The Delayed Depolarization in Cat and Rat Motoneurones

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From numerous studies of motoneurones from different species using the intracellular recording technique it is known that the antidromic spike is generally followed by a short phase of depolarization of varying shape preceding the onset of after-hyperpolarization. Previous studies of this event are not extensive (Brock et al., 1952; Araki and Otani, 1955; Eccles, 1957; Eccles et al., 1958a; Machne et al., 1959; Araki, 1960), and it is mostly described as a ‘true’ after-potential homologous with the well-known after-potentials succeeding the spikes in muscle and nerve fibres. This identification may or may not be legitimate and for the time being we have therefore preferred the neutral designation ‘delayed depolarization’.

As Prof. Granit already mentioned (this Volume, p. 35) we have found that in the rat motoneurones delayed depolarization is very prominent and generally has the shape of a hump taking off from the falling phase of the spike. Similar observations have been reported in work on amphibian motoneurones. Granit et al. (1963) devoted special attention to this phenomenon and thought that it possibly might be a sign of dendritic activation. The aim of the present investigation was to extend the analysis of delayed depolarization.

MATERIAL AND METHODS
In the present work some rats were used, but most of the experiments were performed on cats, partly because the properties of cat lumbar motoneurones are so well-known in other respects. The microelectrodes used were filled with 2 M potassium citrate. Otherwise the technique was as in our earlier work (Granit, this Volume, p. 35; Granit et al., 1963). The delayed depolarization seemed to behave in a very similar way in rats and cats. The reported results refer to cat motoneurones when not otherwise stated.

RESULTS
General characteristics of the delayed depolarization
The records topping Fig. 1 show antidromic spikes from six different cat motoneurones. As is seen, the delayed depolarization could assume quite different forms in different cells of this animal. In some cells (records on the left) the delayed de-
polarization had the shape of a more or less prominent hump. Nearly all of the antidromic spikes from rat motoneurones (Granit et al., 1963), and also those reported from frogs and toads (Araki and Otani, 1955; Machne et al., 1959; Araki, 1960), possess a delayed depolarization in the shape of a hump. In the cat, however, many spikes were followed by a smoothly decaying delayed depolarization in which no hump could be seen (Fig. 1, middle records). There existed several intermediary forms between delayed depolarizations with and without a definite hump. Finally, there were also a few units (Fig. 1, records on the right) practically lacking delayed depolarization.

![Diagram of antidromic spikes from six different cat motoneurones.](image)

Fig. 1. Top: antidromic spikes from six different cat motoneurones. All calibrations 10 mV. Spike amplitudes: left row (type I) upper 66 mV, lower 71 mV; middle row (type II) upper 69 mV, lower 87 mV; right row (type III) upper 64 mV, lower 47 mV. The time mark is 1000 c/sec here and in all the following pictures. Bottom: diagram showing the occurrence of type I, II and III units in cat. Cells with spike amplitudes above 60 mV are plotted upwards from the horizontal line. Black areas indicate units with a duration of 70 msec or more of the after-hyperpolarization.

The diagram (Fig. 1) shows the relative occurrence of these three different kinds of antidromic spikes in a material consisting of 95 normal appearing units. About half of all the cells and 60% of those with a spike amplitude exceeding 60 mV had a delayed depolarization in the shape of a hump. Delayed depolarization, smoothly declining or in the shape of a hump, occurred in cells with high membrane and spike potentials from which stable recordings were obtained, sometimes for several hours. Both varieties of delayed depolarization also occurred irrespectively of moderate variations in temperature or depth of the anaesthesia. Only 12 out of the 95 spikes were not followed by any clearly visible delayed depolarization. However, most of these spikes were of fairly low amplitude, and many of them on the verge of spontaneous activity, indicating that the cells were somewhat depolarized. It should be

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emphasized that all the results reported below were more readily obtained from the
cells with large spike amplitudes than from those with low ones.

The black areas in the diagram represent units with durations of after-hyper-
polarization exceeding 70 msec. Delayed depolarization with a definite hump had a
tendency to be more common in cells with short after-hyperpolarizations than in
those with long ones. However, both shapes of delayed depolarization could occur
together with an after-hyperpolarization of any duration.

