

Interpretation of Supraspinal Effects on the Gamma System

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The microelectrode, be it applied for stimulation or recording, has taught us, if we did not know it before, that motor activity is the outcome of highly complex processes hierarchically organized. Best known at the moment are the spinal cord and the motor cortex, when our criterion is understanding of specific definable functions, but we do not doubt that the cerebellum, the basal ganglia and the reticular formation play roles in what Sherrington once called "motricity" that are within reach of comparable understanding though not yet on a par with the two first mentioned.

My task has been restricted to say something about the gamma-spindle system which is a major instrument for handling unexpected encounters with mechanical forces outside the body. The addition of "supraspinal" to the title emphasizes that the muscle spindle is at the disposal of hierarchic governors at different sites. It is not so necessary here to proceed to enumerate these sites. The gamma neurons are focused on the spindles. No other role for them is known. They sensitize spindles and so both the "how" and "why" of the gamma system concern this act of sensitization.

If I begin by being very general, let me first state that motor organizations are built for timing entry and exit of motoneuronal responses. The most perfect timing circuit known in detail today is the spinal centre organizing locomotion by reciprocal innervation. Apparently evolution has put a premium on creating an organization for timing as low down in the neuraxis as possible in order to make it as swift as possible. The Gothenburg group with Lundberg, Hultborn, Jankowska in the lead (see e.g. Lundberg, 1975) has elucidated this organization so well that I think I can assume it familiar to all those present at this Symposium. I have discussed it elsewhere (Granit, 1975).

If it be essential for the spindles to be sensitized in locomotion, the gamma motoneurons would have to be excited already at the spinal level because it is well known that the spinal cord harbours a locomotion centre of its own that can be activated also in the spinal animal. Grillner and his coworkers have devoted a number of relevant experiments to this question. Grillner and Zanger (1974, 1975) and Sjöström and Zanger (1975, 1976) have shown that in the acutely spinalized cat stepping movements can be generated in the deafferented hindlimb. These are a detailed replica of those in non-spinalized animals. The cat is given an injection of 200–500 $\mu\text{g}/\text{kg}$ of Clonidine and 100 mg/kg of DOPA or, alternatively, 50 mg/kg Niamid plus 50 mg/kg DOPA. Stepping movements can then be elicited by tonic

electrical stimulation at 5 Hz of the two cut dorsal roots. It was found that single gamma efferents to a flexor and an extensor displayed perfect rhythmic activation linked to the supraliminal alpha stepping.

Since DOPA activates static gamma efferents, these at least would have been linked in coactivation with the alpha partners of the stepping generator. The authors hold participation of both static and dynamic gamma motoneurons more likely. The gamma activity generally preceded the alpha activity. Staying for the moment by the timing aspect alone, we conclude that spindle sensitization plays an essential role in this spinal precision instrument for timing entry and exit of different muscles in locomotion.

The existence of a spinal stepping generator in combination with the detailed knowledge of the supraspinal control of the Ia inhibitory interneuron given us by the Gothenburg workers (see e.g., a summary by Lundberg, 1975 and one by Wetzell and Stuart, 1976) means that the mechanism employing reciprocal innervation must be activated in a well-organized manner when started supraspinally, for instance, by mesencephalic stimulation as introduced by Shik et al. (1966). This perfect spinal timing instrument can of course be wrongly approached by a supraspinal governor and this is likely to have happened in the experiments of Brooks (1975) in which local cooling of globus pallidus led to a breakdown of alternating movements. I hope that we shall see much experimentation making use of reciprocal innervation of the limbs as a test of the nature of its supraspinal approaches. And, in particular, one would like to be informed on how the gamma system behaves when disintegration of some kind is noted in the timing machinery of the stepping generator. It is a truism that precise knowledge of the nature of a test favours analytical progress.

I have taken up these experiments on alpha-gamma coactivation in the spinal stepping mechanism also for the light they throw on the nature of alpha-gamma linkage as an anatomical proposition. It means that coactivation, though possible anywhere on a supraspinal route, in many cases could be localized to its final site of action in the spinal cord. Is it hopeless to expect those working with the horseradish peroxidase method to provide precise information on the design of the spinal alpha-gamma link?

That the gamma neurons take precedence over the alpha neurons in coactivation is something we have seen from the beginning of gamma-spindle physiology, even when recording their effect in terms of spindle firing from afferent roots. It is nevertheless worth emphasizing that gamma-spindle precedence now has been confirmed once more with a natural movement as essential as stepping. Grigg and Preston (1971) and Fidone and Preston (1969) in their pyramidal baboon found that cortical stimulation also led to gamma precedence. For the development of such problems it would now be necessary to have recourse to intracellular recording.

