Neuroscience and Behavioral Physiology, Vol. 35, No. 5, 2005

Neuron Activity in the Anterolateral Motor Cortex in Operant Food-Acquiring and Alcohol-Acquiring Behavior

Yu. I. Aleksandrov,[1] Yu. V. Grinchenko,[1] D. G. Shevchenko,[1] V. N. Mats,[2] S. Laukka,[3] and R. G. Averkin[1]

UDC 612.821.44 + 612.822 + 612.825

Translated from Zhurnal Vysshei Nervnoi Deyatel'nosti, Vol. 54, No. 3, pp. 363–372, May–June, 2004. Original article submitted December 31, 2002, accepted March 11, 2003.

The interactions of the neuronal mechanisms of food-acquiring behavior and newly formed operant alcohol-acquiring behavior were studied by recording the activity of individual neurons in the anterolateral area of the motor cortex in chronically alcoholized rabbits. Adult animals learned food-acquiring behavior in a cage with two feeders and two pedals, in the corners (the food in the feeders was presented after pressing the corresponding pedal). After nine months of chronic alcoholization, the same rabbits learned an alcohol-acquiring behavior in the same experimental cage (gelatin capsules filled with 15% ethanol solution were placed in the feeders instead of food). Analysis of neuron activity showed that the set of neurons involved in supporting food-acquiring and alcohol-acquiring behaviors overlapped, though not completely. These experiments not only help us understand the neuronal mechanisms of the newly formed and the previously formed behaviors, but also facilitate the development of concepts of the similarity of the neuronal mechanisms of long-term memory and long-term modifications of the nervous system, occurring in conditions of repeated intake of addictive substances.

KEY WORDS: neuron, operant behavior, memory, learning, alcohol, alcoholism.

The appearance of a new need is associated with the formation of behavior directed to its satisfaction. A model for the de novo formation of a need in adult individuals is provided by the need for alcohol. After chronic alcoholization of animals, this need can be met by operant alcohol-acquiring behavior (AAB). It has been suggested that the "physiological substrate of alcoholic motivation" mediating AAB is formed on the basis of motivations formed premorbidly [12]; the variables controlling the need for addictive substances are similar to those controlling behavior directed to "normal reinforcement," for example, acquisition of food [29]. This is in agreement with the hypotheses developed in psychology that the satisfaction of the need for alcohol involves and transforms various actions directed to satisfying previously existing needs [8]. It is logical to suggest from this that the set of neurons involved in supporting the premorbid and newly formed behaviors will overlap. Whether this is the case can be verified by studying the behavioral specialization of neurons, i.e., the relationships between their activity and the functional systems of defined behavioral acts of different phylo- and ontogenetic "ages" [5, 18, 33].

Our previous studies identified various types of behavioral specialization of neurons in different areas of the brain in rabbits, these mediating operant food-acquiring behavior (FAB) in a cage with two pedals and two feeders, located in the corners (see [2, 13, 14, 18]). It was also observed that the formation of a behavioral act during training is a process of systems genesis. Formation of a system for a formed behavioral act is a process of specialization of a new group of neurons in relation to this system. Different types of specialization can be grouped into two large groups: "old" (O)

[1] V. B. Shvyrkov Laboratory for the Neurophysiological Bases of Mental Activity, Institute of Psychology, Russian Academy of Sciences, Moscow; e-mail: nyualex@psychol.ras.ru.

[2] CNS Morphology Laboratory, Institute of Higher Nervous Activity and Neurophysiology, Russian Academy of Sciences, Moscow.

[3] Department of Behavioral Sciences, Oulu University, Finland.

and "new" (N) neurons. Activation of O neurons realizes the systems formed at the early stages of individual development. Their activation is phenomenologically linked with defined movements by the animal. Activation of N neurons realizes the systems for relatively newer behavioral acts in an animal during learning in an experimental cage.

The aim of the present work was to identify whether the formation of AAB is based on the involvement of neurons previously specialized to the premorbid behavior in this new behavior, i.e., FAB, and on the formation of new specializations of neurons relative to the AAB which is formed. Resolution of this aim is important not only for determining the characteristics of AAB formation, but also to answer the more general question of the interactions between the neuronal support of the newly formed and previously formed behaviors.

METHODS

Experiments were performed on five rabbits (*Oryctolagus cuniculus*, males, weight about 3 kg). Some nine months before experiments, animals were placed in a situation allowing free choice between alcohol (7%) and water. Their "home" cages in the animal house permanently contained two feeders (from Cemic, Finland) containing water and alcohol. Animals preferring alcohol to water were identified during the first 1–2 months (eight of 23 rabbits). Animals were transferred to consumption of 10% alcohol and alcoholization was continued in conditions of a free choice between alcohol and water. In this alcoholization regime, alcohol-preferring rabbits consumed more alcohol than water in an average of 89% of cases (measurements were made every 2–3 days for nine months of alcoholization, with identification of the volume of liquid consumed since the previous measurement). Alcohol consumption by the end of alcoholization was 2.9 ± 1.0 g/kg/day.

Before alcoholization, rabbits were trained to an operant food-acquiring behavior in experimental cages fitted with two pedals and two automatically dispensing feeders in response to pressing of the corresponding pedal. Pedal-feeder pairs were located in the corners of the cage against opposite walls. After seven months of alcoholization of these animals, which already had experience of operant FAB, were trained to AAB.

Our previous experiments on rabbits performing AAB in the experimental cage, like those of other authors in experiments on rats [30], demonstrated that the maximum ethanol consumption occurs at a concentration of 15%. Comparison of the activity of one and the same neuron in AAB and FAB required the means of achieving the result of the newly formed AAB to reproduce externally the means of achieving the result of the premorbid FAB. Since ingestion of a solid substance (food) is very different from that of a liquid substance (alcohol), we placed 15% ethanol in gelatin capsules of volume 0.5 ml, and for AAB rabbits were trained to take 15% ethanol rather than food from the same feeders after pressing the pedal. After training was complete, animals were used in experiments for recording of neuron activity.