The amplitudes of delayed depolarization ranged between 1 and 12 mV and were
mostly around 3–7 mV. The durations measured from the onset of the spike varied
between 2 and 13 msec and generally were of the order of 2.5–6.0 msec. The range of
variation in amplitude or duration was about the same for delayed depolarizations
with a hump as for those without it.

The delayed depolarization, when present, was always in sequence to a SD-spike
and was never seen following an IS-spike. In cases of varying IS-SD-latency the
delayed depolarization preserved a constant time relation to the SD-spike. A delayed
depolarization of the same form and size as the one following an antidromic spike
was also generally seen following a spike elicited by a short depolarizing pulse through
the microelectrode or a threshold monosynaptic excitatory postsynaptic potential.
Increase in strength of the ventral root stimulus was never seen to augment the
delayed depolarization. Evidently the delayed depolarization is therefore directly
or indirectly caused by the SD-spike and does not represent any kind of postsynaptic
phenomenon. In all these respects my observations on cats agree with those of Granit
et al. (1963) on rats.

The effects of preceding antidromic spikes

In our earlier work on the rat (Granit et al., 1963) we found that the delayed
depolarization was often greatly diminished after the second of two antidromic
spikes elicited with a short interval, i.e. one of the factors responsible for the delayed
depolarization seemed to have a refractory period. As will be shown below, this was
the case also with cat motoneurones if the intervals between antidromic spikes were
made short enough. At longer intervals, however, the delayed depolarization following
the second of two antidromic spikes was larger than the one following the first spike,
as is demonstrated in Fig. 2A. In the records is also seen that the delayed depolariza-
tion of the second spike has attained a more prominent hump. In practically all
cases in which this experiment was carried out an increase in amplitude of the second
delayed depolarization was seen. In about half of the cases the increase was ac-
companied by an accentuated hump or by the appearance of a hump if there had been
none from the beginning. The same result was obtained if a spike elicited by a short
depolarizing pulse was used as the conditioning stimulus instead of an antidromic
spike.

This increase in amplitude of the delayed depolarization was often maximal at an
interval of about 5 msec. With longer intervals this effect of the conditioning spike
subsided in rough proportion to the lengthening of the interval. The duration of the
effect was rather variable, ranging as a rule from 20 to more than 55 msec after the
onset of the conditioning spike. The time course of the increase in the delayed depolarization showed no relation to the time course of the after-hyperpolarization.

Fig. 2. Cat motoneurone. Spike amplitude 66 mV. All spikes antidromic. Further explanations in text.

In Fig. 2C:1 is illustrated what happens at extremely short intervals. At the first interval of 1.9 msec the delayed depolarization following the second spike is increased in amplitude but has completely lost its hump and is now of the smoothly decaying variety. In Fig. 2C:2 the interval between the first two spikes is 2.8 msec, and here the delayed depolarization presents a prominent hump. The intervals at which the hump of the delayed depolarization in different units disappeared or was greatly diminished, ranged between 1.9 and 4.0 msec. When the hump had disappeared there always persisted a smoothly decaying depolarization which was of larger amplitude than the unconditioned delayed depolarization. When the delayed depolarization had a smoothly decaying shape from the beginning it was never clearly diminished in amplitude at these very brief intervals, although its rate of fall towards the base-line was often increased. When the antidromic repetition rate was very fast as in Fig. 2B:2 and C:2 the hump was accentuated in the second spike but then gradually disappeared leaving a smoothly declining delayed depolarization. In spite of the change in shape of the delayed depolarization its amplitude was in this case rather constant throughout. It almost looks as if there were a lengthening of the refractory period for the hump under these conditions suggesting that it and the smoothly decaying potential may be different entities.

In Fig. 2B and C, presenting short trains of antidromic spikes, it can be seen that practically no further increase in amplitude of the delayed depolarization occurs beyond the second spike for any frequency of stimulation (the case illustrated here

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was the only one seen where the third delayed depolarization actually was a little larger than the second). This was generally the case irrespectively of whether the delayed depolarization was smoothly decaying or had the shape of a hump. In this respect the delayed depolarization seems to differ from the negative after-potential seen in the squid nerve, the cause of which is assumed to be an accumulation of potassium ions at the membrane (Frankenhaeuser and Hodgkin, 1956).

