Neural Organization for the Long-Term Memory of Paired Associates in the Primate Temporal Cortex

by

Kuniyoshi Sakai

Department of Physics
Faculty of Science
University of Tokyo

Submitted to University of Tokyo
in Partial Fulfillment of the Requirements
for the Degree of Ph.D.

December 16, 1991

Summary

Human memory is assessed by the paired-associate learning test, in which a series of paired words or figures is presented and the subject is then asked to retrieve the other pair member associated with each cue. We prepared 24 computer-generated pictures and sorted the geometrically distinct patterns into pairs. Two Japanese monkeys (*Macaca fuscata*) were trained to memorize these 12 pairs through repeated trials in a pair-association task. In each trial, a cue stimulus was presented on a video monitor, and then two stimuli for choice were shown after a delay period. The monkey obtained fruit juice as a reward for correctly touching the paired associate. By recording extracellular spikes from single neurons (n=577) during the task performance, we found picture-selective neurons (n=91) in the anterior temporal cortex. One type (*pair-coding neurons*, n=10) selectively responded to both pictures of the paired associates during the cue period. Another type (*pair-recall neurons*, n=10), which had the strongest response to one picture during the cue presentation, exhibited increasing activity during the delay period when the associate of that picture was presented as a cue. These results provide new evidence that single neurons acquire selectivity for visual patterns through associative learning. They also indicate neural mechanisms for storage and retrieval in the long-term memory of paired associates.

Introduction

One of the central problems in neuroscience is how the brain recognizes environmental features. The physiological basis of coding for recognition lies in the spatio-temporal patterns of neural discharges. It has been assumed that principal features of sensory information are first analyzed in several specific sensory areas of the cerebral cortex, and that they are combined in association cortices. The most famous study on the early stage of feature detection was the discovery of the functional architecture in the visual cortex by Hubel & Wiesel (1962, 1968, 1977).

The recording of the action potentials or spikes from single cells has revealed that cortical neurons respond selectively to certain parameters of visual stimuli, such as orientation, size, and colour. Furthermore, neural responses selective to more complex stimuli have been reported in the primate temporal cortex, which processes visual information at much higher levels with refinement of receptive fields (Gross 1973; Iwai & Mishkin 1990). These studies have used immobilized and anesthetized monkeys (Gross et al. 1969, 1972; Desimone & Gross 1979; Bruce et al. 1981; Schwartz et al. 1983; Desimone et al. 1984; Tanaka et al. 1991), or alert monkeys during performance of visual discrimination and/or fixation tasks (Ridley & Ettlinger 1973; Ridley et al. 1977; Rolls et al. 1977; Gross et al. 1979; Sato et

al. 1980; Perrett et al. 1982, 1984, 1985; Richmond et al. 1983, 1987; Rolls 1984; Baylis et al. 1985; Rolls & Baylis 1986; Sato 1988, 1989; Yamane et al. 1988; Hasselmo et al. 1989; Gochin et al. 1991). Moreover, there have been neuronal recordings with behaving monkeys in visual memory tasks (Gross et al. 1979; Mikami & Kubota, 1980; Fuster & Jervey 1981, 1982; Baylis & Rolls 1987; Miyashita & Chang 1988; Miyashita 1988; Fuster 1990). Recently, selective neural responses in the human lateral and medial lobe have been reported (Heit et al. 1988; Ojemann et al. 1988; Creutzfeldt et al. 1989).

On the other hand, there have been studies to show that bilateral damage to the inferior temporal cortex of monkeys causes impairment in visual memory tasks (e.g., delayed matching-to-sample task) (Sahgal & Iversen 1978; Fuster et al. 1981; Mishkin 1982; Sahgal et al. 1983). Therefore, the temporal cortex plays a substantial role in visual recognition processing. However, the coding mechanism for recognition remains to be deciphered.

Memory is presumably the last stage of recognition processes. Hence a key issue is how the brain stores information for a long period. Because an organism can recognize a number of faces and objects, there must be a representation of those long-term memories in neural assemblies. If neurons show selective responses to some objects, which can be acquired only through learning under special conditions, then it is certain that they are closely related to the coding elements of long-term memory.

In the anterior temporal cortex of monkeys, it was previously

reported that individual neurons responded selectively to a few of the computer-generated fractal patterns used in a visual delayed matching-to-sample task (Miyashita & Chang 1988). This response selectivity was shown to be acquired through stimulus-stimulus association by the presentation of the patterns in a fixed-order during the training session (Miyashita 1988). These findings led us to the further question of how long-term memory is encoded and retrieved by an ensemble of neurons in the temporal association cortex.

In the present study, we recorded single neurons from the temporal cortex of monkeys during the performance of a pair-association task. This task was redesigned from that used in the behavioural study of memory (Murray et al. 1988), and was applied to the neurophysiological study for the first time. It would be a new promising paradigm which elucidates the neural representation of long-term memory. Here, two types of task-related neurons in the anterior temporal cortex, which organize the long-term memory of paired associates, are reported. These results have been recently published (Sakai & Miyashita 1991b, c).

Methods

Figure 1 shows the experimental set-up designed for this study. Each device will be subsequently explained in the following Methods sections.

Visual stimuli

Figure 2 shows a set of patterns generated from Fourier descriptors, according to the reconstruction theorem with specified sets of harmonic amplitudes and phase angles (Zahn & Roskies 1972). This set was used for one monkey, and coloured fractal patterns (Miyashita et al. 1991) were used for the other. We arranged these patterns into 12 pairs. Sorting into pairs was basically random, avoiding apparent geometrical resemblances such as rotational symmetry. Their resolution was 160 x 160 pixels with 256 colors.

Pair-association task

Each trial begins with the monkey continually pressing a lever in front of him (Fig. 3). Following a warning stimulus, a cue stimulus was presented in the centre of the video monitor for 1 s. After the delay period of 4 s, two stimuli for choice, the paired associate (correct choice) and a distractor (incorrect choice), were shown randomly in two of four possible positions (arranged in two rows of two columns). The distractor was

selected from other pairs randomly in every trial. The monkey obtained fruit juice as a reward for touching the correct paired associate within 1.2 s. If the monkey released the lever before the choice, that trial was aborted. These sequences of the task were controlled by a microcomputer (PC-9801RA21, NEC) based on Turbo-C programs prepared by the author. Interrupt signal input (lever on and off, touch panel coordinates, and neural spikes) and digital signal output (reward supply and external commands) were processed using parallel I/O interfaces. Fruit juice was delivered through an electromagnetic valve (PK0305, Takasago Electric), which was controlled by TTL (HD7438P, Hitachi) for driving a relay switch (G2VN-237P, Tateishi Electronics).

Behavioral training procedures

Two Japanese macaques (*Macaca fuscata*) (weight 6 - 8 kg, males) were trained in a shield room with sound-attenuating tiles. The monkey's behavior during the task was carefully monitored with a CCD video camera. Extraneous sounds were masked by white noise delivered from stereo speakers. Each monkey was comfortably seated in a primate chair during experiments and was returned to his home cage immediately following each session. Daily care and treatment of animals conformed with NIH guidelines (revised 1985).

The monkeys were trained by the successive approximation method with a manual priming switch. Twelve pairs used in neuronal recordings were divided into three blocks (four pairs per block). After separate learning of the three blocks, all 12 pairs were

presented in random order. The direction of association (for example from 1 to 1', or from 1' to 1) was randomized except for in the early training phase. The delay interval was 0.5 s before thorough randomization, and was increased to 4 s. Error correction trials were included in the early training phase. The criterion for acquisition was two consecutive days of 26 correct responses in 30 trials (87%). The two monkeys took 876 ± 303 trials per picture (mean ± s.e.m.) to reach this criterion.

Recording techniques

After the monkey had learned the task as described above, a head-holding device and a cylindrical chamber for microelectrode recording (Evarts 1968) were attached to the skull under aseptic conditions. The axis of the cylinder was vertical in the Horsley-Clarke coordinate system. To secure the implant, stainless steel bolts were run along several slots in the skull. These attachments and an earth terminal were bound together with dental orthodontic resin (Caulk). During the surgical operation, the monkey was anesthetized with ketamine hydrochloride (Sankyo) and sodium pentobarbital (Dainabot). Intramuscular injection of antibiotics was delivered to prevent infection, and the monkey was given sufficient rest for recovery from surgery.

The activity of single neurons was recorded with a glass-insulated tungsten microelectrode (after Levick 1972). The electrode was inserted vertically into the target zone through the intact dura mater along a stainless steel guide tube, by means of a hydraulic microdrive manipulator (MO-95C, Narishige).

Standard chronic single-unit recording techniques were employed (Rolls et al. 1989; Miyashita et al. 1989).

The action potentials of single cells were amplified 5000- to 10000-fold by a preamplifier. The preamplifier must satisfy the following biological specifications. First, high sensitivity and a low noise level are required in order to discriminate the neural spikes of about 50 μV. A suitable selection of operational amplifiers and noise reduction techniques are necessary for this purpose. Second, the DC drift due to the brain structures must be compensated by temperature-stabilized zener diodes (LM399, National Semiconductor) with a wide operating range. Third, a high input impedance operational amplifier (JFET input; LF356) that can neutralize large capacitive loads is required in the first stage because of high microelectrode resistance and a stray capacitance. To meet these requirements, an original preamplifier was designed and constructed by the author.

The output signal from the preamplifier then passed through high-pass (50-200 Hz) and low-pass (5 kHz) filter circuits, and was converted into digital pulses by a time-window discriminator. The isolation of each neuron was carefully monitored by two sets of storage oscilloscope and sound monitor with power amplifier IC (TA7240AP, Toshiba).

Data analysis

On-line analysis of the neural discharges was carried out by using a microcomputer (PC-9801RA21, NEC). The computer collected

and stored peristimulus rastergrams of neural activity for each trial, and displayed them on a printer.

The collected trials shown in the rastergrams of Figs. 5 and 8 were originally separated by intervening trials of other cue stimuli, and were sorted by off-line computation. Error trials were not included in these figures.

