

Fig. 1. Schematic structure of 3C 33. The southerly component has an intensity about 2.5 times greater than its companion. The center of gravity of the radio emission thus falls to the south of the parent galaxy, which is indicated by a small ellipse.

ponents compared with their separation, 3C 33 (8) is a particularly interesting object. This is shown schematically in Fig. 1. Because of its small size, the peak-brightness temperature in the brighter (southern) component is very high, more than 3  $\times$  10<sup>5</sup> °K at 1000 Mcy/sec, which is only an order of magnitude less than that for Cygnus A. Because 3C 33 has a high galactic latitude  $(-49^\circ)$  as well as a high radio surface brightness, it is perhaps the best double source in which to search for optical emission from the radio components. Accurate radio positions (9, 10) may be combined with the brightness distribution information to give the following position (1950.0) for the brighter component:

$$\alpha = 01^{h}06^{m}12^{s} \pm 1.5^{s}$$
  
 $\delta = 13^{o}02'30'' \pm 15''.$ 

The orientation of the major axis of 3C 353 has not previously been determined. It was measured by tracking the source with the interferometer at an effective spacing of 460 wavelengths N-S. There is an indication from the high-resolution observations (3250 wavelengths N-S) that the major axis defined by the bright peaks in 3C 353 differs by about 7° from that defined by the total emission from two components. For the other sources the

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brightness distribution seems fairly symmetrical about the minor axis.

In our initial survey (2) we reported that the components of Hercules A were nearly circular. This is not correct, but an explanation for the discrepancy in our earlier result will require a sequence of observations with gradually increasing resolution along the minor axis.

High-brightness regions at the outward extremities of double radio sources seem to be characteristic features of these objects. In both Hercules A and Cygnus A (and, to a lesser degree, also in 3C 33), the effective component separation increases with resolution along either the major or the minor axis. If the high-brightness regions were in the form of bright ridges at the extreme edges of the double sources and aligned perpendicularly to the major axis, the effect of changing separation with resolution would only be noticed along the major axis. The effect mentioned comes from the nature of the visibility functions and a detailed explanation is inappropriate here. However, the bright regions do tend to be points rather than ridges. It has been suggested (4) that the emission peak represents a shock front of compressed magnetic field formed ahead of an expanding "blob" of energetic plasma. This explanation still seems reasonable, but the shock front is evidently not planar over an area comparable to the minor-axis component diameter.

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## **Tremorine: Its Peripheral Action** on Striated Muscle

Abstract. Tremorine, injected intraperitoneally into rats, induces the same kind of calcium release in the motor end-plates as that induced by acetylcholine-like agents. Since the same effect results even if the appropriate motor nerve has previously been transected, it is concluded that this myoneural action of Tremorine is not due to a central excitation but rather to a peripheral stimulatory property of the drug.

Tremorine (1-4-dipyrrolidino-2-butyne) was described in 1956 by Everett (1) and is known to produce a Parkinsonian-like syndrome in a variety of laboratory animals. Besides tremor (1). hypersecretion of saliva, bradycardia, and transient mydriasis have also been reported to occur in animals treated with Tremorine (2). The Tremorineinduced tremors in rats have been employed in the evaluation of drugs for Parkinsonism (3).

Recently, however, De Groat and Volle (4) found that the active metabolic product, oxotremorine, resulted in ganglionic firing from the cat's superior cervical ganglion, suggesting a peripheral site of action of this drug. Since the myoneural junction shows several characteristics similar to ganglionic synapses, the question arises whether the Tremorine-induced tremor also might be, at least in part, due to some peripheral (myoneural) action of this drug. A convenient way to answer this question is to trace histochemically the release of calcium in the postjunctional cytoplasm of the motor end-plate. It has been shown by Sávay and Csillik (5) that both electrical stimulation and the administration of depolarizing drugs (such as cholinesterase inhibitors and carbaminoylcholine) result in the appearance of histochemically detectable calcium in the post-junctional cytoplasm of the fundamental cells right below the nerve terminal. Experiments performed by this technique, as reported here, prove that Tremorine has both central effects and a well-defined peripheral myoneural action.

