Integration of past and current visual information during eye movements in amblyopia

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Abstract

Combination of signals based on their reliability is an increasingly popular model for sensorimotor processing. However, how reliability is estimated, or how such estimation is affected by prolonged exposure to noisy inputs, is still unknown.

In this study, we compare patients with unilateral functional amblyopia with control subjects tracking either a reliable target, or a blurry, unreliable target, in a task of repeated, sustained smooth pursuit.

We provide evidence for a lower weight of visual information during smooth pursuit in amblyopic and control subjects tracking a blurry target, with no significant difference of prior information weight. In contrast, we found no evidence of lower visual information weight in the catch-up saccades of amblyopic subjects.

We conclude that oculomotor performance in unilateral amblyopia mostly lays within the continuum between our control groups, without significant differences in the relative weights of prior and visual information. However, smooth pursuit exhibits additional deficits that might result from abnormal visual development.

Keywords

Amblyopia, Reliability-based integration, Unilateral functional amblyopia, Kalman filtering, Smooth pursuit, Catch-up saccades, Visual information

1 Introduction

There is a growing consensus about the use of reliability-based integration as a model of the processing of noisy, time-delayed or multimodal sensory sources by sensorimotor systems (Berniker and Kording, 2009; Kording and Wolpert, 2004; Rohe and Noppeney, 2018). As a prime example of sensorimotor behaviors, smooth pursuit eye movements have been extensively studied, and several models relying on reliability-based integration have been proposed (Bogadhi et al., 2013; Dimova and Denham, 2009; Montagnini et al., 2007; Orban de Xivry et al., 2013). Most recently, behavioral studies in both monkeys (Darlington et al., 2017) and humans (Deravet et al., 2018) have shown evidence of reliability-based integration of noisy visual information with prior information, in line with these models.

Numerous unknowns remain, such as the pathways and regions of the brain implicated in the actual integration process (Darlington et al., 2017). One way to explore these questions is to investigate developmental deficits of vision, such as amblyopia. Unilateral functional amblyopia, while typically characterized by an acuity loss in one eye for which no physical cause can be found (Daw, 2014; Von Noorden and Campos, 2002), is also associated with other deficits related to contrast or motion perception (Kiorpes et al., 2006; McKee et al., 2003; Simmers et al., 2003). The fact that some of these deficits, including acuity, can also be found in the fellow, unaffected eye (Ho et al., 2005; Meier and Giaschi, 2017; Varadharajan and Hussaindeen, 2012) shows that amblyopia affects the oculomotor system beyond the monocular level, possibly including pathways responsible for prior integration. Unfortunately, visually guided smooth pursuit in amblyopic patients has received limited attention outside of its potential asymmetry (Ciuffreda et al., 1979; Schor, 1975; Von Noorden and Mackensen, 1962a), except for a recent study that investigated smooth pursuit latency and steady-state gain (Raashid et al., 2016) in anisometropic amblyopia.

In our study, using a target-tracking task, we compare the sensorimotor behavior of amblyopic patients with two groups of controls presented with either reliable or less reliable visual targets. We predicted that, because of their visual acuity deficits, the sensorimotor behavior of amblyopic subjects would be comparable to that of normal subjects presented with a noisy visual target. We also probed the weighting of prior and visual information in patients and controls, which might be expected to be affected by their different history of visual development.

2 Methods

2.1 Participants

We recruited 20 amblyopic patients, 2 of which were set aside because of data quality (see data processing). The remaining 18 patients (8 female) were between 12 and 61 yo (average = 32.56, sd = 16.58, cf. Fig. 1A). We also recruited 38 control
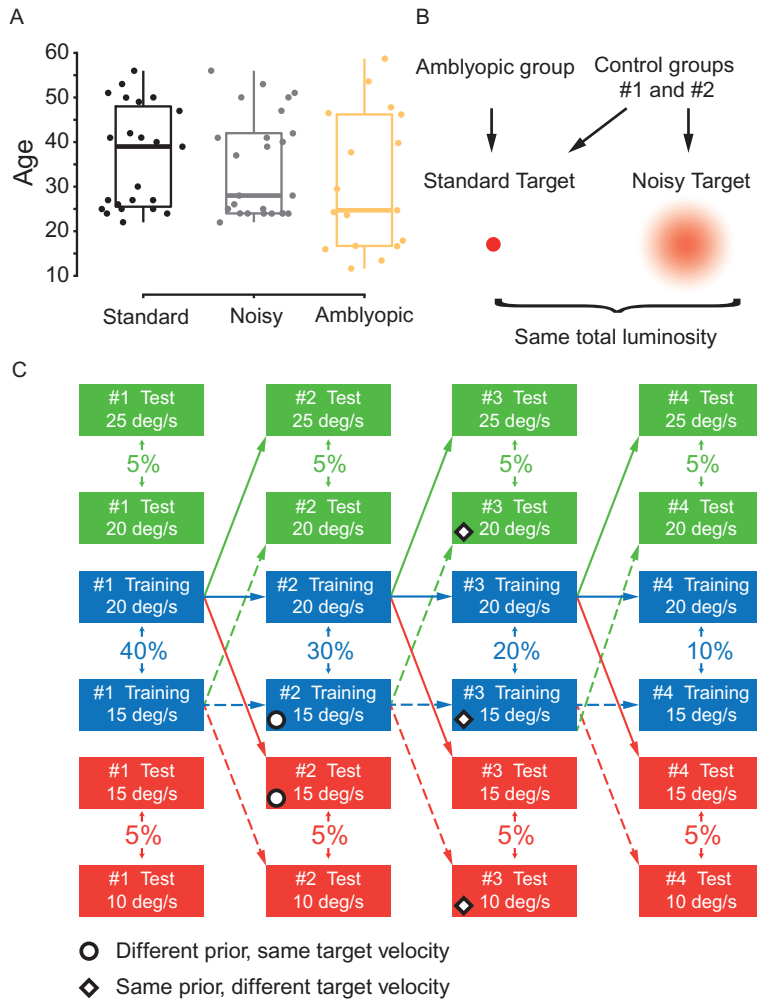
FIG. 1