Identification of recording sites

X-radiographs were used to locate the position of the microelectrode on each recording track, relative to bony landmarks such as the posterior tip of the sphenoid bone and the centre of the external auditory meatus. At the conclusion of the experiment, electrolytic microlesions were made by applying DC currents of 15-20 μA (tip negative) to microelectrodes for 60-120s. Additionally, three electrodes were left in the brain for reference. The monkey was deeply anesthetized with an overdose of pentobarbital sodium (45 mg/kg, intramuscular) and then perfused through the heart with 0.9 % saline followed by 10 % formaldehyde solution in phosphate buffer (pH 7.4). The brain was removed from the skull and sectioned coronally at 40 μm on a freezing microtome (after Rosene et al. 1986). Serial sections were then stained with cresyl violet (Merck).

Results

A paradigm for pair association

We prepared 24 computer-generated pictures for each monkey, and sorted the geometrically distinct patterns into pairs, which were defined as *paired associates* (Fig. 2). One of the advantages of using these artificial patterns is that the visual stimuli were entirely new to the monkey before the training. Since the pair combinations are basically random and fixed, they are not predictable without memorizing these paired associates. Therefore, we can analyze the experimentally controlled association between two pictures in each pair.

Two monkeys were trained to memorize a set of 12 pairs through repeated trials in the *pair-association task* (Fig. 3). In each trial, a cue stimulus was presented on a video monitor. The monkey was required to recall the paired associate of the cue and wait during the delay period of 4 s. After that, two stimuli for choice, the paired associate of the cue and a distractor from a different pair, were shown. The monkey obtained fruit juice as a reward for correctly touching the paired associate with his hand. In the recording sessions after training, the monkeys' performance was 70-100 % correct. Extracellular spike discharges of single neurons were recorded from the anterior part of the temporal cortex. The location of the neurons were later identified by histological studies (Fig. 4).

Pair-coding neurons

Figure 5 shows one type of neuron with picture-selective responses during the cue period. One picture elicited the strongest response during the cue period from a neuron, with some activity during the delay period (Fig. 5*a*). By contrast, another picture elicited no response at all (Fig. 5*c*). This neuron responded reproducibly to only two pictures (Fig. 5*a,b*), but not to other pictures in the set (Fig. 5*c,d*). It might be that the cell responded to geometrically similar patterns. The strongest and the second-strongest responses were ascribed to a particular pair which had no apparent geometrical similarity (Fig. 6, upper). Some other cells showed broader tuning and responded to three or more pictures. Nevertheless, paired pictures were found to be among the most effective stimuli for these cells (Fig. 6, lower). We call this type of cell a *pair-coding neuron*, which manifests selective cue responses to both pictures of the paired associates.

Evaluation of cue responses was done by calculating a mean discharge rate for each picture. First, spike numbers were collected over 400 ms at the beginning of the cue interval. They were averaged across trials for the same cue stimulus and their variances were evaluated to test reproducibility in each cell. Of 577 isolated neurons, 436 cells were unresponsive (Table 1). Since weak responses are susceptible to random fluctuations around a spontaneous discharge level and they cannot be ascribed to the optimal stimulus (Gross et al. 1972), we examined 104

cells whose discharge rates (a spontaneous discharge rate was subtracted for each cell) were distributed beyond 15.5 Hz (the leftmost saddle point in the distribution of 141 responsive cells). Out of the 104 cells, 13 showed nonselective responses to all pictures, whereas the other 91 cells were picture-selective (Table 1).

These 91 cells reproducibly showed a strong picture-selective response during the cue period. The most effective stimuli for each cell covered all pictures in the set. These responsive cells tended to be located near one another (1-2 mm wide) in the temporal cortex. Thirty-two of the 91 cells responded to only one picture, whereas 59 cells responded to two or more pictures.

We further analyzed these 59 cells by calculating two coupling indices for each neuron, defined as

$$CI_p = N_p^{-1} \sum_{\substack{i\ j \\ i<j}} \sum \{(x_i-b)(x_j-b)\}/\{(x_{best}-b)(x_{2nd\text{-}best}-b)\}*100,$$

with $j = i'$ for paired associates and

$$CI_r = N_r^{-1} \sum_{\substack{i\ j \\ i<j}} \sum \{(x_i-b)(x_j-b)\}/\{(x_{best}-b)(x_{2nd\text{-}best}-b)\}*100,$$

with $j \neq i'$ for random combinations, where x_i denotes a mean discharge rate during the cue period for the ith picture (the ith and i'th pictures are one pair), b is a spontaneous discharge rate, x_{best} and $x_{2nd\text{-}best}$ are mean discharge rates for the best and second-best cue-optimal pictures in each cell, and N_p and N_r are the total number of combinations for two cases. Pair index (PI) was then defined as

$$PI = CI_p - CI_r.$$

One coupling index CI_p measures correlated neural responses to paired associates, whereas the other coupling index CI_r estimates responses to other random combinations among 24 pictures. The latter index CI_r serves as an experimental control for untrained association between two pictures. For each cell, we defined a pair index *PI*. The frequency distribution of *PI* values (black and dotted bars in Fig. 7) demonstrated that the paired associates elicited significantly correlated responses ($P<0.015$; Wilcoxon's signed-rank test, $n=59$). In order to clarify the significant contribution of pair-coding neurons, we calculated *PI* for shuffled pairs by exchanging the terms of paired associates and those of other random 12 pairs selected from 264 random combinations. Because 22 sets of shuffled pairs that had no overlap in their components were selected for each cell (i.e. 12 x 22 = 264 distinct combinations in total), there are enough data ($n=1298$) for the control distribution of *PI* values (white and dotted bars in Fig. 7). The difference between these two distributions was statistically significant ($P<0.05$; Kolmogorov-Smirnov two-sample test). The number of pair-coding neurons was estimated to be 10, by the distribution difference for positive *PI* values (black portions in Fig. 7). We conclude that the selectivity of these neurons to paired associates was acquired through learning of the pair-association task.

Pair-recall neurons

We found another type of neuron with picture-selective activities during the delay period. One picture elicited the strongest response during the cue period from a single neuron (Fig. 8*a*). In the trial when the paired associate of this cue-optimal picture was presented as a cue, the same cell had the highest tonic activity during the delay period, in contrast to a weak response during the cue period (Fig. 8*b*). This delay activity gradually increased until the choice of stimuli appeared. Furthermore, the paired associate of the second-best cue-optimal picture still elicited a sustained activity during the delay period (Fig. 8*c,d*). Other pictures evoked weak or no response (Fig. 8*e,f*). The delay activities were confined to a few cue stimuli in the set. We call this type of cell a *pair-recall neuron*, in which the paired associate of a cue-optimal picture elicited the highest delay activity.

Figure 9 demonstrates the stimulus selectivity of another pair-recall neuron. For this cell, only one picture elicited the cue-optimal response. Although there was no cue response when its paired associate was presented, this neuron was selectively activated by this associate during the delay period. All other stimuli elicited an inhibition of delay activities for this cell.

Eleven of 91 cells showed picture-selective delay activities that surpassed cue responses in those trials (Fig. 10). Out of 11 cells, 10 were pair-recall neurons as defined above. The highest delay activity of the pair-recall neurons does not represent mere sensory after-discharge, because it is stronger

than the cue response. Furthermore, a significant augmentation of discharge rates was observed for the highest delay activity when mean discharge rates at two intervals were compared (Fig. 10): 200-1400 ms (near the beginning of the delay interval) and 2760-3960 ms (near the end) after delay onset ($P<0.05$; Wilcoxon's signed-rank test, $n=11$). By contrast, the delay activity elicited by a cue-optimal picture itself was significantly reduced during the delay period ($P<0.005$; $n=11$).

Error analysis

Out of 91 responsive neurons, 18 cells showed three or more error trials (where the monkey made incorrect choices) in which a cue-optimal picture was presented. There was no significant difference in mean discharge rates during the cue period between correct and error trials ($P>0.05$; Wilcoxon's signed-rank test, $n=18$). Out of 10 pair-recall neurons, two cells exhibited three or more error trials in which the paired associate of a cue-optimal picture was presented. One cell showed no significant difference, whereas the other cell showed a higher delay activity in correct trials than in error trials, which correlated with the monkey's choice ($P<0.01$; two-tailed modified t test (Snedecor & Cochran 1989), $t'=3.21$ with 17 d.f.).

Discussion

Associative coding and ensemble coding

It was previously reported that a picture-selective delay activity reflected stimulus-stimulus association caused by the picture presentation in a fixed order during the training session of the delayed matching-to-sample task (Miyashita 1988). But evidence from that experiment was restricted to implicit learning because the monkey could perform the task without memorizing the real sequence of patterns. In the present task paradigm, associative learning was imposed to assess long-term memory more directly. The monkey could not select the correct paired associate without memorizing and recalling the pair combinations.

According to the results reported here, acquired pairing is now regarded as an important coding faculty. This type of coding is here called *associative coding*, in which the involvement of associative learning is essential. The properties of pair-coding neurons indicate that memory storage is organized such that single neurons can code both pictures of the paired associates. A possible basis for associative coding lies in the change of synaptic connections through repetitive learning (Artola & Singer 1987; Frégnac et al. 1988), whereby two pictures are always paired with each other.

In the primate inferior temporal cortex and part of the superior temporal sulcus, neural responses to complex objects

such as hands (Gross et al. 1969, 1972; Desimone et al. 1984), faces (Bruce et al. 1981; Perrett et al. 1982, 1984, 1985; Desimone et al. 1984; Rolls 1984; Baylis et al. 1985; Rolls & Baylis 1986; Yamane et al. 1988; Hasselmo et al. 1989), and Fourier descriptors (Schwartz et al. 1983; Gochin et al. 1991) have been reported. Although responses of 'face neurons' are selective in the sense that these cells do not respond to non-face objects, their selectivity among various faces is rather broad (Rolls 1984; Baylis et al. 1985). This implies that a more distributed type of coding is used among these neurons. Rolls (1987) proposed this to be 'ensemble coding' in contrast to 'grandmother cell' or 'pontifical cell' coding. Barlow (1972) argued that the 'pontifical cell' should be replaced by a number of 'cardinal cells', and that each event must correspond to a specific combination of active cells. Recently, Tanaka et al. (1991) proposed 'combination coding', based on their findings that each cell in the inferotemporal cortex responded selectively to a complex feature unique to particular objects. This coding also assumes the combination of active cells, where each cell represents the presence of a particular partial feature.

