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Spatial, movement- and reward-sensitive discharge by medial ventral striatum neurons of rats

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Abstract

Previous behavioral and acute electrophysiological data have lead researchers to speculate that the nucleus accumbens integrates limbic, reward and motor information [5,12,22,31]. The present study examined the behavioral correlates to single unit activity of the nucleus accumbens and surrounding ventral striatum as a means of evaluating the integrative functioning of this region in an awake animal. Medial ventral striatum (mVS) activity was recorded as rats completed multiple trials on an eight arm radial maze. Neuronal activity was found to correlate with spatial, reward- and movement-related behavioral conditions. While the majority of cells demonstrated correlates of a single type (i.e. either spatial *or* reward correlates), 6 cells encoded multiple correlates of different types (i.e. spatial *and* reward correlates). The data suggests that this integrative process can be active both at the level of the individual neuron, and at the structural level. These results are consistent with the hypothesis that the mVS integrates spatial and reward-related information, which in turn influences voluntary motor output structures in order to achieve accurate navigational behavior.

Key words: Ventral striatum; Hippocampus; Amygdala; Spatial memory; Single unit activity

1. Introduction

It is generally agreed that the hippocampus is an essential structure for normal spatial learning. Many hippocampal neurons preferentially fire when an animal is at a particular spatial location in its environment [25,34,37,38,40,41]. Also, hippocampal lesions produce selective spatial learning deficits [33,42,52]. Therefore the hippocampus may contribute knowledge concerning the spatial context of a situation [39]. The mechanism by which newly formed associations in the hippocampus guide subsequent behavioral output, however, remains to be determined. One possibility is that the hippocampus affects motor output via the medial ventral striatum, in particular the nucleus accumbens. Indeed, based primarily on neuroanatomical data and electrophysiological results from anesthetized animals, many have postulated that the accumbens somehow integrates limbic information with motor systems driven by the ventral pallidum [5,12,22,31]. The accumbens is also known to be involved in reinforcement aspects of behavior [8,19,27,61]. Therefore, the present experiment evaluated the hypothesis that the medial ventral striatum serves to integrate spatial- and reward-related information which in turn can affect the voluntary motor output system of the ventral pallidum to achieve accurate navigational behavior.

Although most of the behavioral literature concerning the ventral striatal area involves the nucleus accumbens (ACC), more recent neuroanatomical evidence suggests that this structure might not be as discretely defined as was once thought. Neurons surrounding the ACC, primarily in the olfactory tubercle, demonstrate similar morphologic and striated characteristics that define the ACC [15]. Therefore Heimer and colleagues proposed that these two structures be collectively referred to as the ventral striatum (VS). Subsequent electrophysiological studies have adopted this terminology, and shown that behavioral correlates to neuronal firing are evenly distributed throughout the medial ventral striatum (mVS) [49].

The mVS is known to play a role in some types of spatial information processing. Ibotenic acid lesions of

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the nucleus ACC cause impairments on a spatial discrimination and reversal learning task, as well as on spatial versions of the Morris water maze task [1]. Additional evidence suggests that, similar to hippocampus, the ACC is selectively involved in the acquisition of spatial information. For example, c-*fos* expression in ACC is associated with the acquisition of conditioned place preferences, and not subsequent activation of the learned response [6].

Given the role of hippocampus in spatial learning, afferent projections from the subiculum or entorhinal cortex of the hippocampus [3,13,20,50,53,56,57,62] might provide spatial information to the mVS. Ventral tegmental area (VTA) derived dopamine activity in the mVS [45,47] appears to modulate incoming hippocampal information since iontophoretic application of dopamine in the ACC attenuates subicular stimulation-induced activation of ACC neurons [63]. The modulatory effects of dopamine appear to depend on the frequency of fornix (which carry subicular afferents to ACC) stimulation: dopamine enhanced ACC responses to high frequency inputs, while inhibition of ACC responses was observed following low frequency stimulation [44]. It was postulated that dopaminergic influences on ACC excitability is determined by the "relative weight of the excitatory and inhibitory components" that define specific environmental events. Similar to observations of hippocampal-ACC system function, dopamine appears to modulate information from the amygdala to the ACC. Dopamine application or VTA stimulation attenuated the excitatory response of ACC neurons to amygdala stimulation [65]. Numerous neuroanatomical studies show that there is significant overlap of terminals from the basolateral nucleus of the amygdala (BLA) and hippocampus within the medial portion of the ACC [13,20,21,23]. Therefore, the ACC is strategically located to integrate amygdaloid and hippocampal information.

While the hippocampus may provide spatial information to the ACC, the amygdala may supply the ACC with information concerning stimulus–reward associations. Cador and colleagues [7] demonstrated that lesions of the BLA reduced responding to a conditioned reinforcer, and that appropriate responding according to these stimulus–reward associations was dependent upon the presence of dopamine in the ventral striatum. A role for the amygdala in stimulus–reward associations was also suggested by Rolls [48] who demonstrated that amygdala neurons selectively respond to stimuli previously related to reward. Control studies illustrated that these cells do not respond to the stimuli or reward per se, but only to their paired association.

In addition to providing a center for limbic integration, the ACC may provide a mechanism by which such information can guide subsequent navigational behavior. The primary output for the ACC is the ventral pallidum (VP) [14,64,66], which is known to be involved with the activation of voluntary movements [15,54]. Jones and Mogenson [18] showed that dopaminergic microinjections into the ACC cause increases in ambulatory locomotion, an effect which is attenuated by the addition of GABA in the ventral posterior globus pallidus. Further neurochemical data from these investigators [17] showed that the ACC projection neurons liberated GABA in the globus pallidus. Thus the GABAergic projections from the ACC were implicated in a mechanism for the initiation of locomotion.

Our working hypothesis regarding the role of the nucleus accumbens in spatial navigation is that this structure associates spatial contextual information (from the HPC) with reward information (from the BLA), to facilitate initiation of appropriate behavioral output via the ventral pallidal system. The first step in evaluating this hypothesis was to examine the nature of information coded by neurons within the mVS. In particular, mVS single unit activity was recorded while rats performed a spatial maze task. Such activity was correlated with spatial, reward and movement aspects of behavior.

2. Materials and methods

2.1. Subjects and apparatus

Twelve male Fischer-344 rats (10–13-month-old retired breeders) were individually housed in a controlled environment (70°C; 12 h light/dark cycle) and maintained at 80% ad libitum body weights during behavioral testing. An automated 8 arm radial maze [28] was constructed of 8 black Plexiglas runways (58.0×5.5 cm) radiating from a center platform (19.5 cm diameter) that was supported 79.0 cm off the ground. The maze was located in a 3×3.7 m room and was surrounded by various pieces of furniture that could serve as visual cues.

2.2. Behavioral training

Animals were trained to perform a spatial memory task according to a partial forced choice procedure [30]. Alternate arms were consistently baited with small and large rewards (1 and 3 drops chocolate milk, respectively). Trials consisted of the random, sequential presentation of 4 different arms followed immediately by the presentation of all 8 arms. The memory portion of the task entailed entering only the arms not previously entered that trial. Thus, repeat entries were considered errors. A trial ended when the rat selected all 8 arms. Once the animal was able to perform 8 such trials within 1 h (with 2 min inter-trial intervals) for 7 consecutive days, recording electrodes were surgically implanted into the striatum.

2.3. Electrode construction

The stereotrode and microdrive design were adopted from McNaughton and colleagues [24,26]. Two lacquer coated tungsten wires were twisted together (25 μm tip diameter) and coated with Epoxylite to serve as stereotrodes. Each stereotrode was then threaded through 30-gauge cannulae leaving at least 2 mm extending from the bottom.

Two cannulae were mounted 1 mm apart on each microdrive. One microdrive was implanted over each hemisphere. Prior to surgery the stereotrode tips were cut at a 45° angle and gold plated to reduce their impedance (70–200 kΩ; tested at 1 kHz). Reference electrodes were constructed from 114 μm teflon-coated stainless steel wire. A ground lead (250 μm insulated stainless steel wire) was soldered to a jeweler's screw. Amphenol pins were crimped onto the stripped ends of all recording electrodes and ground wires.

