

1                                    **The Stochastic Early Reaction,**  
2                                    **Inhibition, and Late Action (SERIA)**  
3                                    **Model for Antisaccades**

4    **SERIA - A model for errors and reaction times in the antisaccade**  
5    **task**

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## 19 **Abstract**

20 The antisaccade task is a classic paradigm used to study the voluntary control of eye  
21 movements. It requires participants to suppress a reactive eye movement to a visual  
22 target and to concurrently initiate a saccade in the opposite direction. Although several  
23 models have been proposed to explain error rates and reaction times in this task, no  
24 formal model comparison has yet been performed. Here, we describe a Bayesian  
25 modeling approach to the antisaccade task that allows us to formally compare different  
26 models on the basis of their evidence. First, we provide a formal likelihood function of  
27 actions (pro- and antisaccades) and reaction times based on previously published  
28 models. Second, we introduce the *Stochastic Early Reaction, Inhibition, and late Action*  
29 *model* (SERIA), a novel model postulating two different mechanisms that interact in the  
30 antisaccade task: an early GO/NO-GO race decision process and a late GO/GO decision  
31 process. Third, we apply these models to a data set from an experiment with three mixed  
32 blocks of pro- and antisaccade trials. Bayesian model comparison demonstrates that the  
33 SERIA model explains the data better than competing models that do not incorporate a  
34 late decision process. Moreover, we show that the race decision processes postulated by  
35 the SERIA model are, to a large extent, insensitive to the cue presented on a single trial.  
36 Finally, we use parameter estimates to demonstrate that changes in reaction time and  
37 error rate due to the probability of a trial type (prosaccade or antisaccade) are best  
38 explained by faster or slower inhibition and the probability of generating late voluntary  
39 prosaccades.

## 40 **Author summary**

41 One widely replicated finding in schizophrenia research is that patients tend to make  
42 more errors in the antisaccade task, a psychometric paradigm in which participants are  
43 required to look in the opposite direction of a visual cue. This deficit has been suggested  
44 to be an endophenotype of schizophrenia, as first order relatives of patients tend to show  
45 similar but milder deficits. Currently, most models applied to experimental findings in  
46 this task are limited to fit average reaction times and error rates. Here, we propose a  
47 novel statistical model that fits experimental data from the antisaccade task, beyond  
48 summary statistics. The model is inspired by the hypothesis that antisaccades are the  
49 result of several competing decision processes that interact nonlinearly with each other.  
50 In applying this model to a relatively large experimental data set, we show that mean  
51 reaction times and error rates do not fully reflect the complexity of the processes that are  
52 likely to underlie experimental findings. In the future, our model could help to understand  
53 the nature of the deficits observed in schizophrenia by providing a statistical tool to study  
54 their biological underpinnings.

## 55 **Introduction**

56 In the antisaccade task ([1]; for reviews, see [2,3]), participants are required to saccade  
57 in the contralateral direction of a visual cue. This behavior is thought to require both the  
58 inhibition of a reflexive saccadic response towards the cue and the initiation of a  
59 voluntary eye movement in the opposite direction. A failure to inhibit the reflexive  
60 response leads to an erroneous saccade towards the cue (i.e., a prosaccade), which is  
61 often followed by a corrective eye movement in the opposite direction (i.e., an  
62 antisaccade). As a probe of inhibitory capacity, the antisaccade task has been widely used  
63 to study psychiatric and neurological diseases [3]. Notably, since the initial report [4],  
64 studies have consistently found an increased number of errors in patients with  
65 schizophrenia when compared to healthy controls, independent of medication and  
66 clinical status [5-8]. Moreover, there is evidence that an increased error rate constitutes  
67 an endophenotype of schizophrenia, as antisaccade deficits are also present in non-  
68 affected, first-degree relatives of diagnosed individuals (for example [5,7]; but for  
69 negative findings see for example [9][10]).

70 Unfortunately, the exact nature of the antisaccade deficits and their biological origin in  
71 schizophrenia remain unclear. One path to improve our understanding of these  
72 experimental findings is to develop generative models of their putative computational  
73 and/or neurophysiological causes [11]. Generative models that capture the entire  
74 distribution of responses can reveal features of the data that are not apparent when only  
75 considering summary statistics such as mean error rate (ER) and reaction time (RT) [12-  
76 15]. Additionally, this type of model can potentially relate behavioral findings in humans  
77 to their biological substrate.

78 Here, we apply a generative modeling approach to the antisaccade task. First, we  
79 introduce a novel model of this paradigm based on previous proposals [16-20]. For this,  
80 we formalize the ideas introduced by Noorani and Carpenter [17] and extend them into  
81 what we refer to as the *Stochastic Early Response, Inhibition and late Action (SERIA)*  
82 model. Second, we apply both models to an experimental data set of three mixed blocks  
83 of pro- and antisaccades trials with different trial type probability using formal Bayesian  
84 inference. More specifically, we compare several models using Bayesian model  
85 comparison. Third, we use the parameter estimates from the best model to investigate  
86 the effects of our experimental manipulation. We found that there was positive evidence

87 in favor of the SERIA model when compared to our formalization of the model proposed  
88 in [17]. Moreover, the parameters estimated through model inversion revealed the  
89 complexity of the decision processes underlying the antisaccade task that is not obvious  
90 from mean RT and ER.

91 This paper is organized as follows. First, we formalize the model developed in [17] and  
92 introduce the SERIA model. Second, we describe our experimental setup. Third, we  
93 present our behavioral findings in terms of summary statistics (mean RT and ER), the  
94 comparison between different models, and the parameter estimates. Finally, we review  
95 our findings, discuss other recent models, potential future developments, and  
96 translational applications.

## 97 **Materials and methods**

### 98 **Ethics statement**

99 All participants gave written informed consent before the study. All experimental  
100 procedures were approved by the local ethics board (Kantonale Ethikkommission Zürich,  
101 KEK-ZH-Nr.2014-0246).

### 102 **Race models for antisaccades**

103 In this section, we derive a formal description of the models evaluated in this paper. We  
104 start with a formalized version of the model proposed by Noorani and Carpenter in [17]  
105 and proceed to extend it. Their approach resembles the model originally proposed by  
106 Camalier and colleagues [21] to explain RT and ER in the double step and search step  
107 tasks, in which participants are either asked to saccade to successively presented targets  
108 or to saccade to a target after a distractor was shown. Common to all these tasks is that  
109 subjects are required to inhibit a prepotent reaction to an initial stimulus and then to  
110 generate an action towards a secondary goal. Briefly, Camalier and colleagues [21]  
111 extended the original 'horse-race' model [16] by including a secondary action in  
112 countermanding tasks. In [17], Noorani and Carpenter used a similar model in  
113 combination with the LATER model [22] in the context of the antisaccade task by  
114 postulating an endogenously generated inhibitory signal. Note that this model, or  
115 variants of it, have been used in several experimental paradigms (reviewed in [20]). Here,  
116 we limit our discussion to the antisaccade task.

