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An internal clock for predictive saccades is established identically by auditory or visual information

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Abstract

Previously we have shown that repetitive predictive saccades to alternating visual targets are mediated by an internal clock. That is, when subjects track a periodic visual stimulus alternating at a high rate (a small inter-stimulus interval, ISI, of 500 or 833 ms), they use an internal estimate of stimulus timing to pre-program the eye movement timing. Auditory pacing tones at the same rate also generate predictive saccades. It is natural to ask if an identical internal clock is used to generate the predictive saccades in each case. We hypothesized that if subjects can use auditory information to establish an internal estimate of stimulus timing – as we demonstrated can be done with visual targets – then the distributions of predictive inter-saccade intervals should demonstrate the well-known “Scalar Property” for either Auditory Cued or Visual Cued stimuli: inter-saccade interval histograms should be almost identical when each is divided by its mean. However, when making reactive saccades to a pacing stimulus (at a low rate), there should be a difference in the timing statistics between Auditory and Visual pacing, due to differences in sensory processing. We report here that the variances of inter-saccade intervals at three predictive pacing rates (ISIs of 500, 833, and 1000 ms) are equivalent, whereas the variance for Auditory Cued Pacing was greater than that for Visual Cued Pacing during reactive saccades at two reactive pacing rates (ISIs of 1667 and 2500 ms). When the inter-saccade interval histograms at the predictive pacing rates were normalized, the distributions were nearly identical for both Visual and Auditory Cued Pacing, which means that the Scalar Property holds for predictive saccades from either pacing stimulus. These results suggest that (1) an internal timing reference (clock) can be established by either auditory or visual information, and (2) during predictive tracking the variability in saccade timing is due to the variability in the internal timing representation, while during reactive tracking the variability in saccade timing depends on the sensory modality used to trigger the saccades.

Keywords

prediction; timing; internal clock; visual; auditory

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Introduction

We have previously shown that repetitive predictive saccades made in response to alternating visual targets are mediated by an internal clock. That is, when subjects track a periodic visual stimulus alternating at a high rate (a small inter-stimulus interval, ISI, of 500 or 833 ms), they use an internal estimate of stimulus timing to pre-program the eye movements (Joiner & Shelhamer, 2006). The distributions of the inter-saccade intervals (time between saccades) at these predictive pacing rates demonstrate the Scalar Property (Gibbon, 1977; Gibbon, Malapani, Dale and Gallistel, 1997; Meck & Benson, 2002): the variance of the time estimate increases with the square of the mean. Thus, inter-saccade interval distributions (which during predictive tracking represent the distribution of the time estimates) at different rates are statistically indistinguishable when each is divided by its mean.

This relationship has been modeled by the following framework (Treisman, 1963; Gibbon et al., 1997; Meck & Benson, 2002): an internal estimate of a time interval is generated by integrating, over time, a signal which represents an internal counter. When the integrated signal reaches threshold (which specifies the required interval duration), a timed event occurs (in this case a saccade), and the integrator is reset to start a new cycle. Typically the integrated signal has a random component due to neural noise, and this leads to randomness in the event times (time estimates). More specifically, the longer the inter-event interval, the longer the integration time of the noisy signal, and hence the more variability there will be in the event times (Schöner, 2002). However, the variability of the time estimate is proportional to the interval length (Weber's Law) and thus the distributions of inter-event intervals for different interval lengths should be nearly identical when each is divided by its mean, demonstrating the Scalar Property. This is not the case when making reactive movements to a visual stimulus as we demonstrated for repetitive saccades made to targets alternating at a lower pacing rate (a large ISI of 2500 ms); in this case, the variability of the inter-saccade intervals is due to the variability in reaction time from trial to trial (the passage of time is not internally estimated) and thus the Scalar Property does not apply (Joiner & Shelhamer, 2006).

