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Inhibition failures and late errors in the antisaccade task: influence of cue delay

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Aponte EA, Tschan DG, Stephan KE, Heinzle J. Inhibition failures and late errors in the antisaccade task: influence of cue delay. *J Neurophysiol* 120: 3001–3016, 2018. First published August 15, 2018; doi:10.1152/jn.00240.2018.—In the antisaccade task participants are required to saccade in the opposite direction of a peripheral visual cue (PVC). This paradigm is often used to investigate inhibition of reflexive responses as well as voluntary response generation. However, it is not clear to what extent different versions of this task probe the same underlying processes. Here, we explored with the Stochastic Early Reaction, Inhibition, and late Action (SERIA) model how the delay between task cue and PVC affects reaction time (RT) and error rate (ER) when pro- and antisaccade trials are randomly interleaved. Specifically, we contrasted a condition in which the task cue was presented before the PVC with a condition in which the PVC served also as task cue. Summary statistics indicate that ERs and RTs are reduced and contextual effects largely removed when the task is signaled before the PVC appears. The SERIA model accounts for RT and ER in both conditions and better so than other candidate models. Modeling demonstrates that voluntary pro- and antisaccades are frequent in both conditions. Moreover, early task cue presentation results in better control of reflexive saccades, leading to fewer fast antisaccade errors and more rapid correct prosaccades. Finally, high-latency errors are shown to be prevalent in both conditions. In summary, SERIA provides an explanation for the differences in the delayed and nondelayed antisaccade task.

NEW & NOTEWORTHY In this article, we use a computational model to study the mixed antisaccade task. We contrast two conditions in which the task cue is presented either before or concurrently with the saccadic target. Modeling provides a highly accurate account of participants' behavior and demonstrates that a significant number of prosaccades are voluntary actions. Moreover, we provide a detailed quantitative analysis of the types of error that occur in pro- and antisaccade trials.

antisaccades; error rate; eye movements; reaction time; SERIA model

INTRODUCTION

The antisaccade task (Hallett 1978) is an oculomotor paradigm widely used in psychiatry and neurology (reviewed in Bittencourt et al. 2013; Everling and Fischer 1998; Gooding and Basso 2008; Hutton and Ettinger 2006), in which participants are required to saccade in the opposite direction of a peripheral visual cue (PVC). This paradigm probes both the ability to inhibit reflexive responses, i.e. (pro)saccades toward a visual cue, and the ability to initiate voluntary actions, i.e. (anti)saccades in the opposite direction of the PVC (Everling and Fischer 1998). Fundamentally, since the seminal study of Hallett (1978), it is known that participants tend to commit more errors (i.e., prosaccades) when required to make antisaccades, than when required to make prosaccades.

The clinical relevance of this paradigm derives from the fact that error rates (ERs) and reaction times (RTs) are altered in many psychiatric and neurological diseases. For example, ERs are elevated not only in schizophrenic patients (Gooding and Basso 2008) but also in their first-order relatives as well as in related psychiatric populations, such as schizoaffective disorder patients (Calkins et al. 2004; Reilly et al. 2014; Myles et al. 2017). Deficits have also been reported in patients with Parkinson's disease (Amador et al. 2006; Antoniades et al. 2015; Chan et al. 2005), attention deficit disorders (e.g., Klein et al. 2003; Munoz et al. 2003), and brain lesions (Guitton et al. 1985; Pierrot-Deseilligny et al. 1991).

Antisaccade errors have mostly been attributed to deficits in inhibitory control (e.g., Broerse et al. 2001; Calkins et al. 2004; Levy et al. 1998). An alternative explanation states that antisaccade errors are also caused by deficits in voluntary action initiation. This view was initially proposed by Fischer et al. (2000), who applied a factor analysis to pro- and antisaccade data from a large cohort of subjects. The analysis revealed two main factors that Fischer and colleagues interpreted as inhibitory control and voluntary action initiation. Using a similar argument, Klein and Fischer (2005) proposed to extend the distinction between "express" (RT $<$130 ms) and "normal-range" (RT $>$130 ms) saccades to antisaccade errors and used indirect statistical evidence to suggest that these evolve differently during development and are correlated with different psychometric constructs (Klein et al. 2010). In particular, Klein et al. (2010) found that the probability of normal-range errors but not the probability of express errors was correlated with psychometric intelligence (Heller et al. 1998; Jäger et al. 1997) and working memory (Sternberg 1966).

From a different perspective, Reuter and colleagues (Reuter and Kathmann 2004; Reuter et al. 2005), on the basis of the

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parallel saccade programming model of Massen (2004), hypothesized that at least some fraction of the errors observed in this paradigm are caused by failures to initiate voluntary actions. More recently, Lo and Wang (2016) incorporated the idea of two sources of antisaccade errors into a biophysical model of eye movement control and speculated that the mechanisms behind prosaccade errors with unusually high latency might be of interest in psychiatric research. In that spirit, Coe and Munoz (2017) suggested that the ratio between express (RT = 90–140 ms) and high-latency errors (RT >140 ms) could distinguish between control and patient populations, such as Parkinson's disease and lateral amyotrophic sclerosis patients.

Recently, using the Stochastic Early Reaction, Inhibition, and late Action (SERIA) model (Aponte et al. 2017), we presented quantitative and qualitative evidence that errors in the antisaccade task can be divided into fast, reflex-like prosaccades and voluntary but erroneous late prosaccades. SERIA is a generative model that extends the LATER model for antisaccades (Noorani and Carpenter 2013) and builds on the idea that RTs are distributed as the threshold hit times of linear, ballistic accumulation processes (Noorani and Carpenter 2016). In this family of models (similar to the model proposed by Kristjánsson et al. 2001), pro- and antisaccades are generated by two competing but independent accumulators. In addition, a third unobservable process can stop reflexive prosaccades, similarly as in the model used for the countermanding saccade task (Camalier et al. 2007; Logan et al. 1984).

Conceptually, SERIA extends Noorani and Carpenter's (2013) work by introducing a further decision process that can generate late prosaccades and competes with the (late) antisaccade process. Errors can therefore be divided into early errors, explained as inhibition failures, and late errors, explained by the race between voluntary pro- and antisaccades. Moreover, according to SERIA, errors on prosaccade trials occur when an early response is inhibited, but the antisaccade process overwrites the late prosaccade process. Thus, SERIA provides a unified account of all types of errors observed in the antisaccade task.

One limitation of the study in Aponte et al. (2017) is that the version of the antisaccade task used there originated from nonhuman primate studies (e.g., Sato and Schall 2003) and has not been widely used in humans (but see Chiau et al. 2011; Irving et al. 2009; Liu et al. 2010; Weiler and Heath 2014). Concretely, in Aponte et al. (2017), subjects performed interleaved pro- and antisaccade trials, in which a PVC signaled both the trial type and the target location (see Fig. 1*A*). We refer to this version of the antisaccade task as the synchronous cue (SC) design.

In humans, the antisaccade task is most often administered in a block design (Antoniades et al. 2013) in which subjects perform either pro- or antisaccedes throughout a block. Even when different trial types are interleaved, participants are usually informed about the task demands before the PVC is presented (e.g., Barton et al. 2006; Cherkasova et al. 2002; Massen 2004; O'Driscoll et al. 2005; Pierce et al. 2015; Pierce and McDowell 2016a, 2016b; Reuter et al. 2006). We refer to this paradigm as the asynchronous cue (AC) design. This version of the task is often used in primate experiments as well (e.g., Amador et al. 1998; Johnston et al. 2014; Koval et al. 2014; Vijayraghavan et al. 2016).

The main goal of the present study was to test whether the conclusions drawn in our previous experiment generalize to the AC design, the most common version of the antisaccade task. We acquired data from 24 participants in both the SC and AC conditions and compared RT and ER as well as SERIA model parameters estimated from the data. We were interested in three main questions. First, we investigated whether in an AC design it was necessary to postulate a late race between voluntary pro- and antisaccades. Hence, we compared models that incorporated a late race against models in which all late saccades were antisaccades. Second, we were interested in differences in the probability of inhibition failures and late errors in the two task designs. Specifically, we investigated if and in what proportions late errors occurred in SC and AC conditions.

Our third main goal was to test whether the effects of trial type probability reported in Aponte et al. (2017) could be

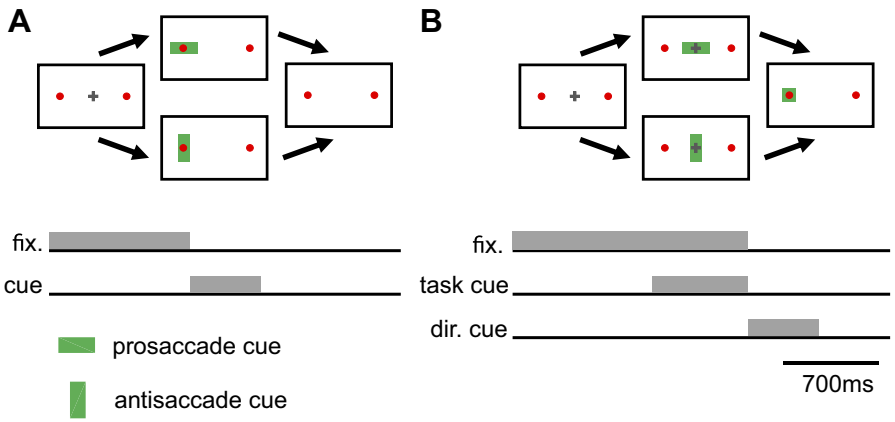

Fig. 1. Task design. *A*: synchronous cue (SC) condition. Similarly to Aponte et al. (2017), subjects were instructed to fixate on a central cross for 500 to 1,000 ms while two red circles were displayed at ± 12°. Immediately after the fixation period, a green bar was displayed centered on one of the red circles for 500 ms. Participants were instructed to saccade as fast as possible to the red circle cued by a green bar and to saccade to the uncued circle when a vertical bar was displayed. *B*: asynchronous cues (AC) condition. As in the SC condition, subjects were instructed to fixate on a central cross for 500 to 1,000 ms. After the initial fixation period, a green bar was displayed at the center of the screen for 700 ms. Immediately afterward, the fixation cross and the green bar were removed, and a green square was displayed centered on one of the red circles. Subjects were instructed to saccade to the cued circle if a horizontal bar was presented and to saccade to the uncued circle otherwise.

replicated and whether these effects generalized to the AC design. Previous studies (Aponte et al. 2017; Chiau et al. 2011) suggest that in the SC design participants leverage contextual prior information in pro- and antisaccades trials, similarly as stablished for other probability manipulations in oculomotor tasks (Carpenter and Williams 1995). In that seminal study, Carpenter and Williams demonstrated that changes in RT distributions can be explained by the principles of Bayesian inference, in which contextual information is combined with perceptual evidence accumulated over time. An alternative possibility is that task uncertainty can affect inhibitory control (Aponte et al. 2017; Olk and Kingstone 2003), indirectly affecting RT and ER. Physiologically, the effects of trial type probability on the antisaccade task could be explained by preparatory activity that precedes stimulus onset in cortical (Everling and Munoz 2000) and subcortical regions (Everling et al. 1998; 1999). Despite these findings in the SC design, several studies have found significant effects of trial type probability on prosaccade but not on antisaccade ER using an AC design (Pierce et al. 2015; Pierce and McDowell 2016b). Yet a third study reported the opposite effect (Pierce and McDowell 2016a). Thus, we investigated to which extent participants used contextual information in the AC design compared with the SC design.