#### 117 *The pro, stop, and antisaccade model (PROSA)*

118 Following [17], we assume that the RT and the type of saccade generated in a given trial  
119 are caused by the interaction of three competing processes or units. The first unit  $u_p$   
120 represents a command to perform a prosaccade, the second unit  $u_s$  represents an  
121 inhibitory command to stop a prosaccade, and the third unit  $u_a$  represents a command to  
122 perform an antisaccade. The time  $t$  required for unit  $u_i$  to arrive at threshold  $s_i$  is given  
123 by:

$$s_i = r_i t, \quad (1)$$

$$\frac{s_i}{r_i} = t, \quad (2)$$

124 where  $r_i$  represents the slope or increase rate of unit  $u_i$ ,  $s_i$  represents the height of the  
125 threshold, and  $t$  represents time. We assume that, on each trial, the increase rates are  
126 stochastic and independent of each other.

127 The time and order in which the units reach their thresholds  $s_i$  determines the action and  
128 RT in a trial. If the prosaccade unit  $u_p$  reaches threshold before any other unit at time  $t$ , a  
129 prosaccade is elicited at  $t$ . If the antisaccade unit arrives first, an antisaccade is elicited at  
130  $t$ . Finally, if the stop unit arrives before the prosaccade unit, an antisaccade is elicited at  
131 the time when the antisaccade unit reaches threshold. It is worth mentioning that,  
132 although this model is motivated as a race-to-threshold model, actions and RTs depend  
133 only on the arrival times of each of the units and ultimately no explicit model of increase  
134 rates or thresholds is required. Thus, for the sake of clarity, we refer to this approach as  
135 a ‘race’ model, in contrast to ‘race-to-threshold’ models that explicitly describe increase  
136 rates and thresholds.

137 Formally (but in a slight abuse of language), the two random variables of interest, the  
138 reaction time  $T \in [0, \infty[$  and the type of action performed  $A \in \{pro, anti\}$ , depend only  
139 on three further random variables: the arrival times  $U_p, U_s, U_a \in [0, \infty[$  of each of the  
140 units. The probability of performing a prosaccade at time  $t$  is given by the probability of  
141 the prosaccade unit arriving at time  $t$ , and the stop and antisaccade unit arriving  
142 afterwards:

$$p(A = pro, T = t) = p(U_p = t)p(U_a > t)p(U_s > t). \quad (3)$$

143 The probability of performing an antisaccade at time  $t$  is given by

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

144 The first term on the right side of Eq. 4 corresponds to the unlikely case that the  
145 antisaccade unit arrives before the prosaccade and the stop unit. The second term  
146 describes trials in which the stop unit arrives before the prosaccade unit. It can be  
147 decomposed into two terms:

$$p(U_a = t) \int_0^t p(U_s = \tau) p(U_p > \tau) d\tau \quad (5)$$

$$= p(U_a = t) \left( p(U_s < t) p(U_p > t) + \int_0^t p(U_s = \tau) p(\tau < U_p < t) d\tau \right)$$

$$= p(U_a = t) \left( p(U_s < t) p(U_p > t) + \int_0^t p(U_s < \tau) p(U_p = \tau) d\tau \right). \quad (6)$$

148 The term  $p(U_a = t) \int_0^t p(U_s < \tau) p(U_p = \tau) d\tau$  describes the condition in which the  
 149 prosaccade unit is inhibited by the stop unit allowing for an antisaccade. Note that if the  
 150 prosaccade unit arrives later than the antisaccade unit, the arrival time of the stop unit is  
 151 irrelevant. That means that we can simplify Eq. 4 to

$$p(A = anti, T = t) = p(U_a = t) \left( p(U_p > t) + \int_0^t p(U_s < \tau) p(U_p = \tau) d\tau \right). \quad (7)$$

152 Eq. 3 and 7 constitute the likelihood function of a single trial, defining the joint probability  
 153 of an action and the corresponding RT. We refer to this likelihood function as the PRO-  
 154 Stop-Antisaccade (PROSA) model. It shares the central assumptions of [17], namely: (i)  
 155 the time to reach threshold of each of the units is assumed to depend linearly on the rate  
 156  $r$ , (ii) it includes a stop unit whose function is to inhibit prosaccades and (iii) there is no  
 157 lateral inhibition between the different units. Finally, (iv) RTs are assumed to be equal to  
 158 the arrive-at-threshold times. Note that the RT distributions are different from the arrival  
 159 time distributions because of the interactions between the units described above. The  
 160 main difference of this model compared to [17] is that we do not exclude *a priori* the  
 161 possibility of the antisaccade unit arriving earlier than the other units. Aside from this,  
 162 both models are conceptually equivalent.

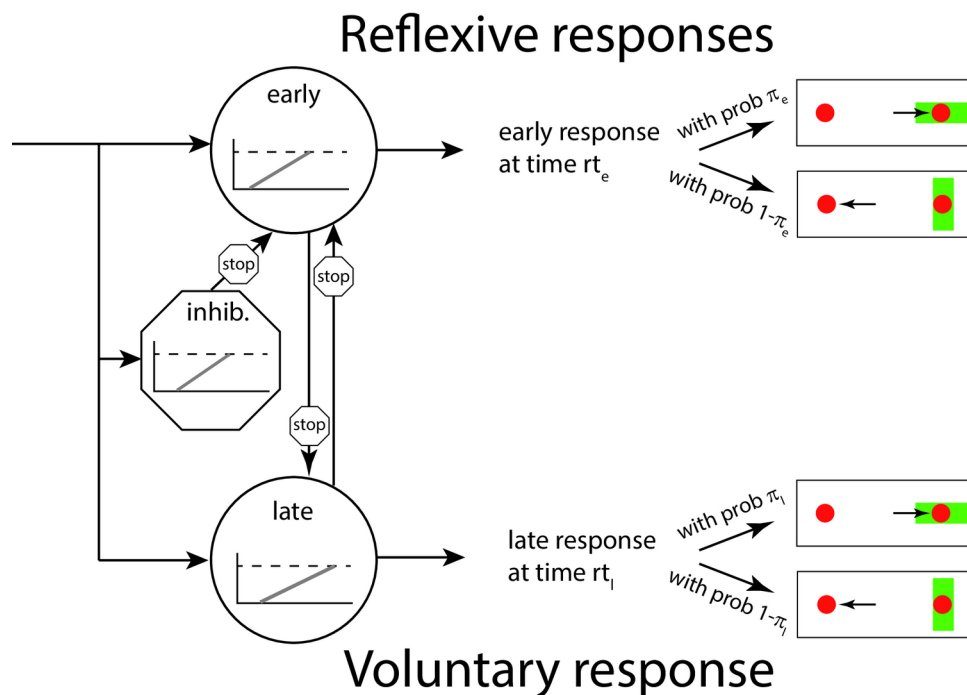
### 163 **The Stochastic Early Reaction, Inhibition, and Late Action Model** 164 **(SERIA)**

165 The PROSA model is characterized by a strict association between units and action types.  
 166 In other words, the unit  $u_p$  leads unequivocally to a prosaccade, whereas the unit  $u_a$   
 167 always triggers an antisaccade. This implies that if the distribution of the arrival times of  
 168 the units is unimodal and strictly positive, the PROSA model cannot predict voluntary  
 169 slow prosaccades with a late peak, or in simple words, the PROSA model cannot account



170 for slow, voluntary prosaccades that have been postulated in the antisaccade task [23].  
 171 Similarly, it has been argued that prosaccade RT can be described by the mixture of two  
 172 distributions (for example [2,22]). To account for this, we introduce the Stochastic Early  
 173 Reaction, Inhibition and Late Action (SERIA) model.

