HIGH-FREQUENCY TRANSITIONS IN CORTICAL SPIKE TRAINS RELATED TO SHORT-TERM MEMORY

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Abstract—Single-unit spike trains recorded from parietal cortex of monkeys performing a tactile short-term memory task show characteristic fluctuations (transitions) in their firing frequency that are related to memory. Spike trains recorded during the memory period, when the animal must retain information for the short term, show a higher rate of such transitions than spike trains recorded during intertrial baseline periods. In the present study, an analysis of multiple temporal resolutions over which these transitions are observed reveals that the memory-related transitions occur most prominently in the 25–50 Hz range. The results of this study suggest that, in the monkey, high frequency fluctuations of neuronal discharge in the parietal cortex are correlated with haptic short-term memory. The presence of such fluctuations are also consistent with theoretical models of short-term memory. © 1998 IBRO. Published by Elsevier Science Ltd.

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Neurons in the cerebral cortex receive numerous local and remote connections of both excitatory and inhibitory nature. Supposedly, cells of an activated memory network of the cortex are subject to increased presynaptic inputs. Because of such processes as temporal and spatial summation, that increase of inputs can be expected to result in an increase of discontinuities in postsynaptic firing. Accordingly, cells recorded from parietal cortex of monkeys performing a haptic short-term memory task show a higher incidence of firing discontinuities (transitions) while the animal must retain tactile information, and thus presumably while a tactile memory network is active. 2 In addition to temporal information, and thus presumably while a tactile memory network is active. 2

Changes in transition rate may not be evident in raw firing. In many cells, it is only after the spike train has been appropriately filtered that those changes can be seen. An outstanding question that appropriate filtering can answer is the frequency domain in which neuroelectrical potentials vary in short-term memory. Experimental data and simulations have implicated 20–70 Hz activity in higher cognitive operations, such as the perceptual binding of stimulus features 8,11,19 and attention, 14,15 related to the activation of memory networks. It is thus reasonable to expect that, during the performance of an active short-term memory task, transitions will occur at temporal resolutions that detect frequency and pattern changes in that range. The present work was intended to verify this expectation.

EXPERIMENTAL PROCEDURES

Animal care and surgical procedures conformed to institutional guidelines-approved by the Animal Research Committee at the University of California, Los Angeles. For present analysis, spike trains were selected from units recorded in the parietal cortex of two male rhesus monkeys (Macaca mulatta) performing a memory task for another study. Twenty-six units were selected for this study because their spike trains during short-term memorization differed in transition rate from baseline condition. During recording, the animal performed a delayed tactile matching-to-sample task. A trial began with a click signalling that the sample (a rod) was in front of the animal, accessible to touch but out of sight. The animal's palpation of the sample rod was followed by a delay period (memory period). At the end of the delay, a second sound signalled that two rods with identical dimensions but different surface features were accessible for choice; one of them was the sample. The monkey's correct choice, that is, a pull at the sample rod, was rewarded with fluid reinforcement delivered to the animal's mouth. The sample rod and its relative position at the choice were changed randomly from trial to trial. The animal was trained to rest its operating hand on a rounded metal ledge at all times, except for sample touch or choice. The removal of the hand from the ledge at other times automatically aborted the trial. The animal's performance of the task was monitored by video cameras. The selected units were mainly from hand-representation areas of somatosensory cortex (Brodman's areas 3a, 3b, 1, and 2). Cellular activity was analysed using a binary mapping technique that detects differences in spike trains with respect to their frequency and/or pattern of firing discontinuities. 2

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Briefly, this technique divides time into bins of equal duration and obtains binary sequences from the spike trains by assigning 1's to bins containing spikes and 0's to bins not containing any (Fig. 1). Spike trains for a given cell are then ranked from highest to lowest with respect to the number of transitions between 1's and 0's in the binary sequence. In this study, each spike train was mapped with 139 different bin sizes (levels of resolution), using all integer bin sizes between 1 and 140 ms.

For every given bin size, a non-parametric ranks test was used to determine transition-number differences between baseline and delay periods in the spike trains from the selected units. The degree of significance, as determined by that test, was expressed by a U-value; the larger the absolute value of U, the greater the confidence of significance. A statistical adjustment was made to take into account the multiple bin sizes used.

A an analysis was carried out to determine at which temporal resolutions the transition differences between baseline and delay periods were most prominent. Histograms were obtained for: (i) the number of cells showing significant differences in transitions with each of the bin sizes, (ii) the distribution of the most significantly differentiating bin sizes. In order to further elucidate the role of transition changes in cognitive operations, transition differences were studied in the delay period as a function of the stimulus in short-term memory.

