

THE EFFECT OF TEMPERATURE ON THE ARTIFICIAL SYNAPSE FORMED BY THE CUT END OF THE MAMMALIAN NERVE

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THE ARTIFICIAL SYNAPSE formed by the cut end of a nerve (14, 18, 11, 12, 17) has several interesting properties. Granit and Skoglund (12) investigated it in cats, with stimulating electrodes on the motor L7 and leads on the sensory L7, and found transmission across the cut end of the sciatic to be a quite regular phenomenon whereas it in frogs, according to Hering (14) presupposes hyperexcitable animals. When in cats a test shock followed a conditioning shock it was noted that, in most experiments, the first shock was succeeded by an oscillatory state of excitability an example of which is found below in Fig. 4. Facilitation and inhibition alternate at frequencies around 250 per second, so that the relayed response to the test shock waxes and wanes depending upon the interval between the stimuli. In their work attention was called to—probably—related results on oscillatory after-potentials by Gasser and his collaborators (cf. 16) and to Arvanitaki's work (1) with the artificial synapse formed by a citrated region in two adjacent crab nerves. The observations by Cole and Curtis (8, 9) on inductance in the squid nerve should also be referred to in this connexion.

In addition Granit and Skoglund described a state of generalized depression or subnormality after the conditioning shock. The observations to be reported below were undertaken in view of the well-known effects of temperature on nerve accommodation (20, 19). The so-called dorsal root reflex of Barron and Matthews (3) is facilitated by a decrease of spinal cord temperature (3, 4, 22), an effect investigated in some detail with respect to accommodation by Skoglund and Uvnäs (22). Reflex excitability seems to be similarly affected (13). The artificial synapse is an ideal preparation for an analysis of a form of transmission which probably is altogether based on an electrical mechanism (18, 12) and the effects of cold are, indeed, striking and should provide good demonstration experiments.

TECHNIQUE

Decerebrate cats were used. The spinal cord was exposed in the lumbar region and the roots S1–L6 on one side severed. The muscles between the hip and the spine were cut at their insertions, all branches along the sciatic severed and the main stem cut. The leg was *completely denervated*. Stimulating electrodes were placed on the motor root L7 and leads to amplifier and oscillograph on the sensory L7. Transmission from motor to sensory fibres takes place at the cut ends of the hamstring and the main sciatic stem (11). For a theoretical analysis of the mechanism of transmission it is best to cut the whole nerve so that the hamstring together with the peroneal and popliteal branches of the sciatic stem form a single

transmitting cross section. The reason for this is that the relayed effects from two transmitting cross sections at different levels can interfere and thus cause undesirable complications (11).

A metal thermode with a cross section like a shallow U took up the end of the nerve and the groove thus formed was closed with a metal lid fitting into the U. Thus a canal, the inside of which was lacquered, was formed for the nerve. The length of the thermode was 2 cm. Its temperature was regulated with running water and measured by a thermocouple placed at the bottom of the groove for the nerve. The severed end of the nerve was just outside the thermode.

The motor root was stimulated iteratively with a pair of shocks at a rate of 1 per sec. Shock interval was adjustable. The conditioning shock started the sweep circuit in the usual manner.

RESULTS

The effects of temperature. The normal and characteristic effect of a sudden drop of temperature at the artificial synapse is a considerable increase

