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Two neuronal systems involved in short-term spatial memory in monkeys

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Abstract. The investigation of the neuronal activity in the monkey cerebral cortex during the delayed spatial choice performance allowed us to develop the hypothesis about two neuronal networks supporting the operative memory. The work of one of them is based on the relay-race and reverberation principles of information transfer. Another neuronal network provides for the reliability of transfer phases of these processes. The two networks are present in both prefrontal and parietal association cortical area.

Key words: short-term memory, operative memory, relay-race reverberation, prefrontal and parietal areas

INTRODUCTION

Classification of different forms of memory poses a complex problem which can be viewed both from physiological and linguistic points of view. Most researchers believe that short-term memory (SM) is a process of storing of a certain image of the environment that will be later used in a forthcoming action in the short-term activity of the neuronal networks (Eccles 1981, Batuev 1987, Batuev et al. 1988). Conditioned reflexes and habits are classical examples of the long-term memory (M), where some relevant information is stored permanently. Hence, the principal difference between SM and LM is that the former, in contrast to the latter, does not necessarily contain relevant information. This follows from the traditional definitions of LM and SM (Batuev et al. 1988).

If, however, one would assume that the relevant information can be retrieved from LM and subsequently incorporated into SM, then the above mentioned definition would be inadequate. In a simple case, the subject is supposed to perceive the most significant information and keep it in SM extracting at the same time some elements of the previous experience from LM and further transferring them into SM. The SM corresponding to the sensory image would be of a probabilistic character. Therefore, in a certain operative situation SM appears to be of a dual nature: it stores the relevant information and in the same time a model (or a programme) of a forthcoming behaviour. The extent to which these two components of the operative memory correspond to one another can be estimated by the goal-directed consummatory act which is mentally modelled and then performed. By relevant information we understand a complex of external and internal signals which are actively selected by the subject from the wide spectrum of influences affecting its brain. In all cases the dominant motivation is the main constructive factor (Batuev 1987). The character and level of motivation define the second component of the operative memory (that is its adequacy to the external signals or adaptivity), the rate of its retrieval from LM and its physiological structure, including motor and visceral components.

This paper describes the distribution of neurones of prefrontal and parietal areas activated in correspondence to various events taking place during the delayed spatial choice test.

METHODS

Behavioural procedure

On the basis of the previously described hypotheses (for details see Batuev et al. 1980, 1981, 1985, Batuev 1987) let us consider a certain model of the monkey behaviour in connection with the rearrangements of unit activity in the higher association cortical fields - prefrontal and parietal.

The experimental situation was as follows. The monkey was seated in the primate chair without head fixation. In front of it there was a panel with signal lamps and levers. A flash of the lamp located on the mid-line was an anticipatory signal. After a certain delay (usually 5 s) a cue followed: one of the two similar lap located in the transparent windows to the right or to the left of the monkey's head was switched on for 5 s. During that period the monkey could not reach the levers which were screened and opened only 5-10 s after the cue had been switched off (a fixed delay). Spatial cues were presented at random order. Thus, the fixed delay served as a test for operative memory which included both the informative components and the elements of programming of a forthcoming action. After the screen was lifted, monkey had to press the lever on the side corresponding to the cue.

An automatic reward system and a device for the reward delivery were fixed to the outside wall of the chamber. These systems were operated by electromagnetic relays switched on by pulling the correct ever. After the correct choice monkey received a food reward in the food box placed on the mid-line. If the choice was erroneous food was not delivered and the screen was closed.

Recording of the unit activity

Unit activity was recorded in the prefrontal (middle portion of the principal sulcus) and parietal (intraparietal sulcus) areas in both hemispheres by 4-microelectrodes bundle. A single electrode consisted of a silver microwire in glass insulation. The diameter of the microelectrode was 40-70 μm and that of the silver core was 5-10 μm. They were sharpened so that the average impedance was 0.5-2.0 MΩ. The electrodes sharpened preliminary were assembled in a plastic plug which was mounted on the micromanipulator. Plugs were implanted into the skull, so they could anchor micromanipulators and a metal holder onto which a small 4-channel source follower was mounted. The holder served as the indifferent electrode. Cortical activity was recorded after the conditioned reflexes became stabilized.

