production of disease, or of pathological lesions, either in the host or in cells in vitro. Likewise, searches for cancer agents have relied on manifestations of overt malignancy, probably under biologically unfavorable conditions. The finding that transmissible, replicating agents can be detected by the induction of a biochemical "lesion" in a normal host, in the form of an abnormal alteration in concentration of a blood enzyme, has apparently permitted the uncovering of agents masked or "silent" in reference to standard criteria. The tumor-producing potential of this factor is unknown at present, although it has been studied only in adult animals and for limited periods in respect to latency. The quantitative correlation of plasma lactic dehydrogenase with experimental mouse tumor growth and regression, however, is now firmly established (*3, 4*) and it seems quite clear that the transmissible enzyme elevation described here is identical to the phase-three plateau previously described as an initial part of the multiphase curve associated with tumor implantation and growth (*4*). The transmissible, enzyme-elevating factor probably also explains the failure of the host plasma lactic dehydrogenase to return to completely normal levels following tumor regression (*4*). Such a five- to tenfold abnormal elevation has persisted for periods exceeding a year following "complete" tumor regression and has been transmissible when such host plasma was injected into normal recipients (*5*).

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## Effect of Pyramidal Tract Activity on Dorsal Column Nuclei

*Abstract.* The response of single units in cuneate and gracile nuclei to cutaneous stimulation can be modified by prior stimulation of the motor cortex of the cat. Both excitation and inhibition of these neurons can be effected via the pyramidal tract.

Direct cortical projections to various sensory nuclei of higher mammals have recently been described (*1*). Although the anatomical descriptions differ slightly, it is evident that the gracile, cuneate, and spinal trigeminal nuclei are abundantly supplied with corticofugal fibers coursing within the pyramidal tract. Concurrent physiological studies (*2*) have shown a depressive effect of central structures on peripherally evoked potentials in the dorsal root (DR reflex), dorsal column relays, dorsal column nuclei, spinal trigeminal nucleus, cochlear nucleus, and the olfactory bulb. Single unit analysis (*3*) of the spinal afferent paths and of the retina, however, have shown not only an inhibition but also an excitation from central structures. We have previously shown (*4*) that the motor cortex of the cat has both an excitatory and an inhibitory influence on cuneate neurons. Responses in some cuneate neurons could be evoked by single shocks (0.02 to 2.0 msec in duration) to the pericruciate cortex, the latencies ranging from 5 to 30 msec. Other cuneate neurons were rendered less excitable for periods of 100 to 200 msec, beginning 10 to 30 msec after a single shock or a train of shocks (300 per second) to the motor cortex. The inhibition was manifested by changes in the response properties of the affected neuron when the footpad was stimulated (decreased probability of response, increased initial spike latency