Other investigators have demonstrated differences in single saccadic responses to auditory and visual stimuli. For example, for horizontal targets less than 40 deg from the point of fixation, the reaction time for a localized auditory target is greater and more variable than that for a visual target at the same eccentricity (Zahn, Abel and Dell'Osso, 1978; Zahn, Abel, Dell'Osso and Daroff, 1979; Zambarbieri, Schmid, Magenes and Prablanc, 1982). In addition, for auditory targets, the mean reaction time decreases as the target eccentricity increases, whereas the opposite relationship is seen for visual targets (Yao & Peck, 1997; Zahn et al., 1978; Zambarbieri et al., 1982). Despite these differences, when tracking a repetitive visual or auditory stimulus alternating at a short ISI (for example 1000 ms), subjects make comparable predictive responses (saccade latency less than 100 ms) regardless of the sensory modality (Zambarbieri, Schmid and Ventre, 1987).

The purpose of this study was to utilize the Scalar Property to compare the inter-saccade interval distributions formed from repetitive saccade tracking when cued by different pacing modalities and at different pacing rates. Based on the findings described above, we hypothesized that if subjects can use auditory information to establish an internal estimate of target timing – as we demonstrated can be done with visual targets – then the distributions of (predictive) inter-saccade intervals at short inter-stimulus intervals should demonstrate the Scalar Property, for both auditory and visual stimuli. For example, the normalized inter-saccade interval distributions for auditory pacing at an ISI of 1000 ms should be statistically indistinguishable from the distributions from visual pacing at a smaller ISI. However, when making reactive saccades at a low pacing rate, there should be a difference in the timing statistics due to differences in the reactive response to the different sensory stimuli. That is, the normalized

inter-saccade interval distributions at reactive pacing rates should not be identical across different pacing rates within a stimulus modality (i.e., comparing visual-cued pacing at an ISI of 2500 to visual-cued pacing at an ISI of 1667 ms) or across different sensory cues within a pacing rate (i.e., comparing visual-cued pacing at an ISI of 2500 ms to auditory-cued pacing at the same ISI).

To test this hypothesis we recorded the eye movements of eight subjects during two pacing conditions: (1) Visual Cued Pacing – subjects tracked LED targets alternating between two fixed positions at a given ISI, (2) Auditory Cued Pacing – both LED targets remained illuminated and subjects made saccades between the two when signaled by a pacing tone from an overhead speaker. We tested two reactive (ISIs of 2500 and 1667 ms) and three predictive (ISIs of 556, 833, and 1000 ms) pacing rates. We report that the variances of the inter-saccade intervals at all predictive pacing rates were approximately equivalent, whereas the inter-saccade interval variance for Auditory Cued Pacing was typically greater than that for Visual Cued Pacing during reactive saccades at the lower pacing rates. When the inter-saccade interval histograms at the predictive rates were normalized, the distributions were nearly identical for both Visual and Auditory Cued Pacing. These results suggest that (1) an internal timing reference can be established by either auditory or visual information, and (2) during predictive tracking the variability in saccade timing is due to the variability in the internal timing representation, while during reactive tracking the variability in saccade timing depends on the sensory modality used to trigger the saccades.

Methods

General

The eye movements of eight subjects (A–H) were recorded while they performed 10 separate blocks of a saccade-tracking task. In each block of trials the timing information was from either a visual or an auditory stimulus. Only subjects G and H had prior knowledge of the goals of the study. Informed consent, according to the local institutional review board, was obtained from each participant. Data were acquired on a PC-compatible Pentium 166-MHz computer running real-time experiment control software developed in-house. Horizontal movements of the eyes were recorded with a Series 1000 Binocular Infrared Recording System (Microguide), sampled at 1000 Hz. The system was calibrated prior to data acquisition by having subjects fixate visual targets at known locations. Subjects were seated in a stationary chair in front of a tangent screen (124 cm in front of the subject) on which were located two LED targets (left and right 15 deg). The head was fixed with a chin rest. Subjects were given no explicit instructions as to timing or accuracy; in the visual tracking tasks they were told simply to “look at the target” and in the auditory tasks, where both lights were illuminated, to “look at the next target when you hear the beep.”

