dase inhibitor (iproniazid). The oxidative deamination catalyzed by monoamine oxidase (MAO) does not play as prominent a part in experiments on cerebral synaptic transmission, because here the DMPEA is given by closearterial injection, thus reducing exposure to the MAO *before* the DMPEA reaches the site of action. Hence, increasing the number of methoxy groups in the ring, that is, masking the hydroxy by converting them to methoxy groups, reduces cerebral synaptic activity and, in contrast, reduces vulnerability to destruction by oxidative deamination. Thus, the resultant effect is influenced by several opposing factors such as the two mentioned.

In the case of LSD, which showed similar impairment of cerebral synaptic function and of behavior in our animal experiments (11, 12), we also measured the impairment of human behavior resulting from synaptic inhibition, which we have shown in animals to be most marked in an area involved in visual association (14), with an objective visual perception test. This test shows that a perceptual dissociation can be induced in schizophrenics by subclinical doses of LSD which have no effect on the normal controls (15). This sensitive quantitative test may reveal behavioral changes in humans where other investigators (16) have been unable to do so by gross observation in an unstated number of subjects given DMPEA orally. This last-mentioned report suggested that more trials should be conducted with amine destruction reduced by MAO inhibitors. Similarly, depending on gross observation, two other groups (17) could not detect changes in a small number of volunteers given higher doses but no MAO inhibitors.

The qualitative identity of the cerebral synaptic and behavioral actions of the structurally similar DMPEA (18) and mescaline supports the possibility that endogenous DMPEA is a potential inducer of psychosis.

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## **References and Notes**

- 1. A. J. Friedhoff and E. Van Winkle, Nature
- A. J. Friedman and E. Van Winkle, *Nature* 194, 867 (1962); M. Takesada, Y. Kakimoto,
  I. Sano, Z. Kaneko, *ibid*. 199, 203 (1963).
  F. A. Kuehl, M. Hickens, R. E. Ormond,
  M. A. P. Meisinger, P. H. Gale, V. J.
  Cirillo, N. G. Brink, *ibid*. 203, 154 (1964).
  - 96

- 3. N. P. Sen and P. L. McGeer, Biochem.
- Biophys. Res. Commun. 14, 227 (1964). R. E. Bourdillon, C. A. Clarke, A. P. Ridges, P. M. Sheppard, P. Harper, S. A. Leslie, 4. Nature 208, 453 (1965).
- Hornykiewiez, Pharmacol. Rev. 18, 925 (1966).
- (1966). T. L. Perry, Science 139, 587 (1963); \_\_\_\_\_, S. Hansen, L. MacIntyre, Nature 202, 519 (1964); A. Faurbye and K. Pind, Acta Psy-chiat. Scand. 40, 240 (1964); T. Nishimura and L. R. Gjersing, Nature 206, 963 (1965); W. Studnitz and G. L. Nyman, Acta Psy-chiat. Scand. 41, 117 (1965). A. J. Friedhoff and E. Van Winkle, Nature 109 (1971, (1963)
- 7. 199, 1271 (1963). F. A. Kuehl, R. E. Ormond, W. J. A. Van-
- denheuvel, *ibid.* 211, 606 (1966). A. S. Marrazzi, *Recent Advances Biol. Psy-chiat.* 2, 379 (1960). 9.
- 10.
- , in Pharmacological Lecturiques .... Drug Evaluation (Year Book, Chicago, 1964), p. 303.

- 11. K. Tanaka and A. S. Marrazzi, Proc. Exp. Biol. Med. 120, 669 (1965).
- A. S. Marrazzi, Ann. N.Y. Acad. Sci. 96, 211 (1962). 12.
- 13. J. Formanek and A. S. Marrazzi, Fed. Proc. 26, 328 (1967).
- A. S. Marrazzi, in *Hallucination* (Grune and Stratton, New York, 1962), p. 36. 14.
- Recent Advances Biol. Psychiat. 9, 15. 197 (1967). 16. K. D. Charalampous and L. W. Tansey, J.
- 17.
- K. D. Charatampous and L. W. Fansey, J. Pharmacol. Exp. Therap. 155, 318 (1967).
  A. L. Shulgin, T. Sargent, C. Naranjo, Nature 212, 1606 (1966); L. E. Hollister and A. J. Friedhoff, *ibid.* 210, 1377 (1966). 18. We thank Dr. J. R. Bergen of the Worcester
- We thank Dr. J. R. Bergen of the motor for Foundation for Experimental Biology for DMPFA IJ. R. Bermaking available the DMPEA [J. R. Ber-gen, Trans. N.Y. Acad. Sci. 28, 40 (1965)]. 19. Supported by USAF grant AF-AFOSR-767-8.
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## Terminals of Single Ia Fibers: Distribution within a Pool of **300 Homonymous Motor Neurons**