When the steady state membrane potential altered spontaneously or was changed by the application of polarizing currents, the difference between the unconditioned delayed depolarization and the one conditioned by a preceding antidromic spike became less and less at more depolarized levels. In the illustrated case (Fig. 3) the

![Fig. 3. Same cat motoneurone as in Fig. 2. All spikes antidromic. Transient spontaneous change in the resting membrane potential from 1-4. The time mark also represents a reference level for comparison of membrane potentials.](image)

change in steady state membrane potential was spontaneous. The unconditioned delayed depolarization is seen to have been transformed from one with practically no hump (Fig. 3:1) to one with a very prominent hump in the depolarized state (Fig. 3:4), and this hump is not very much affected by a preceding antidromic spike.

**The effects of polarizing currents**

The typical changes in size and form of a delayed depolarization provided with a hump which were obtained with polarizing currents are shown in Fig. 4, A-B. All

![Fig. 4. All spikes antidromic and elicited 1.06 sec after the onset of the indicated polarizing currents. A and B from the same cat motoneurone with spike amplitude 65 mV. The depolarization in B is close to the firing threshold of the cell. C is from a cat motoneurone with spike amplitude 42 mV. Note: In this picture the relation to the time mark gives no measure of the relative membrane potentials.](image)

spikes are antidromic. Fig. 4A shows a case of strong hyperpolarizing current and B what happens to the same cell during a depolarizing current. The effects are somewhat similar to what was seen in Fig. 3. With stronger depolarizing currents it was never possible to obtain any reversal of the hump; it merely went below the baseline in a
manner similar to what is seen after the control spike of Fig. 4C:1, which seemed to be depolarized from the beginning. With very strong depolarizing currents the hump sometimes disappeared. The smoothly decaying delayed depolarization on the other hand could be reversed by depolarizing currents (cf. Eccles, 1957). When no hump existed on the delayed depolarization from the beginning it was sometimes possible to make a small one appear by applying depolarizing currents. With hyperpolarizing currents the hump was sometimes diminished, but only in the cell illustrated under Fig. 4C could it be made to disappear completely. As in our previous work (Granit et al., 1963) the amplitude of the delayed depolarization varied with the applied current in a linear manner.

The effects of synaptic activity

When the membrane potential was changed by using tetanic orthodromic stimulation the effects on the shape and size of the delayed depolarization were as a rule much more prominent than when transmembrane currents were applied. They could also be different from those seen with polarizing currents. In Fig. 5A there is a 2 sec interval between each antidromic spike. When a tetanic stimulus to the brain stem is given (A: 3–6) which decreases the membrane potential, the delayed depolarization attains a very prominent hump and has a long duration compared to what is seen in the preceding controls (A:1–2). This happened in spite of the fact that the membrane conductance was increased during the tetanic stimulus. During the subsequent slow return of the membrane potential towards the control value it is seen that the amplitudes of the delayed depolarizations A:7–8 are about the same as those in A:1–2 although the membrane potentials preceding the spikes A:7–8 are lower than those preceding the spikes A:1–2. That these synaptic actions on the delayed depolarization are not any simple functions of the changes in membrane potential occurring in the soma is further stressed by comparison with Fig. 5B. Here, between two experiments such as the one in Fig. 5A, the same antidromic spike was fired into the cell during

Fig. 5. Cat motoneuron with spike amplitude 60 mV. Stable recordings were obtained from this cell for more than 2 h. (A). 2.12 sec interval between each illustrated antidromic spike. The tetanic stimulation is given to the ipsilateral brain stem at the level of the superior colliculus. The time mark also represents a reference level for comparison of membrane potentials. (B). Antidromic spikes fired during the application of different depolarizing currents with strengths as indicated.

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different strengths of depolarizing currents, and now there is almost no accentuation of the hump.

A synaptic stimulus which hyperpolarized the membrane, i.e. an inhibitory stimulus, had effects which were opposite to the typical excitatory actions described above. In Fig. 6 there is again a 2-sec interval between the antidromic spikes. About 7 sec of

![Graph showing spike potentials](image)

Fig. 6. Cat motoneurone with spike amplitude 68 mV. 2.12 sec interval between each illustrated antidromic spike, 7.4 sec of controls left out between A and B. The same tetanic stimulation is given to the peroneal nerve in A and B. The broken line represents a reference level for comparison of membrane potentials.

repeated controls are cut out between A and B. The same inhibitory stimulus is given in A and B. When the inhibition is maximal (A:2–3, B:2) the spikes do not seem to possess any delayed depolarization whatever. When the hyperpolarizing effect of the stimulus is weaker (A:4–5, B:3–5) there is a gradual return of a smoothly decaying delayed depolarization, whereas the hump does not reappear clearly until later, in the controls. B:5 is here actually elicited at a membrane potential which is but a little lower than that of A:6. In spite of this the hump is virtually absent from B:5, which is subject to inhibitory stimulation, while it is well-developed in A:6 which is a control spike.

