Nodular Mechanism of Functional Systems as a Self-regulating Apparatus

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This symposium is dedicated to the memory of a man who by his researches into the reflexes of the brain and discovery of the process of central inhibition had written one of the most brilliant pages in the great history of culture of the human race.

I. M. Sechenov was the first scientist who co-ordinated in the study of the work of the brain fine analytical researches, such as the discovery of inhibition of spino-cerebral reflexes, with the study of brain reflexes, which includes complex forms of man's psychic activity. It is this aspect of the unity of analysis and synthesis in the study of the brain that I would like to discuss in my humble report, dedicated to the memory of our great countryman.

All experiments in neurophysiology aim ultimately at comprehending the law of the entire organism's behaviour, the work of the entire brain. This is true also as far as the microelectrode researches of single neurons of the central nervous system are concerned. Indeed, even the most valuable results of analytical research, aerlier or later, but unavoidably, must raise a question as to what place they occupy in the functioning of the entire brain and what is the degree of their participation in the adaptation activity as far as the external world is concerned.

The conditioned reflex, therefore, as regulatory of the entire organism, has become a favourite object of research of purely neurophysiological laboratories that never raise the question to the study of higher nervous activity, as such. The reflex proved to be that connecting link, which establishes transition from a fine neurophysiological experiment to whole behavioural acts of an animal, *i.e.*, implements that final aim of neurophysiological research, which was formulated above.

If we take the latest and most outstanding works of neurophysiological character, performed by professional neurophysiologists (Fessard, Jasper, Gastaut, Morell, Young, Buser, Hernández Peón and others), then the most interesting part of these researches consists in an attempt to reveal fine neurophysiological mechanisms of the very formation of the conditioned reflex. Moreover, some of the above-mentioned neurophysiologists, making use of contemporary achievements of neurophysiology, in 1958 proposed theories of inhibition of conditioned reflexes (Fessard, Gastaut).

The gap between the finest neurophysiological researches and appraisal of the entire behaviour is so great that it worries neurophysiologists. It has become obvious that a necessity has arisen to work out such a concept, that, on one hand, would represent an expression of a principle of integral behaviour, and, on the other hand, would create facilitated conditions for analysis of details and for finding microprocesses in nervous activity. In other words, it becomes more and more expedient to formulate, speaking figuratively, a 'big address' for fine analytical researches, an exact place for the given concrete analytical research in gross physiological architecture. It is hardly necessary to emphasize that with this approach in use even the finest research gains in the definition of its place and role in maintaining the brain's integral activity.

Proceeding from this urgent necessity of uniting the deductive and inductive approaches to appraisal of material, some years ago we formulated the principle of 'functional system', in which we find the manifestation of general physiological architecture for any act of behaviour or adaptability; at the same time it makes it possible to outline in a neurophysiological sense concrete schemes of research work on a fine analysis of specific nodular mechanisms and architecture.

By 'functional system' we understand such a dynamic organization of processes and mechanisms, which, responding to queries at a given moment, ensures the organism some sort of adaptable effect and simultaneously determines the currents of an adverse effect, *i.e.* resultant afferentation and central nervous system, informing the latter of sufficiency or insufficiency of the obtained adaptable effect. In other words, any functional system, inborn or dynamically formed in the given situation, possesses traits of self-regulation with the main mechanisms characteristic of it.

For a more complete acquaintance of our functional system, as a unit of physiological integration, we refer the reader to our former publications specially dedicated to this question (Anokhin, 1935, 1937, 1947, 1949, 1958, 1961, 1963a, 1963b).

The general architecture of the conditioned reflex, as an elementary act of behaviour, serves as a basis for neurophysiological analysis of functional system. We regard the conditioned reflex as a partially closed formation, in which, as in any other functional system, the final effect or the result of an action, immediately after receiving it, is reflected in a volley of afferent impulses, directed in reverse sense in regard to impulses, which formed an action. These afferent impulses inform the central nervous system as to the degree of sufficiency or insufficiency of the obtained adaptable results, *i.e.*, in the sense of their behaviour they are resultant, inasmuch as they reflect all parameters of the results obtained.

Below we present a principled scheme, which most fully reflects the physiological architecture of the conditioned reflex and at the same time gives an idea about a number of such main mechanisms which are specific only for the functional system, as an integral formation, and not characteristic of separate, anatomically isolated processes and mechanisms (Fig. 1).

Here it is important to point out that the presence of such a general physiological architecture of the act of behaviour, or as it is called Magoun 'model', creates a definite strategy in filling up that gap which at present separates the behavioural act from those most detailed neurophysiological researches and which became possible after successes were attained by contemporary electronics and stereotaxic technology.

Having as a prospect a clearly designated physiological architecture of conditioned reflex, we can correct each fine neurophysiological research in correspondence with the tasks of understanding the whole.

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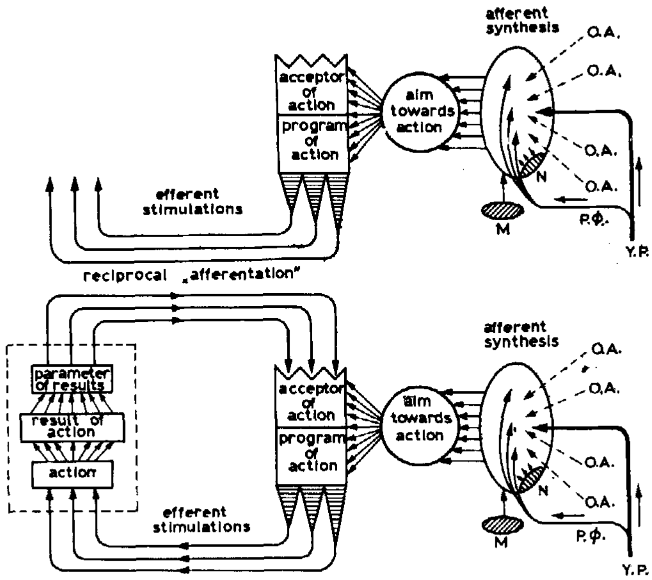

Fig. 1. Principal scheme of physiological architecture of the behavioural act, created in response to the conditioned stimulus. All stages are designed in the figure. I, Stage of formation of efferent excitations. II, Stage of closing a working cycle with the aid of reverse afferentation. In the figure it is clearly seen that the action acceptor, as a model of future results, is formed at the moment when formation of an action starts. M, motivation complex; N, memory as substrate of last experience. It can be observed in the scheme, if the behaviour act is developed on the basis of 'inclination' (hunger, thirst, etc.), then the stage of afferent synthesis is preserved, and the collations of the results with the action acceptor may be consistent and multitudinous (stage after stage reverse afferentations).

In this sense it is necessary to understand neurophysiological (Fessard and Gastaut, 1958, Magoun, 1963) and neurocybernetic views on the physiological architecture of conditioned reflex proposed by us.

The physiological architecture presented above has a number of main mechanisms which may serve as a source for making analytical researches. Some mechanisms or phases of development of physiological architecture of conditioned reflex are so fundamental and so characteristic of any integral behavioural act, that they must be taken and examined separately. However, in this paper I cannot present all the material obtained by us for the characteristics of all properties of the functional system as a whole. I shall confine myself to enumerating and characterizing the role of these phases and main mechanisms with a view later to concentrating the whole attention on experimental materials, characterizing the work on one of these main mechanisms, namely of the one that precedes and defines the trend of the next stages of the whole behavioural act.

