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ON THE ROLE OF THE HIPPOCAMPUS IN THE INTEGRATIVE ACTIVITY OF THE BRAIN

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Abstract. The present evidence plus data from the literature suggest that the hippocampus is concerned with responses to signals having low probability of reinforcement. The theta-rhythm, characteristic of the hippocampus, arises in a situation of pragmatic uncertainty, when stereotypical behavioral patterns have not yet been formed and when decisions are still being sought. The theta-rhythm may serve as a correlate only of orienting-exploratory responses and not as a correlate of the orienting-defensive responses of "biological alertness", in Pavlov's terminology. Functionally, the hippocampus belongs to the system of structures which make decisions about the response to a given stimulus. If, following destruction of the hippocampus, the neocortex gives preference to signals with high probability of reinforcement and in the sphere of unconditioned responses a stronger motivation is predominant, then hippocampal involvement is essential for simultaneous assessment of these two factors. For that reason, the hippocampus plays an important role in the competition among conditioned reflexes having different magnitudes and reinforcement probabilities.

In the extensive literature available, hippocampal functions are associated with conditioned reflex (CR) activity, memory, voluntary movements, orienting and emotional responses. Yet, the question of what exactly the contribution of the hippocampus is to these integrative activities remains unanswered. Two attempts to provide an answer seem to me more validated and deserving further consideration.

First, is the idea of Douglas and Pribram (3) that the hippocampus registers the fact of non-reinforcement of external stimuli as a biologically meaningful event. This idea well accounts for hippocampal involvement in the extinction of orienting and conditioned responses. But

it does not supply an answer to the question of why hippocampal involvement is so important early during the formation of CRs when each presentation of a conditional signal (CS) is invariably attended by reinforcement (8). The Douglas–Pribram concept also contains other inadequacies. Thus, according to this concept, the hippocampus contributes to concentration of attention by blocking the effect of extraneous stimuli (2). In actual fact, however, rats with damaged hippocampus are distracted much less than control animals (4). If the hippocampus really were a “recorder of non-reinforcement”, then following a hippocampal lesion, the animals should have successfully established CRs with a low probability of reinforcement. The experiments of Pigareva (see below), however, have shown that the reverse is true.

As claimed by Vinogradova (20), the hippocampus is a detector of novelty, and abstracts the biological meaning from the stimulus, which is itself assessed by another system comprising mammillary bodies, limbic nuclei of the thalamus, and neocortex. The hippocampus correlates the presented signals (entering via the septum) with the “neural models” stored in secondary zones of the neocortex. The hippocampus does not fix traces but passes them over for recording. The novelty of a signal is revealed in field CA₃. If novelty is not established and the signal is subject to recording, it is fed to field CA₁ which sends axons to mammillary bodies, limbic nuclei of the thalamus, and the limbic cortex (21). Vinogradova’s concept defines more precisely the role of the hippocampus in mnemonic events and in the mechanism and extinction of orienting responses. This concept is thoroughly supported by experimental evidence on the activity of hippocampal neurons upon exposure to external and internal stimuli.

However, this concept may only be used to explain a more or less broad range of facts if the meaning of such terms as “novelty” and “neural model of the stimulus” is extended. For instance, non-reinforcement of a CS will prove to be a new event only if the notion of “novelty” is used to cover not only the CS itself but also its reinforcement. In other words, the model must encompass the CS together with the unconditional stimulus (US). What, then, would be subject to recording: the CS or its non-reinforcement, that is, the change of its meaning for the organism? The time-course of hippocampal electrical activity (theta-rhythm) already shows that the functional state of the hippocampus strongly depends not only on the formal informational characteristics of the stimulus (degree of novelty) but also on the quality of reinforcement — whether defensive or alimentary (12). Apparently, the interesting concept of Vinogradova referred to above, is concerned not with the role of the hippocampus in the integrative activity of the brain but with a narrower and more parti-

cular question of hippocampal involvement in the execution and inhibition of the orienting response.

Of critical importance for the formation of my own concepts concerning the hippocampal role in the organization of adaptive behavior and in the genesis of emotional states, have been experiments by Pigareva on "switching" of CRs of different types in the rat (9, 10). The phenomena, associated with "switching", first described by Asratyan (1) and systematically investigated by his co-workers, have proven highly appropriate for the analysis of hippocampal functions. In the morning an alimentary CR to light and a defensive CR to bell were elaborated; in the evening the stimuli had opposite meaning. Experiments have indicated that attempts to elaborate the switching of defensive and alimentary CRs in intact rats lead to severe disorders of higher nervous activity with marked autonomic components of emotional stress. At the same time, rats with hippocampus destroyed bilaterally according to the method of Mering (Fig. 1), attained consistent "switching" of CRs after 3-6 sessions, while if the hippocampal lesions were produced at different stages of elaboration of the "switching", CR activity was more normal.