2.4. Surgical procedure

Following 24 h of food and water deprivation, maze trained subjects were anesthetized with sodium pentobarbital (40 mg/kg). Animals were secured in a rat stereotaxic apparatus (David Kopf), and electrodes were placed relative to bregma [43]. Burr holes were drilled through the skull and two stereotrodes per hemisphere were implanted above the mVS (AP: +1.0–3.2 mm; L: ±0.8–1.8 mm; D-V: −4.5–5.0 mm). A single reference electrode was placed in corpus callosum, and a ground screw was anchored to the skull. Amphenol pins were inserted into a plastic 9 pin connector [32] that could later be connected to the recording equipment. Additionally, several jewelers screws were secured into the skull. These provided anchors for the dental acrylic, which was allowed to harden around the base of the microdrive posts, onto the 9 pin holder, and over the exposed skull. Animals were allowed 7–10 days recovery at which time they began post-surgical maze training to the same criterion as described above.

2.5. Cell recording

Animals were connected to the recording equipment via a 1× pre-amplification headstage consisting of 5 high input impedance FETs and a light emitting diode. Incoming signals were amplified 3–10,000 times, then filtered at 600 Hz (high pass) and 6 kHz (low pass). The stereotrodes were lowered 20–200 μm per day until spontaneous unit activity was encountered. Electrophysiological and behavioral data were collected and analyzed on a BrainWave Neuroscience Workstation. Single units were isolated by comparing spike characteristics (e.g. spike amplitude, duration, latency to voltage maxima and minima) recorded from the X and Y electrodes. Cells were initially classified on line as either tonic, low frequency phasic, or high frequency phasic firing cells: tonic firing cells discharged constantly, low frequency phasic cells demonstrated episodic bursting with interspike intervals greater than 3 ms, and high frequency phasic cells fired episodically with interspike intervals that did not exceed 3 ms.

2.6. Behavioral monitoring

The animal's position on the maze was recorded with the aid of an automatic tracking system (Dragon Tracker) which monitored the animal's position on the maze via the light emitting diode mounted on the headstage (sampling frequency 20 Hz, resolution 1.5–2.0 cm) [28].

2.7. Histology

Once the electrodes had been lowered through the depth of the mVS (−7.5–8.0 mm) in both hemispheres, rats were perfused with 0.9% saline then 10% formalin. Electrodes were retracted, then the brains were removed and allowed to sink in 30% sucrose formalin solution. Forty μm thick frozen sections were sliced with a cryostat, then stained with cresyl violet. Recording sites were histologically verified by comparing depth measurements at the time of recording with the electrode track reconstruction from serial sections of each hemisphere.

2.8. Data analysis

Various analysis routines (courtesy of B.L. McNaughton and C.A. Barnes, or available from BrainWave) were utilized to analyze behavioral and unit data. The mean spike amplitude, duration and firing rate over the entire recording session were calculated. Also, graphic illustration of the spatial distribution of firing was shown by spot rate diagrams (Fig. 4). In these diagrams, cell firing is presented relative to position. The size of the circles is linearly related to the firing rate of the cell. Dots represent positions occupied by the rat. The direction of diode movement (presumably corresponding with the direction faced by the animal) during cell discharge is shown by a vector projecting from the center of the firing rate circle. This type of visual representation was useful for identifying firing preferences for a particular spatial location (place field), and also for noting directional firing on any or all arms.

To quantify location-related firing, the mean firing rates were calculated across trials as the rat moved inward and outward on all 8 maze arms (16 values total) [25]. The highest rate was divided by the mean of the other 15 rates to arrive at a place specificity score. This score may underestimate actual place specificity because place fields do not always cover the entire length of the maze arms. Also, it should be noted that this calculation considers each direction of movement on maze arms independently. Thus bidirectional place fields are assigned a lower place specificity score than unidirectional fields. Cells with place specificity scores greater than 2.0 were preliminarily classified as having place fields. The reliability of cell firing within these fields was then examined, and used to help confirm spatial correlates (cells which fired less than 50% of the time in the field were excluded). Additionally, spot rate diagrams for the remaining candidate cells were inspected. Only those cells which surpassed the threshold firing rate (30% of the maximum firing rate) more than 3 times anywhere on the maze, were finally classified as spatially correlated. This visual inspection eliminated low rate cells which fired 1–3 super threshold burst(s) and consequently yielded misleadingly high specificity and reliability scores. Place specificity scores were used for classification purposes, and for comparison with previously recorded hippocampal place cells.

A few mVS cells had spot rate diagrams which showed firing rates on 3 or 4 non-adjacent arms that were twice as high as on the remaining arms. For these cells, of the 16 location by direction rates described above, those associated with elevated firing (by more than 100%) were averaged and then divided by the mean of the remaining 12–13 rates.

To evaluate firing rates relative to specific behavioral events, behavior flags were inserted into the position datastream off-line. These flags were used to indicate times at which the animal began outward locomotion on a maze arm (outbound condition), reached the arm end reward site (reward encounter), began to turn around at the arm end (turn), and began inward locomotion on the arm (inbound). Peri-event time histograms (PETHs) were created to indicate the mean firing rate 2.5 s before and after each behavior flag (Fig. 5). For statistical reasons, these graphs were used only for neurons with mean firing rates of at least 1.0 Hz. Mean firing rates during each of the scored conditions (outbound, reward encounter, turns, inbound) as well as during still (non-movement following reward retrieval, just prior to turning) and center crossing (just prior to outbound movement) conditions were extracted from the PETHs. Firing rates during each behavioral condition was divided by the mean still rate in order to normalized the data for comparison between cells. Cells with behavioral condition/still ratios of 2.0 or

Table 1

(A)

	n	Mean firing rate (Hz)	Amplitude (μV)	Duration (μs)	Specificity score
Tonic	25	12.5 (1.62)	107 (6.2)	272 (10.9)	1.3 (0.03)
Low freq. phasic	74	1.5 (0.16)	143 (6.2)	305 (5.6)	2.4 (0.18)
High freq. phasic	4	6.5 (2.83)	197 (41.6)	222 (22.7)	1.8 (0.22)
Total	103	4.4 (0.63)	136 (5.2)	294 (5.3)	2.1 (0.14)

(B)

Group	n	Mean firing rate (Hz)	Amplitude (μV)	Duration (μs)	Specificity score
Spatial	19	1.7 (0.55)	138 (11.7)	300 (8.6)	2.5 (0.28)
Reward	16	5.6 (1.37)	154 (20.6)	300 (11.8)	1.6 (0.13)
Movement	22	6.0 (2.12)	148 (9.8)	310 (11.8)	1.7 (0.08)
Total	51	4.5 (1.04)	143 (8.0)	304 (6.5)	2.0 (0.13)

Summary of cell firing characteristics. Numbers represent mean values (± S.E.M.). (A) The first table illustrates values when cells are grouped as a function of firing pattern. (B) The second table compares the same spike parameters when cells are grouped according to behavioral correlate.

greater (representing 100% increase in firing) and less than 0.50 (representing a 50% decrease in firing) were considered to be correlated with a particular behavior.

3. Results

All of the 103 cells analyzed were histologically verified to have been recorded in the mVS (excluded were cells with mean firing rates less than or equal to 0.1). Within this cell population, 25 cells displayed tonic firing characteristics, 74 showed low frequency phasic firing, and 4 demonstrated high frequency phasic firing. Spike characteristics were compared between cells grouped by firing pattern (tonic, low frequency phasic or high frequency phasic) or by behavioral correlate (spatial, reward or movement) using a one way ANOVA. Mean firing rate, spike amplitude, duration and mean place specificity were significantly different between cells with different firing patterns ($P < 0.01$; Table 1). Tonic and low frequency phasic cells appeared evenly distributed throughout the recorded area, but high frequency phasic cells were only recorded from the ventral border of the ACC within the mVS. This is consistent with acute recordings by Yim and Mogenson [65].