The first stage of any behavioural act consists in the synthesis of all the afferent information, that reach the nervous system from external and internal spheres and in the aggregate compose a necessary stage for forming 'a decision', as an impetus to further formation of effector apparatuses of the behavioural act. We must proceed from an obvious premise that in the sphere of decision it would not be possible to formulate even one aim of behaviour or 'decision to act', if before this, synthesis had not been made of the whole information available at this moment from an animal's external and internal world.

During the growth of cybernetic researches and their contact with biology and physiology, the 'problem of decision' became one of the central problems of a new approach to deciphering mechanisms of the behaviour of animals and especially of man's behaviour. The programme of efferent processes, forming an action with simultaneous formation also of the apparatus of the action acceptor, is an objective physiological expression of 'decision' or 'aim'.

Experimental researches conducted with the aid of various methods, from the classical method of conditioned reflexes up to microelectrode researches inclusive, show that there exist at least four forms of initial information, that enter as the organic first stage components and that never fail to precede the formulation of the aim to action.

The initial stimulus, serving as a concrete impetus to start the formation of the behavioural act, is the first component of the afferent synthesis. A conditioned stimulus may be such an initial stimulus, but it may also be any other stimulus from the external world or the internal medium of the organism, which appears to some degree unexpectedly and enters into the already available broad system of afferent excitors, formed previous to the action of the initial stimulus.

Environmental stimulus serves as a second component of the afferent synthesis. It is not so clearly defined as an initial stimulus, and it includes all those factors that in total represent the general situation, in which the given initial stimulus has begun to function. For work with conditioned reflexes in accordance with the classical method this second category information may be represented by numerous stimuli, which are evoked from the environment of experiment and from all that preceded the formation of an experiment (the room's appearance, table, experimenter, configuration of the passage through which the animal is conducted into the experimental room, etc.). Each of these stimuli was conditionally acquired during the animal's past experience and, composing an organic part of general environmental afferentation, serves as an unavoidable background for its subsequent synthesis with the initial stimulus.

That summary information, which reflects the organism's condition at the given moment in the form of specific excitations ascending in the cortex, serves as the third component of the afferent synthesis, organically entering the process of elaboration of information. Such a state may be dictated by the action of humoral factors in the organism itself and even by the whole complex of environmental stimuli, but having formed such a state it may also subject to itself in the process of afferent synthesis the environment and initial stimuli. The character and the trend of the behavioural act may to a considerable degree be determined by this initial condition. To some extent this initial condition may be compared with what Pavlov called 'basic trends' (Pavlov, 1916) and what some American research workers call 'motivation' (Miller, 1960; Pribram, 1964; etc.).

The fourth component, which is also used at the afferent synthesis stage is the ani-

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mal's or man's past experience, put away in the 'memory's storehouse' and brought out in the process of afferent synthesis for the formation of a decision to act. The usual elaborated conditioned reflex is also developed on the basis of former hardened structural relations and, consequently, an elementary conditioned reflex is already formed in some degree on the basis of the memory's data. The use of memory is far more extensive and diversified when the behavioural act is built into the natural environment in the fo.m of free behaviour and on the basis of the whole complex of a large quantity of external and internal information.

As can be seen from the enumeration of four components of the initial stage of development of behavioural acts, it is a truly all-embracing one. It is precisely at this stage, as in no other stage of development of the behavioural act, that Pavlov's prevision of the decisive (the 'so-called creative') role of the afferent function of the cortex of the great cerebral hemispheres applies. In a way, the most essential thing at this stage is that all the enumerated fragments above comprise a real organic unity, flowing into a single channel, resulting in the formation of the aim of behaviour.

The characteristic feature of the afferent synthesis would be incomplete if we omitted that exclusive role which the orientation-research reaction plays here.

Whenever the process of afferent synthesis is held up or proves to be incomplete, the orientation-research reaction joins in and contributes to the development of additional rising excitations, thus determining an active selection of new information and the process of its cortical synthesis.

As an example of organic unity of the above-mentioned components of afferent synthesis we may cite the results of Shumilina's systematic experiments (1949), conducted in our laboratory, for defining the role of the frontal parts of the cortex in forming a conditioned secretory motor reaction in an environment of active and relatively free choice of one of the sides of reinforcement. These experiments showed that stimuli are organically united in the form of a conditioned stimulus with that specific environment of selection, in which the experiment was conducted.

In place of an initial stimulus here we have a conditioned stimulus, for instance a bell; in place of environmental stimuli we have here both the general stimuli from the entire environment of the experiment, as well as the specific environmental stimulus in the form of alternative selection of one of the sides of a table in correspondence with the conditioned signal.

Removal of frontal parts from a dog that had a well established selection of a corresponding feeding place, demonstrated that here we have an organic interaction of the above-enumerated components of afferent synthesis. Immediately after the removal of frontal parts the animal loses its accustomed integration between the initial and environmental stimuli, and begins to run ceaselessly from one side to the other, performing pendulum-like movements. The environmental stimuli, which were a part of the afferent synthesis as specific stimuli, acquired a role of initial stimuli, and therefore the animal, on being placed on a table, makes movements in order to chose this or the other feeding pan (Fig. 2).

This experiment convinced us that in the stage of afferent synthesis the central nervous system forms a genuine unity of environmental and initial stimuli. Only on

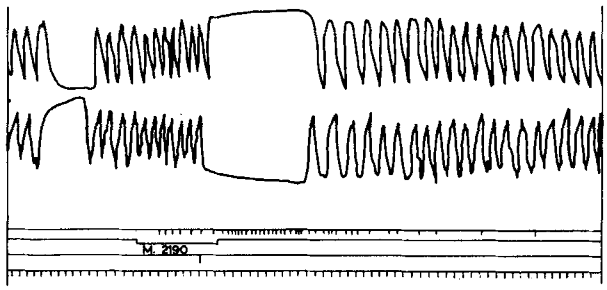

Fig. 2. The dog's behaviour on a two-sided table after the removal of frontal parts of the brain cortex. There can be seen an alternating 'choice' of sides of the table in the intervals between the conditioned stimulus. During the time the conditioned stimulus acts there can be clearly seen more frequent runs and prevalence of the signalled side. What is characteristic is the retardation of the reaction of selection immediately after eating food and greater frequency in intervals. The conditioned secretion has not suffered at all.

this basis does it become clear, though seemingly paradoxical, that being in an experimental environment, which has such a decisive influence on the quality of a conditioned reflex reaction, nevertheless a normal animal in the intervals between the conditioned reflexes sits quietly and does not give the conditioned reflex secretion. The latter flows only at the moment of action of the initial stimulus.

The results given here regarding the role of the frontal parts of the cortex, as implemented in afferent synthesis, are given only to emphasize the significance of that process which is played during the first stage of the formation of the behavioural act. As regards the concrete composition of all afferent information and its neurophysiological analysis, to this the later part of my paper will be dedicated. But now I shall dwell briefly on the form of enumeration on other main mechanisms of the physiological architecture of the conditioned reflex, shown in Fig. 1.