The associative coding proposed here provides one of the definite organizing principles, by which the special selectivity of neural responses is generated. The spatio-temporal patterns of selective neural discharges would thus constitute the basis of ensemble coding. The acquired selectivity through learning is a key feature in the capacity of temporal cortical neurons to establish associations.

Object-centred representation and association

One of the problems with object recognition is that some temporal cortical neurons respond to the optimal stimulus in a manner independent of the angle of view. Perrett et al. (1984) reported cells that responded equally to the face and to other views of the head such as the profile. It should also be noted that more neurons were found to be differentially sensitive to the sight of the object from different vantage points (Perrett et al. 1985). It is not clear whether a number of distinct views would have to be stored separately in the brain.

Marr and Nishihara (1978) previously proposed that a three-dimensional shape representation for recognition should use an *object-centred* coordinate system, which is transformed from a *viewer-centred* coordinate system. Hasselmo et al. (1989) provided evidence that some cells respond to faces on the basis of object-centred coordinates, and that others have responses which are intermediate between object-centred and viewer-centred representations.

For the majority of objects, only learning can specify that the various views of an object belong to the same object (Perrett et al. 1987). Therefore, invariance over changes of vantage points is acquired through associative learning. This situation is a natural extension of our paradigm in that two different views of an object are associated and memorized by temporal cortical neurons. In reality, these visually distinct views are nearly always presented in succession, resulting from relative movement between the observer and the object. Such an associational

mechanism based on temporal contiguity may be a general property of this area of the temporal cortex (Stryker 1991).

Human memory and association

Most of our long-term memories of episodes or objects are organized so that we can retrieve them by association. Anderson & Bower (1980) argued that human memory only stores 'propositions', which are conceived as 'structured bundles of associations between elementary ideas or concepts'. Also in clinical neuropsychology, human memory is assessed by the paired-associate learning test, in which a series of paired words or figures is presented and the subject is then asked to retrieve the other pair member associated with each cue (Wechsler 1987). Patients with lesions of the temporal lobe show marked impairment in this test (Meyer & Yates 1955; Milner 1967; Jones 1974; Petrides 1985; Goldstein et al. 1988). It is also notable that amnesiac patients with bilateral medial temporal-lobe damage could not derive benefit from the instructions to use visual imagery in the recall of verbal paired associates (Jones 1974). This result suggests the special involvement of the medial temporal region in the association process.

Association and categorization of knowledge

Lesions in the right temporal lobe have been shown to produce specific deficits in human cases. Applying the nonsense-figures test, Kimura (1963) reported impairment in the perception and recognition of unfamiliar figures. Milner (1968) also clarified

that the visual disorders associated with right anterior temporal lobectomy affect the retention of the perceived material in face-recognition tasks.

Visual associative agnosia is a syndrome of impairment in recognizing visually presented common objects, although language and visual abilities of the patient are well preserved. Hecaen et al. (1974) studied a patient who was impaired in describing the function and use of common objects, and also impaired in allocating them to a category of similar objects. Another similar case with a left occipito-temporal lesion was reported by McCarthy & Warrington (1986). Other notable clinical reports include prosopagnosia (face agnosia), which generally follows bilateral lesions in occipital and temporal association cortices (Meadows 1974; Whiteley & Warrington 1977; Damasio et al. 1982; Damasio 1985).

Recently, a case with circumscribed damage to the left temporal lobe was reported (McCarthy & Warrington 1988). This patient showed a selective inability to define the characteristics of animals or plants in response to their spoken names, although his knowledge of the visual world was normal. There has been other evidence that our semantic memory may be categorical in its organization (Wilkins & Moscovitch 1978; Warrington & McCarthy 1983, 1987; Warrington & Shallice 1984). Category-related recognition defects would possibly provide a clue as to the neural representation of knowledge (Damasio 1990). Since association within a single category is more easily acquired than that across different categories, as shown by the verbal paired-

associate test, the association process may play an important role in categorization.

It is probable that the visual memory is also categorically organized in classifying various objects. Wilson & DeBauche (1981) showed that monkeys with inferotemporal-cortex lesions did not show categorical perception of visual stimuli. Hence, temporal cortical neurons would be critical for categorization of knowledge, thereby organizing the stored information through associative learning. Pair-coding neurons could serve as basic elements for this process.

Pair-recall neurons and retrieval process

There are two possibilities on the critical processes during the delay period of the pair-association task. One is to hold a *retrospective code*, that is a cue stimulus in memory. The other is to generate a *prospective code* by converting a cue into its paired associate. The highest delay activity of the pair-recall neurons is consistent with the claim that subjects can employ a prospective code.

Anticipatory neural activities with directional selectivity, that precede the initiation of movements and increase during the preparatory period, have been reported in the primate frontal cortex (Niki 1974a, b; Bruce & Goldberg 1985; Mauritz & Wise 1986; Funahashi et al. 1989). In our pair-association task, the increasing delay activity of pair-recall neurons is not related to motor response because the monkey could not predict which position should be touched. As noted before, this delay activity

is not only picture-selective, but also closely coupled with the paired associate that is not actually seen, but retrieved by the cue stimulus. The neural mechanism for the retrieval process remains to be identified, but it may well involve the pair-recall neurons.

Contribution of the medial temporal lobe

A recent lesion study has demonstrated that monkeys with bilateral removal of the medial temporal lobe do not relearn the pair-association task within the training limit, in contrast to the control group (Murray et al. 1988). The type of memory this task used would therefore correspond to one that relies on the integrity of this region.

In the case of humans, electrical stimulation of the temporal cortex is known to produce experiential responses such as imagery recall of visual scenes or objects (Penfield & Perot 1963). Similar mental responses are also evoked by electrical stimulation of the human medial temporal lobe (Halgren et al. 1978). They are idiosyncratic and unrelated to the anatomical site. It is possible that the electrical stimulation activates the retrieval system through the medial temporal lobe, resulting in an imagery association of stored information. The retrieval process would thus need the activation of specific neurons that also participate in categorized memory storage. This hypothesis agrees well with the observation that pair-recall neurons and pair-coding neurons are found in the vicinity.

The medial temporal region is considered to be essential for

the memory consolidation process, by which certain evanescent information is transformed into an enduring representation for long-term memory (Milner 1972; Squire et al. 1984; Sakai & Miyashita 1990, 1991a). Since the anterior temporal cortex links the visual system and the limbic memory system (Insausti et al. 1987; Webster et al. 1991), the unique neurons described here could serve as memory storage elements, also activated in the retrieval process.

Acknowledgments

The author wishes to acknowledge the continuing encouragement of Professor Yoshiki Hotta, who afforded him the valuable opportunity to study higher functions of the brain. The author would like to express his gratitude to Professor Yasushi Miyashita for the constant guidance and for all the inspiring discussion, which opened his eyes to the central problems. Many years of encouragement and the sincere support of his parents are gratefully acknowledged. This work was carried out in the Department of Physiology, Faculty of Medicine, University of Tokyo.

References

Anderson, J. A. & Bower, G. H.: *Human Associative Memory: A Brief Edition* (Lawrence Erlbaum, Hillsdale, 1980).

Artola, A. & Singer, W.: Long-term potentiation and NMDA receptors in rat visual cortex. *Nature* **330**, 649-652 (1987).

Barlow, H. B: Single units and sensation: a neuron doctrine for perceptual psychology? *Perception* **1**, 371-394 (1972).

Baylis, G. C. & Rolls, E. T.: Responses of neurons in the inferior temporal cortex in short term and serial recognition memory tasks. *Exp. Brain Res.* **65**, 614-622 (1987).

Baylis, G. C., Rolls, E. T. & Leonard, C. M.: Selectivity between faces in the responses of a population of neurons in the cortex in the superior temporal sulcus of the monkey. *Brain Res.* **342**, 91-102 (1985).

Bruce, C., Desimone, R. & Gross C. G.: Visual properties of neurons in a polysensory area in superior temporal sulcus of the macaque. *J. Neurophysiol.* **46**, 369-384 (1981).

Bruce, C. J. & Goldberg, M. E.: Primate frontal eye fields. I. Single neurons discharging before saccades. *J. Neurophysiol.* **53**, 603-635 (1985).

Creutzfeldt, O., Ojemann, G. & Lettich, E.: Neuronal activity in the human lateral temporal lobe: I. Responses to speech. *Exp. Brain Res.* **77**, 451-475 (1989).

Damasio, A. R.: Prosopagnosia. *Trends Neurosci.* **8**, 132-135

(1985).

Damasio, A. R.: Category-related defects as a clue to the neural substrates of knowledge. *Trends Neurosci.* 13, 95-98 (1990).

Damasio, A. R., Damasio, H. & Van Hoesen, G. W.: Prosopagnosia: anatomic basis and behavioral mechanisms. *Neurology* 32, 331-341 (1982).

Desimone, R., Gross, C. G.: Visual areas in the temporal cortex of the macaque. *Brain Res.* 178, 363-380 (1979).

Desimone, R., Albright, T. D., Gross, C. G. & Bruce, C.: Stimulus-selective properties of inferior temporal neurons in the macaque. *J. Neurosci.* 4, 2051-2062 (1984).

Evarts, E. V.: A technique for recording activity of subcortical neurons in moving animals. *Electroenceph. Clin. Neurophysiol.* 24, 83-86 (1968).

Frégnac, Y., Shulz, D., Thorpe, S. & Bienenstock, E.: A cellular analogue of visual cortical plasticity. *Nature* 333, 367-370 (1988).

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

Fuster, J. M., Bauer, R. H. & Jervey, J. P.: Effects of cooling inferotemporal cortex on performance of visual memory tasks. *Exp. Neurol.* 71, 398-409 (1981).