174 According to this model, and in analogy to the PROSA model, an early reaction takes place  
 175 at time  $t$  if the early unit  $u_e$  arrives before the late and inhibitory units,  $u_l$  and  $u_i$ ,  
 176 respectively. If the inhibitory or late unit arrives before the early unit, a late response is  
 177 triggered at the time the late unit reaches threshold. Crucially, both early and late  
 178 responses can trigger pro- and antisaccades with a certain probability. Thus, in parallel  
 179 to the race processes which determine RTs, an independent, secondary decision process  
 180 is responsible for which reaction is generated. Fig. 1 shows the structure of the SERIA  
 181 model.



**Fig 1. Layout of the SERIA model.**

The presentation of a visual cue (a green bar) triggers the race of three independent units. The inhibitory unit can stop an early response. Importantly, both early and late responses can trigger pro- and antisaccades. Note that the PROSA model is a special case of the SERIA model in which  $\pi_e = 1$  and  $\pi_l = 0$ , i.e. all early responses are prosaccades, whereas all late responses are antisaccades.

182 To formalize the concept of early and late responses, we introduce a new unobservable  
 183 random variable that represents the type of response  $R \in \{early, late\}$ . The distribution

184 of the RTs is analogous to the PROSA-model, such that, for instance, the probability of an  
 185 early response at time  $t$  is given by

$$p(R = \text{early}, T = t) = p(U_e = t)p(U_i > t)p(U_l > t) \quad (8)$$

186 where  $U_e, U_i,$  and  $U_l$  represent the arrival times of the early, inhibitory, and late units  
 187 respectively. The fundamental assumption of the SERIA model is that a secondary  
 188 decision process, beyond the race between early, inhibitory, and late units, decides the  
 189 action generated in a single trial. An initial approach to model this secondary decision  
 190 process is to assume that the action type (pro- or antisaccade) is conditionally  
 191 independent of the RT given the response type (early or late). Hence, the distribution of  
 192 RTs is not *a priori* coupled to the saccade type anymore; RT distributions for both pro-  
 193 and antisaccades could in principle be bimodal, consisting of both fast reactive and slow  
 194 voluntary saccades.

195 Formally, the conditional independency assumption can be written down as

$$p(A, T|R) = p(A|R)p(T|R), \quad (9)$$

$$p(A, T|R)p(R) = p(A|R)p(T|R)p(R), \quad (10)$$

$$p(A, T, R) = p(A|R)p(T, R). \quad (11)$$

196 The term  $p(A|R)$  is simply the probability of an action, given a response type. We denote  
 197 it as

$$p(A = \text{pro}|R = \text{early}) = \pi_e \in [0,1], \quad (12)$$

$$p(A = \text{anti}|R = \text{early}) = 1 - \pi_e, \quad (13)$$

$$p(A = \text{pro}|R = \text{late}) = \pi_l \in [0,1], \quad (14)$$

$$p(A = \text{anti}|R = \text{late}) = 1 - \pi_l. \quad (15)$$

198 Since the type of response  $R$  is not observable, it is necessary to marginalize it out in Eq.  
 199 [11] to obtain the likelihood of the SERIA model:

$$p(A, T) = p(A, T, R = \text{early}) + p(A, T, R = \text{late}). \quad (16)$$

200 The complete likelihood of the model is given by substituting the terms in Eq. [16]:

$$p(A = pro, T = t) = \pi_e p(U_e = t) p(U_i > t) p(U_l > t) + \quad (17)$$

$$\pi_l p(U_l = t) \left( p(U_e > t) + \int_0^t p(U_e = \tau) p(U_i < \tau) d\tau \right),$$

$$p(A = anti, T = t) = (1 - \pi_e) p(U_e = t) p(U_i > t) p(U_l > t) + \quad (18)$$

$$(1 - \pi_l) p(U_l = t) \left( p(U_e > t) + \int_0^t p(U_e = \tau) p(U_i < \tau) d\tau \right).$$

201 It is worth noting here that the PROSA model is a special case of the SERIA model, namely,  
 202 it corresponds to the assumption that  $\pi_e = 1$  and  $\pi_l = 0$ . The SERIA model allows for  
 203 bimodal distributions, as both early and late responses can be pro- and antisaccades.  
 204 Importantly, one prediction of the model is that late prosaccades have the same  
 205 distribution as late antisaccades.

### 206 **Late race competition model for saccade type**

207 Until now, we have assumed that the competition that leads to late pro- and antisaccades  
 208 does not depend on time in the sense that late actions are conditionally independent of  
 209 RT. This assumption can be weakened by postulating a secondary race between late  
 210 responses; this leads us to a modified version of the SERIA model, that we refer to as the  
 211 late race SERIA model (SERIA<sub>lr</sub>). The derivation proceeds similarly to the SERIA model,  
 212 except that we postulate a fourth unit that generates late prosaccades instead of assuming  
 213 that the late decision process is time insensitive.

214 This version of the SERIA model includes an early unit  $u_e$  that, for simplicity, we assume  
 215 produces only prosaccades, an inhibitory unit that stops early responses  $u_i$ , a late unit  
 216 that triggers antisaccades  $u_a$ , and a further unit that triggers late prosaccades  $u_p$ . As  
 217 before, if the early unit reaches threshold before any other unit, a prosaccade is generated  
 218 with probability

$$p(U_e = t) p(U_i > t) p(U_a > t) p(U_p > t). \quad (19)$$

219 If any of the late units arrive first, the respective action is generated with probability:

$$\text{Antisaccade: } p(U_a = t) p(U_p > t) p(U_e > t) p(U_i > t). \quad (20)$$

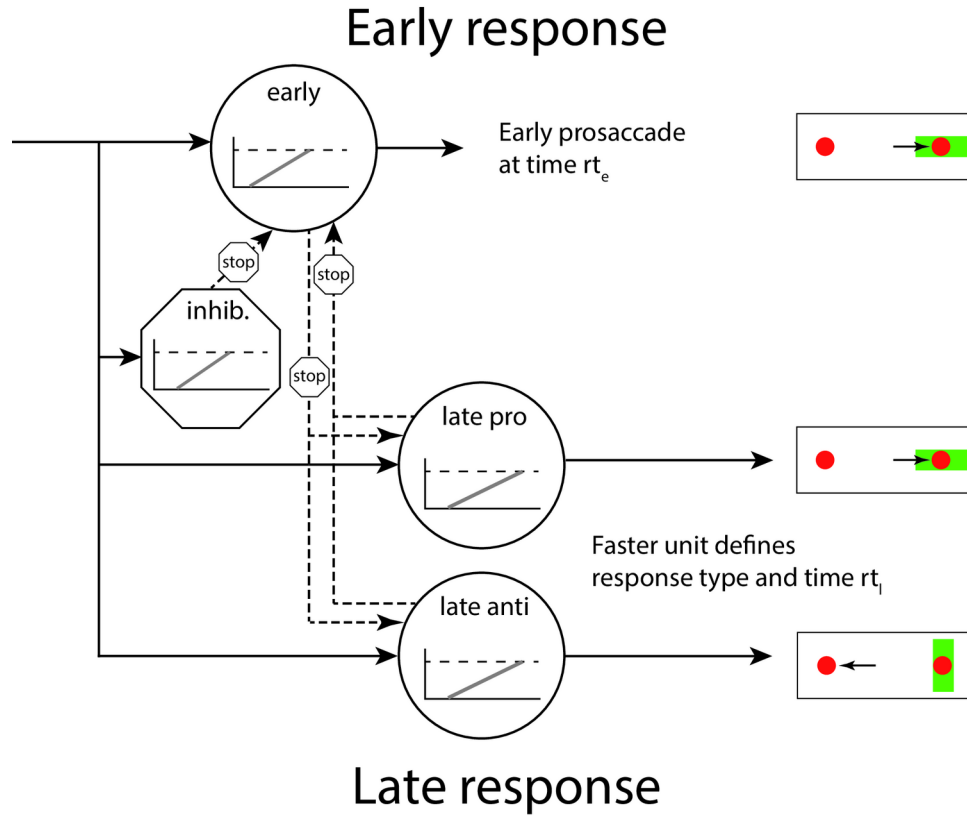
$$\text{Prosaccade: } p(U_p = t)p(U_a > t)p(U_e > t)p(U_i > t). \quad (21)$$