(A) Age distribution of included participants. Boxplots show medians and quartiles; dots are individual data, with some x-jitter for readability. (B) Association between groups and targets. (C) Template of blocks (regardless of target direction). Each block starts with a trial of the first column and ends at a trial with no outgoing arrow. Target direction remains constant within a block. Percentages indicate the % of blocks containing trials of the same type (color) and number (#) at one of the two available velocities (ex: 80% of the blocks have at least one Training trial). Black rings give an example of two trials that can be compared to highlight the effect of previous trials (prior). Black diamonds give an example of trials in which the prior is the same but the visual information differs. Dashed arrows indicate a 15°/s prior target velocity. Solid arrows indicate a 20°/s prior target velocity.

participants, one of which was set aside due to incomplete pupil detection. The remaining 37 controls, between 22 and 56yo (average = 32.43, sd = 10.72; 21 female, cf. Fig. 1A), took part in either one or two versions of the protocol, Standard (23) and Noisy (25), with 11 participating in both (starting with Noisy). Control participants had normal/corrected vision, while amblyopic patients had visual acuity between 2/20 and 10/20 Snellen (0.3–1 logMAR), and exhibited either anisometropic ($n = 4$), strabismic ($n = 8$) or anisometropic and strabismic ($n = 6$) amblyopia.

After full description of the experiment, informed consent was given by the participants. The procedures were approved by the Université catholique de Louvain Ethics Committee and in accordance with the Declaration of Helsinki.

2.2 Protocol

Participants sat in a dark room, 151 cm from a 197×150 cm screen placed in front of them, spanning around 65° (horizontal) by 50° (vertical) of their visual field. Head movements were restrained with chin and forehead rests. A cine8 Barco projector (Barco Inc., Kortrijk, Belgium) displayed the stimuli at a refresh rate of 100 Hz while eye movements were recorded at 1000 Hz using an Eyelink 1000 (SR Research, Ottawa, Ontario, Canada). The display was handled by an in-house toolbox, while Eyelink® interactions were handled by the Psychtoolbox (Kleiner et al., 2007). Calibration targets were presented at the start and every 30 trials, with breaks allowed before each. The duration of an experiment was around 30 min. Importantly, we always recorded the amblyopic or non-dominant eye, masking the other with translucent tape.

In a previous study (Deravet et al., 2018), we established that a blurry Gaussian spot target, with $\sigma = 1.27°$, is able to significantly deteriorate pursuit performance and induce different relative weights of visual and prior information, which we attributed to the lower reliability of the visual information it provides. Since the primary deficit associated with amblyopia is reduced visual acuity, we expected amblyopic patients to exhibit similar pursuit behavior and considered a protocol allowing us to compare their oculomotor behavior with controls presented with either reliable or less reliable visual information. As such, one group of controls (Standard) and all patients tracked a standard target (uniform disk, diameter 0.8°; cf. Supplementary Figs 1 and 2 in the online version at https://doi.org/10.1016/bs.pbr.2019.04.034), while another group of controls (Noisy) tracked a noisy target (Gaussian spot, $\sigma = 1.27°$; cf. Supplementary Fig. 1 in the online version at https://doi.org/10.1016/bs.pbr.2019.04.034). Both targets had the same overall luminance, but different distributions.

This protocol was adapted from Deravet et al. (2018). It consists of blocks (cf. Fig. 1) of 1–4 Training trials, which build a prior through repeated tracking of a pursuit target with identical velocity (15°/s or 20°/s) and direction (−20°, 0°, 20°, 160°, 180° or 200°). In most blocks (80%), the last trial (Test) changes velocity (±5°/s), thereby creating a mismatch between prior and visual information and

probing their weighting. Each trial began with a 500 ms fixation using the same target. Two important differences with the previously published protocol (Deravet et al., 2018) are the absence of passive trial and the use of the same target for both fixation and pursuit.

2.3 Data processing

Data were processed using MATLAB® (MathWorks®). Missing values in the Eyelink® output were considered blinks and removed from the data (along with safety margins of up to the first local minimum of vertical eye movement on each side of the blink). Eye position signals were low-pass filtered at 35 Hz, and both eye velocity and acceleration were obtained using a central difference algorithm on a ±10-ms interval. Data were pooled across all six directions.

   We detected saccade onsets and offsets by implementing the algorithm described in Larsson et al. (2013), slightly altered to handle the noisier data of patients, by detecting over several filtering levels, raising the thresholds for saccades, and checking saccade candidates for consecutive saccades. Once detected, we removed saccades from velocity traces using linear interpolation.

   To remove abnormal trials, we set a few criteria: (1) during the last 100 ms of fixation, median eye position error $<5°$, (2) <90 missed samples in the first 450 ms of pursuit, (3) eye displacement of at least 15% of target displacement, (4) position error during pursuit must not go over $8°$ for >100 ms, (5) no saccade made after target onset may be $>25°$. Finally, we set aside participants whose data were rejected at $>60\%$ (cf. Section 2.1). From remaining participant's data, the criteria took out $\sim11\%$ of trials, distributed as: 7% Standard, 9% Noisy, and 19% Amblyopic groups.

   When analyzing eye velocity during pursuit epochs, we included only trials for which participants (1) had steady state pursuit gain bigger than 0.2, (2) made forward saccades (or none) and (3) moved at least 5% of target displacement using smooth pursuit ($\sim90\%$ of data). In our analysis of smooth pursuit performance during the first trial, we wanted to compare the visual response of the groups. Therefore, we selected trials during which anticipation was low by requiring pursuit onset to occur later than 50 ms ($\sim82\%$ of first training trials).