During the recording of activity from each neuron, the rabbits performed an alternating series of behavioral acts of each type of operant behavior – AAB and FAB. The experiment lasted several days; throughout this time, the "home" cage in which the rabbits spent the night between neuron activity recording periods was fitted with a feeder containing a quantity of ethanol supplementing that consumed during the day's experiment to the mean level of daytime consumption measured during the period of chronic alcoholization. Neuron activity was recorded in the anterolateral area of the motor cortex (coordinates A = 3.0–4.5; L = 3.3–4.3), where stimulation produced movements of the lower limb and where most neurons were activated on taking food (see [2, 6]). Activity was recorded with glass microelectrodes filled with 2.5 M KCl solution, with tip diameters of 1.3 μm and impedances of 1.5-MΩ at 1500 Hz.

Experiments also involved recording of electromyograms (from the deep part of the masseter muscle) and behavior. Electrical signals – event markers for pedal pressings by the animals, lowering of the head to the feeder, and passing of the animal past the midpoint of the wall on moving from the pedal to the feeder and back – were recorded on magnetic tape (see Fig. 1, *A*), and video recordings were made of behavior.

Statistical analysis of neuron spike activity was performed using the following parameters: the mean neuron discharge frequency in each of 10 defined behavioral acts (five on each side of the experimental cage) constituting AAB and FAB and the probability that a neuron would be activated in each of these acts. On the left side of the cage, these acts were identified by numbers 1–5: 1) the start of turning toward the pedal (departure from the feeder and chewing); 2) approaching the pedal; 3) pressing the pedal; 4) turning and approaching the feeder; 5) taking of food from the feeder. On the right side of the cage, the same acts were designated Nos. 6–10 (see Figs. 1–4).

The activity of neurons in different types of behavior was compared by constructing plots showing the patterns of neuron activity in behavioral cycles; the activity of neurons was also compared in this way with the activity of other neurons. The identification numbers of the behavioral acts were plotted on the abscissa and the mean neuron activity frequency in each act, normalized in relation to the maximum mean activity frequency of the neuron in any act, was plotted on the ordinate. Plots were used to assess neuron activity in each behavioral act throughout the entire recording period for identification of the neuron's specialization. The "baseline" frequency was calculated over the whole neuron recording period.

The term neuron activation referred to the appearance of activity (for neurons with no baseline activity) or increas-

