Timing of concurrent visual stimuli determines modulation of saccadic amplitude

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The temporal relation of competing visual stimuli may determine the corresponding oculomotor response. In this study we systematically varied the temporal coincidence of two conflicting stimuli and investigated saccades that were elicited from such stimuli. We varied the time of presentation of two identical spatially separated stimuli between 0 and +165 ms and measured the amplitude of the saccade elicited by these stimuli using infrared eye tracking. In the first experiment, all stimuli were shown for 36 ms only. In the second experiment, stimuli remained on the screen until the subsequent stimulus appeared, whereas in the third experiment all stimuli were removed after saccade onset. Up to an interstimulus interval of 82 ms, we found a significant shift of the saccadic endpoint toward the location of the second stimulus as compared to saccades toward the first stimulus alone. The strongest saccadic bias was observed if a stimulus was shown 36 ms after or before another stimulus. In contrast, time intervals longer than 82 ms elicited saccade adaptation—that is, the saccadic landing point gradually moved toward the second location over time. In more than 99% of trials, the second stimulus appeared before the saccade reached its endpoint. The timing of a conflicting stimulus determines the associated saccadic response: Simultaneous presentation of two stimuli results in a saccadic endpoint at an averaged intermediate position, short interstimulus intervals result in a strong shift of the saccadic endpoint toward the location of the second of two consecutive stimuli, and longer interstimulus intervals elicit saccade adaptation. The timing of two stimuli thus is associated with distinct processes, which complement each other in order to provide an optimal oculomotor response.

Introduction

A saccade is an eye movement bringing the image of an object of interest, a *target*, from the retinal periphery with low spatial resolution onto the fovea with a maximal spatial resolution. Oftentimes a visual scene contains not one single target but rather several, some of more and some of less relevance to the viewer. The neurophysiological processes of conflicting simultaneous stimuli have been extensively investigated in the saccadic system: It has been found that the simultaneous presentation of two visual stimuli leads to saccades with a landing point at an intermediate position (Findlay, 1982). This observation is termed the *global effect* or *saccadic averaging*. It is thought to be the result of saccade-related neuronal-activity peaks of concurrent vectors to two different stimulus locations leading to a new averaged activity peak at an intermediate position (Vokoun, Huang, Jackson, & Basso, 2014). Such averaged neuronal activity has been recorded at the level of the superior colliculus (Glimcher & Sparks, 1993). The global effect can only be observed if the competing visual stimuli are located at an angular distance of less than ~20°. Stimuli farther apart result in a prolonged saccadic latency instead. This has been termed the *remote distractor effect* (Walker, Deubel, Schneider, & Findlay, 1997). The

magnitude of the averaging effect depends on stimulus saliency, size, color, and brightness, as well as higher order signals, for example expectancy (Coren & Hoenig, 1972; Findlay, 1982). For a review of this phenomenon, see Van der Stigchel and Nijboer (2011). This is why some refer to the landing point as the center of gravity: The more prominent a stimulus is, the more it pulls the landing point toward it. Thus, the spatial and contextual influence of simultaneous stimuli on a saccadic response is known in great detail.

Less clear are the temporal requirements for the global effect and more generally the influence of the competing stimuli's timing on a visual response. Two stimuli may be in a temporal conflict in addition to the spatial conflict. The prototypical example of such a temporal conflict is the double-step paradigm, where a saccadic target is moved to a different location during the saccade movement to a first stimulus. If this is done repeatedly, an adaptation of the saccadic amplitude may be observed—that is, the saccadic amplitude gradually changes toward the location of the second stimulus, such that correcting saccades become smaller over time (McLaughlin, 1967). The pathophysiological correlate of this may be a paralytic or mechanical change in the orbit resulting in systematic deviation of the saccadic landing point, which may then be gradually corrected for—adapted—resulting in good spatial accuracy. This mechanism is thought to continuously calibrate the saccadic system to good accuracy (Abel, Schmidt, Dell'Osso, & Daroff, 1978). Saccadic adaptation has been shown in various conditions. It is influenced by stimulus size, stimulus location, stimulus saliency, and top-down control but is independent of nearby distractors (Madelain, Harwood, Herman, & Wallman, 2010), background (Robinson, Noto, & Watanabe, 2000), or attention (Ditterich, Eggert, & Straube, 2000), and it can even be induced using static stimuli rather than a stimulus shift (Schütz, Kerzel, & Souto, 2014). In the majority of saccadic-adaptation studies, the stimulus shift is made during the saccade, and thus little is known about the effect of stimulus timing on saccade amplitude. One exception is the report by Choi, Viswanathan, and Barton (2016), who investigated the saccadic amplitudes elicited by targets and distractors that were shown at different times. They found that a distractor's influence decayed substantially if it was shown between 100 and 300 ms after target onset. They claim that a distractor must appear not later than 100 ms after target onset and that distractor and target must be displayed with a temporal overlap in order to induce a global effect.

Another noteworthy work comes from Panouillères, Gaveau, Socasau, Urquizar, and Pélisson (2013), who found that adaptation could be elicited by intrasaccadic error signals only. This was novel because it had been thought that only targets shown after saccade landing were able to induce an adaptive change of amplitude. In a later study (Panouillères et al., 2016), the crucial time point during the saccadic flight time was further investigated, and the authors concluded that saccade adaptation is induced only when the visual error signal is presented near the time of peak deceleration or saccade termination, not near the time of peak velocity.

One could argue that the global effect and the double-step saccade-adaptation paradigm are two extremes of temporally conflicting stimuli, one with simultaneous onset and another with onset simultaneous to the saccade. In natural nonstatic visual scenes, however, stimuli may appear at any time and any location, thus creating a continuous spectrum of spatial and temporal conflicts. For example, when one looks at the front door and two children enter while running after each other, they appear at close spatial and temporal disparity, creating a conflict in space and time, which challenges the saccadic system with the demand of choosing a saccadic landing point that provides the best overview over the situation. In the current study, we chose two stimuli with a constant distance and systematically varied the temporal properties of presentation to investigate the effect of time on the saccadic landing point.

Methods

Subjects

Thirteen subjects (five women, eight men; median age = 25 years, range = 21–29) participated in Experiment 1. Twelve subjects (four women, eight men; median age = 25 years, range = 22–27) participated in Experiments 2 and 3. All subjects were healthy and had normal vision (no lenses or glasses). Besides the authors who participated (Mathias Abegg and Moritz Feil), subjects were not aware of the study's goal and did not have any experience with eye-tracking studies. They gave informed consent in accordance with the Declaration of Helsinki. No financial compensation was given to the subjects. The study was approved by the local ethics committee.