METHODS

Participants. Twenty-five healthy male volunteers (age: 21.4 ± 2.0 yr) participated in the study approved by the local ethics board of the Canton of Zurich, Switzerland (KEK-ZH-Nr.2014-0246) and conducted according to the Declaration of Helsinki. Because this experiment was part of a larger pharmacological study, only male participants were included. All subjects had normal or corrected-to-normal vision and gave their written informed consent to participate. One subject had to be excluded because of incomplete data. Hence, 24 subjects were included in the final analysis.

Apparatus. The experiment took place in a dimly illuminated room. Subjects viewed a cathode ray tube screen (41.4 × 30 cm, Philips 20B40) operating at 85 Hz from a distance of 60 cm, while their gaze was recorded with an infrared eye tracker (Eyelink 1000; SR Research, Ottawa, ON, Canada). Head position was stabilized using a chin rest. Gaze position was recorded at a sampling rate of 1,000 Hz. Every block started with a 5-point calibration procedure. Absolute calibration error was aimed to be below 1°. The experiment was programmed in the Python programming language (2.7) using the PsychoPy (1.82.02) package (Peirce 2007, 2009). The experiment was controlled by a personal computer (Intel Core i7 4740K) equipped with a Nvidia GTX760 graphics card.

Experimental design. The experimental design used here is an extension of the design used in Aponte et al. (2017). Subjects participated in six blocks of mixed pro- and antisaccade trials. Each block consisted of 200 trials, from which either 20, 50, or 80% were randomly interleaved prosaccade trials. In addition to trial type probability, we also manipulated the temporal order in which the trial type cue and the saccade direction cue were presented: Subjects were either simultaneously informed about the trial type and saccade direction using one peripheral cue (SC condition), or they were informed about the trial type before being presented with the peripheral cue (AC condition). Both conditions are explained in detail below. All task instructions were given in written format at the beginning of the session.

The experiment followed a within-subject, 3 × 2 × 2 factorial design, with factors prosaccade trial probability (PP) with levels PP20, PP50, and PP80, cue type (CUE) with levels SC and AC, and trial type (TT) with levels PRO(saccade) and ANTI(saccade). The blocks belonging to one of the CUE conditions were administered consecutively. The order of presentation of the blocks was pseudo-randomized and counterbalanced across subjects. The same sequence of pro- and antisaccade trials was used for each PP condition independently of the CUE condition. The peripheral cue was presented randomly on the right and left sides of the screen. Again, the same random sequence was used across subjects.

Before participating in the main experiment, subjects underwent a training block of each condition. These consisted of 100 trials, from which the first half were prosaccade trials, followed by 50 antisaccade trials. During training, participants received automatic feedback after each trial indicating whether they had made a saccade in the correct direction. To urge participants to respond quickly, saccades with a latency above 500 ms were signaled as errors.

SC condition. Throughout the experiment, two red circles of 0.25° of radius were presented at 12° to the left and right of the center of the screen. Cueing of the peripheral saccade targets has been used in a number of previous studies (e.g., Barton et al. 2002; Chiau et al. 2011; Sato and Schall 2003) and do not appear to affect pro- or antisaccade RT (Edelman et al. 2006). We introduced these stimuli to facilitate the vector inversion necessary to perform an antisaccade (Munoz and Everling 2004), which is not the main interest of the present study.

Each trial started with a cross (0.6 × 0.6°) displayed at the center of the screen. Subjects were required to fixate for at least 500 ms. If their gaze drifted outside a 3° window, the fixation interval was restarted. The fixation target was presented for a further random interval (500–1,000 ms), after which a green bar (3.48 × 0.8°) centered on one of the peripheral red circles was displayed for 500 ms (Fig. 1*A*). The bar was presented in either horizontal or vertical orientation. A horizontal bar indicated a saccade to the cued stimulus (a prosaccade) and a vertical bar indicated a saccade to the uncued stimulus (an antisaccade). The next trial started 1,000 ms after the peripheral cue was removed.

AC condition. The start of the AC condition (Fig. 1*B*) was identical to the SC condition, but after the initial fixation period a green bar (3.48 × 0.8°) was displayed for 700 ms centered on the fixation cross. The bar could be in horizontal or vertical orientation. The fixation cross and the green bar were removed at the end of the 700-ms period, and subsequently a green square (1.74 × 1.74°) was presented, centered on one of the peripheral red circles for 500 ms. Subjects were instructed to saccade to the cued red circle when a horizontal bar was displayed (prosaccade trial), and to saccade to the uncued circle when a vertical bar was shown (antisaccade trial). The next trial started 1,000 ms after the green square was removed.

Data preprocessing. Data were preprocessed using the Python programming language (2.7). Saccades were detected using the algorithm provided by the eye tracker manufacturer (Stampe 1993), which uses velocity and acceleration thresholds of 22°/s and 3,800°/s^2, respectively. Saccades with a magnitude lower than 2° were ignored. RT was defined as the latency of the first saccade after the fixation cross was removed (henceforth, the main saccade). Trials were discarded if any of the following conditions was true: if a blink occurred between the start of the fixation period and the end of the main saccade; if subjects failed to maintain fixation; if a saccade had a latency above 800 ms or below 50 ms; and, in the case of an antisaccade, if it had a latency below 95 ms.

Errors on antisaccade trials were defined as (pro)saccades toward the cue, and errors on prosaccade trials were defined as (anti)saccades away from the cue. Corrective antisaccades were defined as saccades to the uncued stimulus that followed errors on antisaccade trials. The RTs of corrective antisaccades were defined relative to the cue onset and not relative to the error prosaccade. Corrective saccades were included in the analysis only if they occurred at most 900 ms after cue presentation and if their horizontal end location was not less than 4° and not more than 15° from the center of the screen in the direction of the correct target.

Classical statistical analysis. Mean RTs, ERs, and parameter estimates of the model (see *Modeling* below) were analyzed using a generalized mixed-effects linear model (GLME). The independent variables were PP with levels PP20, PP50, PP80, CUE with levels SC and AC, TT with levels PRO- and ANTISACCADE. The factor SUBJECT was entered as a random effect. All regressors were treated as categorical variables. ERs were analyzed using a binomial regression model with the probit function as link function. When probabilities were analyzed, a Beta regression model (Fournier et al. 2012) was used. For RTs, we report tests based on the F statistic, whereas for ERs and probabilities we report tests based on the χ^2 statistic, as this is more appropriate in models were the dispersion parameter is not estimated from the data (R Core Team 2017). When F-tests were conducted, we used the Satterthwaite approximation to the degrees of freedom (Luke 2017; Satterthwaite 1941).

Statistical significance was asserted at $\alpha = 0.05$. All statistical tests were performed with the *R* programming language (3.4.2) using the functions *lmer, glmer,* and *glmmadmb* (Beta regression model) from the packages *lme4, lmerTest*, and *glmmADMB*.

Modeling. Two models (described in detail in Aponte et al. 2017) were fitted to actions (pro- or antisaccades) and RT. First, we fitted the PRO-, Stop, and Antisaccade (PROSA) model, which structurally resembles the model described in Noorani and Carpenter (2013). According to this model, three linear race decision units determine RTs and ERs in the antisaccade task. Each unit triggers or stops different types of action depending on the order and time at which they hit threshold (henceforth hit time): The early unit triggers a prosaccade if it hits threshold before all other units. These fast reactions can be stopped by the inhibitory unit if the latter hits threshold before the early unit. If an early response is inhibited, the third unit triggers an antisaccade once it hits threshold. This model represents the hypothesis that all voluntary or late responses are antisaccades.

More formally, we assume three independent stochastic accumulation processes or units that represent early responses (u_e), a unit that inhibits them (u_i), and a unit that triggers antisaccades (u_a). The threshold hit time of the units can be represented by the random variables U_e, U_i, and U_a, respectively. According to PROSA, a prosaccade is generated at time t if the early unit hits threshold at time t before all other units

$$p(A = pro, T = t) = p(U_e = t)p(U_i > t)p(U_a > t). \quad (1)$$

Here, the probability on the left-hand side of the equation is the probability that the action *prosaccade* ($A = pro$) is generated at time $t = t$. An antisaccade at time t is elicited when the antisaccade unit hits threshold at time t before all other units

$$p(U_a = t)p(U_e > t)p(U_i > t) \quad (2)$$

or the inhibitory unit hit threshold before the early unit

$$p(U_a = t)\int_0^t p(U_i = \tau)p(U_e > \tau)d\tau. \quad (3)$$

It follows that

$$p(A = anti, T = t) = p(U_a = t)p(U_e > t)p(U_i > t) + p(U_a = t)\int_0^t p(U_i = \tau)p(U_e > \tau)d\tau. \quad (4)$$

Note that, according to PROSA, all early reactions are prosaccades, which can be stopped by the inhibitory unit u_i.