2.4 Data analysis

2.4.1 Pursuit features

Pursuit onset was measured as the intersection of a two-part piecewise linear function (plateau and positive slope) fitted on eye velocity within the interval $[-100,300]$ ms around target onset. The onset time was considered valid if no blink occurred for at least 50 ms afterwards, and if the plateau value remained below $4°/s$.

   Steady-state eye velocity was computed as the slope of a first-order polynomial fitted on the first interval of eye position after the first catch-up saccade that included

no saccades, provided that it lasted at least 70 ms. If there was no such interval (~1.9% of trials), saccadic eye position data were replaced by the integral of their linear interpolation in eye velocity, and included in the fit.

2.4.2 Saccades features
We studied the first catch-up saccade occurring between 100 and 400 ms after target motion onset.

We computed position error (PE), retinal slip (RS) and amplitude (Amp). PE and RS were both assumed to be estimated 100 ms before saccade onset (Becker & Jürgens, 1979), and therefore measured at that time. Retinal slip was computed as the difference between target velocity and a 50 ms average of eye velocity 100 ms before onset.

For each participant and training target velocity, we used data from Training trials #2–#4 to compute linear models of saccade amplitude vs ideal amplitude (difference between target position at saccade offset and eye position at saccade onset). Data from first trials were fitted in a second model because of their later pursuit onset and bigger saccades. We then computed residuals of the corresponding Test trials to quantify their divergence from Training trials, while accounting for individual differences. The computation of the ideal amplitude depended on the type of comparison (prior vs visual) and is further discussed below.

2.4.3 Comparing trials—Prior effect
To assess the effect of prior information, we compared Test and Training trials of matching trial # and visual information, but different experience in prior trials (Test20 vs Train20, Test15 vs Train15, e.g., black circles in Fig. 1C), on measures of pursuit gain and saccade amplitude. Given identical visual information, any behavioral difference is attributed to the prior. To estimate the fraction of the prior that is reflected into the behavior across target velocities, we computed a normalized prior effect on the pursuit according to Eq. (1).

$$NormEffect_{prior} = \frac{mean(Eye\,Velocity\,of\,Training) - Eye\,Velocity\,of\,Test}{Prior\,Target\,Velocity\,of\,Training - Prior\,Target\,Velocity\,of\,Test}$$

(1)

Saccades residuals were computed based on the linear model of saccade amplitude vs the ideal amplitude toward the visible target.

2.4.4 Comparing trials—Visual effect
To estimate the effect of visual information, we compared Test and Training trials of matching trial # and prior information, but different target speed (Train15 vs Test10 or Test20, Train20 vs Test15 or Test25, e.g., black diamonds in Fig. 1C). Comparisons highlight the effect by considering that participants ignored the change of velocity, so that any difference with Training trials is attributed to it. For pursuit, we

achieved this by computing a gain equal to the eye velocity divided by the previous target velocity (15 or 20).

To compare the effect on eye velocity across conditions of opposite effects, we also computed a normalized visual effect, as described by Eq. (2).

$$NormEffect_{visual} = \frac{mean(Eye\,Velocity\,of\,Training) - Eye\,Velocity\,of\,Test}{Target\,Velocity\,of\,Training - Target\,Velocity\,of\,Test} \quad (2)$$

For saccades residuals computation, we considered the ideal amplitude to reach, at saccade offset, a predicted target with the same PE at saccade onset, but moving at the previous target's velocity, i.e., that participants relied on previous RS.

2.4.5 Statistical analyses

We compared several measures from the first training trial of each block, provided anticipation was low, as a way to assess the performance of the visual response to target motion. We analyzed subject averages using a linear mixed effects model, with *group*, *target velocity* and *temporal/nasal direction* as fixed effects, *participants* as random effect, and random slopes for *temporal/nasal direction*.

Further analyses were always respective to participant's own performance in training trials; therefore, we did not include the temporal/nasal direction factor. To assess the existence of a visual effect, we used a model with fixed effects *group*, *type of target* and *training target velocity*, with a random effect for *participants*. When comparing the effect of prior or visual information, we used the same analysis method, but with the following fixed effects: group, training Target velocity and Trial # (first trial/all later ones). We included random intercepts for the participants and random slopes and intercepts for *Trial #* to account for individual differences. We performed hypothesis tests with type III anova, evaluating denominator degrees of freedom using the Kenward-Roger method.

For these analyses, we relied on the afex (Singmann et al., 2018), lme4 (Bates et al., 2015) and lmerTest (Kuznetsova et al., 2017) packages in R (R Core Team, 2018). Post-hocs were pairwise comparisons using robust independent and dependent *t*-tests from the WRS2 R package (Mair and Wilcox, 2018), using 20% trimmed means and 2000 bootstrap samples when applicable (Field and Wilcox, 2017).

