学位申請論文

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論 文 内 容 の 要 旨

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（論文題目）

Responses of monkey perfrontal neurons during a visual tracking task reinforced by substantia innominata self-stimulation.

（無名質自己刺激により強化された視覚性追跡課題遂行中のサル前頭前野ニューロンの応答）

（論文内容の要旨）

本論文は，サルの前頭前野の関与する行動の発現における脳内自己刺激有効部位（無名質）の役割を明らかにする目的で行った。このため，2頭のサルに無名質の刺激を報酬として，視覚性追跡課題を行なわせ，この遂行に伴って活動変化を示す前頭前野ニューロン活動の性質とそれに対する無名質の単刺激（0.2 ms，10 V）の効果を調べた。サルは，手首の屈曲，伸展により，決められたスタート位置からGOシグナルの提示と同時に示される目標位置までハンドルを動かすことにより報酬を受ける。

運動実行時に活動増加を示すもの（タイプ1），報酬出現に約 400 ms 先行して活動増加を示すもの（タイプ2），GOシグナルの提示直後活動増加を始め，報酬出現まで持続的に発火の続くもの（タイプ3），運動時に活動の抑制されるもの（タイプ4）に分類した。一方，無名質の単刺激に対しては前頭前野ニューロンは，順行性応答及び逆行性応答が見られた。

これらの応答は4つのタイプのいずれにも見出された。タイプ1では逆行性応答，順行性応答を示すニューロンがほぼ同程度見られたのに対し，タイプ2では応ずるニューロンの大部分（15/18）が逆行性応答を示し，逆に，タイプ3では応ずるニューロンの大部分（5/6）が順行性応答を示した。また，運動発現に重要な役割を果す運動野のニューロンは無名質の単刺激によっては全く賦活されなかった。

以上の結果により，大脳皮質前頭前野と無名質は相互の線維連絡（求心性線維と遠心性線維）をもち，タイプ1ニューロンに見られる無名質からの求心性，遠心性入力及びタイプ3ニューロンの無名質からの求心性入力により，前頭前野ニューロンが賦活されること，また，タイプ2のような前頭前野よりの遠心性出力により，無名質が賦活されることが考えられる。視覚性追跡運動を遂行するのに無名質－前頭前野でつくられる神経回路が働いていることが示唆される。

RESPONSES OF MONKEY PREFRONTAL NEURONS DURING A VISUAL TRACKING TASK REINFORCED BY SUBSTANTIA INNOMINATA SELF-STIMULATION

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SUMMARY

To examine the role of the reward stimulation of the substantia innominata (SI) in the generation of the behavior that the prefrontal cortex (PF) concerned, PF neuronal activities related to the visual tracking task and their responses to SI stimulations were analyzed in two Japanese monkeys. Monkeys were rewarded by moving a handle by the wrist movement from the start position to the target position simultaneously with the GO signal. Sixty nine neurons showed task-related activities and were classified into four types. These neurons showed the transient activation before the movement initiation (Type 1, n=31) or before the reward presentation (Type 2, n=26), the tonic activation from the GO signal to the reward (Type 3, n=9), and the inhibitory activity during the movement (Type 4, n=3). The antidromic responses and the orthodromic responses to SI stimulations were observed in every type. In Type 1, the number of antidromically activated neurons (8/31) was similar to that of orthodromically activated ones (5/31), but in Type 2, many of responded neurons (15/18) showed the antidromic response, and in Type 3, many neurons (5/6) showed the orthodromic response.

These results show that different types of PF neurons have different anatomical relations to SI and suggest that these mutual connections are important to activate PF neurons in the generation of the behavior.

INTRODUCTION

In chronic single unit studies, it is shown that the prefrontal cortex is related to the performance of the goal directed behavior[6,7,8,9,11]. In the previous study[7], activities of the dorsolateral prefrontal cortex neurons were recorded when the monkeys performed three kinds of visual tracking tasks by the wrist extension and flexion. Many prefrontal neurons showed bidirectional or unidirectional activity before and during the task movement of the delayed response and these activities were compared for three kinds of tasks. As a result, it was concluded that there were the neuronal activities specific to the movement direction prior to the onset of the voluntary movement and that these activities might be involved in the effective execution of the goal directed movement. In a delayed response[7,8] or a delayed alternation task[9], there were neuronal activations prior to the movement execution and these activities presumably reflected the informations about the ensuring movement. That some of the movement-related prefrontal neurons received the visual input was reported[8,11] and these neurons were named visuokinetic neurons[8]. But it was not clear what inputs the movement-

related neurons received from other neuronal systems and how to use these inputs for the generation of the behavior.

The brain region related to the brain-stimulation reward was thought as one of the neuronal systems which affected these movement-related neurons. The brain-stimulation reward might activate these neurons and facilitate the generation of the behavior, because the reward strength and response rates increased in proportion as the current intensity of stimulations increased[1,3]. Olds[13] hypothesized the existence of reward neurons or drive neurons at the lateral hypothalamus and attempted to explain the generation of the intracranial self-stimulation (ICSS) by activations of these neurons. Though these neuronal activities were thought to facilitate the generation of the behavior, this thought has not been verified experimentally.

The aim of the present study is to examine the effects of the substantia innominata (SI) self-stimulation on the prefrontal cortex neurons when the monkeys perform a two-choice visual tracking task by the wrist extension and flexion, more specifically to examine whether the movement-related neurons are activated by ICSS of SI. On the other hand, in the prefrontal

cortex, there were neurons whose activities changed with the reward presentation[12]. These reward-related neurons might relate to the positive site of ICSS. So, the present study also examine whether the reward-related neurons are activated by ICSS of SI. The reasons why the substantia innominata was chosen as a site of ICSS were that the stimulation of SI produced the positive effect of ICSS[10,14] and that the neurons in SI directly projected to the prefrontal cortex in the monkey[4,5].

METHODS

Two young adult Japanese monkeys (Macaca fuscata) weighing at 4.0 kg (M19) and 6.2 kg (M20) were used. Sitting in primate chairs, they performed a two-choice visual tracking task by the wrist flexion and extension. Instruments were the same as the ones used in a previous study[7]. The monkey rotated the vertical handle by his left hand from the start position to the target position. His right hand was restrained by a rope. His left arm was inserted into two pieces of the plexiglass tube interconnected at the elbow joint. Only the wrist joint was movable. The handle was attached by an arm to a potentiometer (Copal, J45S, 50 kΩ). About 25 cm away from the monkey's face, there was a panel with 9 light emitting diodes (LEDs) arranged in two rows (Fig. 1A). The upper row of LEDs indicated the target positions of the handle movement and the lower row, the position of the handle. The movable zone of the handle (110^{o}) was divided into 8^{o} zones. One LED indicated one zone, whose number corresponded to the number of each LED. The upper LEDs were numbered so as to correspond to the number of the lower LEDs. The start position was at P5, being the center of the movable zone, and the target

Fig. 1

positions were T3 and T7.