Fuster, J. M. & Jervey, J. P.: Inferotemporal neurons distinguish and retain behaviorally relevant features of visual stimuli. *Science* 212, 952-955 (1981).

Fuster, J. M. & Jervey, J. P.: Neuronal firing in the

inferotemoral cortex of the monkey in a visual memory task. *J. Neurosci.* 2, 361-375 (1982).

Fuster, J. M.: Inferotemporal units in selective visual attention and short-term memory. *J. Neurophysiol.* 64, 681-697 (1990).

Goldstein, L. H., Canavan, A. G. M. & Polkey, C. E.: Verbal and abstract designs paired associate learning after unilateral temporal lobectomy. *Cortex* 24, 41-52 (1988).

Gochin, P. M., Miller, E. K., Gross, C. G. & Gerstein, G. L.: Functional interactions among neurons in inferior temporal cortex of the awake macaque. *Exp. Brain Res.* 84, 505-516 (1991).

Gross, C. G.: Visual functions of inferotemporal cortex. In: *Handbook of Sensory Physiology* 7, Part 3B, pp. 451-482 (Springer, Berlin, 1973).

Gross, C. G., Bender, D. B. & Rocha-Miranda, C. E.: Visual receptive fields of neurons in inferotemporal cortex of the monkey. *Science* 166, 1303-1306 (1969).

Gross, C. G., Rocha-Miranda, C. E. & Bender, D. B.: Visual properties of neurons in inferotemporal cortex of the macaque. *J. Neurophysiol.* 35, 96-111 (1972).

Gross, C. G., Bender, D. B. & Gerstein, G. L.: Activity of inferior temporal neurons in behaving monkeys. *Neuropsychologia* 17, 215-229 (1979).

Heit, G., Smith, M. E., Halgren, E.: Neural encoding of individual words and faces by the human hippocampus and amygdala. *Nature* 333, 773-775 (1988).

Halgren, E., Walter, R. D., Cherlow, D. G. & Crandall, P. H.:

Mental phenomena evoked by electrical stimulation of the human hippocampal formation and amygdala. *Brain* 101, 83-117 (1978).

Hasselmo, M. E., Rolls, E. T., Baylis, G. C. & Nalwa, V.: Object-centered encoding by face-selective neurons in the cortex in the superior temporal sulcus of the monkey. *Exp. Brain Res.* 75, 417-429 (1989).

Hecaen, H., Goldblum, M. C., Masure M. C. & Ramier, A. M.: Une nouvelle observation d'agnosie d'object: deficit de l'association ou de la categorisation, specifique de la modalite visuelle? *Neuropsychologia* 12, 447-464 (1974).

Hubel, D. H. & Wiesel, T. N.: Receptive fields, binocular interaction and functional architecture in the cat's visual cortex. *J. Physiol.* 160, 106-154 (1962).

Hubel, D. H. & Wiesel, T. N.: Receptive fields and functional architecture of monkey striate cortex. *J. Physiol.* 195, 215-243 (1968).

Hubel, D. H. & Wiesel, T. N.: Functional architecture of macaque monkey visual cortex. *Proc. R. Soc. Lond.* B. 198, 1-59 (1977).

Insausti, R., Amaral, D. G. & Cowan, W. M.: The entorhinal cortex of the monkey: II. cortical afferents. *J. Comp. Neurol.* 264, 356-395 (1987).

Iwai, E. & Mishkin, M. (Ed.): *Vision, Memory, and the Temporal Lobe* (Elsevier, New York, 1990).

Jones, M. K.: Imagery as a mnemonic aid after left temporal lobectomy: contrast between material-specific and generalized memory disorders. *Neuropsychologia* 12, 21-30 (1974).

Kimura, D.: Right temporal-lobe damage: perception of unfamiliar

stimuli after damage. *Arch. Neurol.* 8, 48-55 (1963).

Levick, W. R.: Another tungsten microelectrode. *Med. Biol. Eng.* 10, 510-515 (1972).

Marr D. & Nishihara, H. K.: Representation and recognition of the spatial organization of three-dimensional shapes. *Proc. R. Soc. Lond. B.* 200, 269-294 (1978).

Mauritz, K.-H. & Wise, S. P.: Premotor cortex of the rhesus monkey: neuronal activity in anticipation of predictable environmental events. *Exp. Brain Res.* 61, 229-244 (1986).

McCarthy, R. A. & Warrington, E. K.: Visual associative agnosia: a clinico-anatomical study of a single case. *J. Neurol. Neurosurg. Psychiatr.* 49, 1233-1240 (1986).

McCarthy, R. A. & Warrington, E. K.: Evidence for modality-specific meaning systems in the brain. *Nature* 334, 428-430 (1988).

Meadows, J. C.: The anatomical basis of prosopagnosia. *J. Neurol. Neurosurg. Psychiatr.* 37, 489-501 (1974).

Meyer, V. & Yates, A. J.: Intellectual changes following temporal lobectomy for psychomotor epilepsy. *J. Neurol. Neurosurg. Psychiat.* 18, 44-52 (1955).

Mikami, A. & Kubota, K.: Inferotemporal neuron activities and color discrimination with delay. *Brain Res.* 182, 65-78 (1980).

Milner, B.: Brain mechanisms suggested by studies of temporal lobes. In: *Brain Mechanisms Underlying Speech and Language*, pp. 122-145 (Grune & Stratton, New York, 1967).

Milner, B.: Visual recognition and recall after right temporal-lobe excision in man. *Neuropsychologia* 6, 191-209 (1968).

Milner, B.: Disorders of learning and memory after temporal lobe lesions in man. *Clin. Neurosurg.* 19, 421-446 (1972).

Mishkin, M.: A memory system in the monkey. *Phil. Trans. R. Soc. Lond.* B 298, 85-95 (1982).

Miyashita, Y.: Neuronal correlate of visual associative long-term memory in the primate temporal cortex. *Nature* 335, 817-820 (1988).

Miyashita, Y. & Chang, H. S.: Neuronal correlate of pictorial short-term memory in the primate temporal cortex. *Nature* 331, 68-70 (1988).

Miyashita, Y., Higuchi, S., Sakai, K. & Masui, N.: Generation of fractal patterns for probing the visual memory. *Neurosci. Res.* 12, 307-311 (1991).

Miyashita, Y., Rolls, E. T., Cahusac, P. M. B., Niki, H. & Feigenbaum, J. D.: Activity of hippocampal formation neurons in the monkey related to a conditional spatial task. *J. Neurophysiol.* 61, 669-678 (1989).

Murray, E. A., Gaffan, D. & Mishkin, M.: Role of the amygdala and hippocampus in visual-visual associative memory in rhesus monkeys. *Soc. Neurosci. Abstr.* 14, 2 (1988).

Niki, H.: Prefrontal unit activity during delayed alternation in the monkey. I. Relation to direction of response. *Brain Res.* 68, 185-196 (1974a).

Niki, H.: Differential activity of prefrontal units during right and left delayed response trials. *Brain Res.* 70, 346-349 (1974b).

Ojemann, G. A., Creutzfeldt, O., Lettich, E. & Haglund, M. M.:

Neuronal activity in human lateral temporal cortex related to short-term verbal memory, naming and reading. *Brain* 111, 1383-1403 (1988).

Penfield, W. & Perot, P.: The brain's record of auditory and visual experience - a final summary and discussion. *Brain* 86, 595-696 (1963).

Perrett, D. I., Rolls, E. T. & Caan, W.: Visual neurones responsive to faces in the monkey temporal cortex. *Exp. Brain Res.* 47, 329-342 (1982).

Perrett, D. I., Smith, P. A. J., Potter, D. D., Mistlin, A. J., Head, A. S., Milner, A. D. & Jeeves, M. A.: Neurons responsive to faces in the temporal cortex: studies of functional organization, sensitivity to identity and relation to perception. *Hum. Neurobiol.* 3, 197-208 (1984).

Perrett, D. I., Smith, P. A. J., Potter, D. D., Mistlin, A. J., Head, A. S., Milner, A. D. & Jeeves, M. A.: Visual cells in the temporal cortex sensitive to face view and gaze direction. *Proc. R. Soc. Lond. B.* 223, 293-317 (1985).

Perrett, D. I., Mistlin, A. J. & Chitty, A. J.: Visual neurons responsive to faces. *Trends Neurosci.* 10, 358-364 (1987).

Petrides, M.: Deficits on conditional associative-learning tasks after frontal- and temporal-lobe lesions in man. *Neuropsychologia* 23, 601-614 (1985).

Richmond, B. J., Wurtz, R. H. & Sato, T.: Visual responses of inferior temporal neurons in awake rhesus monkey. *J. Neurophysiology* 50, 1415-1432 (1983).

Richmond, B. J., Optican, L. M., Podell, M. & Spitzer, H.:

Temporal encoding of two-dimensional patterns by single units in primate inferior temporal cortex: I. Response characteristics. *J. Neurophysiol.* **57**, 132-146 (1987).

Ridley, R. M. & Ettlinger, G.: Visual discrimination performance in the monkey: the activity of single cells in infero-temporal cortex. *Brain Res.* **55**, 179-182 (1973).

Ridley, R. M., Hester, N. S. & Ettlinger, G.: Stimulus- and response-dependent units from the occipital and temporal lobes of the unanaesthetized monkey performing learnt visual tasks. *Exp. Brain Res.* **27**, 539-552 (1977).

Rolls, E. T.: Neurons in the cortex of the temporal lobe and in the amygdala of the monkey with responses selective for faces. *Hum. Neurobiol.* **3**, 209-222 (1984).

Rolls, E. T.: Information representation, processing, and storage in the brain: analysis at the single neuron level. In: *The Neural and Molecular Bases of Learning*, pp. 503-539 (John Wiley & Sons, Chichester, 1987).

Rolls, E. T., Judge, S. J. & Sanghera, M. K.: Activity of neurons in the inferotemporal cortex of the alert monkey. *Brain Res.* **130**, 229-238 (1977).

Rolls, E. T. & Baylis, G. C.: Size and contrast have only small effects on the responses to faces of neurons in the cortex of the superior temporal sulcus of the monkey. *Exp. Brain Res.* **65**, 38-48 (1986).

