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Visual and Auditory Inputs into the Cuneate Nucleus

Abstract. *Sound clicks or light flashes modify somatic sensory activity in the cuneate nucleus of the cat. The techniques of gross potential recording in the cuneate nucleus or medial lemniscal tract, of single unit recording in the cuneate nucleus, and of excitability testing of cuneate terminals demonstrate this heterosensory interaction.*

The cuneate nucleus is the first synaptic relay receiving ipsilateral afferent inputs from upper thoracic and cervical body segments. It constitutes part of an important somesthetic projection system, subserving tactile and kinesthetic sensations. Therman's (*1*) concept of this nucleus as a simple and powerful one-to-one relay for somesthetic information on its way to the thalamus has been subsequently modified by anatomical, physiological, and pharmacological studies. It is now established that cuneate transmission can be inhibited or facilitated by a number of central and peripheral influences. Central modulation has been demonstrated by electrical stimulation of the somatosensory cortex (*2–7*) and the reticular formation (*8, 9*). Afferent cutaneous facilitation (*10*) and inhibition (*10, 11*) have also been observed. Inhibition from central or peripheral sources has been shown to be either presynaptic or postsynaptic, or both (*7, 11*). In addition to relay cells projecting directly to the thalamus, the cuneate nucleus contains interneurons that are interposed between the various central and peripheral pathways and the relay cells. These interneurons play an important role in central and peripheral modulations and appear to be associated primarily with presynaptic inhibition (*6*). In this report, the effects on cuneate transmission of two sensory modalities—vision and audition—are demonstrated.

The cuneate nuclei were exposed in decerebrate (midcollicular transection under ether) or anesthetized [α-chloralose (50 mg/kg) or pentobarbital sodium (35 mg/kg)] and paralyzed (gallamine triethiodide or decamethonium bromide) cats. Single electrical test stimuli were applied to the forepaw or the superficial radial nerve ipsilateral to the cuneate recording site. Brief strong flashes or clicks were used as the conditioning photic or acoustic stimuli, respectively. Four types of responses were recorded: (i) gross potentials either at the surface or within the depth of the cuneate nucleus, (ii) extracellular action potentials from cuneate neurons, (iii) the lemniscal response at the caudal end of the contralateral thalamus, and (iv) antidromic compound action potentials from superficial radial nerves in response to brief electrical stimulation of the dorsal column afferents within the nucleus. Details of these techniques appear elsewhere (*11*).

It has previously been shown that ipsilateral cutaneous afferent volleys generate a response on the surface of the cuneate nucleus which consists mainly of a brief (4 to 5 msec) negative potential (N wave) and a prolonged positive potential (P wave) of about 100 msec duration. The N wave is due to synaptic depolarization of

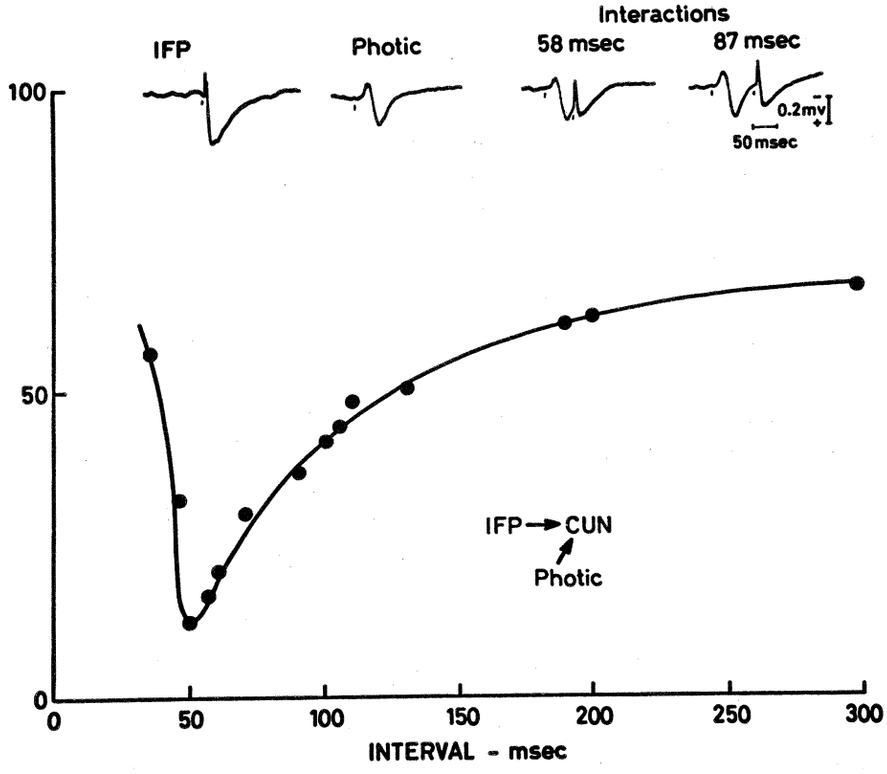

Fig. 1. The effect of photic conditioning stimulation on the size of the surface P wave in the cuneate nucleus (*CUN*) evoked by ipsilateral forepaw (*IFP*) test stimulation. In the sample records above, *IFP* and *Photic* are control records for testing and conditioning stimuli, respectively. In *Interactions*, the conditioning stimulus preceded the test stimulus by the indicated interval. Stimulus artifacts have been retouched. The curve below is a plot of the time course of this inhibition, each dot representing the mean of ten observations at that time interval. Values shown on the ordinate are percentages.