3 Results

In this study, we investigated smooth pursuit in three groups, presented with visual information that was either reliable, noisy, or affected by amblyopia; furthermore, we manipulated the reliability of prior information about target velocity. Here, we first assess how amblyopia and the reliability of visual information affect smooth pursuit latency and gain (Fig. 2). Then, we highlight and compare the weights of visual and prior information in pursuit gain and catch-up saccades amplitude.
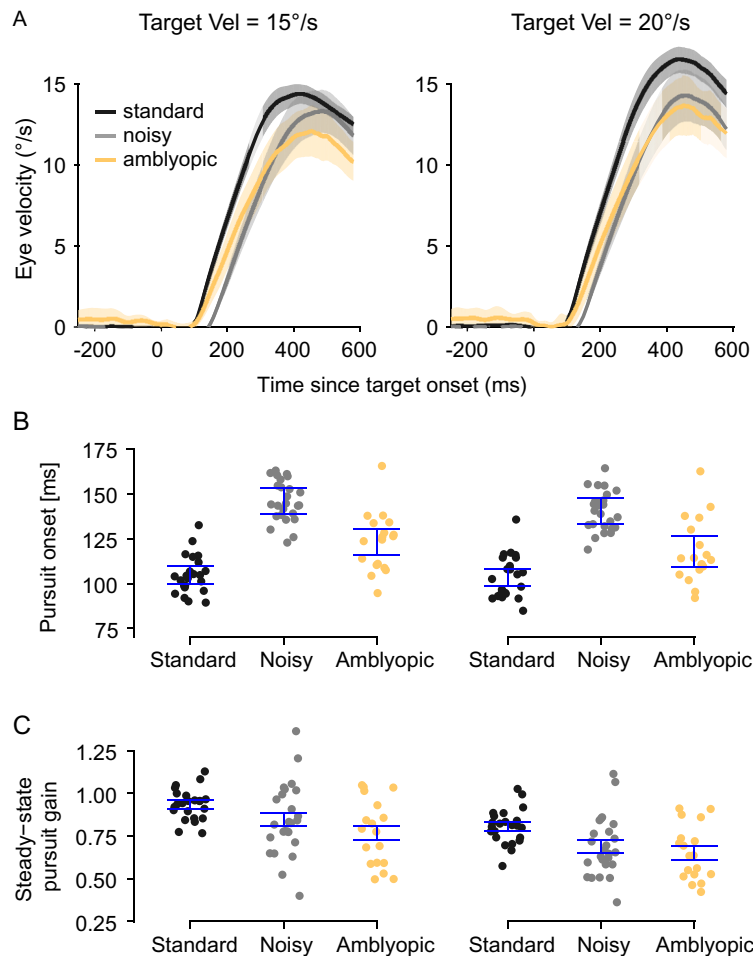
FIG. 2

Overall pursuit performance during Trial #1. (A) Averages, per group, of participant's average eye velocity traces during Training trials at 15°/s and 20°/s. The surrounding shadow indicates 95% CI. (B and C) Respectively, Pursuit onset and Steady-state pursuit gain, for Training trials at 15°/s and 20°/s. Dots correspond to individual participants. Error bars are centered on the average of participant's averages and indicate the average of participant's SEM.

3.1 Performance of smooth pursuit

3.1.1 Pursuit onset is delayed in amblyopic and noisy groups

Given previous studies, we expected to observe delayed pursuit onset in the two groups with less reliable visual information. There was indeed a main effect of *group* ($F(2,63.11) = 68.79$, $P < 0.0001$): the Noisy (trimmed mean differences in FBQ

scores $M_{diff} = +38.97$ ms, 95%CI: [34.80, 43.14], $Y_t = 18.6$, $P < 0.0001$), and Amblyopic ($M_{diff} = +15.18$ ms [9.78, 20.57], $Y_t = 5.34$, $P < 0.0001$) groups initiated pursuit later than the Standard group. Still, amblyopic patients initiated pursuit faster ($M_{diff} = -23.79$ ms, [-29.44, -18.14], $Y_t = 8.1$, $P < 0.0001$) than the Noisy group. In addition, there were main effects of target velocity ($F(1,124.82) = 10.66$, $P = 0.001$) and temporal/nasal direction ($F(1,62.8) = 12.16$, $P = 0.0009$).

3.1.2 Steady-state smooth pursuit gain is lower in amblyopic and noisy groups

The analysis of smooth pursuit steady-state gain revealed main effects of *group* (F $(2,63.08) = 6.22$, $P = 0.003$) and *target velocity* ($F(1,124.27) = 325.77$, $P < 0.0001$). There was no main effect of direction ($F(1,62.35) = 0.7$, $P = 0.41$), and its interactions with *group* ($F(2,62.3) = 2.97$, $P = 0.06$) and *velocity* ($F(1,124.27) = 3.75$, $P = 0.05$) were non-significant. Other effects and interactions were also non-significant, with $P > 0.13$. Overall, the Standard group had higher gain than both Noisy ($M_{diff} = 0.116$ [0.063, 0.17], $Y_t = 4.3$, $P < 0.0001$) and Amblyopic ($M_{diff} = 0.183$ [0.113, 0.253], $Y_t = 5.2$, $P < 0.0001$) groups, while there was no significant difference between Noisy and Amblyopic groups ($M_{diff} = 0.066$ [-0.01, 0.145], $Y_t = 1.7$, $P = 0.09$).

3.2 Weighting of prior and visual information in smooth pursuit

To highlight the effect of prior and visual information on eye movements, we compared, respectively, trials with different prior target velocity but the same current velocity, or trials with the same prior target velocity but different current target velocities (cf. Section 2 and Fig. 1).

3.2.1 Smooth pursuit: Prior information weight does not differ across groups

As can be seen in Fig. 3, panels (A and B), eye velocity during Test trials was modestly biased toward target velocity in previous trials, being either higher (prior at 20°/s—red traces) or lower (prior at 15°/s—green traces) than the Training trials of matching target velocity. Analyzing the normalized effect of the prior on smooth pursuit (cf. Section 2, Fig. 3C), we confirmed its presence (main effect of *Trial #* $F(1,63) = 30.83$, $P < 0.0001$). We found no significant differences between groups. That is, there was no significant main effect of group ($F(2,63) = 2.49$, $P = 0.9$), interaction *group x Trial #* ($F(2,63) = 0.1$, $P = 0.9$) or *group × target velocity × Trial #* ($F(2,126) = 1.47$, $P = 0.23$).