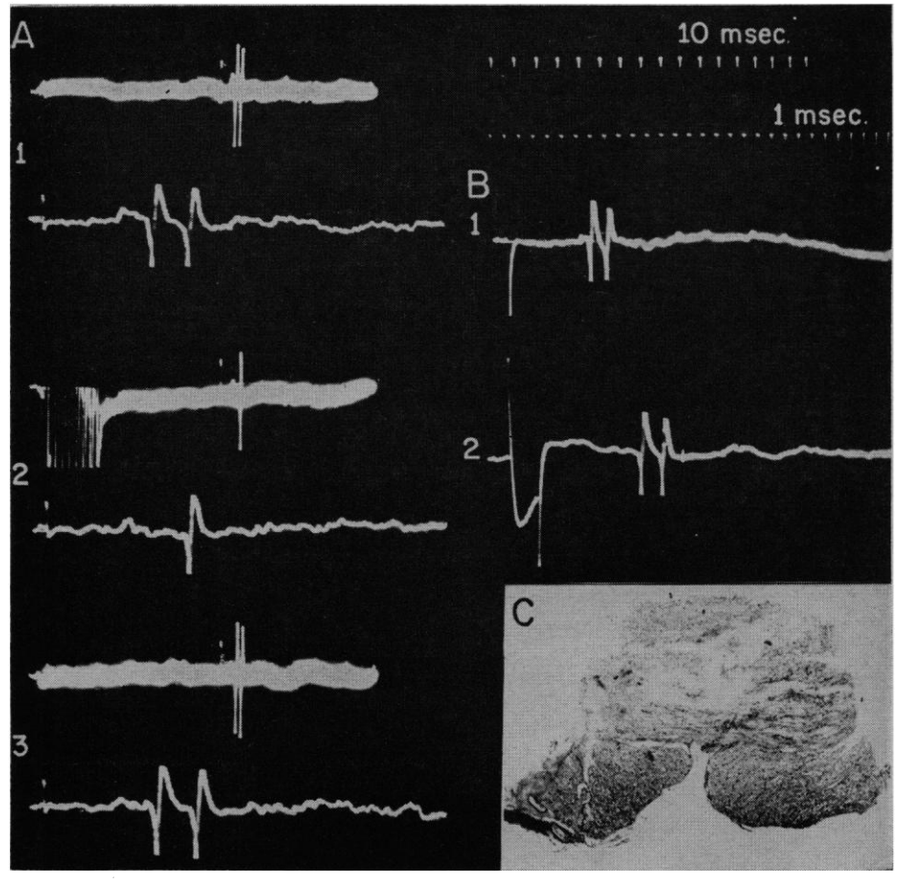


Fig. 1. Responses of two cuneate units recorded after brain-stem transection. (*A*) Inhibitory interaction. Each pair of sweeps shows same event; the upper, slow sweep was triggered 85 msec before the lower, fast sweep. Traces (1) and (3) response of unit in left cuneate nucleus to left forepaw stimulation. (2) Increased latency and decreased number of spikes per discharge to the same forepaw stimulus after a conditioning train (eight shocks at a rate of 312 shock/sec) to the right motor cortex. (*B*) Response of another unit in left cuneate nucleus to peripheral and cortical stimulation. (1) Fired by ipsilateral forepaw shock. (2) Fired by shock to right motor cortex. The 1 msec time trace applies to the fast sweeps in (*A*) and all sweeps in (*B*). (*C*) Luxol-fast section of what remained of the pyramidal tract after transection. Note that lateral borders of the pyramidal tract are damaged (× 17).

and fewer spikes per discharge). Both cerebral hemispheres displayed these modifying capabilities, although the cortex ipsilateral to the unit under observation was uniformly less effective than the contralateral cortex.

In this study (*5*) cats were anesthetized with Nembutal and paralyzed with decamethonium bromide (or Flaxedil). Single units in the cuneate and gracile nuclei were isolated by conventional 0.5 to 1.5 $\mu$ micropipette techniques. Responses in these units were evoked by needle electrodes in the footpads. Because it is not possible to excite only pyramidal tract elements in the intact nervous system, the bulb was isolated from the midbrain so that only the pyramidal tract was intact. The brain stem was exposed by a ventral approach, and the tissue was removed by suction under direct vision. The transection was begun on each side of the pyramids at the level of the trapezoid body and carried through to the bony tentorium. All tissue, including the middle and the superior cerebellar peduncles, was carefully removed so that there was a gap of a few millimeters between the rostral and caudal stumps of the transected brain stem. Bipolar silver-ball electrodes were then placed on the pericruciate cortex of each hemisphere for excitation of corticofugal elements; only the pyramidal tract, however, could carry activity beyond the transection. At the end of each experiment the brain was perfused with formalin, removed, sectioned, and stained in order to assess the extent of pyramidal tract isolation (Fig. 1*C*).