Behaviorally correlated cells appeared to be uniformly dispersed throughout the mVS (Fig. 1). Three distinct behavioral correlates were identified: place, reward and movement. Spike characteristics were compared between cells with behavioral correlates from only one of these groups (e.g. cells demonstrating reward correlates only). Mean rate, amplitude and duration were not significantly different ($P > 0.1$), while

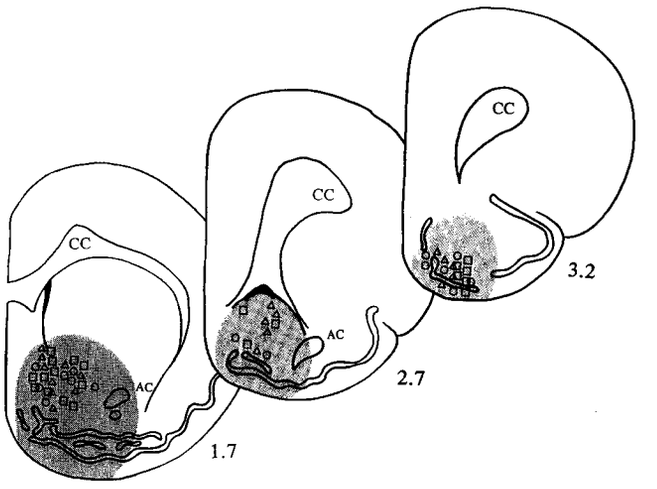

Fig. 1. A schematic of behaviorally correlated recording sites within the mVS. Shaded areas correspond to mVS areas. Open symbols indicate behaviorally correlated cells: triangle = spatial correlate, square = reward correlate, circle = movement correlate. Overlapping symbols indicate single cells demonstrating behavioral correlates of two different types (i.e. an overlapping triangle and square represents a cell with spatial and reward correlates). Non-correlated neurons were evenly distributed throughout the recorded area and are not represented here. (CC = corpus collosum, AC = anterior commissure.)

specificity scores were significantly different between groups ($F_{2,40} = 6.08$, $P < 0.01$; Table 1). Additionally, tonic firing cells were less likely to demonstrate behavioral correlates (7/25 correlated cells; 28%) than either of the phasic cell types (low frequency, 40/74; 54% and high frequency, 4/4; 100%; Fig. 2). Thus, while behavioral correlates were found in all types of spontaneously active neurons, they were most common in cells that fired in phasic bursts. Furthermore, of the

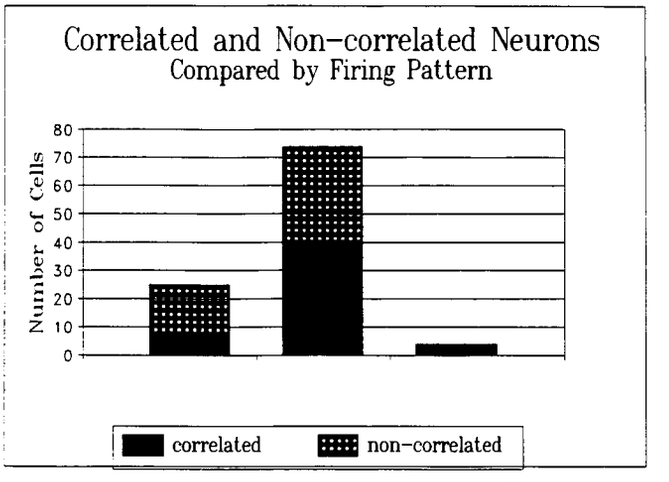

Fig. 2. Ratios of behaviorally correlated and non-correlated neurons, shown as a function of firing pattern. Patterned bar (top) reflects the total number of cells recorded, solid bar (bottom) indicates total number of *correlated* cells of that firing type. From left to right are ratios for tonic firing, low-frequency firing, and high frequency firing neurons.

Table 2

(A)

	Spatial	Reward	Movement	Total
Tonic	0	3	3	6
Low freq. phasic	15	8	14	37
High freq. phasic	0	1	1	2
Total	15	12	18	45

(B)

	Spatial/ reward	Spatial/ movement	Reward/ movement	Total
Tonic	1	0	0	1
Low freq. phasic	0	2	1	3
High freq. phasic	1	0	1	2
Total	2	2	2	6

Summary of the number of cells with behavioral correlates when grouped by firing pattern. (A) Table A represents all cells with correlates within a single behavioral type. (B) The second table shows the numbers of cells demonstrating behavioral correlates of two different behavioral types.

cells *with* behavioral correlates, tonic firing cells tended to demonstrate reward correlates (4/7), low frequency phasic cells often showed spatial and/or movement correlates (17/40 each), and high frequency phasic cells usually had reward correlates (3/4; Table 2). Cells with behavioral correlates were evenly distributed throughout the mVS, with the exception of one type of reward correlated neuron (which coded expectation of reward) which most often corresponded with high frequency phasic cells recorded from the ventral border of the ACC within the mVS.

3.1. Spatial correlates

Nineteen of 51 neurons which demonstrated behavioral correlates in our task were sensitive to the spatial location of the animal. Of these, 3 cells were also correlated with reward or movement conditions. Three types of place fields were recorded: single arm, multiple arm, and center platform place fields.

The frequency distribution of place specificity scores for mVS neurons is illustrated in Fig. 3. The mean place specificity for all cells was 2.1 (range 1.0–10.6), while the mean specificity for cells with arm place fields was 3.3 (range 1.92–5.6).

Three cells demonstrated single arm place fields. One of the 3 place cells fired in both directions (facing inward and outward on the maze arm), while the other 2 had unidirectional fields (Fig. 4A). Three cells demonstrated place fields on 3 or 4 arms, with at least 1 arm non-adjacent to the others (Fig. 4B). All multiple arm place cells fired preferentially as the rat faced one

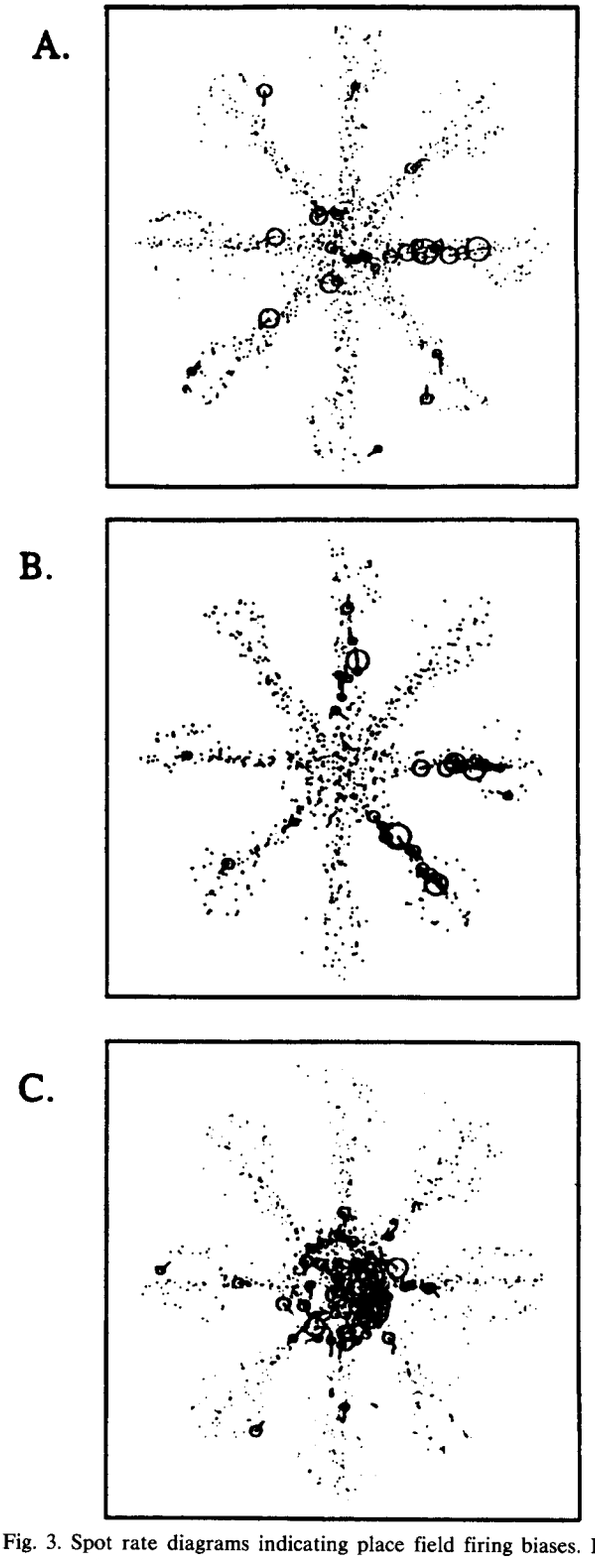

Fig. 3. Spot rate diagrams indicating place field firing biases. Dots represent locations occupied by the rat. Circle size is linearly related to neuronal firing rate, while vector lines projecting from the circles represent the direction faced by the animal during cell discharge. (A) A unidirectional single arm place field on the east arm of the maze. (B) A bi-directional multiple arm place field, with fields on arms pointing north, east, and south-east. (C) A center platform place field demonstrating non-uniform firing on the center platform. This cell preferred to fire when the rat was located on the northwest quadrant of the center platform. (Maximum firing rates 12.5, 14.7 and 34.3 Hz, respectively.)