In this context it is interesting to recall Hagbarth's dictum, based on his experience with direct recording from spindle afferents in human nerves: "When the skeletomotor system is silent, so is the fusimotor system" (Burke et al., 1976). Silence is then defined in terms of spike generation. His condition for silence, which is complete relaxation, may well involve an act of suppression by inhibition. What happens intracellularly is, and will be of course, unknown when the subject is man. I mention such reservations because for those of us who have had their experiences from spindle studies in the cat, absence of tonic firing in man has come as a surprise. Numerous experiments have shown spindle firing in the absence of alpha activity. Long spindle after-discharges are also quite common in the cat. Need we assume that the cat makes more use of its gamma-spindle system than man? But then the baboon also shows

gamma precedence, as stated above. Spindle precedence has been recorded by Burg et al. (1974) from tibial spindle afferents during the Jendrassik manoeuvre, alpha precedence is the general experience of Vallbo (1971) in his studies of human spindle primaries in voluntary contraction of the finger flexors. Are there in man two modes of mobilizing the gamma neurons, a more generalized activation and an exactly timed coactivation in a precise voluntary finger contraction whose spindle firing occurs on its rising phase? Our experience long ago with the cat (Granit and Holmgren, 1955) was that the spindles as well as the gamma motoneurons either could be activated diffusely through a pathway that withstood numerous criss-cross sections in the spinal cord above the segment studied or, alternatively, by a very fast route that was easily interrupted by lateral cuts in the cord. The explanation of the discordant experiences reported above may well lie in the existence of two such possibilities, alternatively, in high conduction velocity of the voluntary monosynaptic component (see Phillips and Porter, 1977).

However, both possibilities imply alpha-gamma coactivation. From the work of Vallbo (1974) and Hagbarth and his colleagues (Burke et al., 1978a, b) we have also learned to look with considerable caution upon reports maintaining lack of alpha-gamma linkage. They have shown how easily an experimenter can be deceived because the selected spindle, that failed to be linked to imitate alpha behaviour, was one that was shunted by activity in a neighbouring muscle. Their warning is especially relevant when experimenters have dealt with freely moving animals or with muscles that have not been properly isolated from one another.

I do not maintain that all reports on absence of alpha-gamma linkage are faulty. Long ago (Granit et al., 1955) we described loss of linked behavior in cooling the cerebellar vermis. Hagbarth tells me (personal communication) that in man he has seen two types of clonus, one with the usual coactivation, another in which the spindles fire on the falling phase and thus behave in the passive fashion of stretch receptors.

What I have said now completes my discourse on a ubiquity of alpha-gamma linkage that elevates it to a principle in motricity. How then should one explain the common gamma precedence? There is the size hypothesis that may be applied but, considering the complex structure of the central nervous system, one should not be forced to swallow the rule of size like a bad pill that has to go down without chewing. Alternatives to be considered are, e.g. a well-developed internuncial apparatus, high synaptic densities and a higher normal level of depolarization than that of the alpha motoneurons which necessarily have to be silent unless used for some specific purpose.

Speaking of gamma precedence in locomotion Sjöström and Zanger (1976) state: "The advantage is an optimal adaptation of the muscle spindle system already at the beginning of the contraction". Their statement made me look up my old views, as formulated in 1954 for the Silliman Lectures (1955): "The interpretation of all these experiments is that the gamma system is there not only to improve the performance of the sense organs but also as an 'ignition mechanism' to initiate movement as well as to maintain tonus... A consequence of this interpretation is that the muscles possessing spindles actually are provided with two motor systems..." "With this arrangement the sense organs in the muscle are immediately ready to 'measure' during the ensuing contraction" (p. 268). Today, later experiments have added substance to these early generalizations.

Significant for the understanding of an important role of coactivity of alpha and gamma motoneurons seem to me particularly two experiments both analyzing an

encounter with the unexpected. The earlier one is by Corda et al. (1965) and demonstrates unequivocally the importance of sensitized spindles in the response to a sudden obstruction in the even rhythmic flow of respiration. The physiological load compensation initiated by the spindle burst was absent after deafferentation. The other one is by Marsden et al. (1972) and shows load compensation to a halting obstruction in the voluntary contraction of the long thumb flexor. The effect undoubtedly was started by its muscle spindles, even though some background facilitation from skin or joint receptors proved necessary. In both cases we are entitled to assume coactivation. There was direct evidence of it in the former experiment, and, as to the latter, it has been proved beyond doubt that voluntary finger movements are coactivated (e.g. Vallbo, 1971).