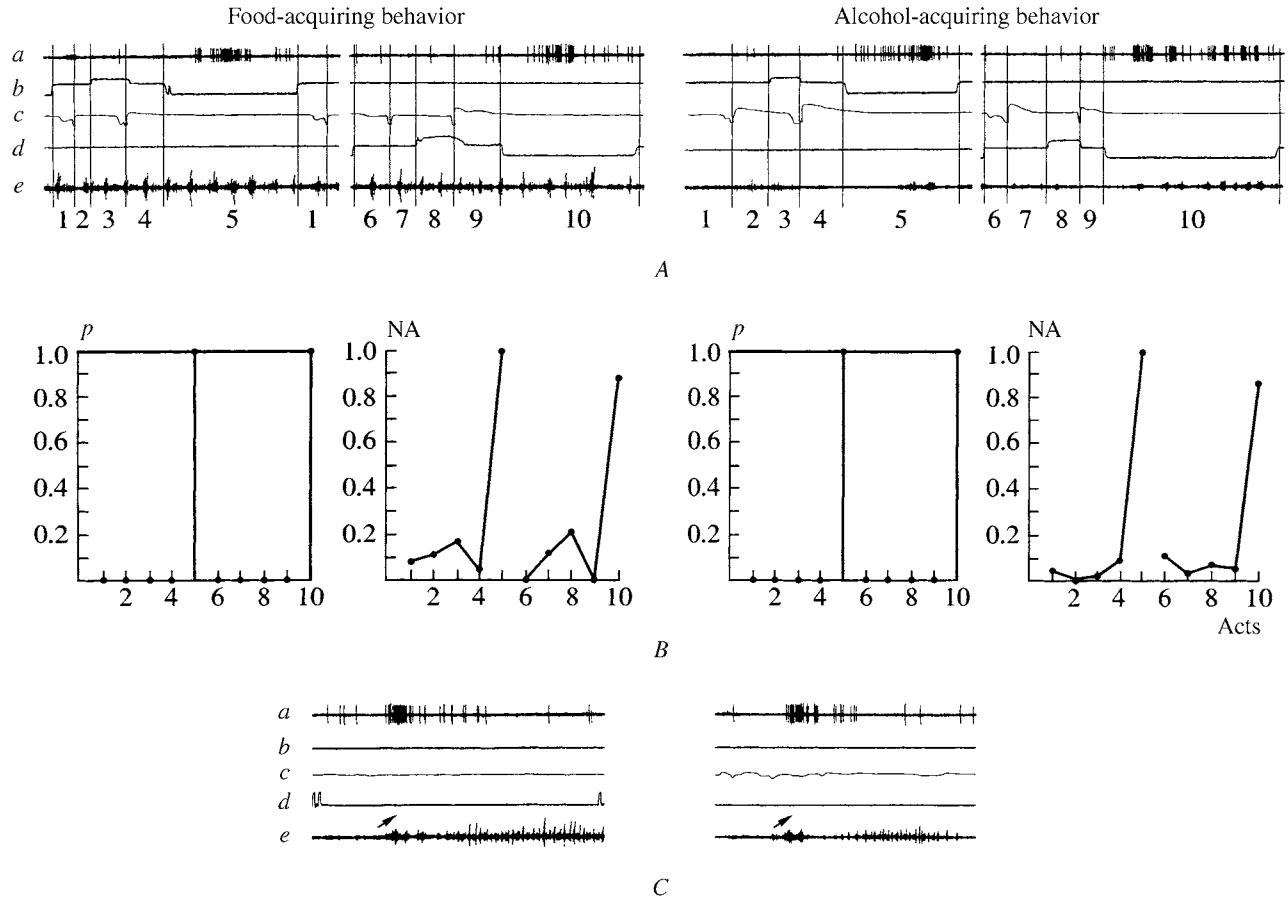

Fig. 1. Activation of O neurons when animals grasped food and alcohol-containing capsules. *A*, *C*) Fragments of crude traces in food- and alcohol-acquiring behavior: (*a*) neuron spike activity (activation corresponds to grasping of food or capsules with the teeth on turning to both feeders – acts 5 and 10 – and grasping food or capsules presented from the experimenter's hand, shown by oblique arrows in (*e*)). Markers for pedal-pressing and lowering the head to the feeders on the left and right walls of the cage are shown in (*b*) and (*d*) respectively (upward deviations are pedal-pressings; downward deviations are lowering of the head to the feeder); (*c*) markers for movement of the animal's head along the mid-part of the wall on movement from the pedal to the feeder and back; (*e*) electrical activity in the deep part of the intrinsic masticatory muscles (activity peaks correspond to the grasping of food in the feeder, gnawing, and chewing). *B*) Plots of the normalized activity frequency (NA) on the ordinate) and the probability that activation will occur (*p* on the ordinate) in each act of the food-acquiring and alcohol-acquiring behaviors; the abscissas on all plots show the identification number of the corresponding behavioral acts (see Methods); numbers and vertical lines on crude traces in (*A*) define these behavioral acts. Activation is shown to have appeared in 100% of cases in acts 5 and 10, increases in activity being by large factors compared to activity in the other acts.

es in the spike frequency to at least 1.5 times the baseline level (for neurons with baseline activity) in all performances of one or the other behavioral act. Neurons were regarded as specialized relative to the system underlying a behavioral act only when each performance of this act produced activation of the neuron, i.e., when the probability of its activation was unity. This type of activation was termed "specific." Unlike "specific" activation, "non-specific" activation was also identified, this also exceeding the mean activity frequency during the act, though this was more variable, arising in less than 100% performances of the behavioral performance. The significance of differences in neuron activity in different acts was assessed using Student's *t* test for comparison of the mean activity frequencies for each pair of acts (see [9] for more detail).

Cells with "specific" activation, according to these criteria, were divided into O and N neurons. N neurons were selectively activated during the act of approaching the feeders or taking food from one feeder, but not the other and during the approach to and/or pressing of one or both pedals. We emphasize that activation of N neurons occurred consistently during the act specific for these neurons, despite the fact that this act, for example, the approach to the pedal or feeder (for neurons active during approaches to both pedals or feeders), was characterized by opposing movements at the opposite walls of the experimental chamber. O neurons were activated during the animals' movements. Activation of O neurons was seen when the movement specific for this neuron was performed (turning to the left and/or right, tilting and/or lowering the head, etc.),

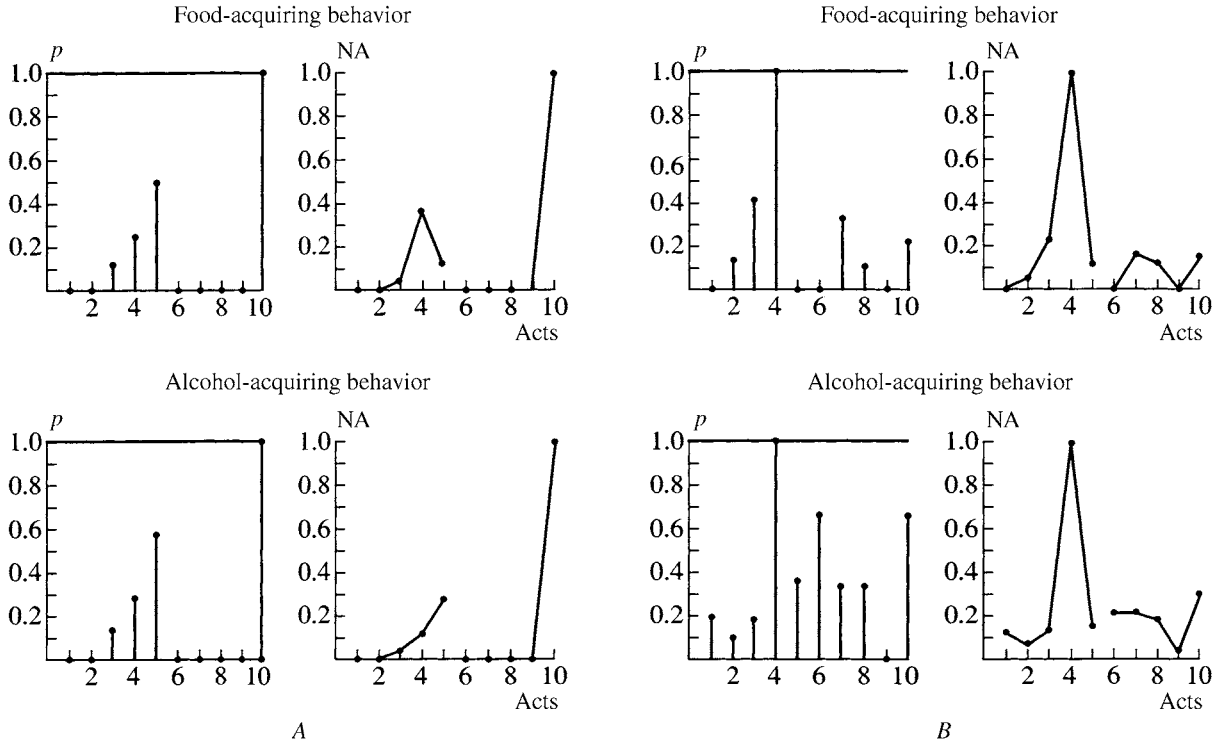

Fig. 2. Plots showing activity frequencies and the probabilities of appearance of activation in each act of the food-acquiring and alcohol-acquiring behaviors in two different N neurons (*A* and *B*) activated during both food-acquiring and alcohol-acquiring behaviors**.** "Specific" activation arises in the neuron shown in (*A*) in both behaviors on grasping from the right feeder (act 10) and in the neuron shown in (*B*) in both behaviors during the approach and tilting to the left feeder (act 4). For further details see caption to Fig. 1.