Visual Cued Tracking Task

In the Visual Cued tracking task subjects tracked LED targets alternating between two fixed positions (± 15 deg) at a given ISI. Each subject made 100 saccades at five pacing rates: ISIs of 2500, 1667, 1000, 833, and 556 ms. There were two pacing rates that generally promoted reactive tracking (ISIs of 1667 and 2500 ms) and three pacing rates that largely promoted predictive tracking (ISIs of 556, 833, and 1000 ms). Examples of tracking at the lowest and highest pacing rates (ISIs of 2500 and 556 ms) for this task are shown in Figure 1A and B for subject B.

Auditory Cued Tracking Task

In the Auditory Cued tracking task subjects made saccades between the two continuously illuminated LED targets (± 15 deg) when signaled by a pacing tone (200 ms in duration) from

a speaker located above the subject (not coincident with either visual target). The pacing tone was not localized to either target position. The tone was given with the same ISIs as in the visual tracking task (ISIs of 2500, 1667, 1000, 833, and 556 ms), for 100 eye movements at each ISI. Examples for the lowest and highest pacing rates for this task (ISIs of 2500 and 556 ms) are shown in Figure 1C and D for subject B.

Pacing rate and stimulus-cue modality were counterbalanced between subjects. Subjects performed one block (consisting of 100 saccades) for each combination of sensory cue and pacing rate (10 blocks total).

Data Analysis

Analysis of eye-tracking data was done off-line. First, eye velocity and acceleration were calculated using a four-point digital differentiator based upon a least-squares derivative algorithm (Savitzky & Golay, 1964). This is an efficient iterative method of fitting a third-order polynomial to each data point and the preceding and following two values, then finding the derivative of the fitted polynomial. This introduces less noise than conventional differentiators. Eye movement latency was determined by comparing the onset of the primary saccade to the onset of the target in each trial. Saccade onset was determined using a velocity threshold ($\geq 60^\circ/\text{s}$). Inter-saccade interval was the time between each primary saccade.

Results

Tracking Variability and Weber's Law

Subjects demonstrated the same tracking behavior for the same pacing rate for both sensory conditions. An example is shown in Figure 2 for subject A. Displayed are histograms of saccade latency from the two sensory stimulus conditions (Visual and Auditory Cued Pacing) for the five pacing rates (ISIs of 2500, 1667, 1000, 833, and 556 ms). The thick black dashed line in each panel represents a latency of 100 ms, which we consider the criterion for defining predictive saccades (Isotalo, Lasker and Zee, 2005; Leigh & Zee, 1999). At the two lowest pacing rates (ISIs of 2500 and 1667 ms) the latency histograms are grouped to the right of the dashed line for both sensory stimuli conditions. This demonstrates that the subject is mainly making reactive movements to both sensory cues at these timing rates. At the three highest pacing rates (ISIs of 1000, 833, and 556 ms) the latency histograms are grouped to the left of the dashed line and distributed below 0 ms. Thus, at these pacing rates the subject is largely making predictive movements (eye movements before the stimulus cue) for both sensory stimuli conditions. These results are also summarized in Tables 1 and 2 for all subjects.

In Figure 3 the standard deviation of the inter-saccade intervals for Visual Cued Pacing is plotted against the variance for Auditory Cued Pacing for all subjects. The two slowest pacing rates (ISIs of 2500 and 1667 ms) are displayed in Figure 3A and the three fastest pacing rates (ISIs of 1000, 833, and 556 ms) in Figure 3B. The thick black dashed line represents equal variance of the eye movement timing (inter-saccade intervals) from the two sensory stimulus conditions. During the slowest pacing rates, the standard deviation of the inter-saccade intervals during Auditory Cued Pacing is generally greater than during Visual Cued Pacing; the points plotted in Figure 3A are mainly grouped below the dashed black line. This was not the case at the three fastest pacing rates displayed in Figure 3B. In this case the points are distributed along the black dashed line demonstrating that the eye movement timing variability is approximately equivalent during the two sensory stimuli conditions. The data in Figure 3B also exhibit Weber's Law in both sensory conditions: timing variability increases as the duration of the timed interval increases. As shown in the Figure 3B, the standard deviation of the inter-saccade intervals made to the ISI of 556 ms during the two sensory stimuli conditions is largely grouped below the ISIs of 833 and 1000 ms.