The typical diminution or abolition of the hump in the delayed depolarization during postsynaptic inhibition can thus take place in relative independence of changes of steady-state membrane potentials recordable in the soma. This conclusion is

![Graph showing brainstem tetanus](image)

Fig. 7. Rat motoneurone with spike amplitude 68 mV. 1.96 sec interval between each antidromic spike. The tetanic stimulation to the brain stem is given ipsilaterally at the level of the superior colliculus. The continuous line represents a reference level for comparison of membrane potentials.

further underlined by the behaviour of the cell in Fig. 7. This is a motoneurone from a rat in which an antidromic spike is elicited about once every second. The slow tetanus given to the brain stem has a weak depolarizing effect on the membrane in
the beginning, and yet it influences the delayed depolarization in a manner otherwise typically seen with synaptic stimuli which hyperpolarize the membrane. When looking at the membrane potentials it is seen that for instance the spikes 3 and 10 lacking the hump are preceded by membrane potentials lower than those in the controls 1–2 and higher than in control 11–12.

**DISCUSSION**

The delayed depolarization in motoneurones from rats and amphibians generally has the shape of a rather pronounced hump (Machne *et al.*, 1959; Araki, 1960; Granit *et al.*, 1963). In the cat the delayed depolarization has this shape only in about half the number of units, being otherwise of a smoothly decaying variety. There was no fundamental difference in amplitude between delayed depolarizations with and without a hump. However, there were several ways of affecting the shape of a delayed depolarization. The hump could be abolished so that the shape of the delayed depolarization became smoothly decaying. It was also possible to make a smoothly decaying delayed depolarization acquire the shape of one with a hump. One possible explanation for these changes in the shape of the delayed depolarization may be that the hump reflects a current of different origin from the one giving rise to the smoothly decaying delayed depolarization.

The hump had certain properties in common with spike processes: it could not be reversed by polarizing currents, it had a refractory period, it could be accentuated or sometimes made to appear with depolarizing currents, and it could also be diminished, in one case even abolished, with hyperpolarizing currents. Typically synaptic stimuli had effects in the same general direction as the corresponding polarizing currents, but their influence was, as a rule, very much stronger. The synaptic effects could thus rarely be imitated by polarizing currents. Sometimes the typical synaptic actions also occurred independently of changes of membrane potential as recorded in the soma. If the synaptic effects also in this case were dependent upon the actions of the synaptic currents on the membrane potentials, these findings would tend to locate at least the main factors responsible for the delayed depolarization to a membrane provided with synapses but situated far from the recording site in the soma, *i.e.* in the dendrites.

The hypothesis that the smoothly declining delayed depolarization and the hump may represent different phenomena receives some support from the facts that a smoothly declining delayed depolarization contrary to the hump, showed no clear signs of refractoriness and that it could be readily reversed by polarizing currents. As earlier pointed out by Eccles (1957) it bears some resemblance to the after-potential following the spike in the IS-segment and in certain intraspinal fibres. The smoothly declining delayed depolarization may thus well represent a 'true' after-potential directly connected with the SD-spike, but it seems probable from the results of Terzuolo and Araki (1961) that this depolarizing potential is very much longer and larger when the spike is recorded in the proximal part of the dendrites than when it is obtained in the soma. Such a long-lasting depolarization in sequence to an

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SD-spike in the dendrites may well be capable of displaying the increase in amplitude and the accentuation of the hump that was seen when the delayed depolarization followed the second of two antidromic spikes. Actually a conditioning antidromic spike changed the shape of the delayed depolarization in a manner very similar to what was seen with depolarizing currents or excitatory postsynaptic activity. The fact that the time course of these effects of a conditioning antidromic spike showed no relation to the time course of the after-hyperpolarization also tends to locate them to the dendrites, or at least to a site outside the soma.