Second, we fitted the SERIA model (see Fig. 2), which extends PROSA by including a fourth unit, which can trigger late, voluntary prosaccades. Hence, SERIA distinguishes between reflexive, early prosaccades, and voluntary, late prosaccades.

Formally, to account for late prosaccades, we model a fourth unit u_p and its hit time U_p. A prosaccade at time t can be generated when the early unit hits threshold before all other units

$$p(U_e = t)p(U_a > t)p(U_i > t)p(U_p > t) \quad (5)$$

or the late prosaccade unit hits threshold before all other units

$$p(U_p = t)p(U_a > t)p(U_i > t)p(U_e > t) \quad (6)$$

or the inhibitory unit stops an early reaction and the late prosaccade unit hits threshold before the antisaccade unit

$$p(U_p = t)p(U_a > t)\int_0^t p(U_i = \tau)p(U_e > \tau)d\tau. \quad (7)$$

Finally, antisaccades are generated either when the antisaccade unit hits threshold before all other units

$$p(U_a = t)p(U_p > t)p(U_e > t)p(U_i > t) \quad (8)$$

or the early prosaccade unit is stopped, and the late prosaccade unit hits threshold after the antisaccade unit

$$p(U_a = t)p(U_p > t)\int_0^t p(U_i = \tau)p(U_e > \tau)d\tau. \quad (9)$$

As for the PROSA model, the probability of a specific action at time t can be calculated by summing the probabilities of the different cases that can trigger the corresponding action.

SERIA distinguishes two types of errors on antisaccade trials: inhibition failures, when the early unit hits threshold before all other units, and volitional or late errors, when the late prosaccade unit hits threshold before the antisaccade unit. An error on a prosaccade trial occurs when an early response is stopped but the antisaccade unit hits threshold before the late prosaccade unit. Note that the model used here corresponds to the SERIA model with late race ($SERIA_{lr}$), introduced in Aponte et al. (2017).

To fit the models to empirical data, we evaluated three different parametric distributions for the increase rate (or reciprocal hit time) of each of the units: We assumed either that the increase rate of all the units was truncated Gaussian distributed, in analogy to the LATER model (Noorani and Carpenter 2016), or that the increase rate of the early and inhibitory unit was Gamma distributed, but the increase rate of the late units was inverse Gamma distributed. We refer to this model as the mixed Gamma model. Finally, we considered a model in which the increase rate of all the units was Gamma distributed.

Initially, we assumed different parameters for the units on pro- and antisaccade trials. However, we also considered a constrained version of the SERIA model in which the early and inhibitory units followed the same distribution on pro- and antisaccade trials but the late units had different parameter values across trial types (Aponte et al. 2017). For PROSA, we investigated a model in which the early unit followed the same distribution across trial types but all others were allowed to differ (Aponte et al. 2017; Noorani and Carpenter 2013). A summary of the model space is presented in Table 1. More details on the model space can be found in Aponte et al. (2017).

We fitted the data from all subjects and PP conditions simultaneously using a Bayesian hierarchical model (Gelman et al. 2003), in which the prior distribution of the parameters of each subject was informed by the population distribution. The two CUE conditions were analyzed independently, because our goal was to evaluate whether different models were favored under different task designs. The population distribution was modeled using a linear mixed-effects model with PP as fixed effect and SUBJECT as a random effect.

Models were fitted using Markov chain Monte Carlo (MCMC) sampling via the Metropolis-Hastings algorithm. The evidence or marginal likelihood of a model was computed with thermodynamic integration (Aponte et al. 2016; Gelman and Meng 1998), with 32 chains and a 5th-order temperature schedule (Calderhead and Girolami 2009). To increase the efficiency of the algorithm, we incorporated a "swap-step" according to population MCMC's accept/reject rule (Calderhead and Girolami 2009). The algorithm was run for 16×10^4 iterations, and the first 6×10^4 samples were discarded as "burn-in" samples. The code was executed on a computer cluster

Table 1. *Model space*

Model	Parametric Distribution	No. of Parameters
Unconstrained/constrained	*PROSA*	
m_1/m_2	Truncated normal	15/13
m_3/m_4	Mixed Gamma	15/13
m_5/m_6	Gamma	15/13
	SERIA	
m_7/m_8	Truncated normal	19/15
m_9/m_{10}	Mixed Gamma	19/15
m_{11}/m_{12}	Gamma	19/15

List of models with corresponding increase rate distributions and number of free parameters. PROSA; PRO-, Stop, and Antisaccade model; SERIA, Stochastic Early Reaction, Inhibition, and late Action model. In constrained models, some of the parameters are assumed to be equal across trial types. Note that besides the parameters of the units, all models include 3 additional parameters that account for no-response time, late-response cost, and frequency of outliers, i.e., saccades with latencies below the no-response time. Further details can be found in Aponte et al. (2017).

running Linux (CentOS 7.4.1708), MATLAB R2015a (8.5.0.197613), and GSL 1.16. The software implemented here is publicly available as part of the TAPAS toolbox (http://www.translationalneuromodeling.org/tapas/; see software note).

The statistic used to compare models was the difference in log model evidence (LME), which corresponds to log Bayes factors (Kass and Raftery 1995). Because our main hypothesis was related to families of models (SERIA and PROSA), we used Bayesian family model comparison (Penny et al. 2010) implemented in the SPM12 software package (release 6470, function *spm_compare_families.m*). Building on random-effects Bayesian model selection (Stephan et al. 2009), this method pools the evidence of models that are assumed to belong to the same family and returns the posterior probability of each family.

RESULTS

A total of 28,815 main saccades were collected from 24 subjects; 1,079 trials (or 3.7%) were discarded due to eye blinks (330), fixation failures (458), missing data (74), no saccade (1), or short saccade latency (203). Only a few saccades (14) had a latency above 800 ms. In the analysis of corrective saccades, 983 and 696 trials were included in the SC and AC conditions, respectively.

Error rate. Figure 3, *A* and *B*, display the mean ER in all conditions and trial types. Participants made more errors on antisaccade trials compared with prosaccade trials [χ^2 (2, n = 144) = 257.06, $P < 10^{-5}$]. ER was higher in the SC condition compared with the AC condition [χ^2 (2, n = 288) = 400.12, $P < 10^{-5}$]. Because there was a significant interaction between the factors PP, CUE, and TT [χ^2 (2, n = 288) = 91.59, $P < 10^{-5}$], pro- and antisaccade ERs were submitted to two independent tests using PP and CUE as explanatory variables.

ER was higher in the SC condition, regardless of trial type [prosaccade trials: χ^2 (2, n = 144) = 402.75, $P < 10^{-5}$; antisaccade trials: χ^2 (2, n = 144) = 257.06, $P < 10^{-5}$]. Moreover, there was a significant interaction between the factors PP and CUE in both trial types, demonstrating that PP

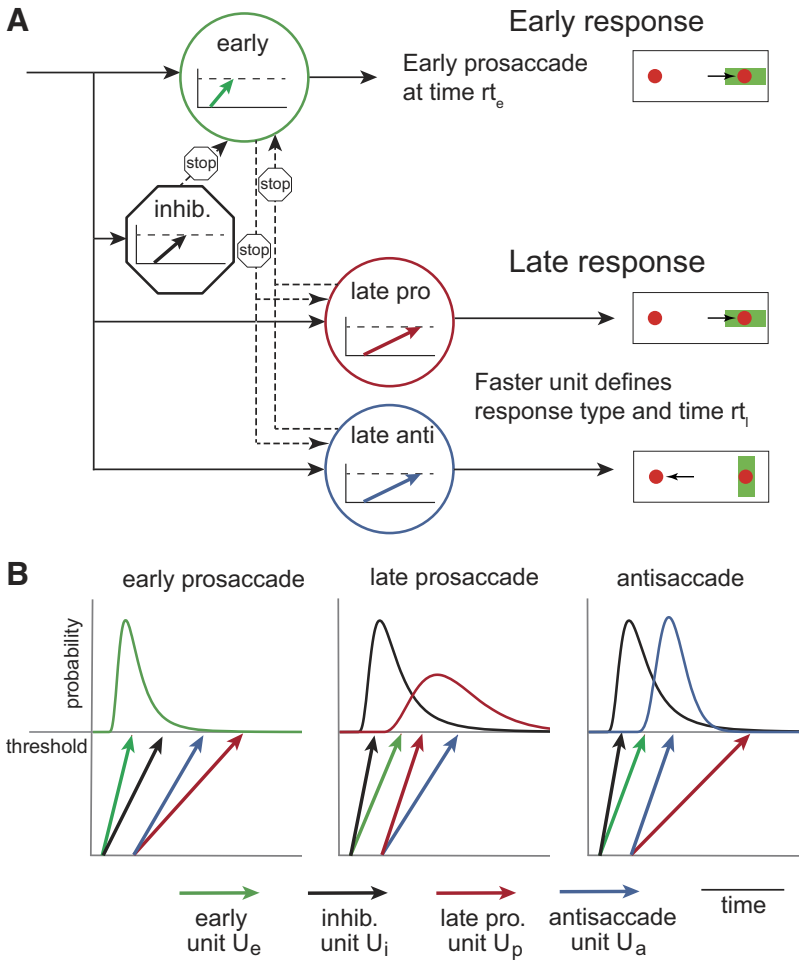

Fig. 2. The Stochastic Early Reaction, Inhibition, and late Action (SERIA) model: *A*: the SERIA model consists of 4 units with different hit time distributions. A reactive, early response is triggered if the early unit (green) hits threshold before all other units. If the early unit is stopped by the inhibitory unit (black), the ensuing late action is decided by the race between the late pro- (red) and antisaccade (blue) units. The unit that hits threshold first determines the action and reaction time (RT). Figure adapted with permission from Aponte et al. (2017). *B*: the order and hit times of the units determine the RT and action performed on a trial. The increase rate of each of the units is assumed to be stochastic. Colors correspond to those in *A*. For simplicity, units are shown as sharing the same threshold, although this assumption is not necessary. Note that in the PRO-, Stop, and Antisaccade (PROSA) model, there is no late prosaccade unit; thereby prosaccades can only be generated by the early unit. *Left*: an early prosaccade is generated when the early unit hits threshold before all other units. *Middle*: a late prosaccade is generated when the inhibitory unit hits threshold before all other units, and the late prosaccade unit hits threshold before the late antisaccade unit. *Right*: an antisaccade is generated when early reactions are inhibited and the antisaccade unit hits threshold before the late prosaccade unit.