Figure 4 plots the mean and standard deviation of the inter-saccade intervals pooled across all subjects for each ISI during Visual and Auditory Cued pacing. An ANOVA on the inter-saccade intervals showed that there was not a significant difference in mean timing performance between subjects ($P > 0.1$ for all pacing rates and sensory conditions), therefore differences in mean saccade timing between subjects did not contribute to the pooled inter-saccade interval variability. The circles represent the average inter-saccade interval and the bars are plus and minus one standard deviation of the pooled data. The mean inter-saccade intervals in the two sensory stimulus conditions were equivalent at all pacing rates, as determined with a paired t -test (P values for the ISIs of 2500, 1667, 1000, 833, and 556 ms: 0.9180, 0.8343, 0.7819, 0.9195, and 0.9880). The variance of the inter-saccade intervals for a given pacing rate was compared between the two sensory stimuli using an F -test (variance of the intervals made during the auditory pacing divided by the variance during the visual pacing). The inter-saccade interval variability was larger for the auditory stimulus at the two lowest pacing rates (P values for the ISIs of 2500 and 1667 ms were less than 1×10^{-16}). At the three highest pacing rates there was no statistical difference in variance between the two sensory stimuli (P values for the ISIs of 1000, 833, and 556 ms: 0.1485, 0.1144, and 0.425).

Scalar Property for Predictive Tracking

In addition to the analysis above, we wanted to determine if the distributions of inter-saccade intervals demonstrated the Scalar Property in the two sensory-pacing conditions. That is, we wished to utilize the Scalar Property to compare the normalized inter-saccade interval distributions when cued by different pacing modalities and at different pacing rates. We begin with an analysis of data from *reactive* saccades. The normalized inter-saccade interval distributions for all subjects are plotted for ISIs of 2500 and 1667 ms in Figure 5A and B. (Inter-saccade interval data from all subjects were pooled and then normalized by dividing these intervals by the mean inter-saccade interval of the pooled data. The normalized data were then plotted as a histogram, where each bin is 1% of the mean inter-saccade interval.) Auditory Cued pacing is represented by the solid line; Visual Cued pacing by the dashed line. As demonstrated in the figure, the duration of the ISI affected the width of the histogram; the normalized histogram for pacing at the ISI of 1667 ms (panel B) has a lower peak for both stimulus conditions than for pacing at 2500 ms (panel A). Consequently, the normalized histograms for the ISI of 1667 ms were wider (indicating more variability) than for 2500 ms. This is true even within the same modality condition. For example, the normalized histogram for Auditory Cued pacing for the ISI of 1667 ms (the solid line in panel B) has a lower peak than for the ISI of 2500 ms (solid line in panel A). This result does not support the Scalar Property: the two distributions should overlap when plotted as a proportion of the mean if the Scalar Property held. This means that there is a statistically significant difference in the normalized histograms from the two stimulus conditions, and between pacing rates, during reactive tracking. That is, the histogram for Auditory Cued pacing at 2500 ms ISI is different from the histogram for Auditory Cued pacing at 1667 ms ISI (chi-square test, $P = 1.20 \times 10^{-12}$). The same is also true for Visual Cued pacing ($P = 0.0014$). In addition, the histogram for Auditory Cued pacing at 2500 ms ISI is statistically different from the histogram for Visual Cued pacing at 2500 ms ISI ($P = 0.0028$). The same is true for pacing at 1667 ms ($P = 1.44 \times 10^{-15}$). These findings indicate that the Scalar Property does not hold with either pacing stimulus, suggesting that an identical timing process is *not* present across sensory modalities and frequencies for *reactive* saccades.