Summarizing the situation, it thus seems probable, both from the experiments with synaptic stimulation as well as from those with a conditioning antidromic spike, that important factors responsible for the delayed depolarization are located to the dendrites. In several situations the hump behaved differently from, and rather independently of, the smoothly declining delayed depolarization, indicating that these two phenomena may represent factors of different origin. The hump has certain properties in common with spike processes whereas the smoothly declining potential seems to reflect a large depolarizing after-potential or even an extremely slow falling phase of the SD-spike which is propagated out into the proximal part of the dendrites (Terzuolo and Araki, 1961). On this view the hump would reflect a spike discharge further out in the dendrites occurring possibly after some delay as a sequence to an SD-spike propagated out into the proximal part of the dendrites. As there are many dendrites in the motoneurone the hump could reflect spike discharges from many different sources which would account for differences in amplitude and temporal dispersion of the hump. Both the amplitude and the shape of the hump as well as its latency would also be modified to a large extent by the rather rapidly changing membrane conductance in the soma membrane following its activation by the SD-spike. Further, these parameters of the delayed depolarization would also be influenced by an electronic spread of the potentials.

If the hump on the delayed depolarization really represents spikes elicited further away in the dendrites it should also be possible in normal motoneurones to elicit such spikes in isolation by synaptic stimulation at the site of its origin. Small spike discharges elicited from the dendrites by stimulation and not directly propagating into the soma have previously been reported to occur in chromatolysed motoneurones (Eccles et al., 1958b) and in the pyramidal cells of the hippocampus (Spencer and Kandel, 1961; and others).

However, it should not be forgotten that a most important alternative explanation of the delayed depolarization has not been ruled out, namely that it may be an after-potential which for unknown reasons can change its shape when subjected to various modifying influences. Fully to exclude this alternative would require an experimental situation in which different parts of the neurone membrane could be investigated separately.

**SUMMARY**

1. The investigation was concerned with the depolarizing potential which follows the intracellularly recorded antidromic spike in lumbar motoneurones, i.e. the delayed
depolarization. Most of the experiments were performed in cats. Some rats were also used.

2. Cat motoneurones in good condition were generally followed by a delayed depolarization of varying size. The delayed depolarization in these cells had the shape of a hump in about half the number of units, being otherwise of a smoothly decaying variety.

3. It was confirmed that the delayed depolarization is directly or indirectly caused by the SD-spike and that it is not a postsynaptic phenomenon.

4. When the delayed depolarization had the shape of a hump and two antidromic spikes were elicited at short intervals (19–40 msec) the hump of the second delayed depolarization disappeared. With the conditioning antidromic spike at longer intervals (5 up to more than 55 msec) the delayed depolarization was increased in amplitude and in about half the number of cases it presented a more prominent hump.

5. Depolarizing currents diminished the amplitude of the delayed depolarization and made it acquire a more prominent hump. The hump was not reversed in direction by depolarizing currents. Hyperpolarizing currents increased the amplitude of the delayed depolarization and made its hump less prominent.

6. Excitatory and inhibitory synaptic stimuli typically had effects on the delayed depolarization in the same general direction as the corresponding polarizing currents, but their influence was, as a rule, very much stronger. Synaptic stimuli had especially marked effects on the shape of the delayed depolarization. The synaptic effects could rarely be simulated by polarizing currents. Sometimes the typical synaptic actions on the delayed depolarization occurred independently of changes of membrane potential as recorded within the soma.

7. Some possible interpretations of the delayed depolarization are discussed. The material seems to lend some support to the hypothesis that important events responsible for the delayed depolarization take place in the dendrites. It should be stressed, however, that the evidence presented is not conclusive at this point.

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DISCUSSION

Eccles: There are many interesting questions concerning the delayed depolarization that you have so thoroughly investigated. If the hump-like component is produced by spikes generated at remote regions of the dendrites, this spike generation would be much later than the latest spikes recorded by Terzuolo and Araki in their intracellular records from dendrites. However, the very slow decline they observed for dendritic spikes certainly would contribute to the smoothly declining phase of the delayed depolarization. I have hitherto assumed that the delayed depolarization of motoneurons was simply homologous with the after-depolarization of nerve fibers, where under conditions of background depolarization the spike declines to a brief notch that rises again to a later after-depolarization.

