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Adaptation of naturally paced saccades

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Gray MJ, Blangero A, Herman JP, Wallman J, Harwood MR. Adaptation of naturally paced saccades. *J Neurophysiol* 111: 2343–2354, 2014. First published March 12, 2014; doi:10.1152/jn.00905.2013.—In the natural environment, humans make saccades almost continuously. In many eye movement experiments, however, observers are required to fixate for unnaturally long periods of time. The resulting long and monotonous experimental sessions can become especially problematic when collecting data in a clinical setting, where time can be scarce and subjects easily fatigued. With this in mind, we tested whether the well-studied motor learning process of saccade adaptation could be induced with a dramatically shortened intertrial interval. Observers made saccades to targets that stepped left or right either ~250 ms or ~1,600 ms after the saccade landed. In *experiment I*, we tested baseline saccade parameters to four different target amplitudes (5°, 10°, 15°, and 20°) in the two timing settings. In *experiments II* and *III*, we adapted 10° saccades via 2° intrasaccadic steps either backwards or forwards, respectively. Seven subjects performed eight separate adaptation sessions (2 intertrial timings × 2 adaptation direction × 2 session trial lengths). Adaptation proceeded remarkably similarly in both timing conditions across the multiple sessions. In the faster-paced sessions, robust adaptation was achieved in under 2 min, demonstrating the efficacy of our approach to streamlining saccade adaptation experiments. Although saccade amplitudes were similar between conditions, the faster-paced condition unexpectedly resulted in significantly higher peak velocities in all subjects. This surprising finding demonstrates that the stereotyped "main sequence" relationship between saccade amplitude and peak velocity is not as fixed as originally thought.

saccade adaptation; motor learning; speed-accuracy trade-off; main sequence

SACCADIC EYE MOVEMENTS are the fastest, most frequent voluntary movements in the human behavioral repertoire. In natural free-viewing conditions, we make saccades more often than our heart beats, at a frequency of roughly 2–3 times per second (Yarbus 1967/1995). In the laboratory, however, experiments often demand much longer periods of fixation between trials, forcing the subject to inhibit his/her natural drive to make exploratory saccades. Such an unnaturally slow pace makes the experiment feel monotonous and fatiguing, potentially affecting the quality of data collected and confounding any experimental effects with changes in arousal levels. Indeed, lowered arousal levels have been associated with reductions in saccadic peak velocities (Di Stasi et al. 2013) and increases in reaction times (Straube et al. 1997). Besides issues of natural temporal conditions, more natural spatial environments, such as complex images, have been reported to quicken latencies (White et al. 2008) and speeds (Jansen et al. 2009) and to change saccade amplitude patterns (Andrews and Coppola 1999). We wondered whether more natural pacing would also affect saccade metrics such as reaction time, velocity, and amplitude.

Saccade amplitudes are modulated by the motor learning process known as saccade adaptation. Because saccades are so short in duration and can reach peak velocities upwards of 900°/s, their trajectories cannot be modified by visual feedback during the movement itself, and accuracy is maintained by an adaptive process based on postsaccadic visual feedback (Noto and Robinson 2001; Wallman and Fuchs 1998). The adaptation is commonly studied by an intrasaccadic step (ISS) paradigm in which a saccade target is repeatedly displaced in one direction during the saccade (McLaughlin 1967). After several repetitions of this systematic error, the saccade gains (saccade amplitude/target amplitude) gradually compensate toward the stepped location of the target.

Saccade adaptation is time sensitive. The error signal is most effective over the first 100 ms of postsaccadic visual feedback, decreasing progressively thereafter (Bahcall and Kowler 2000; Fujita et al. 2002; Panouillères et al. 2011; Shafer et al. 2000). This is consistent with the notion that fixation durations when exploring the natural environment do not last for much longer, and thus any adaptive feedback signals must rely on a very short period of stable visual input. Indeed, after a natural fixation delay of ~400–500 ms, the error signal has a much weaker effect on adaptation. At longer timescales, rest periods of 30 s cause significant reduction in the amount of adaptation retained in several trials after the interruption (Ethier et al. 2008a), suggesting that reduced frequency of saccades, or their consequences, can reduce adaptation. On the basis of these observations, we deemed that saccade adaptation sessions with a short intertrial interval (ITI) might proceed normally. If true, this would allow for much shorter experiments than have been required in the past, which would be especially beneficial in clinical or developmental studies.

Hence, in the present study, we tested a reflexive saccade paradigm with a postsaccadic viewing time of 250 ms, requiring subjects to make visually guided saccades almost continuously. This shortened sessions by almost a factor of 4, compared with control sessions using a more conventional timing. Including reaction time and saccade duration, the intermovement interval (IMI) was similar to natural saccade pacing (479 ms, on average). We employed baseline (nonadaptation) sessions to see whether a naturalistic pacing affected saccade metrics and adaptation sessions to test whether these were unaffected by the pacing.

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A major motivation for this study was to attempt to make saccade adaptation experiments more feasible for use in clinical populations, who may have more difficulty staying awake or focused for the duration of a conventional experiment. Because there is now mounting evidence demonstrating saccade adaptation to be a suitable model for studying motor learning in general (Herman et al. 2013a; Prsa and Their 2011), it has the potential to be a very useful paradigm for studying motor and learning impairments in clinical and developmental populations, but only a handful of studies have taken advantage of this. Existing studies have examined saccade adaptation in patients with cerebellar disease (Alahyane et al. 2008; Choi et al. 2008; Coesmans et al. 2003; Golla et al. 2008; Hubsch et al. 2011; Panouillères et al. 2013; Straube et al. 2001; Xu-Wilson et al. 2009a), thalamic lesions (Gaymard et al. 2001), Parkinson's disease (PD) (Abouaf et al. 2011; MacAskill et al. 2002), schizophrenia (Coesmans et al. 2014; Picard et al. 2012), and autism spectrum disorder (ASD; Mosconi et al. 2013). There have also only been a few saccade adaptation studies in developmental populations (typically developing: Doré-Mazars et al. 2011; Salman et al. 2006a; Chiari malformation: Salman et al. 2006b; children with ASD: Johnson et al. 2013).

Our examination of saccade adaptation during short or long IMIs revealed that saccade adaptation proceeded at least as well in our short-IMI sessions, even though these sessions took <30% of the time of our long-IMI comparison sessions. Our findings demonstrate that the slow pace of typical saccade adaptation experiments may be unnecessary and even detrimental to the amount of adaptation produced.

METHODS

In *experiment I*, we assessed the baseline parameters of alternating blocks of saccades with short (479 ms, on average) and long (1,835 ms, on average) IMIs, which we define as the amount of time between each target-directed primary saccade. That is, the IMI of a given trial is determined by the latency and duration of the primary saccade and the postsaccadic viewing time of the target, which was either fixed at 250 ms or varied between 1,250 and 1,950 ms. *Experiments II* and *III* used the same IMIs in separate sessions to compare their effects on saccade adaptation.

General

Subjects were seated in a dark room, 57 cm away from a 21-in. monochrome CRT display with a vertical refresh rate of 200 Hz (Iiyama Vision Master Pro 514, Oude Meer, The Netherlands) and a resolution of 800 × 600 pixels (visible area 41.5 cm × 30.5 cm). Head and eye position were kept stable by using a table-mounted chin and forehead rest. Subjects viewed the stimuli binocularly, and right pupil position was digitized at 1,000 Hz with an Eyelink-1000 infrared eye-tracking system (SR-Research, Mississauga, ON, Canada).

