

## The relationship between monkey hippocampus place-related neural activity and action in space

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### Abstract

To solve complex spatial problems like visual scanning and spatial navigation, animals must explore and actively sense an array of environmental stimuli. Recent studies have led to an agreement that the hippocampal formation (HF) is essential to the internal representation of spatial relation in animals. In the present study, neural activity was recorded from the HF of three monkeys, which steered a cab to various locations by pressing the appropriate bars (spatial moving task). Place-related activity of most HF neurons persisted even if the direction the monkey faced was rotated during the task. However, when the experimenter, rather than the monkey, controlled the device, the place-related neural activity of most HF neurons turned out to be obscure. The results suggest that the HF represents space effectively in situations in which the animal acts in space. © 1997 Elsevier Science Ireland Ltd.

**Keywords:** Hippocampus; Monkey; Place; Space; Action

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Active sensing is implicit and essential to a primate's cognitive ability to resolve a complex spatial paradigm such as visual scanning or spatial navigation. This implies that neural events during such behavior are highly dependent on the animal's active interaction with the environment. Accordingly, single unit recording studies of the monkey frontal eye field during visual scanning revealed a relationship between vision-related activity and active decision making. Passive tracking, which approximated real scanning but did not require interaction with images, was insufficient to drive the vision-related neurons that had responded to images during scanning [1].

During spatial navigation, the animal must flexibly compare changing sensory inputs arising from locomotion with a stored representation of the environment [4,5]. In the rodent literature, the hippocampal formation (HF) is considered essential to this function [2,6,10,14]. In particular, rat hippocampal neurons have place-correlates; 'place cells' which fire specifically when the animal passes through a specific location, in relation to an arrangement of relevant allocentric cues [7–9,11]. Recently, we reported that place-

related neurons in the monkey HF are comparable to rat place cells [13]. Using a paradigm in which the monkey could change the location of a motorized movable device (cab) in which it rode while performing an operant task, we found several neuronal types. These included one that changed activity when the subject changed location and one that responded selectively to task cues, depending on the subject's location [12,13]. In this report, we show that the monkey HF place-correlate is also highly dependent on the animal's action.

Extracellular neural activity was recorded from the HF of three adult monkeys (*Macaca fuscata*). Conventional surgery and unit recording techniques were used [12,13]. Each monkey steered the cab to various locations by pressing appropriate bars, guided by visual (bar LED) and/or auditory (cue tone) cues (the spatial moving task) [12,13]. Increase or decrease of neural activity during each inter-trial interval (ITI, at least 1 min) in each location was considered to be significant if it exceeded 2.0 SD from the overall mean of the activity at 16–25 different locations. Task-related neural activity was determined by an analysis of the variance between the pretrial discharge rate during ITI and the rate in each phase of the task ( $P < 0.05$ ). To estimate the changes in the place-correlates of HF neurons

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in different conditions, Pearson's correlation coefficient ( $\gamma$ ) between the data obtained in the normal condition and those in other conditions was calculated by comparing corresponding neuronal activities in the same experimental field. The data obtained in the normal condition was, when available, the average of multiple laps.

Of the 238 neurons recorded in the monkey HF, 79 (33.2%) had place-related responses; their neural activity was higher when the monkey was in some specific location in the experimental field. Task-related neural activity was evident in 110 (46.3%) of the neurons in one or more of the task phases: cue signals (cue tone,  $n = 82$ ; bar LED,  $n = 79$ ); stimulus presentation (food or rewarding/non-rewarding object,  $n = 104$ ); bar pressing ( $n = 59$ ) and holding (moving,  $n = 94$ ); reward (food or juice) delivery ( $n = 26$ ). Of these 110 neurons, 33 (13.9%) also demonstrated place-related neural activity. An examination of the histology after recording revealed that these place and/or task-related neurons were distributed throughout the hippocampus proper, the dentate gyrus, the subiculum, and the parahippocampal gyrus; many neurons were located in the pyramidal cell layer in CA1 and CA3.

