MITOGENETIC RADIATION OF NEUROMUSCULAR SYSTEM AS A METHOD OF ANALYZING ITS MOLECULAR SUBSTRATE

PAPER IV. MANIFESTATION OF REGULATORY POWERS OF MOLECULAR SUBSTRATE OF MUSCLES IN VARIOUS FUNCTIONAL STATES

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In our previous papers [2, 3, 4] we developed the idea that an unbalanced state of order of the molecular substrate was a specific feature of the nervous system and muscles in the resting state.

The unbalanced state is maintained by the interaction of different—antibatic—processes produced by the spinal centers and muscles. In other words, the molecular substrate is constantly regulated by the system as a whole.

This gave rise to the question of whether regulative effects might be the basic feature of various functional states, which could then be regarded from a common viewpoint.

Hence, it was of interest to analyze the effects observed in frog muscle in experiments in vivo when the nerve was subjected alternately to subliminal and supraliminal stimulation.

METHOD OF EXPERIMENTS

The frogs (Rana temporaria or Rana ridibunda, mainly males) were pinned on a flat cork board. The gastrocnemius muscle was exposed and its tendon was cut and connected to the recording arm. A small portion of the central part of the sciatic nerve was also exposed and the electrodes were applied to it. The tetanic stimulations from an electric stimulator were characterized by the following parameters: frequency 15-20 cps, pulse duration 8-10 m sec, amplitude 0.1-2 v (the precise data are given in Table 1).

The area of the radiating surface of the muscle varied from 4-5 to 10-12 mm, depending on the aim of the experiments.

In the spectral experiments the muscle radiation was directed into the entrance slit of a spectrograph by reflection from a concave mirror. The radiation was detected by the usual biodetection method used in the laboratory [5, 6].

RESULTS OF EXPERIMENTS

The stimuli were applied in the following order: Supraliminal stimuli followed 20-30 sec later by subliminal stimulation for 5 to 10-12 sec (of the same or lower frequency), and after approximately the same time a second supraliminal stimulation of the same strength and frequency as the initial stimulation.

TABLE 1

Change in State of Muscle and Its Radiation Due to Subliminal Stimulation

Amplitude of stimulus (in v)		Muscle extension	Subsequent increase in muscle excitability	Muscle radiation (effect, %) for radiating surface of 10 mm^2, exposure 3 sec	Nos. of kymograms illustrating individual experiments
supraliminal stimulation	subliminal stimulation				
0,15	0,12	—	+	34	—
0,8	0,4	—	+	45	—
0,4	0,3	—	—	0	—
0,8	0,7	—	+	25	—
1,1	0,9	—	+	33	—
0,2	0,15	—	—	—8	—
0,8	0,5	+	+	40	6
1,8	1,5	—	+	35	—
0,2	0,15	—	—	—4	—
0,15	0,1	—	—	0	—
0,12	0,1	+	+	42	55
2	1,8	+	+	25	—
0,4	0,2	+	+	33	—
0,2	0,15	—	—	—5	—
0,2	0,12	—	+	50	66
0,8	0,5	—	—	—2	—
0,2	0,1	—	—	2	—
0,2	0,15	+	+	32	—
0,15	0,1	—	+	25	—
0,2	0,15	—	—	0	—
0,3	0,2	—	+	45	—
0,15	0,085	+	+	30	43
1,1	0,9	—	+	42	—

In 60-70% of the cases the second supraliminal stimulation resulted in a stronger muscular contraction than the initial stimulation, i.e. the excitability of the muscles was increased.

At the same time (in approximately 30% of the experiments) a slight extension of the muscle was observed during subliminal stimulation.*

In every case where an increase of excitability occurred the radiation intensity during subliminal stimulation increased considerably, irrespective of whether there was an evident extension or not.**

The results of the experiments are given in Table 1 and some of them are shown in the kymograms.

A comparison of the kymograms (see figure) shows that the important factor is the change of intensity of the stimulation, and not the frequency.

