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THE GAMMA-INNERVATION OF PRIMARY MUSCLE SPINDLE ENDINGS AS A TRIGGER MECHANISM IN COLD SHIVERING

The typical rhythmicity of the α-motoneurones during a cold shivering tremor originates not before the spinal level. The experience of different authors leads to this result. (Henatsch et al., 1966; Hufschmidt, 1959; Perkins, 1946; Birzis and Hemingway, 1957; Lippold et al., 1959; Meurer et al., 1967; Klussmann and Henatsch, 1969). But the efforts for finding a pacemaker for the rhythmicity of the α-motoneurones at spinal level were up to now disappointing. This has prompted the idea that the rhythmicity might be generated within closed neuronal feedback loops that become unstabilized for some reason. One of the feedback systems most frequently discussed in this respect consists of the extrafusal muscle, the muscle spindle and their primary afferents ending at the α-motoneurones, and the α-motoneurones themselves.

The first figure shows a schematic drawing of this servocontrol system. One can see the skeletal muscle and parallel to the muscle its stretch receptor, the muscle spindle. The muscle spindle for its part possesses its own motor system that the figure represents in a very simplified manner (Barker, 1967; Boyd, 1968). It comes from the γ-motoneurones of the spinal cord then proceeds to the muscle spindles. The sensory afferent fibres of the muscle spindle lead to the spinal cord and terminate at the α-motoneurones of the same muscle. These elements the extrafusal muscle, the muscle spindle, and the α-motoneurones together form a negative feedback system. This servo-loop might possess stability or instability depending on conditions to be explained. During ordinary movement the servo-loop works stable. During a cold shivering, on the other hand, the stable behavior degenerates into instability. Such a change in the behavior of the servo-loop takes place through an intervention of the central nervous system in the servo-loop. The modulating action of the central nervous system can be pointed out at the α-motoneurone level (Stuart et al., 1966 b; Klussmann, 1969; Meurer et al., 1967) as well as at the muscle spindles (Stuart et al., 1966 a; ten Bruggencate et al., 1964; Schäfer, 1969; Henatsch, 1966). Both elements change their properties during cold shivering.

Our interest concentrated on the kind of changes in the properties of the muscle spindle and how far these changes might account for the onset of an instability. If this question is worked out biocybernatically simple mathematics results in the prediction that the muscle spindle advances the instability of the servo-loop if its first and second order differential sensitivities are reduced during cold shivering and/or its proportional sensitivity is enhanced. Because of the limited time we can not discuss the mathematics of these calculations in detail. Only so much might be mentioned that the transfer function of the servo-loop was optained and that we applied the so-called Hurwitz stability criterion (Oppelt, 1964) to our closed loop system equation to determine the conditions for the instability of the servo-loop.

The decrease in the differential sensitivities and the enhancement in the proportional sensitivity of the muscle spindle that are theoretically required during cold shivering were experimentally examined in the discharge frequencies of primary muscle spindle endings. For this purpose the discharge frequencies of spindle afferents from the gastrocnemius muscle of the cat are recorded in response to ramp stretches of the same muscle. The sensitivities were determined from the discharge patterns before, during, and after cold shivering. The cold shivering tremor was obtained by simply cooling the cats. Figure two shows a discharge pattern of a primary ending during a ramp stretch. The pointed curve represents the discharge frequencies of the spindle with the individual symbols indicating the reciprocal intervals between neighbouring spikes. The upper curve demonstrates the stimulus used to stretch the muscle from a resting length with a definite velocity to a final value. The frequency of impulses coming from the muscle spindle depends upon the acceleration, velocity, and length of the stretch. The acceleration of the stretch is measured in the discharge pattern by the initial burst marked by the first arrow, A. After the first peak the spindle develops a second peak at the end of the stretch rise and then the discharge rate drops to a maintained new frequency value. The difference between the frequency peak at the end of the stretch rise and the maintained value marked with S is proportional to the velocity of the stretch. This value is the dynamic response, D. Finally the length of the stretch is measured by the static response the maintained frequency marked by the third arrow, S.

For the considerations of the instability we are actually not so much interested in the responses of the muscle spindle but instead in their sensitivities. We can extract the first order differential sensitivity from the dynamic response and the second order differential sensitivity from the acceleration response. The proportional sensitivity can be obtained from the static response.