direction in the field. A majority of place cells ($n = 14$) had place fields on the center platform. These fields were not direction specific and often only covered portions of the center platform (Fig. 4C).

3.2. Reward correlates

Sixteen cells (of 51) demonstrated reward correlated firing. Reward encounter cells ($n = 11$) demonstrated altered firing rates within 500 ms after reaching the arm end reward site (9 cells increased firing by at least 100%; 7 cells attenuated firing by at least 50%; Fig. 5).

In order to ensure that reward encounter was the relevant correlate for our cells, two probe trials were run on different animals. During these trials, the maze was not baited. In both cases, the reward encounter cells showed dramatically reduced firing at the arm ends (Fig. 6). Thus, the cells were not responding only to the cessation of movement at arm ends. This probe could not be repeated within subjects, as animals quickly learned not to continue with the trial if reward was absent from the first reward site.

Other reward correlates included expectation of reward and reward magnitude. Seven expectation cells showed altered firing 500 ms or less prior to reward encounter (6 increased firing by at least 100%, and 1 attenuated firing by at least 50%; Fig. 7). Firing just prior to reward encounter has been described previously for the mVS [10,16,49]. Two magnitude cells demonstrated differential firing with large and small reward at the arm ends. The cell shown in Fig. 7 fired at a mean rate of 32.3 Hz just prior to encounter of large rewards, and only 24.7 Hz before small reward encounter (demonstrating both expectation and magnitude reward correlates). Other researchers have also reported differential firing based on the appetitive value of reward [49].

The reward magnitude condition was manipulated for one cell by rotating the arms that held small and large rewards (Fig. 8). Thus, arms which had always been baited with small reward now held large rewards

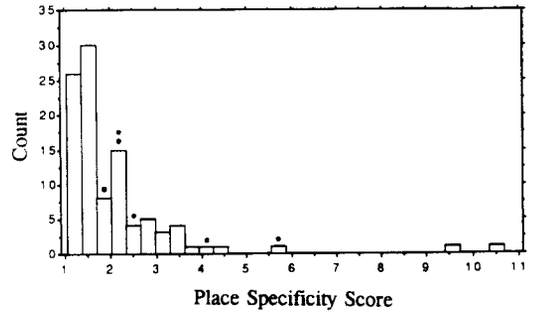

Fig. 4. Frequency distributions of place specificity scores for all neurons recorded in the mVS. Dots represent specificity scores for cells with an arm bias.

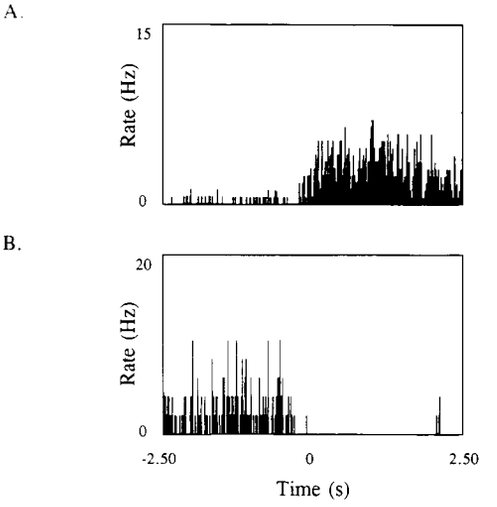

Fig. 5. Peri-event time histograms demonstrating reward encounter correlates. Time is represented on the ordinate with time 0 corresponding to reaching the arm end reward site (bin size, 10 ms). (A) An example of a cell which increased firing when the animal encountered the reward. (B) Another cell which ceased firing with reward encounter.

and vice versa. Prior to reward rotation, cells fired on average 189% higher rate on arms which held the large reward relative to small reward arms. *Immediately* following reward rotation, the firing rate on large reward

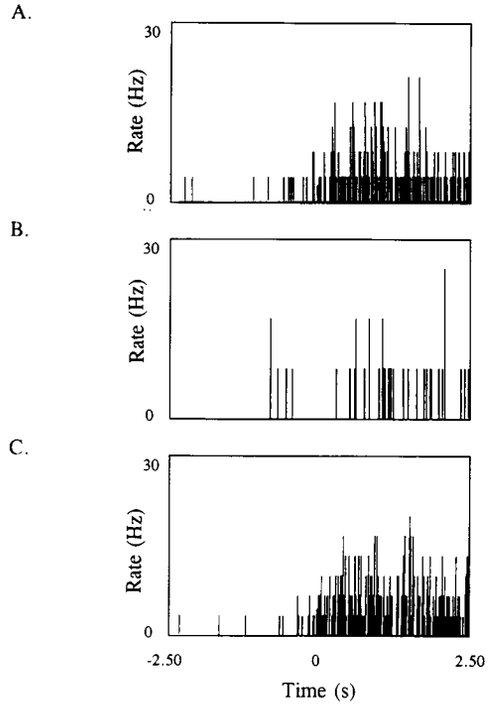

Fig. 6. Dependence on the presence of reward for the reward encounter behavioral correlate. Time 0 represents reaching the arm end reward site. (A) The baseline firing rate when rat encounters reward at the arm end. (B) Firing rate when the rat reached unbaited reward sites. (C) Firing following the return of reward to the arm ends.

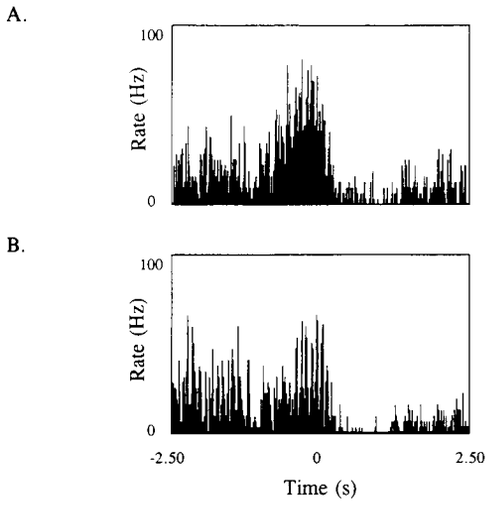

Fig. 7. Peri-event time histograms demonstrating differential firing related to magnitude of reward. Time 0 corresponds to reaching the arm end reward site. Graphs represent outward locomotion towards a location associated with small (A) or large (B) magnitude reward. A) Mean firing rate 1.25 s prior to small reward encounter was 32.3 Hz. B) This cell fired at a mean rate of 24.7 Hz 1.25 s prior to large reward encounter. Note: higher firing rate corresponds to *smaller* reward situation, and thus does not indicate an increased preparation for larger ingestion.

arms (now in a different spatial location) was much higher than on small reward arms (164%), a trend which continued throughout the four rotated reward trials (173% mean rate difference). Upon return to the original reward locations, the highest firing rate again followed the large reward arm (197%). Therefore, differential neuronal firing patterns appeared to rotate with the reward and were not a function of the spatial location of different magnitude rewards. The other cell which appeared to encode reward magnitude demonstrated similar differential firing but 500 ms *prior* to reward encounter. In this case, differential firing appeared to depend on expectations of reward magnitude.

