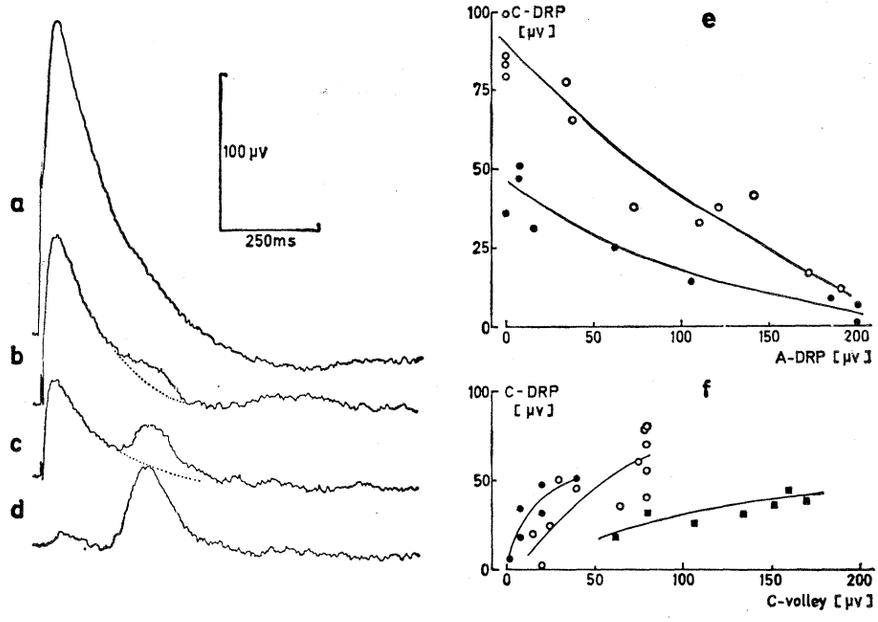

Fig. 2. Factors influencing the size of the C-DRP. (a) An average DRP (16 superpositions) following a sural nerve stimulus (35 volts, 0.2 msec) producing maximum A- and C-volleys. This experiment was on a cat anesthetized with Nembutal (40 mg/kg). In b–d the stimuli were the same as in a, but the A-volley was blocked to an increasing extent. In e the peak values of the C-DRP's are plotted against those of the preceding A-DRP's. The points are from the same experiments as a–d; the circles are from the measurements shown in Fig 1. In f the relation between the size of the C-volley (abscissa) and of the C-DRP (ordinate) is shown. The points are either from single measurements (○) or averaged values from 10 to 16 successive trials (●, ■).

estimated, which was always around the peripheral value (Table 1).

Generally, the C-DRP was greatly reduced by a preceding A-DRP (Fig. 1, k–n; Fig. 2, a–e). This was also the case when the A-volley was generated by a separate stimulus given to other cutaneous nerves, the effect of depression persisting for more than 300 msec. In similar experiments the influences of a C-DRP onto an A-DRP and onto a second C-DRP were tested. The depression of the A-DRP by the preceding C-DRP was less pronounced, but the time course was similar. When pairs of C-fiber stimuli were delivered to the sural nerve, the second C-DRP was strongly suppressed with intervals between stimuli of up to more than 500 msec.

Thus, an afferent C-volley generates a DRP having the same polarity as that caused by an A-volley; that is, the proximal electrode is more negative than the distal one is throughout the potential change. These findings are in contrast to those of Mendell and Wall (*4*), who claimed that afferent C-volleys produce a "positive DRP" (that is, a presynaptic hyperpolarization). As judged from their illustrations, most of the positive DRP's occurred too soon after the peripheral stimulus to have been evoked by C-fiber activity. Their conclusions form one of the basic postulates in a recent pain theory (*5*). According to this "gate control" theory, presynaptic hyperpolarization of afferent fibers by a C-input will facilitate the central effects of all sensory impulses. My experiments do not support this view.