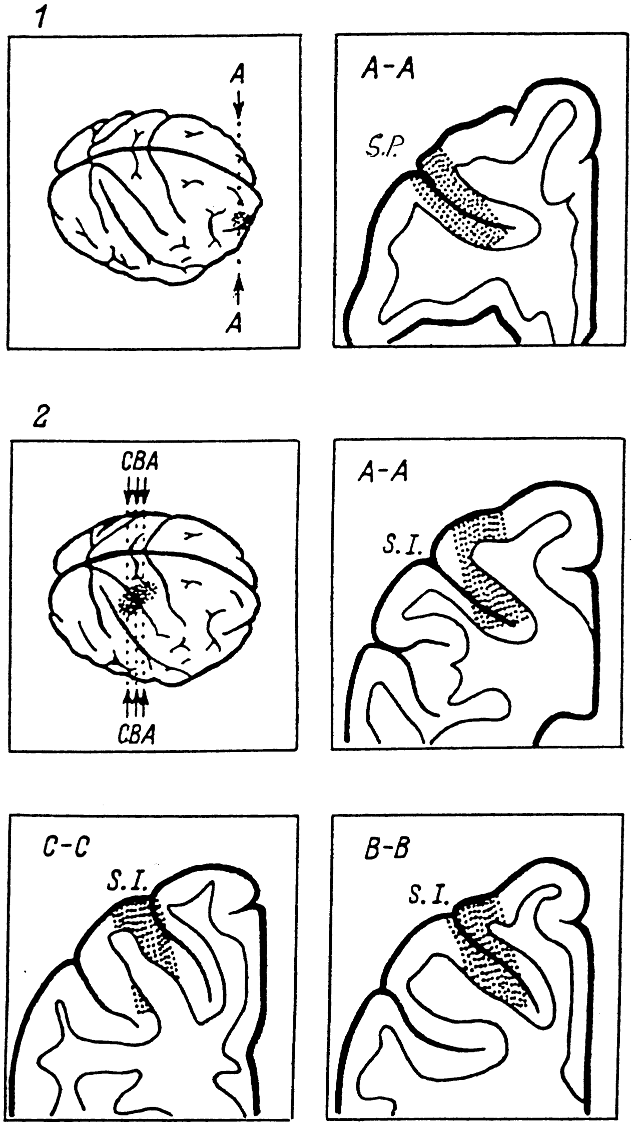


Fig. 1. Areas of unit activity recording in the prefrontal area (s.principalis) (1) and in the parietal area (s.intraparietalis) (2). Summarized data for all hemispheres of three monkeys (1) and summarized data for each monkey (A-A, B-B, C-C).

Data processing

The recordings were processed by storing rasters and plotting peristimulus time histograms of the neurones' activity. In each programme, the maintained activity was recorded for 6 s before the anticipatory signal flashed. Mean firing rates and mean square deviation (δ) were calculated for background activity. Deviations of firing from the mean level which were greater than ±1.96 for the probability of 0.05 and ±2.58 for the 0.01 were considered reliable.

Histology

When the experiments were finished, the animals were deeply anaesthetized and after death their brains were placed in formalin. The brains were cut into blocks and the pieces chosen for examination were then sectioned on a freezing microtome and counterstained. The histological verification showed that the prefrontal unit activity was recorded in a limited area which incorporated only the mid-portion of the principal sulcus.

In two cases (Fig. 1) unit activity was recorded on the borderline of fields 5 and 7, deep in the intraparietal sulcus, in the third case (C-C) unit activity was recorded in the field 7. Note that the activity of most of the parietal area units was recorded from the field 7.

RESULTS

Spatially selective neurones

A total of 355 units were recorded and examined in the sampled cortical areas. Of these, 174 were the parietal neurones and 181 were the prefrontal one. Ninety eight parietal units and 161 prefrontal units were recorded during delayed spatial choice performance.

In this paper, we will consider only this subpopulation of the registered neurones whose frequency and pattern of activity was significantly dependent on the right or on the left-side location of the spatial cue (Kubota et al. 1974, Niki 1974, Batuev et al. 1988). These cells in the prefrontal ($n = 50$) and the parietal ($n = 36$) cortical areas were labelled as spatially selective neurones (Batuev et al. 1981). They are characterized by the low background activity which did not exceed 10 imp/s. It can be generally assumed (Batuev et al. 1989) that the selective reactivity of neurones with a low background activity is determined by a considerable convergence of inhibitory modulating inputs onto them. Investigations using the method of microiontophoretic application of the inhibitory antagonists confirmed this assumption (Batuev 1987).

Neuronal systems of relay-race reverberation on the operative memory

The population of spatially selective neurones which displayed differential activity during the cue presentation (i.e. their frequency rate or discharge pattern differed significantly with the left or the right cue presentation) was found in both sampled cortical areas. Figure 2 reveals the differential activity of one of the unit from the parietal cortex during the cue presentation on the left and on the right side. During other stages of the experimental sequence their activity did not differ. These neurones were named "sensory" since they were involved in the description of the spatial locations of the cue as the major informative feature of the entire experimental situation. They amounted to 6.5% in the total number of spatially selective neurones in the prefrontal cortex and 9% in the parietal cortex.

Another population of cells changed their activity only during the delay. These neurones did not respond to the cue presentation but started a spatially selective activity during the delay. Figure 3 demonstrates the reactions of one of such neurones. Its frequency rate and discharge pattern to the presentation of the cue to the left did not differ from that to the right. However, the significant differences appeared immediately after the cue was switched off and they were present during the entire period of delay (5 s). We named them "neurones of SM" and they amounted to 8% in the total number of spatially selective neurones in the prefrontal and 4% in the parietal cortex. It seems quite probable that neurones of SM are activated by inputs from the "sensory" neurones (the relay-race effect).