The same analysis described above was carried out for pacing at the ISIs of 1000, 833 and 556 ms (Figure 6A, B, and C respectively), where *predictive* tracking occurred. Unlike the results described for ISIs of 1667 and 2500 ms, the histograms at these pacing rates *do* demonstrate the Scalar Property: there is not a statistically significant difference in tracking distributions with different sensory cues at the same ISI (P values for the ISIs of 1000, 833, and 556 ms:

0.33, 1.00, 0.99). In other words, the normalized histogram for Auditory Cued pacing at the ISI of 1000 ms is not significantly different from the histogram for Visual Cued pacing at the same ISI (panel A). All histograms presented in panels A, B, and C are again displayed in panel D for comparison. As shown in panel D, qualitatively all six distributions overlap in maximum value and width. Statistically, there is not a significant difference in 9 of the 15 possible comparisons between normalized histograms ($P > 0.01$, chi-square test). As one example, the normalized inter-saccade interval histogram for Visual Cued pacing at the ISI of 556 ms is statistically indistinguishable from the normalized inter-saccade interval histogram for Auditory Cued pacing at the ISI of 1000 ms ($P = 1.00$). The fact that the Scalar Property holds for predictive saccades in both sensory modalities indicates that they share a common timing mechanism.

Discussion

In this study we have provided evidence that human subjects use the same internal timing mechanism (neural clock) to predictively track targets when cued by a repetitive visual or auditory stimulus. We base this conclusion on two behavioral results: (1) the variance of the inter-saccade intervals at the three predictive pacing rates tested (ISIs of 500, 833, and 1000 ms) were statistically indistinguishable between the two sensory conditions, (2) when the inter-saccade interval histograms at the predictive pacing rates were normalized, the distributions were nearly identical for both Visual and Auditory Cued pacing.

Previous Behavioral Studies that Support Separate Modality-Specific Timing Mechanisms

There are numerous differences in perceptual and motor responses to auditory versus visual stimuli that suggest that repetitive responses to these two stimuli might not be mediated by the same timing mechanism. For example, there is a long line of research that has shown that acoustic intervals are judged longer than visual intervals of the same physical duration (Goldstone, Boardman and Lhamon, 1959; Behar & Bevin, 1961; Goldstone & Goldfarb, 1964a,b; Goldstone & Lhamon, 1972, 1974; Walker & Scott, 1981). This difference led Penney and colleagues (2001) to propose that the two stimuli cause a putative internal clock to run at different rates. In terms of an integrate-to-threshold timing mechanism this would mean that the linear-rising noisy signal grows at a faster rate for visual compared to auditory stimuli. It should be noted, however, that in the study reported here we are examining the time *between* motor responses rather than the *duration* of the sensory stimulus. That is, the integrated signal represents the estimate of the time between motor responses (saccades) rather than the duration of the visual or auditory stimulus. In this way we believe we are engaging the same timekeeping mechanism with each sensory modality, resulting in the equivalence of the distributions of the timing between movements (inter-saccade intervals) for different pacing rates and sensory cues.

Recent imaging studies have also suggested a separation in the neural areas responsible for timekeeping to auditory and visual stimuli. Jantzen and colleagues (2005) examined neural activity in healthy human subjects as they coordinated a finger-thumb opposition movement to either a visual or auditory stimulus presented repeatedly at an ISI of 800 ms. They found increased activity in the superior temporal gyrus during auditory cued pacing, while visual pacing generally increased activity in the superior parietal lobe, the middle temporal area, and right middle frontal gyrus. In addition, the authors reported that there was not a statistical difference in the inter-response interval variability between the two modalities. Another imaging study examined repetitive finger presses to different sensory stimuli presented at an ISI of 400 ms (Jäncke, Loose, Lutz, Specht and Shah, 2000). These authors found that activity generally increased in the premotor cortex, supplementary motor area, and thalamus during auditory pacing, while visual pacing typically activated the inferior parietal lobule and