There was an interaction *target velocity × Trial #* ($F(1,126) = 5.89$, $P = 0.02$), corresponding to a smaller effect of the prior for a Test trial at 15°/s (trimmed means difference $M_{diff} = -0.138$ [-0.219, -0.057], $Y_t(39) = -3.43$, $P = 0.001$) compared to a Test trial at 20°/s ($M_{diff} = -0.319$ [-0.434, -0.206], $Y_t(39) = -5.66$, $P < 0.0001$). This can be observed in Fig. 3, panel (B), by comparing red and green traces.
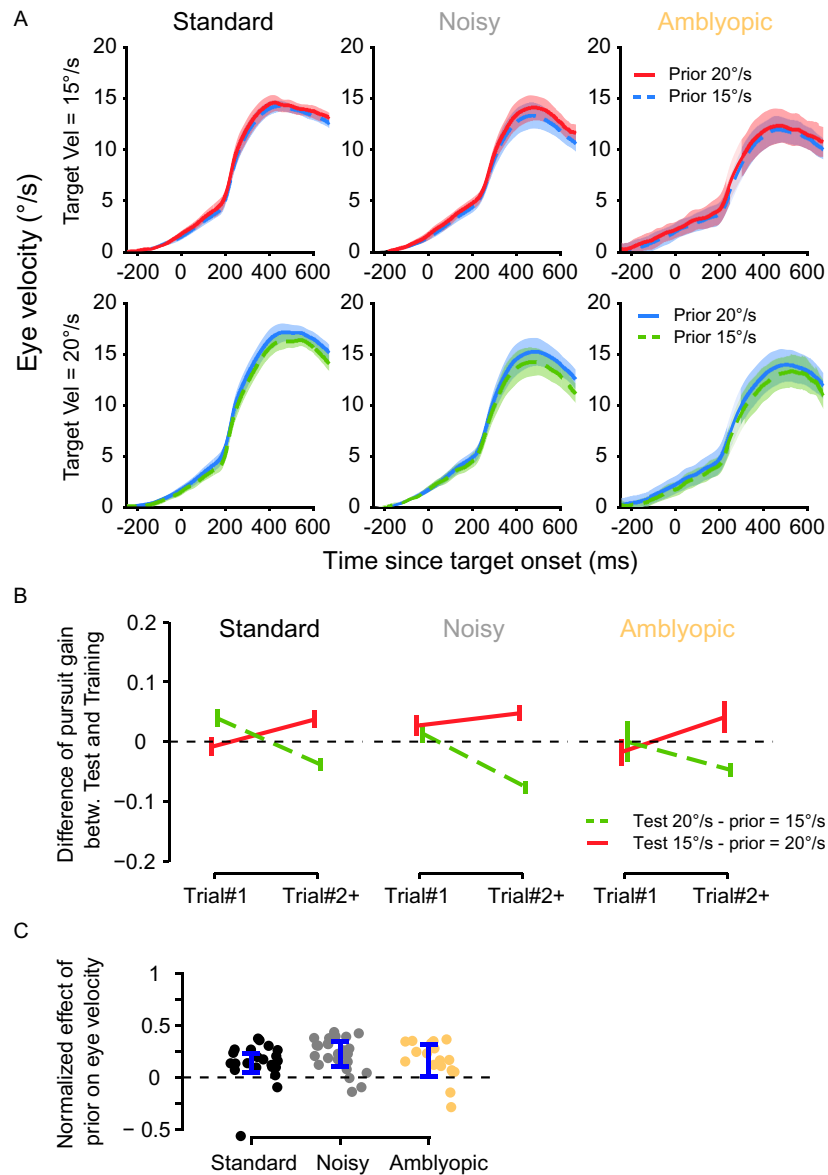
FIG. 3

(A) Averages of participant's average eye velocity traces during Training and Test trials with the same target velocity (first row: 15°/s; second row: 20°/s), but different priors of target velocity, 1 group per column, for trials #2–#4. Blue traces correspond to Training trials, red/green traces to Test trials. The surrounding shadows indicate 95% CI. (B) Averages of participant's average differential gains of the smooth pursuit eye velocity response to a target moving at 15°/s (full red line) or 20°/s (dashed green line), during the first or later trials, either at a higher (20°/s, full red line) velocity or a lower (15°/s, dashed green) velocity. Error bars indicate the SEM. (C) Normalized effect of the prior on eye velocity, with participant's averages as dots, and error bars corresponding to the average of participant's SEM, centered on the average of averages.

3.2.2 Smooth pursuit: Visual information has higher weight in the standard group

As shown in Fig. 4, panels (A and B), participant's eye velocity also reflected the higher (green traces) or lower (red traces) target velocity in Test trials, compared to Training trials (blue traces). To analyze the effect of visual information on smooth pursuit, we first established its presence by comparing Training and Test trials, then we compared the groups using the normalized visual effect.

The analysis of the visual gain of smooth pursuit (cf. Section 2) revealed main effects of *group* ($F(2,63) = 8.21$, $P = 0.0007$), *training target velocity* ($F(1,315) = 452.89$, $P < 0.0001$), and *trial type* ($F(2,315) = 378.27$, $P < 0.0001$), as well as interactions *group* $\times$ *trial type* ($F(4,315) = 35.05$, $P < 0.0001$), *training target velocity* $\times$ *trial type* ($F(2,315) = 48.02$, $P < 0.0001$). The interaction *group* $\times$ *training target velocity* $\times$ *trial type* wasn't significant ($F(4,315) = 2.33$, $P = 0.06$).

To verify the effect presence in all groups, we explored the interaction *group* $\times$ *trial type*. Simple effect analysis with robust *t*-tests showed significant differences between Training trials and Test trials for which target velocity decreased (cf. Fig. 4, panel (B), red traces) in all groups (Standard, Noisy and Ambly: $P < 0.0001$). However, when target velocity increased (cf. Fig. 4, panel (B), green traces) the difference was significant in the Standard ($P < 0.0001$) and Noisy ($P = 0.006$) groups, but not in the Amblyopic group ($P = 0.202$).