I wish to ask if you have ever recorded hump-like potentials superimposed upon EPSP's, and that could be attributed to the production of local responses generated in dendrites by strategic concentrations of excitatory synapses. With chromatolysed motoneurons these local responses are observed, but so far as I remember our observations with chromatolysed motoneurons did not reveal any special tendency for the antidromic spike potential to be followed by hump-like delayed depolarizations. Have you investigated chromatolysed motoneurons?

Kernell: Actually I have occasionally seen such hump-like potentials superimposed upon excitatory postsynaptic potentials, but I am not yet prepared to commit myself as to their nature. I have not investigated chromatolysed motoneurons.

Wall: I would like to ask about an alternative hypothesis. Introducing a micro-electrode from the dorsal direction while the ventral root is being fired, and stopping as soon as the record shows a successful intracellular antidromic volley, I would assume that the most likely place to hit first is a dendrite rather than a cell body. Now if that is the case, let me suggest that your type I with the hump represents an intradendritic recording with a partial block of transmission along the dendrite, your type II represents an intracellular recording, and your type III represents a fully blocked dendrite. One test of that would be to ask what would happen if you were recording of your type I with the hump and simply wait on, pushing the electrode in a little further. Does it convert to the type III? I would appreciate having your comments about this.

Kernell: On your theory one would expect to find IS-spikes to vary in size with the size and shape of the delayed depolarization. On scrutiny of the records this has not been observed. Further, since the size and shape of the hump could be altered rather easily and even abolished or made to appear in a reversible fashion in any one unit, as shown above, your hypothesis does not seem very probable as judged from the present material.
GELFAN: It was not clear to me what percentage of the motor neurons which you impale fire repetitively, and what percentage just once.

GRANIT: While many motoneurons can be made to fire a few spikes to intracellular stimulation, a small number only will be found to fire tonically in the way illustrated above. Undoubtedly the large majority of the penetrated motoneurons will fail to fire tonically for technical reasons beyond control and so calculations of percentages are meaningless.

We have, however, emphasized that some of the — to all appearance — good penetrations giving large spikes may well represent motoneurons in which the adaptive process, described above, is so well-developed that they for this reason respond phasically. As a matter of course, this statement represents a hypothesis.

ECCLES: It is remarkable that we have had to wait till now for the first systematic study of the effect of prolonged steady depolarization on motoneurons. Yet this experimental test provides a good replica of the action of a steady level of excitatory synaptic action; and this is the simplest condition of physiological stimulation of motoneurons. It will be appreciated that the synapses will then be applying a steady depolarizing current to motoneurons exactly as in the experiments with steady current application. The linear relationship of applied current to frequency is thus directly applicable to studies of excitatory synaptic action. In part the accommodation with slowing of frequency during a steady current can be attributed to the fall in potential that occurs after the initial summit, as has been found by Araki, Ito and Oshima. This summit is attained in about 20 msec with an approximately exponential decay governed by the time constant of the membrane, and the subsequent decline continues for about 100 msec to a steady plateau at about 70% of the summit. Hyperpolarizing currents give mirror image effects, and there is a reverse sequence of comparable potential changes on cessation of the currents. The changes in membrane excitability as measured by test current pulses exactly parallel the potential changes.

GRANIT: There is little to add to these statements except that the general problem of accommodation has been discussed in our original paper no. 2 (Granit, Kernels, Shortess). Our belief is that, in view of the change of the type of response during intracellular stimulation, accommodation does not suffice to explain our findings. Furthermore, adaptation varies during tonic and, hence, non-accommodative firing. For this reason we have preferred a neutral descriptive term such as ‘adaptation’.

LUNDBERG: I am in favour of the hypothesis that the delayed depolarization in motoneurons is a sign of dendritic invasion. For the interpretation we also have to consider findings on other types of nerve cells. Kuffler was the first to suggest that the delayed depolarization in the crustacean stretch receptor cell is due to dendritic events. Grampp (Acta physiol. scand., suppl. 213, 59 (1963)) has made a detailed investigation of this phenomenon with intracellular and extracellular recording from the initial segment, the soma and the dendrites. He has given strong evidence that the large delayed depolarization in the crustacean stretch receptor cells is caused by a dendritic action potential that electrotonically spreads to the soma. Furthermore, Grampp has

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shown that under certain defined conditions this delayed depolarization may evoke multiple discharges. There is the possibility that in the CNS synaptic actions exerted on the dendrites may regulate the degree of dendritic invasion and in this way influence the ability of a cell to respond with multiple spike discharges.