regardless of which behavioral act was characterized by these movements. For example, activation seen in these cells on turning to the right corresponded to approach to the pedal on one wall of the chamber and to another act – the approach to the feeder – on the opposite wall. This group also included neurons activated on taking food (see below).

The remaining neurons, with variable activity at different frequencies, comprised the group of cells with undefined specialization.

RESULTS

Observations of the animals' behavior during preexperiment testing showed that the capsules themselves were unattractive for the rabbits – they did not eat empty capsules. AAB in these experiments generally ended earlier than FAB, i.e., a moment arose during the experiment at which the rabbit stopped taking capsules containing ethanol solution from the feeder, while they continued taking the portion of unencapsulated food. However, rabbits which stopped taking ethanol-containing capsules after pressing the pedal immediately and willingly drank significant amounts of ethanol from a syringe held by the experimenter.

Comparison of the durations of the corresponding acts in AAB and FAB revealed significant differences. Most acts forming part of AAB were performed more slowly than the corresponding acts in FAB (for more detail see [20]).

Analysis of neuron activity was performed in 121 neurons. The selection criterion was performance by the animals of the complete programs of both AAB and FAB, i.e., activity had to be recorded from the specified cell in each type of behavior on both sides of the experimental chamber. Of 121 neurons, 74 (61%) showed no "specific" activation in any of the acts of either AAB or FAB. These cells were regarded as having undetermined specialization. "Baseline" frequencies were compared for all 74 neurons (See Methods) in AAB and FAB; there were no significant differences.

Of 47 neurons (39%) which were consistently activated in the behavioral acts studied here, 44 cells (36%) were classified as O neurons. As a rule (42 of the 44 cells), O neurons were "common," i.e., were activated in both AAB and FAB. At the same time, O neurons in other brain structures were mainly cells whose activation was phenomenologically linked with one or another body and/or head movement by the animal (see Methods), while in the area studied here, most O neurons (34 cells) were "grasp-

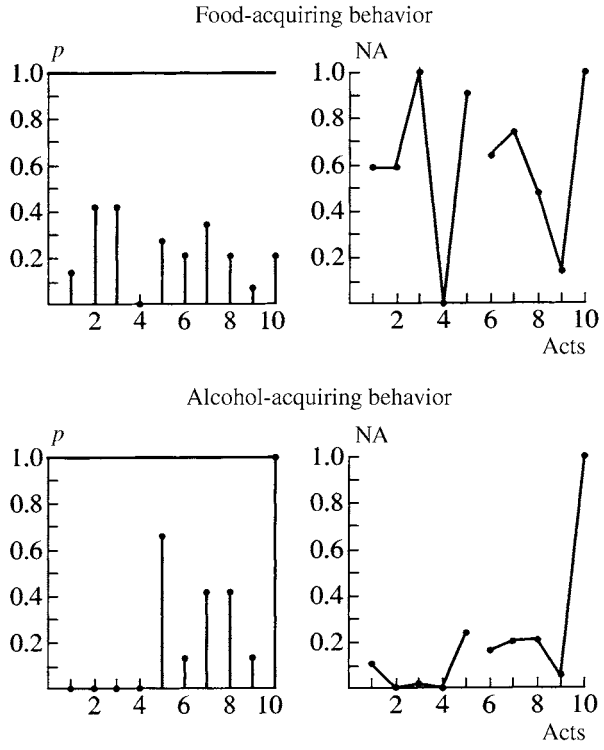

Fig. 3. Plots showing the normalized activity frequency and probabilities of appearance of activation in each act of the food-acquiring and alcohol-acquiring behaviors in an "alcohol-specific" N neuron. "Specific" activation of the neuron appears only in the behavior consisting of grasping alcohol from the right feeder; it was only in this act (10) that the probability of appearance of activation reached unity – see plot at lower left. The plot at lower right shows that the activity frequency during this act was greater than the level of activity in all other behavioral acts (1–9) by a large factor. "Specific" activation was not seen in any act of the food-acquiring behavior. For further details see caption to Fig. 1.