Having confirmed the presence of the effect in all groups, we compared them using the normalized visual effect measure (cf. Fig. 4C), and found significant main effects of *group* ($F(2,63) = 26.98$, $P < 0.0001$) and *training target velocity* ($F(1,126) = 49.62$, $P < 0.0001$). Contrary to the effect of prior information, we found no significant main effect of *Trial #* ($F(1,63) = 2.93$, $P = 0.09$), however, there was a significant *training target velocity* $\times$ *Trial #* interaction ($F(1,126) = 8.72$, $P = 0.004$).

Post-hoc analyses showed the Standard group had the strongest visual effect (Stand vs Noisy: $M_{diff} = 0.293$ [0.230, 0.355], $Y_t = 9.2$; Stand vs Ambly: $M_{diff} = 0.263$ [0.177, 0.349], $Y_t = 6.16$; both P values < 0.0001), while the Amblyopic and Noisy group did not differ (Noisy vs Ambly: $M_{diff} = -0.03$ [-0.114, 0.0545], $Y_t = -0.71$, $P = 0.47$).

3.3 Weighting of prior and visual information in catch-up saccades

Since saccades share inputs with pursuit (Krauzlis, 2005; Orban de Xivry and Lefèvre, 2007) and based on our previous study, we examined how the mismatch between prior and visual information affected catch-up saccades amplitude.

3.3.1 Catch-up saccades: Prior information weight does not differ across groups

Similarly to smooth pursuit, all groups exhibited effects of prior (main effect of *Trial #* $F(1,63) = 27.05$, $P < 0.0001$) on saccade amplitudes. As such, after the first trial, saccade amplitudes made during Test trials were either smaller if the previous target was
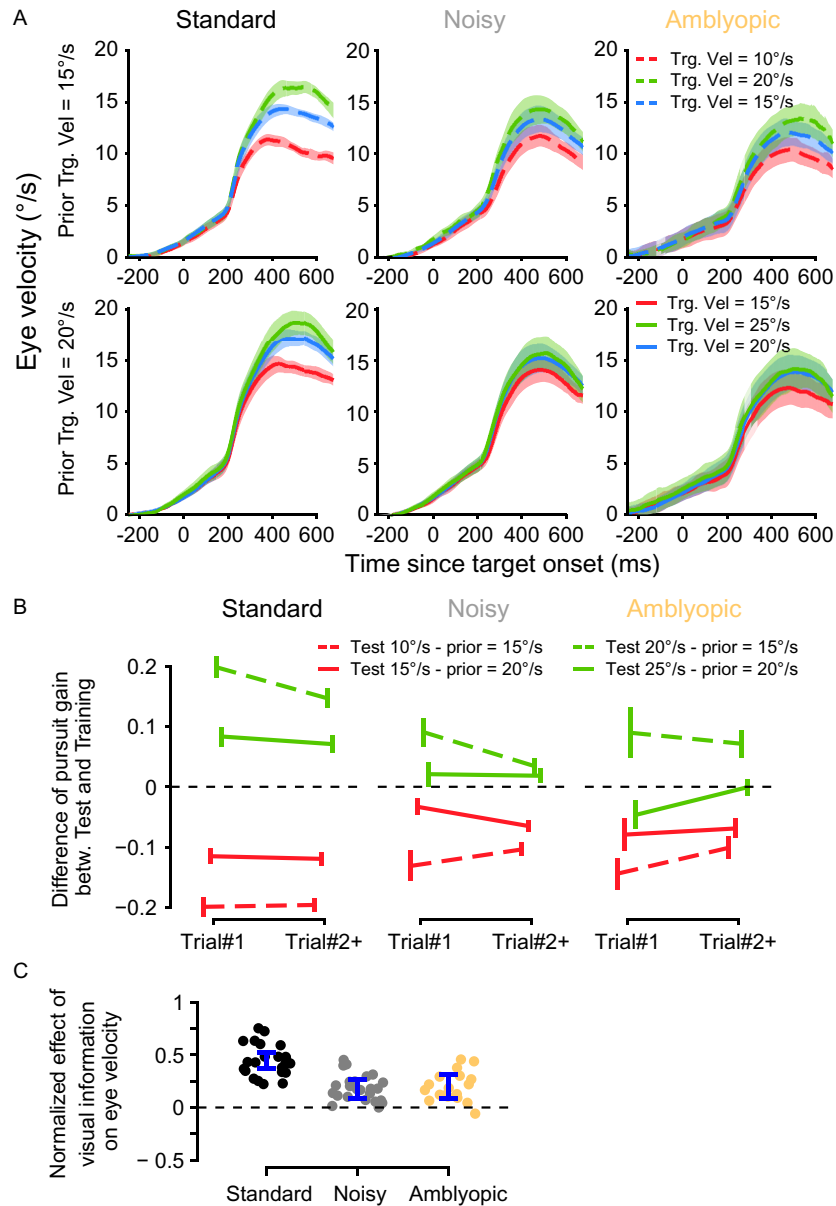
FIG. 4