Apparatus

The subjects were seated 60 cm (50 cm for Experiment 2) away from a screen with their head immobilized by a chin and forehead rest. A 20-in. CRT monitor (ViewSonic G220fb) with dimensions of 1,024 × 724 pixels and a refresh rate of 85 Hz was used for all experiments. The room's luminance was kept constant
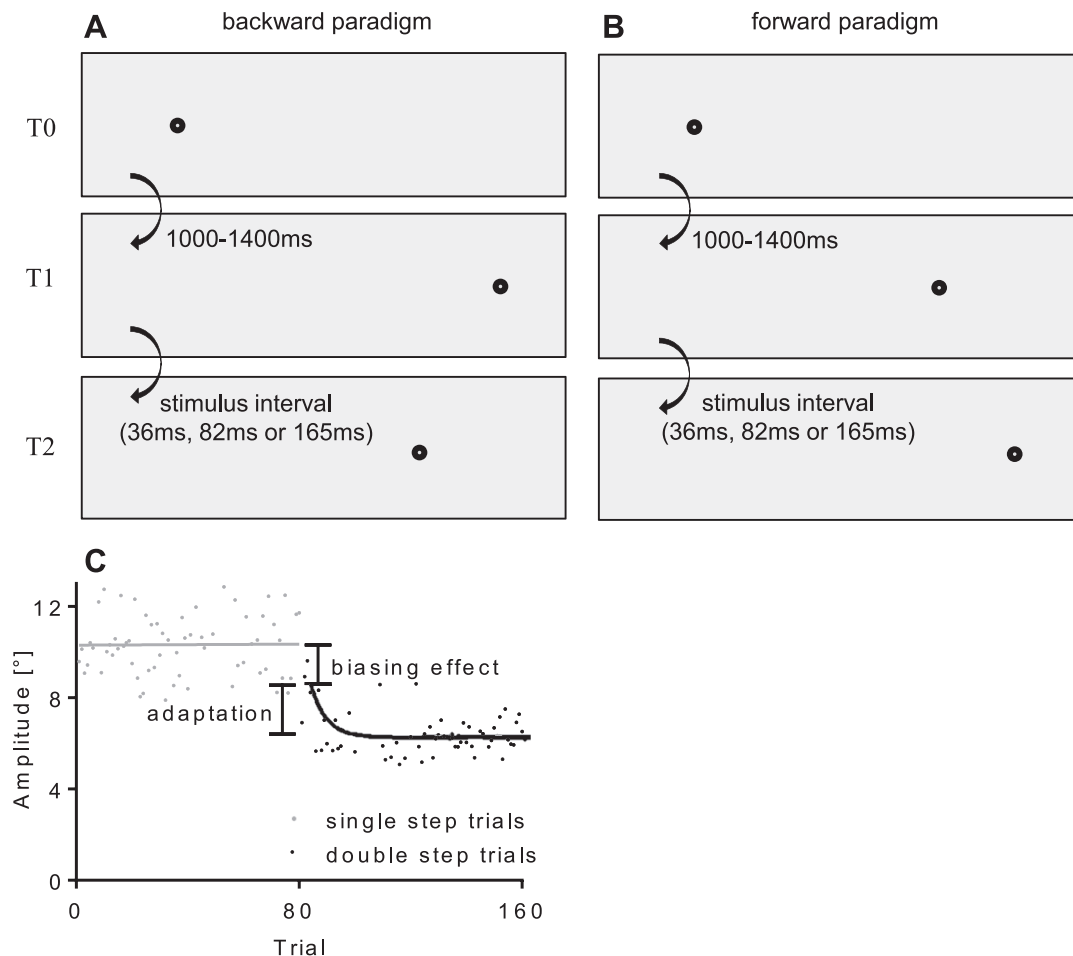
Figure 1. (A–B) The experimental design of the double-step trials. In Experiment 1, T1 and T2 were shown for 36 ms and then disappeared. In Experiment 2, targets were visible until the subsequent target appeared, whereas in Experiment 3 the screen blanked at saccade onset. The stimulus interval is the time between the onset of the first and second stimuli—that I, between T1 and T2. Single-step trials are identical, except that no T2 stimulus was shown. (C) Data for one subject from a backward-paradigm block preceded by a single-step block. It illustrates how the amount of adaptation and averaging effect were calculated: The single-step trials were fitted with a linear regression function, the double-step trials with an exponential model described in Analysis.

at a dim level during all experiments. Eye movements were recorded at 2,000 Hz using the EyeLink 1000 system (SR Research, Mississauga, Canada). The eye tracker was calibrated using a nine-point array. Calibration was considered successful if accuracy was at least 1°. The experiments were designed using ExperimentBuilder 4.56 (SR Research).

Procedure

All experiments started with a single-step block. This was followed by six double-step blocks. Between each pair of double-step blocks, a single-step block was inserted. We used double-step blocks with stimulus intervals of 36, 82, and 165 ms; each stimulus interval was tested in a forward paradigm with the second target farther away from the starting point and a

backward paradigm in which it was closer (see Figure 1). This resulted in six different types of double-step blocks. In Experiments 1 and 3 we added a simultaneous block with simultaneous presence of two stimuli (thus a stimulus interval of 0 ms). This block was also preceded by a single-step block. Thus in total we used 14 blocks in Experiments 1 and 3 and 12 blocks in Experiment 2. The order of the double-step blocks was randomized for each subject. The first block in Experiment 2 consisted of 25 trials; all other blocks contained 80 trials each, which also were newly randomized for each subject. Before each block, the calibration was validated; if accuracy was less than 1° the system was recalibrated. All stimuli were identical black spots of 1° in size with a white dot inside on a light-gray background. The subjects' task was to "always look at the stimulus." We did not give any information on which stimulus subjects had to fixate in

case of ambiguity. The entire experiment lasted about 45 min.

The experimental design is illustrated in Figure 1. All double-step trials began with a starting target (T0), which remained visible for a random period of 1,000 to 1,400 ms and then was replaced with target point T1 (first step). After the stimulus interval (36, 82, or 165 ms), T1 was replaced by target point T2 (second step). If T1 was 8° from the fixation point, T2 was always at 12°. Since this constellation potentially induces forward adaptation—that is, an adaptation with increased saccadic amplitudes—we termed this the *forward paradigm*. Inversely, if T1 was at 12° and T2 at 8°, we termed this the *backward paradigm*. In order to prevent predictability of stimulus locations, the targets appeared randomly to either the left or the right of T0 if the target location (T1 and T2) was within the physical limitations of the screen. If the randomization algorithm selected a target location outside the physical limits of our screen, we reversed the direction of the target. The stimulus location of T2 represented the starting point T0 for the subsequent trial. Before the beginning of the next trial, however, the starting point shifted randomly between 0.5° and 2° to the left or the right with a slow, sinusoidal movement. This ensured that the targets changed their location on the screen over the trials and that stimulus locations were not predictable from preceding trials or visual cues such as the screen frame. In the trials of single-step blocks, no T2 stimulus was shown; instead, T1 of the current trial served as starting point T0 of the subsequent trial, again only after a random horizontal displacement of the stimulus. The amplitude of target points T1 from the following double-step block was used as the single target in the single-step blocks. This was thus 12° for the backward paradigm and 8° for the forward paradigm.

In Experiment 1, stimuli T1 and T2 were each shown for only 36 ms and then disappeared. The starting stimulus of the subsequent trial reappeared at a random time interval ranging from 700 to 900 ms.

In Experiment 2 we explored saccades under conditions with visual feedback. For this we examined six conditions in 12 blocks, using the identical design as for Experiment 1 except that all stimuli remained on the screen until they were replaced by the subsequent stimulus. Thus, T1 remained visible for the duration of the stimulus interval and T2 remained visible for a random duration between 1,000 and 1,400 ms. After that it served as T0 of the subsequent trial.