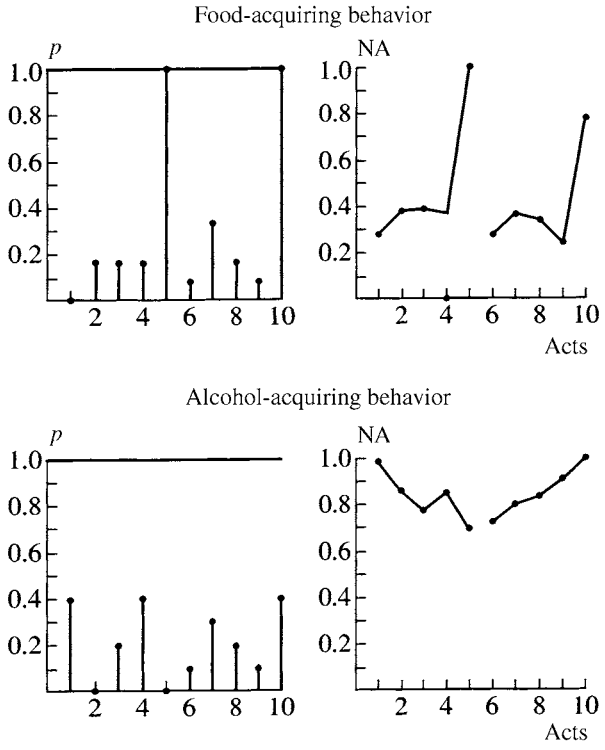

Fig. 4. Plots showing the normalized activity frequency and probabilities of appearance of activation in each act of the food-acquiring and alcohol-acquiring behaviors in a "food-specific" O neuron. The neuron showed "specific" activation with a probability of unity on grasping food from both feeders (plot at upper left, acts 5 and 10). The activation frequency was greater than neuron activity in all other acts (1–4 and 6–9, plot at upper right). "Specific" activation was not seen in any act of the alcohol-acquiring behavior. For further details see caption to Fig. 1.

ing" neurons, whose activity was associated with the behavior consisting of grasping an object, as well as with gnawing and chewing. Unlike N neurons, which are activated during the act of grasping food only in defined conditions, for example, only in relation to one of the feeders (see Fig. 2), the "specific" activation of O "grasping neurons" arose whenever food was grasped, i.e., in relation to both feeders, on taking food from the floor of the experimental chamber, and on taking food from the experimenter's hand. In the latter case, the rabbits had to raise rather than tilt the head to perform the grasping act. Figure 1 shows an example of a "common" O "grasping neuron," activated during grasping of food in FAB and on grasping capsules in AAB (Fig. 1, *A*, *B*). Activation of this neuron occurred in relation to both feeders as well as during grasping of food and capsules from the experimenter's hand (Fig. 1, *C*).

Only three cells (2%) had the properties of N neurons involved in supporting "new" systems formed by training the animal in the experimental cage. We have previously demonstrated that there are insignificant numbers of N neurons in the anterolateral area of the cortex in different types of operant behavior [1] in healthy and chronically alcoholized animals [16, 20]. Of three N neurons, two were "common," showing "specific" activation (in one case on grasping from the right feeder; Fig. 2, *A*; in the other on approaching and turning to the left feeder; Fig. 2, *B*) in both AAB and FAB.

One of the N neurons seen in the present experiments – an "alcohol-specific" neuron – showed "specific" activation (in all behavioral tests) only in AAB on taking capsules with alcohol but not in FAB on taking food (Fig. 3).

Two O "grasping neurons" were "food-specific," their "specific" activation occurring only in FAB. One is shown in Fig. 4.

As already noted, specific activation in the vast majority of O neurons was seen in both AAB and FAB. In 16 (13%) of O neurons, the activation frequency was significantly (with p values from <0.05 to <0.001) different in the cognate acts in AAB and FAB: 12 (10%, all "grasping cells")

showed greater activation in AAB and four (3%; three were "grasping cells" and one was a "movement neuron") showed greater activation in FAB.

Although by definition neurons of undefined specialization did not show constant activation, some of these neurons did show increases in discharge frequency in some performances of defined behavioral acts. Comparison of the activity of neurons of undefined specialization, unlike the approach with O and N neurons, was not performed individually for each neuron but for groups of neurons with similar patterns of activity, i.e., similar distributions of "non-specific" activation in cognate acts within AAB and FAB. The mean frequency and standard deviation for all neurons of the group in each of the acts were calculated and significant differences in frequency for the group were compared for cognate acts in AAB and FAB. Comparison of the overall patterns of the activity of neurons showing "non-specific" activation on grasping food and capsules revealed no significant differences. There were also no significant differences on comparison of the overall patterns of the activity of the group of neurons of undefined specialization in which inhibitory activity was noted during the acts of grasping food and capsules.

DISCUSSION

Despite the relatively small quantity of ethanol consumed by the animals during the experiment involving recording of neuron activity, which lasted eight hours or more (see Methods, regarding the consumption of additional doses of ethanol after experiments), none of the animals showed any signs of physical withdrawal. Such signs are rarely seen in animals taking ethanol in conditions of free choice and are not an obligatory component for determining their dependence on alcohol [28]. At the same time, alcohol-dependent animals have been shown not to stop taking alcohol after addition of noxious substances to their alcohol solution, though there is a tendency to decreases in consumption. AAB is persistent in animals despite the noxious additives, which is regarded as strong evidence in favour of the existence of a high level of dependence on addictive substances, analogous to drug dependence in humans [39]. Our experiments showed that rabbits rejected empty capsules, that AAB is completed more slowly than FAB, and that immediately after cessation of taking ethanol-containing capsules animals drank ethanol from a syringe provided by the experimenter. The behavioral data presented here provide evidence that the capsules used in our experiments can be regarded as a "noxious" additive and that after nine months of alcoholization, our rabbits were dependent on alcohol and a need to obtain it.

Comparison of neuron activity in FAB and AAB provided evidence that the sets of neurons involved in the types of behavior compared here significantly overlapped: 36% of neurons were "common" to these behaviors. As regards neurons with undefined specialization and showing inconstant and variable activity, it can be suggested that their spike activity also plays a role in supporting behavior. Thus suggestion is also supported by our previous reports [15, 17, 20]. These reports presented theoretical and factual arguments supporting the notion that neurons of this group belong to systems associated with behaviors other than those studied here. "Other" behavior is performed in the behavior studied here because of inter-system relationships characterizing the structure of the individual experiment. This suggestion is also in agreement with published data showing that even the most variable discharges are not simply "neuronal noise," but reflect the involvement of the neuron in organizing behavior [25, 36]. If this suggestion is correct, then both "common" neurons and neurons of undefined specialization are involved in FAB and AAB.

