RAPID COMMUNICATION

Functional Differentiation Along the Anterior-Posterior Axis of the Hippocampus in Monkeys

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Colombo, Michael, Tom Fernandez, Katsuji Nakamura, and Charles G. Gross. Functional differentiation along the anterior-posterior axis of the hippocampus in monkeys. J. Neurophysiol. 80: 1002–1005, 1998. We tested whether the primate hippocampus was functionally heterogeneous along its anterior-posterior axis. Two monkeys were trained on both a spatial and nonspatial memory task and the incidence of spatial and nonspatial delay activity in the anterior, middle, and posterior hippocampus was noted. Spatial delay activity (activity in the delay period after the sample stimulus on the spatial memory task) was more common in the posterior than the anterior hippocampus, whereas nonspatial delay activity (activity in the delay period after the sample stimulus on the nonspatial memory task) was evenly distributed throughout the hippocampus. Furthermore, delay neurons in the anterior hippocampus exhibited scalloping delay activity, whereas those in the middle and posterior hippocampus did not. These findings suggest that the hippocampus is functionally heterogeneous and that the posterior regions may be more important for processing spatial information, whereas the anterior regions may be more important for directing or coding movements to points in space.

INTRODUCTION

A review of the hippocampal literature reveals a range of impairments that are difficult to collapse under the umbrella of a single theory. For example, views that the hippocampus is only critical for memory (Eichenbaum et al. 1994; Squire 1992) or cognitive mapping (O’Keefe and Nadel 1978) often fail to consider the well-documented mnemonic and nonspatial impairments that follow hippocampal lesions (Gray and McNaughton 1983) as well as the many findings that hippocampal unit activity is modulated by movement-related factors (Foster et al. 1989; Sharp et al. 1995). Recently, there has been some evidence that the dorsal hippocampus of rats may be more important for the processing of spatial information than the ventral hippocampus (Jung et al. 1994; Moser et al. 1993), and there has been suggestive evidence that the same may be true in primates (Colombo and Gross 1994, 1996; Watanabe and Nike 1985). These findings raise the possibility that the hippocampus may be functionally heterogeneous and that different functions may fall under the jurisdiction of different regions within the hippocampus. The goal of the current experiment was to test for functional differentiation within the primate hippocampus. In particular, we examined whether the posterior hippocampus in monkeys, which is considered equivalent to the dorsal hippocampus in rats (Witter 1993; Witter and Amaral 1991), was more important for processing spatial information than the anterior hippocampus.

METHODS

Two monkeys (Macaca fascicularis) were trained on both spatial and nonspatial delayed matching-to-sample (DMS) tasks. The stimulus for the spatial DMS task consisted of a 16-lobed pattern, whereas the stimuli for the nonspatial DMS task consisted of a picture of a monkey face and a 4-lobed pattern. The DMS procedure was identical for both tasks. At the end of a 10-s intertrial interval (ITI), a high-frequency tone was presented for 0.2 s, followed by the presentation of a sample stimulus for 1 s on either the left or right side of the monitor. The sample stimulus was then turned off and a 5-s delay period followed. At the end of the delay period, two comparison stimuli were presented for 2 s, one on the right side and the other on the left side of the monitor. A response to the correct comparison stimulus resulted in a reward (cranberry juice), followed by the ITI. A response to the incorrect comparison stimulus, or failing to press within the 2-s response window, resulted in a 10-s time-out period, which was then followed by the ITI.

During the comparison period on the spatial DMS task, the 16-lobed pattern stimulus was presented on both sides of the monitor and the monkey had to respond to the stimulus that occupied the same position as the sample stimulus. During the comparison period on the nonspatial DMS task, both the 4-lobed pattern and monkey face stimuli were presented, and the monkey had to respond to the stimulus that matched the sample stimulus. A session consisted of either 80 or 96 trials, with an equal number of spatial and nonspatial DMS trials randomly intermixed. On completion of behavioral training the animals were prepared for alert recording by implanting a head restraint post and recording well (Desimone and Gross 1979). Extracellular activity of single isolated neurons was recorded by using tungsten microelectrodes.

We recorded from a total of 94 neurons. Of these, 34 were located in the anterior regions (A11–A15), 40 in the middle regions (A7–A11), and 20 in the posterior regions (A3–A7) of the hippocampus (Szabo and Cowan 1984). We compared the percentage of neurons displaying spatial and nonspatial delay activity across these areas. A delay neuron is a neuron that fires more (or less) during the delay period of a DMS task than during the ITI (baseline) period. A number of investigators have suggested that delay activity represents a neural correlate of memory (Colombo and Gross 1994; Funahashi et al. 1989; Foster and Jervey 1982; Miyashita and Chang 1988). For each isolated neuron, the average activity in the 10-s ITI (baseline) period was compared with the average activity in the 5-s delay period by using paired t-tests (2-tailed, P < 0.01). Only correct trial data were analyzed. Spatial delay activity occurred...
sponded in the delay period after the spatial stimulus and to either one or both of the nonspatial stimuli.

In contrast to delay activity in inferior temporal cortex, which often occurs in the presence of activity to the sample stimulus, delay activity in the hippocampus appears to be much less dependent on sample activity (Colombo and Gross 1994). The relationship between sample activity and delay activity was again examined in the current study. Delay activity was considered to be related to sample activity if, for example, a neuron fired significantly during the delay period and the presentation of the sample stimulus. In line with our previous findings, there were approximately an equal number of sample-dependent and sample-independent instances of delay activity; this was the case for spatial (50 vs. 50%), nonspatial face (55.6 vs. 44.4%), and nonspatial pattern (52.4 vs. 47.6%) delay activity.