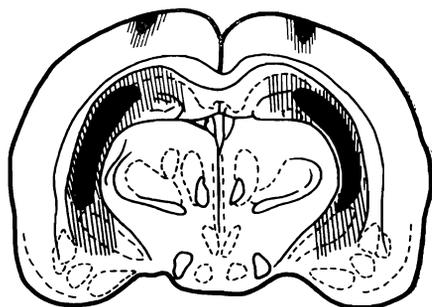


Fig. 1. The largest (hatching) and the smallest (black) hippocampal and neocortical lesions. Frontal sections.

Since hippocampectomized rats completely retained not only the previously acquired connections between reinforcement and CS but also the meaning of the composite situational switching signal, it is not possible to speak of a general memory defect. Similarly, the results of these experiments cannot be accounted for by diminished fear because hippocampectomized rats exceeded control animals in readiness to switch similar alimentary reflexes when the switching signal was reinforced alternately in the left and the right halves of a chamber depending on the situation. The most plausible conclusion one can make is that the behavior of rats with damaged hippocampus is selectively oriented to signals of highly probable events. The behavior is no longer complicated by predictions of events unlikely to happen in a given situation, specifically, in

Pigareva's experiments, by the possibility of painful stimulation in an alimentary situation (16). Consequences of hippocampal destruction are shown schematically in Fig. 2. That the switching signal potentially retains both meanings ascribed to it, is suggested by cases of double responses registered in CR switching by Struchkov (18).

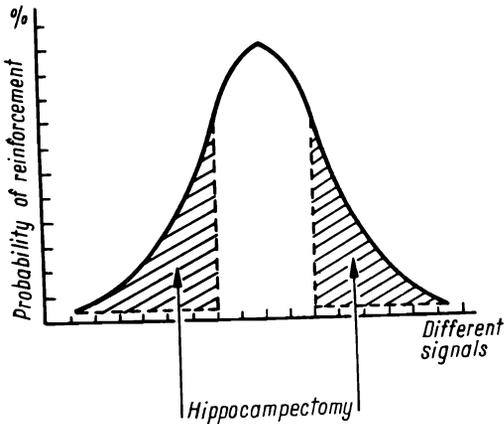


Fig. 2. After-effects of hippocampectomy.

The validity of these conclusion was confirmed by direct experiments of Pigareva with partial (probabilistic) reinforcement of alimentary CRs. With random reinforcement of 100 do 50% of the CS presentations, CR elaboration in hippocampectomized rats showed no substantial differences from the situation in intact animals. When the proportion of reinforcement was further reduced to 33–25%, hippocampectomized rats were unable to form CRs over the period of 10 experimental days. Intract rats attained high response levels by days 8 and 9.

In this context, the numerous facts referred to above, may be explained. Thus it becomes clear why the hippocampus is actively involved in the early stages of CR formation, when the probability of reinforcement remains problematic for the animal; why the hippocampectomized animals are superior to intact ones the two-way avoidance situation (stimulus invariably meaning current) but are inferior to them in the one-way avoidance where only half of the cage is dangerous (stimulus signals shock only when the animal is in a definite position); why perseveration arises in hippocampectomized animals only upon transition from a frequently reinforced lever to one with rare reinforcement and why they exhibit no differences from intact animals with the reverse transition; why the hippocampus is concerned in the extinction of conditioned and orienting reflexes in association with the falling probability of their reinforcement. There are strong reasons to believe that the course of extinction of an

orienting response depends not so much on the formation of a neural model of the stimulus as on ascertaining its indifference for the organism. In this context, it is also possible to explain the impaired development of trace CRs following hippocampal lesions, since the probability of reinforcement of a delayed signal is always lower (more dubious, more problematic) than that of a CS contiguous to reinforcement.

It is difficult to assume that the assessment of reinforcement probability, the probability of satisfying a requirement existing in the animal, occurs in the hippocampus itself. More likely it is made by neocortical structures. According to Luria (5) and Pribram (13), the presence of a requirement for food, water, a mate, etc. is fixed by the mediobasal portions of the cerebral hemispheres. The posterior portions of the neocortex form a program of actions required to meet the requirement that has arisen, while the anterior portions control the actual implementation of the program and predict its effectiveness. In dogs the significance of prefrontal neocortex for evaluating the reinforcement probability of CRs has been demonstrated by Mekhedova (6, 7). The hippocampus is involved in this process only when and as long as there exists a pragmatic uncertainty, *providing for responses with low reinforcement probability*. That is why an animal with destroyed hippocampus becomes unilaterally oriented to signals of low-probability events and is free of "doubt and hesitation". Not only electrical activity but hippocampal functions as well are intimately linked up with functions of the septum whose destruction also affects the evaluation of reinforcement probability by the brain. When a septally operated rat performs two CRs, extinction of one of them is slowed in comparison with control animals unless both responses are reinforced concurrently. If, on the other hand, only one of the responses ceases to be reinforced, the second response extinguishes faster than in intact animals (14). These experiments again show that the consequences of the operation cannot be reduced to the trivial "weakening to inhibition" but have a much more complex nature.