cerebellar vermis. However, unlike the Jantzen study, these authors reported that the inter-tap interval variance during synchronization to the visual stimulus was larger than during synchronization to the auditory stimulus. Other differences in the oculomotor responses to these two stimuli are noted in the introduction section. (It is important to note that the above examples support the hypothesis that temporal processing is mediated by distributed brain areas (Rao, Harrington, Haaland, Bobholz, Cox and Binder, 1997; Buonomano & Karmarkar, 2002; Buhusi & Meck, 2005). It is not our intent to argue that the brain represents time in a central manner, but rather that the data that we present here suggest that the temporal processing, whether centralized or distributed, during predictive saccade tracking is the same when the timing information is provided by different modalities.)

Though in this study, during reactive tracking Auditory Cued pacing elicited greater variability than Visual Cued pacing, there is evidence that the opposite relationship holds for repetitive manual responses (Jäncke et al., 2000; Chen, Repp and Patel, 2002; Kolers & Brewster, 1985). In addition, the greater variability of single saccadic reaction times to auditory targets noted in the introduction is attributed to delays in reconstructing target position from non-visual information (Yao & Peck, 1997; Zambambieri et al., 1982). However, in the current study target position was always visually presented, even when the timing information was auditory. That is, the response time during reactive tracking to a purely visual stimulus was less variable than the response time to a visual stimulus cued by an auditory source. It is possible that the increased variability for the auditory condition is related to having to deliberately disengage fixation whereas during the visual condition the jumping of the target diminishes if not eliminates the duration of this process. An interesting future study would be to compare the reaction time variability to purely visual targets to the response variability to visual targets cued by a non-localized auditory signal.

Previous Behavioral Studies that Support a Modality-Independent Timing Mechanism

Despite the evidence outlined above for separate modality-specific timing mechanisms, there is an abundance of previous reports that support a timing mechanism that performs equally for auditory and visual stimuli. For example, Eijkmann and Vendrik (1965) found, with a duration detection task, that the accuracy of timing was equal for visual and auditory stimuli and also that the combination of both modalities did not increase the accuracy of timing. The fact that performance did not improve by combining the stimuli suggests the use of one common central clock for both modalities. Warm and colleagues (1975) found that training to increase accuracy in temporal discrimination transferred between modalities, again suggesting a common clock. There are also results from non-primates (Roberts, 1982) that suggest that both light and sound cues can be utilized similarly in an internal clock mechanism.

The use of auditory and visual stimuli for timing has also been demonstrated for oculomotor smooth pursuit. In a recent study by Jarrett and Barnes (2005) subjects tracked a visual target moving at a constant velocity to the right and then returning leftward with a variable reversal time. The start and reversal times of the upcoming visual stimulus were provided by either audio cues prior to target presentation or direct visual information (repetitive tracking of the stimulus). The times of eye reversal with respect to the stimulus, for the visual-only and the auditory-cued conditions, were not significantly different. These findings show that timing information derived from auditory cues or from direct visual motion can be used equally well by human subjects to predictively time the anticipatory initiation and trajectory change of pursuit eye movements.

Recent studies of synchronized tapping have also investigated responses to auditory and visual pacing stimuli. Merchant and colleagues (2006) examined the variance of inter-tap intervals (ITIs) as subjects tapped in synchrony to an auditory or visual stimulus presented at ISIs that ranged from 350 to 1000 ms. Similar to the results presented in Figure 3B, they reported similar

variance in the inter-tap intervals during the two sensory stimuli conditions. In addition, consistent with the present results, the inter-tap interval variance increased as interval length increased for both sensory conditions.