The percentage of neurons displaying spatial and nonspatial delay activity in the anterior, middle, and posterior regions of the hippocampus is shown in Fig. 2. Planned comparisons revealed that spatial delay activity was more prominent in the posterior hippocampus than in the anterior hippocampus (Fisher’s exact test, one-tailed, $P \leq 0.05$). There were no differences in the number of neurons displaying spatial delay activity between the anterior and middle ($P = 0.07$) or between the middle and posterior ($P = 0.26$) regions of the hippocampus. In contrast, nonspatial delay activity was evenly distributed throughout the hippocampus. Planned comparisons revealed no significant differences in the number of neurons displaying either of the two types of nonspatial delay activity across the anterior, middle, and posterior regions of the hippocampus (all $P_s \geq 0.08$). Both monkeys showed a similar pattern of results.

In a previous study (Colombo and Gross 1994) we noticed that delay neurons in anterior hippocampus exhibited scalloping activity; that is, the magnitude of the delay activity increased as the delay progressed. Some researchers have suggested that scalloping delay activity may represent a neural correlate of an imminent response (Fuster 1993; Halgren 1991). Given that hippocampal unit activity can be modu-

**FIG. 1.** Coronal reconstructions of the anterior, middle, and posterior recording sites for the 2 monkeys.

**FIG. 2.** Distribution of spatial and nonspatial delay activity across the anterior (A), middle (M), and posterior (P) regions of the hippocampus.
and nonspatial delay activity data with position (3: anterior We thank Dr. Harlene Hayne for statistical assistance.

The dotted line represents the baseline (ITI) activity level. Only data from inhibitory delay neurons are shown.

related by movement-related factors (Foster et al. 1989; Sharp et al. 1995), we were interested in whether there were any regional differences in the expression of scalloping activity by hippocampal delay neurons. Delay activity across the 5-s delay period was collapsed into 1-s bins and plotted as a change in activity compared with the ITI (baseline) activity level. Owing to the small number of excitatory delay neurons (n = 12), we restricted this analysis to inhibitory delay neurons (n = 29). The results are shown in Fig. 3. Repeated-measures analysis of variance conducted on both the spatial and nonspatial delay activity data with position (3: anterior vs. middle vs. posterior) and delay period (5: bins 1-5) as factors revealed a significant position x delay period interaction effect both for neurons displaying spatial delay activity [F(8, 92) = 3.21, P < 0.01] and nonspatial delay activity [F(8, 108) = 4.11, P < 0.01]. Separate univariate tests showed that only for the anterior spatial delay activity [F(4, 20) = 4.57, P < 0.01] and the anterior nonspatial delay activity [F(4, 32) = 5.08, P < 0.01] was there a significant decrease in activity (i.e., became more inhibitory) across the 5-s delay period. In contrast, there was no evidence that the magnitude of delay activity varied across the delay period for either spatial or nonspatial delay activity in the middle or posterior hippocampus (all Ps > 0.07). Thus scalloping delay activity was a feature of delay neurons in the anterior hippocampus but not in the middle or posterior hippocampus.

**DISCUSSION**

Two main findings emerged from the current study. First, spatial delay activity was predominantly located in the posterior rather than the anterior hippocampus, whereas nonspatial delay activity was evenly distributed throughout the hippocampus. Second, scalloping delay activity was noted in the anterior rather than the middle and posterior hippocampus.

The finding that the percentage of delay neurons displaying spatial delay activity increases from anterior to posterior suggests that in monkeys the posterior hippocampus is more concerned with processing spatial information than the anterior hippocampus. This finding is consistent with literature on research in rats (Jung et al. 1994; Moser et al. 1993) suggesting that the dorsal hippocampus (equivalent to the primate posterior hippocampus) is also more involved with processing spatial information than the ventral hippocampus (equivalent to the primate anterior hippocampus).

In addition to playing a major role in processing spatial information, there is also considerable evidence that unit activity in the hippocampus is modulated by movement-related factors (Foster et al. 1989; Halgren 1991; Sharp et al. 1995) and that the hippocampus may be important for learning about directing movements to positions in space (Gaffan 1985). To the extent that scalloping delay activity reflects a neural code of a response, our findings suggest that the anterior hippocampus may play a greater role in the motor aspects of spatial behavior than the posterior hippocampus. The fact that scalloping delay activity has been seen in the frontal cortex of monkeys (Fuster 1993; Miller et al. 1996) [a region strongly implicated in response planning and motor control (Boussaoud et al. 1996; Petrides 1994)] and that the anterior hippocampus has stronger projections with frontal cortex than the posterior hippocampus (Barbas and Blatt 1995; Carmichael and Price 1995) further supports this view.

In conclusion, views that the hippocampus is critical for memory or spatial processing need not conflict with findings that the hippocampus has nonmnemonic, nonspatial, and movement-related functions. Our findings suggest that the hippocampus is functionally heterogeneous, and that spatial and movement-related aspects of hippocampal function may be primarily under the jurisdiction of the posterior and anterior regions of the hippocampus, respectively.

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