220 Finally, if the inhibitory unit arrives first, either a late pro- or antisaccade is generated  
221 with probability

$$\text{Antisaccades: } p(U_a = t)p(U_p > t) \left( \int_0^t p(U_i = \tau)p(U_e > \tau)d\tau \right), \quad (22)$$

$$\text{Prosaccades: } p(U_p = t)p(U_a > t) \left( \int_0^t p(U_i = \tau)p(U_e > \tau)d\tau \right). \quad (23)$$

222 Implicit in the last two terms is the competition between the late units, which are  
223 assumed again to be independent of each other. Formally, this competition is expressed  
224 as the probability of, for example, the late antisaccade unit arriving before a late  
225 prosaccade  $p(U_a = t)p(U_p > t)$ . A schematic representation of the model is shown in Fig.  
226 2. This late race is similar to the Linear Ballistic Accumulation model proposed by [24],  
227 although in that model decisions are seen as the result of a race of ballistic accumulation  
228 processes with fixed threshold but stochastic base line and increase rate. Here we only  
229 assume that the late decision process is a GO-GO race [21].



**Fig 2. Layout of the SERIA<sub>Ir</sub> model.**

The presentation of a visual cue (a green bar) triggers the race of four independent units. The inhibitory unit can stop an early response. The late decision process is triggered by the competition between two further units.

230 The likelihood of an action is given by summing over all possible outcomes that lead to  
 231 that action:

$$p(A = pro, T = t) = p(U_e = t)p(U_i > t)p(U_a > t)p(U_p > t) + \quad (24)$$

$$p(U_p = t)p(U_a > t)p(U_i > t)p(U_e > t) +$$

$$p(U_p = t)p(U_a > t) \left( \int_0^t p(U_i = \tau)p(U_e > \tau) d\tau \right),$$

$$p(A = anti, T = t) = p(U_a = t)p(U_p > t)p(U_i > t)p(U_e > t) + \quad (25)$$

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

232 We have left out some possible simplifications in Eq. 24 and 25 for the sake of clarity.

233 The conditional probability of a late antisaccade is given by the interaction between the

234 late units, such that

$$p(U_a < U_p) = \int_0^{\infty} p(U_a = t)p(U_p > t)dt = 1 - p(U_p < U_a), \quad (26)$$

235 is analogous to the probability of a late antisaccade  $1 - \pi_l$  in the SERIA model. This

236 observation shows that the main difference between the SERIA and SERIA<sub>r</sub> model is that

237 the former postulates that the distribution of late pro- and antisaccades are equal and

238 conditionally independent of the action performed, whereas the latter constrains the

239 probability of a late antisaccade to be a function of the arrival times of the late units.

240 The expected *response time* of late pro and antisaccade actions is given by

$$\frac{1}{p(U_p < U_a)} \int_0^{\infty} t p(U_p = t)p(U_a > t)dt, \quad (27)$$

$$\frac{1}{p(U_a < U_p)} \int_0^{\infty} t p(U_a = t)p(U_p > t)dt. \quad (28)$$

241 We will refer to these terms as the mean *response time* of pro- and antisaccade actions, in

242 contrast to the mean arrival times, which are the expected value of any single unit.

### 243 **Non-decision time**

244 The models above can be further finessed to account for non-decision times  $\delta$  by

245 transforming the RT  $t$  to  $t_\delta = t - \delta$ . The delay  $\delta$  might be caused by, for example,

246 conductance delays from the retina to the cortex. In addition, the antisaccade or late units

247 might include a constant delay  $\delta_a$ , which is often referred to as the antisaccade cost [1].

248 Note that the model is highly sensitive to  $\delta$  because any RT below it has zero probability.

249 In order to relax this condition and to account for early outliers, we assumed that

250 saccades could be generated before  $\delta$  at a rate  $\eta \in [0,1]$  such that the marginal likelihood

251 of an outlier is

$$p(T < \delta) = p(T_\delta < 0) = \eta. \quad (29)$$

252 For simplicity, we assume that outliers are generated with uniform probability in the  
 253 interval  $[0, \delta]$ :

$$p(T = t) = \frac{\eta}{\delta} \text{ if } t < \delta. \quad (30)$$

254 Furthermore, we assume that the probability of an early outlier being a prosaccade was  
 255 approximately 100 times higher than being an antisaccade. Because of the new parameter  
 256  $\eta$ , the distribution of saccades with a RT larger than  $\delta$  needs to be renormalized by the  
 257 factor  $1 - \eta$ . In the case of the PROSA model, for example, this means that the joint  
 258 distribution of action and RT is given by the conditional probability

$$p(A = \text{pro}, T = t_\delta | t_\delta > 0) = p(U_p = t_\delta)p(U_a > t_\delta - \delta_a)p(U_s > t_\delta), \quad (31)$$

$$p(U_a < 0) = 0, \quad (32)$$

$$p(A = \text{anti}, T = t_\delta | t_\delta > 0) = \quad (33)$$

$$p(U_a = t_\delta - \delta_a) \left( p(U_p > t_\delta) + \int_0^{t_\delta} p(U_p = \tau)p(U_s < \tau)d\tau \right).$$

259 A similar expression holds for the SERIA models. However, in the PROSA model a unit-  
 260 specific delay is equal to an action-specific delay. By contrast, in the SERIA model both  
 261 early and late responses can generate pro- and antisaccades. Thus,  $\delta_a$ , represents a delay  
 262 in the late actions that affects both late pro- and antisaccades.