Figure three shows the determination of these sensitivities as well as their changes during cold shivering tremor. One can see in the diagram a) the acceleration response as a function of the acceleration of the stretch. The values of the resting behavior of the cat are marked by crosses and open circles, wheras the value during cold shivering tremor by closed circles. The curves rise linearly over a wide range. One can see, that the slope of the shivering curve is less. The ascent of the curves corresponds to the second order differential sensitivity. Consequently, the second order differential sensitivity decreases during cold shivering tremor. The diagram b) shows the dynamic response

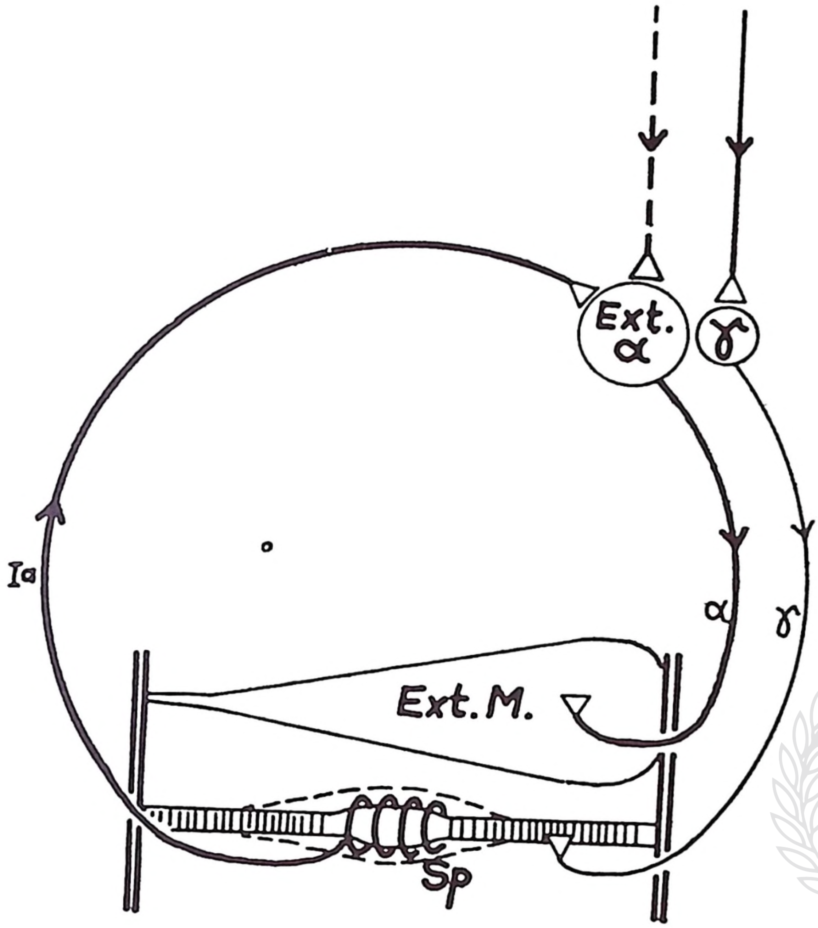

Fig. 1

A simplified reproduction of the stretch reflex feedback system. Ext. M.: extrafusal muscle; ext. α: α-motoneurone; γ: γ-motoneurone; Sp: muscle spindle; Ia: primary afferent fibre, During cold shivering tremor there occurs an instability in the feedback system.

as a function of the velocity of stretch. The resting and shiver values are characterised as in a). As one can see, the ascent of the shivering curve decreases here as well. Because that ascent of these curves corresponds to the first order differential sensitivity, this sensitivity, too, declines during cold shivering. Thus, both differential sensitivities fulfil the conditions of the cybernetical calculations by which the first and second order differential sensitivity becomes smaller if the muscle spindle participates in the instability of the servo-loop.

The proportional sensitivity is evident from the ascent of the curves of the static response, demonstrated in diagram c). Here the values during resting behavior and cold shivering lie on one curve. There were some spindles that showed an increase in their proportional sensitivity but just the same number of spindles had also a decrease in their sensitivity. So on the whole one can say that the proportional sensitivity does not change during cold shivering. By this behavior the proportional sensitivity does not contribute to the onset of an instability. In this case one would expect the sensitivity to increase during cold shivering. But on the other hand, the proportional sensitivity does not counteract an instability, it just behaves indifferent. By these findings the muscle