While seated in the experiment booth, subjects were given general instructions to follow a small annulus that would be moving horizontally about the screen. Before each session began, the eye-tracker was calibrated with a nine-point calibration grid. All subjects gave written informed consent prior to participating, and the experimental protocol was approved by the Institutional Review Board of The City College of New York.

Stimuli

The target stimulus was a small red annulus with a diameter of 0.3° that randomly stepped horizontally to the left or right of its previous location (5°–20° in *experiment I* and always 10° in *experiments II* and *III*). The target steps were contingent upon the bounds of the monitor (±15° from center), thus preventing the target from jumping offscreen. Stimulus generation and display, data storage, and overall experimental session orchestration were controlled with a custom interface in LabVIEW (National Instruments, Austin, TX) running Windows XP (Microsoft, Redmond, WA) on a Dell PC (Austin, TX). Stimulus positions were random but predetermined prior to each session and were the same for every subject.

Experiment I: Baseline Saccades

Data were collected from nine experienced subjects (ages 25–38 yr, 6 men and 3 women). This included three of the authors, who, unlike the other six subjects, were not naive to the purposes of the experiment. *Experiment I* consisted of 400 continuous trials divided into alternating blocks of 50 short-IMI trials and 50 long-IMI trials, giving 200 possible trials per IMI condition. Target amplitudes were equally and randomly distributed among 5°, 10°, 15°, and 20° steps. In this experiment, the target did not step intrasaccadically.

Experiments II and III: Testing Efficacy of Short-IMI Saccade Adaptation

In *experiments II* and *III* we compared gain decrease and gain increase adaptation, respectively, during separate short-IMI and long-IMI sessions. In these sessions the target always made a random horizontal step of 10° and, during the adaptation phase, a backward or forward ISS of 2° to elicit gain increase or gain decrease adaptation, respectively. To examine the effect of session duration (and thus the effect of temporal spacing of trials) on saccade adaptation, we had subjects participate in separate sessions of short (250 trials) and long (800 trials) lengths. We hoped that this would enable a roughly time-equated comparison of the adaptation magnitudes produced by the 250-trial long-IMI sessions and the 800-trial short-IMI sessions. To summarize, there were eight sessions in total resulting from the combination of IMI, session length, and adaptation direction. Because gain increase and gain decrease adaptation likely rely on distinct mechanisms, we conducted separate statistical analyses for *experiments II* and *III*, detailed below.

Data were collected from the same seven subjects in both experiments, six of whom also participated in *experiment I*. Sessions were spaced apart by at least 24 h to avoid any residual adaptation from the previous day. Session run orders were also counterbalanced across subjects. Each session was divided into three phases: a baseline phase in which the target did not make an ISS, an adaptation phase in which the target made 2° ISSs, and a recovery phase in which the target again did not step intrasaccadically. ISSs were triggered once the primary saccade exceeded a velocity threshold of 30°/s. In the short, 250-trial sessions there were 50 baseline trials, followed by 150 adaptation trials and 50 recovery trials. The long sessions contained 150 baseline trials, followed by 500 adaptation trials and 150 recovery trials.

Data Analysis

Saccade gains and other parameters used for analyses were derived from the raw data with a custom software package written for use with MATLAB (The MathWorks, Natick, MA). Primary saccades were detected automatically with a 20°/s threshold, and then each trial was visually inspected for accuracy. During the visual inspection phase, a small number of trials were discarded because of blinks, anticipatory movements (<80 ms or in the wrong direction), and abnormal hypo- or hypermetricity (<65% or >150% of the target step). This amounted to 1,604 of 33,000 trials (4.86%) being rejected.

Statistical analysis in *experiment I* was performed by conducting six separate two-way repeated-measures ANOVAs for each saccade parameter of interest, using IMI length and target amplitude as factors.

For more conservative statistical comparisons between sessions in *experiments II* and *III*, we first estimated population marginal means (PMMs) of the last 50 trials of each phase (*phase 1* = baseline, *phase 2* = adaptation, *phase 3* = recovery) in each session by computing a 3 × 7 × 8 ANOVA, with phase, subject, and session as factors. Adaptation and recovery gain changes were then computed by taking the difference between *phases 1* and *2* or *phases 2* and *3*, respectively. We used the Tukey-Kramer method to do this, which further provided us with simultaneously computed confidence intervals (CIs) on the subject and group levels. The Tukey-Kramer method has the advantage of providing easily graphable comparisons but only gives boundaries for a given α instead of exact P values. The α value is set at 0.05 in all analyses using this method unless otherwise noted. See Herman et al. (2013b) for a similar use of this analysis method.

RESULTS

Assessing whether saccade adaptation proceeds normally during a faster trial pacing than is typically used was the primary goal of this study, but we were also interested in whether faster pacing affects saccade metrics, such as unadapted gains, reaction times, and velocities. In the nonadaptation *experiment I*, we found that short-IMI trials had gains similar to slower-paced trials, facilitating the comparison of adaptation across conditions. Surprisingly, we also found that short-IMI saccades had consistently higher peak velocities and shorter durations and greater amplitude variability without differences in reaction time. In the adaptation experiments, remarkably, we found the adaptation was at least as robust, if not more so, in the short-IMI sessions compared with the long-IMI sessions.

Experiment I: Baseline Saccade Parameters

Short-IMI and long-IMI saccades had very similar spatiotemporal patterns overall. From individual traces in a representative subject (Fig. 1, *A* and *B*), amplitudes and reaction times at all four target step sizes tested were essentially indistinguishable despite the very rapid pacing of the short-IMI conditions. Aligning traces on saccade onset and averaging in this subject showed the highly stereotyped kinematics of saccades (Fig. 1, *C* and *D*) but with greater peak velocities in the short-IMI condition. The same pattern was seen on the group level, as shown in Fig. 1, *E* and *F*. Quantifications confirmed these general patterns across pacing and amplitude conditions (Fig. 2).

Mean saccade gains were unaffected by pacing, but decreased with target amplitude. Across subjects, there was no difference in gain between IMI conditions [Fig. 2*A*; repeated-measures ANOVA, $F(1,8) = 0.08$, $P = 0.79$], but there was a main effect of target amplitude on gain [$F(3,24) = 26.4$, $P < 0.001$]. This "range effect" of target amplitudes on saccade gain is well established in the literature (e.g., Abrams et al. 1989; Kapoula and Robinson 1986), despite recent challenge to it (Gillen et al. 2013). The normality of gain was convenient