Rolls, E. T., Miyashita, Y., Cahusac, P. M. B., Kesner, R. P., Niki, H., Feigenbaum, J. D. & Bach, L.: Hippocampal neurons in the monkey with activity related to the place in which a

stimulus is shown. *J. Neurosci.* 9, 1835-1845 (1989).

Rosene, D. L., Roy, N. J. & Davis, B. J.: A cryoprotection method that facilitates cutting frozen sections of whole monkey brains for histological and histochemical processing without freezing artifact. *J. Histochem. Cytochem.* 34, 1301-1315 (1986).

Sahgal, A. & Iversen, S. D.: Categorization and retrieval after selective inferotemporal lesions in monkeys. *Brain Res.* 146, 341-350 (1978).

Sahgal, A., Hutchison, R., Hughes, R. P. & Iversen, S. D.: The effects of inferotemporal cortex lesions on Konorski delayed pair comparison in monkeys. *Behav. Brain Res.* 8, 361-373 (1983).

Sakai, K. & Miyashita, Y.: Molecule - Hippocampus - Memory. Part I: On the molecular mechanisms of synaptic plasticity. *Brain and Nerve* 42, 1017-1029 (1990).

Sakai, K. & Miyashita, Y.: Molecule - Hippocampus - Memory. Part II: Hippocampus as a memory control apparatus. *Brain and Nerve* 43, 111-128 (1991a).

Sakai, K. & Miyashita, Y.: Single neurons in primate temporal cortex code both of paired associates stored in visual long-term memory. *Soc. Neurosci. Abstr.* 17 (1991b).

Sakai, K. & Miyashita, Y.: Neural organization for the long-term memory of paired associates. *Nature* 354, 152-155 (1991c).

Sato, T.: Effects of attention and stimulus interaction on visual responses of inferior temporal neurons in macaque. *J. Neurophysiol.* 60, 344-364 (1988).

Sato, T.: Interactions of visual stimuli in the receptive fields

of inferior temporal neurons in awake macaques. *Exp. Brain Res.* 77, 23-30 (1989).

Sato, T., Kawamura, T. & Iwai, E.: Responsiveness of inferotemporal single units to visual pattern stimuli in monkeys performing discrimination. *Exp. Brain Res.* 38, 313-319 (1980).

Schwartz, E. L., Desimone, R., Albright, T. D. & Gross, C. G.: Shape recognition and inferior temporal neurons. *Proc. Natl. Acad. Sci. U.S.A.* 80, 5776-5778 (1983).

Snedecor, G. W. & Cochran, W. G.: *Statistical Methods*, 8th ed., p. 97 (Iowa State University Press, Ames, 1989).

Squire, L. R., Cohen, N. J. & Nadel, L.: The medial temporal region and memory consolidation: a new hypothesis. In: *Memory Consolidation: Psychobiology of Cognition*, pp. 185-210 (Lawrence Erlbaum, Hillsdale, 1984).

Stryker, M. P.: Temporal associations. *Nature* 354, 108-109 (1991).

Tanaka, K., Saito, H., Fukada, Y. & Moriya, M.: Coding visual images of objects in the inferotemporal cortex of the macaque monkey. *J. Neurophysiol.* 66, 170-189 (1991).

Warrington, E. K. & McCarthy, R. A.: Category specific access dysphasia. *Brain* 106, 859-878 (1983).

Warrington, E. K. & McCarthy, R. A.: Categories of knowledge: further fractionations and an attempted integration. *Brain* 110, 1273-1296 (1987).

Warrington, E. K. & Shallice, T.: Category specific semantic impairments. *Brain* 107, 829-854 (1984).

Webster, M. J., Ungerleider, L. G. & Bachevalier, J.: Connections of inferior temporal areas TE and TEO with medial temporal-lobe structures in infant and adult monkeys. *J. Neurosci.* 11, 1095-1116 (1991).

Wechsler, D.: *Wechsler Memory Scale - Revised* (The Psychological Corporation, Harcourt Brace Jovanovich, San Antonio, 1987).

Whiteley, A. M. & Warrington, E. K.: Prosopagnosia: a clinical, psychological, and anatomical study in three patients. *J Neurol. Neurosurg. Psychiatr.* 40, 394-430 (1977).

Wilkins, A. & Moscovitch, M.: Selective impairment of semantic memory after temporal lobectomy. *Neuropsychologia* 16, 73-79 (1978).

Wilson, M. & DeBauche, B. A.: Inferotemporal cortex and categorical perception of visual stimuli by monkeys. *Neuropsychologia* 19, 29-41 (1981).

Yamane, S., Kaji, S., Kawano, K.: What facial features activate face neurons in the inferotemporal cortex of the monkey. *Exp. Brain Res.* 73, 209-214 (1988).

Zahn, C. T. & Roskies, R. Z.: Fourier descriptors for plane closed curves. *IEEE Trans. Comput.* 21, 269-281 (1972).

Figures

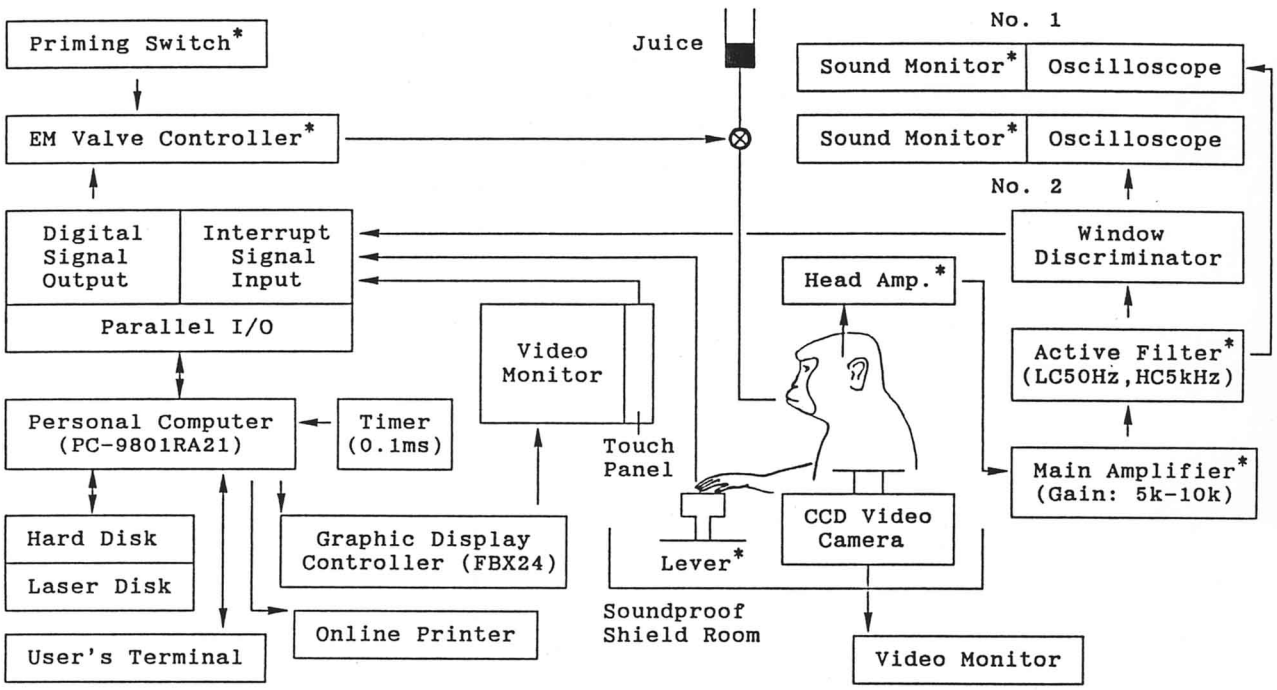

Fig. 1 Experimental set-up for this study. The direction of information flow is indicated by arrows connecting each device shown in a box. The device with an asterisk was specially designed and constructed by the author.

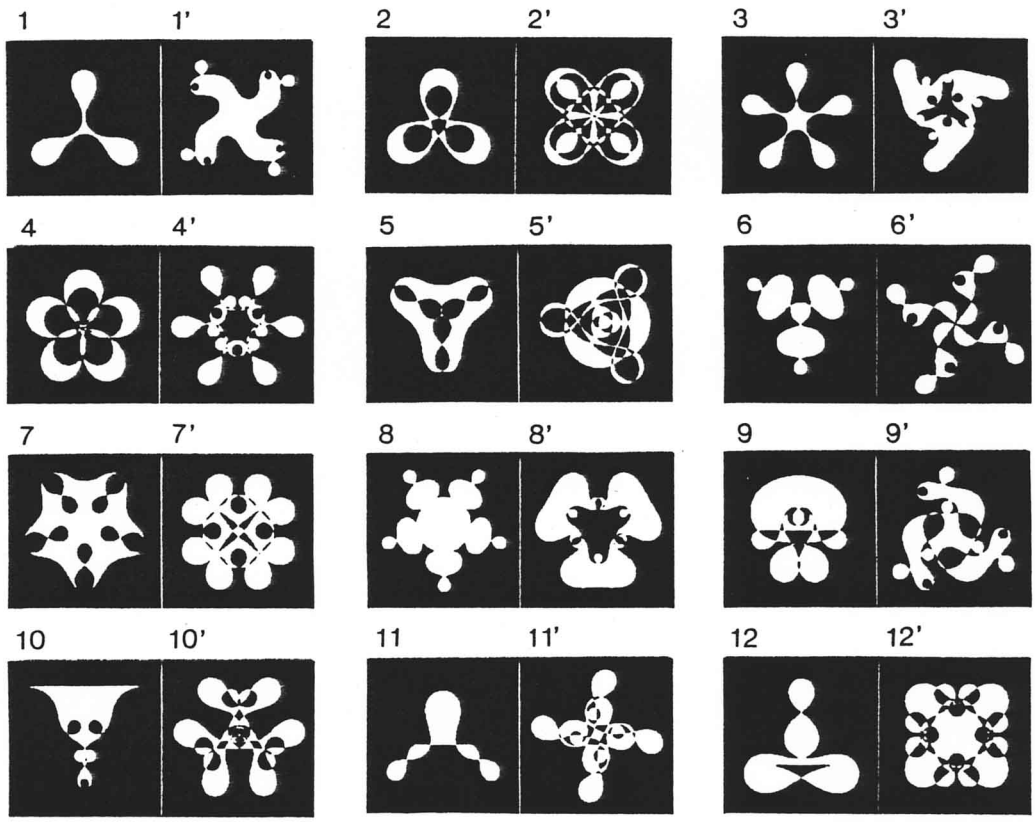

Fig. 2 Visual paired associates. These pictures are 12 pairs of patterns generated from Fourier descriptors (1 and 1' - 12 and 12') for stimuli in the task. The real images on a colour video monitor were yellow monochrome against a black field. The monkeys learned to retrieve the other member of the pair associated with each cue picture.