3.3. Movement correlates

Twenty one of the 51 correlated cells were sensitive to various movement conditions. Units classified as general movement cells ($n = 6$) showed altered firing rates during all movement conditions (turns, inbound, center and outbound) relative to periods of non-movement (3 increased firing by at least 100%, 3 attenuated firing by at least 50%). Units that demonstrated significant alterations in firing during particular movements were classified according to the movement descriptor; e.g. turn (2 increased, 0 attenuated), inbound (4 increased, 3 attenuated) or outbound (7 increased, 2 attenuated; Fig. 9).

3.4. Overlapping correlates

The firing rates of several cells ($n = 10$) were correlated with two behaviors. Five of these cells had multiple correlates within a single category of behavior; 3 cells demonstrated both reward encounter *and* reward expectation correlates, and 2 cells had movement correlates for inward *and* outward locomotion (without corresponding correlates for turns or center crossing movements). The other 6 cells either had correlates to both space and reward ($n = 2$), space and movement ($n = 2$), or reward and movement ($n = 2$; Fig. 10).

Further analysis was necessary to determine whether the overlapping correlates were independently encoded, or conversely if one correlate was a function of another. For example, a cell which demonstrated a multiple arm place field and also increased firing during reward encounter, was analyzed to see if the reward correlate was only evident on arms within the place field. Since firing rates increased during reward irrespective of spatial location, these behavioral correlates were considered to be separately encoded. Simi-

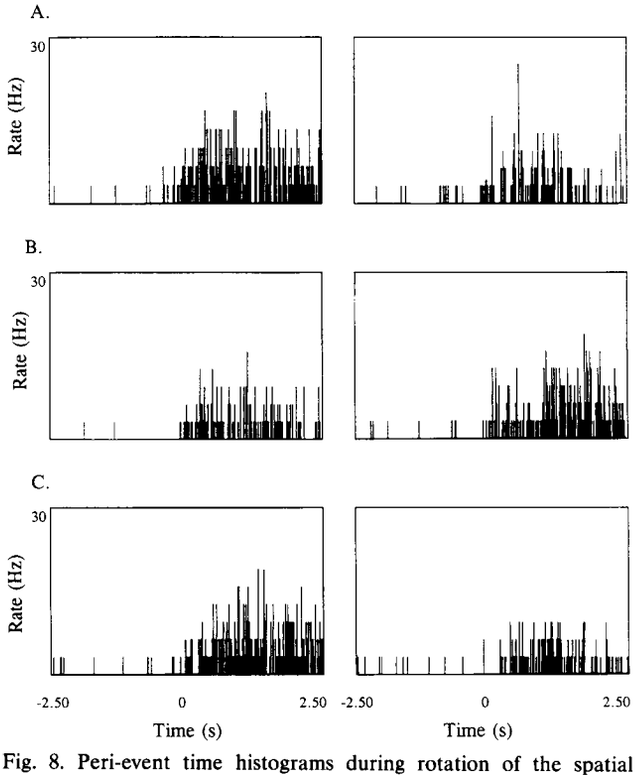

Fig. 8. Peri-event time histograms during rotation of the spatial location of rewards of different magnitudes. Time 0 indicates reward encounter for all graphs. (A) Baseline firing rates upon encountering *large* (left) and *small* (right) rewards (means 6.8 and 3.6 Hz, respectively). (B) Firing during encounter of *small* (left) and *large* (right) rewards following rotation of reward locations, such that arms which previously held large reward, now held small reward and vis versa (mean rates 3.3 and 5.7 Hz, respectively). (C) Firing after reward magnitudes were returned to standard locations (as in A; mean rates 6.1 and 3.1, respectively).

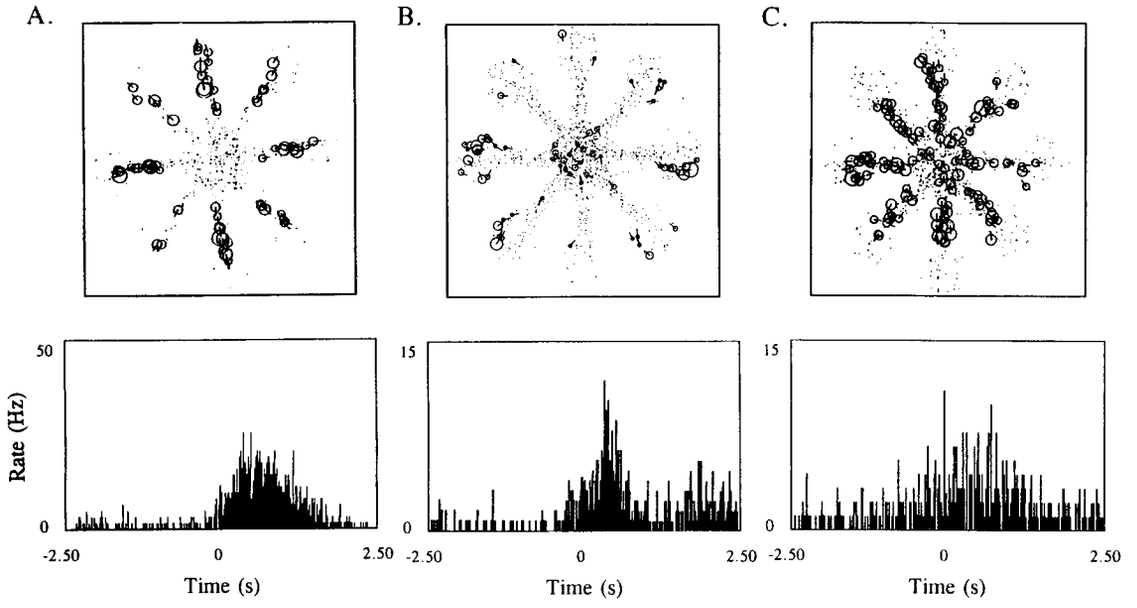

Fig. 9. A spot rate diagram (top) and a peri-event time histogram (PETH; bottom) illustrating movement correlates. (A) This cell fired preferentially during outward locomotion on all maze arms. The maximum firing rate was 41.8 Hz, while the mean firing rate was 13.3 Hz for the 1.25 s following time 0 (representing outward movement). In contrast, the mean firing rate during inward locomotion was 1.5 Hz. (B) This cell demonstrated its highest firing rates when turning at the ends of all arms. The maximum firing rate was 37.8 Hz, while the mean firing rate was 5.0 Hz (time 0 represents the beginning of the turn). (C) This cell was found to fire most during movement in the inward direction on all maze arms. The maximum firing rate was 10.2 Hz, while the mean firing rate was 3.8 Hz for the 1.25 s following time 0 (which represents inward movement). In contrast, the mean firing rate during outward locomotion was 1.5 Hz.

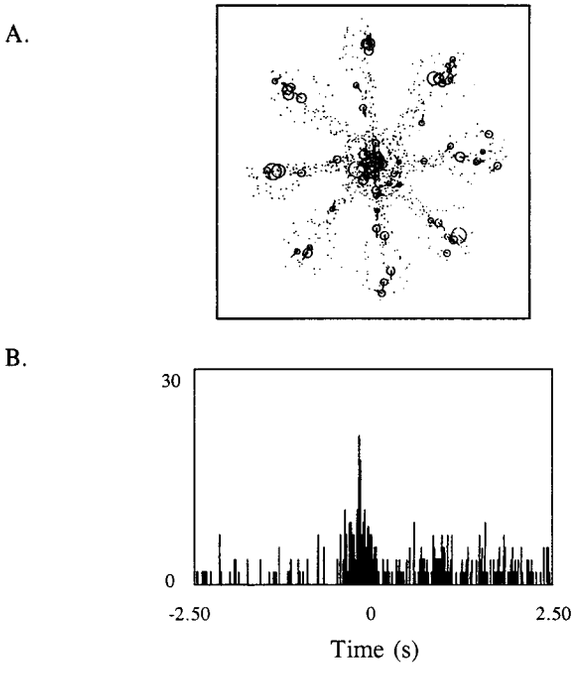

Fig. 10. Overlapping correlates from a single cell. (A) Spot rate diagram illustrating the consistancy of firing at arm ends and in the center platform place field (maximum rate 14.4 Hz). (B) Peri-event time histogram showing increased cell firing 300 ms prior to reaching the arm end (mean rate approximately 7.5 Hz for 500 ms prior to time 0).

larly, reward and movement correlates were determined to be independent because they occurred at different times within a trial. For example, a cell which increased firing just prior to reaching the reward site also attenuated firing during inward locomotion, which occurred more than 1 s later. Cells with both spatial and reward correlates were obviously independent because their spatial fields were located on the center platform while reward related firing was seen on the arm ends. Consequently, it appears that single mVS neurons are able to encode multiple behavioral correlates.