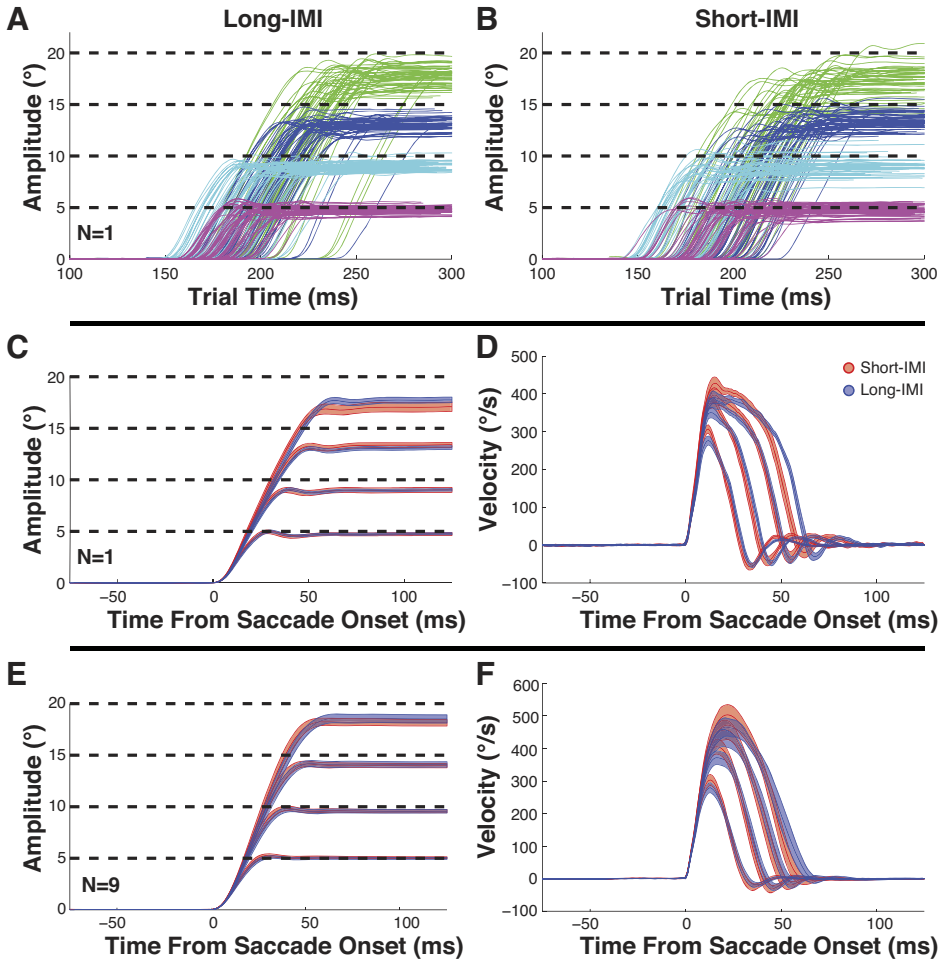

Fig. 1. Position and velocity profiles from nonadaptation *experiment I*. *A* and *B*: horizontal eye movement traces of a representative subject, plotted for long-intermovement interval (IMI) (*A*) and short-IMI (*B*) trials separately. Horizontal dashed lines denote each target amplitude, and saccade traces are color coded according to the target amplitude for that trial. *C–F*: averaged position and velocity profiles for the same subject (*C* and *D*) and across all subjects (*E* and *F*). Shaded fills represent SE. In this figure (*C–F*) and subsequent figures the short-IMI condition is shown in red and the long-IMI condition is shown in blue.

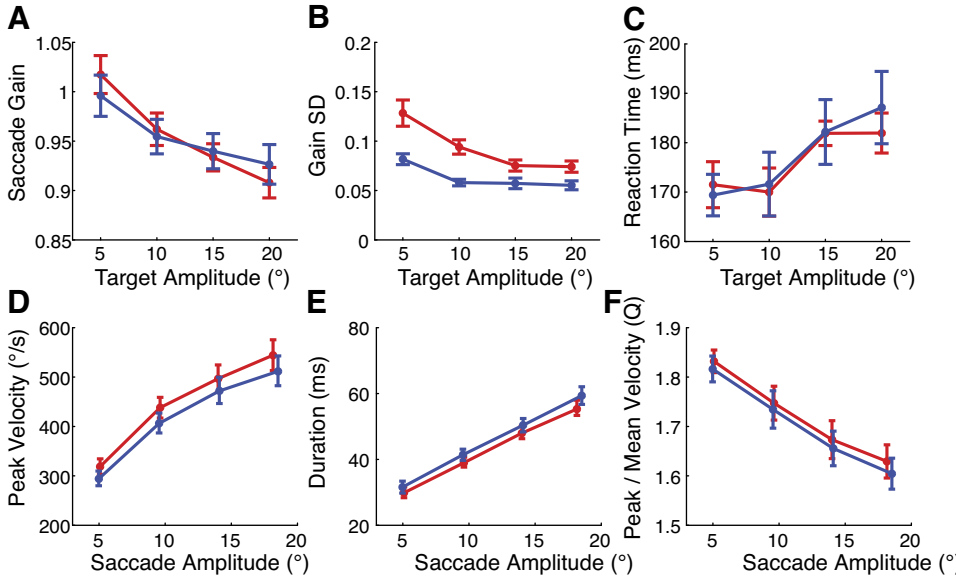

Fig. 2. Baseline saccade metrics. Parameters were computed by averaging across individual subject means. The short-IMI condition is again plotted in red, and the long-IMI condition is plotted in blue. *A–C* are plotted as a function of target amplitude. *D–F* are plotted as a function of saccade amplitude. Error bars are SE.

and reassuring for our aim of studying saccade gain adaptation at faster pacing but was by no means a foregone conclusion. We anticipated that there might well have been a speed-accuracy trade-off, with more urgency to make almost continuous movements, reducing reaction times and reducing landing accuracy.

Although there was surprisingly little effect of pacing on accuracy or reaction times, precision was markedly reduced at faster pacing. Saccade gains were significantly more variable in the short-IMI condition [Fig. 2*B*; $F(1,8) = 42.7$, $P < 0.001$]. There was also a main effect of target amplitude on gain variability [$F(3,24) = 15.8$, $P < 0.001$]. Reaction times were no different between pacing conditions [Fig. 2*C*; $F(1,8) = 0.07$, $P = 0.79$], averaging 179 ± 8 ms (mean ± 95% CI) for the short-IMI condition versus 181 ± 13 ms for the long-IMI condition. Because IMI accordingly varied as a function of reaction time, this meant that average IMIs in the short-IMI condition ranged from 466 to 488 ms. Average IMIs in the long-IMI condition ranged from 1,809 to 1,870 ms. Reaction times increased significantly with increasing target amplitude [$F(3,24) = 10.3$, $P = 0.008$], which is consistent with existing literature for eccentricities upward of 15° (e.g., Kalesnykas and Hallett 1994). Hence, there was no trade-off between speed of reaction and the mean accuracy or precision of saccades. But might there be a trade-off in speed of movement and saccade precision, as typically found in Fitts's law of arm movements (Fitts 1956)?

Saccade speeds increased, and their movement times correspondingly decreased, at faster pacing. The so-called "main sequence" relationships between peak velocity, or duration, and saccade amplitude were shifted by 6–10% at each target amplitude (Fig. 2, *D* and *E*), giving significantly higher peak velocities in the short-IMI condition [$F(1,8) = 40$, $P < 0.001$] as well as significantly shorter durations [$F(1,8) = 9.8$, $P = 0.014$]. Of course, consistent with the classic main sequence pattern, both peak velocity and duration also showed main effects of target amplitude [peak velocity: $F(3,24) = 88.3$, $P < 0.001$; duration: $F(3,24) = 219$, $P < 0.001$]. The main sequence pattern has been modeled as a saccadic equivalent to Fitts's law, but one in which the precision is optimized and essentially fixed (Harris and Wolpert 2006; Tanaka et al. 2006). In other words, the main sequence itself may be the embodiment of a speed-precision trade-off across amplitudes, but we have found the first evidence (of which we are aware) of a speed-precision trade-off within a given amplitude range via the simple manipulation of trial pacing. Because this surprising finding demonstrates that saccade trajectories of the main sequence are not as stereotyped as originally thought, being influenced by the pace at which saccades are made, we looked closer at the shapes of their velocity profiles.