Immediately after the end of afferent synthesis and the emergence of an aim to action, almost simultaneously there are formed two closely-connected neurophysiological mechanisms. One of these mechanisms contains in itself afferent parameters of future results of action, while the other mechanism contains all details of the programme of distribution of efferent excitations, implementing the work of peripheral apparatuses, forming an action and consequently results of that action.

As can be seen from the principal architecture of the behavioural act, the apparatus, anticipating the efferent properties of future results, is a sequence of processes of afferent synthesis that most fully reflects the aim to action itself. To some degree it is a direct reflection of organic synthesis of what has been acquired by the given animal in its 'recent' and 'old' memory. This apparatus, in conformity with its physiological significance, was named by us an acceptor of action. From this name one can see that it takes upon itself real afferent signals from real results of action and compares them with the afferent parameters of required results contained in it.

It follows that, in conformity with our concept, the action acceptor primarily represents dynamic formation, in its composition anticipating combination of afferent

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parameters of precisely those results that were required by the extraordinary situation which arose at the given moment.

Consequently, there are as many action acceptors as there are new situations, as there are afferent syntheses, and as there are aims in the changing stream of an animal's and man's behavioural acts. And just as the results of numerous actions cannot be the same, so the afferent parameters of these results cannot be the same.

From this point of view one must not speak, as is sometimes done, about the 'localization' of the acceptor of action. It cannot represent something forever localized, like 'phrenological bumps', inasmuch as the evaluation of the results of action will be implemented in one example, for instance in visual and tactile afferentation, and in another in auditory and spatial afferentation, etc. One thing is undoubted: integration of all these parameters of results of action, as Shumilina's experiments show, occurs mainly in the frontal parts of the cortex.

As may be seen from the principal architecture, the results obtained, influencing with their parameters the animal's various receptive surfaces, form a stream of afferent impulses, which in the system of the whole behavioural act flows in reverse direction in relation to excitations, that formed an action.

By comparing parameters of reverse afferentation with an action acceptor the behavioural act closes; should they coincide an animal or man is anabled to go over to the next stage of behaviour.

From all that has been said here it is clear that afferent synthesis, formation of an aim to action, formation of an action acceptor and of a programme of action, attaining of results and diverse information about these results compose absolutely necessary main mechanisms of any behavioural act. They may vary in volume and composition, but not one reflex or behavioural act can be of adaptative significance, if it does not contain all these links of physiological architecture.

As can be seen from the general architecture of the act of behaviour, the reflex act or 'reflex arc' in its old Descartes concept is, of course, included in the functional architecture and can be excluded at any moment, if, with the view of carrying out research, we wish to confine ourselves to the linear distribition of excitation, beginning from the initial stimulus and ending only with reflex action.

However we must remember that each real action of an animal, which is an expression of efferent excitations only, unavoidably ends by obtaining results, and by information about these results going into the central nervous system. Consequently, setting up of a 'three-part arc' may now be performed only temporarily and only for research purposes. Recognition of its universal educational significance would now contradict that enormous scientific material and new generalizations, that have appeared during the last ten years in many spheres of science (see, for example, Anokhin, 1935; Wiener, 1958; Magoun, 1963; Drischel, 1960; Klaus, 1961; and many others).

Filling in the neurophysiological detail of each of the main mechanisms of functional architecture of a behavioural act is an extremely big piece of work. It would suffice for many laboratories and perhaps even for entire generations of researchers. The important thing is that each concrete research be defined exactly in conformity with its place in this big architecture, so that it received, so to say, its 'address', which must determine the tactics of research, *i.e.*, orientation in collecting material and explanation of its physiological meaning.

Let us return to the first stage, to the afferent synthesis, and try to understand the composition of the information, which in its entirety determines this stage. According to the work of Magoun and Moruzzi, the ascending information, reaching the cortex of the great hemispheres, consists of two extensive streams of information, which have an entirely different informative significance. The first channel, which ensures the advance of information in the cortex of the great hemispheres in accordance with the lemniscus system to this cortex, was named a specific channel of afferentation, inasmuch as owing to this afferentation the organism obtains information about the fine sensorial modality, ascending excitation. The channel that has been named 'non-specific' begins from collateral branches of the lemniscus system and through subcortical nuclear formations enters the brain cortex. Thus, the first general characteristic of the stage of afferent synthesis in forming a behavioural act consists in expedient utilization of both these channels of afferent signalling and in the study of their interrelation at the level of the cortex and 'the nearest subcortical structures'.

The more detailed study of ways and characteristics of arising afferentations shows, however, that practically all the apparatus of subcortical nuclei thus or otherwise takes part in transmitting information to the cortex of the great hemispheres. Suffice it to recollect the second discharge of Forbes (the urethane second discharge), which was studied in our laboratory by Lu-Juan-Hui, in order to appreciate the multiple character the afferent excitations acquire on reaching the cortex of great cortical hemispheres. The researches of Purpura and other scientists have shown that practically all subcortical nuclei take part in this or other stages in the transfer of peripheral information to the cortex of the great hemispheres.

It follows that even a plain single stimulus, applied to some receptor's surface, unavoidably penetrates into the brain cortex in the form of thousands of rising excitations, directed to its diverse synaptic organizations. In substance this penetration gives us a genuine idea of the volume of afferent synthesis which takes place mainly at the level of the cortex of the great hemispheres.

Our own researches on the so-called non-specific rising activity have demonstrated that the amount of information having a general character is much greater than only one homogeneous non-specific activity, as is assumed by the theory of non-specific rising activity.

It was found that each activating influence, ascending in the cortex of the great hemispheres and having an overall influence on its synaptic organizations, has a specific quality, for which it was necessary to introduce the concept of biological modality in contrast with 'sensorial modality'. This biological modality of the generalized activation of the cortex may be of protective, pain, orientating, sexual, or alimentary character, etc. And each of these excitations, reaching the cortex of the great hemispheres, excites here precisely those extensive synaptic organizations and intraregional connections, that were already formed earlier, first on the basis of inborn connections with subcortical structures, and later on the basis of acquired connections.

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It is not difficult to imagine what different interrelations meet the rising excitations, originating in specific subcortical formations, having a definite biological quality. This is the arena of an afferent synthesis, where the interrelation of the most varied and multitudinous excitations of formation of decision and aim is in complete correspondence with the volume and quality of the afferentations received at the given moment.

In recent years we conducted a study of these rising afferentations in two ways. On the one hand, we compared the quality of rising afferentations, originating in various centres of diverse inborn reflexes, especially in food seeking and protection. This is, so to say, the projection of biological subcortical excitations on the cortex. On the other hand we also analysed the very station of destination, *i.e.*, the interrelation of excitations, coming to cortical neurons and distributed on these neurons in conformity with their functional meaning.

In the first direction special attention is merited by the systematic experiments of our co-worker Sudakov who studied alimentary activation, arising from the hypothalamus, to frontal parts of the cortex of the great hemispheres.

