The effect of entrainment on the timing of periodic eye movements

Brian A. Richardson, Ramesh Balasubramaniam*

Sensorimotor Neuroscience Laboratory, Department of Kinesiology, McMaster University, 1280 Main Street West, Hamilton, ON L8S 4K1, Canada

ARTICLE INFO

ABSTRACT

We performed an experiment in which eight healthy individuals made periodic eye movements at five pacing interval conditions (500 ms, 750 ms, 1000 ms, 1250 ms, and 1500 ms). Three methods of entrainment were used in the synchronization phase: saccade, continuous pursuit and discontinuous pursuit. The stimulus train was extinguished and in the continuation phase, subjects made saccadic eye movements at the entrained movement frequencies between two static targets. Using the Wing–Kristofferson model, clock and motor variance were extracted from the time series of continuation trials for all three entrainment conditions. Our results revealed a main effect of time interval on total variance clock variance (as predicted by Weber's law) and on motor variance. We also report that the pursuit entrainment conditions resulted in and mean duration and variance to the saccade entrainment. These results suggest that the neural networks recruited to support a periodic motor timing task depend on the method used to establish the temporal reference.

Timing of eye movements is an important skill for several tasks involving visuo-motor control. In a typical motor timing experiment, a synchronization-continuation design is employed [1,4,8,23,24,27,28]. Participants make movements to an external pacing signal or stimulus train. This is referred to as the synchronization phase. After a few repetitions, the stimulus train is extinguished, but the subjects continue to generate movements that are now internally paced, referred to as the continuation phase. The nature and the statistics of the inter-response intervals have been studied extensively over the last few decades [29,30]. An issue that has not received much attention is the role of the kind of movements subjects make in the synchronization phase (i.e., during entrainment) in relation to potential effects on the following responses in the continuation phase of the experiment. The question of whether the responses in the entrainment phase have a lasting effect on characteristics of the timekeeping networks that are recruited in the continuation phase remains unanswered. Recent fMRI evidence [10,15] suggests that the cortical and subcortical areas recruited to support a simple motor timing task depend crucially on the method used to establish the temporal reference. These results suggest that the particular type of entrainment in the synchronization phase affects the recruitment of neural networks involved in the continuation phase.

Eye movements provide some advantages over finger tapping as a means to investigate the timing mechanisms that are implicated in many types of movement tasks. For example, the extraocular muscles that move the eyes, are controlled more via open-loop control and efference copy signals than proprioception [3,7,19,22]. This suggests the existence of an extremely low latency feedback mechanism which allows for the observed online control. There are two classes of eye movements that are commonly studied: saccadic and smooth-pursuit movements. Whereas the control of saccadic responses is largely accomplished through exclusive subcortical networks, smooth-pursuit involves many more distributed cortical and subcortical areas. The cortical areas implicated in both, such as the frontal eye field (FEF) have specific regions for each type of movement [18]. Given that the two kinds of eye movements show both neural and behavioral differences in organization, we ask the following question: does entrainment to different classes of eye movements in the synchronization phase affect the subsequent responses in the continuation phase?

In a large range of voluntary timing tasks, the widely successful Wing–Kristofferson (WK) model [21,27,28] suggests two distinct and independent processes, the clocking and motor networks, and that each process is variable within itself. So, the observed total variability (TV) in series of response intervals is a summation of the variability in each network. The model suggests that a timekeeping process, the clock, generates open-loop periodic output signals, which are received by the motor system to elicit the desired response. However, integration of the clocking signal is delayed by a variable amount due to processing and implementation delays in the motor networks. As the model suggests that variability between these two processes is independent, one can estimate the variability in each process. Whereas clock variability (CV) has been shown to scale according to duration of the target interval [8] the estimated motor variability (MV) remains constant across target intervals but

* Corresponding author. Tel.: +1 905 525 9140x21208; fax: +1 905 523 6011.
E-mail address: ramesh@mcmaster.ca (R. Balasubramaniam).

varies with effector [23,24]. Although the WK model was developed using data from finger tapping paradigms, subsequent research has confirmed that the model can be used with similar validity to examine periodic saccades for timed responses [4].