Pacing does not significantly change the shape of saccadic velocity profiles. A simple shape parameter is the ratio between the peak and mean velocities, known as the Q ratio: (peak velocity × duration)/saccade amplitude. This gives a measure of how peaked a profile is and has proven useful in describing abnormal saccade metrics in clinical populations (Garbutt et al. 2003). We found no difference in the Q ratio between IMI conditions [Fig. 2*F*; $F(1,8) = 2.9$, $P = 0.13$] but once again did observe a main effect of target amplitude [$F(3,24) = 20.6$, $P < 0.001$]. Figure 2 shows that as target amplitude increases the Q ratio decreases, meaning that the relative velocity profiles are less sharply peaked at higher target amplitudes.

The striking IMI-related differences in peak velocity, duration, and gain variability were consistent within single subjects. To compare peak velocities within subjects, we first normalized each single-trial peak velocity by dividing it by the square root of its amplitude (see Lebedev et al. 1996). As shown in Fig. 3, we found that every subject showed higher normalized peak velocities and higher gain variability in the short-IMI condition. Paired Student's *t*-tests confirmed that normalized peak velocity was significantly higher for all subjects ($P < 0.02$). Likewise, two-sample *F*-tests of variance revealed significantly greater variability in short-IMI saccade gains within every subject ($P < 0.03$). Duration, on the other hand, was only significantly shorter in four of nine subjects ($P < 0.01$). Hence, the velocity-precision trade-off we observed was not due to individual differences between subjects.

Finally, corrective saccades were common in both pacing conditions. Because the target started each trial from its previous landing position and remained visible during the ITI,

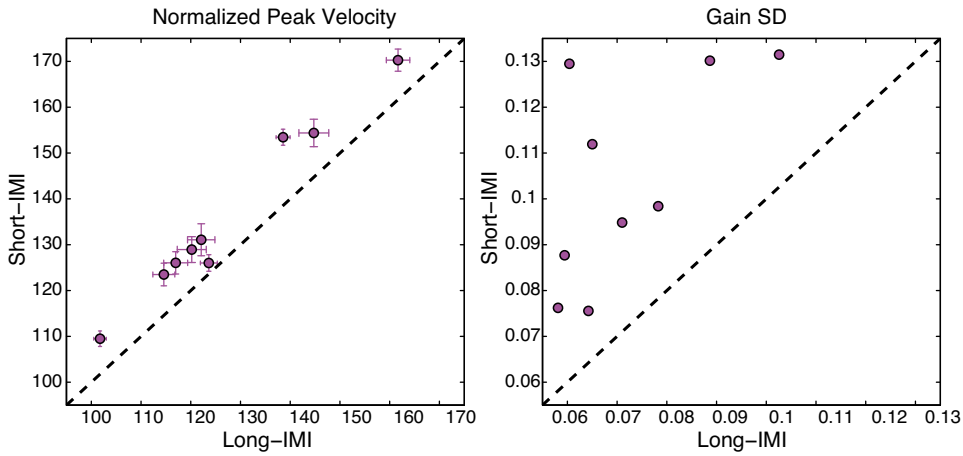

Fig. 3. Speed and precision comparison between short-IMI and long-IMI in individual subjects. *Left*: average normalized peak velocities for every subject, plotted with a line of equality. All data points lie above the equality line, indicating that short-IMI trials resulted in higher normalized peak velocities in every subject. 2D error bars are SE. *Right*: short-IMI trials also resulted in greater gain variability in every subject. In this analysis, gain variability was assessed across all trials, irrespective of target amplitude.

long-IMI trials had more time for subjects to correct for small postsaccade errors. Thus it is unsurprising that long-IMI trials tended to have a higher proportion of correctives than short-IMI trials (39% vs. 31%), but these differences were not significant [$F(1,8) = 3.9$, $P = 0.084$].

Experiments II and III: Ultrarapid Saccade Adaptation Using Short IMIs

There were eight sessions total in these experiments, examining both gain decrease and gain increase adaptation. A short and a long IMI were tested in separate short (250 trials) and long (800 trials) sessions for each experiment such that the 800-trial, short-IMI session was comparable in time to the 250-trial, long-IMI session. Comparing these time-equated sessions allowed us to examine whether there is any influence of time passage on saccade adaptation. The short and long IMIs were evoked by the same postsaccadic viewing times used in *experiment I* (250 ms or 1,250–1,950 ms, respectively).

To validate the main findings of *experiment I*, we conducted paired *t*-tests on the baseline gains and peak velocities across the short-IMI and long-IMI sessions. For both comparisons we obtained one mean value for each subject by first averaging across the last 50 baseline trials in each session and then across sessions. Confirming the findings of *experiment I*, we found that the short-IMI sessions had significantly higher peak velocities [$t(6) = 3.78$, $P < 0.01$; short IMI: 445 ± 39°/s, long IMI: 412 ± 29°/s] and a nonsignificant trend toward higher gains in the short-IMI sessions [$t(6) = 2.06$, $P = 0.085$; short IMI: 0.96 ± 0.03, long IMI: 0.91 ± 0.04].

Experiment II: Gain Decrease Sessions

Adaptation proceeded similarly in the short- and long-IMI sessions, gradually adapting over many trials. Figure 4*A* shows the time course from a typical subject in the long sessions. The gains were more variable throughout in the short IMI, but the time course was similar for the adaptation and then deadaptation in the nonadapting recovery period. Figure 4*B* shows robust lowess fits and associated 95% CIs for gain values averaged across subjects, and again it is apparent that the short- and long-IMI sessions proceed quite similarly.

Adaptation gain changes were significant for short and long IMIs in both the short (150 adaptation trials) and long (500 adaptation trials) sessions. For example, in Fig. 5, *left*, the short-IMI data are shown by the group mean and CI ($\alpha = 0.05$) by the red bar, with the CIs of the seven subjects overlaid. The group- and subject-level CIs were computed simultaneously (but separately for each pair of sessions) via the conservative Tukey-Kramer method for comparing PMMs (see METHODS). Because none of the four group CIs in Fig. 5 overlap the zero gain change reference dashed line, they all adapted significantly. In both short sessions, the same five of seven subjects showed significant adaptation (Fig. 5; $\alpha = 0.05$). In the long sessions, all subjects showed significant adaptation (Fig. 5; $\alpha = 0.05$).

There were no significant group-level differences between IMI conditions, but, surprisingly, there was a trend toward short-IMI adapting more. Within each panel of Fig. 5, the CIs between IMI conditions overlapped and were not significantly different from each other (as indicated by the brackets below the *x*-axis). However, the short-IMI sessions produced slightly larger overall gain changes (short sessions: 0.09 ± 0.01 vs. 0.07 ± 0.01; long sessions: 0.12 ± 0.01 vs. 0.11 ± 0.01). There were also no significant within-subject differences between either pair of short- and long-IMI sessions, as illustrated in Fig. 5 by the overlapping CIs for every subject. Thus it appears that both IMIs affect adaptation similarly after 150 and 500 trials.

To better examine the effect of the number of ISS trials and session durations on adaptation, we compared three other group pairings: short versus long session for each IMI and the time-equated sessions (long session of short IMI vs. short session of long IMI). We applied the same procedure mentioned above to compare group- and subject-level PMMs to establish significant differences between the 250-trial (150 adaptation trials) and 800-trial (500 adaptation trials) adaptation sessions for short and long IMIs separately, and also between the time-equated 800-trial short-IMI session and the 250-trial long-IMI session.