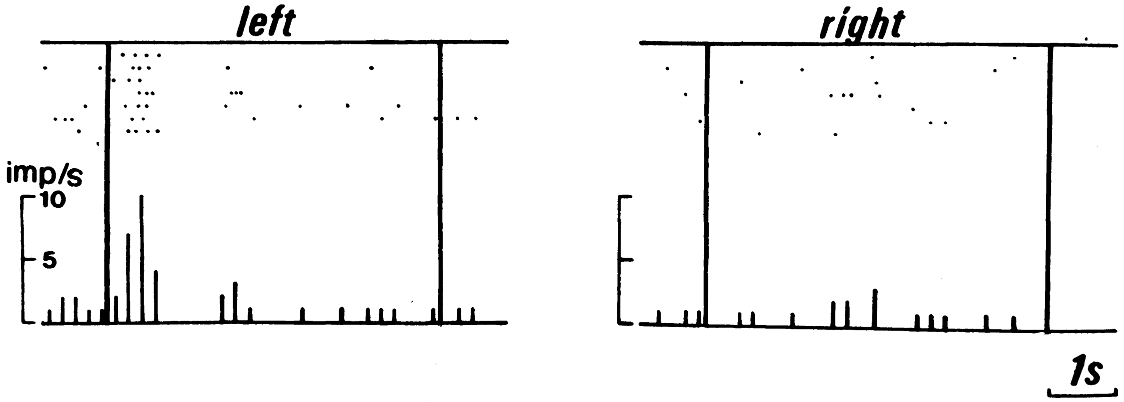


Fig. 2. Differences in the activity of a single parietal neurone during the cue presentation on the left or on the right side. Raster oscillograms and histograms for the neurone firing for 7 repetitions of the experimental sequence ending with the correct choice of the lever. Vertical line on the left and right, the cue onset and offset. Abscissa: time in s: the ordinates, number of impulses for $\Delta t = 200$ ms. Time calibration, 1 s.

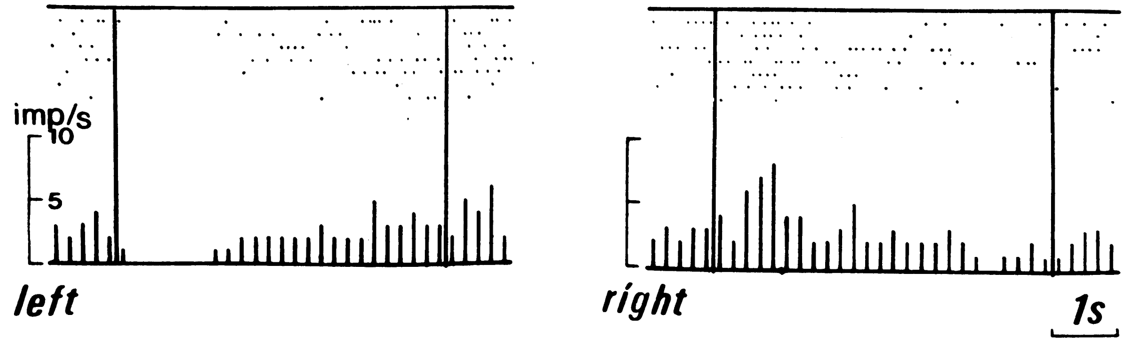


Fig. 3. Differences in the activity of a single parietal neurone during the delay after the cue was presented on the right or on the left side. Vertical line, the moments of beginning and the end of the delay (trigger markers). Other descriptions are the same as in Fig. 2.

What happens during the delay? In a special series of experiments we increased the delay up to 10-18 s. It appeared that in the prefrontal area the delay (or the interval between the cue and the trigger stimulus) was filled up with the bursts of discharges (1.5-2 s) of various neuronal circuits which were observed at the beginning (A), in the middle (B), or at the end (C) of the delay, or with bursts of the same circuits (D). Only 5% of cells were in the activated state during the whole period of the delay (E) (Fig. 4).

It seems that various neuronal circuits are successively involved in the short-term activation which is based on the relay race principle as well.

The fact that the delay is divided into shorter periods can be explained with the idea of reverberation mechanisms which were described for the cerebral cortex (Eccles 1981). There is also a morphological substrate for that: in layers II and III of the prefrontal area there exist certain neurones whose axons return and end on their own dendrites. These neurones may serve as a basis for the impulse reverberation in such a neuronal "trap". It can be seen in Fig. 5 that in cortical layers III-IV there are located groups of pyramidal neurones whose axons exhibit U-like branching towards the cells of the same group. Stellate neurones may be present here as well. Their axons send collaterals to another type of neuronal clusters - the large pyramidal cells in layers V-VI.Here these axons come in contact with the zones of branching of the basal dendrites of the pyramids. A cluster of neurones of the first type is an example of the trap in which the discharge may reverberate until it is switched to an efferent module