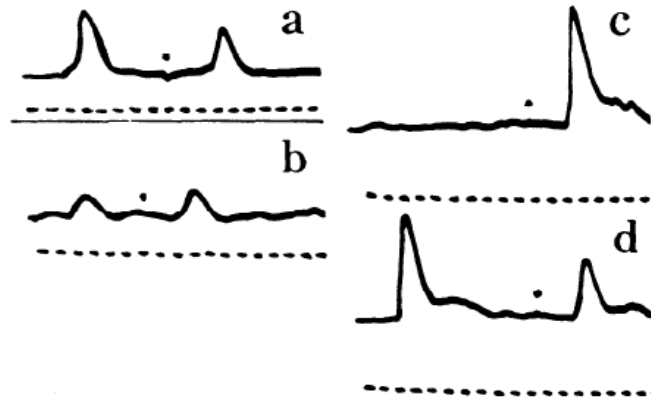


FIG. 1. Transmission motor to sensory fibres. *a*, conditioning shock followed by test shock at 36.6° . *b*, same at 40.4° . *c* and *d* at 16° , *c* test response alone, *d* as above. Time in this and all figures to follow in millisecc. Shock artifact for test shock indicated by a point above the records.

of the transmitted response. Conditioning and test response are shown in Fig. 1*a* at 36.6° . In *b* the temperature has been raised to 40.4° which resulted in a diminution of the size of the relayed discharge. Then the temperature was suddenly dropped to 16° . In *c* is shown the large increase of the transmitted effect in terms of the test response alone, in *d* conditioning response followed by the response to the test shock. This record, compared with *a*, illustrates the second characteristic effect of cold, the increase in the depression left by the conditioning shock. The response to the test shock is far more depressed in *d* than in *a*. Comparison with *c*, the test response alone, shows that it has been reduced to 47 per cent of the size of the control. The interval between conditioning shock and test shock happens to be longer in *d* than in *a*.

The same experiment will now be performed with conditioning and test shock at a constant interval of 11 msec. At the same time another phenomenon will be illustrated. Granit, Leksell and Skoglund (11) have shown that transmission across the artificial synapse is of a much smaller order, or entirely absent, if the discharge is forced in the opposite direction, *stimulating*

electrodes on *sensory L7* and *leads on motor L7*. The unidirectional properties of the artificial synapse have been explained by Skoglund's observation on cats (21), i.e., accommodation and rheobase both are lower in sensory than in motor nerves. His results confirmed for this animal and with a different technique the observations by Erlanger and Blair (10) on frogs.

This fact formed the starting point for the following experiment which is particularly well suited for demonstrations. The sensory L7 is stimulated and, unless a high degree of amplification is used, nothing originally is seen in the motor root. Then the artificial synapse is suddenly cooled. Immediately both conditioning and test shock, caused a relayed discharge, illustrated in Fig. 2*a*. In the records *b—m* the increase of the relayed response is fol-

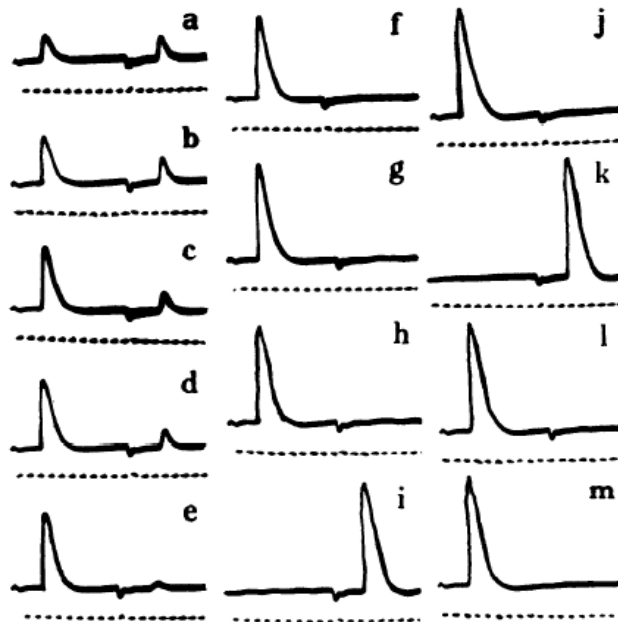


FIG. 2. Transmission sensory to motor fibres stimulated by cold.
Full explanation in text.

lowed by a series of successive photographs. Already in *b* it is seen that the response to the test shock did not take part in the large rise of the response to the conditioning shock. In *e* the response to the test shock is but a small hump on the base line and in *f—h* merely its shock artifact is left. The response to the conditioning shock continued to increase. In *i* the test shock was put in alone as control and the relayed effect is here found to be even larger than the response to the conditioning shock in *h*. The effect of cold is followed in *j—m* up to its maximum, *k* and *m* being controls of respectively test shock and conditioning shock alone, *j* and *l* combined shocks.