Longer sessions gave greater adaptation, indicating that adaptation in the short sessions did not reach asymptotic levels. This is shown by the group-level comparisons of the red and blue brackets in Fig. 5 showing significance at the $\alpha = 0.05$ level. The relevant mean comparisons are now 0.09 ± 0.01 and 0.12 ± 0.01 for the short-IMI condition and 0.07 ± 0.01 and 0.11 ± 0.01 for the long-IMI condition. Despite these group-level differences, there were no significant within-subject differences between the short and long sessions in the short-IMI

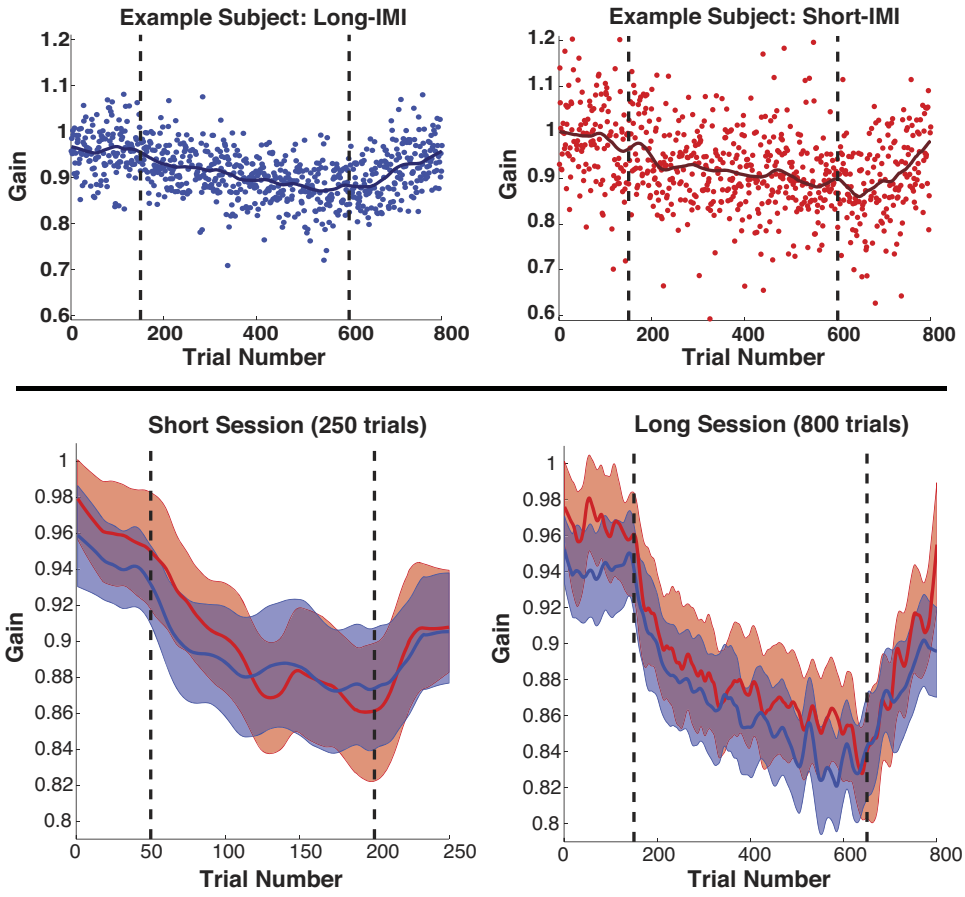

Fig. 4. Gain decrease adaptation sessions. *Top*: raw data from an example participant in the 800-trial gain decrease sessions (long IMI on *left*, short IMI on *right*). Trials in which the target stepped intrasaccadically lie between the dashed vertical lines. *Bottom*: averaged data for the 250-trial (*left*) and 800-trial (*right*) sessions. Solid lines indicate robust lowess fits over the trial-by-trial data after averaging across subjects, using a moving average window of 35 trials. Shaded fills represent SE.

condition, suggesting that the increase in adaptation magnitude after 500 adaptation trials was marginal (but significant across subjects). A similar trend is apparent in the long-IMI sessions, where only two subjects showed significantly greater adaptation magnitudes after 500 adaptation trials (Fig. 5, *right*; $\alpha = 0.05$).

The roughly time-equated sessions revealed significantly greater adaptation in the long, short-IMI session compared with the short, long-IMI session. Examining group-level PMM CIs, the significance of the relevant comparison is indicated by the gray bracket between the two panels in Fig. 5 ($\alpha = 0.05$; adaptation magnitudes: 0.12 ± 0.01 vs. 0.07 ± 0.01), whose average durations were 6 min 54 s and 7 min 40 s, respectively. Only two subjects showed significantly greater adaptation in the long, short-IMI session (Fig. 5; $\alpha = 0.05$).

Recovery. Gain recovery in the postadaptation period, where the target stops making an ISS, proceeded similarly for both IMI conditions. Group means and standard errors for the eight sessions are shown in Table 1. For recovery from gain decrease sessions, there were no significant differences between IMI conditions, both within and between subjects. At the group level, gain recovered in all four session types ($\alpha = 0.05$). At the subject level, in the short sessions (50 recovery trials), most subjects did not show a significant change in gain compared with the end of the adaptation phase. In the long sessions (150 recovery trials), substantially more recovery occurred. Six of

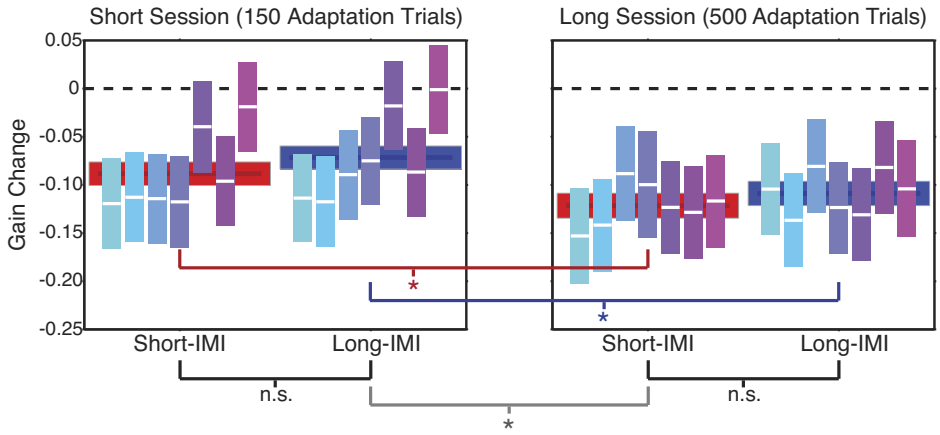

Fig. 5. Statistical comparison of adaptation gain changes in the gain decrease sessions. Adaptation gain changes were calculated by subtracting the population marginal means (PMMs) of the last 50 trials of the baseline phases from the PMMs of the last 50 trials of the adaptation phases. Then the Tukey-Kramer method was used to simultaneously compute confidence intervals on the subject and group levels at an α level of 0.05. Each bracket represents a separate statistical comparison using this method. *Significance at $\alpha = 0.05$ level. n.s., Not significant.

Table 1. *Postadaptation recovery gain changes*

	Gain Recovery	
	Short IMI	Long IMI
Gain decrease		
Short session	0.025 ± 0.013	0.021 ± 0.013
Long session	0.077 ± 0.014	0.063 ± 0.013
Gain increase		
Short session	−0.026 ± 0.016	−0.003 ± 0.016
Long session	−0.051 ± 0.015	−0.039 ± 0.015

Values are group means ± SE. IMI, intermovement interval.

seven subjects showed significant recovery in the short-IMI session, and five of seven subjects showed significant recovery in the long-IMI session.

