



Relation between Size of Neurons and Their Susceptibility to Discharge

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of northward distance. The bloom was also about 1 day later for every 100-foot increase in elevation in the mountainous areas.

As more information is accumulated in subsequent surveys, analyses will be made to determine the relation between weather measurements at the climatological stations and plant development.

Figure 1 shows the periods when lilacs came into bloom throughout Montana in the spring of 1956. In "early" areas, indicated by horizontal lines, lilacs bloomed before 20 May. Areas with no lines were intermediate, with bloom beginning between 20 and 25 May, and the areas of slanted lines were last, with the onset of bloom coming after 25 May. Due to the scarcity of reports from areas above 5000 feet and to the great influence of the irregular terrain at these altitudes, this initial analysis does not extend to higher elevations.

Two large early-blooming areas are

shown on the map, one in the east-central part of the state and the other in the far western valleys. Earliest reports of bloom dates came from Hardin (elevation 2895 feet), in southeastern Montana. A number of reports of early bloom also came from the north-central part of the state, including locations in and near Great Falls and Highwood and the towns of Chinook and Dodson.

Lilacs bloomed late in the northern communities bordering on Canada, in the northeastern section near North Dakota, and in some of the mountain valleys of the western section. Latest reports of bloom dates came from Elliston (elevation 5075 feet), in west-central Montana.

Figure 2 shows the duration, in days, of the period between the beginning and the end of the lilac bloom. Lilacs remained in bloom less than 14 days in the areas where there are horizontal lines and more than 20 days in regions covered

by slanted lines. This map tends to reflect the weather which occurred during the blooming period, and it could provide a basis for understanding relationships between weather and plant development.

For the state as a whole, it required an average of 7 days for the lilacs to advance from opening of first bloom to the date of peak of full bloom and 9 days to develop from peak of full bloom to the end of bloom. The highest station reporting lilac bloom was Lima, in southwestern Montana, with an elevation of 6265 feet, and the lowest station to report lilac bloom was Hinsdale, in the northeastern section, which has an elevation of 2170 feet.

A number of countries have well-organized phenological networks and are effectively utilizing such information in their agricultural planning. It is interesting to note that phenological observations have been made in Europe from the mid-18th century up to the present time, whereas very little has been done in the United States to obtain phenological information on a regional basis.

In 1957 phenological reports are being obtained from individual farmers throughout the state as well as from the climatological observers and garden club members who cooperated last year. Since lilacs are not available for observation purposes in some parts of Montana, an alternate indicator plant, the large common *Caragana* (Siberian pea), is also listed for this year's survey. The *Caragana*, a yellow flowering perennial, completes its various stages of bloom at about the same time as the lilac. Study of the additional reports now being received will permit greater detail and accuracy in the charting and statistical analyses of the phenological information.

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Note

1. This survey was made possible through the cooperation of R. A. Dightman, state climatologist, U.S. Weather Bureau, and of V. E. Iverson and H. N. Metcalf, Horticulture Department, Montana State College.

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Relation between Size of Neurons and Their Susceptibility to Discharge

Neurons in the central nervous system differ widely in the size of their cell bodies. Even in relatively homogeneous groups of cells, such as motor neurons, the differences in volume and surface area are considerable. The functional significance of these variations in size is not known. It is, of course, a well-established fact that the voltage required to



Fig. 1 (Top). Periods when lilacs came into bloom in Montana in 1956. Fig. 2 (Bottom). Duration of the period of bloom.

excite axons electrically increases as their diameter decreases (1). It does not follow, however, that large neurons can be more easily discharged synaptically than small ones. The situation, in fact, appears to be just the reverse, to judge from the studies on spinal reflexes described in this report (2).