The purpose of this study was to investigate how various measures of human timekeeping abilities are influenced by task dynamics during entrainment. To accomplish this, we tailored the saccade synchronization-continuation methods, previously used by Collins et al. [4] towards the analysis of series of response intervals as performed with various types of periodic eye movements. In the present study, we first entrained the eye movements of test subjects differentially to the periodic stimulus train (either using saccade or smooth-pursuit). Next, the pacing stimulus was extinguished and subjects performed continuation saccade between two fixed points. Following work of Jantzen et al. [10,15], we hypothesized that the synchronization condition or the type of entrainment would affect the variability in continuation responses because of a lasting effect on clocking networks. It is important to keep in mind that smooth-pursuit eye movements are not implemented in unpaced timing studies because it is necessary that a stimulus exists for which pursuit movements can follow.

Eight healthy individuals (three female, five male) from the local student body participated and completed the experiment. The protocol was approved by the McMaster Ethics Review Board. Our experimental apparatus consisted of a PC workstation and an Eye-Link II head-mounted eye tracker (SR Research). Gaze data were sampled at 500 Hz while subjects tracked visual targets that were displayed on a flat-style 17 in. CRT monitor, running at a resolution of 640x480 pixels and refresh rate of 125 Hz. The display was positioned 510 mm in front of the subject, and moving visual targets and the fixed crosshairs had consistent positions 7.5° of visual angle apart, each 3.75° from away from the center of neutral gaze. On an otherwise blank computer display, we presented moving visual targets (5 mm circles, similar in characteristics to a standard light emitting diode) that would move horizontally in a periodic fashion for 20 intervals. Subsequent to these 20 synchronizing intervals the pacing target was removed and subjects continued periodic eye movements for an additional 25 intervals. As the primary manipulation of entrainment dynamics during the synchronization phase, the pacing target's kinematic properties were manipulated in three different conditions. As depicted by the sample target time series plot in Fig. 1, the target trajectory that evoked saccades followed a square waveform. The target requiring discontinuous pursuit tracking with rather abrupt reversals in movement direction has a triangular waveform. Also, a continuous pursuit target with smoother kinematics, or rather a less salient event structure, is illustrated by the sine waveform. Once 20 synchronization intervals were completed, the pacing target disappeared and two crosshairs appeared on the screen in place of the pacing target. Subjects were instructed to continue making periodic eye movements at the same rate. Again, we would like to call attention to the fact that continuation eye movements were always performed with saccades because of the aforementioned incompatibility between unpaced timing tasks and the conditions required to evoke pursuit. We used a fully within-subjects repeated-measures design. Subjects performed all three entrainment conditions across five pacing interval conditions (ISI of 500 ms, 750 ms, 1000 ms, 1250 ms, and 1500 ms), for a total of 15 trial conditions. Subjects were initially asked to complete three iterations of each trial condition and were called back for follow-up trials when required.

Prior to recording data, subjects were shown six familiarization trials to facilitate proper tracking in synchronization and in the transition to saccades for continuation. All the data were carefully examined to ensure that the subjects complied with the instructions in both synchronization and continuation. Specifically, we examined the data to ensure that the pursuit targets were tracked
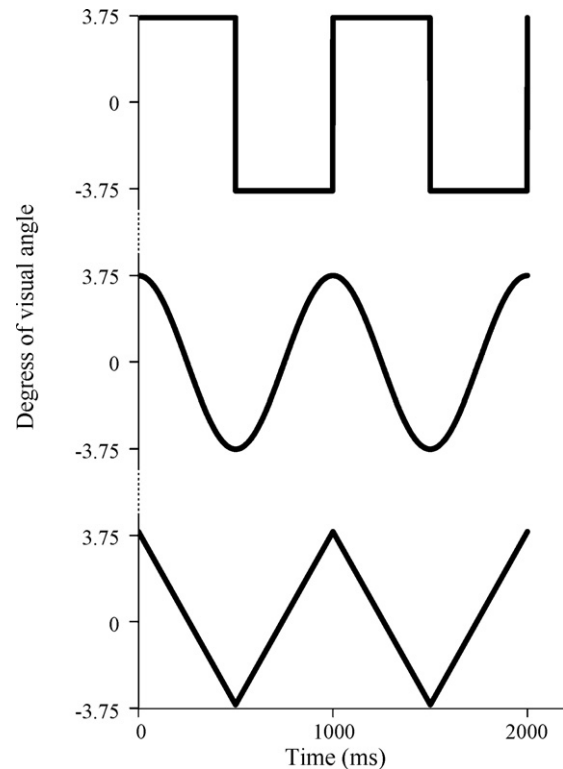