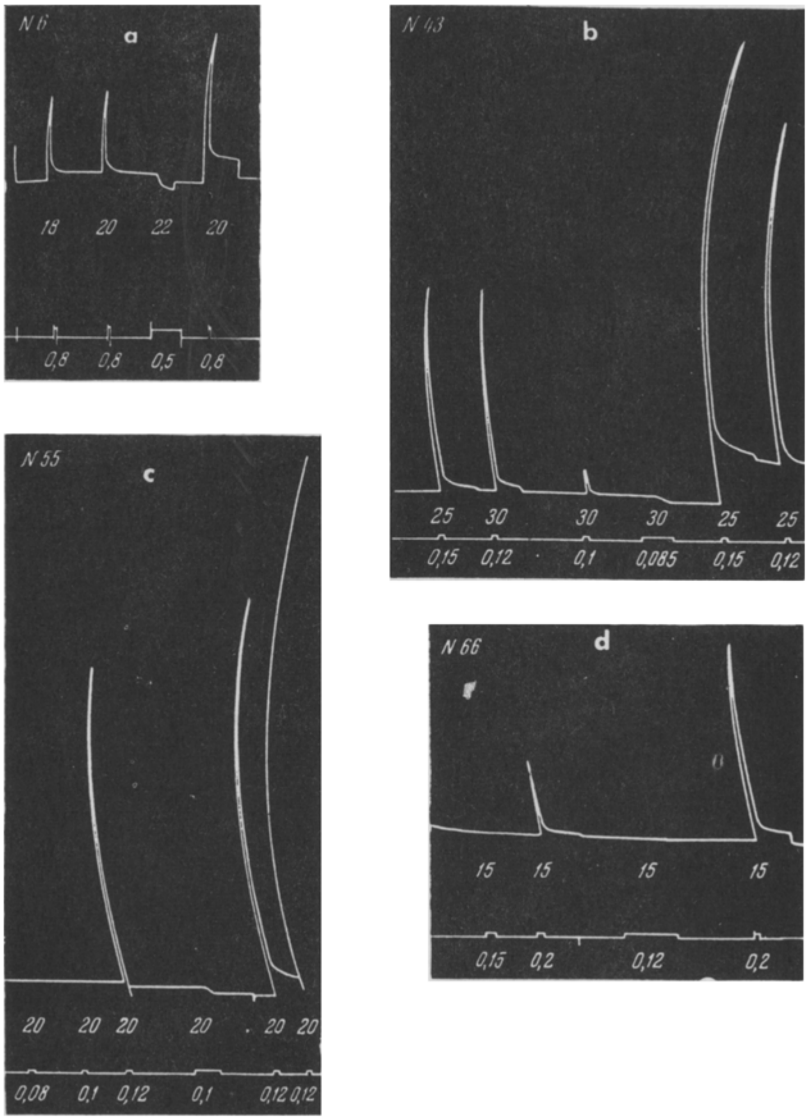
From previous laboratory data we knew that muscular contraction was also associated with a considerable intensification of radiation [5, 6]. But at the same time it seemed very probable that the states of the molecular substrate of the muscle during subliminal and supraliminal stimulation were different.

Hence, as criteria for assessing the state of the substrate we studied the changes in intensity of the muscle radiation during the action of stimuli lasting as long as 10-12 sec, and the presence of lines characteristic of free end-groups of peptides in the spectrum.

* Apparently the same effects resulting from weak stimulation were observed by Rauh [7]. In their phenomenology the described effects were also very similar to the picture of true pessimal inhibition discovered by I. A. Arshavskii and M. N. Kondrasheva [1].

** The radiation intensity was determined, as usual, from its inverse dependence on the threshold exposure. As we know, for a resting muscle the threshold exposure for the same radiating surface is equal to 8 sec, i.e. the radiation of a resting muscle is about a third of that observed in these experiments [2, 3, 6].

As already noted, the increase and decrease in the number of free end-groups of peptides indicates not only corresponding changes in the dispersion of the substrate in the chemical sense of the term, but also changes in the weak intermolecular interactions responsible for the mutual orientation of the molecules [2]. In application to the unbalanced molecular substrate of the nervous system and muscles effects of such kind are involved.



Change in state of muscles during and after subliminal stimulation. Distinct extension of muscle during subliminal stimulation with subsequent increase in excitability (Nos. 6, 43, 55). Subsequent increase in excitability with scarcely noticeable extension (No. 66).

The effects discovered in muscle during subliminal and supraliminal stimulation were, in fact, different.

During subliminal stimulation a spectrum typical of peptide end-groups $R-NH_2$ and $R-OH$ was clearly displayed (Table 2).

During supraliminal stimulation, i.e. during muscular contraction, there was a rapid decrease in the intensity of these lines.

TABLE 3

Intensity of Muscle Radiation at Different Times After Start of Subliminal and Supraliminal Stimulations of Nerve

Subliminal stimulations		Supraliminal stimulations	
exposure	effect (in %)	exposure	effect (in %)
3 sec after start of stimulation	3	3 sec after start of stimulation	0
	23		−5
	10		8
	30		3
	−3		35
	40		
	0	3 sec in the period 3-7 sec after start of stimulation	12
	40		−9
	10		0
3 sec in the period 3-7 sec after start of stimulation	42	5 sec after start of stimulation	43
	33		53
	45		37
	40		30
	50		44
			49
3 sec in period 7-11 sec after start of stimulation	35		
		5 sec in period 3-8 sec after start of stimulation	30
			20
		5 sec in period 5-10 sec after start of stimulation	−10
			3

If the state of the substrate of the neuromuscular system owes its character to the continuous interaction of elements contained in it, i.e. for each element "bound" in some degree to it, then the applied stimulations, by introducing even local changes in the substrate, must, as it were, increase the autonomy of the elements of the system, since they inevitably destroy or weaken the interaction. The direct consequence of this both for centers and muscles must be an intensification of the processes specific to them [2]; for muscles—intensification of their specific processes of a prepolymerization nature, which may lead to a decrease in free end-groups of peptides and a weakening of radiation; for centers—intensification of processes of a dispersive nature.