RESULTS

The firing frequency of the 26 cells of the database ranged between 4 and 50 Hz. Because of the selection criterion, the spike trains of all cells showed significant differences in transition rate between baseline and delay periods. In two of those cells (8%) such spike-train differences were also observed between trains from delay periods depending on the memorandum.

Figure 2 shows the distribution of cells by bin size at which significant differences in transition number between delay and baseline periods were observed. The bin sizes at which the greatest number of cells...
show those differences fall in the range between 21 and 40 ms, with a maximum (20 out of 26 cells) at 28 ms. In each of the 26 cells, the particular bin was determined at which the greatest degree of differentiation occurred between baseline and delay. The distribution of such bins is shown in Fig. 3, where the resolution range has been partitioned to fit one entire interval to the 21 to 40 ms range (48 to 25 Hz). In 13 of the 26 cells (50%), the most significant discrimination between baseline and delay occurs in that interval (P <0.01, binomial distribution).

Based on the finding of increased transitions in delay periods, and on the evidence that most cells differentiated delay from baseline at 28 ms resolution, we attempted to verify that spike trains, especially during the delay, contained patterns giving rise to high transition rates at that resolution. Specifically, we focused on the alternating binary pattern yielding the highest transition rate (01010101). In seven out of 20 cells that pattern was significantly present at the 28 ms resolution, and more prevalent in delay than baseline (Fig. 4A).

**DISCUSSION**

The memory-related changes in transient firing frequency between baseline and delay periods indicate changes in the state of activity of memory networks. The present study shows that those changes occur most frequently in the 25–50 Hz range. The increased frequency of transitions during the memory period (delay) supports the hypothesis that in that period the cells are subject to increased inputs from the network(s) to which they belong. These inputs may come, for example, from the sectors of the cortical network representing associated properties of the memorandum.

Increased inputs upon a cell in an active memory network may be expected to impose constraints in the

**Fig. 4.** Binary mapping of spike sequences from two cells (A and B) that differentiated baseline and delay periods by transition number at 28 ms resolution (the maximum in Fig. 2). Mapped trains were scanned for sequences of alternating 0’s and 1’s, which give high rate of transitions, as observed in delay periods. Only sequences of at least eight digits in length were considered (i.e., 01010101). The significance of that pattern was assessed by comparing the number of its occurrences, in the binary mapping of any given train, with that of its occurrences in the binary maps of 1000 randomly shuffled versions of the interspike interval sequence of that train.\(^3,7\) If the number of occurrences in the original mapped train exceeded that found in 95% of the mappings of the shuffled versions, the presence of the pattern was considered significant. The alternating pattern may be occasionally replaced (cell B) by series of filled bins (1111...). Applying the finer resolution of 13 ms binning reveals a pattern of alternation that corresponds to 40 Hz firing frequency.
temporal structure of the cell’s firing. As a result, changes in that temporal structure will arise which the analysis of the binary sequence may reveal by virtue of its filtering property. A complete characterization of the patterns observed in binary sequences would require further analysis than that conducted in this study. However, the binary mapping at a resolution yielding higher transitions in short-term memory reveals at least one periodic pattern, either as expression of periodic spiking or bursting (Fig. 4).

This is consistent with unit behaviour in computational models (e.g., see Refs 20 and 24), where active short-term memories are sustained by re-entry of impulses in recurrent cortical networks. The activity of the units in these models shifts between frequency attractors. Viewed in the context of such models, the increases in transitions observed during delay periods of visual or tactile memory tasks may be at least partly a function of a network’s activity shifting between these attractor states. Input from subcortical structures involved in perception, such as the thalamus,13 could also contribute to the generation of periodic transitions of the type shown in Fig. 4. Further, intrinsic cellular mechanisms are another potential source of those transitions.4,6,10,12,17,21

All cells used in the present study differentiated between baseline and delay on the basis of transition number differences. However, it is difficult to determine which aspect of memory the transitions reflect. The fact that the majority of cells do not show memorandum-specific transition differences in delay periods suggests several possible interpretations. First, a given cell’s activity may be specific for attributes that are common to the two memoranda of the task. This might reflect binding of those associated features in memory, much as similar binding (of sensory stimuli) has been suggested in perception.3,11,16,19 It is possible that activity generated by common attributes overshadows the activity from specific memorandum features. It is also possible that the transition differences observed between baseline and delay near the 40 Hz resolution are associated with attention, which is a necessary requirement for performance of a memory task. This interpretation is consistent with recent results obtained by studies of local field potentials in somatosensory areas of the cortex.14,15,22

**CONCLUSION**

The activity of single neurons recorded from S1 in monkeys show differences in firing fluctuations that are related to short-term memory. These fluctuations, which are generally higher during short-term memory, are mainly observable in the 21 to 40 ms resolution range. This finding is consistent with theoretical models of short-term memory.

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