Cold thus had a truly enormous effect in facilitating transmission from sensory to motor fibres. From practically zero the volley reached values of the order of 3 mV (*k* and *m*). But at the same time the generalized depression, caused by the conditioning shock, increased at a still faster rate so that the

response to the test shock soon became completely blocked, despite the long interval of 11 msec.

The facilitation of the relayed response and the generalized depression after the conditioning shock are the typical effects of cold. But sometimes other phenomena are seen. These are illustrated in Fig. 3, referring to the standard arrangement with stimulating electrodes on the motor L7 and leads on the sensory L7. The records *a-e* are controls at temperature 36°.

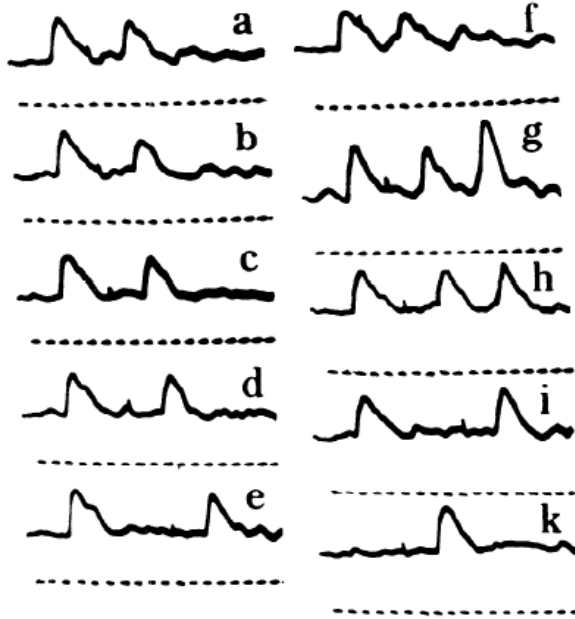


FIG. 3. Transmission motor to sensory fibres. *a-e* at 36.6°, *f-k* at 15.2°. In both sets of records shock interval decreasing downwards.

nated from the synapse. In rhythmic artificial synapses it is quite common to find the oscillations sufficiently marked to cause a small secondary volley at the root in response to the first shock. (A small secondary volley after the first response is thus indicated in several of the records of Fig. 3 but are far more pronounced in the records of Fig. 4.)

Other agents, such as *e.g.*, electrotonus, may cause similar changes in the artificial synapse, as shown by Skoglund in experiments soon to be published. The secondary responses will be analyzed in this work in which better conditions have been provided for penetrating this aspect of the problem.

The effect of cold generally disappears after some time, varying a great deal from experiment to experiment.

The generalized depression. Some experiments on the effect of low temperature on the artificial synapse suggested that the increase in the generalized depression is dependent on the facilitation in such a manner that whenever the transmitted effect of the conditioning shock is large this automatically leads to a heavy subsequent depression. In the wake of depression the

temperature is then brought down to 15.2° and the effect shown in *f-k* for increasing shock intervals. There is hardly any increase in the size of the responses but nevertheless something has happened since at the intervals *g* and *h* a large secondary wave (the third wave seen in the records) has turned up in response to the single test shock. Now the effect of this test shock is shown alone as control in *k* which is a single volley just as the volley, caused by the test shock at the interval reproduced in record *i*. It is probable therefore that in this particular experiment cold facilitated the rhythmic oscillations of excitability, set up by the shocks, to such an extent that at a *suitable interval* for interference between the excitatory phases of the rhythms a second discharge emanated from the synapse.

oscillatory changes of excitability may still be displayed (12). When the artificial synapse was kept cold for a long time until the response gradually diminished, then the test volley again turned up.