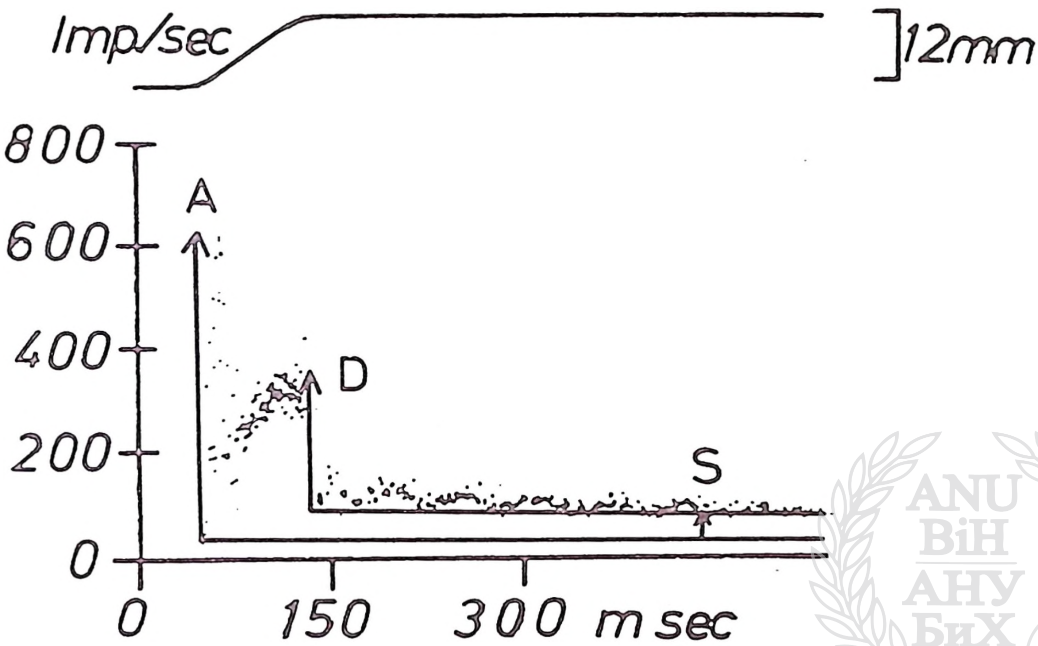

Fig. 2

Response pattern of a primary spindle ending during a ramp stretch to the extrafusal muscle. A: acceleration response; D: dynamic response; S: static response.

spindle does give rise to an instability in the servo-loop extrafusal muscle, muscle spindle, spinal cord by a decrease in their first and second order differential sensitivities.

The change in the slope of the characteristic curves is generated by central γ-inervation of the muscle spindle. The type of central γ-innervation had now to be identified, in order to become acquainted with the activity of the central nervous system which descends during cold shivering and leads to the change in the sensitivities of the muscle spindle.

To this end the fusimotor fibres innervating the muscle spindles were artificially stimulated at the ventral roots and the curves during γ-stimulation were compared with those during cold shivering tremor. Figure fous shows in diagram a) the curves of the dynamic response with and without γ-stimulation. As in the afferent system it is customary to distinghuish between a static and a dynamics component also in the

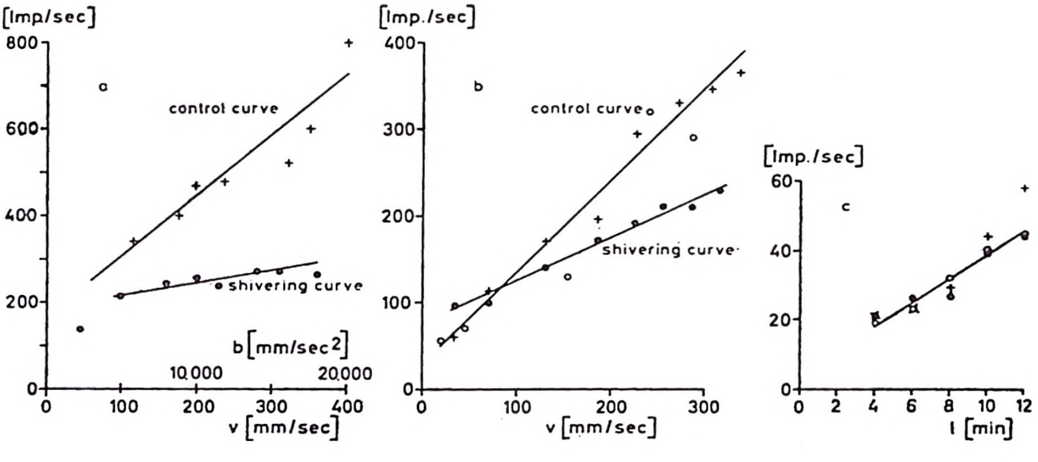

Fig. 3

Characteristic curves of primary spindle endings before (+), during (●) and after (o) cold shivering tremor. a: Acceleration response as a function of the acceleration of stretch. b: Dynamic response as a function of the velocity of Stretch. c: Static response as a function of the length of stretch. The slope of the curves shows the sensitivities of the muscle spindle. Note that the differential sensitivities (a, b) decrease during cold shivering tremor.