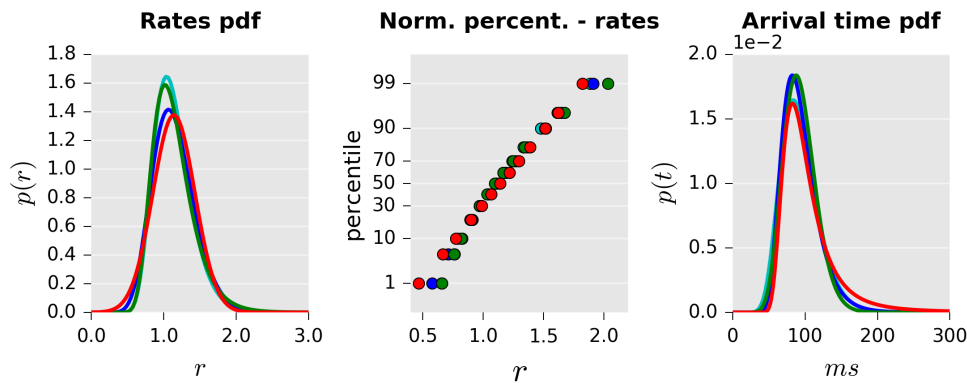
### 263 **Parametric distributions of the increase rate**

264 The models discussed in the previous sections can be defined independently of the  
 265 distribution of the rate of each of the units. In order to fit experimental data, we  
 266 considered four parametric distributions with positive support for the rates: gamma [13],  
 267 inverse gamma, lognormal [25] and the truncated normal distribution (similarly to [22]  
 268 and [24]). Table 1 and Fig 3 summarize these distributions, their parameters, and the  
 269 corresponding arrival time densities. We considered five different configurations: 1) all  
 270 units were assigned *inverse gamma* distributed rates, 2) all units were assigned *gamma*  
 271 distributed rates, 3) the increase rate of the pro and stop units (or early and the inhibitory  
 272 units) was *gamma distributed* but the antisaccade (late) unit's increase rate was *inverse*  
 273 *gamma* distributed, 4) all the units were assigned *lognormal* distributed rates or 5) all  
 274 units were assigned *truncated normal* distributed rates.

**Table 1: Parametric density functions of the increase rates.**

Name	Parameters	Rate p.d.f.	Arrival time p.d.f.
Gamma	$k, \theta$	$\frac{\theta^{-k}}{\Gamma(k)} e^{-r/\theta} r^{k-1}$	$\frac{\theta^k}{\Gamma(k)} e^{-\theta/t} t^{-k-1}$
Inv. gamma	$k, \theta$	$\frac{\theta^k}{\Gamma(k)} e^{-\theta/r} r^{-k-1}$	$\frac{\theta^{-k}}{\Gamma(k)} e^{-t/\theta} t^{k-1}$
Log normal	$\mu, \sigma^2$	$\frac{1}{\sqrt{2\pi\sigma}} e^{-\frac{1}{2}\left(\frac{\ln r - \mu}{\sigma}\right)^2}$	$\frac{1}{\sqrt{2\pi\sigma t}} e^{-\frac{1}{2}\left(\frac{\ln t + \mu}{\sigma}\right)^2}$
T. normal	$\mu, \sigma^2$	$\frac{1}{Z} e^{-\frac{1}{2}\left(\frac{r-\mu}{\sigma}\right)^2}$	$\frac{1}{Zt^2} e^{-\frac{1}{2}\left(\frac{t^{-1}-\mu}{\sigma}\right)^2}$

Z is the normalization constant  $Z = \int_0^\infty \exp\left(-\frac{(r-\mu)^2}{2\sigma^2}\right) dr$ .



**Fig 3. Illustration of probability distributions used to model increase rates.**

Left: Distribution of the rates based on different probability density functions: Normal (red), gamma (blue), inverse gamma (green), and log-normal (cyan). All distributions were matched to have equal mean and variance. Center: Probit plots of the same distributions. While the gamma and lognormal distributions are very close to the straight line induced by the normal distribution, the inverse gamma distribution diverges slightly more from linearity. Right: Arrival time distribution (scaled to ms).

275 All the parametric distributions considered here can be fully characterized by two  
 276 parameters which we generically refer to as  $k$  and  $\theta$ . Hence, the PROSA model is  
 277 characterized by the parameters for each unit  $k_p, k_a, k_s, \theta_p, \theta_a, \theta_s$ . The SERIA model can  
 278 be characterized by analogous parameters  $k_e, k_l, k_i, \theta_e, \theta_l, \theta_i$  and the probabilities of early  
 279 and late prosaccades  $\pi_e$  and  $\pi_l$ . In the case of the SERIA<sub>lr</sub> model, the probability of a late



280 prosaccade is replaced by the parameters of a late prosaccade unit  $k_p, \theta_p$ . In addition to  
281 the unit parameters, all models included the non-decision time  $\delta$ , the antisaccade (or late  
282 unit) cost  $\delta_a$ , and the marginal rate of early outliers  $\eta$ .

## 283 **Experimental procedures**

284 In this section, we describe the experimental procedures, statistical methods, and  
285 inference scheme used to invert the models above. The data is from the placebo condition  
286 of a larger pharmacological study that will be reported elsewhere.

### 287 *Participants*

288 Fifty-two healthy adult males naïve to the antisaccade task were invited to a screening  
289 session through the recruitment system of the Laboratory of Social and Neural Systems  
290 Research of the University of Zurich. During screening, and after being debriefed about  
291 the experiment, subjects underwent an electrocardiogram, a health survey, a visual acuity  
292 test, and a color blindness test. Subjects were excluded if any of the following criteria  
293 were met: age below 18 or above 40 years, regular smoking, alcohol consumption the day  
294 before the experiment, any possible interaction between current medication and  
295 levodopa or benserazide, pulse outside the range 55-100bpm, recreational drug intake in  
296 the past 6 months, history of serious mental or neurological illness, or if the medical  
297 doctor supervising the experiment deemed the participant not apt. All subjects gave their  
298 written informed consent to participate in the study and received monetary  
299 compensation.

### 300 *Procedure*

301 Each subject was invited to two sessions. During both visits, the same experimental  
302 protocol was followed. After arrival, placebo or levodopa (Madopar® DR 250, 200mg of  
303 levopa + 50 mg benserazide) was orally administered in the form of shape- and color-  
304 matched capsules. The present study is restricted to data from the session in which  
305 subjects received placebo. Participants and experimenters were not informed about the  
306 identity of the substance. Immediately afterwards subjects were introduced to the  
307 experimental setup and to the task through a written document. This was followed by a  
308 short training block (see below).

309 The experiment started 70 minutes after substance administration. Subjects participated  
310 in three blocks of 192 randomly interleaved pro- and antisaccade trials. The percentages  
311 of prosaccade trials in the three blocks were 20%, 50%, or 80%. This yielded three  
312 *prosaccade probability* (PP) conditions: PP20, PP50, and PP80. Thus, in the PP20 block,  
313 subjects were presented a prosaccade cue in 38 trials, while in all other 154 trials an  
314 antisaccade cue was shown. The order of the trials was randomized in each block, but the

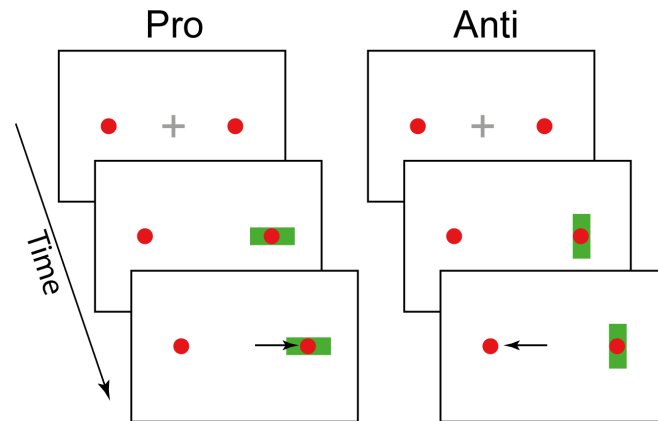
315 same order was used in all subjects and sessions. The order of the conditions was  
316 counterbalanced across subjects.