**Kernell:** Thank you for this interesting comment.

**Willis:** Another type of neuron showing a delayed depolarization after the spike potential is the reticular formation neuron. Dr. Magni and I have seen several instances of this phenomenon, and in some the threshold was low enough that a second spike arose from the depolarization.

**Kernell:** Thank you for the interesting information. It is interesting to compare the antidromic responses reported from different kinds of nerve cells because it seems like cells lacking dendrites, as for instance spinal ganglion cells (Ito, 1957), giant cells from *Aplysia* (Tauc, 1957) or sympathetic ganglion cells from the frog (Nishi and Koketsu, 1960), generally have no or a smoothly decaying delayed depolarization whereas cells with extensive dendrite trees, like the pyramidal cells of the hippocampus (Kandel and Spencer, 1960) or the retinal ganglion cells (Tomita *et al.*, 1961) often display a delayed depolarization with the shape of a hump.

**Sears:** Has Dr. Granit made any measurements of motoneuron discharge frequency in terms of membrane depolarization? The reason I ask this, is that in experiments on respiratory motoneurons using repetitive stimulation of ‘Ia’ type afferents in the intercostal nerves, I have found that there is a linear relationship between synaptically induced depolarization and discharge frequency.

**Granit:** No, for the time being only in terms of current as described.

**Creutzfeldt:** In addition to Prof. Granit’s report on intracellular stimulation of motoneurons and to Sir John’s remark on accommodation of motoneurons to intracellularly applied currents I should like to mention shortly our own experience with cortical nerve cells (experiments with Dr. Lux and Dr. Nacimiento). The threshold of nerve cells in the cats motor cortex (Betz cells and unidentified cells) is about 10 times below that of motoneurons probably because of their smaller size. Injured cells with a decreased membrane potential have a still lower threshold. The time constant measured with the strength-latency method lies in different cells between 5 and 12 msec. Using long supra-threshold pulses of about 0.5 sec, the initial high frequency discharge drops down within 70–100 msec to a steady state. The initial frequency as well as the steady state discharge are linearly related to the strength of the applied current. The steady discharge stays unchanged for several seconds and only with just supra-threshold stimuli it finally drops down to the spontaneous level. Using slowly rising currents with slopes of even more than 1-sec duration no sign of accommodation could be observed, i.e. the neuron begins to discharge always if the current reaches the same absolute threshold value. These observations show that the phasically discharging cortical cells react to long depolarizing intracellular currents in the same way as spinal motoneurons do.
Granit: I can merely repeat what I have said above, namely that the concept of accommodation provides little aid for the understanding of tonic firing which by definition is non-accommodative. Slowly rising currents may provide information about accommodation when the preparation consists of a single node in a nerve fiber, the adjacent nodes having been cocainized, but not when the index used is the spike fired by the soma of a motoneuron.

I do not understand why the time constant of motoneurons should necessarily be related to repetitive firing.

As to the explanation of tonic firing in terms of the ionic theory, I am aware of work, soon to be published, which will deal with this question in detail.

Sears: I have just one other point that seems relevant. The after-hyperpolarization of the motoneuron has this specific action of wiping out the pre-existent EPSP. So even if there is a static barrage on the motoneurons this is converted to a post-depolarization.

Gelfan: If you are going to treat the spinal neurons as sense organs, as indeed they are, with such large receptive surface as represented by dendrites, the adaptation to conduct stimulation will vary, as it does in peripheral sense organs. I should imagine that 'phasic' motoneurons adapt rapidly; tonic motoneurons less so, and spontaneously discharging interneurons not at all. This implies different physical characteristics of neurons. Phasic motoneurons with relatively long subnormality, for example, are not apt to fire repetitively at high frequency under normal conditions.

Kernell: When talking of tonic and phasic motoneurons I would like to mention that I have made some further investigations on the rhythmic properties of cat motoneurons as related to the duration of the after-hyperpolarization. Both neurons with very short and very long after-hyperpolarization could give well-maintained rhythmic discharges to depolarizing currents, and the duration of the after-hyperpolarization could not be correlated to the ability of rhythmic firing. Also it is interesting that differences in adapted slope constants show no evident relation to the duration of the after-hyperpolarization. The frequency range, however, seems to be related to the duration of the after-hyperpolarization.

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