Twelve normal, 150- to 200-g albino rats were injected intraperitoneally with Tremorine (50 mg/kg). In another 12 animals, the left phrenic nerve was transected intramuscularly 1 to 14 days prior to the administra-

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Fig. 1. (A) Release of calcium in the post-junctional cytoplasm of a motor endplate (diaphragm of the rat) 10 minutes after an intraperitoneal injection of Carbachol (1 mg/kg) ( $\times$  1000). (B) Release of calcium 30 minutes after an intraperitoneal injection of Tremorine (50 mg/kg). Arrows point to nuclei.

tion of the drug. Tremor started 4 to 10 minutes after the injection and was accompanied later by a supersecretion of the Harderian glands and salivation. Thirty to sixty minutes after the injection, the rats were killed by decapitation; the diaphragms were excised and frozen on specimen holders by means of dry ice. Longitudinal sections were cut on a cryostat, dropped immediately into acetone, floated in 2 percent sodium barbital, and stained for liberated calcium according to the method described by us earlier (5, 6).

In the diaphragms of normal rats, Tremorine induced the release of calcium in well-localized areas in the postjunctional cytoplasms ("soleplates") of the myoneural junctions. The patterns obtained were virtually the same as those obtained after supramaximal electrical stimulation (5), or after the administration of neostigmine or Carbachol (carbaminoylcholine). Heavily stained granules outlined the fundamental cells, outlining the nuclei (Fig. 1). Smaller doses of intraperitoneally injected Tremorine (10 and 25 mg/kg) resulted in less characteristic microscopic patterns, even though the outlines of the soleplates could also be easily distinguished in these experiments.

served in those animals in which the phrenic nerve had been transected 1 to 3 days prior to the administration of the drug. There was a marked decrease in the intensity of the reaction and in the number of granules showing evidence of liberated calcium on the 4th day after the nerve was transected; by the 5th day there was no evidence of liberated calcium. Thus the reaction was entirely similar to that observed earlier in animals treated with Carbachol. From the 8th day after transection onward, after injection of the same doses of Tremorine, there appeared a peculiar linear reaction on the surfaces of muscle fibers, extending up to 100 to 200  $\mu$  in length. This kind of "surface reaction" was observed previously in animals under similar experimental conditions injected with neostigmine or Carbachol. The reaction has been ascribed to the altered sensitivity of denervated muscles to acetylcholine and related compounds (6). It appears, therefore, that the action

Virtually the same pattern was ob-

of Tremorine on the myoneural junction resembles in all histochemical details that of acetylcholine-like agents. The experiments reported here support the conclusion that the main action of Tremorine is peripheral rather than central. On the basis of pharmacological studies with this drug (1-4, 7), there remains little doubt that cholinergic effects on various central and ganglionic levels contribute to the general picture evoked by Tremorine. Thus, it appears that the total effect of Tremorine consists of a composite action on cholinergically mediated junctions, probably due to the liberation of acetylcholine in a variety of synapses.

Whether the actual effect observed in our experiments was due to Tremorine itself or to its activated oxo-derivate (7) should be decided in the future by similar experiments carried out with oxotremorine.

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## **Protein Synthesis Enhanced** in the Liver of Rats Force-Fed a Threonine-Devoid Diet

Abstract. There is enhanced incorporation of leucine-C<sup>14</sup> into proteins in cell-free preparations from livers of young rats force-fed a threonine-devoid diet for 3 days. This increased protein synthesis in the liver is related predominantly to enhanced activity of ribosomes. The aggregates of liver ribosomes (ergosomes or polysomes) as measured in a sucrose gradient indicated a shift from lighter toward heavier ergosomes with a decrease in monomers.

In earlier studies (1-3) we found that young rats force-fed for 3 to 8 days purified diets devoid of single essential amino acids developed pathologic changes that closely resembled many of those found in infants with kwashiorkor (4). The morphologic changes consisted of a periportal fatty liver, excess hepatic glycogen, and atrophy of the pancreas, submaxillary gland, stomach, spleen, and thymus. Among the biochemical changes in the livers of these experimental animals were increases in lipid, glycogen, total RNA, and in the incorporation in vivo of amino acids into protein (2, 3). The last-mentioned finding was particularly surprising in an animal in which obvious pathologic changes were readily produced by a regimen deficient in an amino acid. However, subsequent reports by others (5) substantiated the occurrence of enhanced protein synthesis in the livers of animals with amino acid or protein deficiencies under a variety of experimental conditions. The studies in vitro which we are now reporting show that the increased protein synthesis in the livers of rats forcefed a threonine-devoid diet is related predominantly to enhanced activity of ribosomes.

Male and female Sprague-Dawley rats (70 g) were force-fed for 3 days a purified complete diet or one devoid of threonine (3). Each animal received