In spite of this radical surgical intervention, units in the dorsal column nuclei were affected by stimulation of the motor cortex to the same extent as were those in intact preparations. Nearly one-third of the units could be driven and two-thirds could be inhibited from the cortex; occasionally, a unit which could not be affected was isolated. Figure 1 shows the responses of two units, the first inhibited and the second driven by the motor cortex. The histological section shows the extent of pyramidal tract that remained in this animal; examination of other sections revealed nearly complete destruction of the overlying medial lemniscus-trapezoid complex, which can be seen in Fig. 1*C*. The remaining brain stem was totally transected. Evidently both excitation and inhibition can be transmitted to the bulb by way of the pyramidal tract. The excitatory effect appears to be direct. This is deduced from the following of high stimulus frequencies (in excess of 100 per second), the brief latency and the small latency dispersions found in some cortically driven units, and the profound difficulty of demonstrating excitation when the pyramidal tracts alone were transected. The inhibitory pathway, on the other hand, appears to be less direct. Perhaps the pyramidal tract projections to the reticular formation (*6*) are involved; certainly inhibition remains, albeit with altered characteristics, after transection of the pyramidal tract. Nevertheless, it is interesting that both anatomical and functional evidence points to a direct connection between the somatic motor and sensory systems via that phylogenetically recent system, the pyramidal tracts.

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## Hormonal Induction of Vascular Tissue in Tobacco Pith in vitro

*Abstract.* The direct addition of indole-3-acetic acid into sterile-cultured stem pith sections of *Nicotiana tabacum* through inserted glass pipettes has induced cell division and differentiation where such activity would not normally occur. This evidence lends support to the theory that indole-3-acetic acid is the hormone that limits xylogenesis.

There is considerable evidence that indole-3-acetic acid (IAA) plays a major role in the differentiation of vascular tissue in plants. The classical study of Jacobs (*1*) illustrated that vascular tissue can be induced around a wound in vivo when the original vascular strand has been severed and external IAA is introduced through a petiole in the node above the wound. Other workers (*2*) have demonstrated in vitro that vascular tissue can be induced in undifferentiated callus tissue either by grafting a bud into the callus, thus providing it with hormones diffusing from the apical tissue, or by applying indole-3-acetic acid or naphthaleneacetic acid in a lanolin paste into an incision in the callus. Pith tissue which is, essentially, undifferentiated parenchyma presents a region which has a definite orientation in the plant as opposed to the nonpolar orientation of callus. Previous work (*3*) has shown that no vascular tissue was induced in sterile cultures of tobacco pith sections when the culture medium contained only IAA as the growth-promoting substance. In fact, no cell divisions were initiated at any concentration of the hormone. Since it was shown that division could be induced with mixtures of IAA and other growth-promoting substances, the supposition was that, although IAA may cause differentiation, another growth-promoting substance is necessary to promote cell division.

The experiment described in this report is part of a study designed to give quantitative and qualitative evidence of the amount and type of differentiation induced in response to IAA and other differentiation factors in undifferentiated tissues. The observations were made during a study of the response of tobacco pith to IAA supplied through glass pipettes inserted directly into the center of the tissue (Fig. 1). Pith cylinders were removed from *Nicotiana tabacum* by boring through lengths of stem with a sterile cork borer slightly smaller in diameter than the entire pith cylinder. The pith sections were cut into 15 mm pieces and, after insertion of Pyrex glass pipettes into the morphological apical end, were placed in culture tubes containing agar-solidified Riker's tobacco medium (*4*), a nutrient mixture which contains no IAA and does not support growth of the pith. The pipettes were filled with the additives through holes pierced in the polyethylene caps that cover the tubes. The caps were sealed with small squares of cellophane tape. The pipettes were refilled as they emptied. The cultures were maintained in a culture room at 25°C with a 12-hour light-dark cycle to a maximum of 42 days, some sections being terminated each week and fixed for sectioning. In the present experiment the concentration of hormone supplied to the tissue was 0.5 mg/liter. Control cultures were set up with pipettes that contained sterile water or nothing.

The results indicate that no cell divisions occurred until the tissue had been subjected to a prolonged exposure to IAA, for no divisions were observed