Experiment III: Gain Increase Sessions

Once again, adaptation proceeded similarly in the short- and long-IMI sessions. Figure 6, *top*, shows data from a typical subject in the long sessions. Figure 6, *bottom*, shows the time course of the averaged group data, which suggests that the short-IMI condition adapts more rapidly than the long-IMI condition over the first 100 adaptation trials—a trend similar to, but stronger than, that in the gain decrease sessions. Overall, adaptation magnitudes were slightly smaller for the gain increase compared with gain decrease sessions, particularly in the short, 150-adaptation trial sessions, which is in line with previous literature showing a smaller slope/longer acquisition period for gain increase adaptation.

All gain increase sessions produced significant adaptation on the group level (Fig. 7; $\alpha = 0.05$). On the subject level in the short sessions, only three subjects showed significant adaptation in the short-IMI session and only two subjects showed significant adaptation in the long-IMI session (Fig. 7; $\alpha = 0.05$). In the long sessions, all seven subjects showed significant adaptation in the short-IMI session while only five subjects showed significant adaptation in the long-IMI session (Fig. 7; $\alpha = 0.05$).

The major difference from the gain decrease data was the surprising finding that short-IMI led to more adaptation in the longer trial sessions than long-IMI pacing. The average magnitudes (0.11 ± 0.01 vs. 0.08 ± 0.01) for short IMI and long IMI, respectively, were significantly different (Fig. 7, black asterisk; $\alpha = 0.05$). Comparing IMI conditions in the short sessions, there was a similar but nonsignificant trend (Fig. 7; average magnitudes: 0.07 ± 0.02 vs. 0.06 ± 0.01).

We again conducted further Tukey-Kramer corrected comparisons to examine the effect of number of ISS trials and session duration on adaptation magnitudes. These additional comparisons revealed significantly greater adaptation after 500 ISS trials in the short-IMI sessions (Fig. 7; $\alpha = 0.05$; average magnitudes: 0.07 ± 0.02 vs. 0.11 ± 0.02) and a smaller such difference between the long-IMI sessions that was not significant at $\alpha = 0.05$ (Fig. 7; average magnitudes: 0.06 ± 0.01 vs. 0.08 ± 0.01).

Comparing the time-equated sessions again revealed significantly greater overall adaptation in the long, short-IMI session compared with the short, long-IMI session (Fig. 7; $\alpha = 0.05$;

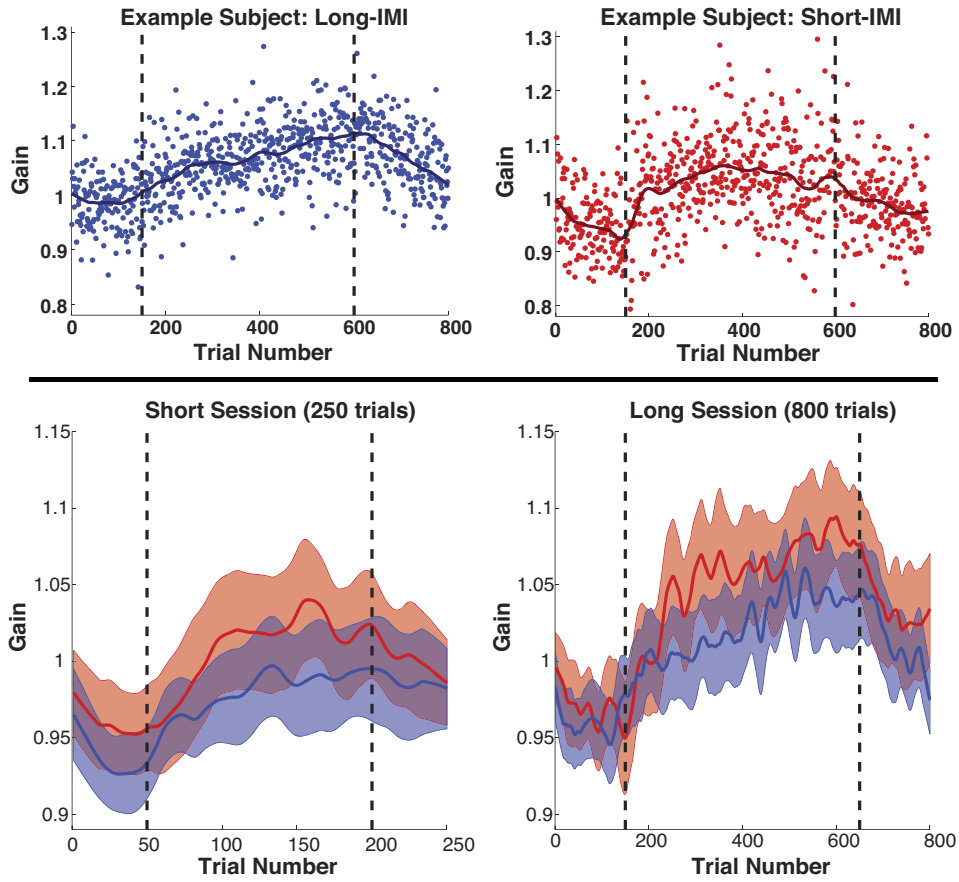

Fig. 6. Gain increase sessions. *Top*: raw data from the same subject as in Fig. 4 in the 800-trial gain increase sessions. *Bottom*: averaged data for the 250-trial (*left*) and 800-trial (*right*) gain increase sessions. Solid lines indicate robust lowess fits over the trial-by-trial data after averaging across subjects, using a moving average window of 35 trials. Shaded fills represent SE.

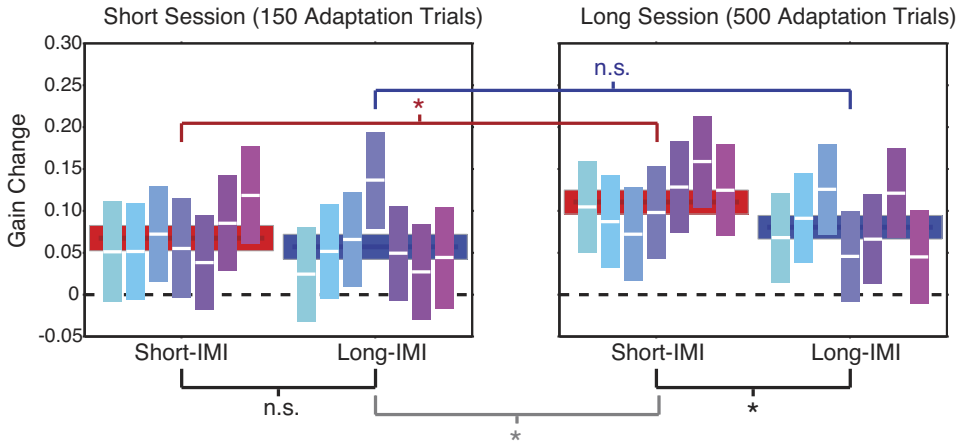

Fig. 7. Statistical comparison of adaptation gain changes in the gain increase sessions. Adaptation gain changes were calculated by subtracting the PMMs of the last 50 trials of the baseline phases from the PMMs of the last 50 trials of the adaptation phases. Then the Tukey-Kramer method was used to simultaneously compute confidence intervals on the subject and group levels at an α level of 0.05. Each bracket represents a separate statistical comparison using this method. *Significance at $\alpha = 0.05$ level.

average magnitudes: 0.11 ± 0.01 vs. 0.06 ± 0.01; session durations: 6 min 24 s vs. 7 min 35 s). This supports the often-assumed notion that saccade adaptation depends more on the number of ISS trials than on the duration of the session.