He demonstrated that in a hungry cat under urethane narcosis the frontal parts of the brain cortex are in the state of desynchronization, while other parts of the cortex of the great hemispheres remain in the characteristic sleep state of slow electrical activity (Sudakov, 1962). The artificial 'satiation' of an animal under narcosis led to a decline in activation and emergence of slow electrical activity. In the same manner the coagulation of lateral nuclei of the hypothalamus always produced emergence of slow electrical activity into the brain's frontal part. Comparison of both these experiments enabled us to draw the conclusion that activation is indeed of a specific alimentary character, and the initial point of activation, so to say, its 'pacemaker' is in the lateral nucleus of the hypothalamus, which corresponds to the alimentary centre, discovered by Annand, Brobek and Andersen.

If an animal, which is under urethane narcosis and displaying hunger activation, is subjected to tetanic sciatic stimulation in the brain's frontal parts by electric current then the whole cortex of the great hemispheres proves to be in a state of general desynchronization. In this we may see the generalization of the ascending excitation throughout the whole cortex of the great hemispheres. But then we must recognize that at this moment a hungry cat has in the frontal parts of its brain cortex the simultaneous presence of two activating excitations: one alimentary organized before the stimulus, arising from the hypothalamus, and the other protective, originating on the basis of gentle sciatic stimulution (Fig. 3).

The question is into what relations these two excitations enter in synaptic organization of the frontal parts of the cortex of the great hemispheres. Are we witnessing the incompatability of these two excitations varied in biological modality, or can they coexist as in convergence on the same cortical neurons?

The search for an answer to this question developed in two ways. On the one hand, for the dissociation of two rising activations, alimentary and pain, we applied aminazine (chlorpromazine), as a substance of which we had already had experience and that showed selective blocking action on the pain ascending activation. On the other hand, we undertook microelectrode researches on solitary cortical cells of frontal

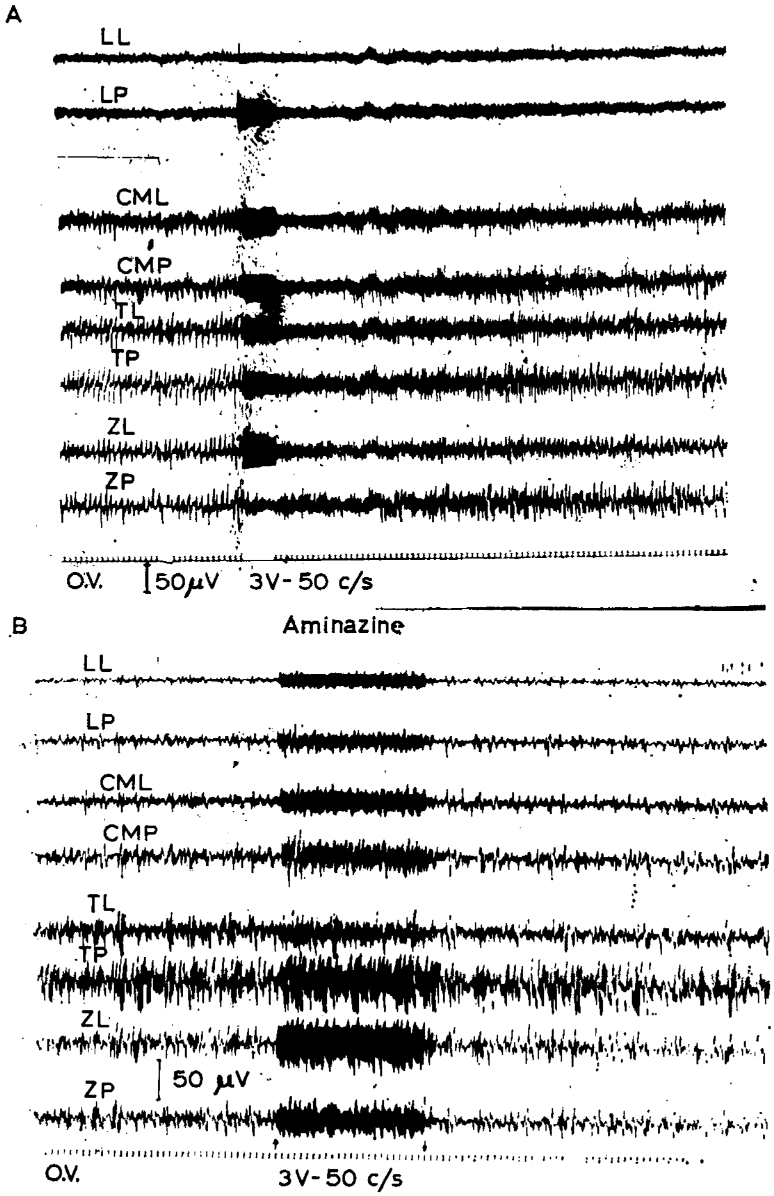

Fig. 3. Comparison of the chemical nature of pain and alimentary activation. A, activated state of all parts of the brain after a brief application of the sciatic pain stimulation of 3 V and 50 c/s. B, the same experience with pain stimulation after a preliminary aminazine injection. One can notice the elimination of the activated state in all parts of the cortex with the exception of frontal parts.

parts of the cortex of the great hemispheres both against the background of separately produced rising activations of varied biological modality, and against the background of their simultaneous influences on cortical neurons.

Experience has shown that there are at least two biologically different rising activations, which may enter into the most varied interactions in the cells of the cortex of the great hemispheres.

Thus, for instance, aminazine fully blocks that subcortical substrate, which ensures in the cortex the generalized pain activations, but at the same time leaves untouched the activation of frontal parts of the brain's cortex, depending on the rising excitations of the alimentary centre of the hypothalamus. Through this the important fact is stressed that rising activations of diverse biological modalities are adressed to various synaptic organizations of the cortex cells of the great hemispheres (Fig. 3).

Perhaps the most interesting consequence of the experiments described above is the observation that synaptic organizations of one and the same cortical cell may be an arena of struggle of two rising excitations having different biological modalities. This phenomenon was named by us 'multibiological convergence' in correspondence with the established terminology for convergence of various sensorial excitations in one and the same nerve cell (Fessard, 1961; Young 1963) (Fig. 4).

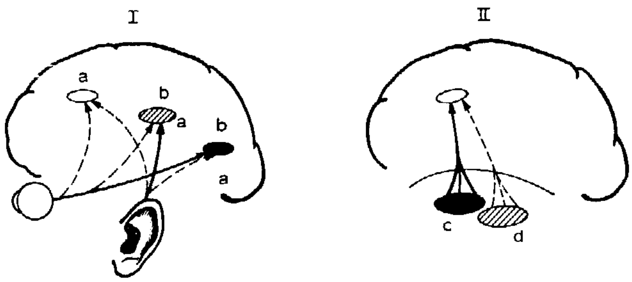

Fig. 4. Schematic depiction of two categories of convergence in cortical cells. I, multisensorial convergence; II, multibiological convergence. Marks: a, zone of convergence; c, pain subcortical centre; d, alimentary subcortical centre.

We were led to this experience by new variants of the experiments described above. Thus, for instance, Panfilov and Loseva (1964) conducted experiments on the prolongation of the starvation time. In all the experiments described above cats were hungry for 2 days before the experiment started. But in experiments conducted by Panfilov and Loseva they hungered for 4 to 6 days. As the researches showed, the general picture of electric activity differed considerably from that picture, described above for a 2-day starvation (Fig. 5, A) (Panfilov and Loseva, 1964).