Fig. 1. An example of the various entrainment stimuli, with saccade (top), continuous pursuit (middle), and discontinuous pursuit (bottom) target trajectories. All of these sample trajectories have a 500 ms inter-stimulus interval event structure.

with minimal error in pursuit gain, and that participants necessarily performed saccadic jumps between the crosshairs with minimal time spent in gaze towards extraneous areas of the screen. We also carefully inspected the data to make sure that subjects did not engage in saccadic pursuit or make frequent catch-up saccades when engaged in pursuit tracking.

Average gaze data was analyzed using MATLAB^{TM} and in-house developed scripts to extract inter-response intervals (IRI) from the continuation phase eye movements. Gaze position data was smoothed using a 21-sample windowed equally weighted moving average filter, and was then used to derive gaze velocity. Saccade onset was determined when absolute gaze velocity exceeded a 15°/s threshold that directly led to a crossing the screen's midline before the velocity fell under the threshold. The first IRI in continuation responses was discarded and the subsequent twenty IRIs were used for analysis. Each series of twenty IRIs was linearly detrended to bring the datasets towards stationarity as required for WK decomposition. The mean latency values and IRIs are provided in Table 1. The values of the saccade latencies (<100 ms) suggest that these eye movements are essentially clock-driven and not reactive [12]. Whereas the latency of reversing pursuit direction at the target boundaries does not change across interval conditions, it seems that this entrainment behavior is instead locked to the stimulus.

Using the previous methods for unbiased autocovariance estimators [26], our first investigation flagged the trials which violated the WK predictions for the lag-1 autocorrelation function (lag-1r). To assure meaningful WK measures, trials where the lag-1r was less than −0.5 and greater than 0 were then excluded from further variability analysis. If it was discovered that a subject performed any one trial condition where the lag-1r was in WK violation for all three completed iterations, the subject was asked to return for a follow-up retesting of only these conditions. After all of the participants had completed every trial condition with a minimum of one

Table 1
Mean and standard deviation of the inter-response intervals (IRIs) for the three entrainment conditions are shown in the top of the table. The response asynchrony values during the entrainment conditions are listed below. The negative values indicate the early arrival of the eye (before the target). All values are shown in ms.

Entrainment condition	Saccade		Continuous pursuit		Discontinuous pursuit	
	Mean	SD	Mean	SD	Mean	SD
Continuation inter-saccade interval (ms)						
500 ms	563.85	50.01	551.92	36.25	578.68	37.47
750 ms	818.19	59.28	846.20	86.62	881.43	131.09
1000 ms	1043.53	90.80	1135.44	154.39	1151.42	138.38
1250 ms	1296.15	143.89	1291.01	175.23	1351.21	175.77
1500 ms	1509.74	145.47	1521.94	240.46	1677.99	195.54
Response asynchrony during entrainment (ms)						
500 ms	47.23	68.88	17.35	7.72	39.31	10.96
750 ms	−65.52	72.12	19.07	13.44	33.38	13.07
1000 ms	−87.91	145.67	18.78	14.91	27.71	11.08
1250 ms	−98.96	142.36	35.41	23.98	40.61	20.75
1500 ms	4.22	139.68	32.86	23.46	42.67	24.31

acceptable trial per condition, the total variance (TV), clock variance (CV), and motor variance (MV) components of the WK model were computed with standard calculations [26]. For each variance measure we ran a 3 (synchronization condition) × 5 (target interval) repeated-measures ANOVA.

The percentage of trials in violation of WK lag-1r predictions were computed for each subject then averaged across subjects and pacing interval conditions. During saccade entrained trials the total WK violations were 22.3%, similar to that reported in previous literature [4]. The rate of WK violation was higher when subjects entrained timing to continuous, 30.5%, and discontinuous, 32.1%, pursuit targets.