Recovery. Recovery from gain increase adaptation was overall smaller in magnitude compared with gain decrease recovery (Table 1), but then adaptation magnitudes between experiments were also smaller. Again there were no within- or between-group differences in IMI condition. In the short sessions, the short-IMI session showed a significant change in gain on the group level, with two subjects also showing significant gain changes ($\alpha = 0.05$). In the long-IMI session on the other hand, there was no significant gain recovery on the group and single-subject levels. In the long sessions, there were significant group-level gain changes in both sessions, with three subjects showing significant recovery in the short-IMI session and two subjects showing significant recovery in the long-IMI session ($\alpha = 0.05$).

DISCUSSION

Effective Saccade Adaptation to Short IMIs

We sought to test whether a more naturally paced, shortened IMI would have an effect on the magnitude of saccade adaptation. In our short-IMI sessions, subjects were paced to make saccades about twice a second, which reduced the duration of these sessions by 75% compared with our more traditionally timed long-IMI sessions. In fact, this meant that the 250-trial short-IMI sessions were completed in just under 2 min, while the 250-trial long-IMI sessions took slightly longer than 7.5 min. Despite this drastic reduction in session duration, saccade adaptation proceeded remarkably similarly for both IMIs. Our findings conclusively show that very short trial durations can be effectively used in saccade adaptation experiments without affecting the completeness of adaptation. This represents a significant methodological advance that we hope will further facilitate the study of saccade adaptation in clinical populations.

The unimpaired adaptation seen in the short-IMI sessions is consistent with studies showing that complete saccade adaptation can occur from postsaccadic target durations of as little as 80–100 ms (Panouillères et al. 2011; Shafer et al. 2000). However, some integration of the visual error driving adaptation can still occur for quite some time after a saccade. When a target is extinguished during a saccade, significant gain changes can still be elicited if the stepped target is reilluminated up to 600 ms later (Bahcall and Kowler 2000; Fujita et al. 2002). Hence, it was not by any means certain whether an average IMI of 479 ms, equivalent to a postsaccadic viewing time of ~250 ms (the difference arising from reaction and movement times), would produce the same amount of adaptation.

Indeed, contrary to what might have been expected, there was actually a small trend toward greater adaptation in the short-IMI sessions, which was significant on the group level in the 800-trial gain increase session. Thus not only were the short-IMI sessions almost four times shorter in duration, they were also somewhat more effective than the long-IMI sessions in eliciting adaptation. This finding can be interpreted in two ways: *1*) the increased rate at which saccadic errors were experienced in the short-IMI session facilitated learning and increased the level at which adaptation magnitudes asymptote and/or *2*) adaptation in the slower session did not reach true asymptotic levels because of reduced arousal and/or a greater impact of learning decay.

It has been proposed that the motor memory serving saccade adaptation is composed of a fast and a slow state that learn and decay on different timescales while both simultaneously contributing to saccade amplitude on a given trial (Ethier et al. 2008b). If we conjecture that short IMI affects a fast process more than a slow one, because of its faster-paced error exposure, it could explain two trends in our data. First, because the fast timescale contributes more to adaptation rate in gain-increasing paradigms than in gain-decreasing paradigms (Ethier et al. 2008b), a stronger fast process in short IMI would be more easily revealed in gain-increasing than gain-decreasing sessions. As stated above, this is what we found (compare Figs. 5 and 7). Second, there should be more recovery during short IMI, the trend for which can be seen in Table 1.

As a way of further exploring the contribution of time passage to saccade adaptation, we conducted a 250-trial and a 800-trial session for both IMIs and both adaptation directions, which allowed us to have pairs of short-IMI and long-IMI sessions of comparable durations. In these comparisons we found that there was significantly more adaptation in both of the 800-trial short-IMI sessions compared with the 250-trial

long-IMI sessions, indicating that the number of errors experienced was more important than the time elapsed. This finding also suggests that there is no observable cost of massed practice in saccade adaptation, contrasting other types of motor learning, where it has been shown that massed practice has a detrimental effect on learning (e.g., Lee and Genovese 1988; Stelmach 1969).

Proof of Utility of Short-IMI Adaptation: Parkinson's Disease Patient

Since all of the subjects in this experiment were at least somewhat experienced with eye movement experiments, it remains to be seen how successful short-IMI saccade adaptation paradigms might be in more naive subjects, or patients for that matter. As a step toward establishing our simple short-IMI saccade adaptation paradigm's viability for use in patients, we recently had the opportunity to test a 250-trial short-IMI saccade adaptation session on a patient with PD. Before participating in the short-IMI session, the patient unsuccessfully attempted a more conventionally timed saccade adaptation paradigm. His failure in the conventional paradigm was mainly due to a marked impairment in initiating saccades, a common problem in the disease. Perhaps to compensate for this impairment, the patient often made microsaccades in the opposite direction just before the primary saccade or synkinetic blinks with the saccade. [These would both interrupt omnipause neuron (OPN) activity, perhaps facilitating saccade initiation.] The patient's ptosis (droopy eyelids) additionally made recording difficult. Remarkably, however, when he attempted the short-IMI gain decrease paradigm, all of these problems were alleviated enough for usable data to be recorded. Although the data were noisy, Fig. 8 shows that this patient exhibited a steady decrease in gain to the back-stepping target. This result is in line with the finding that adaptation of reactive saccades is not impaired in PD (MacAskill et al. 2002). Importantly for the present study, it demonstrates that even in one of the most difficult cases to record, the short-IMI was remarkably effective—perhaps paradoxically so, given the patient's initiation problems.

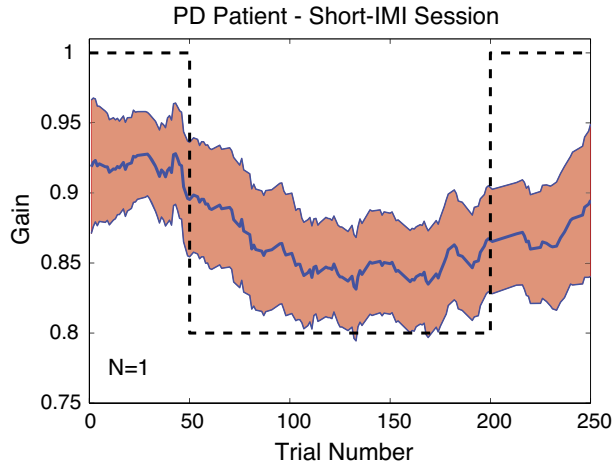

Fig. 8. Short-IMI gain decrease adaptation in a patient with Parkinson's disease (PD): moving average of gains (blue curve; span 40 trials) with 95% confidence intervals shown by shaded region. Superimposed is the final target amplitude in gain units (black dashed line) showing the 50 trials before and after adaptation and 150 adaptation trials in which the target stepped back to 8° upon saccade.

Baseline Effects on Short-IMI Saccades

Experiment I unexpectedly revealed that faster-paced saccades had peak velocities that were consistently higher across all four target amplitudes tested, demonstrating that the highly stereotyped main sequence relationship between peak velocity and saccade amplitude can be shifted simply by changing the pace at which an observer makes saccades. This finding is quite surprising, as very few studies have observed robust task-related increases of saccadic peak velocity. A strong increase in peak velocity has been observed in monkeys when saccades to a target were rewarded (Chen et al. 2013; Takikawa et al. 2002). In humans, very small peak velocity increases (~1%) have been reported when subjects were putatively rewarded with upright face stimuli compared with inverted faces or noise patches (Reppert et al. 2012; Xu-Wilson et al. 2009b). Larger (4%) velocity increases were found when subjects finger tapped an array of targets compared with making saccades alone (Epelboim et al. 1997). Velocity increases comparable to ours (10%) were found in a perceptual task in which a discriminandum was only present for 13 ms at the median of subjects' latencies, thus encouraging both shorter latencies and faster saccades (Montagnini and Chelazzi 2005); subjects varied considerably in their task-related velocity changes. All these previous studies involved different stimuli or task demands. We find our results more surprising given that the stimuli and task were always the same and only the pacing varied; moreover, all our subjects showed significant velocity increases.