In Experiment 3 we examined saccades under conditions of no visual feedback. For this, T1 also was visible until T2 was shown. However, all stimuli disappeared at saccade onset, defined by a velocity of more than 22°/s, independent of whether T2 had already appeared on the screen. As computing time and

refresh rate induced some additional delay, the screen was only blanked at a median of 31 ms after saccade onset. The median saccade duration was 51 ms. In a trial-by-trial analysis (data not shown), we found that the screen was blanked before saccade end was detected in every trial of Experiment 3. As in Experiment 1, we added a simultaneous block with a stimulus interval of 0 ms at the end, thus resulting in a total of 14 blocks for this experiment.

Analysis

We used saccadic amplitude as the primary outcome measure. For this we used the first saccade after the onset of T1 with an amplitude greater than 5° and a starting point within 1° of T0, thus resulting in one saccade per trial. Saccades with amplitudes larger than 15° or latencies less than 80 ms or more than 300 ms were excluded as obvious outliers. Saccades containing blinks were also excluded. On this basis, a total of 18.1% of all saccades were rejected. Two subjects had to be excluded altogether from Experiment 1 due to more than 60% rejected trials.

To analyze the double-step measurements, which are expected to follow an exponential distribution, we fitted the following model to the data as proposed by Souto, Gegenfurtner, and Schütz (2016):

$$S(t) = \alpha + \beta e^{-\lambda t}$$

The asymptotic level is α, the adaptation rate λ, and the amplitude of the decay β. We used the nls-function of R to determine the least-squares estimates of the parameters of this nonlinear model by minimizing the sum of squared differences between the model and the data. To find starting estimates, we log transformed the data, which allowed us to determine suitable values from a linear model fit. The single-step trials were fitted with a linear model applying a least-squares regression. Saccadic amplitudes were determined from these fitted values for each participant and each condition as described later. As two stimuli may elicit a saccade with a landing point at an averaged—that is, intermediate—position, we determined the *bias of the saccadic endpoint* induced by a second stimulus as compared to the saccadic endpoint of the preceding single-step trial. For this we subtracted the first point of the double step's fitted curve from the last point of the single step's fitted line (Figure 1). To measure saccadic adaptation we examined the amplitude change in the course of subsequent double-step trials. We then used the difference between the first and last points of the double step's fitted curve to determine the magnitude of the adaptation (Figure 1). This was done for each subject and each stimulus interval.
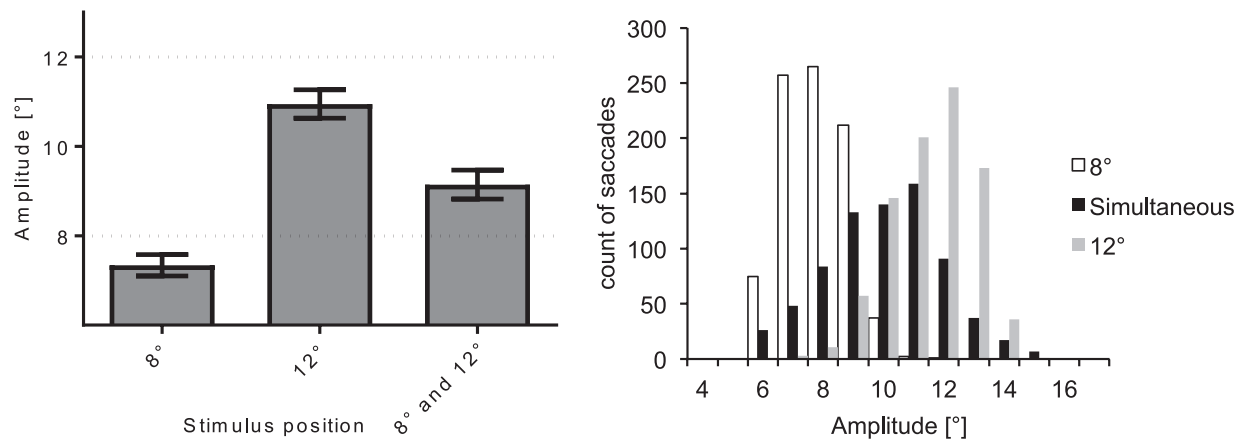
Figure 2. Left: Mean saccadic amplitude across all subjects' means elicited by stimuli at different positions in Experiment 1. The bars show the standard error of the mean across all subjects. Right: Overlapping histograms of the single-step trials (8° and 12°, white and gray bars) and the simultaneous trials (black bars). The simultaneous trials show a single peak at an intermediate position, indicating averaging of saccadic amplitude rather than a bimodal amplitude distribution.

Statistical analysis

To statistically investigate whether the magnitude of the saccadic bias was different for the different stimulus conditions, we used repeated-measures analysis of variance (ANOVA). To test for the presence of bias in a given stimulus condition, we used Student's *t* test to compare the biasing amplitudes for each block and see whether it differed from 0. Using paired *t* tests, we also compared the magnitude of the saccadic bias between the forward and backward paradigms using absolute values from both stimulus intervals. When several groups were tested at once, we adapted the significance level according to the Bonferroni correction for multiple comparisons.

In order to statistically examine adaptation—that is, change of amplitude over time—we used a linear mixed-effects model with saccade amplitude as the dependent variable and stimulus interval and trial number as independent variables. Subjects were used as a random effect. Trial number was used as a measure of time, and a change of amplitude over time is here defined as adaptation. To compare the adaptation between different blocks, we used the interaction term of the six stimulus intervals and trial number. To detect significant adaptation in individual timing conditions, we fitted separate mixed-effects models for each timing condition, with amplitude as the dependent variable and trial as the independent variable. The best-fitting model (random intercept, random slope, combined) was chosen by the smallest Akaike information criterion. Again, the significance level was adjusted to 0.008 after Bonferroni correction for multiple comparisons.

For the analysis of saccadic latency, we calculated each subject's median saccadic latency for each stimulus interval and then took the mean across all subjects. Comparisons between two groups were done with unpaired *t* tests.

All values are displayed as mean ± standard error of the mean. For analysis and figures we used EyeLink Data Viewer, Microsoft Excel, SPSS (Version 21), R, and GraphPad Prism (Version 7.02, www.graphpad.com).

Results

First we investigated how two stimuli instead of a single stimulus affected the saccadic landing point. For this we used a typical averaging paradigm with two simultaneously presented stimuli (simultaneous block) at 8° and at 12° for 36 ms and compared the elicited amplitude with saccades to stimuli at 8° and at 12° alone (single-step blocks). We found that simultaneous stimuli elicited saccades with a landing point at an intermediate position (saccadic amplitude = 9.1° ± 0.3°), thus significantly shorter than saccades to targets at 12° (11.0° ± 0.3°), $t(10) = 13$, $p < 0.001$, and significantly longer than saccades to targets at 8° (7.3° ± 0.2°), $t(10) = 13$, $p < 0.001$ (Figure 2). This indicates the presence of saccadic averaging for targets shown simultaneously.