### 317 *Stimulus and apparatus*

318 During the experiment, subjects sat in front of a CRT monitor (Philipps 20B40, distance  
319 eye-screen:  $\approx 60\text{cm}$ , refresh rate: 75Hz). The screen subtended a horizontal visual angle  
320 of 38 degrees of visual angle (dva). Eye movements were recorded using a remote  
321 infrared camera (Eyelink II, SR-Research, Canada). Participants' head was stabilized with  
322 a chin rest. Data were stored at a sampling rate of 500 Hz.

323 During the task, two red dots (0.25dva) that constituted the saccadic targets were  
324 constantly displayed at an eccentricity of  $\pm 12\text{dva}$ . Displaying the saccadic target before  
325 the execution of an antisaccade has been reported to affect saccadic velocity and accuracy,  
326 but not RTs [26], and arguably decreases the need for sensorimotor transformations [27].  
327 At the beginning of each trial, a gray fixation cross ( $0.6 \times 0.6\text{ dva}$ ) was displayed at the  
328 center of the screen. After a random fixation interval (500 to 1000 ms), the cross  
329 disappeared, and the cue instructing either a pro- or an antisaccade trial (see below) was  
330 shown centered on either of the red dots. As mentioned above, in each block, subjects  
331 were presented with a prosaccade cue in either 20, 50, or 80 percent of the trials. The  
332 order of the presentation of the cues was randomized. The cue was a green rectangle  
333 ( $3.48 \times 0.8\text{ dva}$ ) displayed for 500ms in either horizontal (prosaccade) or vertical  
334 orientation (antisaccade). Once the cue was removed and after 1000ms, the next trial  
335 started.

336 Subjects were instructed to saccade in the direction of the cue when a horizontal bar was  
337 presented (prosaccade trial) and to saccade in the opposite direction when a vertical bar  
338 was displayed (antisaccade trial, see Fig. 3). See [28,29] for similar task designs.



**Fig 4. Task design.**

After a variable fixation period of 500-1000ms (top) the cue (green rectangle) appeared on the screen for 500 ms. The orientation of the cue (horizontal or vertical) indicated the required response (prosaccade or antisaccade).

339 Prior to the main experiment, participants were trained on the task in a block of 50  
340 prosaccade trials, immediately followed by 50 antisaccade trials. During the training,  
341 subjects were automatically informed after each trial whether their response was correct  
342 or not (see below), or whether they had failed to produce a saccade within 500ms after  
343 cue presentation (CP). No feedback was given during the main experimental blocks.

#### 344 *Data preparation*

345 Data were parsed and preprocessed using the Python programming language (2.7).  
346 Saccades were detected using the algorithm provided by the eyetracker manufacturer  
347 (SR Research), which uses a velocity and acceleration threshold of  $22dva/s$  and  
348  $3800dva/s^2$  [30]. We only considered saccades with a magnitude larger than  $2dva$ . RT  
349 was defined as the time between CP and the first saccade larger than  $2dva$ . A prosaccade  
350 trial was considered correct if the end position of the saccade was ipsilateral to the cue  
351 and, conversely, an antisaccade trial was considered correct if the end position of the  
352 saccade was contralateral to the cue.

353 Trials were excluded from further analysis if a) data were missing, b) a blink occurred  
354 between CP and the main saccade, c) the trial was aborted by the experimenter, d)  
355 subjects failed to fixate in the interval between fixation detection and CP, e) if a saccade  
356 was detected only later than 800ms after CP, f) if the RT was below 50ms, and in the case  
357 of an antisaccade if it was below 110ms. Corrective antisaccades were defined as saccades  
358 that a) followed a prosaccade error, b) occurred no later than 900ms after CP, and c) had  
359 less than  $3dva$  horizontal error from the red circle contralateral to the cue.

360 Besides the fitted non-decision time  $\delta$  we assumed a fixed non-decision time of 50ms for  
361 all participants [17]. This was implemented by subtracting 50ms of all saccades before  
362 being entered into the model. In order to avoid numerical instabilities, RT were rescaled  
363 from millisecond to tenths of a second during all numerical analysis. All results are  
364 presented in ms.

## 365 **Modeling**

366 We aimed to answer three questions with the models considered here. First, we  
367 investigated which model (i.e. PROSA, SERIA or SERIA<sub>lr</sub>) explained the experimental data  
368 best, and whether all important qualitative features of the data were captured by this  
369 model. We did not have a strong hypothesis regarding the parametric distribution of the  
370 data and hence, comparisons of parametric distributions were only of secondary interest  
371 in our analysis. Second, we investigated whether reduced models that kept certain  
372 parameters fixed across trial types were sufficient to model the data. Third, we  
373 investigated how the probability of a trial type in a block affected the parameters of the  
374 model.

### 375 *Model space*

376 Initially, we considered 15 different models as shown in Table 2. Each model was fitted  
377 independently for each subject and condition. Since our experimental design included  
378 mixed blocks, we allowed for different parameters in pro- and antisaccade trials, i.e.,  
379 different increase-rate distributions depending on the *trial type* (TT). Under this  
380 hypothesis, the PROSA model had 12 free parameters (6 for each TT), whereas the SERIA  
381 model required 4 further parameters ( $\pi_e$  and  $\pi_l$  in each TT). The late race SERIA<sub>lr</sub> model  
382 included 16 parameters for the units (8 for each TT). We did not investigate the case that  
383 early reactions could trigger antisaccades but rather fixed the probability of an early  
384 antisaccade  $1 - \pi_e$  to  $10^{-3}$ . The rationale behind this was that if early reactions are a  
385 priori assumed to never trigger antisaccades, rare but possible early antisaccades might  
386 cause large biases when fitting a model.

387 Regarding the non-decision time  $\delta$ , antisaccade cost  $\delta_a$ , and rate of outliers  $\eta$ , we assumed  
388 equal parameters in both TT. Consequently, the full PROSA model had 15 free parameters  
389 whereas the full SERIA and SERIA<sub>lr</sub> models had both 19 free parameters.

**Table 2. Model families with the respective increase-rate distributions.**

<b>PROSA</b>			
<b>Model</b>	<b>Prosaccade/ stop units</b>	<b>Anti. unit</b>	<b># Param. full/const.</b>
$m_1/m_1^c$	Inv. gamma	Inv. gamma	15/13
$m_2/m_2^c$	Gamma	Gamma	15/13
$m_3/m_3^c$	Gamma	Inv. gamma	15/13
$m_4/m_4^c$	Lognorm.	Lognorm.	15/13
$m_5/m_5^c$	T. norm.	T. norm.	15/13
<b>SERIA</b>			
	<b>Early/stop units</b>	<b>Late unit</b>	
$m_6/m_6^c$	Inv. gamma	Inv. gamma	19/13
$m_7/m_7^c$	Gamma	Gamma	19/13
$m_8/m_8^c$	Gamma	Inv. gamma	19/13
$m_9/m_9^c$	Lognorm.	Lognorm.	19/13
$m_{10}/m_{10}^c$	T. norm.	T. norm.	19/13
<b>SERIA<sub>lr</sub></b>			
	<b>Early/stop units</b>	<b>Late pro./anti. units</b>	
$m_{11}/m_{11}^c$	Inv. gamma	Inv. gamma	19/15
$m_{12}/m_{12}^c$	Gamma	Gamma	19/15
$m_{13}/m_{13}^c$	Gamma	Inv. gamma	19/15
$m_{14}/m_{14}^c$	Lognorm.	Lognorm.	19/15
$m_{15}/m_{15}^c$	T. norm.	T. norm.	19/15

Models with parameters constrained to be equal across trial types are referred through the superscript *c*.