(A) Averages of participant's average eye velocity traces during Training and Test trials with the same priors of target velocity (first row: 15°/s; second row: 20°/s), but different target velocity, 1 group per column, for trials #2–#4. Blue traces correspond to Training trials, red/green traces are Test trials. The surrounding shadows indicate 95% CI. (B) Averages of participant's average differential gains of the smooth pursuit eye velocity response to a target moving either at 10°/s or 20°/s (resp. red and green dashed lines) or at 15°/s or 25°/s (resp. red and green solid lines) during the first or later trials, at either a higher (all red lines) or lower (all green lines) velocity. The error bars correspond to the SEM. (C) Normalized effect of visual information on eye velocity, with participant's averages as dots, and error bars corresponding to the average of participant's SEM centered on the average of averages.
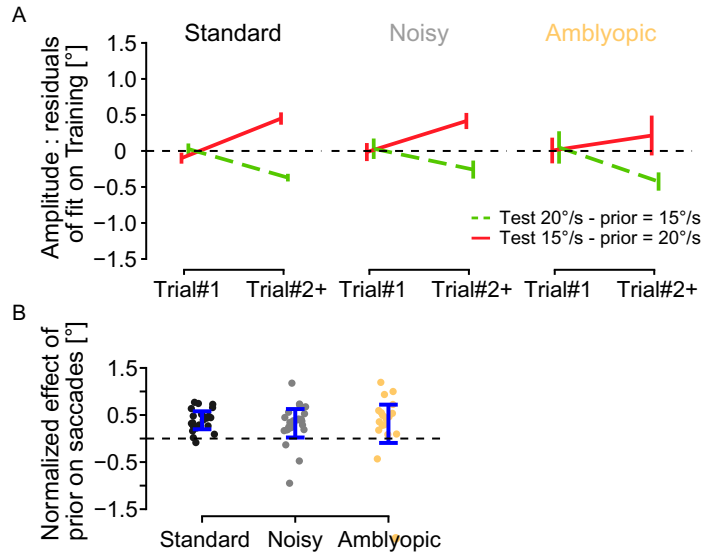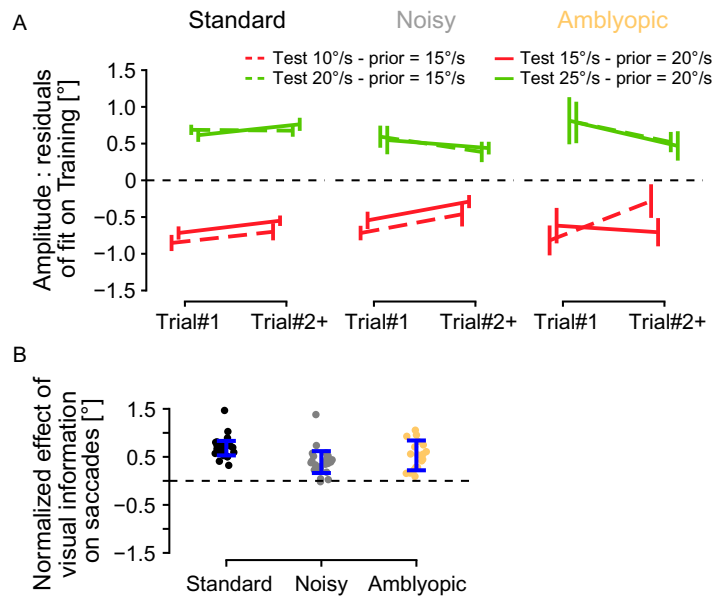
FIG. 5

(A) Effect of prior information on the amplitude of saccades, shown by the averages of each participant's residuals average, for each trial group (first or later). Red/green traces show data from Test trials. Error bars indicate the SEM. Dashed lines indicate a 15°/s prior target velocity. (B) Normalized effect of prior information on saccade amplitude, in later trials. Dots are individual averages of normalized residuals, blue error bars correspond to SEM.

slower (cf. red traces in Fig. 5A), or larger if it was faster (green traces in Fig. 5A). Once again, there was no difference between groups (no main effect of group: F $(2,63) = 0.02$, $P = 0.98$, no interaction group x Trial #: $F(2,63) = 0.31$, $P = 0.74$), which is apparent in the Fig. 5B comparing the normalized effect of the prior in later trials between groups. All remaining effects and interactions were non-significant ($P > 0.47$), including the interaction *training target velocity* $\times$ *Trial #*.

3.3.2 Catch-up saccades: Visual information weight is higher in standard and amblyopic groups

Of course, saccades were still impacted by visual information. We compared the amplitude of catch-up saccades in Test and Training trials, highlighting significant main effects of *group* ($F(2,63) = 8.34$, $P = 0.0006$), *training target velocity* ($F(1,315) = 504.14$, $P < 0.0001$) and *type of trial* ($F(2,315) = 330.86$, $P < 0.0001$), as well as an interaction *group* $\times$ *trial type* ($F(4,315) = 3.90$, $P = 0.004$). Post-hoc analysis on the interaction *group* $\times$ *trial type*, showed that all groups exhibited significant effects of visual information ($P < 0.001$) in both types of Test trials. This proved that, in all groups, Test trials induced larger/smaller amplitudes in reaction to faster/slower targets (Fig. 6A).

FIG. 6

(A) Effect of visual information on the amplitude of saccades, shown by the averages of each participant's residuals average, for each trial group (first or later). Red/green traces show data from Test trials. Error bars indicate the SEM. Dashed lines indicate a 15°/s prior target velocity. (B) Normalized effect of visual information on saccade amplitude, in later trials. Dots are individual averages of normalized residuals, blue error bars correspond to SEM.

To compare groups, we analyzed the normalized effect of visual information on saccades (cf. Section 2, Fig. 6B), revealing significant group differences (main effect of *group* $F(2,63) = 5.45$, $P = 0.007$). Direct comparisons showed that the Noisy group exhibited weaker visual effect on saccades than both the Standard ($M_{diff} = -0.191$ $[-0.273, -0.108]$, $Yt = -4.49$, $P < 0.0001$) and Amblyopic ($M_{diff} = -0.143$ $[-0.28, -0.009]$, $Yt = -2.09$, $P = 0.038$) groups. The Standard and Amblyopic groups did not differ ($M_{diff} = 0.048$ $[-0.078, 0.173]$, $Yt = 0.77$, $P = 0.459$).

In addition, there was a significant main effect of *Trial #* ($F(1,63) = 8.73$, $P = 0.004$), but no significant effect of *training target velocity* and no significant interaction (all $P > 0.07$). Post-hocs showed, as seen in Fig. 6A, that the effect of visual information on catch-up saccades decreased after the first trial ($M_{diff} = -0.144$ $[-0.218, -0.069]$, $Y_t = 3.82$, $P < 0.0001$).