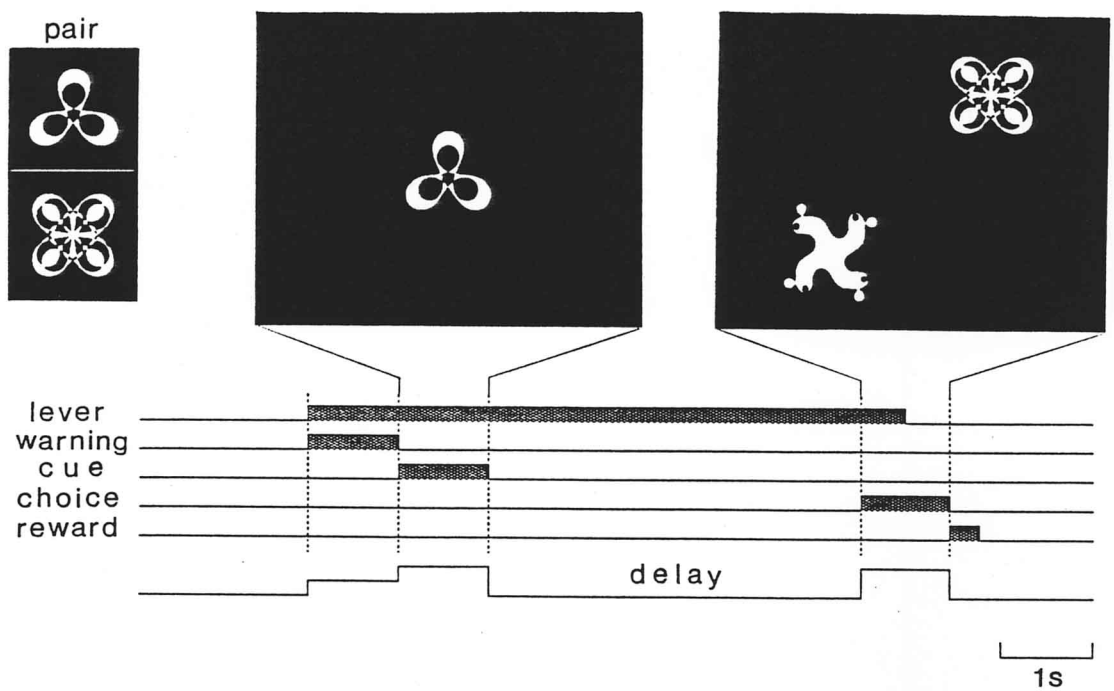

Fig. 3 Pair-association task for monkeys used to assess long-term memory. A sequence of events in a trial is shown with an example of one pair. Lever, lever press by the monkey to initiate a new trial; warning, green square (1 s); cue, one of 24 pictures as a cue stimulus (1 s); delay, green square (4 s); choice, A choice between two stimuli, the paired associate of the cue and one from a different pair; reward, fruit-juice reward for touching the correct paired associate. Bottom trace, events chart used in Figs 5 and 8.

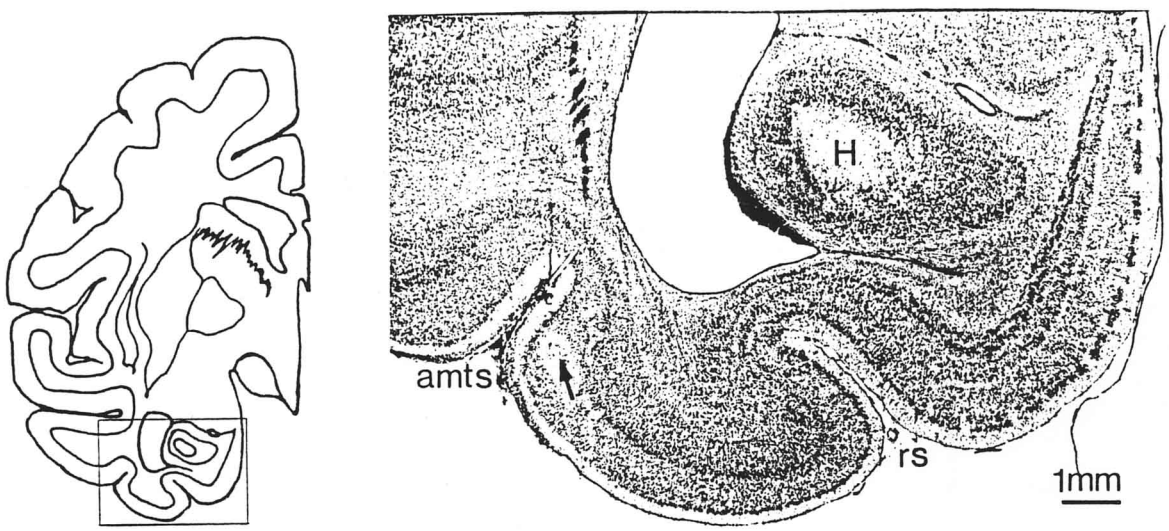

Fig. 4 Location of recorded neurons. Left, coronal-section of the monkey's brain. Right, Nissl-stained section indicated by a box on the coronal-section. The arrow shows a recording electrode site.

Abbreviations: *H*, hippocampus; *amts*, anterior middle temporal sulcus; *rs*, rhinal sulcus.

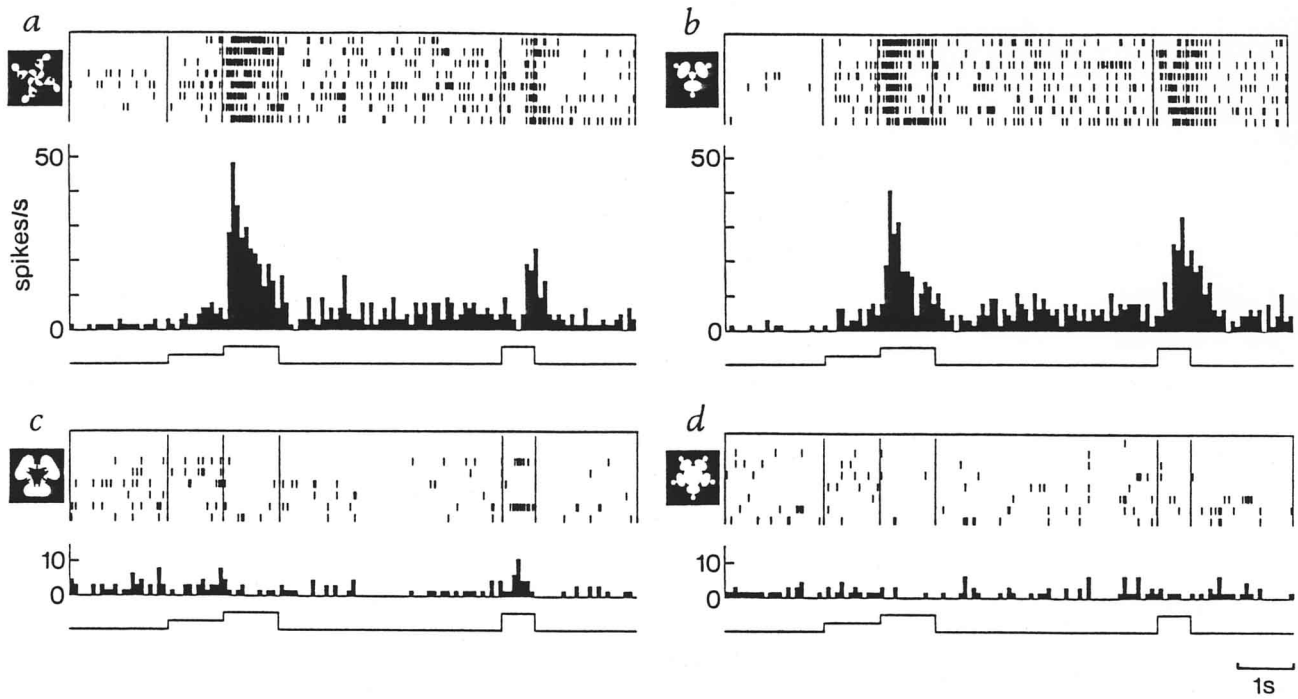

Fig. 5 Response of a *pair-coding neurons* which were selective to both pictures of the paired associates. In each panel, rastergrams of neural discharges in each trial (upper) and spike-density histograms (lower) are shown. Bin width, 80 ms. The data were obtained from a single neuron. *a*, These trials were collected for picture 6' as a cue (shown on the left of the rastergrams). This picture elicited the strongest response during the cue period. *b*, Trials for cue 6 that resulted in the second-strongest cue response. *c, d*, Trials for cue 8' and cue 8, respectively, that elicited no response at all in the same cell. This neuron selectively responded to both pictures of the paired associates 6 & 6'.