390 In addition to the full models, we evaluated restricted versions of each of them by  
 391 constraining some parameters to be equal across TT. In the case of the SERIA model, we  
 392 hypothesized that the parameters of all units were equal, irrespective of TT (i.e., that the  
 393 rate of the units was not affected by the cue presented in a trial). However, we assumed  
 394 that the probability that an early or late response was a prosaccade was different in pro-  
 395 and antisaccade trials. Therefore, in the case of the SERIA model, instead of 12 unit  
 396 parameters (6 per TT), the restricted model had only 6 parameters for the units' rates.  
 397 The parameters  $\pi_e$  and  $\pi_l$  were allowed to differ in pro and antisaccade trials. In the case  
 398 of the restricted SERIA<sub>lr</sub> model, the units that underlie the late decision process were  
 399 allowed to vary across TT, yielding a restricted model with 4 parameters for the early and  
 400 inhibitory units, and 8 for the late decision process, half of them for each trial type. In the

401 case of the PROSA model, similarly to [17], it is possible to assume that the parameters of  
402 the prosaccade unit remain constant across TT, and that the parameters of the stop and  
403 antisaccade units depend on TT, yielding 10 parameters for the units.

#### 404 *Prior distributions for model parameters*

405 To complete the definition of the models, the prior distribution of the parameters was  
406 specified. This distribution reflects beliefs that are independent of the data and provides  
407 a form of regularization when inverting a model. In order to avoid any undesired bias  
408 regarding the parametric distributions considered here, we reparametrized all but the  
409 truncated normal distribution in terms of their mean and variance. We then assumed that  
410 the log of the mean and variance of the rate of the units were equally normally distributed  
411 (see Table 3). Therefore, the parametric distributions had the same prior in terms of their  
412 first two central moments. In the case of the truncated normal distribution, instead of an  
413 analytical transformation between its first two moments and its natural parameters  $\mu$   
414 and  $\sigma^2$ , we defined the prior distribution as a density of  $\mu$  and  $\ln \sigma^2$ . To ensure that  $\mu$  was  
415 positive with high likelihood (96%) we assumed that  $\mu \sim N(0.55, 0.09)$ . The variance term  
416 was distributed as displayed in Table 3. As a further constraint, we restricted the  
417 parameter space to enforce that the first two moments of the distributions of rates and  
418 RTs existed. We relaxed this constraint for the late units of the SERIA<sub>lr</sub> in order to allow  
419 for ‘flat’ distributions with possibly infinite mean and variance. This can describe a case  
420 in which the increase rate of one of the late units is extremely low.

**Table 3. Prior probability density functions.**

Parameter	Probability density function	Expected value	Variance
$\mu_r$	$\mathcal{N}(\ln \mu_r; -1.08, 0.97)$	0.55	0.5
$\sigma_r^2$	$\mathcal{N}(\ln \sigma_r^2; -2.64, 0.69)$	0.1	0.01
$\delta$	$\mathcal{N}(\ln \delta; -1.58, 1.79)$	0.5	1.25
$\delta_a$	$\mathcal{N}(\ln \delta_a; -0.87, 1.17)$	0.75	1.25
$\pi_e$	$Beta(\pi_e; 0.5, 0.5)$	0.5	0.145
$\pi_l$	$Beta(\pi_l; 0.5, 0.5)$	0.5	0.145
$\eta$	$Beta(\eta; 0.5, 0.5)$	0.5	0.145

421 For the non-decision time  $\delta$  and the antisaccade cost  $\delta_a$ , the prior of their log transform  
 422 was a normal distribution, consistent across all models. Note that the scale of the  
 423 parameters  $\delta$  and  $\delta_a$  in Table 3 is tenths of a second. The fraction of early outliers  $\eta$ , and  
 424 early and late prosaccades  $\pi_e$  and  $\pi_l$  were assumed to be Beta distributed, with  
 425 parameters 0.5 and 0.5. Thus, for example, the prior probability of an early outlier is given  
 426 by

$$p(\eta) \propto \eta^{0.5}(1 - \eta)^{0.5}. \quad (34)$$

427 This parametrization constitutes the minimally informative prior distribution, as it is the  
 428 Jeffrey's prior of  $\eta$ ,  $\pi_e$  and  $\pi_l$ . Table 3 displays the parameters used for the prior  
 429 distributions.

### 430 Bayesian inference

431 Inference on the model parameters was performed using the Metropolis-Hastings  
 432 algorithm [31]. To increase the efficiency of this sampling scheme, we iteratively modified  
 433 the proposal distribution during an initial 'burn-in' phase as proposed by [32]. Moreover,  
 434 we extended this method by drawing from a set of chains at different temperatures and  
 435 swapping samples across chains. This method, called population MCMC or parallel  
 436 tempering, increases the statistical efficiency of the Metropolis-Hasting algorithm [33]  
 437 and has been used in similar contexts before [34]. We simulated 16 chains with a 5-th  
 438 order temperature schedule [35]. For all but the models including a truncated normal  
 439 distribution, we drew a total of  $4.1 \times 10^4$  samples per chain, from which the first  $1.6 \times 10^4$



440 samples were discarded as part of the burn-in phase. When a truncated normal  
441 distribution was included (models  $m_5$ ,  $m_{10}$ , and  $m_{15}$ ), the total number of samples was  
442 increased to  $6 \times 10^4$ , from which  $2 \times 10^4$  were discarded. The convergence of the algorithm  
443 was assessed using the Gelman-Rubin criterion [33,36] such that the  $\tilde{R}$  statistic of the  
444 parameters of the model was aimed to be below 1.1. When a simulation did not satisfy  
445 this criterion, it was repeated until 99.5 percent of all inversions satisfied it.

446 Models were scored using their log marginal likelihood or log model evidence (LME). This  
447 is defined as the log probability of the data given a model after marginalizing out all its  
448 parameters. When comparing different models, the LME corresponds to the log posterior  
449 probability of a model under a uniform prior on model identity. Thus, for a single subject  
450 with data  $y$ , the posterior probability of model  $k$ , given models 1 to  $n$  is

$$p(m_k|y) = \frac{p(y|m_k)p(m_k)}{\sum_{i=1}^n p(y|m_i)p(m_i)} = \frac{p(y|m_k)}{\sum_{i=1}^n p(y|m_i)}. \quad (35)$$

451 Importantly, this method takes into account not only the accuracy of the model but also  
452 its complexity, such that overparameterized models are penalized [37]. A widely used  
453 approximation to the LME the Bayesian Information Criterion (BIC) which, although easy  
454 to compute, has limitations (for discussion, see [38]). Here, we computed the LME  
455 through sampling using thermodynamic integration [33,39]. This method provides  
456 robust estimates and can be easily computed using samples obtained through population  
457 MCMC.