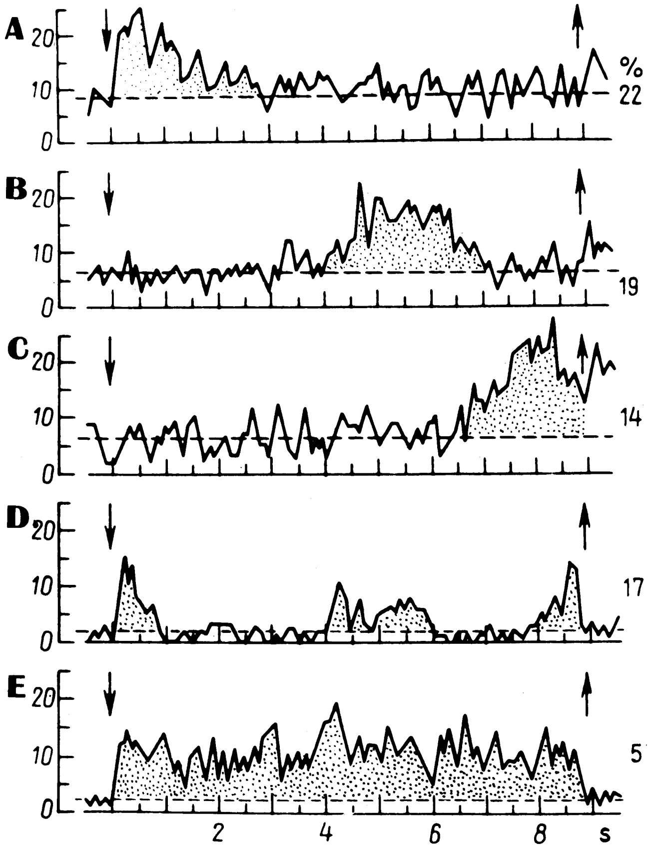


Fig. 4. Main type (A-E) of changes in the firing rate of prefrontal neurones during the delay period. Arrows indicate the beginning and the end of the delay. Numbers on the right side stand for the percentage of neurones. The ordinates: firing rate (cps) Δt = 200 ms; n = 10; abscissa: time (s). For other explanations, see text.

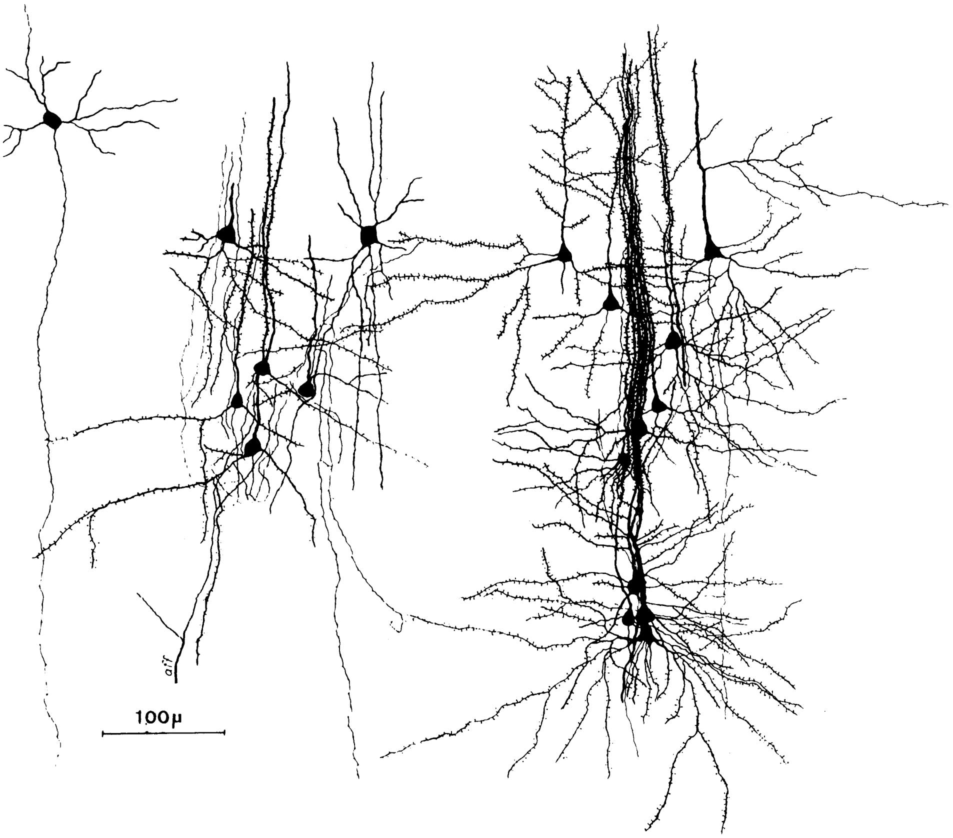


Fig. 5. Main types of neuronal clusters (modules) in prefrontal cortex. 1, circuit-like neuronal trap: thalamic afferent; 2, cylindrical vertical cluster. For other explanations, see the text.

of the large pyramids. Predominance of closed neuronal clusters of the first type in the principal sulcus can serve as a structural prerequisite for storing impulse discharges and for the relay switching of activation from one neuronal cluster to another.

These neuronal traps were found only in the prefrontal but not in the parietal areas. In the latter large single pyramidal cells or their vertical modules predominated (Batuev et al. 1988). It should be noted that in the parietal cortex, long delays (up to 18 s) were not divided into brief bursts of discharges. The activity which helps to store information about the cue location in the neurones of SM is manifest throughout the entire delay.