efferent γ-motor supplies sometimes referred to as γ_1 and γ_2. Here the effect of the stimulation of a dynamic fusimotor fibre is demonstrated. The behavior of the dynamic response without γ-stimulation is given by the curve marked with crosses. The dynamic response during γ-stimulation is shown by closed triangles. During the dynamic γ-stimulation there occurs a decrease in the slope of the curve as it was the case during cold shivering. Not only the decrease of the slope but also the intersection with the control curve corresponds with the behavior during cold shivering. Since the characteristics during γ-stimulation and during cold shivering show the same course it is safe to say that during cold shivering an enhanced dynamic γ-innervation is present.

The static γ-innervation during cold shivering was read from the behavior of the spontaneous activity of secondary muscle spindle endings. In many experiments they were simultaneously recorded. Here regularly a decrease of the spontaneous activity took place. From this finding (Appelberg et al., 1966; Brown et al., 1967) one is led to conclude that during cold shivering the static γ-innervation is depressed simultaneously from supraspinal levels.

Thus, during cold shivering there occurs a changed fusimotor innervation to the effect that the dynamic innervation is enhanced and static γ-innervation is decreased, which then leads to the described decrease of the differential sensitivities first and second order.

The change in the γ-innervation seems to be essential for the rise of a typical cold shivering tremor. So the enhancement of the dynamic γ-innervation regularly parallels the appearance of the visible tremor (Klussmann, 1969; Henatsch et al., 1966). And the γ-innervation was changed just before the beginning of a burst of tremor from the supraspinal centres. A few seconds later, directly as a consequence of the changed γ-innervation, one notices the beginn of the tremor. When the tremor commes to an end also the enhanced γ-inner-

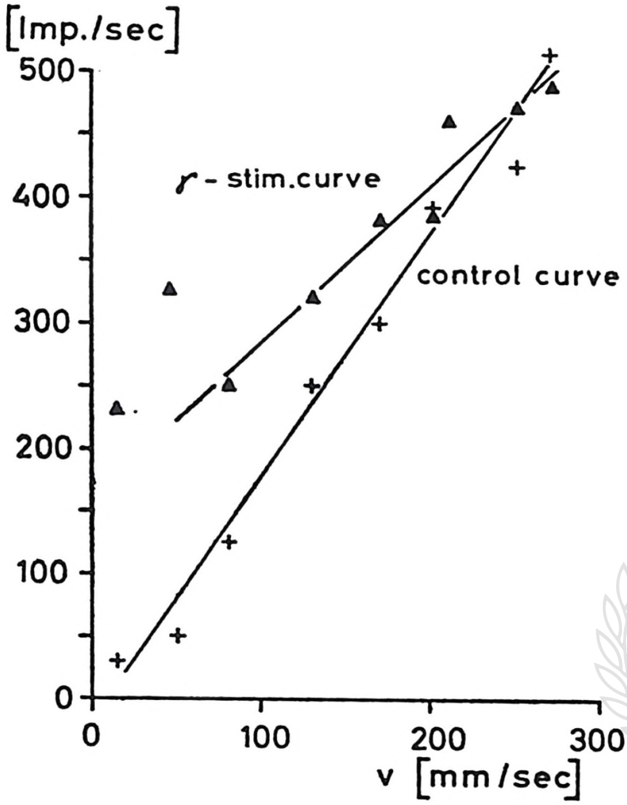

Fig. 4

Characteristic curves of the dynamic response with (▲), and without (+) dynamic γ-stimulation. During dynamic γ-stimulation there occurs a decrease in the slope of the curve and an intersection with the control curve as it happend during cold shivering tremor (Fig. 3b)

vation stops. Moreover, it was possible to establish that in those cases in which the cats showed a pronounced cold shivering tremor with large amplitudes a high dynamic γ-innervation had taken place, wheras a weak tremor with small amplitudes showed only a stightly enchanced γ-innervation. The above given results together with these observations can be interpreted in that way, that by the muscle spindle the servo-loop is brought into the instability.