Concurrent with our own experiments, another group has also recently shown that IMI has an effect on peak velocity and duration (Haith et al. 2012). The premise of their modeling study was that simply making a successful saccade is rewarding in some sense, and that the expected value of this reward is discounted as a function of time. They further proposed that in sequences of saccades the goal of the oculomotor system might then be to maximize the rate of reward. Hence, increasing the pacing increases the rate of the most rewarding (least discounted) visual information, which increases the "value" of each saccade leading to faster movements. To test their model predictions, they conducted an experiment in which subjects made ~40° horizontal saccades to two alternating targets while the ITI was parametrically varied on a trial-by-trial basis. They found that peak velocities increased and durations decreased with decreasing IMIs. Although temporal discounting is usually used to explain behavior on a much longer timescale, they provide an interesting explanation for why IMI has such a robust effect on saccade kinematics.

Our data both support and question facets of their model. We extend their empirical findings to a more natural oculomotor range, and at an individual rather than group level. All nine of our subjects had significantly faster normalized velocities at short IMI compared with long IMI (Fig. 3, *left*). The 10% speed increase to 10° targets matches their model well, but we found a slight downward trend as target amplitude increased (e.g., 7% at 15°), opposite to their model prediction of increasingly fast velocities at larger amplitudes. More importantly, their model was based on a binary success criterion of landing

within 1° of the target and, empirically, their ITI started when the eye was within 3° of the target. Given that saccades are known to undershoot more at larger target amplitudes (Fig. 2*A*; Abrams et al. 1989; Becker 1991), saccades landing within 3°, let alone 1°, of a 40° target in a single movement should be rare. The inevitable presence of corrective saccades may have increased their IMI well beyond their intended/reported IMI, and these corrective movements were not considered by the model. Finally, they did not report finding any change in precision of saccade accuracy or include modulations of that in their model.

Speed-Precision Trade-Off

A striking feature of our data was the increased variance of gain in the short-IMI pacing (Fig. 2*B*). Increases in gain variability were associated with increases in peak speed (Fig. 3), suggesting that a speed-precision trade-off might underlie these effects of changing pacing. This observation fits with the notion that saccade amplitude variability is primarily governed by signal-dependent noise: faster movements with their larger control signals incur more neural noise, which results in greater inaccuracy (Harris and Wolpert 1998). This speed-accuracy model predicts saccade trajectories in remarkable detail (Harwood et al. 1999). By adding a proportionate cost-of-time to the movement, Harris and Wolpert (2006) predicted the peak velocity-amplitude and duration-amplitude relationships ("main sequence") well. They included a "postmovement fixation period" factor, reasoning that the longer a given fixation lasts, the greater the cost of an inaccurate eye movement. They predicted that this would have an effect on peak velocity/duration very similar to what we observed. Hence, the Harris and Wolpert model is sufficient to explain our findings without including the hyperbolic temporal discounting functions of Haith and colleagues.

In summary, the surprising plasticity of the main sequence due to pacing found by us and Haith et al. is not easily explained from earlier ideas that the main sequence resulted from limitations on motoneuronal firing (e.g., "bang-bang control models," Lehman and Stark 1979). Modern optimization models provide provocative and exciting explanations of this novel finding, with or without invoking hyperbolic temporal discounting.

A Neurophysiological Explanation?

Is there a plausible physiological explanation, either in opposition to the above models or as a biological implementation thereof? OPNs pause during saccades in all directions and otherwise fire tonically during fixation (Luschei and Fuchs 1972). Consequently, OPNs have typically been thought to act as a gating mechanism for saccade generation, through their inhibitory action on excitatory burst neurons (EBNs) (Sparks 2002). However, an alternative role has been proposed more recently in which OPNs act as a gain controller for EBNs (Optican 2008). Optican reasoned that since OPNs use glycine to inhibit EBNs, as opposed to GABA, OPNs have the potential to exert an additional facilitatory influence on EBN activity through glycine's excitatory action on NMDA receptors. Using a simplified model of this proposed mechanism, he showed that OPNs could thus have a modulatory effect on peak velocity, which could explain monkey studies showing that OPN lesions reduce peak velocities in otherwise normal saccades (Soetedjo et al. 2002). Optican viewed OPN activity as signaling that information useful to reorienting to a target of interest was about to arrive, and hence OPNs go silent during saccades when no useful information is incoming. Perhaps this would also explain the observed postsaccadic enhancement of OPN tonic firing rates observed from analysis of the 50 ms (Gandhi and Keller 1999) or 50–150 ms window (Everling et al. 1998) after saccade when new visual or reafferent information comes in. We propose that this expectation/arousal signal might increase with increased saccade pacing, since the expectation of useful information to orient toward would increase, leading to increased OPN tonic firing before saccades and thence higher peak velocities in the Optican model. Thus an active expectation or arousal mechanism might both increase OPN firing after saccades and also explain how increased pacing increases peak velocities by increasing OPN activity before saccades. A similar connection between OPN activity, saccadic peak velocity, and arousal has also recently been suggested particularly in the context of the more common finding of reduced saccade speed with decreasing arousal levels (Di Stasi et al. 2013). It remains to be determined whether the effects of saccade pacing on velocity are due to a generalized arousal mechanism or a specific expectation signal corresponding to the value of expected rewards inherent in either the Harris and Wolpert or, particularly, the Haith and colleagues model.

An alternative OPN mechanism to explain our pacing changes based on the biophysics of membranes seems unlikely. Gandhi and Keller (1999) suggested that their postsaccadic OPN enhancement might be due to postinhibitory rebound: a transient depolarization following a hyperpolarization. As pacing increases, the postsaccadic interval becomes closer in time to the presaccadic interval. Might postsaccadically increased OPN activity, due to rebound, linger such that higher OPN firing before the next saccade leads to higher peak velocities? The timing of our short IMI seems too long to make this explanation plausible. However, little is yet known of how very rapid, repeated on-off switching of OPNs affects their intersaccadic firing.

Conclusions

Testing a natural pacing of saccades leads to increases in peak velocities and variability but leaves mean gain accuracy unaffected, with gain adaptation being as effective as at slower pacing, if not more so. Perhaps the greater adaptive efficacy of error signals immediately after the saccade (Panouillères et al. 2011; Shafer et al. 2000) originates from the same mechanism as the peak velocity effects but was only revealed in one of our adaptation conditions because of the inherent greater variability in adaptation between and within subjects compared with the more stereotyped main sequence. In addition to these novel theoretical and empirical considerations, we have demonstrated the potential utility of faster pacing for clinical and developmental studies.

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DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the author(s).

AUTHOR CONTRIBUTIONS

Author contributions: M.J.G., J.P.H., J.W., and M.R.H. conception and design of research; M.J.G. and M.R.H. performed experiments; M.J.G. and J.P.H. analyzed data; M.J.G., A.B., and M.R.H. interpreted results of experiments; M.J.G. prepared figures; M.J.G. drafted manuscript; M.J.G., A.B., and M.R.H. edited and revised manuscript; M.J.G., A.B., J.P.H., and M.R.H. approved final version of manuscript.

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