Next we explored the effect of stimulus timing on saccadic averaging—that is, the bias of the saccadic landing point induced by the presence of a second stimulus separated in time and space. We found that the magnitude of the saccadic bias depends significantly on stimulus timing, $F(5, 50) = 20$, $p < 0.001$ (repeated-measures ANOVA, Figure 3), such that shorter stimulus intervals lead to a larger bias than longer stimulus intervals, $F(1, 75) = 18$, $p < 0.001$ (linear mixed-effects model). An analysis of saccadic
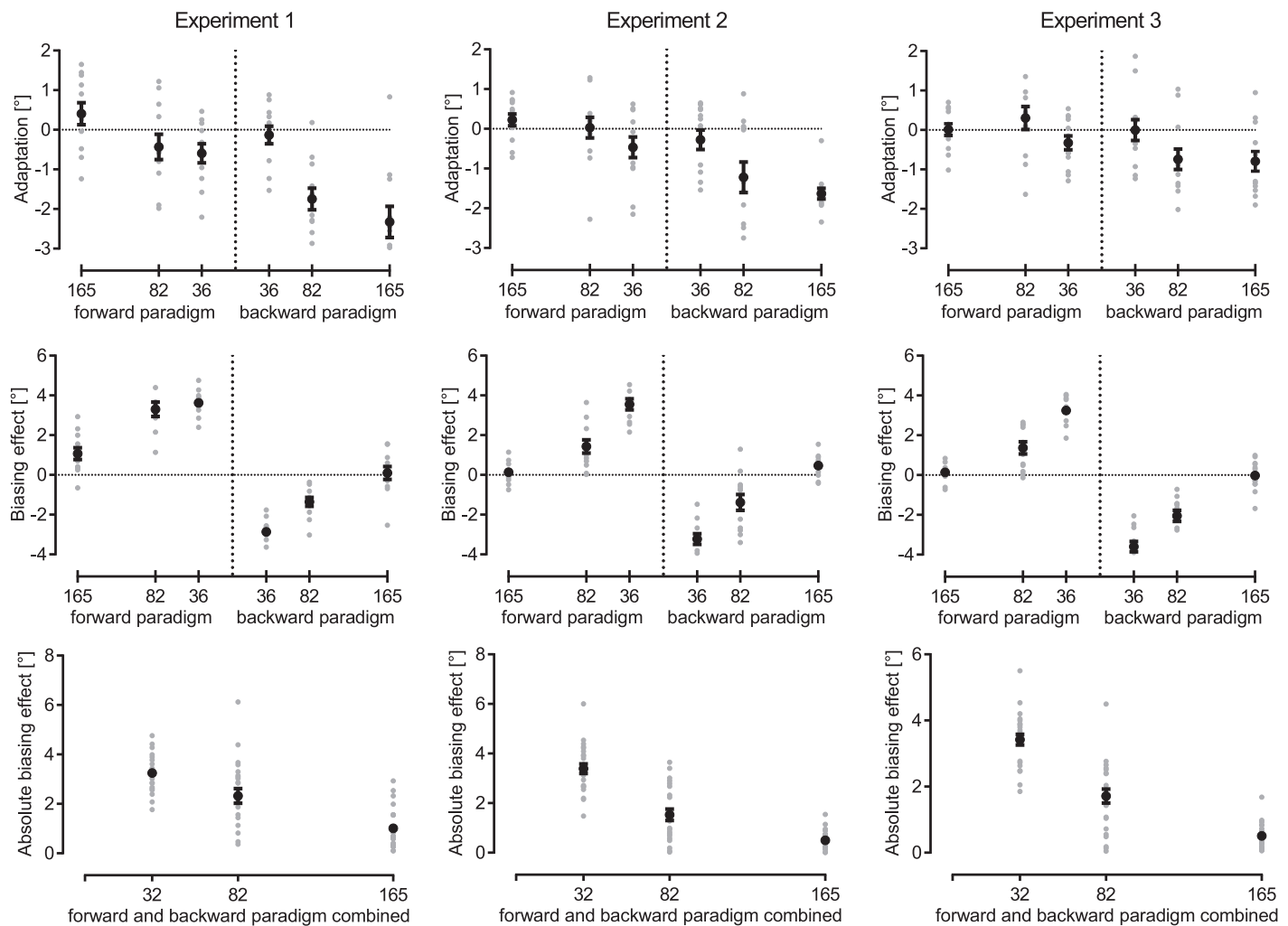
Figure 3. Summary results showing the magnitude of adaptation and of the saccadic biasing effect for all experiments. The *x*-axis indicates the stimulus interval in milliseconds for the paradigm indicated below. Black points show the mean of all subjects ± standard error of the mean; gray points are individual subject means.

bias for each time interval individually showed the presence of a significant saccadic bias for stimulus intervals of 36 ms—forward paradigm: $3.6° \pm 0.19°$, $t(10) = 19$, $p < 0.001$; backward paradigm: $-2.9 \pm 0.2°$, $t(10) = 13$, $p < 0.001$—and 82 ms—forward paradigm: $3.3° \pm 0.4°$, $t(10) = 9$, $p < 0.001$; backward paradigm: $-1.35 \pm 0.2°$, $t(10) = 13$, $p < 0.001$. There was, however, only borderline and no significance, respectively, for forward- and backward-paradigm stimulus intervals of 165 ms—forward paradigm: $1.1° \pm 0.3°$, $t(10) = 3$, $p = 0.07$; backward paradigm: $0.1° \pm 0.3°$, $t(10) = 0$, $p = 0.792$ (Figure 3). Two stimuli presented at an interval of 36 ms elicited saccades with a landing point that was not different from the endpoint of a saccade toward a single stimulus at the location of the second of two stimuli in the backward paradigm: $10.6° \pm 0.3°$ versus $11.0° \pm 0.3°$ for 12° single-step stimuli, $t(10) = 2$, $p = 0.073$). There is still a significant difference in the forward paradigm,

though: $7.9° \pm 0.3°$ versus $7.4° \pm 0.3°$ for 8° single-step stimuli, $t(10) = 3$, $p = 0.007$. A comparison of the size of saccadic bias between the forward- and backward-paradigm trials showed a larger bias in the forward-paradigm trials with a stimulus interval of 82 ms than the corresponding interval in the backward paradigm, $t(10) = 5$, $p < 0.001$. The magnitude of the saccadic bias was not different for intervals of 36 ms, $t(10) = 2$, $p = 0.045$, or 165 ms, $t(10) = 3$, $p = 0.031$.