In this context I would like to emphasize that it has been so easy to study coactivation in relation to the most sensitive alpha motoneurons that its role in the action of the large and fast alphas has been neglected. They have merely been regarded as the end point in the progress of recruitment, as laid down by the size hypothesis. However, recruitment thresholds have been found variable by several authors, most recently again by Kanda et al. (1977) in the decerebrate cat and by Garnett and Stephens (1978) in man. Thus there are possibilities for studying the link between fast alpha motoneurons and gamma neurons in appropriately designed experiments. Vallbo's experience with alpha preceding may then turn out to be characteristic of fast motoneurons.

As I pointed out in my introduction to this Symposium vibratory stimulation in man has drawn attention to a slow mobilization of a polysynaptically determined rise of excitability ultimately emerging in a contraction, the vibratory reflex (TVR). This process, though held to be spinal (Gillies et al., 1971; Burke et al., 1976), is under strong supraspinal control. It is easily suppressed by an act of will and the ensuing relaxation of the muscle augments the firing rate of the spindles (Marsden et al., 1969; Burke et al., 1976). Hagbarth's group (Burke et al., 1978b) postulates a mechanism of gain regulation, centrally controlled. If gain be centrally put down, the spindles cannot alone re-establish it. The normal operation of the postulated gain control would – I suppose – follow automatically by alpha-gamma linked commands to the muscles, the gamma system contributing its share through the mediation of the loop across the spindles. Setting of the gain would be an alpha affair. Marsden et al. (1976), who reported that gain in their thumb flexor experiment is boosted in proportion to the requirements of opposing force, also refer this effect to the alpha motor system. However, somehow the organism must be informed about the increase in external force and also in this sense the sensitized spindles are bound to add their contribution to the total performance.

In this, as in most other experiments dealing with the gamma-spindle system, one encounters its two major roles, i) the sensory one of information, as delivered by the sensitized spindles, mostly in cooperation with other sensory instruments such as tendon organs, skin and joint receptors, ii) the motor one across the gamma loop on the alpha motoneurons.

The motor role of the gamma loop is more accessible to interpretation than its sensory role as informant. One important reason for this is the known role of the spindles in connexion with reciprocal innervation; they produce monosynaptic excitation and disynaptic inhibition on the antagonist. In voluntary isometric contractions the spindles fire in rough proportion to the effort and therefore, as this increases,

become relatively more significant both for monosynaptic "ignition", and maintained load compensation. The gamma loop is likely to be used also for maximizing motor efforts. The range of firing frequencies is not known for spindles in man because of the difficulties in maintaining the flexible tungsten microelectrode in a fixed position. In the cat the range by supraspinal stimulation at a well chosen site was as high as about 160 impulses/sec compared with the basic value of the defferented spindle at the same length (soleus between 8 and 12 mm muscle extension, according to Eldred et al., 1953).

However also in man the coactivated spindle, despite experimental constraints, has been shown by Hagbarth et al. (1970) to add a substantial amount to the voluntary contraction studied in a finger flexor. After removing the gamma contribution by a Xylocaine block the sustained isometric response was "very much reduced". Full power could then be restored by adding a vibratory stimulus. In the cat Severin (1970) applied a procaine gamma block in experiments on controlled locomotion. The amplitude of the extensor EMG was then found reduced by approximately one half while the rhythm of stepping was essentially unchanged.

The numerous experiments from Hammond (1956) onwards on unexpected loading and the effect of instruction on the stretch reflex have all been concerned with alpha motoneurons. As a rule, parallel records showing how the spindles have behaved in motor volleys succeeding the early monosynaptic "ignition" of the system have not been published. We know that this later activity, the functional stretch reflex of Melvill, Jones and Watt (1971a, b), is the one responsible for muscular force and, on present knowledge, can make a fair guess as to how sensitized spindles have behaved, case for case. The papers by Hagbarth and his coworkers (Burke et al., 1978) provide decisive information.

When in these experiments the subject was ordered to hold a given position of the foot, a spindle burst was elicited by a displacement produced by loading. This led to an alpha load compensating response after a latency of 175–300 msec that with background activity of a stretch reflex was shortened to 40–80 msec. In such experiments dislocation of the microelectrode prevents use of heavy loads but the authors assume that by its short latency the early spindle contribution plays an important role in preparing the ground for an increased voluntary alpha-gamma linked compensation. It is hardly possible fully to evaluate the role of the monosynaptic "ignition" without intracellular studies of its effect on the level of depolarization. Clearly every early effect must be significant for the speed of action of the muscles because this is highly sensitive to the fast firing rates characteristic of the early response of the motoneurons (Buller and Lewis, 1965).