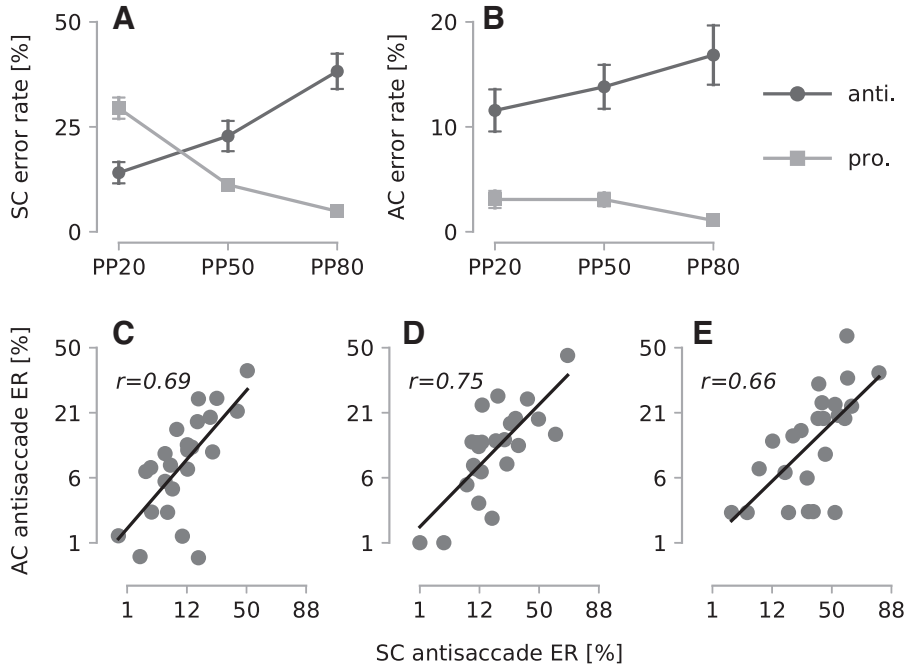

Fig. 3. *A*: mean error rate (ER) vs. prosaccade trial probability (PP; 20/50/80, percents randomly interleaved prosaccade trials), synchronous cue (SC) condition. *B*: mean ER vs. PP, asynchronous cue (AC) condition. Error bars depict SE of the mean. *C–E*: ER correlation between AC and SC conditions in PP20, PP50, and PP80 conditions, respectively. ERs are displayed in the probit scale.

had a much more pronounced effect in the SC condition [prosaccade trials: χ^2 (2, n = 144) = 43.00, $P < 10^{-5}$; antisaccade trials: χ^2 (2, n = 144) = 63.43, $P < 10^{-5}$].

Next, we submitted ERs in the two CUE conditions to two separate tests with explanatory variables TT and PP. Thus, we could test whether PP had a significantly different effect on pro- and antisaccade trials. We found that in both CUE conditions the interaction between PP and TT was significant [SC: χ^2 (2, n = 144) = 700.46, $P < 10^{-5}$; AC: χ^2 (2, n = 144) = 42.24, $P < 10^{-5}$].

Finally, we investigated ER correlations between the two CUE conditions (Fig. 3, *C–E*). The probit-transformed ERs in each PP block were analyzed separately. For numerical reasons, zero percent ERs were set to a nonzero value, pretending that the respective subjects had committed a single error. There was a significant correlation ($R^2 > 0.43$, $P < 0.001$) between ERs on antisaccade trials in all three PP conditions, but we found no comparable results on prosaccade trials ($R^2 < 0.01$, $P > 0.56$). ERs were not generally correlated across trial types in either the SC or AS condition. In particular, we found only significant correlations in the SC+PP50 ($R^2 = 0.16$, $P < 0.04$) and AC+PP20 ($R^2 = 0.31$, $P < 0.01$) conditions.

Reaction times. The mean RTs of correct saccades are displayed in Fig. 4. Initially, pro- and antisaccade trials were analyzed together in a model including the factors PP, CUE, and TT. On average, RTs were higher in the SC condition compared with the AC condition (ΔRT = 124 ms; $F_{1,253} = 1469.5$, $P < 10^{-5}$). Prosaccades had a lower latency than antisaccades (ΔRT = 32 ms; $F_{1,253} = 105.5$, $P < 10^{-5}$). The three-way interaction between the factors PP, CUE, and TT was significant ($F_{1,253} = 9.6$, $P < 10^{-3}$).

To explore this interaction, RT on pro- and antisaccade trials were submitted to two separate models with PP and CUE as independent variables. The factor PP was significant on both pro- ($F_{2,115} = 3.46$, $P < 0.03$) and antisaccade trials ($F_{2,115} = 4.32$, $P < 0.01$). However, there was a significant interaction between the factors CUE and PP on antisaccade ($F_{2,115} = 11.25$, $P < 10^{-3}$) but not on prosaccade trials ($F_{2,115} = 1.79$, $P = 0.17$).

We then investigated both CUE conditions separately in a model with factors PP and TT. In the AC condition, pro- and antisaccade RT slightly decreased with increasing prosaccade trial probability, as previously reported by Pierce et al. (2015). However, neither the main effect of PP ($F_{1,115} = 2.40$, $P < 0.09$) nor the interaction PP $\times$ TT was significant ($F_{2,115} = 0.48$, $P = 0.61$). However, the main effect of TT was significant ($F_{1,115} = 238.93$, $P < 10^{-5}$). In the SC condition, PP had the opposite effect on pro- and antisaccades, which resulted in

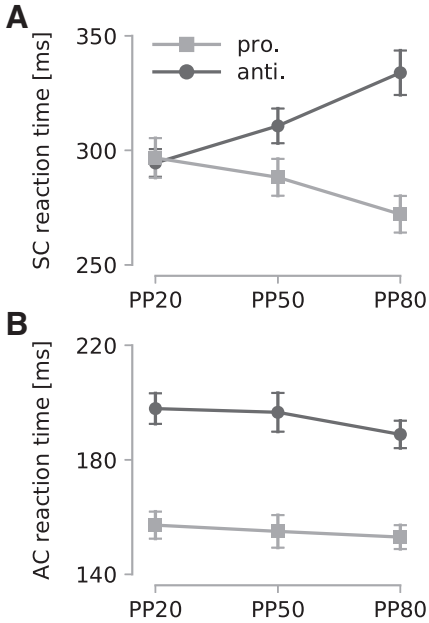

Fig. 4. *A*: Mean reaction time (RT) vs. prosaccade probability (PP; 20/50/80, percents randomly interleaved prosaccade trials), synchronous cue (SC) condition. *B*: mean RT vs. PP, asynchronous cue (AC) condition. Only the mean RTs of correct trials are displayed. Error bars depict SE.

a significant interaction between PP and TT ($F_{2,115} = 12.99$, $P < 10^{-5}$).

The correlation between RT across CUE conditions was significant only on antisaccade trials in the PP50 block (PP50 + AS: $R^2 = 0.27$, $P = 0.008$). There was a positive but not significant correlation in all other blocks and trial types (PP20 + AS: $R^2 = 0.14$, $P = 0.064$; PP80 + AS: $R^2 = 0.14$, $P = 0.068$; PP20 + PS $R^2 = 0.08$, $P = 0.159$; PP50 + PS: $R^2 = 0.08$, $P = 0.178$; PP80 + PS: $R^2 = 0.11$, $P = 0.105$).

Model comparison. To compare models, we used the differences in LME or log Bayes factors between the hierarchical models fitted to our data (Table 2).

We first compared families of models in each of the conditions separately. In the SC condition, the SERIA family was favored compared with the PROSA family (posterior probability nearly 1). In the SERIA family, constrained models were favored compared with models in which the early and inhibitory unit were allowed to differ across trial types (posterior probability nearly 1). When we considered each model independently (Table 2), analogously to the findings in Aponte et al. (2017), a constrained SERIA model (m_{12}) obtained the highest evidence ($\Delta LME > 26.6$).

In the AC condition, while the SERIA family was favored compared with the PROSA family (posterior probability ~1), SERIA models in which the early and stop units were not constrained obtained the highest evidence (posterior probability ~1). When models were compared individually, the unconstrained mixed Gamma SERIA model (m_9) was favored among all possibilities ($\Delta LME > 79.5$).

To facilitate the comparison across CUE conditions and our previous study (Aponte et al. 2017), in the following we report the parameter estimates obtained using mixed Gamma models (SC condition: m_{10}; AC condition: m_9).

Model fits. Qualitatively (Gelman et al. 2003; Gelman and Shalizi 2013), we evaluated the PROSA and SERIA models by plotting the histogram of RTs of all saccades and the fit of the best model in each family (Fig. 5). For the PROSA model, we used model m_5 in both conditions. Fits were computed by weighting the expected probability density function in a given block by the corresponding number of trials.

Table 2. *Differences in LME*

Model	Parametric Family	SC	AC
	PROSA		
m_1	Truncated normal	103.0	295.0
m_2	Truncated normal	0.0	0.0
m_3	Mixed Gamma	540.7	291.7
m_4	Mixed Gamma	518.3	92.3
m_5	Gamma	572.5	364.1
m_6	Gamma	557.4	140.2
	SERIA		
m_7	Truncated normal	1,162.7	740.1
m_8	Truncated normal	1,177.8	717.7
m_9	Mixed Gamma	1,230.4	**874.8**
m_{10}	Mixed Gamma	1,264.9	542.6
m_{11}	Gamma	1,248.0	795.3
m_{12}	Gamma	**1,291.5**	769.9

Model comparison. Log model evidences (LME) are given relative to the worst model (m_2) in each condition. PROSA; PRO-, Stop, and Antisaccade model; SERIA, Stochastic Early Reaction, Inhibition, and late Action model. Models with the highest evidence are highlighted in boldface. SC, synchronous cue; AC, asynchronous cue.