Next we checked for the presence of adaptation. We found that saccadic amplitude significantly depended on trial number—that is, saccadic amplitude changed over time, $F(1, 21) = 2,565$, $p < 0.001$ (linear mixed-effects model, Figure 4). The Stimulus interval × Trial number interaction was also significant. It showed that the magnitude of adaptation depended on timing condition, $F(6, 73) = 30$, $p < 0.001$ (linear mixed-effects model). Next we looked for adaptation in each timing condition separately.
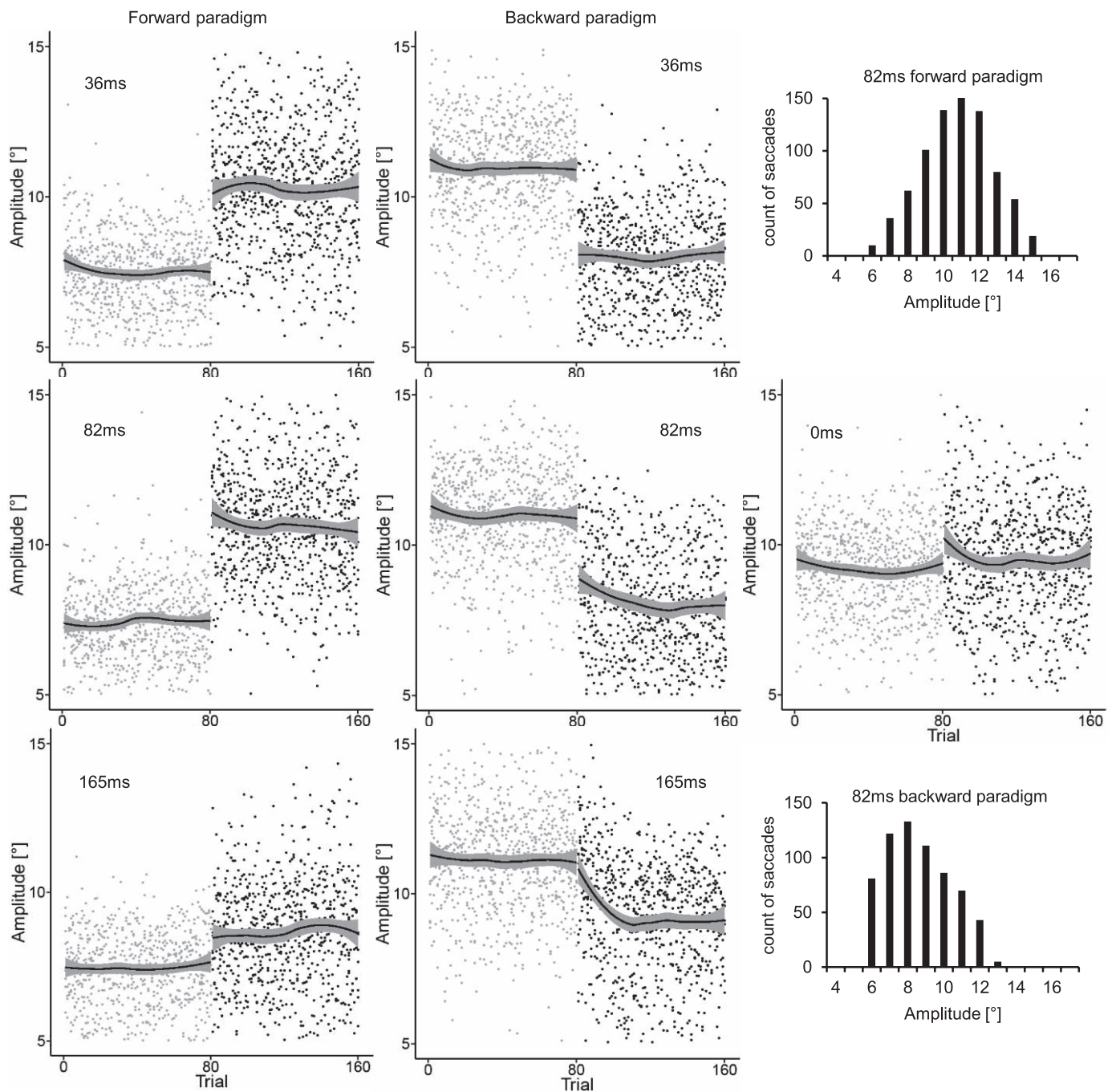
Figure 4. Illustration of saccadic amplitude for each stimulus interval in Experiment 1. Each point represents one subject's trial, in gray for a single-step trial or black for a double-step trial. Smoothed line (moving average) by local polynomial regression fitting with 95% confidence interval. Amplitude histograms for the 82-ms condition show a monophasic distribution with a single peak at the mean saccadic amplitude.

We found significant adaptation for the backward paradigm at 82 ms, $F(1, 640) = 16$, $p < 0.001$ (linear mixed-effects model), and 165 ms, $F(1, 718) = 49$, $p < 0.001$ (linear mixed-effects model), but not for any other condition—forward paradigm, 165 ms: $F(1, 714) = 4$, $p = 0.044$; forward paradigm, 82 ms: $F(1, 780) = 1$, $p = 0.300$; forward paradigm, 36 ms: $F(1, 742) = 4$, $p = 0.037$; backward paradigm, 36 ms: $F(1, 679) = 0$, $p = 0.976$ (all linear mixed-effects models, Figure 3). Thus, timing condition determines whether adaptation occurs or not. Taken together, we found in this experiment a biasing effect for short stimulus intervals and backward adaptation at longer time intervals.

In the next experiments we tested whether visual feedback of the landing position influences adaptation.

	Forward 165 ms	Forward 82 ms	Forward 36 ms	0 ms	Backward 36 ms	Backward 82 ms	Backward 165 ms	Mean
Experiment 1	176 ± 40	164 ± 16	162 ± 18	176 ± 26	179 ± 32	161 ± 26	177 ± 32	171 ± 28
Experiment 2	148 ± 16	149 ± 19	155 ± 21		181 ± 20	166 ± 34	161 ± 22	160 ± 25
Experiment 3	160 ± 15	165 ± 22	172 ± 19	166 ± 22	199 ± 19	180 ± 36	169 ± 16	173 ± 25
Mean	161 ± 28	159 ± 20	163 ± 20	170 ± 24	187 ± 25	169 ± 24	169 ± 24	168 ± 26

Table 1. Mean of each subject's median latency (± standard deviation) in milliseconds.

Induction of adaptation may depend on visual feedback of the second stimulus's location after saccadic landing, which provides an error signal at the end of a first saccade and may drive adaptation. So we tested for the presence of a biasing effect and adaptation in conditions with visual feedback (Experiment 2) and without (Experiment 3). Again two stimuli were presented 36, 82, or 165 ms apart. The second stimulus remained visible in one experiment (Experiment 2) but not in one without visual feedback (Experiment 3).

We then compared the magnitude of saccadic bias in the visual-feedback and no-visual-feedback conditions. As in Experiment 1, we found the greatest biasing effect when stimuli were 36 ms apart: visual feedback—forward paradigm, 36 ms: 3.6° ± 0.3°, $t(11) = 12$, $p < 0.001$; backward paradigm, 36 ms: −3.2° ± 0.3°, $t(11) = 12$, $p < 0.001$; no visual feedback—forward paradigm, 36 ms: 3.2° ± 0.2°, $t(11) = 16$, $p < 0.001$; backward paradigm, 36 ms: −3.6° ± 0.3°, $t(11) = 13$, $p < 0.001$. There was also a smaller, yet still significant biasing effect for stimulus timing of 82 ms—visual feedback, forward paradigm: 1.4° ± 0.3°, $t(11) = 4$, $p = 0.002$; backward paradigm: −1.4° ± 0.4°, $t(11) = 3$, $p = 0.007$; no visual feedback, forward paradigm: 1.4° ± 0.3°, $t(11) = 4$, $p = 0.001$; backward paradigm: −2.0° ± 0.3°, $t(11) = 7$, $p < 0.001$—and no or a very small biasing effect in trials with a stimulus interval of 165 ms— visual feedback, forward paradigm: 0.1° ± 0.1°, $t(11) = 1$, $p = 0.399$; backward paradigm: 0.5° ± 0.2°, $t(11) = 3$, $p = 0.015$; no visual feedback, forward paradigm: 0.1° ± 0.1°, $t(11) = 1$, $p = 0.347$; backward paradigm: 0.0° ± 0.2°, $t(11) = 0$, $p = 0.919$. There was a significant decrease of bias with increasing stimulus intervals in both experiments, $F(1, 75) = 18$, $p < 0.001$ (linear mixed-effects model).