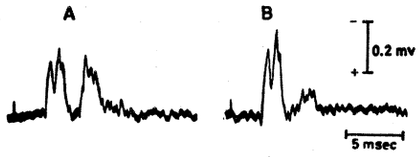

Fig. 2. Excitability change in cuneate tract terminals produced by acoustic stimuli. Sample records from the superficial ulnar nerve in response to microelectrode stimulation at a depth of 1.2 mm in the cuneate nucleus. (A) Testing stimulation (alone). (B) Testing stimulation preceded at 50 msec by conditioning acoustic stimulation.

cuneate cells (*1, 4*), while the P wave has been postulated to be due to prolonged depolarization of the presynaptic terminals of cuneate tract fibers (*4, 5, 7*). Brief flashes or clicks generated similar N and P waves on the surface of the cuneate nucleus (Fig. 1). In response to photic and acoustic stimuli, however, the N wave (10 msec latency) was more prolonged and the P wave reached its peak at 55 msec and lasted about 80 msec. When a P wave was evoked in the cuneate nucleus in response to conditioning photic or acoustic stimuli, it depressed the test P wave evoked by an ipsilateral cutaneous volley. This P wave depression reached its maximum at conditioning-testing interval of about 50 msec and lasted over 200 msec (Fig. 1). This was similar to the effects on the P wave by conditioning stimulation of the adjacent forelimb nerves (*7*), the contralateral sensorimotor cortex (*7*), or remote skin areas in the other limb (*11*).

Another evidence for a visual and auditory influence on the cuneate nucleus was observed by the method of excitability testing (*5, 12*). Microelectrode stimulation within the cuneate nucleus evoked an antidromic response in the superficial radial nerve consisting of an initial spike complex conducted antidromically over the faster cutaneous nerves and a second spike complex that is analogous to the dorsal root reflex (*5*). Conditioning photic or acoustic stimuli caused an increase in the initial spike complex and a depression in the secondary spike complex (Fig. 2), with a similar time course for both effects. This time course was also similar to that observed during the P wave interaction just described. These changes and their time courses are suggestive of presynaptic inhibition (*5, 11*).

A third line of evidence was observed from the effects of photic and acoustic conditioning stimuli on the test mass discharge in the contralateral medial lemniscus evoked by stimulation of the ipsilateral forepaw. Photic and acoustic stimuli depressed the test discharge in the medial lemniscus.

A fourth line of evidence was provided from observations that conditioning photic and acoustic stimuli also inhibited spontaneously firing cuneate neurons as well as those driven by peripheral cutaneous stimulation. The latter influence was demonstrated by a decrease in the probability of discharge, a decrease in the number of spikes per discharge, a lengthening of initial spike latency, or a combination of these effects.

Convergence and interaction between visual, auditory, and somatic sensory stimuli have already been demonstrated in cortical "polysensory" areas of the cat (*13*), monkey (*14*), and man (*15*). Little is known about these interactions at subcortical levels (*16*), and nothing is known about them at the level of the first somatic sensory relay.

Although we have demonstrated modulatory influences of photic and acoustic stimuli on the cuneate nucleus, we have no precise information about the pathways involved. These influences were present but attenuated when the cats were under pentobarbital anesthesia. The persistence of auditory inhibition in decerebrate preparations rules out the necessity for reflex stimulation through the somatosensory cortex. Recently, Chu (*17*) demonstrated that the pyramidal tract was not essential for auditory and visual facilitatory and inhibitory effects on the spinal cord. We cannot, however, rule out a role for the brainstem reticular formation which can receive a multisensory input (*18*) and can exert modulatory influences on the gracile and cuneate nuclei (*8, 9*).

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24 August 1971

Comparative Ability of Hycanthone and Miracil D to Interact with DNA

The report of Hartman *et al.* (*1*) on the mutagenic activity of the antischistosomal agent hycanthone in *Salmonella* concludes with the comment that while published reports are available on the interaction of the related compound, miracil D, with DNA and its effects on bacterial metabolism, comparable information on hycanthone is lacking. It is the purpose of this brief note to summarize the data on the latter agent which have been recorded recently in rather scattered fashion.

In standardized test systems, hycanthone exhibited activity equivalent, on a molar basis, to miracil D in increasing the melting temperature and relative viscosity of DNA—two measures of their ability to complex with this macromolecule. Both compounds inhibited the growth of *Bacillus subtilis* in vitro and of mouse leukemia L1210 in vivo and interfered at equivalent concentrations with DNA and RNA synthesis in these tumor cells in vitro.

In addition to these data from our laboratories (*2*), Waring has recently adduced elegant evidence for the capacity of hycanthone to intercalate between the base pairs of DNA on the basis of measurements of the sedimentation coefficient of circular duplex DNA of bacteriophage øX174 (*3*). Wittner *et al.* (*4*) have demonstrated pronounced activity of hycanthone against RNA synthesis, but not DNA or protein synthesis, in HeLa cells.

These similarities between the two closely related antischistosomal com-