Replicating our previous findings (Aponte et al. 2017), the RT distribution of correct prosaccades in the SC condition was bimodal and could not be captured by the PROSA model but was accounted for by the SERIA model. More importantly, since this is the first time that SERIA has been applied to the AC task, the RT distributions in the AC condition were also fitted better by the SERIA model. This was particularly clear in correct prosaccades in the PP50 and PP80 conditions (Fig. 5, *bottom row, middle* and *right*).

To further examine the fits of the SERIA model, Fig. 6 displays the empirical and predicted cumulative density function (cdf) of the reciprocal RT[1] of correct pro- and antisaccades. Cdfs are displayed on the probit scale (Noorani and Carpenter 2016) but in contrast to previous studies (Aponte et al. 2017; Noorani and Carpenter 2013), we did not normalize by the total number of saccades.

The distribution of reciprocal (inverse) RTs on correct trials in the SC condition echoed the findings of Carpenter and Williams (1995) and suggests that prosaccades are the result of two processes (Noorani and Carpenter 2016). Moreover, the RT distribution of late prosaccades converges to the distribution of correct antisaccades. This provides further evidence for the hypothesis that late prosaccades are the result of a slow accumulation process analogous to the one used to model antisaccades (Aponte et al. 2017).

SERIA also yielded accurate fits in the AC condition. Although the RT distribution of pro- and antisaccades deviated from the linear behavior observed in the SC condition, the model correctly predicted the empirical cdfs. Arguably, because late responses had latencies as low as 95 ms, early and late prosaccades were disguised in a single unimodal distribution that did not follow the linear pattern observed in the SC condition. For a similar reason, antisaccades did not follow a linear pattern in the AC condition, as their hit time was early enough to be influenced considerably by the race between the early and inhibitory units.

RT distribution of corrective antisaccades. Errors on antisaccade trials (prosaccades) are often followed by corrective antisaccades toward the uncued location. We investigated the frequency and RT distribution (relative to the onset of the peripheral cue) of these secondary saccades behaviorally and with SERIA. In the following, we did not take into account the PP factor, as the number of errors per block varied widely over subjects and blocks.

On average, participants corrected most antisaccade errors in both conditions (SC: 63%, SD 26%; AC: 74%, SD 24%). The mean corrective antisaccades latency after cue onset was 412 ms (SD 32 ms) in the SC condition. Corrective antisaccades had a lower latency in the AC condition (281 ms, SD 54 ms). We first investigated whether the RT of the error prosaccade on a corrected trial was different from the RT of noncorrected errors. To test this hypothesis, the mean RT of errors on antisaccade trials was submitted to a GLME with factors CUE and CORRECTED (CORR), their interaction, and SUBJECT as a random effect. While the effect of CORR was not significant ($F_{2,66} = 2.3$, $P = 0.13$), the interaction between CORR

[1] Reciprocal RTs are often used to compare cumulative RT distributions. In these plots, the *x*-axis is rescaled proportionally to 1/RT and flipped such that RTs increase from left to right. A detailed description of reciprobit plots can be found in Noorani and Carpenter (2016).

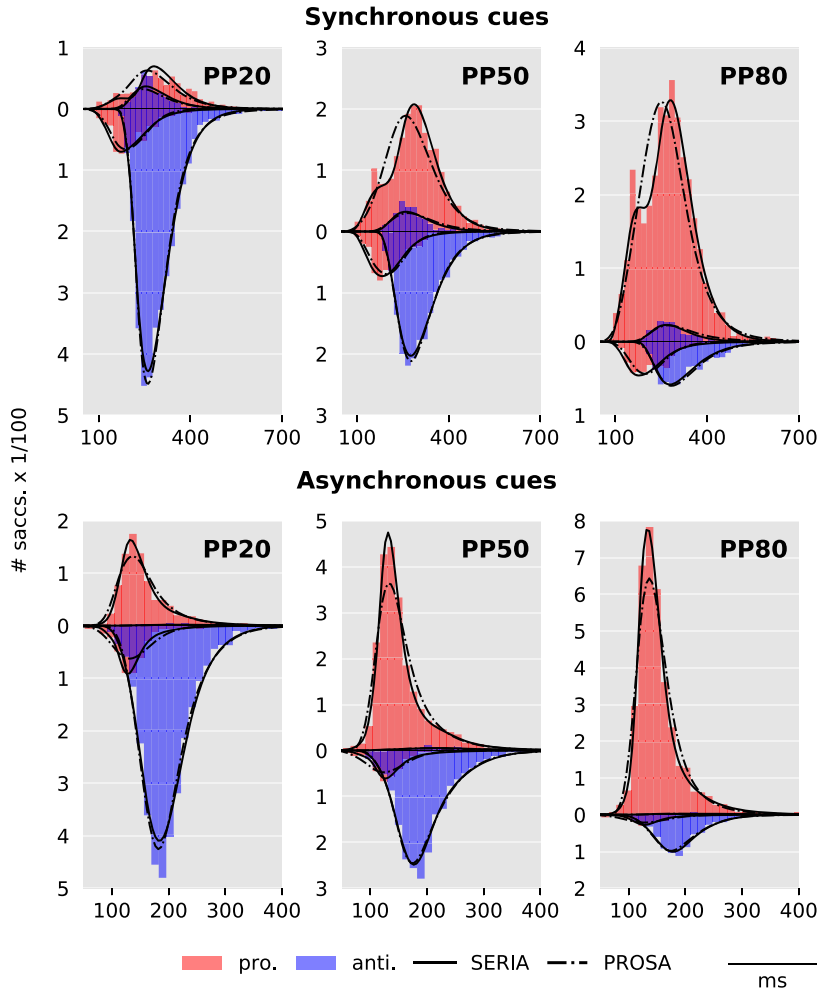

Fig. 5. Histogram of reaction times (RTs) and model fits. PP, prosaccade trial probability (20/50/80, percents randomly interleaved prosaccade trials). Each panel displays RT histograms of prosaccade trials in the positive half-plane. Antisaccade trials are displayed in the negative half-plane. Prosaccades are displayed in red, antisaccades in blue. Hence, errors on prosaccade trials (antisaccades) are displayed in blue in the positive half-plane, whereas errors on antisaccade trials (prosaccades) are displayed in red in the negative half-plane.

and CUE was significant ($F_{2,65} = 5.4$, $P = 0.02$). This effect was driven by a significant difference ($t(18.9) = 3.4$, $P = 0.003$) in the AC condition, in which corrected errors were, on average, 22 ms faster than uncorrected errors.

Previous studies have shown that the RT distribution of corrective antisaccades can be predicted using computational modeling (Aponte et al. 2017; Cutsuridis 2015; Noorani and Carpenter 2014a). To predict the RT distribution of corrective antisaccades, the distribution of the hit time of the late antisaccade unit of each subject in each condition was weighted by the corresponding number of corrective antisaccades. The estimated distribution was time-shifted to optimize the predictive fit; i.e., we tried to predict the shape of the RT distribution, not its mean. Figure 7*A* displays the predicted distributions in the SC (time shift = 93 ms) and AC (time shift = 63 ms) conditions. Visual inspection suggests that SERIA predicted correctly the shape of the distribution of corrective antisaccades.

Finally, we considered the possibility that the probability of a corrective antisaccade (i.e., the fraction of errors that were corrected) was related to the mean fraction of antisaccade errors that were inhibition failures as estimated by the model (Fig. 7, *B* and *C*). For this, both quantities were probit transformed as in previous analyses. Although in the AC condition both metrics were strongly correlated ($R^2 = 0.44$, $P < 0.001$), this was not the case in the SC condition ($R^2 = 0.04$, $P = 0.30$).

Model parameters: inhibition failures and late errors. We then turned our attention to inhibition and volitional or late errors. The latter occur when the late prosaccade unit hits threshold before the antisaccade unit on an antisaccade trial, or when the antisaccade unit hits threshold before the late prosaccade unit on a prosaccade trial. We also investigated the probability of an inhibition failure, i.e., the probability that the early unit hits threshold before all other units. On an antisaccade trial, an inhibition failure is an early error.

In the SC condition (Fig. 8*A*), the findings were in line with our previous results (Aponte et al. 2017). Whereas the probability of a late error on a prosaccade trial was negatively correlated with PP [χ^2 (2, $n = 72$) = 156.66, $P < 10^{-5}$], the opposite behavior was observed for the probability of an inhibition failure [χ^2 (2, $n = 72$) = 22.5, $P < 10^{-3}$] and a late error on an antisaccade trial [χ^2 (2, $Nn = 72$) = 23.5, $P < 10^{-5}$].

By contrast, in the AC condition it was necessary to consider the number of inhibition failures on pro- and antisaccade trials separately, because model comparison favored models in which the early and inhibitory units behaved differently across trial types. When we considered the effect of PP in the AC condition, we found a significant effect only on the probability