In a similar study (Chen et al., 2002) subjects tapped in synchrony to either an auditory (tone) or visual (LED) stimulus presented repetitively at an ISI of 488 ms. The authors performed spectral analysis on the ITIs and on the latency time series. (The power spectra represent fluctuations in each quantity as a function of frequency, not tapping performance at different pacing frequencies.) They found that there were differences in ITIs and in latency variability (as seen by differences in the power spectra) above a critical frequency that corresponded to fluctuation intervals longer than 3 seconds. That is, over time intervals of more than 3 seconds, the variability of the visual condition was greater than that of the auditory condition. However, for intervals of less than 3 seconds the variances of the two sensory conditions were similar. The authors state that, “This integration process may be mostly determined by a central mechanism, and less dependent upon different modalities. This could be the reason that we observed similar variances in auditory and visual synchronization within 3 seconds... This time scale may represent a modality-independent temporal integration window which operates in sensorimotor integration” Supporting our findings, these results suggest that the timing mechanisms in synchronized tapping to ISIs below 3 seconds are similar across modalities, but when synchronized to ISIs above 3 seconds there are variability difference across sensory modalities.

This 3-second interval has been shown to be a threshold in tapping behavior in other studies as well (MacDorman, 1962; Engström, Kelso and Holroyd, 1996; Miyake, Onishi and Poppel, 2004). When tapping to a pacing metronome, if the stimulus period is longer than 3 seconds, subjects typically respond after the stimulus, indicating that participants are reacting to the stimulus. When the period is shorter than 3 seconds, participants usually anticipate the stimulus, responding before each click. In duration-discrimination tasks Weber’s Law (the observation that the variability of the time estimate is proportional to the interval length) is violated for durations longer than 2 seconds (Getty, 1975). There is also a difference in brain evoked potentials and accuracy when participants reproduce intervals above and below 3 seconds (Elbert, Ulrich, Rockstroh and Lutzenberger, 1991). These results led Mates and colleagues (1994) to suggest that this interval is the upper limit of a temporal integration process in sensorimotor synchronization.

These results complement our previous findings (Shelhamer & Joiner, 2003; Shelhamer, 2005), where we showed that sequences of predictive saccades are correlated over a span of approximately two seconds. We hypothesize that this correlation represents feedback on the performance of previous movements that occurred within this time window. This information on past performance is then used for updating the estimate of the next stimulus interval (feedforward). In this manner the timing between saccades can be estimated, and a response can be initiated in anticipation of the next in a sequence of repetitive stimuli. (We note that with no prior timing information, initial predictive saccade tracking can only occur after at least three eye movements (two intervals) (Zorn, Joiner, Lasker and Shelhamer, 2007). That is, the subject must make a reactive response to the first two target jumps of the sequence and can only use the acquired timing information to affect the third and later eye movements. Therefore, predictive tracking typically occurs at ISIs where three or more eye movements fall within the approximate two-second time span ($ISI \leq 1000$ ms).) We hypothesize that this manner of estimating the time between upcoming movements is identical during Auditory and Visual Cued pacing, which results in the distributions of the inter-saccade interval being statistically indistinguishable. However when the intervals cannot be estimated (stimulus timing falls outside this time window, typically ISIs > 1000 ms) the subject must react rather than anticipate the stimulus. In this way the processing of the sensory information (as

previously demonstrated for single reactive saccades, Zahn et al., 1978,1979;Zambarbieri et al., 1982) determines the time between reactive saccades and results in differences between inter-saccade interval distributions in the two sensory conditions.

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Figure 1.

Representation of the experimental conditions. During Visual Cued Pacing (panels A and B) subjects tracked LED targets alternating at a fixed interval (ISI) between two fixed positions. During Auditory Cued Pacing (panels C and D) subjects made saccades between the two constantly illuminated LED targets when signaled by a pacing tone (gray trace) given at a fixed ISI. At low pacing rates (e.g., an ISI of 2500 ms) subjects generally made reactive eye movements after the sensory stimulus (panels A and C). At high pacing rates (e.g., an ISI of 500 ms) subjects largely made predictive movements before the sensory stimulus (panels B and D).

Figure 2.