The experiments were carried out on cats whose spinal cords had been transected just below the obex. Reflexes were elicited in lumbar ventral roots by electrical stimulation of dorsal roots or large nerve trunks (3). When shocks of sufficient strength were used, the response consisted of two phases (Fig. 1): a brief, relatively synchronous discharge

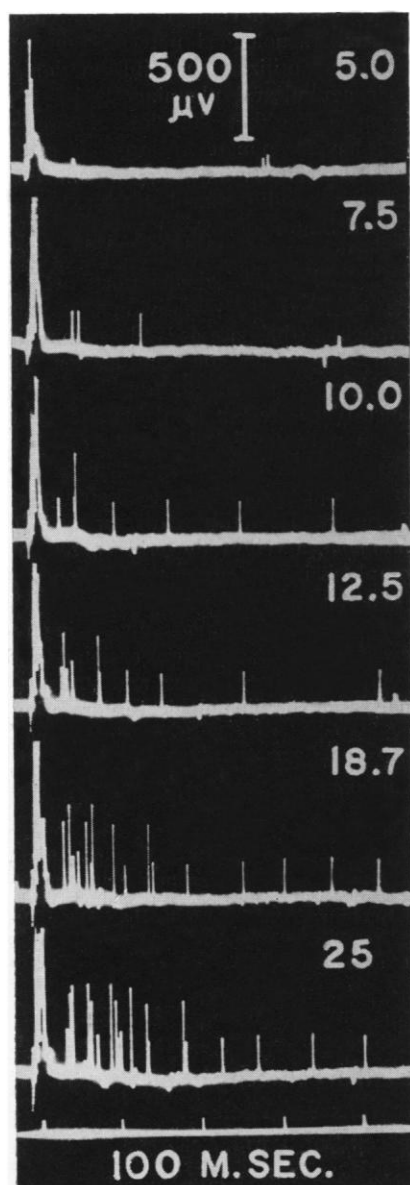


Fig. 1. Reflex discharges recorded from a filament of the seventh lumbar ventral root in response to stimulation of the ipsilateral sciatic nerve. Figures at the right of each tracing indicate the intensity of the stimulation, in volts. The initial deflection at the left of each tracing is the early discharge referred to in the text.

of short latency, followed by rhythmical firing, sometimes lasting a second or more (4). In order to analyze the second phase of the reflex in detail, recordings were taken from fine filaments of ventral roots dissected under a low-power binocular microscope. In these it was possible to distinguish the individual impulses of single motor neurons discharging repetitively. As may be noted in Fig. 1, these impulses may differ considerably in amplitude. The amplitudes vary directly with the diameters of the fibers in which the impulses are conducted (5). It is assumed here that the diameter of axons is related to the size of their cell bodies. Large spikes, accordingly, will be taken to signify discharge of large motor neurons.

Figure 1 illustrates progressive changes in the late response recorded from a ventral root filament as the stimulus applied to the ipsilateral sciatic nerve was increased from 5.0 to 25 v. In the upper record the stimulus was well above threshold for the early reflex but was too weak to evoke the later discharge. The three small spikes shown in this record were probably spontaneous impulses in gamma or "small motor" fibers innervating muscle spindles. Increase in the stimulus strength to 7.5 v caused a single alpha motor neuron to discharge three times. With further increases in the intensity of stimulation, this motor neuron, identifiable by the amplitude of its spikes, responded with progressively longer trains of impulses. At a stimulus strength of 10.0 v, a second unit, with spikes about twice the amplitude of the first, made its appearance, thereafter discharging two, four, and five times in response to stronger shocks. A third and still larger unit appeared at 18.7 v, firing twice at this intensity and four times at 25 v. Further increases in shock strength did not bring any additional motor neurons into the late discharge.

The intensity of stimulation required to elicit prolonged repetitive discharges varied with the level of excitability of each preparation. At times it was only three to four times that necessary for monosynaptic reflexes. Recruitment of progressively larger motor neurons with increase in stimulus intensity was observed regularly. Discharges of slightly smaller neurons with stronger shocks were occasionally noted in single tracings but never as a regular occurrence. In general, units which differed most in spike amplitude differed most in the strength of stimulation necessary to discharge them. Even small differences in the spike amplitude of motor neurons, however, were accompanied by measurable differences in what might be called their reflex threshold.