There is some evidence to suggest that the hippocampus plays an important role in the creative activity of the brain (as well as in the mechanism of dreams), providing for the low-probability combinations of neural traces. The evidence on the predominant effect of hallucinogens (lysergic acid diethylamide) on hippocampal structures favors this assumption. On the other hand, the reference to the hippocampus as an "organ of hesitation and doubt" prompts the speculation that selective and reversible suppression of its activity might be effective in treating neurotic states.

It seems interesting to consider, hippocampal electrical activity in this context, particularly since the pertinent evidence on this point is as

abundant as it is contradictory. Almost any form of behavior, whether emotional, orienting, motor or conditioned, may be accompanied both by desynchronization of the hippocampal EEG and by well synchronized theta-rhythm. First of all, it is necessary to find out to which functional state of the hippocampus itself, the two main kinds of its total electrical activity correspond. According to Vinogradova, during the reaction to new stimuli (theta-rhythm) the activity of hippocampal neurons is predominantly inhibited, while that of the reticular formation is enhanced. As the orienting reflex extinguishes, hippocampal neuronal activity becomes maximal while reticular activity falls (22). Thus, the theta-rhythm may be regarded as an electrophysiological manifestation of an inhibited, inactivated state of the hippocampus (20). The available data agree with the Volterra's theoretic calculations of interactions between excited and inhibitory elements. According to Volterra (23), the theta-rhythm results from a concurrent decrease of the number of excited and inhibited elements, with a predominant decrease of excited elements. At the same moment the ascending activating influences on the higher divisions of the brain attain considerable intensity. Such an interpretation agrees well with the high correlation of theta-rhythm enhancement with changes in heart rate (11).

As the hippocampus pertains to the system regulating the level of arousal in higher divisions of the brain, its state is always affected both by fluctuations in the magnitude of a requirement (motivation) and by the degree of uncertainty (novelty, stage of CR elaboration, etc.). It is only necessary to bear in mind that according to the "law of the dominant", strong motivation makes presumptively meaningful (i.e., certain) any stimulus, including new ones. For that reason, the response to a quite new stimulus is accompanied by desynchronization rather than by theta-rhythm (19) because the theta-rhythm in the hippocampus is *an electrophysiological correlate of pragmatic uncertainty*.

From this point of view, it makes no sense to look for correlations between hippocampal EEG and movements as such. A motor act may be performed at different levels of motivation and with different degrees of uncertainty, including both the degree of consolidation of the given motor habit and the probability of its reinforcement. No less varied is the motivation of orienting responses, which is negative in the case of fright and alertness (the reflex of biological alertness according to Pavlov), and positive in the case of searching for factors which are biologically meaningful for the organism (the Pavlovian orienting-exploratory reflex). The generic name "orienting reflex" actually unites a whole group of very different responses: the action of quite unknown stimuli, the primitive response of fright, the activity directed to a more thorough acquaintance

with the novel stimulus, etc. Naturally enough, both desynchronization and theta-rhythm may be recorded in the hippocampus in this case. No universal electrophysiological correlate of the orienting reflex exists in nature, as there is no single, universal orienting reflex.

Thus it can be concluded that hippocampal destruction and the results of studies of global hippocampal electrical activity well agree with each other at least in one respect. Among a multitude of factors of the external and internal environment, the degree of uncertainty of forthcoming events and the degree of motivation most of all affect the functional state of the hippocampus as judged by the hippocampal EEG.

It can be readily seen that the theoretical basis of this approach to the analysis of hippocampal functions is the information theory of emotions (15, 17). It may be recalled here that this theory postulates that the degree of emotional stress is determined by the magnitude of the requirement (motivation) and by the assessment of the probability of its satisfaction at a given moment. From this viewpoint, the hippocampus is associated neither with motivational excitation (which forms in other structures, primarily in the hypothalamus) or with the assessment of reinforcement probability which is performed by neocortical mechanisms. The hippocampus pertains to that system in which motivational and informational excitation are integrated and serves as an intermediate station through which these two streams of excitation exert a modulating effect on the neural substrate of emotions.

Among the systems recognized by modern neuropsychology (behavioral motivation, programming and control of actions, neural substrate of emotions, etc.), the hippocampus is most closely associated with the decision-making system concerned with what action to take in response to a given signal.

If, following hippocampal destruction, the neocortex gives preference to signals with high probability of reinforcement, and in the sphere of URs a stronger motivation proves to be dominant, then hippocampal involvement is essential for simultaneous assessment of these two factors. The role of the hippocampus is particularly obvious in those situations where there is competition between requirements of different magnitudes and different probabilities of satisfaction.

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