Abstract. The excitatory postsynaptic potentials produced in motoneurons by impulses in single afferent fibers (Ia) have been recorded with the aid of an averaging computer. These responses were used to map the distribution of the terminals of single fibers within the pool of 300 motoneurons of the medial gastrocnemius muscle. Twelve Ia fibers were studied in separate experiments. Monosynaptic excitatory postsynaptic potentials were found in 94 percent of the 77 motoneurons investigated. This finding indicates that each of the 300 motoneurons must receive afferent fibers from almost all of the spindles of the muscle it innervates.

Recent studies (1) on stretch reflexes have raised questions regarding the organization of input to motoneurons. The afferent fibers from primary spindle receptors in skeletal muscle make direct connections with motoneurons which innervate the muscle of origin (2), but the precise distribution of the afferent terminals within the pool of motoneurons has never been established. Limitations in existing anatomical techniques make it difficult to follow all the axonal ramifications of a single neuron in the central nervous system, especially if the branches are widely distributed. In particular, the number of motoneurons receiving terminals from a single afferent fiber and the spatial extent of the terminal branching are unknown. We explored several approaches to this problem before adopting the one described below. In brief, we have recorded the excitatory postsynaptic potentials (EPSP's) produced in gastrocnemius motoneurons of the cat by impulses in a single afferent fiber (Ia) from that muscle. We have used these responses to map the distribution of the Ia terminals among the approximately 300 motoneurons of this muscle. Since these EPSP's are very small, an averaging computer was used to extract the signals from the baseline noise.

Two types of experiments, differing slightly, were carried out on cats anesthetized with sodium pentobarbital. In both, all of the hindlimb nerves were cut, except for the nerve supplying the medial gastrocnemius muscle. Some of the branches of this nerve were also severed, reducing the sensory input from the medial gastrocnemius to about one third of normal. The dorsal roots through which this remaining input was channeled were repeatedly subdivided and tested until a rootlet was found which yielded electrical records meeting all criteria (3) for identification of discharges from a single group Ia fiber. All other dorsal roots from lumbar 6 through sacral 2 were then cut so that the afferent connections of the medial gastrocnemius were finally reduced to a single group Ia fiber. Using 3- to 5megohm micropipettes filled with 3MKCl, we made intracellular recordings of the EPSP's produced in medial gastrocnemius motoneurons by impulses in this fiber when the intact branch of the nerve to this muscle was stimulated electrically. An averaging computer (CAT 400B) was used to summate a large number of individual EPSP's and thus to improve the ratio of signal to noise.

In later experiments a more flexible variation of this technique was introduced in which Ia impulses, evoked by stretch and recorded from the dorsal root filament, were used to initiate the sweep of the averaging computer. The remaining dorsal roots were not severed, since only the EPSP's which were locked in time with the trigger signal (that is, the afferent impulse) were extracted from the baseline noise. If the first rootlet selected for study was subsequently found to be blocked, other filaments could be examined until a satisfactory input was found.

In Fig. 1 a series of recordings from a motoneuron are reproduced illustrating an unusually large EPSP, which was clearly apparent in single sweeps. The electrical stimulus applied to the muscle nerve was adjusted to be just at threshold for the single Ia fiber whose activity was recorded on the lower traces, so that an impulse was observed in approximately half of the sweeps. When no afferent impulse was recorded, no EPSP was evoked, whereas an EPSP was evoked when an impulse was recorded. The results indicate that the EPSP's with which we are concerned were caused by single, all-or-none impulses in a group Ia fiber.

Figure 2 illustrates a "summated EPSP," too small to detect in single sweeps, which was extracted from the

Table 1. Distribution and amplitudes of individual EPSP's evoked by impulses in single Ia fibers. The numbers of EPSP's given in the last column are sometimes less than the numbers of positive responses. Some of the motoneurons from which positive results were obtained deteriorated during the recording period as evidenced by a decrease in their membrane potentials. The amplitudes of the EPSP's obtained from these cells have been omitted from the table.