In accordance with Weber's law, a main effect of target interval on CV ($F_{4,28} = 18.53$, $p < 0.0001$) which in turn leads to the effect on TV ($F_{4,28} = 15.75$, $p < 0.0001$) was replicated. The trend of concomitantly increasing CV and TV with longer target intervals durations is illustrated in Fig. 2A and B for each entrainment condition. It is important that this trend is evident in both of these measures; these findings suggest that, regardless of entrainment condition, the continuation saccades are initiated through a timing network
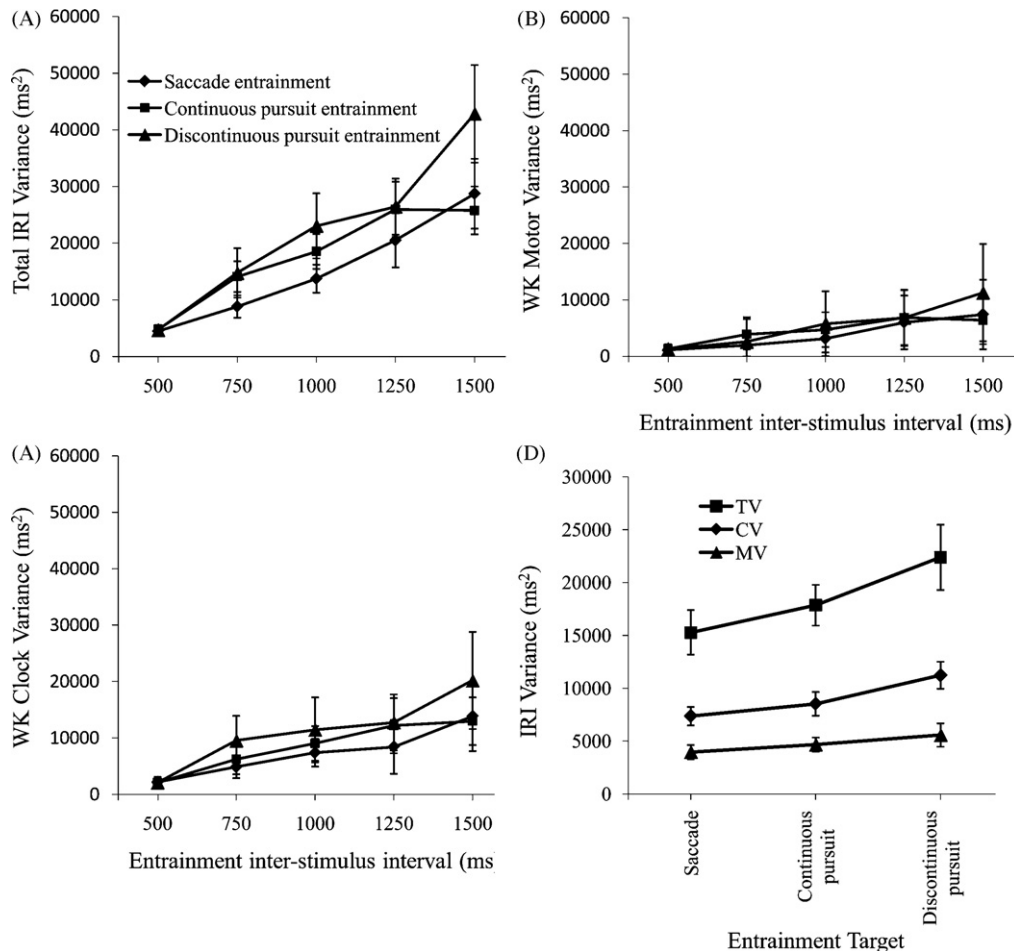

Fig. 2. Panels A–C: WK variance measures across all entrainment conditions and target intervals. Variance is presented as a function of entrainment interval. Error bars represent standard error of the mean (SEM). Panel D: WK variance measures presented as marginal means (±SEM) according to each entrainment condition. *$p < 0.05$; **$p < 0.01$.

that becomes increasingly variable as its representations of cycles become longer.

We also note a main effect of target interval on MV ($F_{4,28} = 8.12$, $p < 0.001$), plotted in Fig. 2C. This is consistent with previous continuation saccade research [4]. The WK model suggests that MV should be invariant of target interval, as they noted in finger tapping [25]. However, the trend is casually reported throughout many previous publications, including reports by the WK authors [27]. Detailed analyses of the trend and long-range correlations (if any) are beyond the scope of the present study.

With regard to the primary experimental manipulation, that is the pacing target's kinematic properties, we found significant main effects of entrainment condition on TV ($F_{2,14} = 7.57$, $p < 0.01$) and CV ($F_{2,14} = 6.73$, $p < 0.01$), but not on MV. Marginal means for the three entrainment conditions are plotted in Fig. 2D for all WK variance measures. Post-analyses using the Bonferonni/Dunn criterion were used to determine significant differences between groups, with significance applied at a corrected $p < 0.0167$.