First it was found that activation did not confine itself to the frontal parts, but embraced the whole cortex of the great hemispheres and consequently became generalized (Fig. 5). Such a picture was not unexpected. If a 2-day starvation led to a regional activation of the frontal parts of the brain cortex, then it was natural to expect that, with the increase in excitability in the sphere of the hypothalamus nuclei from a more powerful stimulation by famine blood, there should also have appeared a more extensive generalization of excitations in the brain cortex. Two possibilities of this transfer from regional activation to a generalized one were feasible.

(1) In the first place there could be widening of a stream of rising activations in connection with the increase in excitability of the alimentary centre of the hypothalamus, *i.e.*, generalization of excitability of a 'vertical type'.

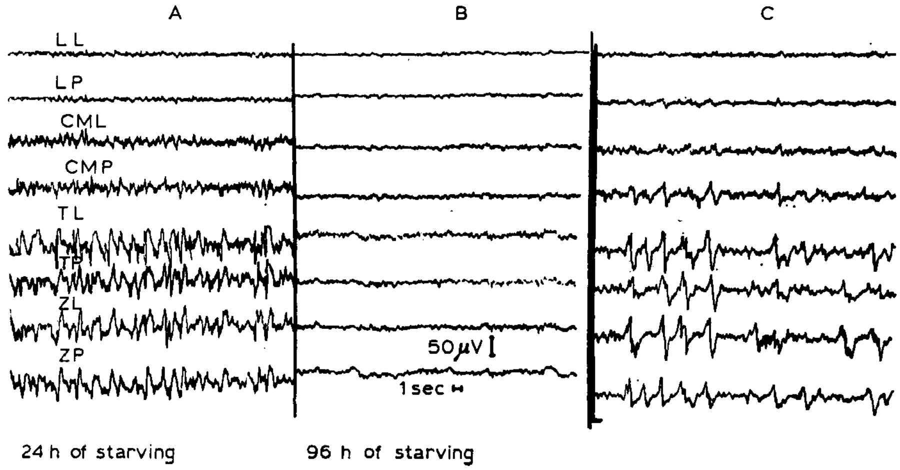

Fig. 5. An example of long hungering and discovery of the chemical nature of the activation evoked by it. A, 24-h starvation. Activation is observed in frontal parts and slow activity in all remaining zones of the cortex. B, 4-day hungering. Activation is spread over the whole cortex of the great hemispheres. C, the same animal after the aminazine injection. One can observe the restoration of the slow electrical activity.

(2) It could be presumed that the excitability irradiation throughout the brain cortex from the frontal parts of the cortex activated by the hypothalamus for the first time could also occur on the basis of the classical theory of the spread of excitations in the cortex, *i.e.*, of a 'horizontal type' (Fig. 6).

In both these possibilities the biological modality of generalized excitations, despite the various mechanisms of their spreading, should have been similarly preserved, *i.e.* alimentary. To check this assertion we made a special control experiment.

In view of the diverse chemical properties of alimentary and protective excitations described above, it might be expected that the injection of aminazine into an animal that had gone without food for 4 days, would not be able to eliminate the preformed generalized activation.

However, the experimental result was different. Injection of aminazine gave totally unexpected results: as with pain generalization, which sets in after the stimulation of the sciatic nerve, aminazine put an end to the whole activation in the occipital, temporal and parietal regions, but left untouched the frontal parts of the brain cortex.

We were thus confronted with a new aspect of interrelation in the cortex of the great hemispheres among the rising activations of diverse biological modality.

It is clear that the rising alimentary activation from the hypothalamus has only a regional importance in the form in which it manifests itself after a 2-day hunger. And as the hunger period grows, there occurs in the region of the hypothalamus a rise in the initial alimentary excitation, which leads to irradiation of excitation into the adrenergic substrate of the reticular formation, possessing the ability to produce rising activation, already generalized throughout the cortex of the great hemispheres.

Results of experiments definitely influence us to such a concept of phenomena witnessed, especially since this concept coincided to a considerable extent with the

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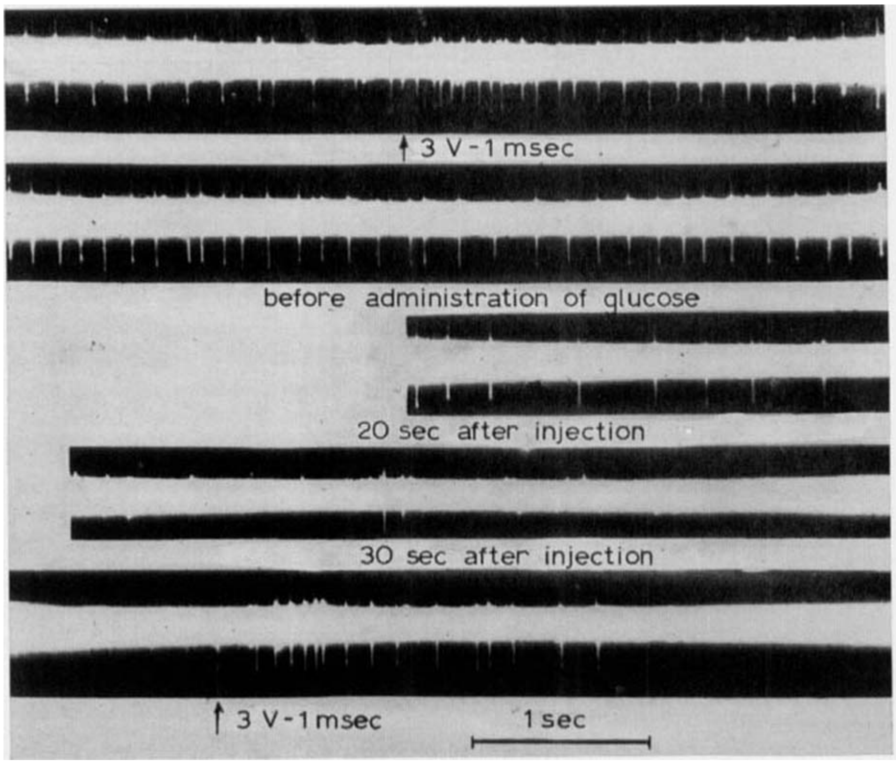

Fig. 6. Microelectrode research of individual neurons in the frontal parts of the cortex. The figure shows a neuron, activated by the ascending alimentary excitation of the hypothalamus. The sciatic nerve stimulation increases the discharge frequency, which points to multibiological convergence. The subsequent injection of glucose leads to gradual elimination of background discharges. Additional sciatic stimulation performed for control purposes results in the restoration of discharges, which points to a full preservation of the cell in respect to other non-alimentary ascending excitations.

biological meaning of the phenomenon. Most probably the long-famished animal is in a more intense general condition and its food-acquiring reaction is more active, requiring the intervention of the sympatho-adrenal system (Kennon, 1928).

Returning to the initial statement of a question regarding afferent synthesis, we can thus observe that one of the undoubted mechanisms of this synthesis represents the interaction of rising activations of varied biological modality in synaptic organizations of the brain cortex. This conclusion was inescapable and made us start experiments requiring the use of the microelectrode technique.