4. Discussion

The predominant finding of this study was that there is spatial-, reward and movement-sensitive neuronal firing in the medial ventral striatum (mVS) of rats performing a spatial memory task. Although some single mVS neurons were correlated with several behaviors within a trial, the firing of the majority of cells occurred relative to a single category of behavior.

4.1. Spatial correlates

Although spatial correlates to unit firing have been well documented in pyramidal cells of the hippocampal

formation [25,34,37,38,40,41] the present study demonstrated for the first time that such correlates can be observed 'downstream' from the hippocampus. Medial VS place fields which covered all or a portion of one maze arm most closely resembled hippocampal place fields. Barnes and colleagues [4] reported mean place specificity scores for different regions of the hippocampus proper as follows; CA1 = 4.5, CA3 = 7.5, subiculum = 2.0 and entorhinal cortex = 2.0. Mean place specificity for all mVS neurons in the present study was 2.1, while the mean specificity of cells with arm place fields was 3.3. Thus, while mVS neurons are able to demonstrate spatial selectivity, they do not tend to have place fields as specific as those reported in CA1 and CA3 of hippocampus. Instead, mean mVS place specificity scores fall between those expected for CA1 and the subiculum and entorhinal cortex. The moderate nature of mean mVS place specificity may reflect the range of spatial information entering the mVS. More specifically mVS neurons which demonstrate place fields with low specificity may be receiving input from hippocampal regions also with low place field specificity such as the subiculum and entorhinal cortex. Medial VS neurons with very specific place fields may receive input from an alternate population of hippocampal neurons originating from CA1 pyramidal cells, which are assiciated with more specific place fields [55,58]. Alternatively, the lower specificity seen in the mVS could reflect the integration of spatial with other non-spatial information within these individual neurons. That is, mVS specificity could be a function of the integration of hippocampal spatial information with other context specific information provided by, for example, the amygdala.

Multiple arm place fields were recorded as often as single arm fields in the mVS. Some hippocampal place cells have also been reported with fields that covered more than one arm of the radial maze [25,28], but most often the arms were adjacent and the two arm field was considered to be a single, larger place field. Hippocampal place fields found on non-adjacent arms have been interpreted by some to belong to different cells that could have been more well isolated using the tetrode technique [51]. Multiple arm fields that were recorded from mVS neurons were never restricted to adjacent arms and thus were not considered to represent larger single fields. Since these neurons were recorded with stereotrodes and not a tetrode, one could question whether mVS multiple arm fields represented the cumulative fields of several non-isolated cells. This is not likely to be the case. Firstly, neurons in the mVS are sparsely distributed and seen predominantly singly, or in clusters of 2 and 3 neurons [11]. Supporting this, our mVS recording sessions did not include the abundance of multiple cell recording observed in our previous hippocampal experiments. If we presume that spatial mVS neurons receive afferent input from the HPC, then it is noteworthy that hippocampal-mVS afferents tend to avoid clusters of neurons in preference of single, isolated neurons [13]. Additional mVS recording using a tetrode recording technique would be necessary to resolve this issue.

The majority of spatially sensitive mVS neurons fired preferentially on the center platform of the radial maze. Center platform spatial firing has also been reported for hippocampal interneurons [26,28,29]. These hippocampal cells fire as the animal crosses the center platform from any direction, and thus the firing distribution is symmetrical about the central platform. In contrast, mVS center platform place cells often fired within distinct regions of the center platform, and thus their place fields did not merely reflect behaviors unique to crossing the center platform. Rather, these cells appear to encode location specific information.

Given that both the mVS and hippocampus code spatial information, and that hippocampus comprises a major mVS afferent system, it is likely that such information is passed from limbic to striatal structures within the mVS. Limbic spatial information may become associated with other non-spatial data such as reward associations.

4.2. Reward correlates

Medial VS neurons appear to be involved with reward encounter, expectation and magnitude. Schultz and colleagues [49] reported similar reward related neuronal activity in the monkey mVS. They found reward encounter associated activity in both ACC, and in the surrounding mVS, but a higher percentage of non-ACC mVS neurons were active during reward expectation. These results are consistent with our own distribution of reward encounter and expectation neurons.

One possible explaination for reward correlates is that cells are firing in response to oral motor muscle activity. Two pieces of evidence indicate that masseter EMG recording is not necessary to infer that reward correlates are independent from oral motor activity. First, increased firing was found to correlate with smaller magnitudes of reward, indicating that muscle activity was not directly correlated with cell activity. Secondly, reward cells were found which fired *prior* to reward encounter, presumably before oral-motor muscles were active. This was consistant with Apicella and colleagues [2] who recorded similar reward delivery correlates in monkey mVS. Using EMG recordings of masseter muscle, these researchers were able to conclude that reward delivery neuronal activation was independent of the oral-motor movements of reward consumption.

Reward information could be accessing the mVS via

the basolateral amygdala (BLA). Chronic recordings from monkey amygdala have shown that BLA neurons respond to reward presentation [36] in a manner that resembles mVS encounter correlates. To our knowledge, no one has tested the response of BLA to reward expectation. However, reward expectation correlates have been demonstrated in the medial prefrontal cortex [59]. Based on this and our own electrophysiological data, it is possible that reward encounter signals reach the mVS through BLA afferents, while reward expectation information accesses the striatum through other routes, possibly via association cortex.

Other researchers have speculated that the mVS may also be involved with encoding hedonistic evaluations [60]. We recorded 2 mVS neurons which were sensitive to reward magnitude, and other researchers have reported finding monkey mVS neurons which alter their firing rate depending on the appetitive value of the reward [49]. Given that magnitude correlates have also been reported in the ventral tegmental area (VTA), but not in other mVS afferent structures [35], the VTA (dopaminergic or non-dopaminergic) projections to the mVS could be responsible for the hedonistic encoding of reward.

4.3. Movement correlates

Movement correlated activity in our study involved goal directed locomotion through a spatial environment. Other movement correlates have been reported in rat mVS during exploration in an open field [9] and food procurement-related body movements in an operant chamber [10] (i.e. raising head, rearing and touching lever). No movement correlates were reported in monkey mVS recordings where locomotion was prohibited. Although one must be cautious when evaluating results from such diverse tasks, the combined results suggest a trend towards mVS activity involving food procurement body movements (including locomotion). This would contrast with dorsal striatal movement correlates reported in monkeys which appear primarily concerned with specific consummatory behaviors (i.e. arm extension/flexion, bar pressing, chewing, grasping or gazing) [35]. If one considers the differential inputs to dorsal and ventral striatum (primarily neocortex and limbic structures, respectively) [31], and their parallel outputs to pallidal motor structures (dorsal and ventral pallidum, respectively) then it is not surprising that these structures might encode different aspects of goal directed motor movement.

Several mVS afferents code movement information, and could supply this information to the mVS. Hippocampal interneurons have been reported to demonstrate movement correlates [28,29,46]. For example, most of these neurons fire consistently during active locomotion, while a small subpopulation is inhibited during movement. There is some evidence of projections from the interneuron population of CA1 to the nucleus accumbens [55]. Whether activity in this interneuron population is sufficient to allow the transfer of motor information to the mVS via the fornix, is presently undetermined.

