

Neuronal correlates of visual time perception at brief timescales

J. Patrick Mayo^{a,b,1} and Marc A. Sommer^{a,c}

^aDepartment of Neuroscience, Center for Neuroscience at the University of Pittsburgh, and Center for the Neural Basis of Cognition, Pittsburgh, PA 15213; ^bDepartment of Neurobiology, Harvard Medical School, Boston, MA 02115; and ^cDepartment of Biomedical Engineering, Center for Cognitive Neuroscience, and the Duke Institute for Brain Sciences, Duke University, Durham, NC 27708

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Successful interaction with the world depends on accurate perception of the timing of external events. Neurons at early stages of the primate visual system represent time-varying stimuli with high precision. However, it is unknown whether this temporal fidelity is maintained in the prefrontal cortex, where changes in neuronal activity generally correlate with changes in perception. One reason to suspect that it is not maintained is that humans experience surprisingly large fluctuations in the perception of time. To investigate the neuronal correlates of time perception, we recorded from neurons in the prefrontal cortex and midbrain of monkeys performing a temporal-discrimination task. Visual time intervals were presented at a timescale relevant to natural behavior (<500 ms). At this brief timescale, neuronal adaptation—time-dependent changes in the size of successive responses—occurs. We found that visual activity fluctuated with timing judgments in the prefrontal cortex but not in comparable midbrain areas. Surprisingly, only response strength, not timing, predicted task performance. Intervals perceived as longer were associated with larger visual responses and shorter intervals with smaller responses, matching the dynamics of adaptation. These results suggest that the magnitude of prefrontal activity may be read out to provide temporal information that contributes to judging the passage of time.

vision | frontal eye field | superior colliculus | macaque | latency

Systems neuroscience research has focused on the spatial aspects of vision, including form, orientation, and size (1, 2). However, the role of time in vision is no less important. Research on the temporal aspects of primate vision has largely consisted of studies of the temporal dynamics of neural activity in the early stages of visual processing, where neurons are exquisitely sensitive to changes in spatial and temporal frequency (3, 4). Neuronal correlates of visual timing in higher-order visual areas, and potential associations between that activity and the perception of timing, remain unexplored.

A major consideration when studying primate vision is that it is interrupted by saccadic eye movements. Consequently, each “snapshot” of the visual world, during an intersaccadic interval, is less than a half-second long (5). The accurate perception of time intervals at such brief timescales is important in itself (e.g., for estimating the speed of briefly appearing objects) and is elemental for longer timing judgments that span multiple saccades. However, despite a growing interest in time estimation in the visual system (6), few experiments have studied it at subsecond timescales.

Our overall goal was to determine the relationship between neuronal activity and the perception of visual timing at subsecond timescales. The simplest possibility is that the latency of sensory responses dictates subsecond temporal perception. However, this straightforward hypothesis is complicated by the fact that visual time perception can vary on the order of tens to hundreds of milliseconds (7), even though stimulus-evoked visual activity is timed precisely across brain regions (<10 ms) (8, 9). Therefore, additional factors, such as the strength of responses, may influence time perception.

The encoding of time by response strength is supported by psychophysical studies showing that stimulus changes that typically lead to increased firing rates also lead to longer time judgments, but those eliciting relatively lower firing rates lead to shorter judgments (for review, see ref. 10). Furthermore, at subsecond timescales, changes in response strength predominate; a ubiquitous property of sensory neurons is adaptation, in which responses to sequential stimuli increase with the time between stimuli (11). Inherent to brief sensory adaptation is an intrinsic strength code of time (12–14). Thus, adaptation-like changes in response strength could contribute to the perception of brief time intervals in multiple sensory modalities.

We tested whether the timing or the strength of visual activity covaried with changes in time perception. Monkeys reported the relative amount of time between two flashes of light presented at intervals <500 ms while we recorded the activity of single neurons in the prefrontal cortex or, for comparison, the midbrain. Surprisingly, we found that the strength of prefrontal responses, not their timing, correlated with the animals’ perception of time. Strength changes matched those naturally present in adaptation: just as longer time intervals elicit larger second responses and shorter intervals elicit smaller responses, intervals perceived as longer and shorter were associated with larger and smaller second responses, respectively. This effect was not evident in midbrain neurons despite otherwise similar response properties. Our results suggest that time-interval perception is not dictated by neuronal response timing but is influenced strongly by systematic changes in neuronal response magnitude in the prefrontal cortex, and likely in other visual areas.

Results

Monkeys Are Capable of Fine Temporal Discrimination. Monkeys were trained to perform a time-interval discrimination task (Fig. 1A). On each trial, we varied the amount of time between two flashes of light [stimulus onset asynchrony (SOA): 250–450 ms at 16.7-ms intervals] presented during fixation. This range of times was chosen to approximate timescales regularly encountered by the visual system during natural behavior, and to elicit adapted yet easily detectable neuronal responses (15, 16). Monkeys were rewarded for making a saccade to one of two choice targets, “short” or “long,” based on that trial’s SOA relative to a learned reference interval of 350 ms. Although SOAs incremented by only ~17 ms and varied within a total range of 200 ms, monkeys readily discriminated the time intervals such that performance scaled with task difficulty (i.e., proximity to the reference interval) (Fig. 1B). Mean Weber fractions across SOAs were 0.11 and 0.14 for monkeys K and C, respectively, nearly equivalent to those of human subjects in comparable tasks (17, 18). These

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¹To whom correspondence should be addressed. E-mail: patrick_mayo@hms.harvard.edu.