Comparison of the marginal TV means grouped for entrainment condition revealed that, saccade entrained trials ($M = 15,278.63$, SD = 13,350.17) had significantly less variability than discontinuous pursuit entrained trials ($M = 22,379.10$, SD = 19,549.58). Accordingly, marginal CV means across the same groupings revealed similar differences. The computed CV from saccade entrained trials ($M = 7363.96$, SD = 5516.47) was significantly less than the CV measured in discontinuous pursuit entrained trials ($M = 11,231.37$, SD = 8079.30). Although the violations noted earlier highlight some inherent limitations with using the WK model for studying periodic eye movements, the fact that TV and CV increased due to the entrainment manipulation (even in trials with violations) suggests that there are important changes in the underlying control structures in the continuation phase. These findings are particularly important for supporting our hypothesis; the properties of the timekeeping networks show lasting properties that are a function of the prior context. Statistical examination of the Weber functions [8] did not reveal significant differences across entrainment conditions. Table 1 reveals mean continuation intervals that are longer following pursuit entrainment.

We predicted that movement parameters during entrainment to a periodic visual target would influence the way timekeeping networks function. We expected to see evidence for this in the structure of timed self-paced responses subsequent to various entrainment conditions. Most importantly, our data reveal that the type of eye movements used for entrainment can have a significant effect on subsequent self-paced responses. Similar to the Jantzen et al. [10,15] findings that informed our hypothesis, our results demonstrate that timing behavior during self-paced saccades is influenced by the movement characteristics of the entrainment stimulus and synchronization task.

The differences between CV measures across entrainment conditions suggest that the task is performed with the least variability when entrained and performed with the same types of movement. In other words, once the subjects began continuation saccades, the clock persisted with the least variance when entrained with saccades. Furthermore, the internal representation of the interval is most variable after entrainment to the discontinuous pursuit target. One may at first attribute these differences to the fact that the timekeeping networks were perturbed by the change from a pursuit target to a saccade target. We see this explanation as unlikely, because clock generated saccades are quite resilient to perturbation [11]. Furthermore, in many timing studies, the transition from synchronization to continuation often results in a shortening of the following response intervals; here we see the opposite trend of longer response intervals. We interpret this as support for the notion that clocking networks may be entrainment dependent.

As the properties of many repetitive smooth movements are generally considered to be "emergent" and different from the structure of event-driven discrete timing tasks [29,30,5], it is demonstrated here that some parameters of continuous smooth eye tracking are better indicators of periodic structure than discontinuous ones. This is an important observation and contrasts trends in periodic limb movement literature [1,2,6]. It is thus surprising that discontinuous pursuit task results in the most variable continuation timing. Given the motor timing literature for finger movements one could predict that the well defined saliency of the interval boundaries would result in a more accurately perceived and stored temporal representation. On the contrary, our findings indicate that smooth and continuous movements, at least those made with the eyes, can indeed facilitate entrainment to an explicit pacing stimulus with more stability than similar movements with a more pronounced event structure.

In the context of eye movements, we must also consider how the event structure of the various stimulus trajectories are perceived and integrated by timekeeping networks. Generally, at the point where the pursuit target reversed directions there was greater tracking error in the discontinuous task as compared with the continuous task. Although the abrupt target reversal may be a very salient event, the tracking error at these times may contribute negatively to the timing entrainment processes. On the other hand, the event structure of the continuous pursuit stimulus is salient in different ways. The velocity structure of this target also introduces a peak velocity mid-flight across the screen. In addition to the reduced tracking errors in continuous pursuit, the pursuit system might lead to more interval entrainment with the change from speeding up to slowing as compared with direction reversals.