Fig. 1 is a typical example of place-related neural activity. The locations at which the monkey could get rewards, and then stay until the next trial, are shown numbered from P0 to P15. The activity of this neuron increased markedly in locations P10–P6 and was restored during the three successive laps using the same clockwise route. The average activity of the neuron in three successive laps is shown in Fig. 1A, which is the control under the monkey-controlled condition during the spatial moving task. The average neural activities at P10–P6, and outside of P10–P6 (P5–P0 and P15–P11) in Fig. 1A were 4.38 and 0.74 spikes/s, respectively. This neuron had no task-related neural activity. That is, no correlates with the task phases ( $P > 0.05$ ). When the room light was extinguished, the increase in the activity of this neuron in the P10–P6 region was suppressed (Fig. 2A), although the animal's overt behavior appeared to be normal. Pearson's correlation coefficient ( $\gamma$ ) between the average place-related neural activity in Fig. 1A and the activity shown in Fig. 2A was insignificant ( $\gamma = 0.059$ ,  $P > 0.05$ ). This indicates that the place-related neural activity of this neuron depended on visual signals from the environment outside of the cab. The place-related increase in neural activity was restored at P10–P6 when the room was illuminated again (Fig. 2B,  $\gamma = 0.748$ ,  $P < 0.01$ ). In Fig. 2B, although alternative routes to these locations were used, for example different bars or sequences of bars were pressed to reach the target area, the place-related neural activity at P10–P6 was replicated. This indicates that the place-related neural activity does not reflect direction or motion influence, but reflects the animal's location in the room. When we rotated the cab  $90^\circ$  counterclockwise, the place-related neural activity still remained, although it was decreased (Fig. 2C,  $\gamma = 0.475$ ,  $P < 0.05$ ). This means that the place-correlate of neural activity cannot simply be ascribed

to responses to specific objects visible outside the cab; the place-related neural activities remained similar although the monkey faced a different scene when it was rotated  $90^\circ$  counterclockwise. Of 22 place-related neurons tested intensively, the activity of 19 neurons corresponded to the above description.

Fourteen neurons displaying place-related activities were further analyzed when the experimenter controlled the moving cab without imposing any operant task on the monkey. This was compared to results obtained when the animal

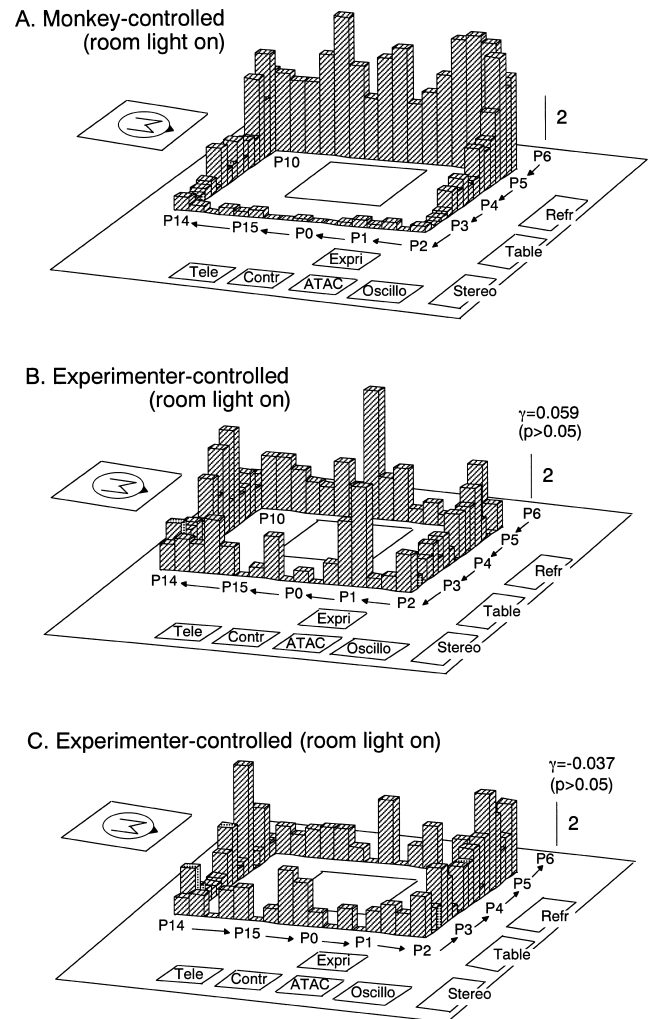


Fig. 1. Profiles of place-related neural activity of a monkey HF in the monkey- and experimenter-controlled conditions. Neuronal activity during the spatial moving task in each location is depicted. (A) The average of the first three laps in the monkey-controlled condition. Direction of the cab and the monkey is also illustrated, facing west. (B) The experimenter-controlled condition (clockwise). (C) The experimenter-controlled condition (counterclockwise). The cab was motorized to move in a  $2.5 \times 2.5$  m field. The monkey normally faced west during the spatial moving task. The entire apparatus was in a  $5 \times 6$  m experimental room. Vertical bars, spikes/s;  $\gamma$ , Pearson's correlation coefficient between control and various conditions; Expri, an experimenter; Refr, a refrigerator; Stereo, a stereotaxic apparatus; Oscillo, an oscilloscope; ATAC, a signal processor (ATAC 3700); Contr, a device controller; Tele, a telemeter receiver. Inset in left, direction of the monkey (M) during the spatial moving task is indicated.

solved the task and moved the cab around the room (e.g. control condition in Fig. 1A). Under the experimenter-controlled condition, the experimenter translocated the cab successively, with no task requirements, along the same route used in the normal condition. The cab stopped at the corners, where a few drops of juice reward were delivered to the monkey. In this condition, the place-related neural activity at P10–P6 disappeared (Fig. 1B,C); in this case, not only did the average activity at P10–P6 decrease, the average activity outside, at P5–P0 and P15–P11, increased. In Fig. 1B, in the experimenter-controlled condition (clockwise), the average neural activities at P10–P6, and outside of P10–P6 were 1.68 and 1.42 spikes/s, respectively. In Fig. 1C, in the experimenter-controlled condition (counterclockwise), the average neural activities at P10–P6 and outside of P10–P6 were 1.32 and 1.77 spikes/s, respectively.