The results of studies performed in our laboratory suggest that the basis of learning a new behavior is the specialization of previously silent neurons, which become active and start to take a role in supporting newly formed behavior [10, 13, 18, 33]. Data obtained by other authors [26, 34, 35, 37, 38] support the suggestion that new neurons become involved rather than that relearning takes place, i.e., "respecialization" of previously specialized cells, and that the newly formed specialization of the neuron does not change (in experimental conditions over a period of days, weeks, and even months of recording).

The performance of any behavioral act is supported by the simultaneous actualization of a multitude of systems, arising at sequential stages of the formation of the behavior and "fixing" these stages. Actualization occurs, as already noted, by activation of neurons specialized in relation to systems of different ages – from the oldest, formed in early ontogenesis (O neurons) to the newest, arising when animals learn an operant behavior in the experimental cage (N neurons) [3, 13].

In our experimental situation, the formation of systems of premorbid FAB can be regarded as the stage preceding the formation of AAB. From these positions and with calculation of the position regarding the constancy of the behavioral specialization of the neuron, the existence of "common" neurons involved in both types of behavior can be regarded as supporting the view that the neuronal mechanisms of pre-existing (in this case premorbid) behavior provide the basis for the formation of the neuronal mechanisms of the new behavior (in this case AAB) directed at satisfying the new need – for alcohol. It can be suggested that "common" neurons are cells specialized in relation to systems of previously formed behavior which do not lose their specialization, but undergo modifications associated with the fact that the systems in relation to which they were specialized are involved in performing the newly formed behavior – AAB. Previously, this type of modification

occurring on training of cells belonging to systems formed before the training was termed "accommodative" reconsolidation [1, 4, 20].

It is likely that these modifications can also explain the differences in the activity of O neurons observed here: a significant proportion of neurons of the "grasping" group, the quantitative characteristics of whose specific activation were significantly different in the behavior to which their specialization was formed at the earliest stages of ontogenesis (different types of food grasping), as compared with the newly formed behavior – AAB.

The initial stage of consolidatory changes associated with the formation of neuronal specialization for newly formed systems is in all probability the expression of early genes [7, 11]. The literature contains data suggesting that early genes are expressed in association with accommodative reconsolidation of the type which motor cortex O neurons undergo during the formation of AAB. Castro-Alamancos et al. [24] showed that the training of rats to press a pedal with the paw was associated with significant increases in the level of early gene expression in the projection zone of the motor cortex. These data can only be regarded as evidence supporting this suggestion, taking cognizance of the fact that most of the changes in the motor cortex during training do not consist of the formation of new specializations, but of modifications of systems previously formed, associated with the reorganization of pre-existing structures of individual experience during learning [1, 2].

The sets of neurons associated with FAB and AAB do not overlap completely: we observed cells showing specific activation only in FAB and only in AAB. The literature contains data showing that the mechanism of juice-acquiring and cocaine-acquiring behaviors in monkeys and rats are "at least partially separated at the neuronal level" [22, 23, p. 1072]. The "food-specific" and "alcohol-specific" neurons observed in the present studies provide evidence supporting the view that analogous relationships are also seen in the organization of FAB and AAB.

We have previously identified "alcohol-specific" cells (at a level of 5%) in another area of the brain in identical experimental conditions in studies in chronically alcoholized animals, i.e., the posterior cingulate cortex [19]. Assuming that the formation of new specializations of new neurons underlies learning, we believe that "alcohol-specific" neurons are specialized during the formation of AAB and are members of the group of N neurons.

As regards the two "food-specific" neurons, both were members of the O group – and were activated during grasping of food in both feeders and food offered by the experimenter. In all probability, this means that *all neurons* belonging to "old" systems supporting the act of grasping, are not obligately involved in supporting any newly formed behavior involving the grasping of an object, its chewing and swallowing and/or the *whole set* of "old" systems is not obligately also involved in the newly formed behavior. "Food-specific" N neurons were not seen in the anterolateral area, and we also did not find them in the posterior cingulate cortex [19].

Bearing in mind the energy value of alcohol, it might be suggested that alcohol-acquiring behavior is in essence food-acquiring behavior. However, the behavioral data referenced above, demonstrating differences in the dynamic characteristics of alcohol-acquiring and food-acquiring behaviors, along with data demonstrating the existence of neurons specifically associated with supporting one behavior but not the other, provide evidence against the possible identify of alcohol-acquiring and food-acquiring behaviors. However, that there is some commonality between them cannot be negated; one indicator of this is the significant number of "common" neurons.

Ever increasing amounts of data are accumulating which suggest that there is significant similarity between the neuronal mechanisms underlying the formation of long-term memory during learning on the one hand and long-lived adaptation arising during chronic exposure to addictive substances on the other [31, 32]. Taking cognizance of the chronic effect of alcohol, at least two aspects of neuronal modifications determining this similarity can be suggested.

First is loss of synapses and death of some cells with simultaneous hyperinnervation of others, due to the toxic action of ethanol [27]. Changes in the numbers of synapses are also known to be an important component of the structural rearrangements accompanying the formation of long-term memory [21].

Secondly, bearing in mind the discussion presented above, it can be suggested that a particular type of "long-lived adaptation," which occurs in chronic alcohol consumption, is not merely similar, but actually identical, to the modifications underlying the formation of new experience. These include rearrangements of neurons associated with the formation of new specializations for AAB and with processes of accommodative reconsolidation of premorbid specializations.

Nestler and Agadzhanyan [31] analyzed the mechanisms of the chronic effects of addictive substances and in turn formulated the question, very important for both theoretical and practical reasons, of why alcoholism recurs even after many years of abstinence. Within the framework of the concepts presented above, the answer is evident: because neuronal specializations newly formed during abstinence do not replace previously formed specializations for AAB, but, rather, supplement them.