The task sequences in the case of a flexion trial, controlled by a minicomputer PDP-11/10, were as follows (Fig. 1B). The monkey rotated the handle. As soon as the handle entered the start position (P5), a green lamp was lit at P5 (Fig. 1B-1). It was lit as long as the monkey held the handle at P5. If it was held there for 1 s, the P5 color changed from green to red. Simultaneously T7 lamp (red) was lit, indicating a GO signal (Fig. 1B-2). The monkey rotated the handle to the target position (P7) and held it there for 0.5 s (Fig. 1B-3). Then, the reward (ICSS or water) was given. In the case of a extension trial, T3 lamp (red) was lit at the GO signal. Then, the monkey rotated the handle to P3 and held it there for 0.5 s. This task was exactly the same as a choice task used in a previous study[7]. A drop of water (0.2 ml/trial) was used as the reward in the early stage of the training, then changed to ICSS. The target position was selected randomly according to a Gellerman series.

Intracranial self-stimulations

After the monkey securely performed this task reinforced by water, 3 or 4 stimulation electrodes were

implanted in the substantia innominata (SI) (A: 22-18, L: 7.0, V: +2.8) contralateral to the moving hand under pentobarbital sodium anesthesia. During the surgery the tip positions of the electrodes were estimated by observing lateral and frontal X-ray photographs of the skull, and later these locations were confirmed histologically. Concentric stainless steel electrodes (i.d.: 0.2 mm, o.d.: 0.6 mm) were used. Parameters of ICSS were 24 pulses of 100 Hz, 0.2 ms duration, square-wave, negative-going pulses generated monopolarly from an electronic stimulater (ME-6012, ME Commercial). To measure a current intensity, the voltage between both ends of a resistor (1 kΩ), being in series with the stimulation electrode, was monitored by an oscilloscope (5103N, Tektronix). An indifferent electrode was a screw implanted in the occipital bone. To infer the effect of ICSS, response rates (the number of the reward presentation) were recorded by a cumulative recorder (Model C-3, Ralph Gerbrands). A response rate of 30 in 5 minutes with no intermission longer than 30 s was set as criteria for the positive ICSS effect[14]. The threshold current intensity of ICSS behavior was measured by gradually increasing the current intensity from 0.5 to 1.5 mA and then gradually decreasing from

1.5 to 0.5 mA. The threshold values of ICSS in the two monkeys were summarized in Table I. In M19, all four stimulation electrodes showed the positive effect. In M20, one electrode (05) did not show the positive effect, even if the current intensity was raised to 2.0 mA.

Table I

Recording and data analysis

After determining the threshold intensities of the electrodes, the monkey was anesthetized with pentobarbital sodium and a stainless steel cylinder (19 mm in diameter) and an L-shaped metal plate to fix the skull to the primate chair were implanted in the skull with dental resin. After a recovery from the surgery, single unit recording were started. During recording sessions, the monkey was seated in the primate chair with his head tightly fixed to the chair frame. A hydrauric microdrive (TO-8, Narishige) was attached to the cylinder. Glass-coated platinum iridium microelectrode (3-5 MΩ) were used for recording. Single unit activities, responding to ICSS or related to the tracking task, were sampled while the monkey was performing the task reinforced by ICSS (1.5 mA). Then, changing the reward from ICSS to water, the responses to water were examined. After these,

the responses to single or double pulse stimulations at SI were recorded. In 27 units, the threshold current intensity of the response was determined.

Unit discharge, lamp signals, reward signal, and hand displacement were recorded on an FM tape recorder (R-260, TEAC). During recording sessions, unit discharges and these signals were monitored by an oscilloscope. During off-line analysis, unit discharges were converted into 1 ms pulses by a window discriminator and stored in a PDP-11/10 computer memory. Collected data were displayed on an oscilloscopic screen as averaged histograms and dots aligned at the moment of the GO signal, the initiation of the movement, and the reward presentation. The responses to SI stimulations were displayed on a screen of the storaged oscilloscope (5103N, Tektronix) and were photographed. After SI stimulations two types of responses were observed : antidromic and orthodromic responses. In the present study, the following criterion was used to determine whether a response was antidromic or not; the responses which repetitively occurred at least with a fixed latency at the threshold and suprathreshold current intensity by 3 ms interval double shocks were classified as the antidromic response[2]. The rests were classified as

the orthodromic response.

Histology

At the end of the study, these two monkeys were also used in 2-deoxyglucose incorporation studies. (Matsunami et al, in preparations). They were sacrificed by an overdose of pentobarbital sodium. The brain was removed and serially sectioned (50 μm). Every third section was stained by the Nissl method. The tip positions of the stimulation electrodes and the recording sites in the prefrontal cortex were determined.

The recording region of monkey M19 was an anterior part of the arcuate area and a posterior part of the periprincipal area, and that of monkey M20 was an anterior part of the ventral arm of the arcuate sulcus and a ventral part of the principal sulcus. The tip positions of the stimulation electrodes are shown in Fig. 2 and summarized in Table I. In M19, two electrodes were in the substantia innominata, one was in the globus pallidus, and the remaining one was at the border region between the substantia innominata and the globus pallidus. In M20, the tip positions of two electrodes were in the substantia innominata and the other tip was in the lateral hypothalamus.

RESULTS

A total of 116 prefrontal (PF) neuronal activities were recorded while monkeys were performing a visual tracking task and their responses to reward stimulations were examined. Among them, 69 neurons changed their activities during the task. If a change of activity was recognized visually in the averaged histograms in relation to the task events, that change was taken as task-related. These task-related neurons were classified into 4 types (Type 1, 2, 3, and 4) depending on the phase of the task during which the change of activity occurred. As for the responses to ICSS at SI, 66 neurons responded antidromically or orthodromically. In the following three sections, the responses of PF neurons to SI stimulations, four types of PF neuron activities during the tracking movement, and the relationships between the four types of activities and the responses to SI stimulations are analyzed.

(1) Responses of prefrontal neurons to SI stimulations

Responses to single or double shocks at SI were examined. Among a total of 116 neurons, 43 neurons (37.1%) showed the antidromic response and 23 (19.8%)

showed the orthodromic response. Examples of the antidromic and orthodromic responses are shown in Fig.3. Fig. 3A is an example of the antidromic response. The response latency is 2.4 ms. This response occurred with the same fixed latency at the threshold stimulations (0.7 mA) by 3 ms interval double shocks as at 1.5 mA stimulations. Antidromic latencies were distributed from 0.9 to 12.5 ms. The mean latency of these was 2.31±1.65 ms (mean ± standerd deviations). Fig. 3B is an example of the orthodromic response. In this example the responses show an early excitation (25-50 ms) followed by inhibition (50-100 ms). In two neurons, the response latencies were 7.5-8.8 ms, but in all other neurons the exact latencies were hard to be determined because they were usually long (20-80 ms), variable, and inconstant.