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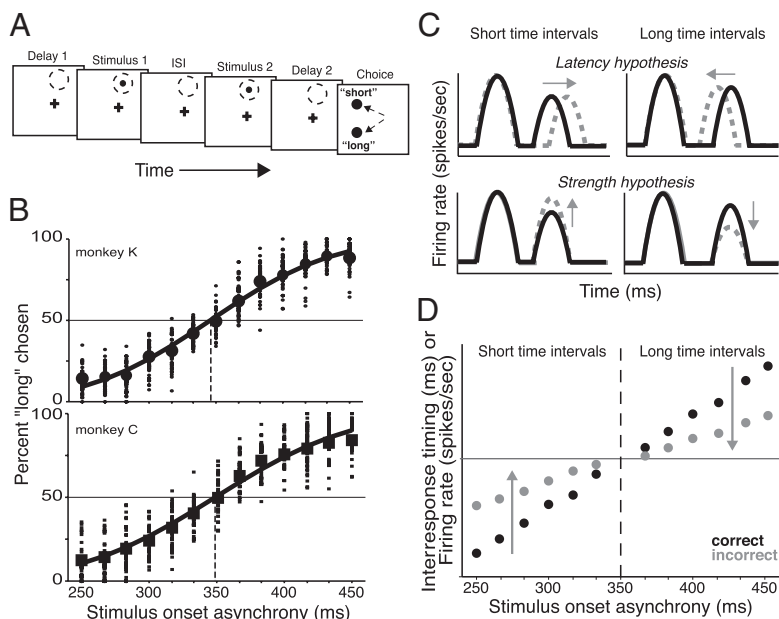


Fig. 1. Temporal-discrimination task, performance, and predictions. (A) Monkeys fixated a spot (cross) followed by a randomized delay period (Delay 1). Two identical stimuli (Stimulus 1 and 2) flashed successively in the receptive field (dashed circle), separated by an ISI. ISI plus the duration of stimulus 1 is equivalent to the SOA. Monkeys reported whether the SOA was shorter or longer than 350 ms by making a saccade to one of two choice targets in the ipsilateral hemifield. (B) Percentage of “long” choices as a function of presented time interval for monkey K (Upper; circles) and C (Lower; squares) over all recording sessions. Task difficulty increases as SOAs approach 350 ms. Small symbols indicate performance in individual sessions. Cumulative Gaussian curve was fit to the average performance (large symbols) across SOAs. Vertical dashed line indicates point of subjective equality. (C) Predicted responses of latency (Upper) and strength (Lower) hypotheses are shown for short (Left) and long (Right) time intervals. Schematics of average activity are shown for correct trials (black traces) and incorrect (dashed gray traces) trials. Arrows indicate the direction of change predicted for incorrect trials. (D) Predicted changes in the inter-response timing or strength of the population’s second visual response (both on ordinate) at each SOA (abscissa).

results extend previous findings of visual time discrimination in monkeys (6, 19) and demonstrate that they can perform fine temporal discrimination at brief timescales.

Predicted Changes in the Timing and Strength of Neuronal Activity.

We recorded from visually responsive neurons in the frontal eye field (FEF) in the caudal prefrontal cortex. The FEF contains visuomotor and cognitive activity (20, 21) that has been shown to correlate with visual perception (22–24), suggesting that it may play a central role in perisaccadic distortions of time (17). The FEF also receives inputs from the basal ganglia and cerebellum (25), two structures thought to play key roles in time keeping (26, 27). We compared neuronal activity in trials in which the time interval (i.e., SOA) was identical but the monkey’s reported percept (i.e., “short” or “long” relative to the reference interval) differed.

If the latency hypothesis is true and the perceived time between stimuli is represented by the time between visual responses, then we would expect to see changes in the interresponse times that correspond to the monkey’s behavioral report. Thus, when short time intervals (<350 ms) are presented, the interresponse time would be longer on incorrect trials, corresponding to the erroneous “long” choice, compared with that of correct trials (Fig. 1C, Upper Left). For long time intervals (>350 ms), the opposite result is expected; the interresponse time on incorrect trials would be shorter than that of correct trials (Fig. 1C, Upper Right). Across time intervals, we would then expect to see contrasting directions of change in interresponse timing as a function of task performance on either side of the 350-ms reference interval (Fig. 1D).