Thus, the results of the present experiments not only help us understand how the neuronal mechanisms underlying newly formed and previously formed behaviors interact, but also aid in developing concepts of the similarity of the neuronal mechanisms of long-term memory and long-lived modifications of the nervous system occurring in conditions of repeated dosage with addictive substances.

CONCLUSIONS

1. The sets of neurons in the anterolateral area of the motor cortex involved in supporting a premorbid (learned before chronic alcoholization of rabbits) operant food-acquiring behavior and an operant alcohol-acquiring behavior formed after alcoholization show significant overlap, with the result that "common" neurons consistently activated in both types of behavior were observed.

2. The systems of previously formed premorbid food-acquiring behavior can be regarded as the basis for the formation of the alcohol-acquiring behavior directed to satisfying the new need – the need for alcohol.

3. The overlap of the sets is not complete: there were "specific" neurons consistently activated only in one of the two types of behavior.

4. The formation of alcohol-acquiring behavior can be regarded as a systems-generating process, consisting of two types of modification: consolidatory, underlying the formation of new specializations of neurons for the systems corresponding to the newly formed alcohol-acquiring behavior, and reconsolidatory, consisting of changes in cells previously specialized for the systems related to the premorbid behavior.

5. The results support the suggestion that there is significant similarity between the neuronal mechanisms underlying the formation of long-term memory during learning, on the one hand, and "long-lived adaptation" arising in conditions of chronic exposure to addictive substances, on the other.

6. It is suggested that recurrences of alcoholism after many years of abstinence are partially explained by the fact that neuron specializations newly formed during abstinence do not replace previously formed specializations related to alcohol-acquiring behavior, but supplement them.

This study was supported by the Russian Fund for Basic Research (Project No. 02-06-00011) and The Grants Council of the President of the Russian Federation of the Major Scientific Schools of Russia (Project No. NSh-1989.2003.6).

REFERENCES

1. R. G. Averkin, Yu. I. Aleksandrov, Yu. V. Grinchenko, V. N. Mats, and A. A. Sozinov, "Activity of neurons in the anterolateral area of the motor cortex of the rabbit brain during grasping of food and non-food objects in operative behavior," *Zh. Vyssh. Nerv. Deyat.*, **51**, No. 6, 752–757 (2001).
2. Yu. I. Aleksandrov, *The Psychophsyiological Significance of Central and Peripheral Neuron Activity in Behavior* [in Russian], Nauka, Moscow (1989).
3. Yu. I. Aleksandrov, "Functional systems theory and systems psychophysiology," in: *Systems Aspects of Mental Activity* [in Russian], K. V. Sudakov (ed.), URSS Editorial, Moscow (1999), pp. 97–152.
4. Yu. I. Aleksandrov, *Systems Psychophysiology. Psychophysiology* [in Russian], Yu. I. Aleksandrov (ed.), Piter, St. Petersburg (2001), pp. 263–324.
5. Yu. I. Aleksandrov and I. O. Yu. I. Aleksandrov, "Neuron activity in the visual and motor areas of the cerebral cortex during performance of a behavioral act with open and closed eyes," *Zh. Vyssh. Nerv. Deyat.*, **30**, No. 6, 1179–1189 (1980).
6. Yu. I. Aleksandrov, Yu. V. Grinchenko, V. N. Mats, O. Laukka, and A. V. Korpusova, "Involvement of rabbit motor cortex neurons in supporting operant behavior before and after chronic alcoholization: comparison with the limbic cortex," *Zh. Vyssh. Nerv. Deyat.*, **52**, No. 1, 85–96 (2002).
7. K. V. Anokhin and K. V. Sudakov, "The systems organization of behavior: novelty as a leading factor in early gene expression in the brain in learning," *Usp. Fiziol. Nauk*, **24**, No. 3, 53–77 (1993).
8. B. O. Bratus', *Psychological Analysis of Personality Changes in Alcoholism* [in Russian], Moscow State University Press, Moscow (1974).
9. A. G. Gorkin, "Behavioral specialization of cortical neurons at different stages of learning," in: *EEG and Neuronal Activity in Psychophysiological Studies* [in Russian], V. B. Shvyrkov, V. M. Rusalov, and D. G. Shevchenko (eds.), Nauka, Moscow (1987), pp. 73–80.
10. A. G. Gorkin and D. G. Shevchenko, "Differences in the activity of limbic cortex neurons in rabbits with different behavioral strategies," *Zh. Vyssh. Nerv. Deyat.*, **45**, No. 1, 90–100 (1995).
11. O. E. Svarnik, K. V. Anokhin, and Yu. I. Aleksandrov, "Distribution of behaviorally specialized neurons and expression of the transcription factor c-Fos in the rat cerebral cortex in learning," *Zh. Vyssh. Nerv. Deyat.*, **51**, No. 6, 758–761 (2001).
12. K. V. Sudakov, A. V. Kotov, and L. F. Kelesheva, "Neurophysiological bases of the formation of alcoholic motivation in experimental conditions," *Vopr. Narkologii*, No. 3, 7–14 (1988).
13. V. B. Shvyrkov, *An Introduction to Objective Psychology. Neuronal Bases of the Mind* [in Russian], Institute of Psychology, Russian Academy of Sciences, Moscow (1995).
14. D. G. Shevchenko, Yu. I. Aleksandrov, V. V. Gavrilov, A. G. Gorkin, and Yu. V. Grinchenko, "Comparison of the activity of neurons in different parts of the cortex in behavior," in: *Neurons and Behavior: Systems Aspects* [in Russian], Nauka, Moscow (1986), pp. 25–35.
15. Yu. I. Alexandrov, Yu. V. Grinchenko, O. Laukka, T. Jarvilehto, V. Maz, and I. Svetlaev, "Acute effect of ethanol on the pattern of behavioral specialization of neurons in the limbic cortex of the freely moving rabbit," *Acta Physiol. Scand.*, **140**, 257–268 (1990).
16. Yu. I. Alexandrov, Yu. V. Grinchenko, O. Laukka, T. Jarvilehto, and V. N. Maz, "Acute effects of alcohol on unit activity in the motor cortex of freely moving rabbits: Comparison with the limbic cortex," *Acta Physiol. Scand.*, **142**, 429–435 (1991).
17. Yu. I. Alexandrov, Yu. V. Grinchenko, O. Laukka, T. Jarvilehto, V. Maz, and A. Korpusova, "Effect of ethanol on hippocampal neurons depends on their behavioral specialization," *Acta Physiol. Scand.*, **149**, 105–115 (1993).
18. Yu. I. Alexandrov, T. N. Grinchenko, V. V. Gavrilov, A. G. Gorkin, D. G. Shevchenko, Yu. V. Grinchenko, I. O. Aleksandrov, N. E. Maksimova, B. N. Bezdenezhnych, and M. V. Bodunov, "Formation and realization of individual experience in humans and animals: A psychophysiological approach," in: *Conceptual Advances in Brain Research*, R. Miller, A. M. Ivanitsky, and P. M. Balaban (eds.), *Complex Brain Functions. Conceptual Advances in Russian Neuroscience*, Academic Publishers, Harwood (2000), Vol. 2, pp. 181–200.
19. Yu. I. Alexandrov, Yu. V. Grinchenko, M. V. Bodunov, V. N. Matz, A. V. Korpusova, O. Laukka, and M. Sams, "Neuronal subserving of behavior before and after chronic ethanol treatment," *Alcohol*, **21**, 1–10 (2000).
20. Yu. I. Alexandrov, Yu. V. Grinchenko, D. G. Shevchenko, R. G. Averkin, V. N. Matz, O. Laukka, and A. V. Korpusova, "A subset of cingulate cortical neurons is specifically activated during alcohol-acquisition behaviour," *Acta Physiol. Scand.*, **171**, 87–97 (2001).
21. C. H. Bailey and E. R. Kandel, "Structural changes accompanying memory storage," *Ann. Rev. Physiol.*, **55**, 397–426 (1993).