Fig. 3

(2) Prefrontal neuron activities

Among 69 task-related neurons, the neurons whose activities increased around the initiation of the movement were classified as Type 1 (n=31). These activities gradually increased around the GO signal presentation, peaked during the movement execution, and then gradually decreased after the end of the movement. All these increasing activities were bidirectional

(increase of the discharge rate for both movement directions)[7]. The neurons with a differential activity to the different movement directions (unidirectional type of activity)[7] were not recorded in the present study. Fig. 4 is an example of Type 1 neuron activity. Fig. 4 shows dot displays, averaged displacements, and histograms aligned at the moment of the GO signal presentation (A), at the initiation of the movement (B), and at the reward presentation (C). Short continuous lines in the dot displays indicate the artefacts of ICSS. This neuronal activity, as seen in Fig. 4A, increased after the GO signal for both flexion (F) and extension (E) movements but increased before the movement initiation, peaked during the movement execution, as seen in Fig. 4B. Then it decreased after the handle entered the target position. As seen in Fig. 4C, this neuron was not activated before or after the reward presentation. A weak difference of the activity magnitude depending on the difference of the movement directions was observed in Fig. 4A and 4B. More discharges were observed during the extension movement (E) than during the flexion movement(F) in this example. The differences of the activities between flexion and extension movements were observed in 42.0% of the neurons of this Type. In some

Fig. 4

of Type 1 neurons, the activity increase started before the GO signal, but their discharge rates peaked during the movement, and then gradually decreased.

The neurons whose activities increased 300 to 500 ms prior to the reward presentation were classified as Type 2 (n=26). The activities of Type 2 neurons were not related to the movement execution, because their discharge rates increased after the end of the movement.

Fig. 5 Fig. 5 is an example of Type 2 neuron activity. In this neuron, a gradually increasin activity started about 500 ms prior to the reward presentation (Fig. 5C). This corresponded to the moment when the handle entered the target position. This increased activity was maintained until the reward presentation. It ceased at the time of the reward presentation (not illustrated). The difference in magnitude of increased activity depending on the movement directions was not apparent, as seen in Fig. 5C. As seen in Fig. 5A and 5B, these activities were not activated during the movement. In 18 neurons, the activities were compared between the natural reward (water) and ICSS. In 61.1% of these neurons, more increased activity was observed during the task performance reinforced by ICSS than by the natural reward. In the remaining neurons, the degree of increasing activity

Fig. 6 was not different between ICSS and water. Fig. 6 is an example of these activities. Fig. 6 shows the activity during task performances reinforced by ICSS (07 electrode, A ; 05 electrode, B) and the natural reward (water, C), respectively. These dots and histograms include activities during both extension and flexion movements. Increasing activities prior to the reward presentation were observed during the task performances with ICSS (Fig. 6A and 6B), but were not observed reinforced by water (Fig. 6C). In general, more clearly increasing activity was observed when more effective stimulation electrodes in the behavioral examination were used.

The neuron activities which continued tonically from the GO signal presentation until the reward

Fig. 7 delivery were classified as Type 3 (n=9). Fig. 7 is an example. Their activities started increase at about 60 ms after the GO signal (Fig. 7A), and were maintained tonically until the reward presentation. These increased activities ceased after the reward presentation (Fig. 7C). In Fig. 7C, the neuronal activities during the task with the natural reward are displayed in the upper 10 trials and those during the task reinforced by ICSS are in the lower three trials. Increased activities ceased as soon as the natural reward was presented (see

upper 10 trials in Fig. 7C). These changes were also observed when ICSS was used as the reward. In this neuron, if the reward was not given at the moment of the reward presentation, increased neuronal activity extended after the reward moment.

The neurons whose activities increased after the handle entered the start position and decreased during the movement execution were classified as Type 4 (n=3). This neuronal activity increased after the handle entered the start position and were maintained tonically until the movement initiation and decreased during the movement execution. Type 4 neurons did not relate to the reward presentation. They showed decreased type activity bidirectionally during the movement.

Thus, the activities of the task-related neurons were classified into four types. Type 1 neurons increased their discharge rates transiently before the movement initiation and Type 2 neurons increased transiently before the reward presentation. Type 3, on the other hand, showed tonic activity from the GO signal presentation until the reward delivery. Type 4 neurons showed a decreased activity during the movement execution.

(3) Neuron types and responsiveness to SI stimulation

Table II

Table II shows the relationships between the response types to SI stimulation and the neuronal types during the task. Among 31 Type 1 neurons, 13 neurons (42.0%) responded to SI stimulations antidromically (n=8) or orthodromically (n=5). In 26 Type 2 neurons, 18 (69.2%) responded to SI stimulation. Among them, 15 neurons (83.3%) responded antidromically. These results show that there are significant differences ($<0.05\%$, Chi-square test) between Type 1 and Type 2 as for the percentage of responding neurons to SI stimulation and the ratio of antidromically activated neurons to orthodromically activated neurons. Among 9 Type 3 neurons, 6 responded to SI stimulations and, of these, 5 showed the orthodromic response. These results were different from those of Type 2 ($<0.02\%$, Chi-square test). Among three Type 4 neurons, 2 showed the antidromic response. On the other hand, of 69 task-related PF neurons, 30 (43.5%) did not respond to SI stimulations. Sixty percent of these neurons belonged to Type 1.

To sum up these results, both antidromic and orthodromic responses were observed in every type of PF neurons. But more Type 2 and Type 3 neurons responded

to SI stimulations than Type 1 neurons did. In Type 2 many neurons showed the antidromic response and, in Type 3, many showed the orthodromic response. But 58 % of Type 1 neurons did not respond antidromically and orthodromically.

DISCUSSION

The present study showed that task-related prefrontal neurons were activated by ICSS of SI. Task-related prefrontal neurons were classified into four types. They showed the transient activation before the movement initiation (Type 1) or before the reward presentation (Type 2), the tonic activation until the reward presentation (Type 3), and the inhibitory activity during the movement (Type 4). The antidromic and orthodromic responses to SI stimulations were observed in every type of neurons. But there were significant differences among these four types as for the percentage of responding neurons and the ratio of antidromically activated neurons to orthodromically activated neurons.