4 Discussion

In this study, we examined the smooth pursuit performance and the weighting of prior and visual information of patients with unilateral amblyopia, and drew comparisons with two control groups tracking either a reliable uniform target (Standard

group) or a noisy Gaussian blob target (Noisy group). Our prediction was that, due to abnormal early visual development (Daw, 2014; Kiorpes and Daw, 2018), the relative weights of visual and prior information in amblyopic patients might differ from both Standard and Noisy groups, despite the fact that the Noisy group is also confronted to less reliable visual information.

Our results show that amblyopic patients exhibited clear deficits of smooth pursuit (latency, gain, reaction to velocity change) compared to the Standard group, which was similar to the Noisy group and consistent with a lower weight of visual information. Also, despite visual information reliability differences, we found no difference in the weight of prior information across groups. It therefore appears that amblyopia affects smooth pursuit in a way consistent with less reliable visual information, while catch-up saccades and prior information integration are less affected.

To our knowledge, our study is the first to investigate sustained, non-sinusoidal smooth pursuit in amblyopic patients with and without strabismus. While a few studies investigated visually-guided and sustained smooth pursuit in amblyopia (Ciuffreda et al., 1979; Schor, 1975; Von Noorden and Mackensen, 1962a), all considered sinusoidal motion, and, apart from (Von Noorden and Mackensen, 1962b), low target velocities ($<10°/s$). Still, we also observed lower pursuit gains in most amblyopic patients. More recently, Raashid et al. (2016) conducted a study of the sustained smooth pursuit of 11 anisometropic amblyopic patients, finding delayed pursuit onset but no difference of steady-state gain.

4.1 Lower reliability of visual information in amblyopia differentially affects smooth pursuit and catch-up saccades

As expected based on reliability-based models of smooth pursuit (Bogadhi et al., 2013; Darlington et al., 2017; Orban de Xivry et al., 2013) and on our previous study (Deravet et al., 2018), the noisy target offered less reliable visual information, inducing lower pursuit gain and delayed pursuit onset in the Noisy group. In addition, when presented with an increase or decrease in target velocity, the Noisy group reacted less than the Standard group, indicating that visual information had lower weight.

Similarly, amblyopic patients showed evidence of lower reliability of visual information compared to the Standard group. However, while smooth pursuit movements showed clear deficits, catch-up saccades remained unaffected. In addition, most amblyopic patients showed no significant oculomotor difference compared to the Noisy group, had shorter pursuit latency and higher weight of visual information in catch-up saccades.

Such differences between saccades and pursuit in amblyopic patients suggest that their saccadic system has access to more reliable visual information than their pursuit system, or that additional deficits affect their smooth pursuit (Bedell et al., 1990), or a combination of the two, possibly as a result of development in presence of noisy visual inputs.

4.2 Prior information integration is not affected by amblyopia

Despite similar protocols, we did not find significant differences of prior information weight between the control groups, therefore not reproducing results of Deravet et al. (2018). We believe this to be due to the differences between the protocols. In the previous experiment, the fixation target was always a uniform dot, from which disengaging was easier for Standard than for Noisy groups (Krauzlis et al., 2017). Also, while passively viewing target motion can suffice to acquire a prior, its reliability is lower than through active viewing (Barnes and Hill, 1984). We think these differences made the pursuit gain of Noisy controls in Deravet et al. (2017) lower than in the present study, possibly making the effect of the prior more salient.

Our hypothesis was that the weight of prior information might be different in amblyopic patients, due to a different development of their visual system (Daw, 2014; Kiorpes and Daw, 2018) or the imbalance in their ocular dominance (Kiorpes et al., 1998). For example, prior information could be given more weight to compensate for the lower reliability of information from the amblyopic eye.

However, we found no significant differences of prior effect between controls and amblyopic patients. One hypothesis to explain this result is that, in everyday life, our amblyopic patients have access to more reliable visual information through the fellow eye (Clavagnier et al., 2015), which allows their prior integration pathways to develop similarly to controls. This would likely require prior integration to be processed binocularly, after the integration of visual information coming from both eyes. As such, the integration of visual and prior information about target motion could be done, respectively, in the Area MT (Osborne et al., 2004, 2007), and in the Frontal Eye Fields (Darlington et al., 2017).

4.3 Neural basis of smooth pursuit deficits in amblyopia

Neural deficits within V1, such as losses of sensitivity and acuity, are well documented in amblyopia (Clavagnier et al., 2015; Kiorpes et al., 1998, 2006), but do not suffice to explain deficits in visuomotor behavior and in extrastriate areas (Kiorpes et al., 1998; Kiorpes and Daw, 2018; Shooner et al., 2015). However, because extrastriate areas are downstream from V1, their development (and feedback) can be affected by these deficits (Kiorpes and Daw, 2018). As such, one explanation for amblyopia is that of an "immature" system in which projections from the amblyopic eye to early visual areas (V1–V3) are characterized by lower spatial resolution and a disordered topographical map (Clavagnier et al., 2015). The Noisy group, processing noisy visual information through an intact neuroanatomical pathway, would therefore be expected to diverge from acuity-matched Amblyopic patients on behaviors whose development was affected by noisy visual inputs. Based on behavior differences suggested in our results, we would expect future investigations using similar protocols and visual acuity—matched groups (matching the Gaussian spots of controls to the acuity of amblyopic patients) to outline an even better picture of the specificities of reliability-based integration in Amblyopia.

4.4 Conclusion

In conclusion, oculomotor performance of amblyopic patients mostly lays within the continuum between that of controls tracking a reliable target and tracking a noisy Gaussian target. While their smooth pursuit showed evidence of a lower weight of visual information, their catch-up saccades did not, which suggests that their smooth pursuit pathways incur additional noise, possibly as a result of developing in presence of noisy visual inputs. Despite these differences, the integration of prior information did not differ between groups, suggesting that the relative weights of prior and visual information are not significantly affected by unilateral amblyopia.

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