Additionally, motor information could access the mVS via reciprocal connections with the ventral pallidum (VP) [14]. The VP is thought to be involved with the activation of voluntary motor movements[15, 54] and thus its connections with the mVS might serve as a feedforward and/or feedback to motor output structures. To our knowledge, no electrophysiological recordings from the VP of freely moving animals have been published to substantiate this idea.

4.4. Overlapping correlates

Some cells demonstrated correlates to more than one type of behavior (i.e. spatial and reward, spatial and movement, or reward and movement correlates). These correlates were shown to be expressed independently during mVS firing. Thus, single mVS neurons appear to be able to represent different types of information, presumably derived from different afferent sources. Since these diverse afferent inputs converge on single mVS neurons, which then project primarily to a single source (i.e. motor output structures), integration of spatial, reward and movement information may be possible at the level of the individual neuron.

4.5. Conclusion

This study provides evidence that mVS neurons encode spatial, reward and motor information in freely navigating animals. Integration of such information may occur at the single cell level, as well as at the structural level. Together these data are consistent with the hypothesis that spatial contextual information (from hippocampus) is integrated with specific stimulus reward associations (from amygdala) in the mVS to affect subsequent behavior. In this way limbic structures can directly affect the accuracy of ongoing navigational behavior.

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5. References

[1] Annett, L.E., McGregor, A. and Robbins, T.W., The effects of ibotenic acid lesions of the nucleus accumbens on spatial learning and extinction in the rat, *Behav. Brain Res.*, 31 (1989) 231–242.

[2] Apicella, P., Ljungberg, T., Scarnati, E. and Schultz, W., Responses to reward in monkey dorsal and ventral striatum, *Exp. Brain Res.*, 85 (1991) 491–500.
[3] Aylward, R.L.M. and Totterdell, S., Neurons in the ventral subiculum, amygdala and entorhinal cortex which project to the nucleus accumbens: their input from somatostatin-immunoreactive boutons, *J. Chem. Neuroanat.*, 6 (1993) 31–42.
[4] Barnes, C.A., McNaughton, B.L., Mizumori, S.J.Y., Leonard, B.W. and Lin, L.-H., Comparison of spatial and temporal characteristics of neuronal activity in sequential stages of hippocampal processing. In J. Storm-Mathisen, J. Zimmer and O.P. Ottersen (Eds.), *Understanding the Brain Through the Hippocampus: The Hippocampal Region as a Model for Studying Brain Structure and Function, Progress in Brain Research*, Elsevier, 1990.
[5] Beninger, R.J., The role of dopamine in locomotor activity and learning, *Brain Res. Rev.*, 6 (1983) 173–196.
[6] Brown, E.E., Robertson, G.S. and Fibiger, H.C., Evidence for conditional neuronal activation following exposure to a cocaine-paired environment: role of forebrain limbic structures, *J. Neurosci.*, 12 (1992) 4112–4121.
[7] Cador, M., Robbins, T.W. and Everitt, B.J., Involvement of the amygdala in stimulus–reward associations: interaction with the ventral striatum, *Neuroscience*, 30 (1989) 77–86.
[8] Cador, M., Robbins, T.W., Everitt, B.J., Simon, H., Le Moal, M. and Stinus, L., Limbic-striatal interactions in reward-related processes: modulation by the dopaminergic system. In P. Willner and J. Scheel-Kruger (Eds.), *The Mesolimbic Dopamine System: From Motivation to Action*, John Wiley and Sons, Ltd., 1991, pp. 225–250.
[9] Callaway, C.W. and Henriksen, S.J., Neuronal firing in the nucleus accumbens is associated with the level of cortical arousal, *Neuroscience*, 51 (1992) 547–553.
[10] Chang, J.Y., Sawyer, S.F., Lee, R.S. and Woodward, D.J., Correlation between nucleus accumbens neuronal activity and cocaine self-administration behavior in rats, *Neurosci. Abstr.*, 17 (1991) 681.
[11] Domesick, V.B., Further observations on the anatomy of nucleus accumbens and caudatoputamen in the rat: similarities and contrasts. In R.B. Chronister and DeFrance, J.F. (Eds.), *The Neurobiology of the Nucleus Accumbens*, Haer Institute, Brunswick, Maine, 1981, pp. 7–41.
[12] Graybiel, A.M., Input-output anatomy of the basal ganglia. In Symposium Lecture, *Proc. Soc. Neurosci.*, Toronto, Canada, 1976.
[13] Groenewegen, H.J., Vermeulen-Van der Zee, E., te Kortschot, A. and Witter, M.P., Organization of the projections from the subiculum to the ventral striatum in the rat, A study using anterograde transport of *phaseolus vulgaris* leucoagglutinin, *Neuroscience*, 23 (1987) 103–120.
[14] Hakan, R.L., Berg, G.I. and Henriksen, S.J., Electrophysiological evidence for reciprocal connectivity between the nucleus accumbens septi and ventral pallidal region, *Brain Res.*, 581 (1992) 344–350.
[15] Heimer, L., Switzer, R.D. and Van Hoesen, G.W., Ventral striatum and ventral pallidum; components of the motor system? *Trends Neurosci.*, 5 (1982) 83–87.
[16] Jeziorski, M. and White, F.J., Effects of repeated morphine treatment on the sensitivity of dopamine receptors in the nucleus accumbens, *Neurosci. Abstr.*, 17 (1991) 329.
[17] Jones, B. and Mogenson, G.J., Nucleus accumbens to globus pallidus GABA projection: electrophysiological and iontophoretic investigations, *Brain Res.*, 188 (1980) 93–105.
[18] Jones, D.L. and Mogenson, G.J., Nucleus accumbens to globus pallidus GABA projection subserving ambulatory activity, *Am. Physiol. Soc.*, 20 (1980) R65–R69.
[19] Joseph, M.H. and Hodges, H., Lever pressing for food reward and changes in dopamine turnover and uric acid in rat caudate and nucleus accumbens studied chronically by in vivo voltammetry, *J. Neurosci. Methods*, 34 (1990) 143–149.
[20] Kelley, A.E. and Domesick, V.B., The distribution of the projection from the hippocampal formation to the nucleus accumbens in the rat: an anterograde- and retrograde-horseradish peroxidase study, *Neuroscience*, 7 (1982) 2321–2335.
[21] Krettek, J.E. and Price, J.L., Amygdaloid projections to subcortical structures within the basal forebrain and brainstem in the rat and cat, *J. Comp. Neurol.*, 178 (1978) 224–255.
[22] Lopes da Silva, F.H., Arnolds, D.E.A.T. and Neijt, H.C., A functional link between the limbic cortex and ventral striatum: physiology of the subiculum accumbens pathway, *Exp. Brain Res.*, 55 (1984) 205–214.
[23] McDonald, A.J., Topographical organization of amygdaloid projections to the caudatoputamen, nucleus accumbens, and related striatal-like areas of the rat brain, *Neuroscience*, 44 (1991) 15–33.
[24] McNaughton, B.L., Barnes, C.A., Meltzer, J. and Sutherland, R.J., Hippocampal granule cells are necessary for normal spatial learning but not for spatially-selective pyramidal cell discharge, *Exp. Br. Res.*, 76 (1989) 485–496.
[25] McNaughton, B.L., Barnes, C.A. and O'Keefe, J.A., The contributions of position, direction, and velocity to single cell unit activity in the hippocampus of freely moving rats, *Exp. Brain Res.*, 52 (1983) 41–49.
[26] McNaughton, B.L., O'Keefe, J. and Barnes, C.A., The stereotrode: a new technique for simultaneous isolation of several single units in the central nervous system from multiple unit records, *J. Neurosci. Methods*, 8 (1983) 391–397.
[27] Milner, P.M., Brain-stimulation reward: a review, *Can. J. Psychol.*, 45 (1991) 1–36.
[28] Mizumori, S.J.Y., McNaughton, B.L., Barnes, C.A. and Fox, K.B., Preserved spatial coding in hippocampal CA1 pyramidal cells during reversible suppression of CA3 output: evidence for pattern completion in hippocampus, *J. Neurosci.*, 9 (1989) 3915–3928.
[29] Mizumori, S.J.Y., Barnes, C.A. and McNaughton, B.L., Behavioral correlates of theta-on and theta-off cells recorded from hippocampal formation of mature young and aged rats, *Exp. Brain Res.*, 80 (1990) 365–373.
[30] Mizumori, S.J.Y., Perez, G.M., Alvarado, M.C., Barnes, C.A. and McNaughton, B.L., Reversible inactivation of the medial septum differentially affects two forms of learning in rats, *Brain Res.*, 528 (1990) 12–20.
[31] Mogenson, G.J., Jones, D.L. and Yim, C.Y., From motivation to action: functional interface between the limbic system and the motor system, *Prog. Neurobiol.*, 14 (1980) 69–97.
[32] Molino, A. and McIntyre, D., Another inexpensive headplug for electrical recording and/or stimulation of rats, *Physiol. Behav.*, 9 (1972) 273–275.
[33] Morris, R.G.M., An attempt to dissociate 'spatial-mapping' and 'working memory' theories of hippocampal function. In W. Seifert (Ed.), *Neurobiology of the Hippocampus*, Academic Press, London, 1983, pp. 405–432.
[34] Muller, R.U., Kubie, J.L. and Ranck Jr., J.B., Spatial firing patterns of hippocampal complex-spike cells in a fixed environment, *J. Neurosci.*, 7 (1987) 1935–1950.
[35] Nishino, H., Hattori, S., Muramoto, K. and Ono, T., Basal ganglia neural activity during operant feeding behavior in the monkey: relation to sensory integration and motor execution, *Brain Res. Bull.*, 27 (1991) 463–468.
[36] Nishijo, H., Ono, T. and Nishino, H., Single neuron responses in amygdala of alert monkey during complex sensory stimulation with affective significance, *J. Neurosci.*, 8 (1988) 3570–3583.
[37] O'Keefe, J., Place units in the hippocampus of the freely moving rat, *Exp. Neurol.*, 51 (1976) 78–109.

