Inhibition of Evoked Potentials by Striatal Stimulation and Its Blockage by Strychnine

Abstract. *Brief stimulation of the basal ganglia in cats deeply anesthetized with chloralose produces a selective, prolonged inhibition of multisensory peripherally evoked potentials at different levels of the neuraxis without altering activity in primary sensory pathways. The inhibition is blocked by small amounts of strychnine, administered intravenously.*

The properties of peripherally evoked heterotopic and multisensory potentials, and their cortical and subcortical distribution, have been studied extensively by Albe-Fessard, Buser, and others (*1*). These authors have demonstrated similar responses to somesthetic, visual, and auditory stimulation, particularly in the intralaminar thalamus, nucleus ventralis lateralis, brainstem reticular formation, caudate nucleus, and association cortex; unit analyses of these structures have shown the convergence on single cells of impulses from diverse body regions and sense organs. In an effort to elucidate some of the neural mechanisms involved in the production and modification of these evoked potentials, the effect of prior striatal stimulation was investigated, especially in the intralaminar thalamus and the association cortex (*2*).

In 107 cats, deeply anesthetized with chloralose (80 mg/kg) and immobilized with Flaxedil, peripherally evoked heterotopic and multisensory potentials (*1*) were partially or totally suppressed by prior stimulation of the basal ganglia (*2*). The inhibiting stimulus consisted of 2- to 8-v square wave pulses of 0.5 msec duration, usually delivered as a brief volley (25 msec, 150 to 200 cy/sec), although single shocks did prove adequate for some electrode placements.

The inhibition was selective for the responses which had long latent periods and were recorded cortically and subcortically in regions of convergence for somesthetic, visual and auditory impulses. Figure 1 shows the effects of striatal stimulation on the association cortex (suprasylvian gyrus), intralaminar thalamus (centrum medianum), and brainstem reticular formation (nucleus gigantocellularis).

The onset of inhibition was gradual with a latency of 5 to 10 msec, and maximum inhibition occurred after 40 to 100 msec; recovery was complete after 350 to 400 msec. There were no effects on the primary sensory projection systems such as have been observed with caudate stimulation under different experimental conditions (*3*). The inhibition was not associated with cortical activity (Fig. 1, *B1*) of the type attributed by some authors to the spread of current into the internal capsule (*4*).

The inhibitory effect has been observed as far caudally as the nucleus gigantocellularis of the ventromedial reticular formation of the brainstem (*5*) and, in a preliminary study, hyperpolarizing potentials (IPSPs) have been recorded intracellularly in two cells of the center median-parafascicular complex of the thalamus after caudate stimulation (*6*). Extracellular microelectrode recordings from 76 units have shown that numerous cells are present in the center median which, unlike the inhibited cells of the same nucleus, were excited by striatal stimulation. It is possible that these excited cells are interneurons in the pathway of striatal inhibition.

In systems of simpler synaptic organization, such as spinal reflex arcs, the inhibition of motoneurons can be blocked by the administration of small, subconvulsive doses of strychnine (*7*). The action of strychnine has been attributed to a specific blocking of the inhibitory synapses of motor neurons and of several other postsynaptic junctions (*8*).