There was no difference of bias between the respective forward and backward paradigms in the visual-feedback condition—36 ms: $t(11) = 1$, $p = 0.191$; 82 ms: $t(11) = 1$, $p = 0.538$; 165 ms: $t(11) = 1$, $p = 0.417$—or the no-visual-feedback condition—36 ms: $t(11) = 2$, $p = 0.118$; 82 ms: $t(11) = 3$, $p = 0.027$; 165 ms: $t(11) = 2$, $p = 0.143$.

We again found a significant adaptation for the stimulus intervals of 82 and 165 ms in the visual-feedback condition—respectively, $F(1, 751) = 26$, $p < 0.001$, and $F(1, 788) = 81$, $p < 0.001$ (linear mixed-effects model)—and for 165 ms in the no-visual-

feedback condition, $F(1, 649) = 10$, $p = 0.002$ (linear mixed-effects model). Importantly, the magnitude of the adaptation was different depending on whether visual feedback was present: In the backward paradigm we found a bigger adaptation in conditions with visual feedback (165 ms: −1.63° ± 0.1°) than without (165 ms: −0.79° ± 0.3°), $t(11) = 3$, $p = 0.012$. The other timing conditions did not evoke adaptation in either experiment: visual feedback—forward paradigm, 165 ms: $F(1, 812) = 2$, $p = 0.195$; 82 ms: $F(1, 816) = 1$, $p = 0.286$; 36 ms: $F(1, 830) = 1$, $p = 0.274$; backward paradigm, 36 ms: $F(1, 832) = 0$, $p = 0.665$; no visual feedback—forward paradigm, 165 ms: $F(1, 713) = 0$, $p = 0.786$; 82 ms: $F(1, 722) = 0$, $p = 0.923$; 36 ms: $F(1, 750) = 3$, $p = 0.089$; backward paradigm, 36 ms: $F(1, 743) = 0$, $p = 0.913$; 82 ms: $F(1, 692) = 5$, $p = 0.022$ (linear mixed-effects models).

Next we analyzed saccadic latencies for all experiments: We found significant differences among the three experiments, $F(2, 230) = 5$, $p = 0.004$ (ANOVA). Experiment 2 showed significantly shorter latencies than both Experiment 1, $t(71) = 2$, $p = 0.020$, and Experiment 3, $t(71) = 5$, $p < 0.001$. Backward-paradigm trials had a significantly longer latency (175 ± 2 ms) than forward-paradigm trials (161 ± 2 ms) across all experiments, $t(104) = 5$, $p < 0.001$. Latency values for each condition are shown in Table 1.

Then we examined the dependence of the saccadic bias and the adaptation from timing the second stimulus (T2) with saccade onset rather than the first stimulus T1. For this we measured the interval between saccade onset and the appearance of T2 in each trial (saccade–T2 interval). Positive values indicate that the stimulus appeared after saccade onset, and negative values before. Table 2 shows this saccade–T2 interval for each block in Experiment 1; the numbers are very similar in Experiments 2 and 3 (data not shown).

Next we qualitatively examined the effect of the saccade–T2 interval on saccadic amplitude. For this, we created a scatterplot with the saccade–T2 interval of all double-step trials of Experiment 1 on the x-axis and the corresponding saccadic amplitude on the y-axis (see Figure 5). Saccades tended to land on the second target if T2 was shown more than 100 ms before saccade onset. The landing point gradually shifts toward the first stimulus the closer T2 appears to saccade onset. Stimulus shifts during or after saccade onset do not

	Forward 165 ms	Forward 82 ms	Forward 36 ms	0 ms	Backward 36 ms	Backward 82 ms	Backward 165 ms
Saccade–T2 interval	−11 ± 40	−82 ± 16	−126 ± 18	−176 ± 27	−143 ± 32	−80 ± 25	−17 ± 34
Before	47%	100%	100%	100%	100%	100%	53%
During	52%	0%	0%	0%	0%	0%	46%
After	1%	0%	0%	0%	0%	0%	1%

Table 2. Mean of each subject's median saccade–T2 interval (± standard deviation) in all conditions of Experiment 1. Values in the lower part of the table indicate the percentage of trials in which T2 appeared before saccade onset (before), during saccade execution (during), and after the saccade landed (after).

affect the saccadic amplitude: The saccades then land on the location of the first stimulus (T1).

Finally, we analyzed the dependence of saccadic adaptation on the individual saccade–T2 interval. Since adaptation cannot be measured in a single trial, we took advantage of the natural difference of saccade–T2 intervals between different subjects. Again in a qualitative analysis we plotted the median saccade–T2 interval of a given subject in a given block against the corresponding adaptation (see Figure 6). This was done for all stimulus intervals except 0 ms, resulting in six points per subject. A linear fit of this data suggests no correlation of saccade–T2 interval and adaptation.

Discussion

Our results show that the timing of two concurrent visual stimuli determines the corresponding oculomotor response: If stimuli were presented in close temporal relation—that is, less than 82 ms—the saccadic endpoint shifted toward the location of the second stimulus. For a stimulus interval of 36 ms the saccadic landing point was strongly biased, such that the saccadic endpoint was similar to a second stimulus alone. If the stimuli were shown simultaneously, however, the elicited saccades had an amplitude at an intermediate position. The situation is entirely different for stimuli that are further apart than 82 ms: For such stimuli, saccadic adaptation predominates—that is, saccades initially land on the position of the first stimulus and the saccadic amplitude gradually shifts over time toward the location of the second stimulus. However, we found adaptation only in the backward paradigm (see discussion later). The magnitude of this saccadic adaptation depends on visual feedback: If the second stimulus was still present after saccadic landing, thus providing visual feedback about the landing error, then the magnitude of the adaptation was bigger. But even when the stimulus was extinguished after saccade onset, preventing visual feedback, we found a small but significant saccadic adaptation. Taken together, our results demonstrate the importance of the timing of visual stimuli on the corresponding saccade and show
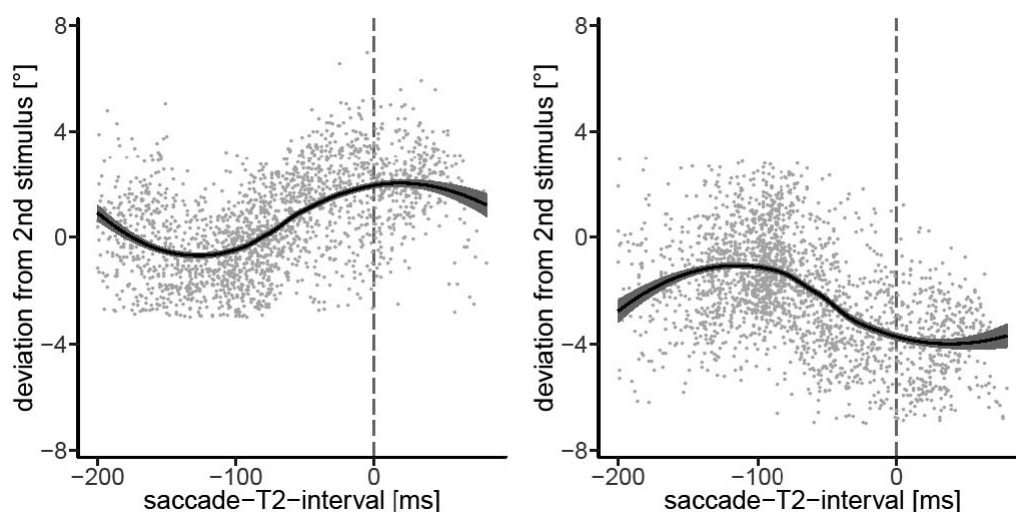