Further investigations in which intraspinal potential field measurements, spinal reflex interactions, and presynaptic excitability testing of single afferents fibers are used should identify the origin of the C-DRP, and determine whether this DRP is also linked to presynaptic inhibition.

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15 March 1968

Exencephalia: Its Occurrence in Untreated Mice

Abstract. *Exencephalia has been reported in irradiated CF1 mice but there are no reports of its occurrence in untreated mice of this strain. In the course of establishing disease-free breeding colonies from CF1 female mice delivered of their offspring by cesarean section, exencephalia was seen frequently. During a 2-week period, 90 litters were delivered; 11 contained exencephalic fetuses, at the rate of one per litter (11 of 90 litters, 12.2 percent; 11 of 1056 fetuses, 1.04 percent). The prevalence of this anomaly in untreated mice of this strain could contribute to overestimates of the effectiveness of low doses of radiation.*

In view of reports of exencephalia in irradiated CF1 mice (*1*) it is important to report the natural occurrence of this anomaly in this strain, because lack of evidence of its prevalence in untreated mice could contribute to overestimates of the effectiveness of low doses of radiation.

Doses of x-irradiation of 200 r produce exencephalia in a high incidence (26 percent) in CF1 mice (*2*), and low incidences (0.7 to 2.3 percent) have been noted after small exposures to radiation (15 r) (*3*). Naturally occurring exencephalia has been reported in several strains of mice (T_1, DB′, Cd/Cd, and AKR-T × Brachy) (*4*), but there are no reports of the occurrence of this anomaly in untreated CF1 mice.

In the course of establishing disease-free breeding colonies at the Argonne National Laboratory, many CF1 female mice were delivered of their offspring by cesarean section. Naturally occurring exencephalia was seen frequently enough to make it necessary to measure its incidence more precisely.

The breeders used to initiate our laboratory's colonies were obtained from Carworth, Inc. Those used for this study were first-, second- and third-generation descendants of the original stock. All were housed in plastic shoebox-type cages (*5*) with white pine shavings as bedding, at a room temperature of 22° to 24°C, a 30 to 40 percent relative humidity, and a light cycle of 12 hours light and 12 hours dark. The diet was Wayne Lab-Blox (*6*) and water. The cesarean sections were performed between the 14th and 20th day of gestation.

During a 2-week period, 90 cesareans were performed and 1056 fetuses examined. Eleven litters contained exencephalic fetuses, one per litter. Thus, the incidence of litters affected (11 of 90) is 12.2 percent, and the incidence of fetuses affected (11 of 1056) is 1.04 percent. No other anomalies were seen.

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22 March 1968

Caudate Unit Responses to Nigral Stimuli: Evidence for a Possible Nigro-Neostriatal Pathway

Abstract. *Electrical stimulation of the substantia nigra evokes depressant and facilitatory responses from individually recorded caudate nucleus neurons. These effects resemble those elicited from caudate cells by microiontophoretic ejections of dopamine. Since histochemical evidence suggests that dopamine-containing fibers link the substantia nigra with the caudate, this pathway may mediate the changes in caudate spike rates produced by nigral stimuli.*

Andén *et al.* (*1*), using fluorescence histochemical methods, have described a dopaminergic pathway consisting of fine fibers which arise from the substantia nigra and terminate in the neostriatum, especially the caudate nucleus. Numerous clinical and biochemical observations suggest possible involvement of this pathway both in the control of caudate dopamine levels and in the production of "extrapyramidal" motor deficits such as parkinsonism (for a review, see *2*). When dopamine is applied iontophoretically from multibarrel micropipette assemblies (microiontophoresis) near caudate cells, the rate of discharge of 50 to 60 percent of these neurons is depressed, while the spike rate of approximately 10 percent of the cells is facilitated (*3*, *4*). Presumably, then, electrical activation of a dopaminergic neural input into the caudate should also elicit both depression and facilitation of caudate unit firing. Several investigators, however, have reported only facilitatory responses from caudate cells following nigral stimuli (*4*, *5*). The present experiments demonstrate that the effects of nigral stimuli are entirely consonant with local caudate pharmacologic responses. In addition to facilitation, electrical stimulation of the substantia nigra markedly depresses the discharge rates of a relatively large percentage of caudate neurons.