Stilmulus mode	Ia con- duction velocity (m/sec)	Moto- neurons recorded (No.)	Positive responses (No.)	Longi- tudinal limits (mm)	Amplitude of EPSP's $(\mu v)$
Electrical	76	4	4	2.0	
Electrical	103	10	10	2.5	50, 50, 56, 63, 88, 100, 150, 175, 200, 225
Electrical	88	10	9	1.9	50, 69, 81, 88, 312, 312
Stretch		2	2		
Stretch	72	3	3	0.1	19, 25
Stretch	87	8	8	2.2	41, 59, 63, 75, 125, 125, 144
Stretch	92	13	12	2.4	18, 19, 19, 29, 37, 63, 81, 162, 190
Stretch	82	6	5	3.6	25, 44, 66, 113, 116
Stretch	95	3	3	1.9	74, 77, 111
Stretch	85	5	4	1.1	74, 107, 126, 192
Stretch		9	8	3.8	17, 37, 54, 80, 89, 120, 141, 190
Stretch	100	4	4	2.7	24, 100, 185, 400

background activity by repeating it many times. Traces A, B, and C demonstrate the linearity of the summation technique over a wide range of repetitions. The absence of any response in trace D, recorded with the microelectrode withdrawn to a point just outside the membrane, establishes the fact that the technique used in these experiments did not detect responses of nearby motoneurons, interneurons, or activity in branches of the afferent fiber. All of the responses observed, therefore, were generated across the membrane of the impaled cell. The summated responses in Fig. 2 have the characteristic shape and time course of individual EPSP's seen in Fig. 1. They occur with a latency of

0.6 to 1.0 msec after the initiation of the sweep of the CAT, and they are increased in amplitude during posttetanic potentiation (not illustrated). Hence, they may be identified as summated, individual, monosynaptic EPSP's, produced by repetition of impulses in a single afferent fiber. Such a response denotes a direct projection from the afferent fiber under study.

A summary of the results is presented in Table 1. The responses evoked by 12 afferent fibers in a total of 77 different motoneurons are summarized in Table 1. Each Ia fiber investigated projected to the great majority of the motoneurons which were penetrated in that experiment. Seven of the 12 fibers which



Fig. 1 (left). Simultaneous recordings from a group Ia nerve fiber in a dorsal root filament (lower trace) and from inside a medial gastrocnemius motoneuron (upper trace) to which this fiber projects. An electrical stimulus to the nerve of the medial gastrocnemius was adjusted to be just at threshold for the Ia fiber, causing it to discharge in approximately 50 percent of the sweeps. Six consecutive frames, out of a long series, are reproduced. Frames 2, 4, and 5 show an all-or-none action potential in the Ia fiber and the EPSP evoked by it in the motoneuron; frames 1, 3, and 6 show no responses in either. Time and amplitude calibrations for upper traces only; lower traces at lower speed. Fig. 2 (right). "Stimulated EPSP's" produced in a gastrocnemius motoneuron by repetition of many individual EPSP's. Traces A, B, and C illustrate the results of summing 100, 500, and 1000 sweeps, respectively; trace D is the sum of 1000 sweeps recorded after the microelectrode had been withdrawn to a point just outside the motoneuron, as indicated by the sudden disappearance of the resting membrane potential. The summation technique simply adds trace to the sum of the preceding traces, allowing signals timelocked with the trigger pulse to produce a much larger sum than that produced by randomly occurring signals distributed evenly throughout each sweep. The result is not a true average. A calibrating pulse of 200  $\mu v$  was injected at the end of each sweep and summated in the same manner as the signal.

were isolated projected to all of the motoneurons from which recordings were taken. In each of the five remaining cases a single negative result was obtained. Clear-cut evidence for a projection was thus found in 72 of the 77 motoneurons. The results when stretch (53 units) or electrical stimulation (24 units) was used were not different.

There are approximately 300 alpha motoneurons innervating the medial gastrocnemius muscle (4). When these cells were discharged antidromically, field potentials were recorded with microelectrodes over a 6-mm length of the spinal cord. According to Sterling and Kuypers' recent study (5) on motoneurons, their "predominant dendritic orientation is longitudinal." Since these dendrites contribute to the field potentials, increasing their total extent, we infer that the cell bodies of the motoneurons are distributed over a more limited range, probably a 4- to 5-mm length of spinal cord. In all experiments we tried to obtain recordings throughout the full extent of the medial gastrocnemius pool. It was difficult, however, to find and record from motoneurons at the limits of this cell column. The maximum longitudinal separations of cells from which positive responses were obtained in each experiment is given in Table 1. The greatest separation found in this rather small sample was 3.8 mm, but studies on projections of Ia fibers to heteronymous motoneurons (lateral gastrocnemius) indicate that the terminals of a single Ia fiber are distributed more widely.