It was reported that in the prefrontal cortex, there were neurons whose activities changed with the reward presentation[12]. These reward-related neurons were thought to have a relation to the positive site of ICSS by receiving the informations of the reward presentation or sending the anticipatory informations of the reward presentation. In the present study, it was found that many neurons whose activities increased 300 to 500 ms prior to the reward presentation and ceased

at the reward presentation (Type 2 neurons) had fiber connections with the reward region. These Type 2 activities were considered similar patterns to Sakai's gradually increasing activity during waiting period before the GO signal in a visual-guided lever press task[16]. So, these activities might be related to the expectancy of the reward in the present study. Most Type 2 neurons responded antidromically to SI stimulations. Accordingly, these Type 2 neurons may send the anticipatory informations of the reward to the positive site of ICSS. Routtenberg and Santos-Anderson[15] suggested that the efferent fibers from the prefrontal cortex to other ICSS positive sites were important in the generation of ICSS behavior and that ICSS from the medial forebrain bundle in the rat might have been derived, in part, from stimulations of the axons of the prefrontal cortex neurons. From the results that many Type 2 neurons showed the antidromic response and the activity related to the reward expectancy, these neurons may be one of the important members of this efferent fiber system from the prefrontal cortex and may play an important role of the generation of the ICSS behavior.

As to the relationships between ICSS positive sites and the movement-related neurons, it was thought that

the rewarding brain stimulations activated these movement-related neurons and facilitated the generation of the behavior, because the reward strength and response rates increased in proportion as the current intensity of ICSS increased[1,3]. In the present study, Type 1 neurons showed similar activity to the ones in the choice task of the previous study[7] and thought to belong to the movement-related neurons. About 40% of these Type 1 neurons responded to SI stimulations. Though fewer Type 1 neurons responded to SI stimulations than Type 2 and Type 3 neurons did, some Type 1 neurons (5/31) responded to SI stimulations orthodromically. This result indicates the posibility that ICSS facilitates the generation of the behavior through orthodromically responded movement-related neurons.

Type 3 neurons showed similar activity to Type 2 neurons as regards that the increasing activity ceased at the reward presentation. But the functions of Type 3 were considered to be different from those of Type 2. Though Type 2 showed transient activation before the reward presentation, Type 3 showed tonic activity from the GO signal to the reward presentation and seemed to relate not only to the reward presentation but also to the GO signal presentation. The functions of Type 3

neurons are not obvious, but these neuronal activities might reflect a certain internal state such as an anticipation of the reward. It is very interesting that many Type 3 neurons, differing from Type 1 and 2, show the orthodromic response with very long latency. Both in Type 2 and Type 3, though the percentage of responded neurons was similar to each other, the ratio of antidromically activated neurons to orthodromically activated neurons was different, namely many neurons showed the antidromic response in Type 2 but many showed the orthodromic response in Type 3.

Thus, these results show that functionally different neurons in the prefrontal cortex during a visual tracking task have a different fiber connection to ICSS positive site. The results that ICSS positive site are connected not only to the reward-related neurons but also to the movement-related neurons in the prefrontal cortex suggest that these connections may be important in the generation of the ICSS behavior.

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Table I Tip position of each stimulation electrode and threshold current intensity of ICSS positive effect.

M. 19

	Tip position	ICSS effect	Threshold
01	GP, SI	positive	0.8 mA
03	SI	positive	1.0 mA
05	GP	positive	1.4 mA
07	SI	positive	0.7 mA

M 20

	Tip position	ICSS effect	Threshold
01	SI	positive	0.9 mA
03	SI	positive	1.1 mA
05	HL	negative	------

* Abbreviations are the same as Fig. 2. "GP, SI" indicates the border region between GP and SI.

Table II Relationships between the responses to SI stimulations and the neuronal activity types during the task performance.

Type	Antidromic	Orthodromic	No-response	Total
1	8	5	18	31
2	15	3	8	26
3	1	5	3	9
4	2	0	1	3
Total	26	13	30	69

LEGENDS FOR FIGURES

Fig. 1 Schematic illustrations of experimental set-ups and temporal sequence of a visual tracking task. A : a panel with 9 LEDs arranged in two rows and a handle coupled to the axis of a potentiometer. Upper LEDs (T3 and T7) are the target lamps. Lower LEDs (P2 to P8) are the position lamps of the handle. P5 is also used as the start position lamp. The movable zone of the handle was divided into 8^{o} zones. One LED indicated one zone whose number corresponded to the number of each LED. B : schematic illustrations of the temporal sequences of the visual tracking task. Only 5 LEDs corresponded to T3, T7, P3, P5, and P7 are illustrated. Displacement (Disp.) of the handle was measured by the potentiometer. The zone between broken lines is the zone of the start zone or the target position. The filled square on the ICSS trace indicates the timing of ICSS. Filled circle in the panel indicate that the red lamp is lit and the hatched circle indicates that the green lamp is lit. Further details about the temporal sequences of the task are in the text.

Fig. 2 Tip positions of ICSS electrodes implanted

in M19 monkey (filled circles) and M20 monkey (open circles). In M19, four electrodes were implanted. In M20, three were implanted. Abbreviations : Amy, amygdala; CA, anterior commissure; Cd, caudate; GP, globus pallidus; HL, lateral hypothalamus; Put, putamen; S, septum; SI, substantia innominata; TO, optic tract.

Fig. 3 Prefrontal neuron responses to SI stimulations. A : antidromic response. These show 10 superimposed traces at 100 Hz double shocks (1.5 mA). The latency is 2.4 ms. B : orthodromic response. These show 15 superimposed traces at 100 Hz double shocks (1.5 mA). These responses have a early excitation (25-50 ms) and a following suppression (50-100 ms). Calibrations : A, 1 ms, 200 μV; B, 20 ms, 200 μV.

Fig. 4 An example of Type 1 neuron activity. A : dot displays, averaged displacements, and histograms aligned at the moment of the GO signal presentation. B : those aligned at the moment of the initiation of the movement. C : those aligned at the moment of the reward presentation. The figures in the left row indicate the activities during the flexion movement (F) and those in the right row indicate the activities

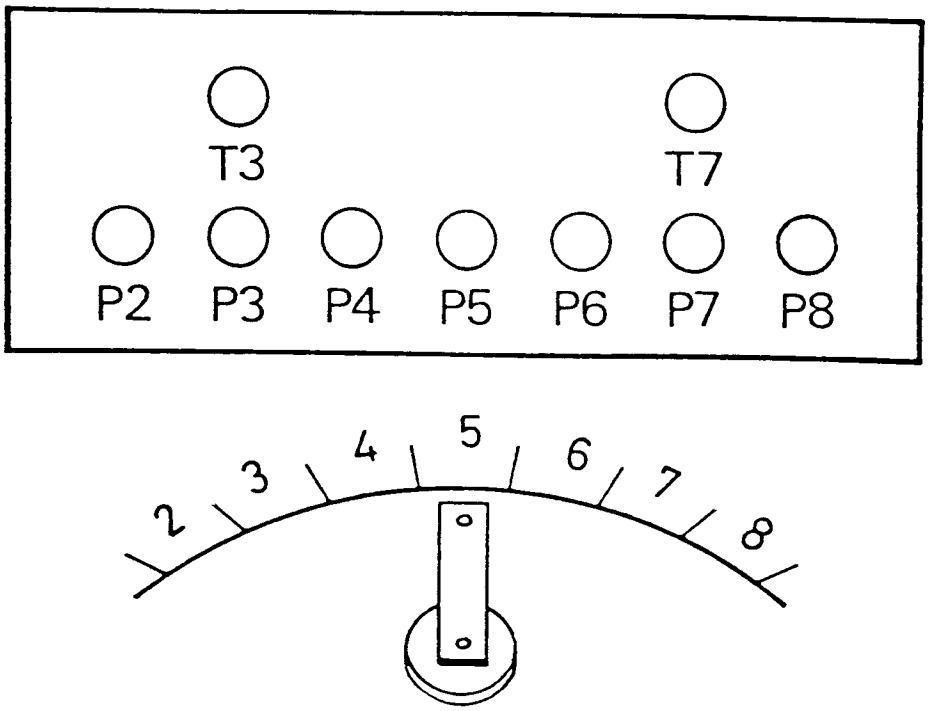
during the extension movement (E). Short continuous lines in the dot displays indicate the artefacts of ICSS and these artefacts are included in the histograms.