Twenty cats were anesthetized with ether, then electrolytically decerebrated at the midpontine level. After the ether was discontinued, the right cerebral hemisphere was exposed and protected with a pool of warm mineral oil. Bipolar stimulating electrodes were advanced downward through the cortex into the posterior portion (pars compacta) of the right substantia nigra (Fig. 1A). The nigra was stimulated with 10-msec trains at intervals of 1.3 seconds; each stimulus consisted of 4- to 5-volt rectangular pulses of 1 msec duration at a frequency of 400 per second. Multibarrel micropipette electrodes, prepared according to previously published methods (*6*), were placed in the head of the right caudate under stereotaxic control. The boundaries of the area sampled within the caudate were defined by the coordinates (*7*): A 14.5–16.5, L 3.5–6, D (+) 4–7.5 (Fig. 1B). Poststimulus time histograms (*8*) of caudate extracellular spike discharges were obtained with a computer of average transients (CAT 1000).

Most recordings were made from "silent" caudate units made to fire by the continuous ejection with 5 na of current of an excitant amino acid, *dl*-homocysteic acid, at a concentration in the micropipette of 0.5 to 1.0*M* and at *p*H 8.5. The firing patterns of activated units were monitored on an oscilloscope. Only neurons producing spikes uncomplicated by the firing of neighboring cells were studied. In addition, continuous contact with a neuron for a minimum of 10 minutes was required in order to obtain two successive summations of the effects elicited by nigral stimuli on unit discharges. The discharge patterns of 42 of the 100 caudate neurons meeting these criteria were not altered by electrical stimulation of the substantia nigra (Table 1) (Fig. 2D). Nigral stimuli, however, reproducibly depressed the discharge frequencies of 44 caudate cells. The depression periods had a mean poststimulus latency of 18.3 msec and a duration of 58.8 msec; the rates of discharge during the periods of depression were reduced by 75 to 80 percent (Fig. 2A). About half of the units initially depressed by nigral stimuli had periods of later facilitation (Fig. 2B). These delayed facilitations had a mean poststimulus latency of 124 msec and a mean duration of 187 msec. In contrast to the delayed facilitation just described, 14 caudate neurons responded to nigral stimuli with patterns of apparently "pure" facilitation having a much earlier latency of 14.2 msec (Table 1). The number of spikes during

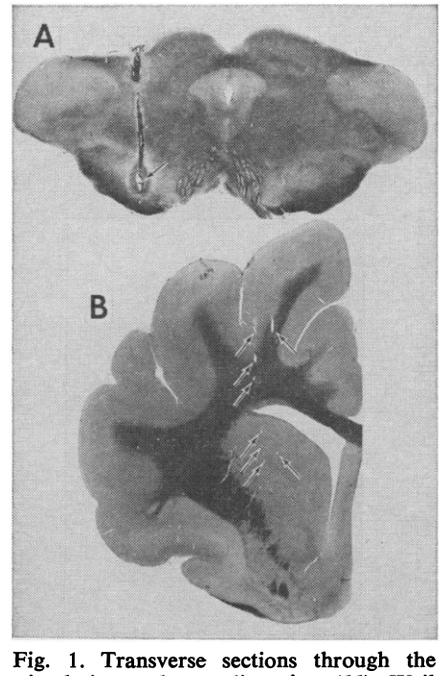

Fig. 1. Transverse sections through the stimulating and recording sites (*11*); Weil stain, 30 μ thickness. (A) Mesencephalon at plane A 3.5–4.0 (*7*). Lesion (arrow) in the substantia nigra was produced postexperimentally by passing electrolytic current through the stimulating electrode. (B) Telencephalon at plane A 15.5–16.0 (*7*). Arrows indicate recording electrode paths of two separate stabs at this level. Units were recorded in the caudate nucleus (lower cluster of arrows).