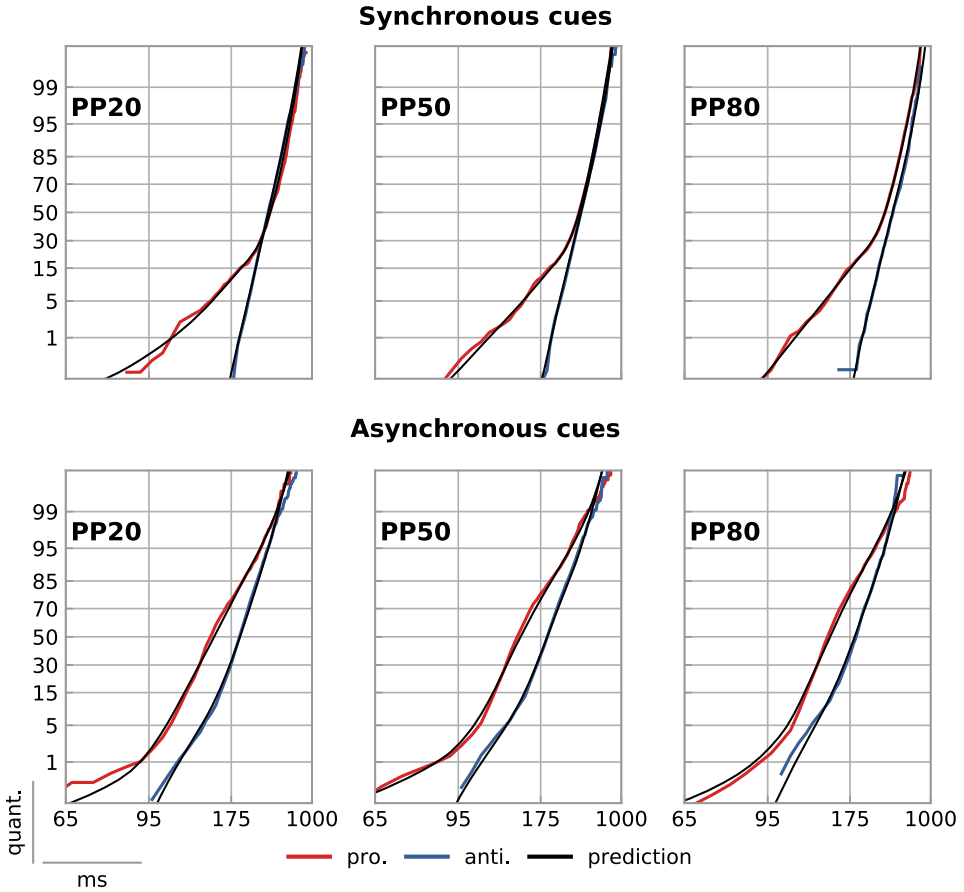

Fig. 6. Empirical and predicted reciprobit of reaction times (RTs) on correct trials. In the synchronous cue (SC) condition, the Stochastic Early Reaction, Inhibition, and late Action (SERIA) model clearly captured the apparent bimodality of the RT distributions. PP, prosaccade trial probability (20/50/80, percents randomly interleaved prosaccade trials). Please note the deflection in the prosaccade cumulative density function (cdf), which demonstrates a bimodal distribution. In the asynchronous cue (AC) condition, the SERIA model accounted for most of the relevant aspects of the RT distribution, including left and right tails.

of late errors on antisaccade trials [χ^2 (2, n = 72) = 6.31, P = 0.04].

In the AC condition, the percentage of late responses on prosaccade trials was estimated to be ~39% of all trials (Fig. 8*B* and Table 3). On antisaccade trials, the percentage of inhibition failures was estimated to be 9% of all trials, or 61% of all errors. Hence, 39% of all errors could be attributed to the late decision process. In the SC condition, the number of antisaccade errors predicted by the model was ~2% higher than the empirical error rate. On average 21% of all errors in antisaccade trials were cataloged as late decision errors. To assess the posterior predictions of the model, we report the correlation coefficient between the empirical and predicted ER in Table 3.

Model parameters: hit times. Finally, we investigated the effect of PP on the expected hit times of the units. In the SC condition (Fig. 8*C*), the early ($F_{2,46}$ = 7.39, P = 0.001), as well as the antisaccade ($F_{2,46}$ = 36.34, $P < 10^{-5}$) and inhibitory units ($F_{2,46}$ = 18.12, $P < 10^{-5}$) were significantly af-

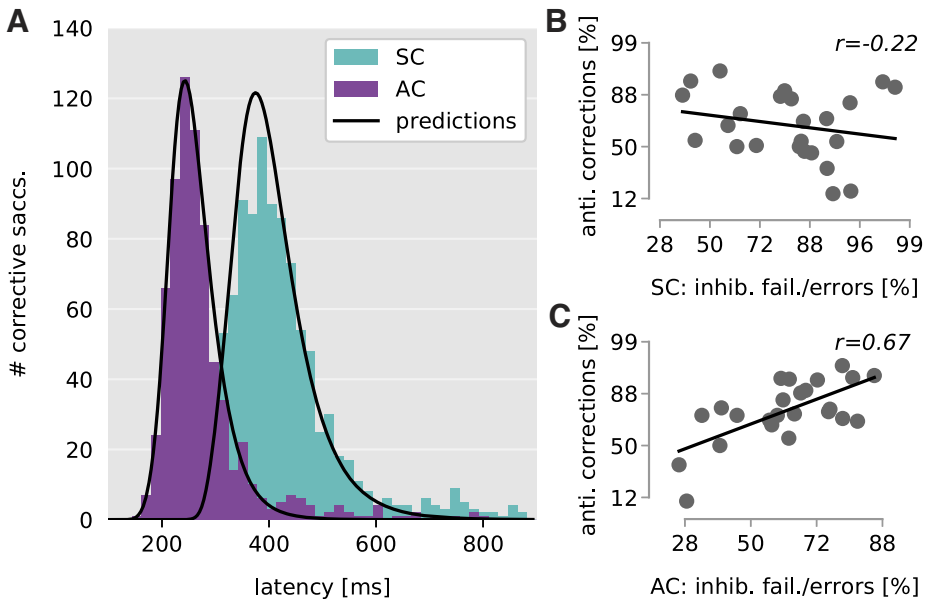

Fig. 7. Corrective antisaccades. *A*: histogram of corrective antisaccades and model predictions. Depicted are distributions of hit times of the antisaccade unit and the histogram of corrective antisaccade reaction times (RTs) relative to cue onset. The location or time-shift of the predicted distributions was optimized using the data. *B*: correlation between percentage of corrected antisaccades and percentage of inhibition failures in the synchronous cue (SC) condition (R^2 = 0.04, P = 0.30). *C*: correlation between percentage of corrected antisaccades and percentage of inhibition failures in the asynchronous cue (AC) condition (R^2 = 0.44, $P < 0.001$).

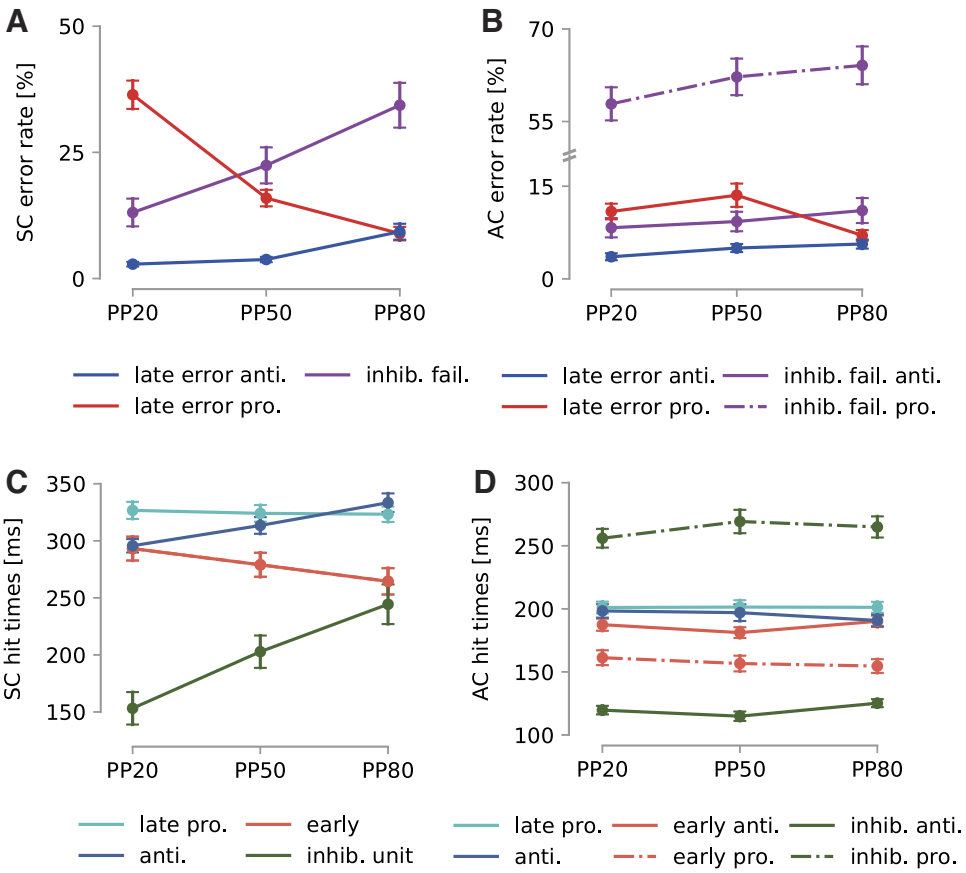

Fig. 8. *A*: probability of late errors and inhibition failures in the synchronous cue (SC) condition. PP, prosaccade trial probability (20/50/80, percents randomly interleaved prosaccade trials). Late errors occur when an early prosaccade is stopped by the inhibitory unit, but the incorrect late action is performed. Nonstopped early reactions are called inhibition failures. *B*: probability of late errors and inhibition failures in the asynchronous cue (AC) condition. *C*: Expected hit time of units in the SC condition. Note that we report a single estimate for the early and inhibitory unit because in a constrained model both units are assumed to have the same behavior across trial types. *D*: expected hit time of units in the AC condition.

fected by PP: high prosaccade trial probability led to slower inhibition, slower antisaccades, and faster early responses. However, we did not find a significant effect of PP on the hit times of the late prosaccade unit ($F_{2,46} = 0.22$, $P = 0.79$).

We then investigated whether the percentage of inhibition failures in the SC condition was correlated with the percentage of inhibition failures on antisaccade trials in the AC condition. Results are displayed in Fig. 9. In each of the PP conditions, we found a significant correlation ($P < 0.005$), with correlation coefficients between 0.67 and 0.77 (Fig. 9). This indicates that the tendency of individual subjects to respond with an early saccade was comparable across task designs.