We were of the opinion that a study of the regime of the activity of one and the same cortical neuron, influenced by various biological modalities rising from the hypothalamic activations, could yield more exact data on the interaction of these activations through the synapses of one and the same neuron (Fadeev's experiments). We knew, of course, that these interactions take place in the synaptic organizations of one and the same cortical neuron. But it is precisely these interactions that compose the neurophysiological basis for analysis and synthesis of rising afferent influences —

synthesis without which neither 'the decision' nor 'the aim to action' can be formed, nor can the formation of subsequent stages of the behavioural act begin. Therefore the study of real interactions of biologically characterized rising excitations at the level of the cortical neuron is a totally unavoidable stage on the road of learning of afferent synthesis in its entirety.

Systematic microelectrode researches were conducted in our laboratory by Fadeev in conditions of special formation of rising activations with a clearly defined biological modality.

First it was proved that it is possible to apportion at least 5 types of cortical cells in conformity with their relation to rising excitations of varied biological modality.

In obtaining from a hungry animal a cortical cell with spontaneous discharges, we had to be sure that these spontaneous discharges are exactly a result of concrete alimentary rising influences in the sphere of the alimentary centre of the hypothalamus. This was ascertained through the gradual elimination of phonal discharges after an intravenous injection of glucose (Fig. 7). Having convinced ourselves that we had an 'alimentary' cell activated by rising influences from an alimentary centre in the hypothalamus, we inflicted a pain stimulation on the sciatic nerve and watched the reaction of the same nervous cortical element.

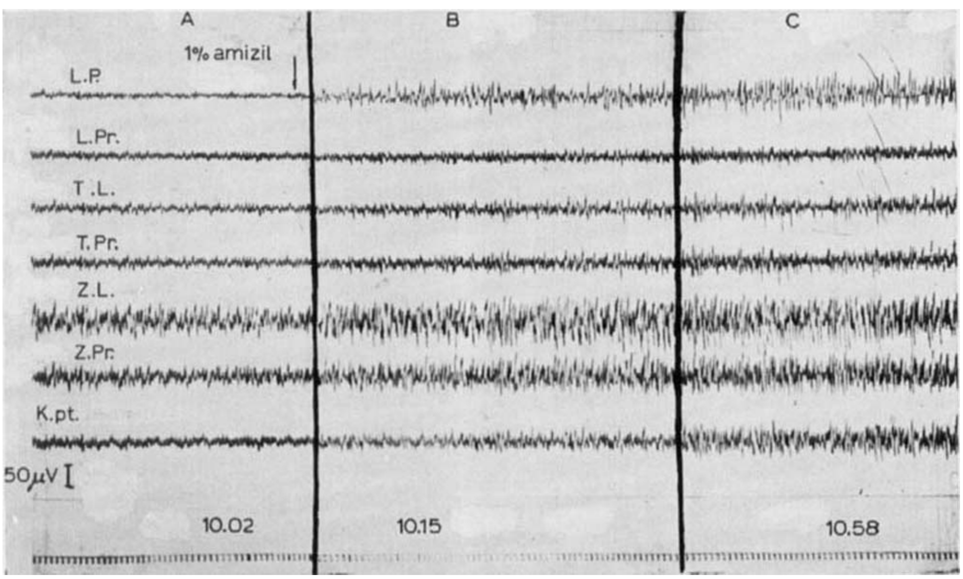

Fig. 7. Experience of application of amizil to the frontal parts of the cortex of the great hemispheres in conditions of their alimentary activation. A, state of electrical activity before the application of amizil. B, 13 min after the application of amizil (the upper part). C, 56 min after the application of amizil. One can see the slowing down of electrical activity at the point of application of amizil.

The most interesting observation made from these experiments was the convergence of the pain rising excitation precisely to those cortical neurons which up to this time were aroused deliberately by the alimentary rising excitation from the region of the hypothalamus. In other words we observed the convergence to one and the same cortical cell of excitations of varied biological modality, which, as we mentioned above, we called 'multi-biological convergence'.

Such a convergence takes place in two ways. In one the pain rising excitation inhibits the spontaneous alimentary discharges, and in the other it increases the frequency of these discharges. In either type of action we must presume the meeting of two heterogeneous influences on one and the same nerve cell.

The interactions of this sort of excitation at the cortical level show that in the process of afferent synthesis various complexes involve not only individual neurons, but also individual synaptic organizations of one and the same neuron.

It is true that according to Bullok (1957), who demonstrated an extraordinary chemical and functional heterogeneity of the membrane of one and the same nerve cell, we can no longer be surprised that various chemical processes may take place in it simultaneously.

Consequently we have now on hand new possibilities for explaining analytical and synthetic processes of the brain cortex.

Here too the problem becomes prominent of the convergence of heterogeneous rising excitations in one and the same cortical cell. And, indeed, how is the cell 'taken apart' as to rising excitations varied in nature? How can these excitations, being chemically heterogeneous, in their entirety determine the exit to a definite axon specific for the given neuron excitation? What is the mechanism of this work of the neuron in bringing numerous excitations 'to one denominator', and what informative value has each of them in this peculiar synthesis?

As can be seen from these questions, the neuron represents a fully developed cell of synthesis, and, receiving (through dendrites and the neuron's body) heterogeneous excitations, generates on an axon an excitation, which in some still incomprehensible manner combines in itself in latent form all the properties of excitations converged upon it.

Today it is clear that in order to understand the afferent synthesis of the whole brain it is necessary also to know the particulars of those mechanisms on the basis of which heterogeneous and numerous chemical processes of the membrane of the nerve cell are transformed into impulses on the axon, well charged with information.

Obviously this represents a new and fascinating aspect in comprehending those synthetic processes which define the natural passage to the next stages of development of the behavioural act, to forming 'the aims of behaviour', the apparatus for envisaging results and formulating a concrete programme of action.

In this exceptionally ramified way we may be helped only by a systematic approach to a problem, but just now, to our regret, we must satisfy ourselves with only initial approaches to this problem.

As a first attempt to undertake the chemical characterization of processes that take place at the level of synaptic organizations of brain cortical cells, we utilized the method of application to the cortex of diverse inhibitors of synaptic activity in conditions of deliberately required convergences on cortical cells of excitations that had biological and sensorial modalities known beforehand. The experiences of many authors in application of diverse substances to the cortex with a view to making analyses permit us to hope for success in our own experiments (see Richrich, 1960).

The general course of the argument preceding the start of these experiments was as follows. If the rising excitations of varied origin converge in the sense of biological and sensorial modality to one and the same cell of the brain cortex, then it is natural to expect that the synaptic formations themselves on the cortical cell used to conduct these excitations may be of different functional importance, they may be depolarized, hyperpolarized and in general have a wide range of changes in the chemical nature of their subsynaptic membranes. This was indicated both by our own results, as well as the data obtained by other authors (Ata-Muradova, 1963; Bullok, 1957, 1958; and others). If this be so, then by applying various specially selected substances directly to points of the cortex, we may create some dissociation of synaptic formations located in the given region. Some of them may be blocked; others, on the contrary, may even be alleviated in the conduct of excitations, and, consequently, we may observe changes in electric potential.