Fig. 5 Type 2 neuron activity. The arrangements of figures are the same as Fig. 4. Short continuous lines in the dot displays indicate the artefacts of ICSS.

Fig. 6 Type 2 neuron activities reinforced by ICSS and water. Rewards are ICSS through O7 electrode (A), ICSS through O5 electrode (B), and a drop of water (C). All figures show neuronal activities during 10 trials including both directions of the movement.

Fig. 7 Type 3 neuron activity. The arrangements of figures are the same as Fig. 4. In all figures, upper 10 trials indicate the neuronal activities during the task reinforced by the natural reward and lower three trials indicate the activities during the task reinforced by ICSS. In C, artefacts of ICSS are displayed in dots and these histograms contain these artefacts.

A


T3
T7
P2
P3
P4
P5
P6
P7
P8
2
3
4
5
6
7
8

B

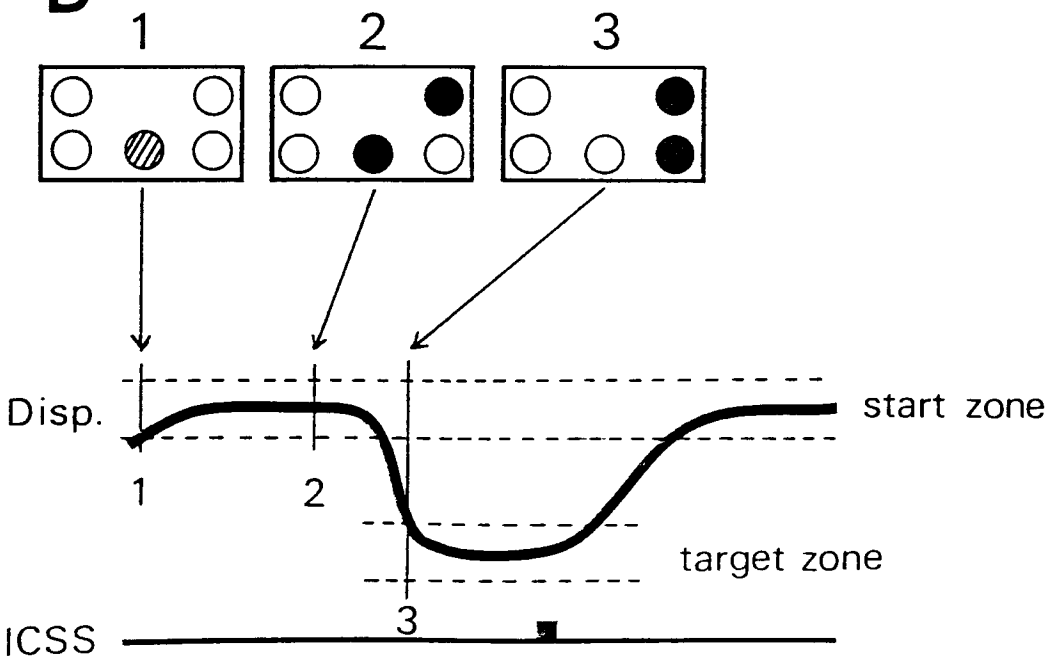

1
2
3
Disp.
start zone
target zone
ICSS

Fig 1

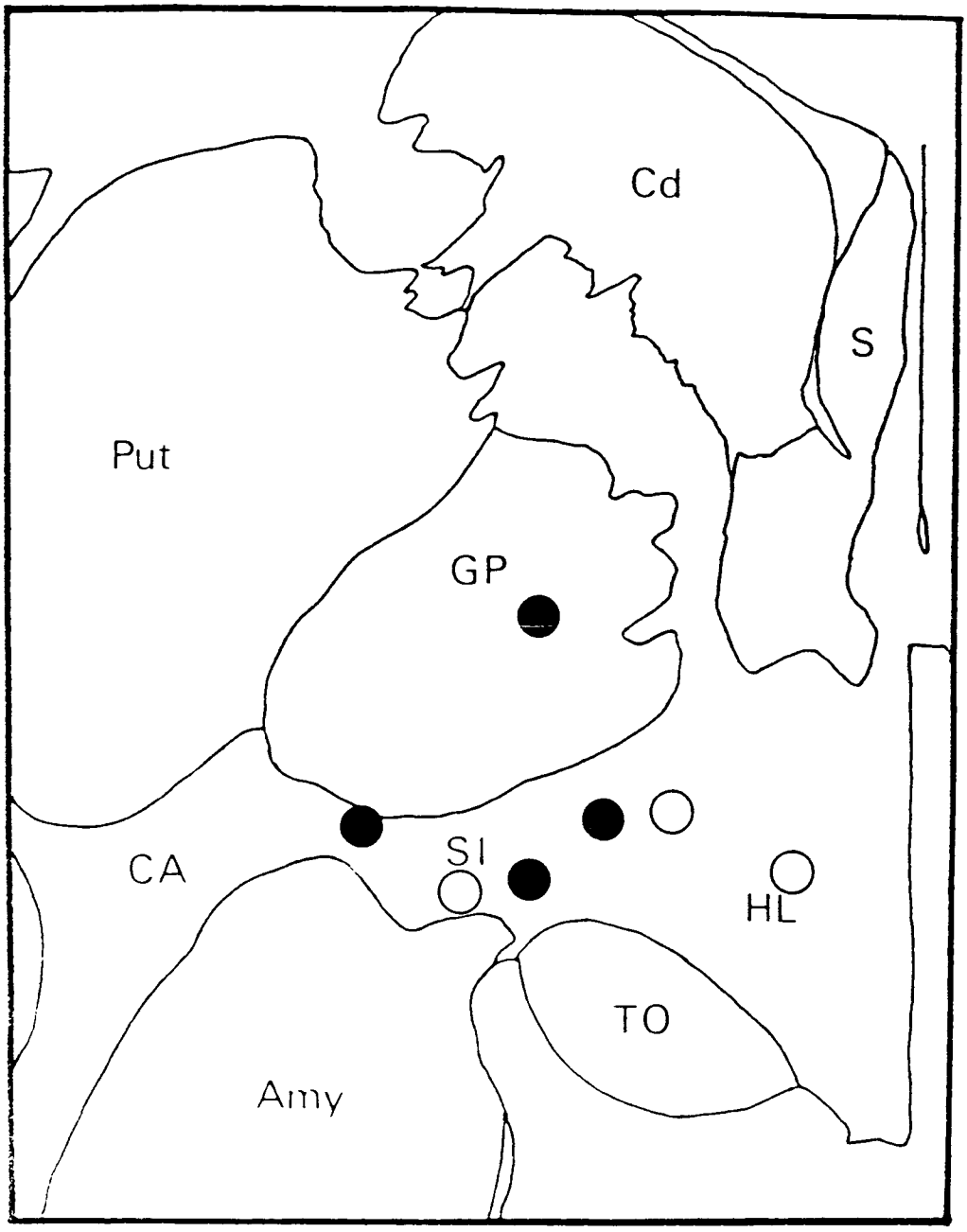


Fig 2

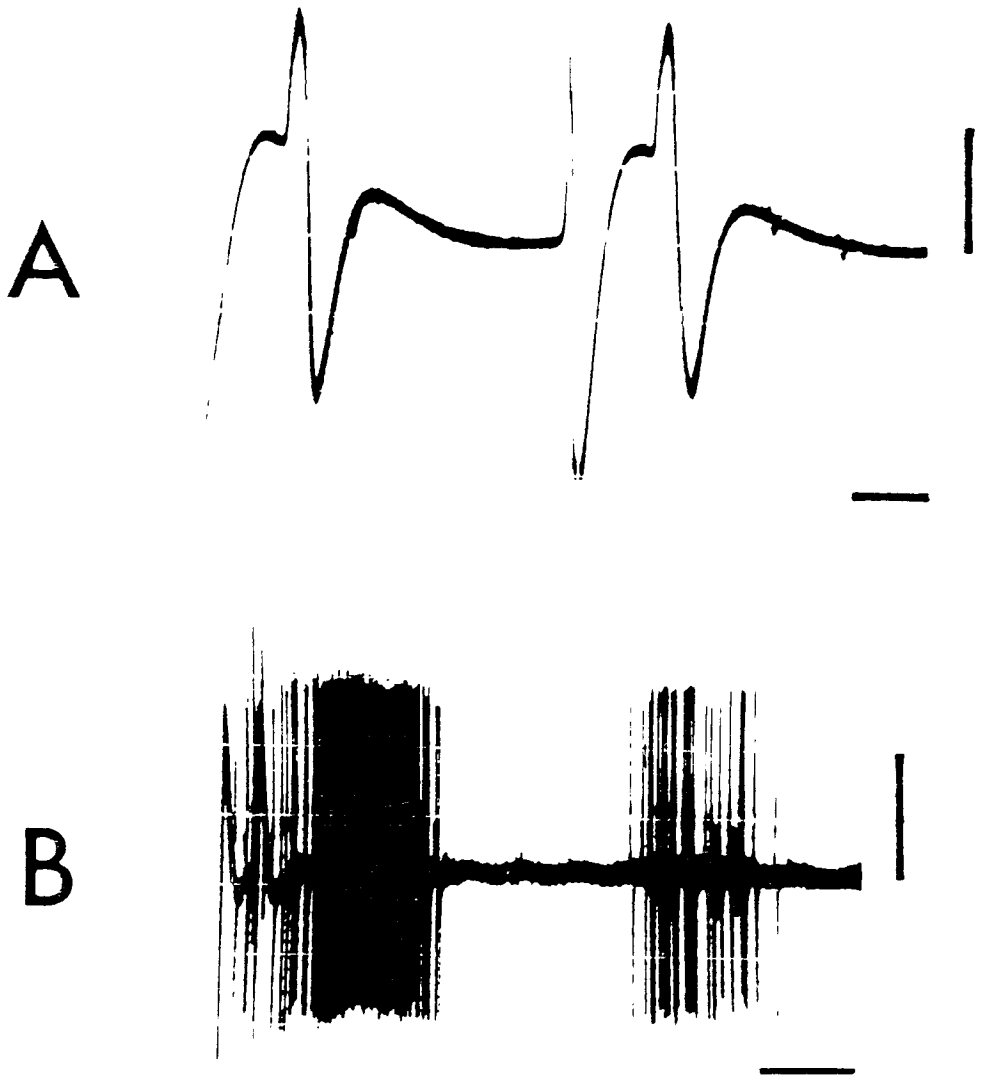
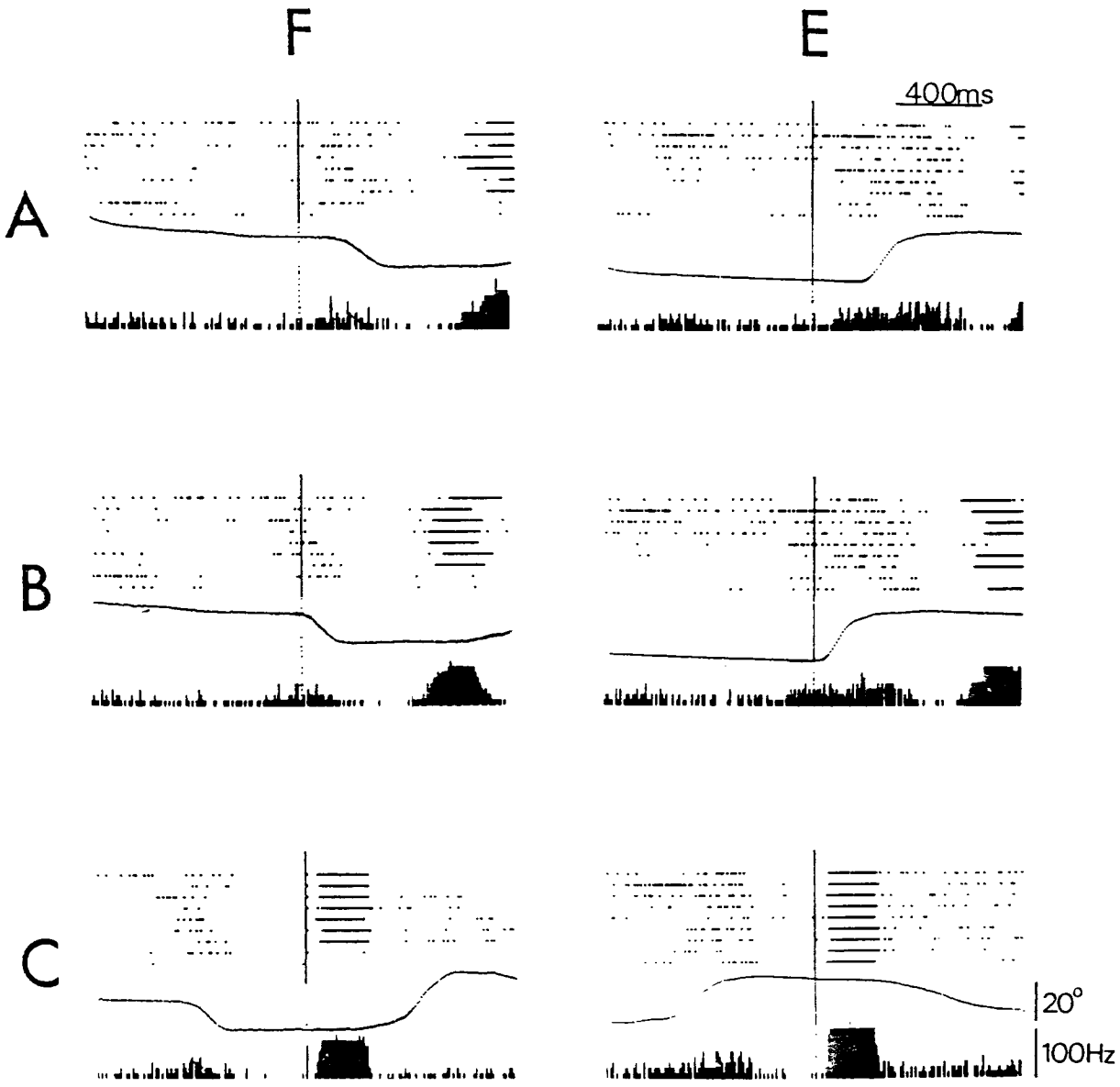
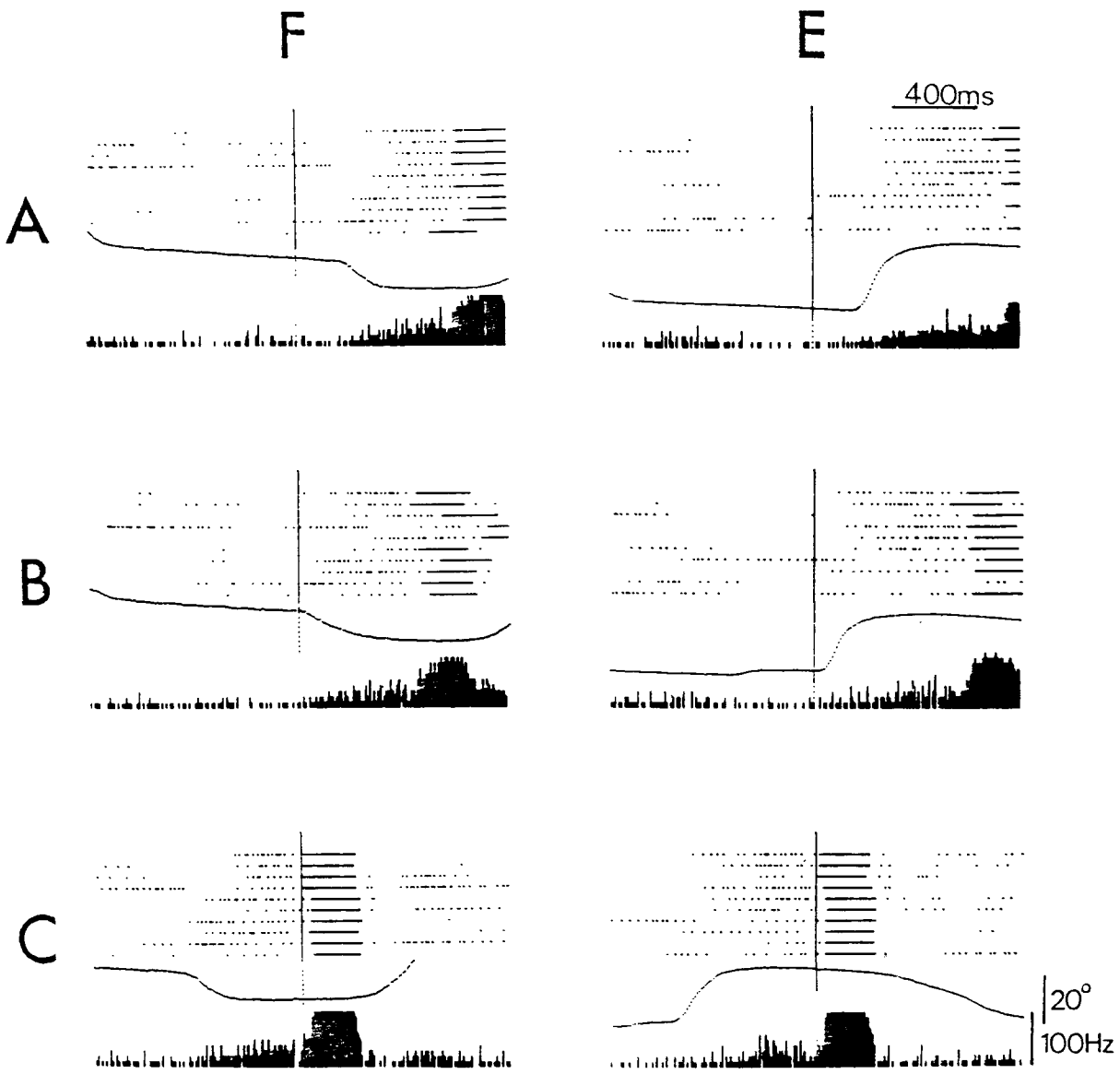