This allows us to speculate about the differences between the functions of the prefrontal and parietal cortices in the operative memory. In the prefrontal area we observe intracortical reverberative activity of the relay-race type while in the parietal cortex the same mechanism is based on the thalamo-cortical interactions involving long loops of direct connections and feedbacks. Regional differentiation within the parietal cortex is much less pronounced than in the prefrontal cortex (Batuev et al. 1985, 1988). The third population of the spatially selective neurones revealed itself only after the opening of the screen, when the monkey was able to prepare and to perfrom a goal-directed movement. These cells did not change their activity during the instructive period of the sequence but when the monkey was solving the problem of which lever to press (on the left or on the right), these neurones showed differential activities (Fig. 6). This Figure shows the responses of a parietal neurone to screen opening. This neurone did not show a differential activity to the right and to the left cue presentations and during the delay. However, the differences of the pattern of discharge became well-pronounced immediately after screen opening. When the pattern of discharges of those neurones during correct and erroneous

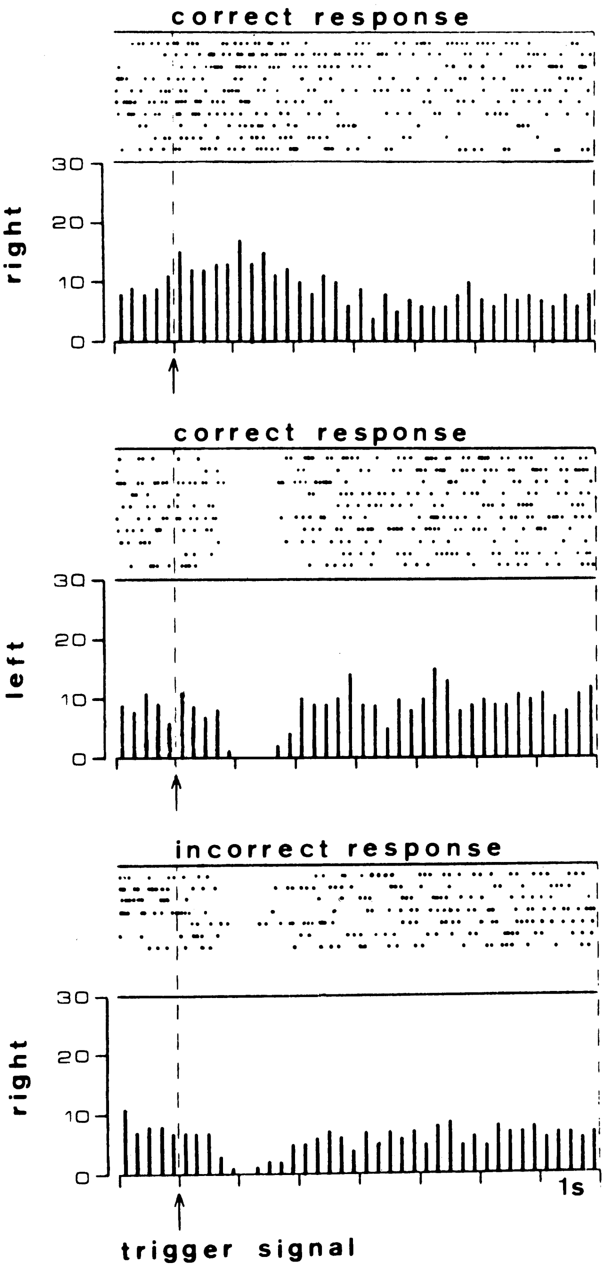


Fig. 6. Activity of a parietal neurone during the experimental sequence ending with the correct and erroneous choice of the lever. Two upper rasters were plotted for 10 repetitions of the sequence, the lower most raster, for 7 repetitions. Shown on the histograms are: abscissa, time in s; the ordinates, number of impulses for $\Delta t = 200$ ms. A dashed line on the left, the moment of the screen opening, that on the right, the end of the programme.

choices, i.e. the performance of the same movement in response to the left or the right cue were compared, no differences were found. Therefore, these neurones were named "the neurones of motor programmes". They seem to be triggered by the neurones of SM, on the basis of the relay-race principle and to store these impulse codes of motor programmes up to the execution of a corresponding motor act. The discharge patterns of the neurones of this group was always consistently similar during correct and erroneous choices.

The mechanism of relay-race transfer from the neurones of SM to the neurones of motor programmes is fragile, as the interfering influences during the delay, as a rule, lead to an erroneous choice of the lever (Fig. 6).

Neuronal system ensuring the reliability of operative memory

It is well known that both in the living beings and in the lifeless systems transition processes are the most fragile links of the sequence. The same holds true for our experiment: the relay-race transfer from the sensory neurones to the neurones of SM and further to the neurones of motor programmes as well as from one reverberating neuronal trap to the next one during the delay in the prefrontal cortex are the least reliable periods in the activity of a neuronal network. In attempt to find some mechanisms ensuring the reliability of the transition process we have first paid attention to the neurones which are responsible for putting together the neighbouring events of the given behavioural sequence. It appears that in both prefrontal and parietal areas there exist neurones (3%) which become spatially selective during both cue presentation and delay (Figs. 7 and 8). Even less numerous are the neurones which are spatially selective during the delay and after the trigger signal: 2% in the prefrontal and 1% in the parietal cortex. Thus, these cells together with the above described modality-specific units are involved in the information transfer from the sensory neurones to the neurones of SM and further to the neurones of motor programme.