[38] O'Keefe, J. and Dostrovsky, J., The hippocampus as a spatial map, Preliminary evidence from unit activity in the freely moving rat, *Brain Res.*, 34 (1971) 171–175.
[39] O'Keefe, J. and Nadel, L., *The Hippocampus as a Cognitive Map*, Clarendon Press, Oxford, 1978.
[40] O'Keefe, J. and Speakman, A., Single unit activity in the rat hippocampus during a spatial memory task, *Exp. Brain Res.*, 68 (1987) 1–27.
[41] Olton, D., Branch, M. and Best, P.J., Spatial correlates of hippocampal unit activity, *Exp. Neurol.*, 58 (1978) 387–409.
[42] Olton, D.S., Becker, J.T. and Handelmann, G.E., Hippocampus, space, and memory, *Behav. Br. Sci.*, 2 (1979) 313–322.
[43] Paxinos, G. and Watson, C., *The Rat Brain in Stereotaxic Coordinates*, Academic Press, Australia, 1986.
[44] Pennartz, C.M.A., Dolleman-Van der Weel, M.J., Kitai, S.T. and Lopes da Silva, F.H., Presynaptic dopamine D1 receptors attenuate excitatory and inhibitory limbic inputs to the shell region of the rat nucleus accumbens studied in vitro, *J. Neurophysiol.*, 67 (1992) 1325–1334.
[45] Phillips, J.G., Pfaus, J.G. and Blaha, C.D., Dopamine and motivated behaivor: insights provided by *in vivo* analyses, *The Mesolimbic Dopamine System: from Motivation to Action*, John Wiley and Sons, Ltd., 1991, pp. 199–224.
[46] Ranck Jr., J.B., Studies on single neurons in dorsal hippocampus formation and septum in unrestrained rats. Part I. Behavioral correlates and firing repertiores, *Exp. Neurol.*, 41 (1973) 461–535.
[47] Roberts, D.C.S., Koob, G.F. and Klonoff, P, Extinction and recovery of cocaine self-administration following 6-OHDA lesions of the nucleus accumbens, *Pharm., Biochem. Behav.*, 12 (1980) 781–787.
[48] Rolls, E.T., Neurophysiology and functions of the primate amygdala. In J.P. Aggleton (Ed.), *The Amygdala: Neurobiological Aspects of Emotion, Memory, and Mental Dysfunction*, Wiley-Liss, Inc., New York, 1992, pp. 143–165.
[49] Schultz, W., Apicella, P., Scarnati, E. and Ljungberg, T., Neuronal activity in monkey ventral striatum related to the expectation of reward, *J. Neurosci.*, 12 (1992) 4595–4610.
[50] Sesack, S.R. and Pickel, V.M., In the rat medial nucleus accumbens, hippocampal and catecholaminergic terminals converge on spiny neurons and are in apposition to each other, *Brain Res.*, 527 (1990) 266–279.
[51] Speakman, A. and O'Keefe, J., Hippocampal complex spike cells do not change their place fields if the goal is moved within a cue controlled environment, *Eur. J. Neurosci.*, 2 (1990) 544–555.
[52] Sutherland, R.J. and Rodriguez, A.J., The role of the fornix/fimbria and some related subcortical structures in place learning and memory, *Behav. Brain Res.*, 32 (1989) 265–77.
[53] Swanson, L.W. and Kohler, C., Anatomical evidence for direct projections from the entorhinal area to the entire cortical mantle in the rat, *J. Neurosci.*, 6 (1986) 3010–3023.
[54] Swerdlow, N.R. and Koob, G.F., Lesions of the dorsomedial nucleus of the thalamus, medial prefrontal cortex and pedunculopontine nucleus: effects on locomotor activity mediated by nucleus accumbens-ventral pallidal circuitry, *Brain Res.*, 412 (1987) 233–243.
[55] Totterdell, S. and Hayes, L., Non-pyramidal hippocampal projection neurons: a light and electron microscopic study, *J. Neurocytol.*, 16 (1987) 477–485.
[56] Totterdell, S. and Smith, A.D., Cholecystokinin-immunoreactive boutons in synaptic contact with hippocampal pyramidal neurons in the nucleus accumbens of the rat, *Neuroscience*, 19 (1986) 181–192.
[57] Totterdell, S. and Smith, A.D., Convergence of hippocampal and dopaminergic input onto identified neurons in the nucleus accumbens of the rat, *J. Chem. Neuroanat.*, 2 (1989) 285–298.
[58] Van Groen, T. and Wyss, J.M., Extrinsic projections from area CA1 of the rat hippocampus: olfactory, cortical, subcortical, and bilateral hippocampal formation projections, *J. Comp. Neurol.*, 302 (1990) 515–528.
[59] Wantanabe, M., Prefrontal unit activity during delayed conditional go/no-go discrimination in the monkey. II. Relation to go and no-go responses, *Brain Res.*, 382 (1986) 15–27.
[60] Wise, R.A., Neuroleptics and operant behavior: the anhedonia hypothesis, *Behav. Brain Res.*, 5 (1982) 39–87.
[61] Wise, R.A. and Bozarth, M.A., Brain mechanisms of drug reward and euphoria, *Psychia. Med.*, 3 (1987) 445–461.
[62] Witter, M.P., Groenewegen, H.J., Lopes da Silva, F.H. and Lohman, A.H.M., Functional organization of the extrinsic and intrinsic circuitry of the parahippocampal region, *Prog. Neurobiol.*, 33 (1989) 162–253.
[63] Yang, C.R. and Mogenson, G.J., Electrophysiological responses of neurones in the nucleus accumbens to hippocampal stimulation and the attenuation of the excitatory responses by the mesolimbic dopaminergic system, *Brain Res.*, 324 (1984) 69–84.
[64] Yang, C.R. and Mogenson, G.J., An electrophysiological study of the neural projections from the hippocampus to the ventral pallidum and the subpallidal areas by way of the nucleus accumbens, *Neuroscience*, 15 (1985) 1015–1024.
[65] Yim, C.Y. and Mogenson, G.J., Response of nucleus accumbens neurons to amygdala stimulation and its modification by dopamine, *Brain Res.*, 239 (1982) 401–415.
[66] Zahm, D.S. and Heimer, L., Two transpallidal pathways originating in the rat nucleus accumbens, *J. Comp. Neurol.*, 302 (1990) 437–446.