Histograms (20 ms bins) of saccade latency for subject A during Visual (top row) and Auditory Cued Pacing (bottom row). Each column represents one of five pacing rates (ISIs of 2500, 1667, 1000, 833, and 556 ms). The thick black dashed line in each panel marks a latency of 100 ms, which is considered the criterion for predictive saccades.

Figure 3.

The standard deviation of the inter-saccade intervals during Visual Cued Pacing is plotted against the standard deviation of the inter-saccade intervals during Auditory Cued Pacing for all subjects. Panel A shows the respective stimulus-cued standard deviations during reactive pacing at ISIs of 2500 and 1667 ms. Panel B shows the respective stimulus-cued standard deviations during predictive pacing at ISIs of 1000, 833, and 556 ms. The thick black dashed line represents equal inter-saccade interval variance in both sensory stimuli conditions.

Figure 4.

Mean and standard deviation of the inter-saccade intervals pooled across all subjects for each ISI during Visual (black trace) and Auditory (gray trace) Cued pacing. The circles represent the average inter-saccade interval and the bars signify ± 1 SD across the pooled data.

Figure 5.

Normalized inter-saccade interval histograms (each bin represents 1% of the mean inter-saccade interval) across all subjects during Visual (dashed lines) and Auditory Cued (solid lines) pacing. Histograms for ISIs of 2500 and 1667 ms are displayed in panels A and B. All histograms presented in panels A and B are displayed for comparison in panel C.

Figure 6.

Normalized inter-saccade interval histograms (each bin represents 1% of the mean inter-saccade interval) across all subjects for ISIs of 1000, 833, and 556 ms (panels A, B, and C respectively). Interpretation of the data is the same as for Figure 5. All histograms presented in panels A, B, and C are displayed for comparison in panel D.

Table 1
The mean and standard deviation of saccade latency at each ISI for Visual Cued pacing for all subjects.

Subject	Saccade Latency – Visual Cued Pacing Rate (ms)				
	2500 ms	1667 ms	1000 ms	833 ms	556 ms
A	142.4±77.7	165.6±55.7	-95.0±102.4	-94.8±83.8	-93.1±65.4
B	106.2±151.7	107.0±165.6	-71.7±88.7	-110.66±80.2	-134.09±73.7
C	122.7±165.1	107.5±133.0	-157.8±179.9	-113.3±154.0	-139.5±99.9
D	179.1±96.9	138.9±41.0	4.4±88.7	96.8±94.2	7.08±83.4
E	173.7±122.4	111.2±154.7	10.4±100.7	-25.1±122.3	8.3±75.2
F	208.7±30.8	183.7±49.3	114.1±86.3	108.1±74.2	97.27±66.3
G	180.0±27.9	147.5±47.5	-24.8±140.0	-39.5±99.1	-26.6±67.7
H	246.4±46.0	177.6±37.1	83.7±74.3	87.8±94.1	82.3±73.8

Table 2
The mean and standard deviation of saccade latency at each ISI for Auditory Cued pacing for all subjects.

Subject	Saccade Latency – Auditory Cued Pacing Rate (ms)				
	2500 ms	1667 ms	1000 ms	833 ms	556 ms
A	188.7±67.8	176.6±84.9	-113.6±92.2	-133.3±100.1	-82.8±63.2
B	111.1±120.7	128.5±126.7	-99.8±81.8	-137.7±91.2	-119.9±53.0
C	171.1±64.4	105.8±139.7	-72.1±166.9	-94.5±169.9	-37.9±112.5
D	149.7±96.7	103.5±130.7	-122.8±120.8	-82.1±83.2	-112.9±69.5
E	187.3±146.7	122.7±123.9	-157.5±154.7	-137.8±122.5	-87.1±102.1
F	153.7±107.5	105.8±73.6	33.0±106.1	53.3±77.7	69.0±62.5
G	176.1±46.8	208.0±69.1	-64.4±113.3	-63.0±92.4	-28.2±54.2
H	236.4±129.8	232.5±70.4	91.0±61.6	90.5±85.5	82.8±71.9