To determine whether an analogous

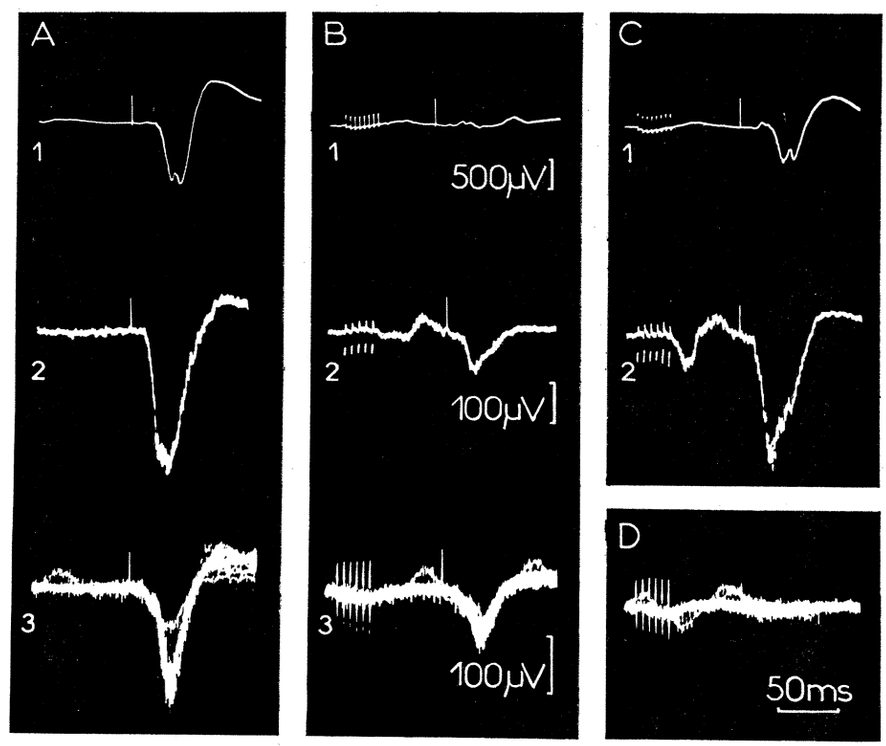

Fig. 1. Inhibition by striatal stimulation of peripherally evoked multisensory responses and blockage of inhibition by strychnine. (*A*) Positive potentials are evoked in the association cortex (*A1*), centrum medianum (*A2*), and brainstem reticular formation (*A3*) by a shock to the homolateral foreleg. (*B*) Brief repetitive stimulation of the head of the caudate nucleus inhibits the peripherally evoked potential in the same three regions. The differences in the degree of inhibition shown in column *B* are representative of variations encountered in different animals. (*C*) The inhibition is blocked by the intravenous administration of strychnine. The caudate volley has no effect on the peripherally evoked potential of the cortex (*C1*) or intralaminar thalamus (*C2*). The same blockage is observed in the brainstem reticular formation but is not shown. The caudate volley alone evokes no reticular response (*D*) nor is the inhibition associated with caudate evoked cortical activity (*B1*). A slight response to caudate stimulation is apparent in the center median (*B2*) which is enhanced after strychnine administration (*C2*). Cotton wick electrodes were used for cortical derivations and bipolar, concentric metal electrodes for subcortical recordings. Positivity is shown as downward deflections. Superimposed traces used for the brainstem reticular formation (*A3, B3, D*).

blockage of inhibition could be obtained in an anatomically more complex system we injected similar doses of strychinine and observed the effect on striatal inhibition.

In ten cats the effect was uniformly the same at all three levels of the neuraxis (association cortex, intralaminar thalamus, and brainstem reticular formation). The intravenous injection of 0.1 to 0.2 mg/kg of strychnine sulfate completely blocked the inhibition produced by stimulating the head of the caudate nucleus. With the doses used, no increases in spontaneous background activity, or in the amplitude of the evoked response were observed after drug administration; hence, no general hyperexcitability could account for the blocking of inhibition.

In the centrum medianum the slight response to caudate stimulation (Fig. 1, *B2, C2*) may reflect the discharge of those cells which microelectrode recordings have shown to be excited by striatal stimulation (*9*). After strychnine administration, this response, though enhanced, does not inhibit the peripherally evoked potential. This would be consistent with the notion that these cells may represent interneurons in the inhibitory pathways and that their synaptic action has been blocked by strychnine. It also shows that occlusion cannot be the cause of the inhibition, because, if it were, the increased response to the caudate volley (Fig. 1, *C2*) would have resulted in even more effective occlusion of the peripherally evoked potential.

Little is yet known about this finding, that strychnine blocks the inhibition of impulses in supraspinal polysynaptic systems (*10*). Not all types of postsynaptic inhibition are susceptible to strychnine (*11*), but the small amounts of this substance used in the present experiments suggest a postsynaptic mechanism of response. Also, the transmitter is probably similar to that of spinal motoneurons; this would be consistent with the notion of Eccles (*12*), that there are relatively few inhibitory transmitters in the mammalian central nervous system.

The cortex does not appear to be an active site of inhibition since subcortical inhibition was still observed after acute and chronic hemidecortication. The inhibitory effect on the cortex (Fig. 1, *B1*) is thus merely the passive reflection of an active subcortical process.

It is probably that the intralaminar thalamus represents only one of several regions which show postsynaptic inhibition in response to striatal stimulation; other thalamic structures such as the nucleus ventralis lateralis, certain reticular regions, and even regions in the spinal cord, may generate postsynaptic inhibition to striatal stimulation (*13*).

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Cytochrome Function in Relation to Inner Membrane Structure of Mitochondria

Abstract. *Projecting subunits of an average diameter of 80Å are found on the cristae of mitochondria prepared from the muscle of* Ascaris lumbricoides. *A spectroscopic examination of the cytochrome content of these mitochondria shows no detectable cytochrome* c_1, a, *or* a_3 *and does reveal cytochromes of types* c *and* b. *Subunits in the same size range are found in cytochrome c deficient mitochondria of the emergent bee, while the frequency of their occurrence along the cristae is decreased relative to the adult bee. Apparently, the cytochrome content of the respiratory chain is not related to the size of the subunits, but may be related to the frequency of occurrence of the subunits.*

Spectrophotometric studies of the stoichiometry and reaction kinetics of components of the cytochrome chain indicated, some time ago, that macromolecular assemblies containing approximately one each of the cytochrome respiratory enzymes might be sufficient for the function of electron transfer and oxidative phosphorylation (*1*). Models of such a system have been shown to be consistent with mitochondrial structure by Estabrook and Holowinski (*2*) and by Lehninger (*3*). More recently, the term "oxysome" has been introduced to represent the concept of a macromolecular assembly of enzymes capable of carrying out all the functions of electron transport and oxidative phosphorylation and specifically including the coupling factors of oxidative phosphorylation and the pathways of energy-linked reversal of electron transfer (*4*).

Observation by electron microscopy of the fine structure units of the inner membrane (IMS), in the size range, 80 to 100 Å, by Fernandez-Moran (5), and more recently by Parsons (*6*), Stoeckenius (*7*), Smith (*8*), and Sjostrand (*9*) has led Green and his coworkers to suggest that these units consist either of the entire assembly of respiratory enzymes (*5, 10*), a "lumped oxysome or "elementary particle" (*10*), or of one or more components of the respiratory chain (*4*), a "distributed" oxysome. There are differences of opinion whether these fine-structure units