In the AC condition (Fig. 8*D*), most of the units had a much shorter hit time compared with the SC condition. Moreover, the fitted parameters suggested that most differences between pro- and antisaccade trials could be attributed to changes in the hit time of the inhibitory unit, which was over 100ms higher on prosaccade trials than on antisaccade trials. To further support this observation, we fitted a mixed Gamma SERIA model in which the early prosaccade unit (but not the inhibitory unit)

Table 3. *Empirical and predicted ER, inhibition failures, and late errors*

	Empirical and Fitted ERs					
	PP20	PP50	PP80	PP20	PP50	PP80
			Antisaccade trials			
		SC			AC	
Empirical ER, %	14.06	22.79	38.22	11.56	13.81	16.83
Predicted ER, %	15.18	24.90	40.53	11.50	13.82	16.07
Correlation coefficient	0.99	0.97	0.98	0.99	0.94	0.99
Inhibition failures, %	12.65	22.00	34.63	8.27	9.28	11.06
100 × late errors / (late errors + inhib. fail.)	26.82	18.62	22.13	39.44	40.01	37.28
			Prosaccade trials			
Empirical ER, %	29.11	11.18	4.88	3.07	3.07	1.07
Predicted ER, %	30.91	11.70	5.21	3.13	3.14	1.12
Correlation coefficient	0.98	0.96	0.99	0.97	0.98	0.90
Inhibition failures, %	13.08	22.42	34.34	57.86	62.23	64.10

To evaluate the error rate (ER) estimates, we display the correlation coefficient between predicted and observed ERs. AC, asynchronous cue; PP, prosaccade probability (20/50/80, percents randomly interleaved prosaccade trials); SC, synchronous cue. Please note that inhibition failures (inhib. fail.) on prosaccade trials correspond to correct early prosaccades. Errors on prosaccade trials can be explained only as late, volitional errors.

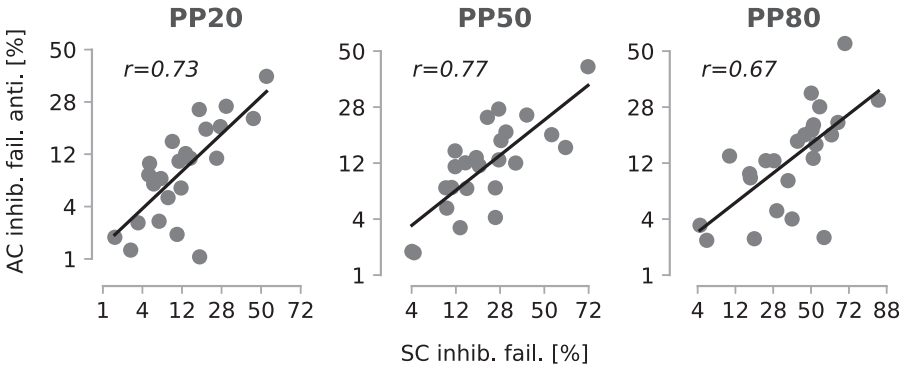

Fig. 9. Correlation of inhibition failures on antisaccade trials. Values are displayed in the probit scale. There was a significant and strong correlation between the percentage of inhibition failures across task designs.

was identical across trial types. This is analogous to the restricted model originally proposed by Noorani and Carpenter (2013). This post hoc model obtained the highest evidence in the AC condition ($\Delta LME > 7$ log units). Crucially, this model was also better than one in which the early unit but not the inhibitory unit was allowed to change across trial types ($\Delta LME > 80$). Thus, most variance in the probability of early prosaccades could be explained by changes in the inhibitory unit, which indicates that displaying the trial type in advance of the saccade direction cue mainly influenced the inhibition of early responses.

There was no significant effect of PP on the hit time of the late pro- and antisaccade units (late pro: $F_{2,46} = 0.00$, $P = 0.99$; anti: $F_{2,46} = 2.08$, $P = 0.13$). However, we found a significant effect of PP on the inhibitory unit regardless of the trial type (pro trials: $F_{2,46} = 3.23$, $P = 0.04$; anti trials: $F_{2,46} = 14.11$, $P < 10^{-3}$). Finally, there was a significant effect of PP on the early unit in antisaccade trials ($F_{2,46} = 8.62$, $P < 10^{-3}$) but not on prosaccade trials ($F_{2,46} = 2.15$, $P = 0.12$). Taken together, our results suggest that manipulating the trial type probability in AC tasks had an effect only on the early and inhibitory units, and this effect was weak on prosaccade trials.

DISCUSSION

The present study resulted in four main findings. First, the SERIA model better accounted for RTs and ERs than the PROSA model in both the SC and AC conditions. This indicates that even in AC designs the prosaccade RT distribution is best described by more than one process. Second, according to the model fits, a significant proportion of errors on antisaccade trials were late errors, irrespective of the CUE condition. Third, we found that in the AC condition the main factor explaining the differences in ER and RT between pro- and antisaccade trials was the hit time of the inhibitory unit and, consequently, the probability of inhibiting an early response. Finally, the effects of manipulating the probability of a trial type were almost completely abolished when subjects were cued about task demands in advance of the peripheral cue. This suggests that SC task designs are more appropriate for studies interested in probability-dependent effects. Moreover, all effects of trial type probability were restricted to the early and inhibitory unit in the AC condition. We proceed to discuss these findings.

SERIA accounts for antisaccade behavior regardless of CUE condition. The main question that we addressed in this study is which model explains RT and ER distributions in the SC and AC antisaccade task designs. Qualitatively, evidence for the SERIA model can be easily observed in histograms of RT in the SC condition (Fig. 5, *top row*): RTs of correct prosaccades follow a bimodal distribution, and their late component resembles the distribution of correct antisaccades. Moreover, errors on prosaccade trials are relatively common in this version of the antisaccade task, and their latency is similar to the latency of correct antisaccades.

None of these patterns is present in the AC condition; correct prosaccade RT are not bimodally distributed and errors on prosaccade trials are rare (<4%). However, a more in-depth analysis revealed that prosaccade RT distributions in the AC condition can be better explained by a model that postulates early as well as voluntary prosaccades (Fig. 5, *bottom row*). In addition, our data suggest that prosaccades do not appear to be bimodally distributed in the AC condition, because voluntary prosaccades are fast enough to overlap with early prosaccades. This is obvious in Fig. 6, *bottom row*, in which the distribution of correct prosaccades deviates from the linear pattern usually observed in other conditions (see Fig. 6, *top row*, and Noorani and Carpenter 2016). Thus, while the AC and SC conditions display very different qualitative patterns, these are captured by the SERIA model, but not by the PROSA model.

Quantitatively, our results are supported by Bayesian model comparison. This method prevents overfitting by penalizing models for their number of parameters (MacKay 2002; Stephan et al. 2009). Hence, while the number of parameters of the winning models (15 and 19) might seem elevated, our analysis indicates that a simpler model (PROSA) does not account satisfactorily for our data. Nevertheless, it is not impossible that further restrictions on the parameter space within the SERIA family could result in more parsimonious models. However, an exhaustive exploration of the space of all models was outside the scope of this paper.

Reallocation of attention and antisaccade cost. Arguably, the main novelty of the SERIA model is the distinction between early responses, which are always directed toward the PVC (i.e., a prosaccade) and can be inhibited by a stop process, and voluntary late responses, which can trigger both pro- and antisaccades. The units that trigger this type of saccades can generate rule-guided behavior (e.g., an antisaccade), at the cost of higher RTs. Moreover, voluntary saccades are also subject to a race-to-threshold decision process (Aponte et al. 2017).

By contrast, voluntary and involuntary saccades are often distinguished by the paradigm in which they are elicited (Walker et al. 2000) and not by the mechanism that generates them: On the one hand, involuntary saccades are associated with paradigms in which a suddenly displayed stimulus elicits

a saccade. On the other hand, voluntary saccades are associated with paradigms in which the target needs to be retrieved from memory or it depends on specific task instructions, such as in the antisaccade task.

Because the SERIA model distinguishes between reflex-like and voluntary saccades toward a visual cue, the distinction between voluntary and involuntary saccades can be reformulated in terms of the processes that generate them. Accordingly, the antisaccade "cost" (Hallett 1978) might be also understood as a voluntary saccade cost (ignoring remapping costs). Our reconceptualization might explain the finding that under certain circumstances pro- and antisaccades exhibit the same (Chiau et al. 2011; Weiler and Heath 2014) or similar RTs (Olk and Kingstone 2003); if all early responses are inhibited, pro- and antisaccades can have the same latency.

This is congruent with the findings of Olk and Kingstone (2003), who showed that, when the inhibitory requirements on pro- and antisaccade trials are matched, the RT difference between pro- and antisaccades is strongly reduced. Olk and Kingstone concluded, however, that inhibitory control slows down pro- and antisaccades. By contrast, according to SERIA, higher inhibition does not intrinsically slow down saccades. Exemplarily, higher inhibition in the SC+PP20 condition (see Fig. 8*C*) is accompanied by faster antisaccades. Rather, SERIA predicts that more inhibition leads to more voluntary saccades, but not necessarily to slower voluntary actions.

An alternative explanation of the "antisaccade cost" in terms of the premotor theory of attention (Rizzolatti et al. 1987) is that participants allocate attention to the peripheral cue and then relocate it to the opposite target. Presaccadic allocation of attention has been widely observed and is important in a model of antisaccades (Heinzle et al. 2007) as well as word skipping during reading (Heinzle et al. 2010). Our modeling suggests that presaccadic attention is not strictly serial. The reason is that the hit times of the late pro- and antisaccade units are comparable in both the SC and AC conditions (Fig. 8, *C* and *D*). In other words, antisaccades are not much slower than late prosaccades, as would be predicted by a serial attention reallocation model. Rather, our findings support the idea that attention might be allocated in parallel to both targets. In line with this, a recent study demonstrated that attention is distributed to cued and uncued stimulus location before correct antisaccades (Klapetek et al. 2016).

Early and late errors on antisaccade trials. SERIA provides a formal account of errors in the antisaccade task, which distinguishes it from two prominent models in the literature. On the one hand, the model in Noorani and Carpenter (2013) does not incorporate a late decision process, and thereby it explains all errors as inhibition failures. On the other hand, lateral inhibition models (Cutsuridis et al. 2007, 2014; Cutsuridis 2015) explain errors as the result of connected accumulators that represent pro- and antisaccades without the intervention of a third inhibitory unit. Accordingly, an error occurs when a voluntary action does not inhibit a reflex-like prosaccade. Along this line, Reuter et al. (2005) have argued that deficits in the ability to initiate an antisaccade contribute to the elevated ERs observed in patients with schizophrenia.

The SERIA model is closer to the idea proposed by Fischer and colleagues (Fischer et al. 2000; Klein and Fischer 2005), who extended the distinction between "express" and "normal latency" saccades to antisaccade errors. Although conceptually similar to the approach presented here, these authors used a simple time threshold to distinguish between the two types of saccades (Klein and Fischer 2005). In this context, SERIA offers a model-based, statistically sound separation between early and late errors that goes beyond simple thresholding of RTs.