Notably, our data also reveal that there was no significant effect of the entrainment conditions on the motor variance, which is not supported by the WK model [23,27,28]. Since our data show that the central clock acted with increased variability in response to pursuit entrainment, it would be tempting to speculate that there is an interaction between clock and motor networks, contrary to the suggestion of the WK model. Aside from the anecdotal suggestions of the model, there is also convincing evidence for this motor and clock segregation in recent finger tapping literature [14,16,20]. In these reports, a disruption to the motor cortex M1 area briefly affects the variability of local responses, yet no measurable change to an increase in timekeeper variability was apparent. Our current data suggest that motor and timing networks interact more than evinced by these TMS studies. In consideration of the task dynamics, one may ask which neural networks are implicated in the kinds of timing tasks presented here. These results also make us question the suitability of the WK model to studying timed eye movements, given the strong assumptions it makes about the independence of CV and MV. Conservatively, we would say that a large portion of the total variance change as a function of entrainment is accounted for by the extracted clock variance. It is then reasonable to conclude that aspects of timekeeper performance are indeed history-dependent.

The current research focuses on the unpaced continuation responses, but another specific domain of timing research focuses on behavior in paced repetitive eye movement tasks [11–13,17]. An important conclusion of this body of research is that timekeeping networks are not necessarily the exclusive source for initiating periodic eye movements in all pacing conditions. At relatively short intervals, >0.5 Hz or <∼1000 ms, predictive saccades arrive at the target destination ahead of the pacing stimulus and rely on clocking mechanisms to do so. Long intervals generally show none of the characteristics of active timekeeping and are likely initiated through sensory mediated reactions to target motion. Furthermore, whether behavior is predictive or reactive also depends on the

history of the system [17] as well as the nature of the instructions given to subjects [9]. In relation to our current findings, should task dynamics be an integral part of establishing a timekeeper, it appears that these effects are consistent at all target IRIs, even though our protocol involves short and long IRI conditions. Further, the saccade latency values (<100 ms) strongly suggest that the eye movements were in a clock-driven control regime while pursuit was stimulus locked. Therefore, it does not seem likely that active implementation of the timekeeper output is needed for passive entrainment.

While investigating the dynamics of syncopating finger tapping responses, Jantzen et al. [10,15] used fMRI to localize brain areas that were selectively activated when producing syncopated responses. Functional imaging allowed for the authors to see that the brain activation specific to setting up syncopated tapping persists after the pacing stimulus was removed and subjects continued to make responses. The difference in controlling saccades and pursuit movements are similar to the differences in syncopated and non-syncopated timing: syncopation, as does pursuit tracking, requires much more distributed set of neural systems. Accordingly, one may expect that the widespread brain activation during pursuit tracking may persist through the continuation phase saccades. Functional neuroimaging studies of eye movements can be used to confirm this prediction.

In summary, our results show that the type of stimulus (and consequently the motor network) that is used to entrain a specific timekeeper network affects the clock accuracy and variability of the responses in the continuation phase. While confirming the findings of Jantzen and Kelso, it also raises important questions about the differences between the networks that are used for discrete/event-based (saccadic) and continuous (pursuit) movements. Further research is required on the behavioral and neural fronts to investigate the distinction between these two classes of movements.

Acknowledgements

References

[1] R. Balasubramaniam, Trajectory formation in timed repetitive movements, in: M.L. Latash, F. Lestienne (Eds.), Motor Control & Learning, Springer, New York, 2006, pp. 47–54.

[2] R. Balasubramaniam, A.M. Wing, A. Daffertshofer, Keeping with the beat: movement trajectories contribute to movement timing, Exp. Brain Res. 159 (2004) 129–134.

[3] B. Bridgeman, L. Stark, Ocular proprioception and efference copy in registering visual direction, Vision Res. 31 (1991) 1903–1913.

[4] C.J.S. Collins, M. Jahanshahi, G.R. Barnes, Timing variability of repetitive saccadic eye movements, Exp. Brain Res. 120 (1998) 325–334.

[5] D. Delignieres, L. Lemoine, K. Torre, Time intervals production in tapping and oscillatory motion, Hum. Movement Sci. 23 (2004) 87–103.

[6] M.T. Elliott, A.E. Welschman, A.M. Wing, Being discrete helps keep the beat, Exp. Brain Res. 192 (2009) 731–737.

[7] B.L. Guthrie, J.D. Porter, D.L. Sparks, Corollary discharge provides accurate eye position information to the oculomotor system, Science 221 (1983) 1193–1195.

[8] E. Hazeltine, L.L. Helmuth, R.B. Ivry, Neural mechanisms of timing, Trends Cogn. Sci. 1 (1997) 163–169.