It appears, then, that motor neurons may be graded according to the ease with which they may be discharged syn-

aptically. At the upper end of the scale are the largest cells, requiring the most intense stimulation. Intermediate on the scale are the smaller, alpha motor neurons, requiring less intense stimulation but not discharging spontaneously. At the lower end of the scale are the "small motor" or gamma neurons innervating muscle spindles. In most recordings from ventral root filaments, these cells can be seen firing steadily without externally applied stimulation. This tendency to be continuously active is perhaps an indication that small cells are so susceptible to excitation that the spontaneous activity of the spinal cord is sufficient to keep them firing.

Although the discharge patterns recorded from different ventral root filaments varied, certain features were regularly observed. The most notable were recruitment of larger units and lengthening of the trains of discharge with stronger shocks; regularity in the rhythm of discharges in each train of impulses, with progressive decrease in their rate; and an inverse relationship between spike height and train length. These characteristics suggest that the excitatory process responsible for the discharge of motor neurons is an intense, prolonged firing of internuncial cells. This activity presumably reaches an early peak of intensity, from which it declines smoothly to resting level. At its maximum, the barrage of impulses from internuncial cells is apparently intense enough to produce repetitive discharges in motor neurons of all sizes. As the excitatory activity subsides, it falls below the levels necessary to discharge the larger cells but remains adequate to fire the smaller motor neurons. Hence the patterns observed in Fig. 1: short trains of large spikes and longer trains of smaller spikes.

It would be premature to draw definite conclusions from these observations, suggestive as they are. It has been shown that the reflex threshold of individual motor neurons varies with the amplitude of the spikes recorded from their axons. The extent to which these findings apply elsewhere in the nervous system remains to be determined. The properties of particular nerve cells are seldom unique except in degree. What little is known, in fact, suggests that they are remarkably alike. This being so, the hypothesis may be advanced for consideration that throughout the nervous system the susceptibility of neurons to discharge is a function of their size.

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References and Notes

1. J. Erlanger and H. S. Gasser, *Electrical Signs of Nervous Activity* (Univ. of Pennsylvania Press, Philadelphia, 1937).
2. This investigation was supported by research grant No. B970(C-1) from the National Institute of Neurological Diseases and Blindness,

National Institutes of Health, U.S. Public Health Service.

3. The stimuli were single square wave pulses of 20 μ sec duration. Reflexes were recorded monophasically from cut ventral roots, usually the seventh lumbar or the first sacral. D-Tubocurarine chloride was administered to prevent reflex movements.
4. In recordings from peripheral nerves, this prolonged firing can only be found in those supplying physiological flexor muscles. Hence it is undoubtedly the late phase of the well-known flexor reflex.
5. H. Gasser, *Ohio J. Sci.* 41, 145 (1941). In fine nerve filaments the position of the fibers with respect to the recording electrodes is relatively unimportant in determining the amplitude of the recorded impulses. This can be corroborated by separating a filament into several finer strands and rearranging these on the recording electrodes.

23 September 1957

Infantile Experience and the Maturation of the Pituitary Adrenal Axis

It has previously been proposed (1) that repeated handling of the infant animal constitutes a stress situation and that experience in infancy with stress results in a greater ability of the organism to adapt to stress in adulthood. Although there have been numerous experiments which have shown that infantile experience affects adult behavior, there has been little work on the effects of infantile experience on developmental processes in the infant organism.

Jailer (2) reported that infant rats, when they were subjected to cold stress, failed to show adrenal ascorbic acid depletion prior to 16 days of age. At 16 days of age, a 19 percent depletion in adrenal ascorbic acid was found. Jailer (3) postulated that the pituitary of rats

younger than 16 days released ACTH as rapidly as it was synthesized, so that, prior to the 16th day, there was no intracellular storage of ACTH to be liberated under stress. As a result, before 16 days of age, the animals were not able to respond to an acute stress with increased release of ACTH. Jailer further reasoned that chronic stress prior to 16 days of age should lead to facilitation of ACTH production and intracellular storage, resulting in increased liberation of the hormone in response to later acute stress. Since it has been postulated that handling in infancy is a stress, it would be expected, on the basis of Jailer's hypothesis, that rats that had been handled up to 16 days of age would liberate more ACTH than nonhandled rats when subjected to cold and would show greater adrenal ascorbic acid depletion. The experiment described in this report (4) was designed to investigate the effects of handling during infancy on ACTH release as measured by adrenal ascorbic acid depletion (5) in the 16-day-old rat.