For this reason it was deemed important to complete these experiments by grading the strength of conditioning and test shock relative to one another. In most cases oscillating artificial synapses of the type shown in Fig. 4 were used. This record was taken with a slow sweep in order to illustrate short and long shock-intervals on the same film. The shock intervals are shortened from *a* to *f*. The two crests of excitability are seen in records *b* and *d*, the trough of inhibition between them in *c*.

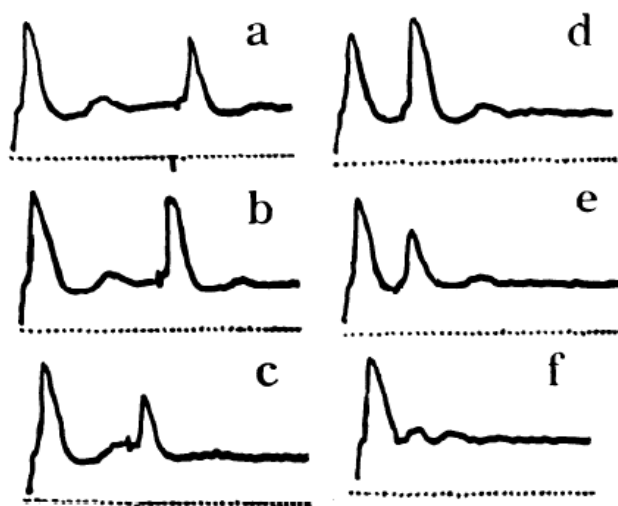


FIG. 4. Transmission motor to sensory fibres. Shock interval decreases from *a* to *f*. Note secondary volleys.

If now conditioning shock and test shock both are adjusted to give maximal relayed responses, a reduction in the strength of the latter may first cause an increase in the amplitude of the oscillations between excitation and inhibition, when excitability is measured at different intervals by the test response in per cent of its control (12). The reason for this is that with both volleys maximal the mechanism of transmission had been driven so near its maximum capacity that few fibres could be added by further increase of facilitation. A reduction of stimulus strength for the test response therefore left a greater margin of fibres available for facilitation. In the terminology of Sherrington and his coworkers (7) this could be expressed by stating that the facilitatory effect on the strong test shock had been "occluded." The test response had been so large that facilitation could not add to it. But this "occlusion" is limited to a narrow range of stimulus strengths. A further diminution of the test shock strength always leads to complete depression of its effect, just as in the above experiments on mobilizing a large number of fibres for the conditioning shock by cooling the synapse. Sometimes, in diminishing test shock strength, "occlusion" was absent and a slight diminution

of test stimulus strength, as judged by the control test volley, sufficed to block the test response altogether.

From these experiments it is concluded that the large generalized depression or subnormality following a conditioning response, facilitated by cold, is due to the large number of fibres involved in the conditioning volley with consequent increased depression and not to any specific effect of the low temperature as such. This, of course, is according to expectation.

DISCUSSION

At least three factors may contribute to developing the facilitatory effect of cold. There is first the increased spike height and increased spike duration of the action potential in a cooled region of nerve, demonstrated with a single fibre preparation by Schoepfle and Erlanger (19). Secondly, the lowered accommodation, mentioned above. This effect on accommodation may be due to the possible third factor, known since the days of Du Bois-Reymond (23) and Bernstein (5). This is that a difference of potential can be noted between a cold and a warm region of a nerve. These temperature potentials were later studied by Verzar (24), Kolb (15) and Bremer and Titeca (6). We confirmed them preliminarily in these experiments with an instrument of limited sensitivity and have now taken up temperature potentials for a detailed investigation.

SUMMARY

When the artificial synapse, formed by the cut end of the cat's sciatic, is cooled, transmission across it is facilitated so that the relayed volleys increase in size. Conversely, they diminish in size when the synapse is warmed.

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