On the basis of these logical prerequisites we conducted experiments with application of cholinolytics to diverse spots of frontal parts of the brain cortex of animals that were in a state of hunger and, consequently, had the activation described above. If we proceed from the point that this initial activation is a result of rising activating influences on the cortical cell, then it would be interesting to discover of what neurochemical nature are the given synapses on the cortical cell.

Experience has shown that aminazine and atropine radically change the electrical activity of the point of application. Thus, for instance, a clearly desynchronized electroencephalogram turns into a slow electroencephalogram of the usual quiet type (Fig. 8).

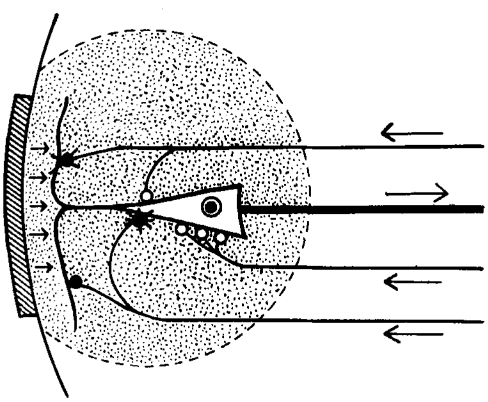

Fig. 8. Schematic depiction of the action of applied substances to the point of cortex. It shows the possible action of applied substances to the synaptic formation of varied localization and varied chemical nature.

If we are to organize this experiment in such a way as to record the produced potential from a zone of application, then we may hope to obtain an interesting result. As was demonstrated in our laboratory's former researches, in conditions of

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hunger activation of the frontal parts of the brain cortex, the potential evoked loses its usual form.

Only a positive part is clearly revealed, while the negative impulse is absent. If we are to proceed from ideas expressed in the figure, then we conclude that the digestive ascending activation 'subtracts', *i.e.*, utilizes exactly those synaptic organizations that are absent from the produced potential, obtained against the background of this activation.

If these suppositions are correct, then the animal's satiation in applying cholinolytics at the point of leading off the evoked potential should have acted in one direction. Both these factors would have to restore the usual form of the evoked potential, positive, negative and 'secondary'. And, indeed, application at this point of amizil and atropine leads to the evoked potential acquiring its usual appearance with positive and negative components (Turenko) (Fig. 9).

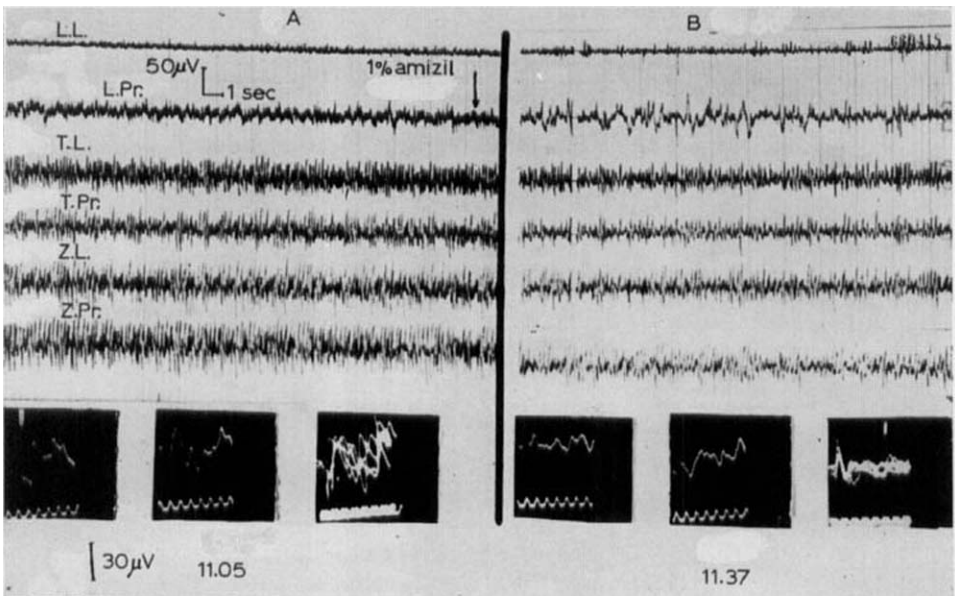

Fig. 9. Comparison of slow electrical activity with the evoked potential at the point of amizil application. We can see a distinct expression of the evoked potential 30 min after the application of amizil.

It can also be said that an animal's satiation alongside the return of the exact and slow electrical activity in the frontal parts also restores the fully valued evoked potential (Sudakov, 1962) (Fig. 10).

We obtained one more illustration, perhaps the most demonstrative, of the fact that each rising activation, having a specific biological modality, is addressed to its own specific synapses on the cortical cells.

After the application of cholinolytics converts the alimentary activation of the cortex into slow electric activity, the stimulation of the sciatic nerve against this background very rapidly transforms this slow activity into desynchronization, but

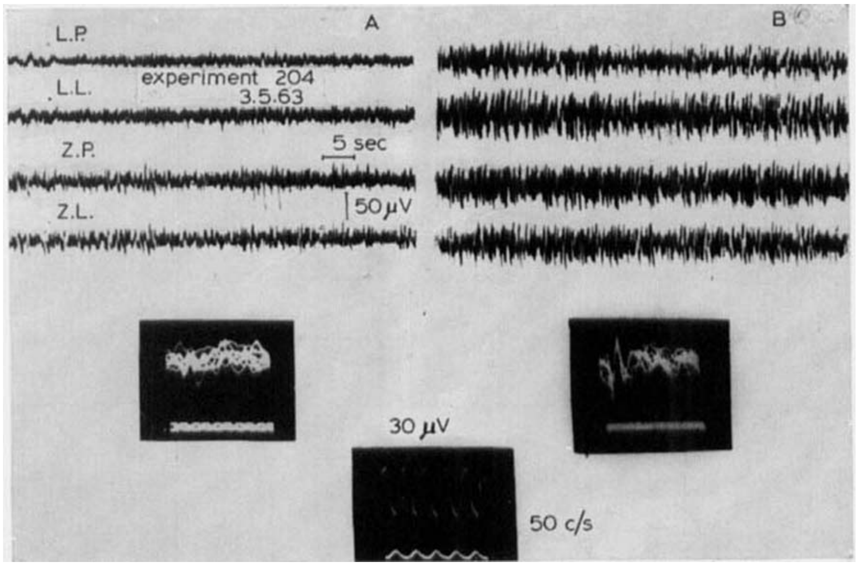

Fig. 10. Experiment demonstrating changes in the evoked potential in the frontal parts of the brain cortex during the process of the animal's transformation from the state of hunger to artificial satiation. A, state of 1-day hunger; activated condition can be seen of electrical activity in frontal parts. The evoked potential is expressed indistinctly. B, electric activity of frontal parts after the intravenous injection of glucose. Electroencephalogram shows the slowing down of electrical activity, which is accompanied by the distinctly expressed evoked potential.

this time of pain character. Thus, synapses responsible for the production of rising activation of different biological modalities proved not to be blocked (Gurenko) Fig. 11).

Considering all the observations cited above, we can say that they give us every ground for assuming that the initial alimentary activation of the brain cortex depends on excitation of cholinolytic synapses on the cells of the brain cortex, and that these synapses serve as a final station for perception of rising excitations from lateral nuclei of the hypothalamus. On the contrary, we may presume that a negative component of the potential produced is formed by synapses, being of different nature, inasmuch as it frees itself from the application of cholinolytics.