Sixty-five infant Sprague-Dawley-Holtzman albino rats were used as subjects. Thirty pups were handled from day 1 through day 15, and 35 were not handled in any manner during the first 15 days of life. The handling procedure was the same as that previously described (6). At 16 days of age the pups were randomly assigned to either the stress or control condition. There were thus four groups: (i) handled, nonstressed ($N=15$); (ii) handled, stressed ($N=15$); (iii) nonhandled, nonstressed ($N=17$); and (iv) nonhandled, stressed ($N=18$). The nonstressed animals were removed from their cages, killed by cervical spinal separation, and weighed. Their adrenals were removed, weighed on a 25-mg Roller-Smith balance, and analyzed for ascorbic acid content. The stressed animals were removed from their cages, placed in small individual compartments, and subjected to a cold stress of 5°C for 90 minutes. They were then killed, and their adrenals were removed, weighed, and assayed.

Adrenal ascorbic acid was assayed by a modification of the micro technique of Glick *et al.* (7). After being weighed, the adrenals were placed in a 15-ml ground-glass stoppered centrifuge tube and were thoroughly ground in 2 ml of 0.5 percent oxalic acid. Five milliliters of *N*-amyl alcohol were added to the tube; next were added 3 ml of a 4 mg percent aqueous solution of sodium 2,6-dichlorophenol indophenol dye. The tubes were then thoroughly shaken and centrifuged, the colored alcohol layer was removed, and its optical density was determined on the Beckman DU spectrophotometer at a wavelength of 546 m μ .

The handled and nonhandled groups

showed essentially the same body weights and adrenal-weight/body-weight ratios at 16 days of age. In addition, the mean adrenal ascorbic content of the handled and nonhandled control groups was almost identical (nonhandled, nonstressed = 359 mg percent; handled, nonstressed = 365 mg percent). The handled, stressed animals showed a mean depletion of 109.73 mg percent and the nonhandled-stressed group, a mean depletion of 73.05 mg percent (Fig. 1). Thus, the handled animals showed 36.68 mg percent greater depletion, a difference significant beyond the 0.025 level of confidence ($t=2.42$, $P<0.025$). In terms of percentage depletion, the nonhandled animals showed 20 percent depletion, corresponding to the 19 percent obtained by Jailer, whereas the handled animals had a depletion of 30 percent.

The results of this experiment tend to support both (i) the hypothesis that infantile handling constitutes stress and (ii) Jailer's hypothesis concerning the effects of chronic stress on the facilitation of ACTH production in the infant animal. It should be noted that whereas Jailer's 16-day animals and our nonhandled animals showed only a 20 percent depletion, the 30 percent depletion exhibited by the handled animals in this study closely resembles the adult response to stress, which has been reported to be between 30 percent and 60 percent depletion (8). The question remains whether these results indicate greater intracellular storage, which results in more ACTH liberation at 16 days of age, or more rapid maturation of the pituitary adrenal axis. Preliminary results obtained in our laboratory indicate that handled infant rats respond to cold stress with increased ACTH release earlier than 16 days; this indicates that handling leads to more rapid maturation of the pituitary adrenal axis.

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26 September 1957

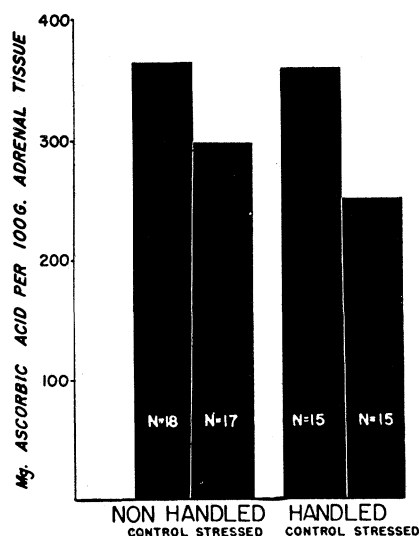


Fig. 1. Comparison of adrenal ascorbic acid concentration in the various groups of infant albino rats.