Interesting light is thrown on coactivation by alpha-gamma linkage in isotonic contractions (Vallbo, 1973; Burke et al., 1978b). If the contraction is slow, the spindles may start immediately to discharge in proportion to the anticipated effort instead of, so to speak, waiting for the completed alpha recruitment process or of following it slavishly by a proportionate increase in firing. The least one can say about this experiment is that it really presents a case of gamma precedence in man, unless one is willing to apply psychological concepts such as "effort" and "anticipation" and assume these to be channelled more easily to gamma neurons than to alpha neurons. At any rate it seems permissible to assume that slow isotonic muscular contractions picture the gamma-spindle contribution better than fast ones in which the intrafusal shortening is counteracted by the unloading effect of surrounding extrafusal muscula-

ture. If this be accepted, the spindles in slow isotonic contractions measure effort leaving measuring of force to the tendon organs. Velocity and length could be measured by a differential of the frequency responses of the two end organs.

In strong voluntary contractions velocity loses in significance. In this case spindles and tendon organs both respond similarly. Noting that the "mean firing rate" of the spindles follows increasing force rather than decreasing length. Burke et al. (1978b) consider that its motor role then has replaced its sensory functions, or perhaps they mean that the motor role then is wholly dominant. While unwilling to follow them to that length, I am in full agreement about the greater contribution of the spindles to motoneuron depolarization with strong efforts (Granit, 1975). This seems to be an inevitable consequence of its monosynaptic projections. To what extent this effect is counteracted by Golgi tendon organs is dependent upon the state of the interneurons by which their effect is controlled.

Segmental vs. supraspinal is too large an issue for my attempt to interpret some supraspinal effects on the gamma-spindle system. Owing to the labours of the Gothenburg group we now have detailed knowledge not only of some segmental circuits and their organization but also of their supraspinal controlling pathways. We realize that the properties of sensitized spindles may be used in so many different combinations that it hardly makes sense to submit a list of potentialities. Elsewhere I have made some comments on this question (Granit, 1975).

While the experiments on man with direct recording from spindle afferents lately have seemed to me the most interesting ones from the viewpoint of supraspinal control, they also have their limitations that one should be aware of. One has been mentioned: that the intracellular approach is excluded. Another is that the difference between the actions of static and dynamic gamma motoneurons does not stand out well. As to primaries and secondaries, the experience of Vallbo (1974) is that they respond in the same general way. Their different roles have to be elucidated in animal experiments. A further restriction is that the range of possible experiments on man is narrow in comparison with the total resources of his motricity. There is a great deal more to do, I think, for instance, of Nashner's (1976) experiments on adaptability in the stretch reflex. A forced stretch reflex that runs counter to its normal purposiveness adapts to the new situation by gradually disappearing. Would then the gamma neurons follow suit or would they prove even more adaptable than their alpha partners? In view of Buchwald and Eldred's (1962) experiment on learning in the gamma system, the latter alternative seems at least as likely as the former. Finally, I must not suppress a secret suspicion that I have nourished for some time, namely that the voluntary mode of activating gamma motoneurons makes preferential use of one particular supraspinal pathway. There may be others with slightly different properties.

In finishing this brief discourse on the interpretation of supraspinal effects on the gamma system I have left out much that merely would have been a repetition of what I have said over the years, some of my summaries being as late as from 1975 and 1977. And I have already apologized for not going through supraspinal sites from which the gamma neurons can be activated. I have of course abstained from presenting much high-quality work on spindle innervation and internal design that suggests possibilities for differential use of this sensorimotor instrument in the muscles. Our methods have not yet permitted more than a few basic interpretations. Also it seems to me that present knowledge of spinal circuitry and descending pathways of control carries greater promises for interpretation than do the details of spindle design that extend beyond the differentiation of static from dynamic gamma control.

SUMMARY

The paper is written as a review evaluating contributions from the last ten years. It discusses likely interpretations of the functional role of the gamma system in the light of experimental work. Among major themes might be mentioned: spinal alpha-gamma linkage in reciprocal innervation, in relation to slow and fast muscles, the alternatives of alpha respectively gamma precedence in their coactivation, the compensatory response to unexpected loading, gain control in relation to vibratory reflexes, mono- and polysynaptic spindle control of motor activity, the role of the gamma system in maximizing motor effects etc.

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