Both these results are in good agreement with our laboratory's former experiments, performed by Shumilina, 1949; Gavlichek, Makarov, Sudakov, 1962; and others. In these experiments the influence of aminazine quite distinctly revealed the difference between the activity, depending on the functions of the cholinolytic substrate and activity, connected with the activation of the adrenergic substrate. The experiments made above strengthen the opinion that activities and synaptic organizations, unyielding to the action of aminazine, may be of cholinergic character.

Experiments cited in my paper represent only a beginning of systematic researches of these mechanisms at the level of cortical synaptic organizations. And already the first results, as you have seen, permit us to presume that it is precisely at the level of the brain cortex that we have an extraordinary coincidence of diverse excitations both in a quantitative as well as in a qualitative chemical respect.

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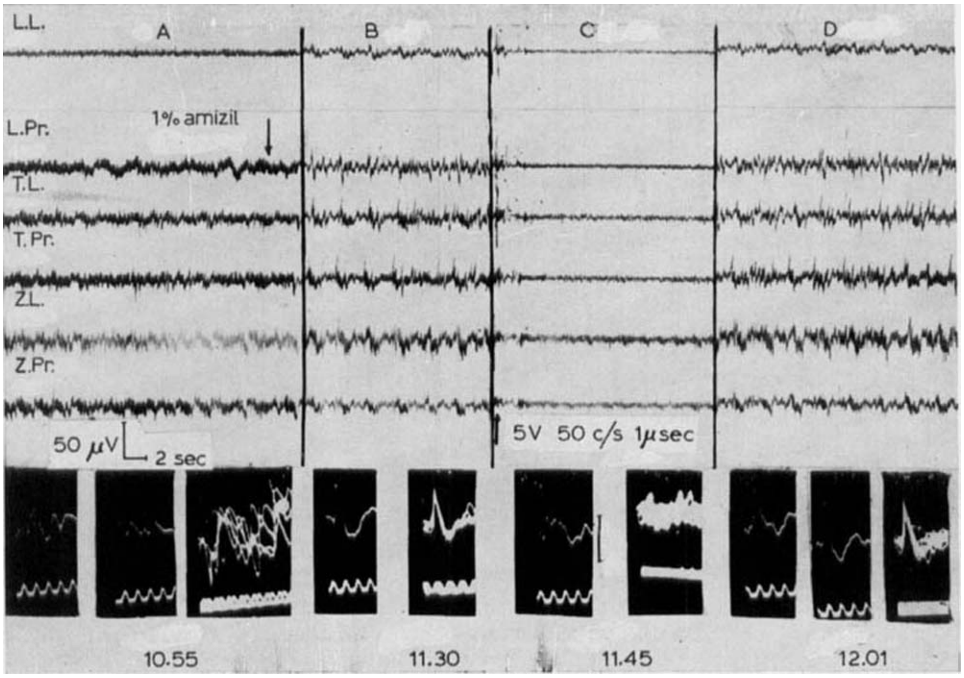

Fig. 11. Comparison of electroencephalogram and evoked potential in conditions of application of amizil and pain stimulation. A, the initial background during the 1-day hungering. The activated state in the frontal parts of the cortex is seen. B, 35 min after application of amizil in the frontal part, on the left side (upper section). Slowing down of activity in the frontal part and appearance of a distinct evoked potential can be seen. C, sciatic nerve pain stimulation. Activation can be seen in all parts of the brain cortex. The evoked potential is shown indistinctly. D, 16 min after inflicting the pain stimulation. The initial background of slow electrical activity is restored, and a distinct evoked potential has appeared. Comparison of electroencephalogram and evoked potential shows that amizil does not block the synaptic organizations, but performs pain activation in the brain cortex.

Figuratively speaking we have at the level of cortical cells an enormous quantity of excitations varied in quality, which may be synthesized on the body of one and the same cortical cell. At the same time we must not forget that a tremendous quantity of excitations, which rises to the cortex of the large hemispheres from the most varied subcortical formations and exterior receptor apparatus, determines both the direction and the main exit of effective corticofugal excitations, *i.e.*, excitations forming the behavioural act.

Only a thorough and fine analysis of all excitations ascending to the cortex of the great hemispheres and appraisal of quantitative correlations of these excitations can give us objectively tangible concepts of those multiform and numerous processes which accompany the stage of afferent synthesis. And it can hardly be doubted that only then, when all these boundless types of interrelations create a final model of the given situation, may the nervous processes swoop down in a free stream on the final stages of formation of the behavioural act.

SUMMARY

The investigation of the individual mechanisms maintaining all parts of the arborized functional system in a state of integration, logically led us to the necessity of characterizing most completely the first phase of the system activity — the afferent synthesis, which precedes the formation of the goal to act and detailed programming of all successive steps of the given action. This task should be performed through revealing the concrete neurophysiological mechanism of cortico-subcortical interaction.

With accumulation of our knowledge in the field of physiology of different brain parts and their interaction under different conditions of functioning, it becomes more and more difficult to regard the cortex and the subcortical structures as something separate, isolated. The question of the function of those structures nowadays is gradually substituted by the following question: which specific parameter is carried by the cortex or subcortex into organically integrated brain work?

As an illustration we may point out the decisive role played by the apparatus of the ascending subcortical activation in associative activity of the cortex (Magoun, 1963). The corticofugal influences on the subcortical apparatus without which the whole brain work would lose its adaptive essence is an example to the contrary.

Consequently, the problem of cortico-subcortical interactions has radically changed both in its neurophysiological aspect and in the evaluation of the integrated behavioural acts of self-regulatory character, especially of the conditioned reflex activity. It implies a new approach to interpretation of already existing data as well as to tactics of obtaining new facts which reveal integrative and self-regulatory character of brain work as a whole.

The most general neurophysiological mechanisms of the adaptive behavioural acts should include in accordance with well elaborated architectonics of these acts, the following stages.

(a) Recognition and identification of the 'exterior' situation, *i.e.* afferent synthesis, which is formed on the basis of ascending activating influences connected with the orienting reflex.

(b) Corticofugal mobilization of subcortical apparatuses in accordance with the situation.

(c) Selective excitation of the cortical neurons or synaptic organizations in accordance with the biological quality of the ascending activations.

(d) The formation of the goal to act and simultaneous formation of the afferent apparatus for the acceptor of the results of the action to be performed in future.

(e) The formation of efferent mechanisms of manifestation of the behavioural act and the achievement of the corresponding results.

(f) The reverse afferentation from these results and their comparison in the acceptor of action with previously formulated purpose.

Special experiments were performed to investigate the fine neurophysiological characteristics of these key processes. These experiments allowed us to reveal the following mechanisms in the cortico-subcortical relationships.

The specific character of the ascending activations to the cortical cells, and the

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convergence of the same cortical cells of sensory as well as specific ascending activations from subcortical apparatuses of different biological quality (multisensory and multibiological convergence).

The combination and interaction of subcortical apparatuses of different biological and chemical specifity in the process of the organism's adaptation to the peculiarities of its internal and external media.

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