The amplitudes of the EPSP's recorded in this series ranged from 17 to 700  $\mu$ v, which encompass the values reported by Kuno (6). The "rhythmic EPSP's" described by Burke and Nelson (7) were much greater in amplitude and probably represent the largest EPSP's to be found in gastrocnemius motoneurons. They were noted in only 10 percent of the cells examined and probably were produced by impulses in large Ia fibers terminating on the somas of small motoneurons with large input impedances (8). In our experiments the responses produced by the same afferent in different motoneurons varied widely in their amplitudes, rise times, and subsequent time courses, suggesting that the numbers of boutons terminaux and their locations on the motoneurons differed from cell to cell in a manner consistent with the model of Rall and his colleagues (9).

Two different types of negative results were encountered. One type resulted from conduction blocks produced during the dissection of dorsal root filaments. Blocks which were distal to the recording electrodes were readily recognized, but those occurring at the zone of root entry proximal to the recording electrodes were not suspected until intracellular recordings revealed a complete absence of EPSP's in all motoneurons. We discarded four filaments for this reason and did not enter the negative results in Table 1. The other type of negative result occurred in experiments in which the afferent fiber was known to be conducting normally as evidenced by positive results in the initial penetrations and in penetrations subsequent to the negative finding. Five examples of this type were found and tabulated. In all cases the negative results were obtained after numerous insertions of the microelectrode into the spinal cord. It is possible that a branch of the afferent fiber had been damaged by the microelectrode or by bleeding within the spinal cord.

We conclude that a primary spindle afferent fiber sends its terminals to a large percentage of the motoneurons of its muscle. Conversely, a single motoneuron must receive afferent fibers from almost all of the spindles of the muscle it innervates. In view of the nearly complete projection of a Ia fiber found experimentally, one is tempted to conclude that the projection is, in fact, complete and that in the case of the medial gastrocnemius each primary afferent fiber sends terminals to all 300 of the motoneurons.

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## **References and Notes**

- E. Henneman, G. Somjen, D. Carpenter, J. Neurophysiol. 28, 560 (1965); *ibid.* p. 599,
  S. Ramón y Cajal, Histologie du Système Nerveux de l'Homme et des Vertébrés (Maloine, Paris, 1909); D. P. C. Lloyd, J. Neurophysiol. 6, 287 (1943); *ibid.* p. 317.
  C. C. Hunt and S. W. Kuffler, J. Physiol. 113, 298 (1951).
- Roy. Soc. London Ser. B. 106, 326 (1930). P. Sterling and H. G. J. M. Kuypers, Brain 4. 5.
- Res. 4, 16 (1967). M. Kuno, J. Physiol. London 175, 81 6.
- (1964)7.
- R. E. Burke and P. G. Nelson, Science 151, 1088 (1966); R. E. Burke, J. Neurophysiol. 30, 1114 (1967).
- 30, 1114 (1967).
  D. Kernell, Science 152, 1637 (1966).
  W. Rall, J. Neurophysiol. 30, 1138 (1967);
  W. Rall, R. E. Burke, T. G. Smith, P. G. Nelson, K. Frank, *ibid.* p. 1169.
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## Agonistic Behavior in Organized and **Disorganized Cotton Rat Populations**

Abstract. Agonistic interaction rate is significantly lower in groups of caged cotton rats (Sigmodon hispidus) from naturally occurring organized populations than in groups composed of strangers. Some type of social structure is apparently present between animals sharing a common area under natural conditions. After a 24-hour period, there is no significant difference in the behavior of the two groups, an indication that a social structure is rapidly formed in the disorganized groups.

Most observations on the social behavior of rats and mice are made on caged populations under artificial conditions due to the fact that these primarily nocturnal animals inhabit areas where observation on naturally occurring populations are impossible. Social disorganization (forcibly placing strangers together) is probably a major factor influencing the intense agonistic behavior commonly observed in caged populations (1, 2). Data on social encounters under natural conditions are very limited and suggest that mutual avoidance may be a common (1, 3) but not universal (4) result of encounters between strange mice.

Calhoun (5) reported on the results of social disorganization caused by introducing aliens into natural populations of Norway rats, but there has been no comparison of the social behavior of animals taken from naturally occurring organized populations with that of disorganized populations created by placing strangers together. We now provide information on the presence or absence of social structure or organization in natural populations of cotton rats, the effects of social disorganization on the behavior of groups of strangers, and the development of social structure in the disorganized groups.

Adult cotton rats (Sigmodon hispidus), one of the most widespread and successful mammal species in southern North America, were trapped live from an area of 0.2 hectare or less. Trapping of these "organized" groups was conducted in Tuscaloosa, Etowah, and Mobile counties, Alabama. No estimate of the home range of the species is available for this area, but recapture of approximately 40 animals indicates that individuals usually move over areas larger than this. Animals in the "disorganized" groups were trapped from areas several kilometers apart. The pos-