When stimulation ceases, the development of interacting processes again becomes possible. But their effectiveness cannot be the same for some period of time. Owing to the more balanced state of muscle substrate during contraction its energy level immediately after stimulation is lowered, i.e. central processes of a dispersive nature must predominate for a time.

But, proceeding from the idea of an unbalanced molecular order of the substrate, sustained by the interaction of antibatic processes, we must assume that the response to a predominance of dispersive processes will be an intensification of polymerizing process produced by the muscles. In other words, the active interaction of centers and muscles will be restored.

From our viewpoint this is a necessary condition for the return of the muscle to the resting state.

The increase in lability of the substrate, i.e. the greater excitability of the muscles, may be associated with these processes.

The suggested sequence of processes can be described as the manifestation of the regulative interactions of centers and muscles and, thus, the view that continuous regulation of the molecular substrate by the system as a whole is the basic feature of various functional manifestations, seems to us well-founded.

The last result corresponds with the data given below, which show that the total intensity of radiation of contracting muscle, the spectrum of which in the first few seconds contained many bands, gradually fell. On the other hand, the radiation intensity during subliminal stimulation even increased a little.

TABLE 2

Spectrum of Peptide End-Groups in Muscle Radiation During Subliminal Stimulation of Nerve

Functional group	Wavelength (in A)	Effect (in %)*
$R-NH_2$	2065—2070	41
$R-NH_2$	2260—2270	45
R—OH	1980—2000	35
R—OH	2400—2440	36

* Each figure is the mean from five experiments.

The radiating surface of the muscle in the experiments described below was reduced to 4-5 mm^2. In this case the stability of the positive effects was more clearly demonstrated (Table 3).

Thus, the data given in Table 3 show that the intensity of muscle radiation during subliminal stimulation exceeded the intensity during supraliminal stimulation and that the distribution of the intensity in time was different. During subliminal stimulation the intensity increased during the first 3-4 sec and then remained at the same level—the results were variable in the first few seconds and the reproducibility was good at subsequent times.

During supraliminal stimulation the level of radiation, comparatively high in the first 7-8 sec, subsequently fell.

In our examination of the obtained results we proceeded from the view that regulative rearrangements of the molecular substrate underlay the observed effects.

The most general definition of the effects observed during subliminal stimulation is that they have the nature of a possible response, and not of an obligate reaction, i.e. in contrast to the obligatoriness of muscular contraction under the action of a stimulus of corresponding intensity stimuli of lesser, but variable, intensities cause distinct changes in state in most cases, but can also fail to produce results.

We think that this distinctive type of phenomenology can be understood on the basis of the following viewpoint.

The dynamicity of the substrate of the nervous system and muscles, i.e. the continuous maintenance of an unbalanced state by the interaction of centers and periphery is clearly expressed, as we know, in the resting state. We assume that the unbalanced state is still continuously maintained during subliminal stimulation. But it is obvious that for this the substrate changes introduced by stimulation* must be compensated to a certain extent by the system itself. We regard the effects observed in the majority of cases as a manifestation of such compensation or, in other words, as the active manifestation of the regulative power of the substrate. These effects, of course, like any regulative processes, do not necessarily occur.

The mitogenetic data do not give direct evidence of this general view, but they certainly help to substantiate it.

A decrease in aggregability of the substrate (increase in free end-groups of peptides) lending to an increase in its mobility can only promote its dynamicity, i.e. the manifestation of regulative powers. A lesser degree of aggregability may also favor extension of the muscle and its subsequent increase of excitability.

At the same time, the increase in intensity of muscle radiation during subliminal stimulation (increasing with increasing stimulation), and which is presumably due to the more frequent occurrence of disturbances and restorations of the molecular order of the substrate, is quite naturally regarded as a manifestation of its increased dynamicity.

In the case of supraliminal stimulation the very fact of the obligatoriness of the contraction response, the gradual weakening of radiation and, in particular, the rapid disappearance of the spectrum of peptide end-groups, show that under continuing stimulation the muscle substrate passes into a new, i.e. more balanced, state. After stimulation, however, the muscle returns to the initial state, and we will attempt to examine this phase from the standpoint of the antibatic nature of the interacting processes produced by the centers and muscles.

* Particularly effective, presumably, during the short interval after supraliminal stimulation.

SUMMARY

This work deals with the reaction of M. gastrocnemius to the subliminal stimulation of the sciatic nerve in experiments on frogs (in vivo). In the majority of the cases there occurs a slight extension of the muscle with a subsequent rise of its excitability, connected with a considerable intensification of mitogenetic radiation. These phenomena are the manifestation attending the regulatory reconstructions of the molecular muscular substrate caused by an active interaction of the centers and muscles. The changes in the substrate connected with the supraliminal stimulation, especially during the return of the muscle from the state of contraction into the state of rest, are regarded from the same point of view.

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All abbreviations of periodicals in the above bibliography are letter-by-letter transliterations of the abbreviations as given in the original Russian journal. *Some or all of this periodical literature may well be available in English translation.* A complete list of the cover-to-cover English translations appears at the back of this issue.