Figure 5. Left: Dependence of saccadic amplitude on saccade–T2 interval in the backward paradigm of Experiment 1. Right: Corresponding data for the forward paradigm. Each trial is represented by a single gray dot. All double-step trials of all subjects in Experiment 1 are included. The amplitude is shown as deviation from the second stimulus, which is 8° for backward-paradigm trials and 12° for forward-paradigm trials. Thus a value of 0 indicates saccadic landing on the location of T2.
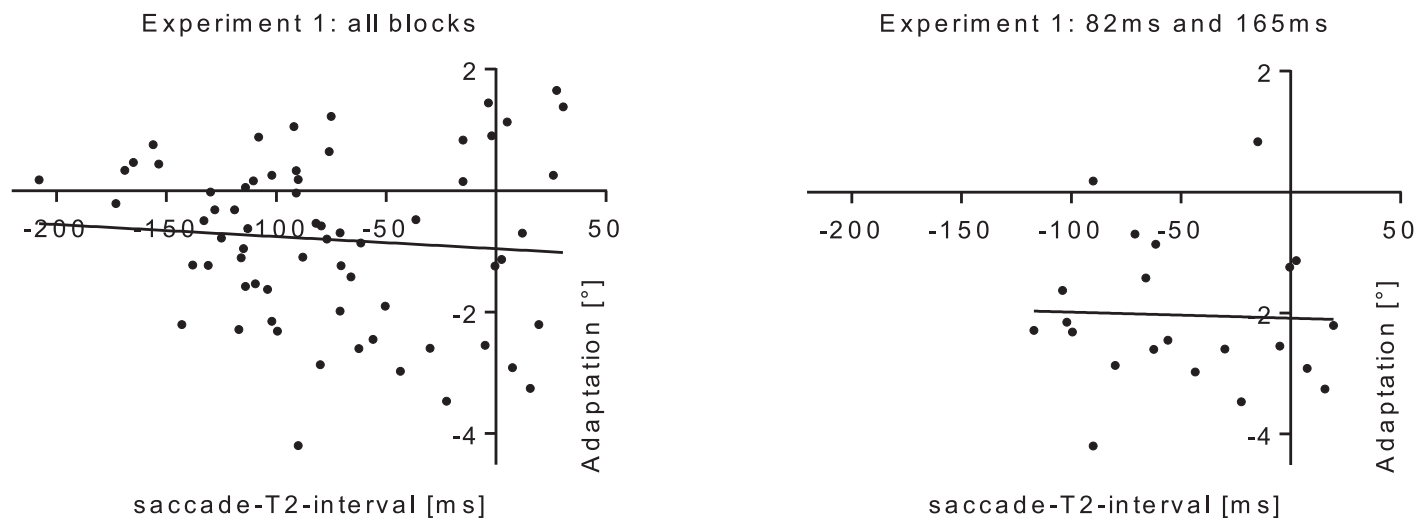
Figure 6. Saccade adaptation versus median saccade–T2 interval. Backward adaptation is represented with negative values. The value 0 corresponds to no adaptation. Each dot represents the magnitude of the adaptation from a backward-paradigm block in one subject; the line represents a linear fit. All blocks for all subjects are shown. In a separate plot we included only those blocks in which adaptation was found—that is, 82 and 165 ms in the backward paradigm.

two complementary oculomotor strategies to cope with conflicting stimuli in the oculomotor system.

Our finding of intermediate saccadic landing points elicited by two simultaneously presented stimuli is in agreement with the well-known global effect (Findlay, 1982). The visual and spatial properties of conflicting stimuli have been extensively studied for the global effect, but the temporal properties of visual stimuli have barely been examined. In a recent article, Choi et al. (2016) described how the size of global effect depends on the duration and delay of distractor presentation. Their distractor corresponds roughly to our T2 stimulus. When they showed the distractor for 100 ms, saccadic bias was observed only when the distractor was visible simultaneously with the target. For longer lasting distractors a global effect was found only if the target was presented within 100 ms after distractor onset. The authors concluded that either two stimuli have to be temporally overlapping or the distractor's duration has to be longer than 100 ms. This is not what we found. All three of our experiments clearly show that the duration of the stimuli can be far less than 100 ms to induce saccadic biasing, and that the stimuli do not have to be temporally overlapping.

Our plot of saccade–T2 interval and saccadic amplitude (Figure 5) suggests that a global effect—or, as we called it, a biasing effect—of saccadic amplitude occurs if T2 is presented up to about 50 ms before saccade start. After that, up to T2 shown at saccade start, no biasing was observed. We presume that at that time point saccadic programming is completed. When T2 was shown at saccade start or during a saccade, adaptation was found instead. Not surprisingly, we found no or only very small biasing at stimulus

intervals of 165 ms. We also found that with decreasing stimulus intervals, saccades were gradually biased toward the location of the second stimulus, such that at an interval of 36 ms the saccadic landing point could no longer be distinguished from a saccade to the second stimulus alone. We have not found a report of this strong effect in the literature, and the origin of this effect is not known to us. In analogy to the global effect and saccadic biasing, one could postulate that the center of gravity—that is, saccade-related activity—is biased heavily toward the second location. One speculative mechanism promoting this could be a surround inhibition induced by the second stimulus. Such center–surround suppression is present throughout the visual system and has been found, among other places, in V1 (Jones, Grieve, Wang, & Sillito, 2001), the frontal eye field (Thompson & Bichot, 2005), and the superior colliculus (Keller & McPeek, 2002). It postulates that the perception of a given stimulus leads to inhibition in areas adjacent to the stimulus location. This surround inhibition has also been found in other sensory systems (audition: Knudsen & Konishi, 1978; touch: Vega-Bermudez & Johnson, 1999; olfaction: Olsen, Bhandawat, & Wilson, 2010).

In contrast to the global effect—which has been shown to be more pronounced if the competing stimulus is located proximally rather than distally for targets within 20° to 30° (Coren & Hoenig, 1972; Findlay, 1982)—we found a bias that was equally strong independent of whether the first stimulus was at 12° or 8°, and thus the second stimulus at 8° or 12°. The bias to the location of a second stimulus in a sequence of two stimuli shares similarities with perceptual experiments: In a hand-movement experiment using

asynchronous stimuli, Lee (1999) showed that with increasing stimulus asynchrony, hand movements gradually shifted toward the first target. In trials with 100 ms between the two stimuli, approximately 75% of the movements were directed to the first stimulus, as compared to 93% of the trials with a 300-ms interval. So, as in our experiments, Lee found a bias toward the second stimulus with shorter intervals, suggesting that our observations may also apply to hand motion.

With greater stimulus intervals, we found saccadic adaptation—that is, a gradual change of saccadic amplitude over time—rather than a biasing effect. A comparison of the magnitude of adaptation showed that we found adaptation only in the backward paradigm, not in the forward paradigm; thus, we found adaptation only if the second stimulus was located closer to the starting point. This observation is consistent with previous studies on saccadic adaptation that have also found more pronounced backward than forward adaptation (Miller, Anstis, & Templeton, 1981; Straube & Deubel, 1995). It is possible that 80 trials provide insufficient statistical power to detect forward adaptation. An alternative explanation is that forward adaptation may involve a different mechanism than backward adaptation. In their review article, Hopp and Fuchs (2004) assert that this type of adaptation can be observed only with 200–400 trials. A series of experiments by Panouillères and colleagues (Panouillères et al., 2013; Panouillères et al., 2016) demonstrated reduced adaptation when the stimulus was presented for less than 20 ms. Given that we do not see a difference between Experiment 1, with a target duration of 36 ms, and Experiment 2, with a persistent target, our results are in line with those of Panouillères and colleagues, who suggest that target durations of less than 20 ms are necessary to reduce adaptation.