The correlation coefficient between place-related activ-

ities in the monkey- and experimenter-controlled conditions was not significant (Fig. 1B,  $\gamma = 0.059$ ; Fig. 1C,  $\gamma = -0.037$ ;  $P > 0.05$ ). Similarly, the place-related neural activity of the other 11 HF neurons turned out to be obscure ( $P > 0.05$ ) under the experimenter-controlled condition, and the remaining two neurons retained similar place-related activity ( $P < 0.05$ ).

Rat HF place-cells behave in a slightly different manner; they fire in a specific location during the animal's spatial navigation. They also fire in a specific manner during the translation of the animal by the experimenter [3,8–10,15], which is similar to the experimenter-controlled condition in our present experiment. However, restraining procedures preventing any locomotion of the subject suppress place-specific firing of the rat HF [3]. Locomotion is probably an important source of information for path integration in rodents [4]. In the present study, we demonstrated that the monkey HF place-related activity is more sensitive to differences in the experimental situation; in the experimenter-controlled condition, place-correlates became strikingly vague in comparison with the monkey-controlled condition. In our experimental setup for monkeys, locomotion is not a primary concern for place-correlates: throughout the experiment with our head-restraining system, the monkey's actual locomotion was constrained. The place-related activity proves to be obscure in the experimenter-controlled condition. The results imply that the animal's action, which implicitly requires interaction between the subject and its environment and consequently requires attention to the environment, but does not necessarily correspond to its fine locomotion, influences the place-correlates. The attention required just for driving was insufficient to maintain the place-correlates since place-related activity was not restored in darkness (Fig. 2A). The dissociation between the primate and the rodent might be ascribed to differences in internal representations of space. Further studies are necessary to prove or disprove this theory.

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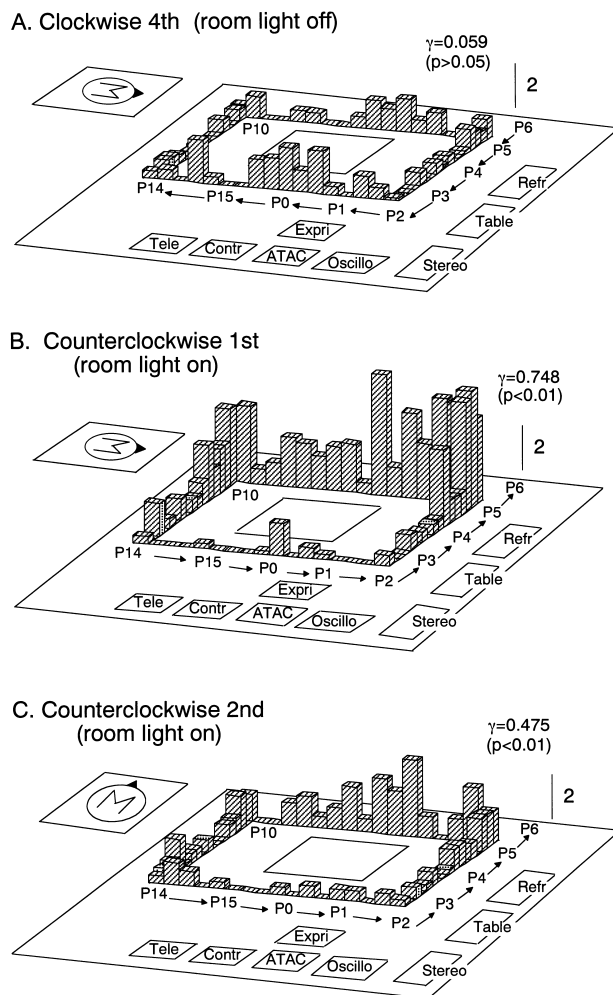


Fig. 2. Activity of a place-related neuron during various conditions. This neuron is the same depicted in Fig. 1. (A) The same clockwise route but the room light is extinguished. (B) The counterclockwise route with the room light turned on again. (C) The counterclockwise route but the cab and the monkey are rotated  $90^\circ$  counterclockwise, now facing the north. Other descriptions as for Fig. 1.

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