A similar pattern is observed for the relay-race activity of neuronal populations in the prefrontal area during the delay. It was found that 5% of all

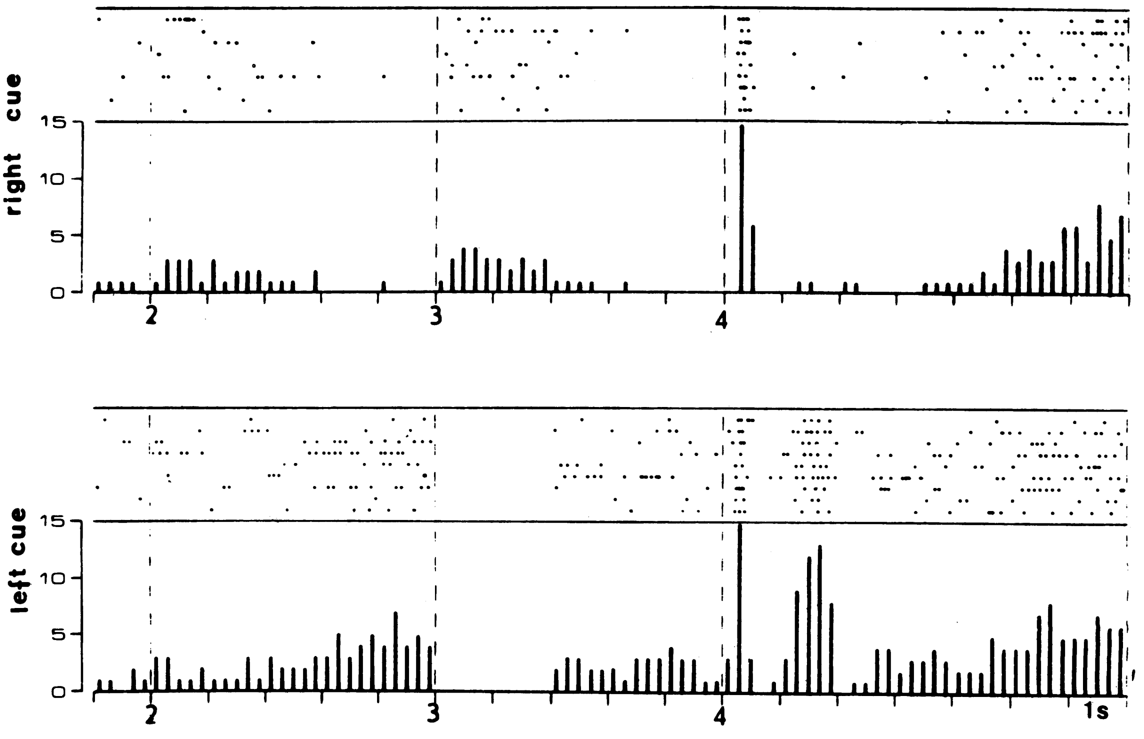


Fig. 7. Responses of a specially selective neurone to the cue location on the right or on the left side. Upper panel, dot displays; lower panel, corresponding peristimulus time histograms. The ordinates, firing rate (cps), Δt = 200 ms; n = 10, abscissa, time (s). Dashed lines from the left to right: the cue onset and offset, trigger signal, the end of the sequences.

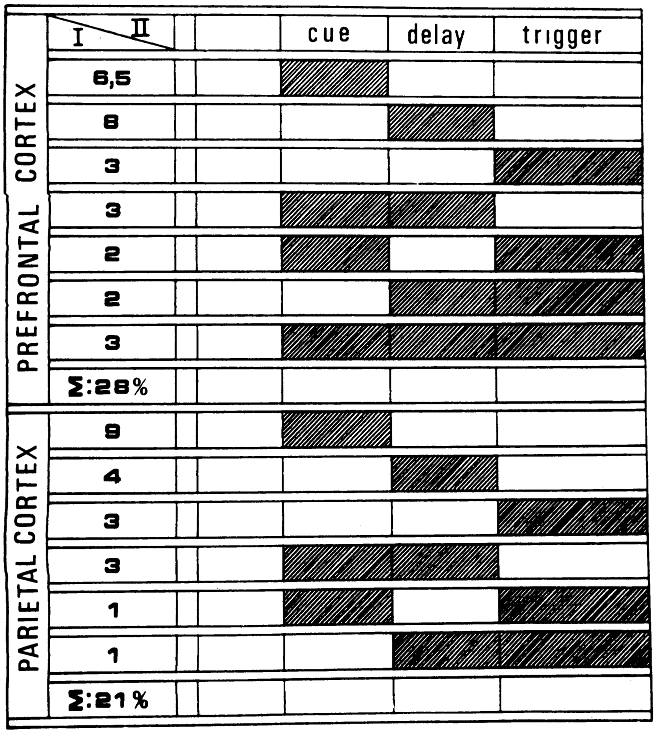
prefrontal units showed high impulsation rates throughout the entire 10 s of delay (Fig. 3E). For these cells 1.5-2 s bursts of discharges were not typical.