While the saccadic bias that we observed possibly originated from averaging of neural activity in key oculomotor structures such as the superior colliculus (Van der Stigchel & Nijboer, 2011), saccadic adaptation has been attributed to different brain areas. Studies have confirmed the importance of the cerebellum (Kojima, Soetedjo, & Fuchs, 2010; Robinson, Fuchs, & Noto, 2002; Sun, Barash, & Thier, 2016), but cortical areas such as the parietal cortex and the frontal cortex, as well as brain-stem premotor areas, also seem to be involved (Alahyane et al., 2007; Hopp & Fuchs, 2004; Panouillères et al., 2009; Pélisson, Alahyane, Panouillères, & Tilikete, 2010). The neuronal network responsible for saccadic adaptation is yet to be determined.

Our adaptation resembles the adaptation found with the classical two-step paradigm: A first stimulus is extinguished after saccade onset and replaced by a stimulus at a different location (McLaughlin, 1967). This paradigm is associated with a mean stimulus

interval of the saccadic latency—that is, about 170 ms—although it may vary in individual trials (Smit, Van Gisbergen, & Cools, 1987). In this respect our 165-ms condition is close to the classical paradigm, with the main difference that we used a fixed interval rather than a saccade-onset-dependent stimulus. Nevertheless, the second target T2 appeared during the saccade in about half of the trials in our 165-ms backward paradigm, which was the condition with the strongest adaptation. This suggests that the adaptation we observed is mediated by a similar mechanism as in a classical double-step paradigm. In comparison with other reports, the magnitude of our adaptation was moderate, with a change of about 2.3° over 80 trials. At the end of the fitted curve in the adaptation block, the saccadic landing point was at a mean of 8.7°, which corresponds to a gain of 0.73. This comes close to saccades to the second stimulus alone, which exhibit a gain of 0.67. This is comparable to findings from classical two-step paradigms (Panouillères et al., 2009; Straube & Deubel, 1995). Given the fact that starting point and stimulus onset were different in each trial, our paradigm was associated with minimal spatial and temporal predictability.

Bahcall and Kowler (2000), as well as Fujita, Amagai, Minakawa, and Aoki (2002), also changed the stimulus interval by delaying the displaced target after saccade onset. They found an exponential decrease of adaptation with increasing intervals until a delay of 400 ms in humans and 750 ms in monkeys, after which no adaptation was found anymore. Together with the finding that brief stimuli (shorter than 80 ms) shown after saccade onset induce less adaptation than stimuli shown for a longer period (Shafer, Noto, & Fuchs, 2000), Pélisson et al. (2010) concluded "that the shifted target must be visible within a critical time-window nearly immediately after primary saccade termination to induce maximal saccadic adaptation" (p. 1106). Then Panouillères et al. (2013) discovered adaptation in trials with a purely intrasaccadic stimulus shift. Overall, our results are in agreement with these findings even though our experimental design is not targeted at this question. We were also able to induce significant adaptation with our paradigm even when the shifted stimulus was shown before saccade termination in the great majority of trials and even though the second stimulus was only present for 36 ms (in Experiment 1). This means that targets shown before saccade landing can lead to adaptation as well. The fact that we found some adaptation in Experiment 3, where all stimuli disappeared after saccade onset, also supports this finding.

What drives saccadic adaptation? In the beginning, it was thought that correcting saccades are needed to induce adaptation; this idea was discarded when adaptation was found without correcting saccades
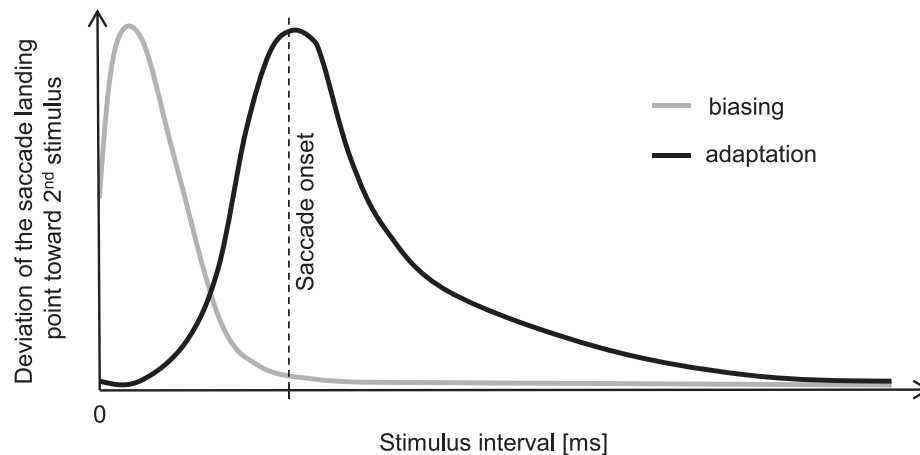
Figure 7. Hypothetical model indicating a possible relation of the stimulus timing, saccade timing, and saccadic landing point.

(Noto & Robinson, 2001; Wallman & Fuchs, 1998). Several groups suggested that the retinal error is crucial instead—that is, the difference between the foveal picture at saccadic landing and the target stimulus (Hopp & Fuchs, 2004; Noto & Robinson, 2001; Wallman & Fuchs, 1998). This theory, however, was challenged with the observation that saccades that land directly on the target may also undergo adaptation (Havermann & Lappe, 2010; Henson, 1978; Robinson, Noto, & Bevans, 2003). This led to the assumption that the predicted error of the postsaccadic picture is critical for adaptation (Bahcall & Kowler, 2000; Collins & Wallman, 2012). This prediction paradigm, a so-called forward model, was also found in other systems, such as the impossibility of self-tickling (Blakemore, Wolpert, & Frith, 2000): The predicted feeling calculated by the efference copy of the motor act is compared to the sensory feedback. Because there is not much discrepancy with self-produced movements, there is no tickling sensation.

The fact that we were able to induce adaptation even when the shifted stimulus was shown before saccade end as well as when the stimulus was extinguished during the saccade is compatible with this theory: The appearance of a new stimulus location at the end of saccade planning allows a person to predict an error and thus drive adaptation, even though the saccade has not been actually terminated.

Thus, in conclusion, our results suggest the following: Adaptation is present only when a stimulus shift induces an error or allows prediction of an error. The magnitude of adaptation is greatest if the error is introduced around the motor execution of an eye movement and decreases if the stimulus is presented earlier or later (Bahcall & Kowler, 2000; Choi et al., 2016; Fujita et al., 2002; Panouillères et al., 2016; Shafer et al., 2000). If conflicting stimuli appear shortly after each other, the saccadic response is shifted toward the location of the second of two consecutive stimuli,

possibly by a mechanism of saccadic averaging and possibly by center–surround inhibition. These two complementary mechanisms provide an optimized oculomotor response (see Figure 7 for illustration).

Keywords: saccade, saccade adaptation, global effect, saccadic averaging, stimulus timing

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