22. E. M. Bowman, T. G. Aigner, and B. J. Richmond, "Neural signals in the monkey ventral striatum related to motivation for juice and cocaine rewards," *J. Neurophysiol.*, **75**, 1061–1073 (1996).
23. R. M. Carelli and O. A. Deadwyler, "Cellular mechanisms underlying reinforcement-related processing in the nucleus accumbens: electrophysiological studies in behaving animals," *Pharmacol. Biochem. Behav.*, **57**, 495–504 (1997).
24. M. A. Castro-Alamancos, J. Borrell, and L. M. Garcia-Segura, "Performance in an escape task induces fos-like immunoreactivity in a specific area of the motor cortex of the rat," *Neurosci.*, **49**, 157–162 (1992).
25. D. Ferster, "Is neural noise just a nuisance?" *Science*, **237**, 1812 (1996).
26. M. O. Jog, K. Kubota, C. I. Connolly, V. Hillegaart, and A. M. Graybiel, "Building neural representations of habits," *Science*, **286**, 1745–1749 (1999).
27. M. A. King, B. E. Hunter, and D. W. Walker, "Alterations and recovery of dendritic spine density in rat hippocampus following long-term ethanol ingestion," *Brain Res.*, **459**, 381–385 (1988).
28. G. F. Koob, L. Stinus, M. Le Moal, and F. E. Bloom, "Opponent process theory of motivation: neurobiological evidence from studies of opiate dependence," *Neurosci. Biobeh. Rev.*, **13**, 135–140 (1989).
29. R. A. Meisch, "Factors controlling drug reinforced behavior," *Pharmacol. Biochem. Behav.*, **27**, 367–371 (1987).
30. J. M. Murphy, G. J. Gatto, W. J. McBride, L. Lumeng, and T.-K. Li, "Operant responding for oral ethanol in the alcohol-preferring P and alcohol-nonpreferring NP lines of rats," *Alcohol*, **67**, 127–131 (1989).
31. E. J. Nestler and G. K. Aghajanian, "Molecular and cellular basis of addition," *Science*, **278**, 58–63 (1997).
32. T. W. Robbins and B. J. Everitt, "Drug addiction: bad habits add up," *Nature*, **398**, 567–570 (1999).
33. V. B. Shvyrkov, "Behavioral specialization of neurons and the system-selection hypothesis of learning," in: *Human Memory and Cognitive Capabilities*, Elsevier, Amsterdam (1986), pp. 599–611.
34. H. A. Swadlow and T. P. Hicks, "Subthreshold receptive fields and baseline excitability of 'silent' S1 callosal neurons in awake rabbits: contributions of AMPA/kainate and NMDA receptors," *Exptl. Brain Res.*, **115**, 403–409 (1997).
35. L. T. Thompson and P. J. Best, "Long-term stability of the place-field activity of single units recorded from the dorsal hippocampus of freely behaving rats," *Brain Res.*, **509**, 299–308 (1990).
36. E. Vaadia, I. Haaiman, M. Abeles, H. Bergman, Y. Prut, H. Slovin, and A. Aertsen, "Dynamics of neuronal interactions in monkey cortex in relation to behavioural events," *Nature*, **373**, 515–518 (1995).
37. M. A. Wilson and B. L. McNaughton, "Dynamics of the hippocampal ensemble code for space," *Science*, **261**, 1055–1058 (1993).
38. J. Wolffgramm, "An ethopharmacological approach to the development of drug addiction," *Neurosci. Biobehav. Rev.*, **15**, 515–519 (1991).
39. D. J. Woodward, P. H. Janak, and J.-Yu. Chang, "Ethanol action on neuronal networks studied with multineuron recording in freely moving animals," in: *Alcohol: Clin. Exp. Res.*, **22**, 10–22 (1998).