Histological studies of the prefrontal cortex revealed in addition to the neuronal traps another type of a neuronal assembly, i.e. vertical modules of pyramidal cells (Batuev et al. 1988). We assume that continuous high-rate impulsation during the delay is somehow generated by these neuronal modules. In this way the reliability of storing of information about the cue location may be secured in the operative memory.

A similarity of structural and functional organization of the prefrontal and parietal areas has been shown. The difference between the prefrontal and parietal areas lies in the following: only in the prefrontal area there are cells which connect the transition phases of the behavioural programme depending not only on the spatial location of the cue, but also on the direction of a forthcoming movement. In other words, this neuronal system is not modality-specific but it is characterized by differential activation by the cue presentation and by the programme of the forthcoming motor act extracted from the LM. The connection between these two sources of activation is so strong that judging by the discharge pattern during the delay we can predict the direction of the would-be motor act and subsequently evaluate the adequacy of the motor programme extracted from the LM and loaded into the operative memory. We think that the retrieval of one of the alternative motor programmes inhibits the other ones.

DISCUSSION

Unit activity of the monkey's association cortical areas studied during performance of the delayed spatial choice allowed us to work out a hypothesis as to the neuronal systems underlying operative memory.



	I \ II			cue	delay	trigger
PREFRONTAL CORTEX	6,5			▨		
	8				▨	
	3					▨
	3			▨	▨	
	2			▨		▨
	2				▨	▨
	3			▨	▨	▨
	Σ:28%					
PARIETAL CORTEX	9			▨		
	4				▨	
	3					▨
	3			▨	▨	
	1			▨		▨
	1				▨	▨
	Σ:21%					

Fig. 8. Distribution of spatially selective neurones in the prefrontal and parietal cortex of monkeys. I, number of spatially selective neurones, recorded in the given region of the cortex, as the percentage of all units sampled ($n = 50$ for prefrontal and $n = 36$ for parietal zones) and the ratio of spatially selective neurones to the total number recorded in the region in question. II, cue: period of cue presentation; delay period: trigger period of the program (opening of the screen, pressing the lever, food reward). Black rectangles designate periods of the programme during which neurones display reliable differences in the firing rates as determined by the cue location.

One of them is based on the principle of the relay-race reverberation. The presentation of the cue elicits the activity of the population of spatially selective sensory neurones. By the delay (i.e. operative memory) this information is transferred to the neurones of SM. Within the delay brief bursts of discharges are observed during which several populations of cells are involved, one by one, into the reverberating activity. Each of these populations is a certain "neuronal trap" in which impulsation is reverberating for 1.5-2 s. After this delay, impulsation is transferred to another neuronal circuits related to the preparation of a goal-directed movement (neurones of motor programmes).

Another neuronal system serves to ensure the reliability of these transition processes, i.e. (1) information transfer from sensory neurones to the neurones of SM and further to the neurones of motor programmes, (2) fixation of the entire period of operative memory without the relay-race reverberation, (3) storing of the information in the activity of one neuronal population up to the

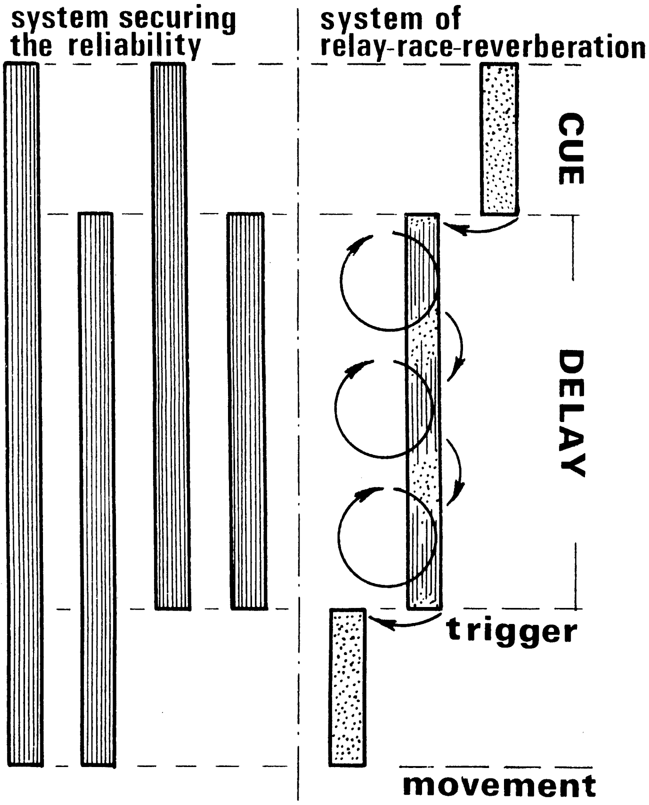


Fig. 9. A hypothetic scheme illustrating several neuronal systems supporting the operative memory. During the cue, sensory neurones are activated. At the end of the period, the information about the spatial location of the cue is relayed to neurones of SM. The latter are involved in local circuits (traps), each one reverberating impulsation. Information thus stored is further transferred in a relay-race manner from one circuit to another. At the end of the delay, neurones of the motor programme are activated, thus inducing an aimed movement. A system securing the reliability of the above described transitions maintains permanent activity in another neuronal population during all transfer phases of the investigated processes. Thus, it retains the same information for the same kind of aimed movement.

point when the goal-directed movement is performed (Fig. 9).