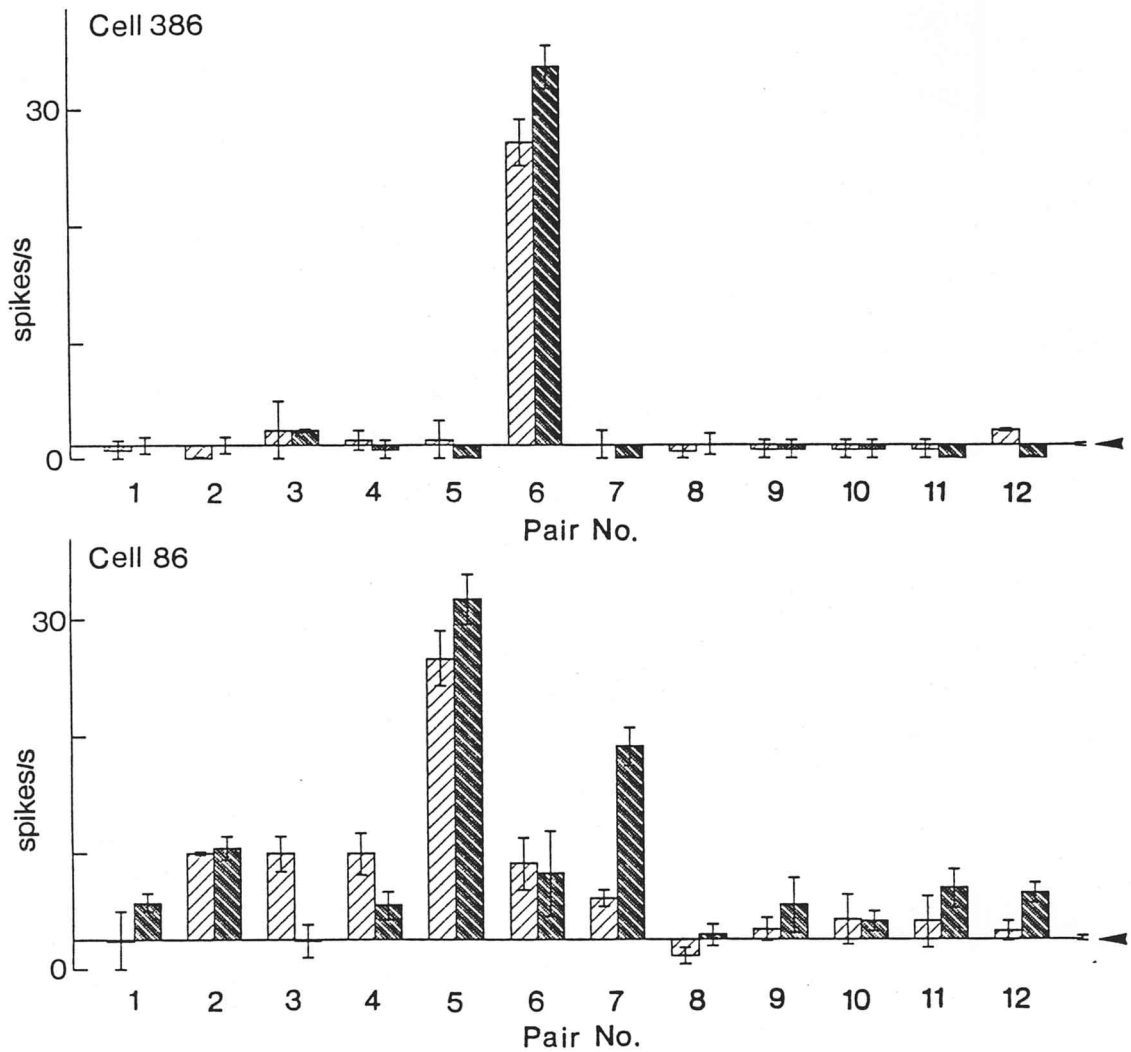

Fig. 6 Stimulus selectivity of pair-coding neurons. The data shown in the upper panel is from the same neuron as in Fig. 5. The lower panel shows a different neuron. These histogram bars are the mean discharge rates for each cue presentation (mean ± s.e.m.) relative to the spontaneous discharge rate (denoted by an arrowhead). Cue stimuli are labelled as 'Pair No.' on the abscissa (light histogram bar in No. 1: cue 1, dark histogram bar in No. 1: cue 1' and so on). Paired associates were among the most effective stimuli for these pair-coding neurons.

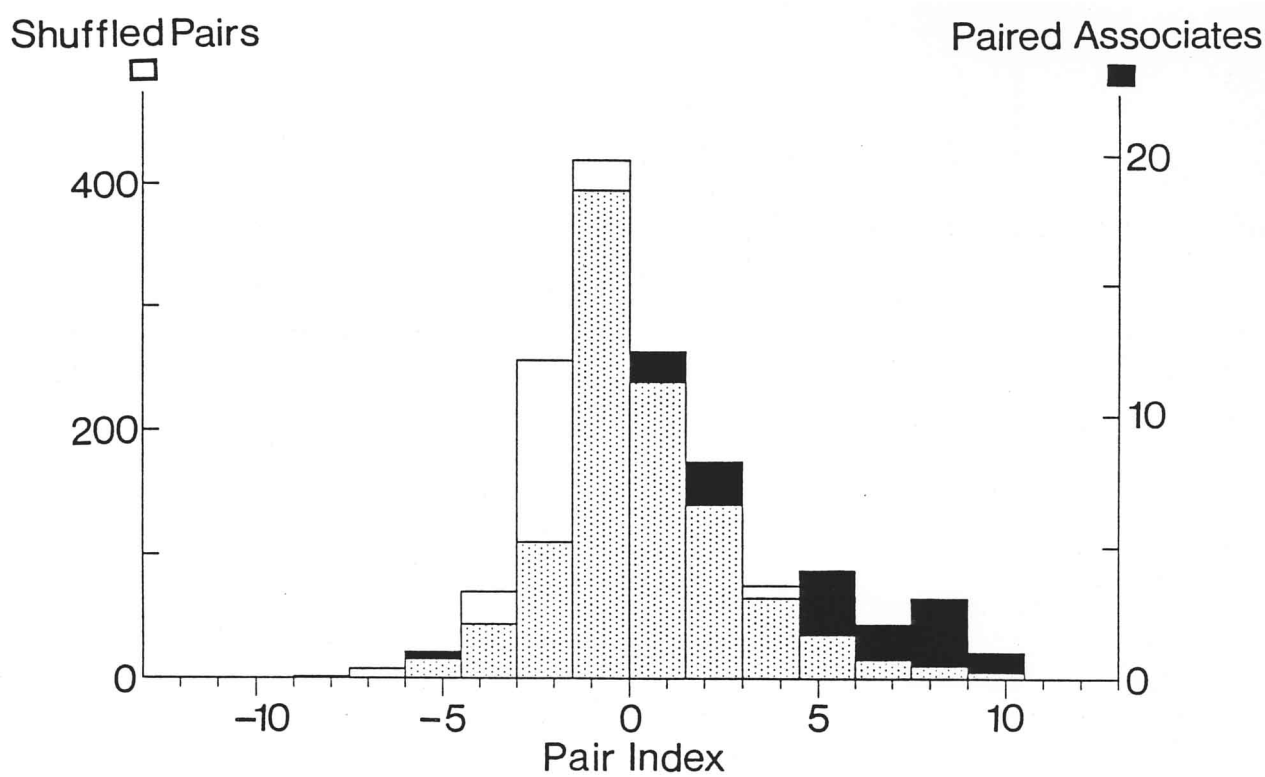

Fig. 7 Frequency distribution of the pair indices in 59 picture-selective neurons in two monkeys. Positive values of pair indices indicate that the neurons exhibited more correlated responses to paired associates (black and dotted bars; n=59) or randomly-selected shuffled pairs (white and dotted bars; n=1298) than other combinations, whereas negative values indicate the converse. These two distributions were adjusted for the size of data and superimposed. The overlapped portions were marked with dots.