This statement is in contrast with the interpretation of other investigators (Stuart et al., 1966b; Pierau et al., 1965; Meurer et al., 1967) who claim that the oscillations of a cold shivering tremor are generated only in the spinal cord respectively only by the α-motoneurones. Deafferentation experiments are quoted as evidence for this idea since after cutting the dorsal roots only the behavior of the α-motoneurones is observed because the muscle spindles are eleminated. And indeed under this experimental condition in some cases a tremor occurs when the cats are cooled. But the tremor differs considerably in its frequency and amplitude from the oscillations of a physiological cold shivering tremor. Consequently, these experiments show that the spinal cord by itsself is able to become an unstable control element. But this observation does not imply that the whole feedback system becomes unstable. So it is possible that a feedback loop consisting of two unstable control elements shows a stable control behavior (Opelt, 1964, S. 447). The stable or unstable behavior of the feedback system is dependent on the properties of all control elements forming the feedback system. On the basis of this assumption the postulated contribution of the spinal cord to the instability is not conclusive. However, our results show that the muscle spindle by a decrease in their differential sensitivities rendres the feedback system into an instability.

S. S. SCHÄFER

GAMA-INERVACIJA PRIMARNIH VRETENASTIH ZAVRŠETAKA MIŠIĆA KAO OBARAČKI MEHANIZAM HLADNOG TREMORA

KRATAK SADRŽAJ

Prilikom drhtanja usljed hladnoće uočena je, pored promjene alfa-inervacija, i promjena gama-inervacija. Gama-inervacija za vrijeme drhtanja usljed hladnoće sastoji se od povišene aktivnosti dinamičkih gama-neurona i od povećanja aktivnosti statičkih gama-neurona. Ova vrsta promjene gama-inervacije rezultira povećanjem senzitiviteta primarnih vretenastih završetaka mišića u odnosu i na brzinu i na akceleraciju.

Prema biokibernetičkim razmatranjima, ova povećanja senzitiviteta mogu dovesti do instabiliteta (= tremor) u feedback-sistemu (ekstrafuzalni muskulo-muskularni vretenasto-kičmeni stub). Prema tome, za drhtanje usljed hladnoće dovoljni su impulsi iz nivoa kičmenog stuba.

Dalje, iz eksperimentalnog i biokibernetičkog dokaza slijedilo bi da su vretenasti završeci mišića preko porasta senzibiliteta ti koji prouzrokuju drhtanje usljed hladnoće. Zbog toga što vrijednost povećanja senzitiviteta vretenastih završetaka mišića zavisi od istovremene gama-inervacije iz viših centara, ti centri mogu započeti, modificirati ili završiti periferni mehanizam drhtanja usljed hladnoće.

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DISCUSSION

Jurna: Dr Schäfer, I had the feeling that you tried to discard the spinal cord as an important rife for tremor generation. Does that mean that could influences the spindle discharge peripheraly? Has it something to do with changes in the initiation of generator poteties? If not, then the spinal cord is still necessary for tremor generation?

Schäfer: Changes in the behavior of the alpha-motoneurones. I think are necessary for the rize of a cold shivering tremor. But on the other hand it is not possible to say that only the alpha motoneurons are responsible for the generation of shivering tremor. For, if the cold shivering tremor generates in the feedback loop than all control element forming the nervo system have the same importance for the rise of an instability. That means that there is no priority between the spinal cord and the muscle spindle for the generation of a cold shivering tremor.

Štern: Have you tried in your experiments to give Atropine or Holinomimetica? Also it would be interesting to know how does succinilholin act.

Schäfer: I only looked for the physiological cold shivering tremor, so I have not had treatments with drugs. But a test with succinilholin would be very interesting for it enhances the dynamic fusimotor effect at the muscle spindle discharge frequencis. Perhaps, it is possible to test by this way the idea that the muscle spindle and the changes in their sensitivities are important for the generation of the tremor at spinal level.

Bruggencate: Dr Schäfer, what is your definition of dynamic gamma-stimulation? Although obviously both with dynamic gamma-stimulation and cold shivering the slope of your curves was diminished, in cold shivering the whole curve was very much below the control. Can this also be explained whith an increase in dynamic gamma activity? Did you also record from filaments efferent gamma-activity under the condition of cold shivering.

Schäfer: The dynamic gamma-stimulation is difined by an increase of dynamic response during the stimulation.

During the cold shivering tremor occurs not only an increase in the dynamic but also decrease of the static gamma innervation. A decrease of the static gamma innervation results in a decrease of the slope of the dynamic response (unpublished results) so the marked diminution of the slope of the shivering nerve results by an addition of the effects of the changes in the static and dynamic gamma innervation. We did not recorded the gamma-activity from ventral root filaments for the sorte of gamma innervation is more precisely read from the changes in the discharge frequencis of the spindle efferents.