[9] E. Isotalo, A.G. Lasker, D.S. Zee, Cognitive influences on predictive saccadic tracking, Exp. Brain Res. 165 (2005) 461–469.

[10] K.J. Jantzen, F.L. Steinberg, J.A.S. Kelso, Brain networks underlying human timing behavior are influenced by prior context, Proc. Natl. Acad. Sci. U.S.A. 101 (2004) 6815–6820.

[11] W.M. Joiner, M. Shelhamer, An internal clock generates repetitive predictive saccades, Exp. Brain Res. 175 (2006) 305–320.

[12] W.M. Joiner, M. Shelhamer, Pursuit and saccadic tracking exhibit a similar dependence on movement preparation time, Exp. Brain Res. 173 (2006) 572–586.

[13] W.M. Joiner, J.E. Lee, A. Lasker, M. Shelhamer, An internal clock for predictive saccades is established identically by auditory or visual information, Vision Res. 47 (2007) 1645–1654.

[14] N. Levit-Binnun, N.Z. Handzy, A. Peled, I. Modai, E. Moses, Transcranial magnetic stimulation in a finger-tapping task separates motor from timing mechanisms and induces frequency doubling, J. Cogn. Neurosci. 19 (2007) 721–733.

[15] J.M. Mayville, K.J. Jantzen, A. Fuchs, F.L. Steinerg, J.A.S. Kelso, Cortical and subcortical networks underlying syncopated and synchronized coordination revealed using fMRI, Hum. Brain Mapp. 17 (2002) 214–229.

[16] B.H. Repp, Phase attraction in sensorimotor synchronization with auditory sequences: effects of single and periodic distracters on synchronization accuracy, J. Exp. Psychol. Hum. 29 (2003) 290–309.

[17] M. Shelhamer, W.M. Joiner, Saccades exhibit abrupt transition between reactive and predictive; predictive saccade sequences of long-term correlations, J. Neurophysiol. 90 (2003) 2763–2769.

[18] D.L. Sparks, The brainstem control of saccadic eye movements, Nat. Rev. Neurosci. 3 (2002) 952–964.

[19] M.J. Steinbach, Proprioceptive knowledge of eye position, Vision Res. 27 (1987) 1737–1744.

[20] T. Verstynen, T. Konkle, R.B. Ivry, Two types of TMS-induced movement variability after stimulation of the primary motor cortex, J. Neurophysiol. 96 (2006) 1018–1029.

[21] D. Vorberg, A.M. Wing, Modeling variability and dependence in timing, in: H. Heuer, S.W. Keele (Eds.), Handbook of Perception and Action, Academic Press, San Diego, USA, 1996, pp. 181–262.

[22] G. West, T. Welsh, J. Pratt, Saccadic trajectories receive online correction: evidence for a feedback-based system of oculomotor control, J. Motor Behav. 41 (2009) 117–127.

[23] A.M. Wing, Effects of type of movement on the temporal precision of response sequences, Br. J. Math. Stat. Psychol. 30 (1977) 60–72.

[24] A.M. Wing, Perturbations of auditory feedback delay and the timing of movement, J. Exp. Psychol. Hum. Percept. Perform. 3 (1977) 175–186.

[25] A.M. Wing, The long and short of timing in response sequences, in: N.E. Stelmach, J. Requin (Eds.), Tutorials in Motor Behavior, North-Holland, Amsterdam, 1980, pp. 469–486.

[26] A.M. Wing, Voluntary timing and brain function: an information processing approach, Brain Cogn. 48 (2002) 7–30.

[27] A.M. Wing, A. Kristofferson, Response delays and the timing of discrete motor responses, Percept. Psychophys. 14 (1973) 5–12.

[28] A.M. Wing, A. Kristofferson, The timing of interresponse intervals, Percept. Psychophys. 13 (1973) 455–460.

[29] H.N. Zelaznik, R.M. Spencer, R.B. Ivry, Dissociation of explicit and implicit timing in repetitive tapping and drawing movements, J. Exp. Psychol. Hum. Percept. Perform. 28 (2002) 575–588.

[30] H.N. Zelaznik, R.M. Spencer, R.B. Ivry, A. Baria, M. Bloom, L. Dolansky, S. Justice, K. Patterson, E. Whetter, Timing variability in circle drawing and tapping: probing the relationship between event and emergent timing, J. Motor Behav. 37 (2005) 395–403.