Hence, an important conclusion from our analysis is that late errors are a significant fraction of all errors regardless of task design. Concretely, in the present sample, ~39% of the errors on antisaccade trials in the AC condition were quantified as late errors, with large variability across subjects (Fig. 9). This number was estimated to be 21% in the SC condition. This is significant, as the ability to separate between early and late errors might be of relevance in computational psychiatry and future patient studies (Coe and Munoz 2017; Fischer et al. 2000; Heinzle et al. 2016; Lo and Wang 2016).

Corrective antisaccades. Here, we have shown that the RT distribution of corrective antisaccades that follow errors on antisaccade trials can be well predicted by SERIA in both conditions. This is strong evidence that antisaccades are programmed in parallel to prosaccades (Massen 2004). Moreover, the rather short time shift (AC 63 ms, SC 93 ms) between correct antisaccades and corrective antisaccades indicates that corrective antisaccades are planned in advance of the execution of an error prosaccade (Aponte et al. 2017).

There seem to be some differences across the two CUE conditions. The RTs of corrected errors in the AC design were significantly shorter than the latency of noncorrected errors. Moreover, the probability of correcting an error was strongly correlated with the fraction of errors that were catalogued as inhibition failures. None of this was true in the SC, which suggests that in this condition corrections followed both early and late errors.

Our findings in the AC condition are compatible with the previous report of Camalier et al. (2007); see also the classical analysis of Becker and Jürgens (1979). Camalier and colleagues presented a target which in a subset of trials was shifted to a second location before subjects performed a saccade. When the target was shifted, participants sometimes saccaded first to the initial location. This was followed on some occasions by a compensatory saccade to the secondary target. Similarly to our results, compensated trials were characterized by shorter RTs toward the initial target. Moreover, the probability of a corrective saccade was well predicted by a modified race model (Logan et al. 1984), in which the second saccade was initiated in parallel once the target was shifted.

AC vs. SC designs. The most obvious difference between the AC and SC conditions was an overall reduction in RTs and ERs in the AC task. This observation replicates previous findings (Weber 1995; Weiler and Heath 2014).

There are two main explanations for these differences. First, in the SC condition the mapping between a cue and an action can only be started once the peripheral stimulus is presented. Thus, one would expect robust inhibition of reactive saccades that affords enough time to select the correct action (Weber 1995). Second, in the AC condition subjects could anticipate the presentation of the peripheral cue, because the task cue was always displayed for 700 ms. Despite this general reduction in RTs, ERs were lower in the AC condition than in the SC condition.

Model comparison suggests differences in the type of anticipatory preparation in the two tasks: whereas in the SC condition the early and inhibitory unit followed a similar hit time distribution across trial types, this was not the case in the AC condition. Furthermore, a model in which the prosaccade unit was fixed across trial types obtained the highest model evidence, indicating that most of the differences in the number of early responses could be accounted for by changes in inhibitory control.

Arguably, in the SC condition the peripheral cue does not influence the inhibition of early responses, because it is integrated in the decision-making process too late to strongly affect the early and inhibitory units. Nevertheless, contextual information about trial type probability was exploited by the participants to drive inhibitory control. By contrast, in the AC condition early prosaccade inhibition is almost entirely determined by the trial type cue and only weakly modulated by the probability of a trial type, as discussed below.

Importantly, the probability of antisaccade errors was correlated between both CUE conditions. Thus, relative ERs were consistent across the two tasks, suggesting that the same cognitive processes are involved in both conditions. In conclusion, SC designs are likely to provide more variability in terms of ER and RT while probing the same cognitive processes involved in an AC paradigm.

Effect of trial type probability. Our results replicate the finding that in the SC condition the probability of a trial type has a large impact on both ER and RT (Aponte et al. 2017; Chiau et al. 2011). Concretely, RTs of correct responses were negatively correlated with the corresponding trial type probability. These effects were strongly reduced in the AC condition, as reported before (Massen 2004; Pierce et al. 2015; Pierce and McDowell 2016a). In fact, in AC designs, randomization of trials seems to have only little impact on RT (Barton et al. 2006).

One limitation of our experiment is that we did not include blocked conditions in which there is no uncertainty about the task demands. However, our main interest was to investigate how contextual information (trial type probability) is leveraged by participants to improve performance in the presence of uncertainty.

On the AC condition, modeling indicated no significant effect of PP on late responses and a significant but relatively small effect on the early and inhibitory units. One interpretation of this is that the early presentation of the task cue in the AC condition essentially removes all uncertainty about the task, rendering the probabilistic manipulation largely ineffective, especially for late responses. This is in contrast to the SC condition, in which contextual information is of relevance for the optimal execution of the task. Thus, the effects of contextual or prior information in the antisaccade task are best studied using the SC design.

Relation to the neurophysiology of antisaccades. In this section, we review aspects of neurophysiology that are relevant for the interpretation of our findings. The execution of an antisaccade recruits cortical and subcortical areas of the oculomotor system (Hikosaka et al. 2000; Munoz and Everling 2004; Pouget 2015), as demonstrated by lesion (Guitton et al. 1985; Pierrot-Deseilligny et al. 1991) and activation studies in humans (McDowell et al. 2008; for a meta-analysis, see Jamadar et al. 2013) and single cell recording (Johnston and Everling 2008; Munoz and Everling 2004) as well as inactivation studies in primates (Condy et al. 2007; Johnston et al. 2014; Koval et al. 2014). Early lesions studies (Guitton et al. 1985; Pierrot-Deseilligny et al. 1991) demonstrated that the prefrontal cortex (PFC) plays an essential role in the correct execution of antisaccades. Historically, the predominant view in this regard has been that the PFC is in charge of inhibiting reflex-like prosaccades (reviewed in Everling and Johnston 2013). Thereby, PFC lesions forestall antisaccades by limiting the ability to stop fast prosaccades.

More recently, this view has been challenged by unilateral deactivation studies of the PFC in nonhuman primates (Everling and Johnston 2013). One central prediction of the "inhibitory model" of the PFC is that, if it is in charge of inhibiting saccades, unilateral deactivation of the PFC should facilitate contralateral saccades to the deactivated hemisphere and impede ipsilateral saccades. However, two studies (Condy et al. 2007; Johnston et al. 2014) have reported that unilateral deactivation hinders antisaccades contralateral to the injection site (increasing ER and RT) and facilitates ipsilateral antisaccades. Moreover, unilateral microstimulation of the PFC (Wegener et al. 2008) hinders antisaccades ipsilateral to the stimulation site. Overall, these studies suggest that the PFC is involved in generating pro- and antisaccades and not simply in stopping early prosaccades (although note that Condy et al. 2007 interpreted their findings in the opposite direction, but see Johnston et al. 2014 for discussion).

One alternative hypothesis is that the PFC implements the competition process between voluntary pro- and antisaccades. This is supported by the observation that the PFC contains rule-sensitive neurons (e.g., Funahashi et al. 1993; Johnston and Everling 2006) that could encode the rule-action mapping (Miller and Cohen 2001) necessary to correctly execute the mixed antisaccade task. This alternative might explain why high latency (RT $>$130 ms) ER, but not early ER, is correlated with cognitive functions such as working memory (Klein et al. 2010). A similar idea has been proposed by Lo and Wang (2016) using a winner-take-all competition model, instead of the independent accumulators used in SERIA. However, both models use competition between voluntary actions to explain high-latency errors in the antisaccade task. Even if the hypothesis that the late decision process is implemented by the PFC is correct, it remains unclear how reflex-like prosaccades are inhibited.

In this context, it has been proposed that prosaccades are stopped by the basal ganglia (BG) (Noorani and Carpenter 2014b), through inhibition of the superior colliculus (Hikosaka et al. 2000), an area fundamentally involved in the generation of eye movements. This idea has been worked out in detail in the computational model proposed by Wiecki and Frank (2013; see also Brown et al. 2004), in which the hyperdirect pathway in the BG (Hikosaka et al. 2000) is activated by neurons in the anterior cingulate cortex that detect the conflict between the visual grasp reflex that triggers prosaccades and the antisaccade cue-action mapping.

The evidence for this theory is not yet decisive, in that lesions of the BG have been shown not to affect antisaccade performance (Condy et al. 2004). Moreover, a meta-analysis of fMRI studies (Jamadar et al. 2013) did not find significant differences in the BG when pro- and antisaccades were compared, although significant activations of the BG were found

when antisaccade and fixation conditions were contrasted. Nevertheless, Ford and Everling (2009) demonstrated that neurons in the caudate nucleus are selective of pro- and antisaccades. Hence, it remains unclear how early prosaccades are stopped in the antisaccade task.

Summary. This study investigated whether and to what extent cue presentation order (task cue and spatial cue) influenced ER and RT in the antisaccade task. Overall, we found that the impact of trial type probability was strongly reduced in the AC condition compared with the SC condition. From a modeling perspective, our results demonstrate that the combination of an early and a late race between voluntary pro- and antisaccades better accounts for RT and ER in an AC design compared with models that incorporate only an early race. Furthermore, modeling revealed that early inhibitory processes are strongly influenced by trial type in the AC condition but not in the SC condition. By contrast, trial type probability had a strong effect on early units in the SC condition but not in the AC condition. SERIA also provided a good prediction of the shape of the distribution of corrective antisaccades in both tasks. Finally, our quantitative analysis supports the hypothesis that a nonnegligible fraction of errors in the antisaccade task can be categorized as late errors, irrespective of task design.

SOFTWARE NOTE

The models used herein are available under the GPL license as part of the TAPAS toolbox (http://www.translationalneuromodeling.org/tapas/).

GRANTS

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DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the authors.

AUTHOR CONTRIBUTIONS

E.A.A., K.E.S., and J.H. conceived and designed research; E.A.A. and D.G.T. performed experiments; E.A.A., D.G.T., and J.H. analyzed data; E.A.A., D.G.T., and J.H. interpreted results of experiments; E.A.A. and J.H. prepared figures; E.A.A. and J.H. drafted manuscript; E.A.A., D.G.T., K.E.S., and J.H. edited and revised manuscript; E.A.A., K.E.S., and J.H. approved final version of manuscript.

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