The strength hypothesis predicts that the magnitude, not the timing, of the visual response should correspond with the behavioral report. Specifically, the second visual response should vary in size but the first response remains relatively constant, matching the strength changes seen during adaptation (15). Thus, when presented with a short interval, the monkey should erroneously deem it “long” if the second visual response is relatively large compared with responses on correct trials (Fig. 1C, Lower Left). Conversely, when presented with a long interval, erroneous “short” judgments should correlate with relatively smaller second visual responses (Fig. 1C, Lower Right). Again, we would expect to see an inflection point around the reference interval, indicating differential strength changes in the second visual response as a function of task performance (Fig. 1D).

Response Strength in the Prefrontal Cortex Correlates with Time Perception.

Fig. 2 shows the responses of three individual FEF neurons to various time intervals. An effect common to all three neurons, for most time intervals, was a systematic difference in the strength of second visual responses in correct vs. incorrect trials. In short-interval trials (red), second visual responses were generally larger when the monkeys incorrectly judged the interval as “long” (lighter traces) versus when they correctly judged them as “short” (darker traces). In long-interval trials (blue), the effect was reversed. The same changes in response strength with time estimation performance were present at the FEF population level as well (Fig. 3). On short-interval trials, second visual responses were larger in incorrect trials compared with correct trials using identical stimuli ($P < 0.001$) (Fig. 3A, Right). Conversely, second visual responses were smaller in incorrect long trials compared with their correct counterparts ($P = 0.003$) (Fig. 3B, Right). First visual responses showed no significant changes between correct and incorrect trials ($P > 0.05$) (Fig. 3A and B, Left). Relative measures of the visual responses (second – first) were subject to uncorrelated variability between responses, yet they still yielded a significant effect for short trials ($P = 0.002$) and a trend for long trials ($P = 0.08$). In sum, larger second responses were associated with longer time percepts and smaller responses with shorter percepts, consistent with the strength hypothesis.

The strength hypothesis also was supported at the level of individual time intervals across FEF neurons. Second visual responses were larger on average in incorrect trials for all short time intervals (Fig. 3C, Left half) and smaller, as predicted, for nearly all long time intervals (Fig. 3C, Right half). Pooled differences in second response strength grouped by short and long choices were each significantly different from zero in the directions predicted by the strength hypothesis ($P = 0.002$; short median = -2.62 ± 0.82 spikes per second, long median = 3.15 ± 0.99 spikes per second, $n = 6$, \pm SE of median). In contrast, time judgments were unrelated to changes in the first visual responses ($P > 0.05$) or in the interresponse timings ($P > 0.05$) (Fig. 3D; see also *Response Timing Does Not Account for Changes in Time Perception*, below).

When the reference interval of 350 ms was presented, there was no correct answer and reward was randomly dispensed at a 50% rate. Average performance at the reference interval was near chance (Fig. 1B), and trial-by-trial performance was unrelated to neuronal activity (no difference in second visual responses as

Behavioral studies that presumably manipulate the size of neuronal visual responses elicit strong time illusions. For example, the time between stimuli presented just before a saccadic eye movement is perceptually compressed relative to baseline measures (17). Our results suggest that presaccadic suppression of visual activity (44) leads to a relatively diminished second visual response associated with a shorter percept of time. A similar understanding of the relationship between stimulus changes and response dynamics can also explain contrast-dependent compression of time judgments, as well as elongation of time perception during rapid serial visual processing (45).

Visual response magnitudes must be read out to affect temporal judgments and provide an estimate of time. Because the nervous system's ability to integrate spike rates is well-established, one attractive feature of the strength hypothesis is that it does not invoke specialized neural circuitry. In this way, magnitude-encoding of temporal intervals in cortical neurons may be one of many simultaneous, overlapping timing processes in the brain (46), thus providing a physiologically plausible alternative to dominant "central clock" models of time perception (47).

Methods

Two adult male monkeys (*Macaca mulatta*) were surgically prepared for neuronal recordings in the FEF and SC. All experiments were conducted under the supervision of the University of Pittsburgh Institutional Animal Care and Use Committee and complied with the guidelines of the United

States Public Health Service Guide for the Care and Use of Laboratory Animals. The FEF and SC were identified through stereotaxic coordinates, structural MRI, and established properties of neuronal activity and stimulation-evoked saccades. Receptive field centers were mapped with memory-guided or visually guided saccades using stimuli presented at eight target directions and at least eight amplitudes (1–35°). Eye position was monitored using a scleral search coil and timings of stimuli were documented with a photodiode.

On each trial, monkeys viewed two sequential stimuli presented in the receptive field center. The monkeys then made a two-alternative forced-choice temporal discrimination (Fig. 1A) by reporting whether the SOA (250–450 ms) was shorter or longer than a learned reference interval of 350 ms. To ensure that the monkeys judged the time between stimuli and no other temporal parameter, delay periods (randomized duration, range of 800 ms) preceded and followed presentation of the paired stimuli. Monkeys reported their percept ("short" or "long") by making a saccade to one of two targets in the ipsilateral visual hemifield. Liquid reward was dispensed for correct judgments. Action potential times, eye-position samples, photodiode output, and task-event timings were stored at 1-ms resolution for offline analysis.

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