Fig. 3



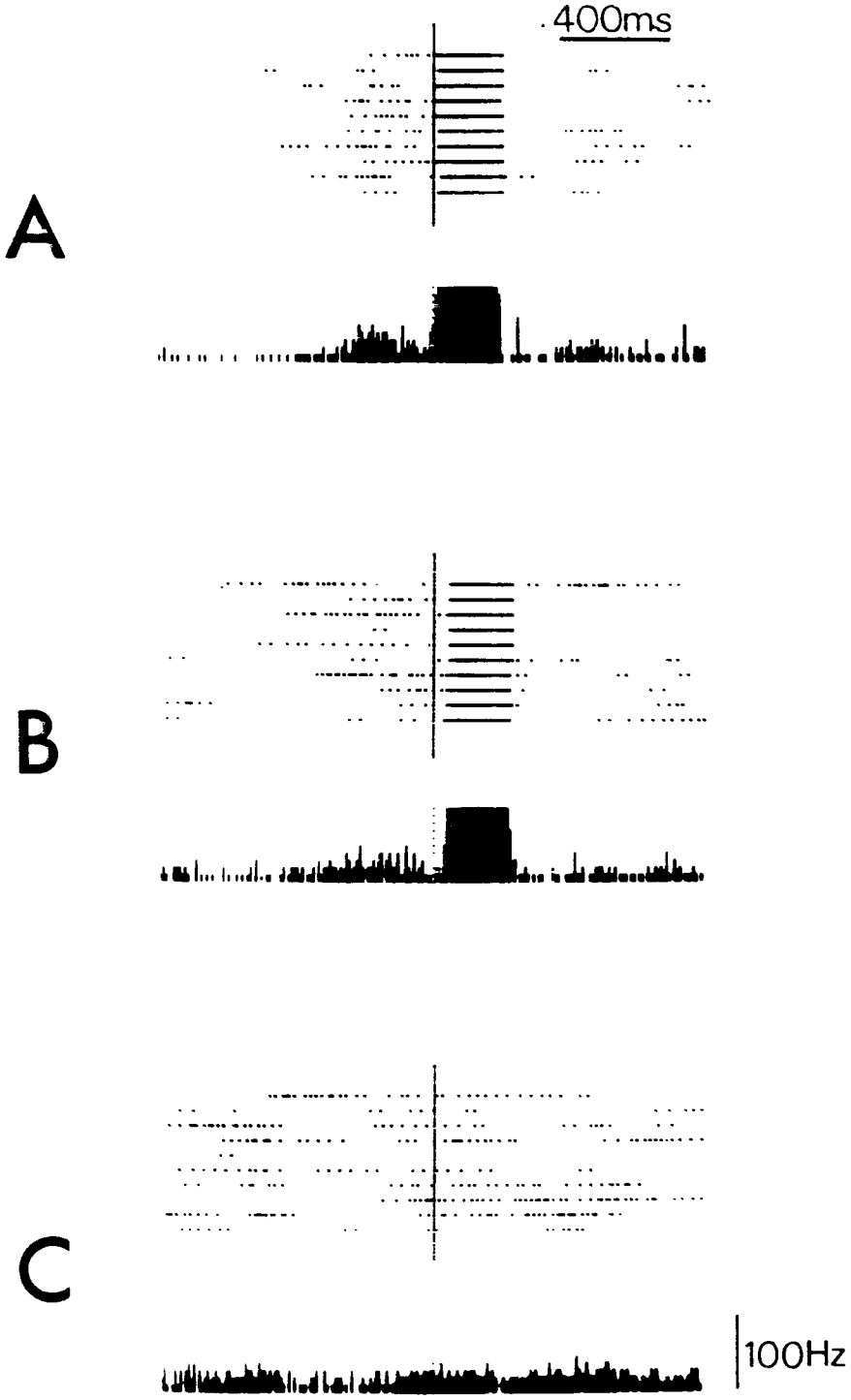
19R(PF):186-2

Fig. 4



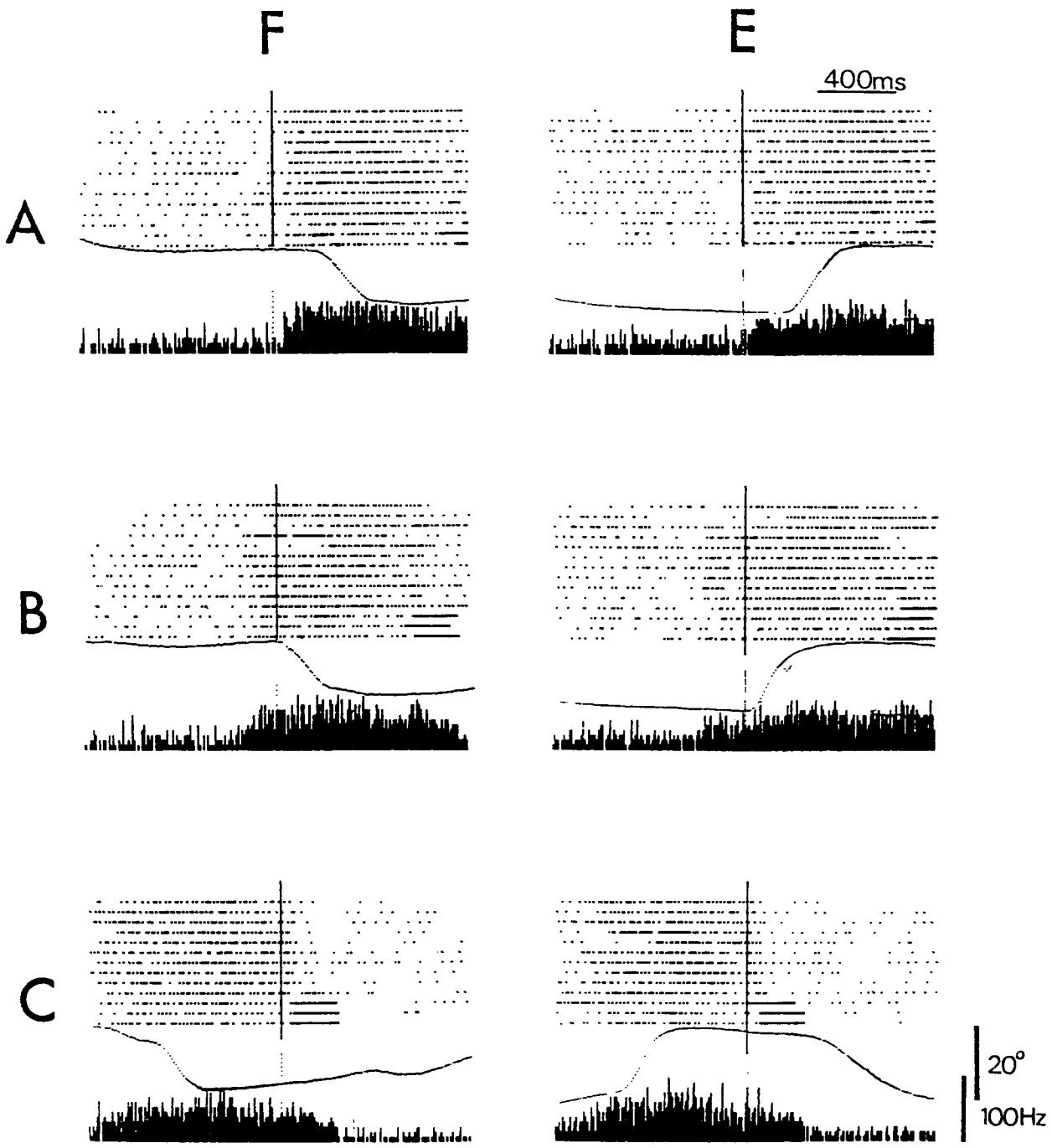
19R(PF):256-1

Fig. 5



19R(PF), 256-1

Fig. 6



19R(PF):178-2

Fig. 7