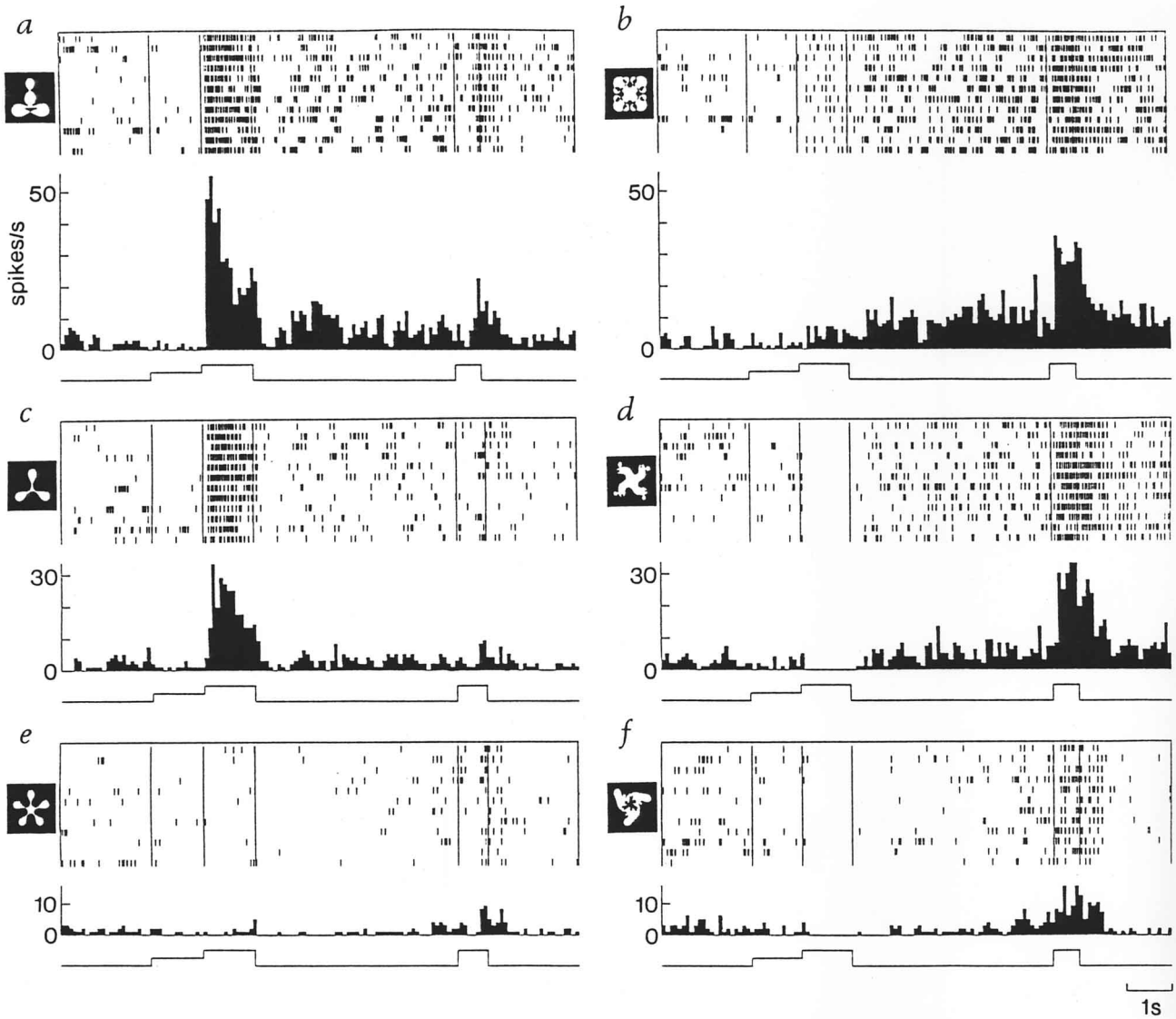

Fig. 8 Responses of a *pair-recall neuron* which exhibited picture-selective activity during the delay period, presumably reflecting retrieval of the paired associate. In each panel, rastergrams and spike-density histograms obtained from a single neuron are shown. Bin width, 80 ms. *a*, Trials for cue 12 which elicited the strongest cue response. *b*, Trials for cue 12'. Note the tonic increasing activity during the delay period, which is much higher than the cue response. *c*, Trials for cue 1 that resulted in the second-strongest cue response. *d*, Trials for cue 1'. Note the sustained delay activity and the inhibitory cue response. *e*, Trials for cue 3 that elicited no response. *f*, Trials for cue 3'. In *f*, the discharges during the choice period are due to stimuli for choice other than 3, such as 1.

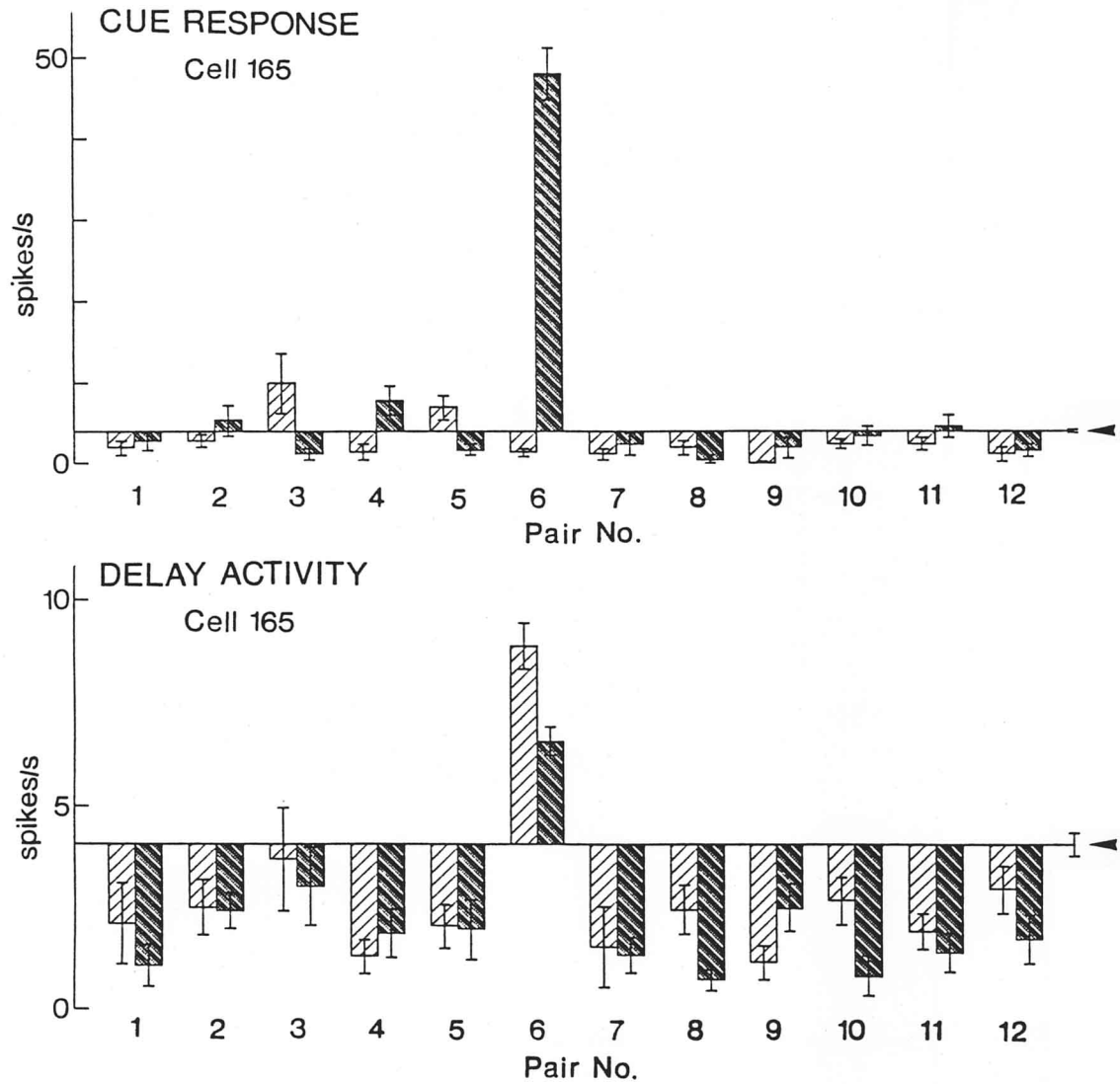

Fig. 9 Stimulus selectivity of a pair-recall neuron. In the upper panel, the histogram bars are the mean discharge rates for each cue presentation (mean ± s.e.m.) relative to the spontaneous discharge rate (denoted by an arrowhead). In the lower panel, the histogram bars represent the delay activities (averaged for 40 - 3960 ms after delay onset) following each cue in the same neuron. Cue stimuli are labelled as 'Pair No.' on the abscissa (light histogram bar in No. 1: cue 1, dark histogram bar in No. 1: cue 1' and so on). The paired associate of a cue-optimal picture elicited the highest picture-selective delay activity.

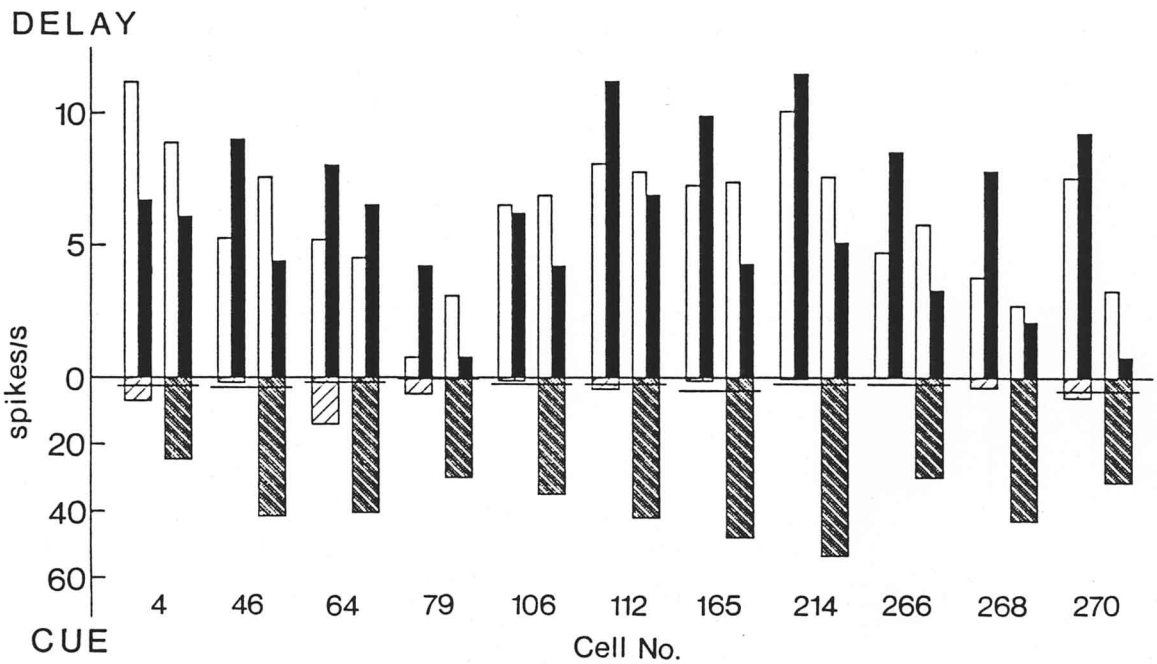

Fig. 10 The relationship between cue response and delay activity in picture-selective neurons. The upper ordinate shows delay activity (mean), whereas the lower ordinate shows cue response (mean) in each cell. The cell numbers are listed on the abscissa. These cells are pair-recall neurons (see text) except one cell (cell 270). For each cell, a dark histogram bar (cue) corresponds to a cue-optimal picture, whereas a light histogram bar (cue) corresponds to the paired associate of this cue-optimal picture. Subsequent delay activity was divided into two intervals; a white bar is for 200 - 1400 ms, and a black bar is for 2760 - 3960 ms after delay onset. An augmentation of delay activity was observed for the associate of a cue-optimal picture, whereas a reduction was seen for the cue-optimal picture itself.

Table 1 *Distribution of cell properties*

Total Units (577)
Cue responsive (141)
Picture selective (91*)
Responsive to two or more pictures (59**)
Responsive to only one picture (32)
Nonselective (13)
Responses too weak to study (37)
Unresponsive (436)

* This number includes pair-recall neurons (10).
** This number includes pair-coding neurons (10).