Representation of these systems in the prefrontal and parietal cortex is different (see, also Fuster 1980, Sakata et al. 1980, Watanabe 1981, 1990, Hyvärinen 1982, Goldman-Rakic 1987, Tanila et al. 1992). The first system provides an input into the operative memory of the spatio-temporal, signalling and programming features of the forthcoming movement, while the second system is used for external (signal) and internal (programming) information which is stored in the same neuronal networks starting from the cue onset.

During the period of the behavioural sequence as well as during the delay there occur neuronal processes of operative memory which underlie the programming function of the brain.

Both association cortical areas are not only directly interconnected (Pandya and Kuypers 1969, Goldman-Rakic 1987) but are also involved in the operative memory processes.

Other authors (Mishkin et al. 1984, Squires and Butter 1984) distinguish two independent types of memory (i.e. declarative and procedural memories or memory for signal recognition and the corresponding reaction). This distinction is convenient from the didactic point of view but it is difficult to separate the systems during neuronal recordings in the paradigm of delayed spatial choice. In these situations some neurones within the same cortical area are distinct in their functional characteristics (sensory neurones, neurones of SM and neurones of motor programmes), whereas other neurones in the same area are subsequently involved into all these operations (Funahashi et al. 1989).

REFERENCES

Batuev A.S. (1987) Higher integrative systems of the brain. Gordon and Breach, New York.

Batuev A.S. (1990) Neuronal mechanisms of short-term memory. Soc. Sci. Rev. F. Physiol. Gen. Biol. 4: 53-93.

Batuev A.S., Alexandrov A.A., Scheynikov N.A, Kharazia V.N, Chan Chin An (1989) The role of inhibitory processes in the formation of functional properties of neurones in vibrissal projection zones in the cat somatosensory cortex. Exp. Brain Res. 76: 198-206.

Batuev A.S., Demianenko G.P., Orlov A.A., Shaefer V.I. (1988) Neuronal mechanisms of the awake brain in monkeys (in Russian). Nauka, Leningrad.

Batuev A.S., Orlov A.A., Pirogov A.A. (1981) Short-term spatio-temporal memory and cortical unit reactions in the monkey. Acta Physiol. Hung. 58: 207-217.

Batuev A.S., Orlov A.A., Shaefer V.I. (1985) Comparative characteristics of unit activity in the prefrontal and parietal areas during delayed performance in monkeys.Behav. Brain Res. 16: 57-70.

Batuev A.S., Pirogov A.A., Orlov A.A., Shaefer V.I. (1980) Cortical mechanisms of goal-directed motor acts in the Rhesus monkey. Acta Neurobiol. Exp. 40: 27-49.

Eccles J.C. (1981) The modular operation of the cerebral neocortex considered as the material basis of mental events. Neuroscience 6: 1839-1855.

Funihashi S., Bruce C.J., Goldman-Rakic P.S. (1989) Mnemonic coding of visual space in the monkey's dorsolateral prefrontal cortex. J. Neurophysiol. 61: 331-349.

Fuster J.M. (1980) The prefrontal cortex. Anatomy, physiology and neuropsychology of the frontal cortex. Raven Press, New York, 222 p.

Goldman-Rakic P.S. (1987) Circuitry of primate prefrontal cortex and regulation of behaviour by representational memory. Handbook of physiology. Vol. V. The nervous system. Chapter 9. Am. Physiol. Soc., Bethesda, p. 373-417.

Hyvärinen J. (1982) The parietal cortex of the monkey and man. Springer Verlag, Berlin, 202 p.

Kubota K., Iwamoto T., Suzuki H. (1974) Visuokinetic activities of primate prefrontal neurones during delayed response performance. J. Neurophysiol. 37: 1194-1212.

Mishkin M., Malamut B.L., Bahevalier J. (1984) Memories and habits: two neural systems. In: Neurobiology of learning and memory (Eds J.L. McGaugh, G. Lynch and N.M. Weinberger). Gouldfeld Press, New York.

Niki N. (1974) Differential activity of prefrontal units during right and left delayed response trails. Brain Res. 70: 346-349.

Pandya D.N. Kuypers H.G.J.M. (1969) Cortico-cortical connections in the rhesus monkey. Exp. Brain Res. 13: 13-36.

Sakata H., Shibutani H., Kawana K. (1980) Spatial properties of visual fixation neurones in posterior parietal association cortex in the monkey. J. Neurophysiol. 43: 1654-1672.

Tanila H., Carlson S., Linnankoski I., Lindroos F., Kahila H. (1992) Functional properties of dorsolateral prefrontal cortical neurones in awake monkey. Behav. Brain Res. 47: 169-180.

Watanabe N. (1981) Prefrontal unit activity during delayed conditional discrimination in the monkey. Brain Res. 225: 51-65.

Watanabe M. (1990) Prefrontal unit activity during associative learning in the monkey. Exp. Brain Res. 80: 296-309.

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