458 One important observation here is that the LME is sensitive to the prior distribution, and  
459 thus can be strongly influenced by it [40]. We addressed this issue in two ways: On one  
460 hand and as mentioned above, we defined the prior distribution of the increase rates of  
461 all models in terms of the same mean and variance. This implies that the priors were equal  
462 up to their first two moments, and hence all models were similarly calibrated. On the  
463 other hand, we complemented our quantitative analysis with qualitative posterior checks  
464 [33] as shown in the results section.

465 Besides comparing the evidence of each model, we also performed a hierarchical or  
466 random effects analysis described in [38,41]. This method can be understood as a form  
467 of soft clustering in which each subject is assigned to a model using the LME as  
468 assignment criterion. Here, we report the expected probability of the model  $r_i$ , which

469 represents the percentage of subjects that is assigned to the cluster representing model  
470 *i*. This hierarchical approach is robust to population heterogeneity and outliers, and  
471 complements reporting the group-level LME. Finally, we compared families of models  
472 [42] based on the evidence of each model for each subject summed across conditions.

### 473 **Classical statistics**

474 In addition to a Bayesian analysis of the data, we used classical statistics to investigate  
475 the effect of our experimental manipulation on behavioral variables (mean RT and ER)  
476 and the parameters of the models. We have suggested previously [11,43,44] that  
477 generative models can be used to extract hidden features from experimental data that  
478 might not be directly captured by, for example, standard linear methods or purely data  
479 driven machine learning techniques. In this sense, classical statistical inference can be  
480 boosted by extracting interpretable data features through Bayesian techniques.

481 Frequentist analyses of RT, ER, and parameter estimates were performed using a mixed  
482 effects generalized linear model with independent variables *subject* (SUBJECT),  
483 *prosaccade probability* (PP) with levels PP20, PP50 and PP80, and when pro- and  
484 antisaccade trials were analyzed together, *trial type* (TT). The factor SUBJECT was always  
485 entered as a random effect, whereas PP and TT were treated as categorical fixed effects.  
486 In the case of ER, we used the probit function as link function.

487 Analyses were conducted with the function *fitglm*.m in MATLAB 9.0. The significance  
488 threshold  $\alpha$  was set to 0.05.

### 489 **Implementation**

490 All likelihood functions were implemented in the C programming language using the GSL  
491 numerical package (v.1.16). Integrals without an analytical form or well-known  
492 approximations were computed through numerical integration using the Gauss-Kronrod-  
493 Patterson algorithm [45] implemented in the function *gsl\_integration\_qng*. The sampling  
494 routine was implemented in MATLAB (v. 8.1) and is available as a module of the open  
495 source software package TAPAS ([www.translationalneuromodeling.org/tapas](http://www.translationalneuromodeling.org/tapas)).

## 496 **Results**

### 497 **Behavior**

498 Forty-seven subjects (age:  $23.8 \pm 2.9$ ) completed all blocks and were included in further  
499 analyses. A total of 27072 trials were recorded, from which 569 trials (2%) were excluded  
500 (see Table 4).

**Table 4. Summary of trials per subject**

	<b>Valid</b>	<b>Blink</b>	<b>Missing</b>	<b>Aborted</b>	<b>FE</b>	<b>Late S.</b>	<b>Early S.</b>	<b>Total</b>
Total	26503	188	60	42	249	0	30	27072
Mean	563.9	4.0	1.3	0.9	5.3	0.0	0.6	576
Std.	9.9	5.1	2.5	1.5	5.0	0.0	1.3	-
Min.	536	0	0	0	0	0	0	-
Max.	576	22	15	6	19	0	8	-

FE: Fixation errors. Late saccades are saccades elicited after 800ms. Early saccades are prosaccades elicited before 50ms after CP or antisaccades elicited before 110ms after CP.

501 Both ER and RT showed a strong dependence on PP (Fig 5 and Table 5). Individual data  
502 is included in the S1 File and is displayed in S2 Figure. The mean RT of correct pro- and  
503 antisaccade trials was analyzed independently with two ANOVA tests with factors  
504 SUBJECT and PP. We found that in both pro- ( $F_{2,138} = 46.9, p < 10^{-5}$ ) and antisaccade  
505 trials ( $F_{2,138} = 37.3, p < 10^{-5}$ ) the effect of PP was significant; with higher PP,  
506 prosaccade RT decreased, whereas the RT of correct antisaccades increased. On a subject-  
507 by-subject basis, we found that between the PP20 and PP80 conditions, 91% of the  
508 participants showed increased RT in correct antisaccade trials, while 81% demonstrated  
509 the opposite effect (a decrease in RT) in correct prosaccade trials. Similarly, there was a  
510 significant effect of PP on ER in both prosaccade ( $F_{2,138} = 376.1, p < 10^{-5}$ ) as well as in  
511 antisaccade ( $F_{2,138} = 347.0, p < 10^{-5}$ ) trials. This effect was present in all but one  
512 participant in antisaccade trials and in all subjects in prosaccade trials. Exemplary RT  
513 data of one subject in the PP50 condition is displayed in Fig 6.



**Fig 5. Error rate and reaction times as a function of prosaccade trial probability (PP).**

Left panel: Mean error rates for pro and antisaccades. Right panel: Mean reaction time in *ms*. Error bars indicate standard errors of the mean. Only correct responses are displayed.

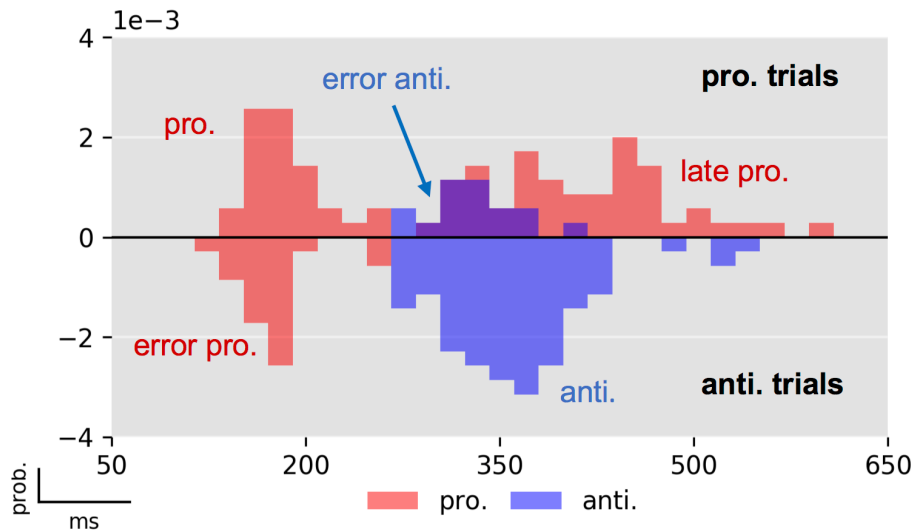
514

**Table 5. Summary of mean RTs and ERs.**

Trial type	Action	Reaction times [ms]		
		PP 20	PP 50	PP80
Pro.	Pro.	330(72)	319(67)	284(59)
Pro.	Anti.	326(68)	329(46)	336(57)
Anti.	Anti	354(60)	378(57)	389(61)
Anti.	Pro	234(50)	231(47)	225(31)
		Error rates [%]		
Pro.		26(15)	11(8)	4(4)
Anti.		23(17)	35(21)	51(20)

Standard deviations are shown in brackets.

515



**Fig 6. Exemplary RT histogram of one subject in the PP50 condition.**

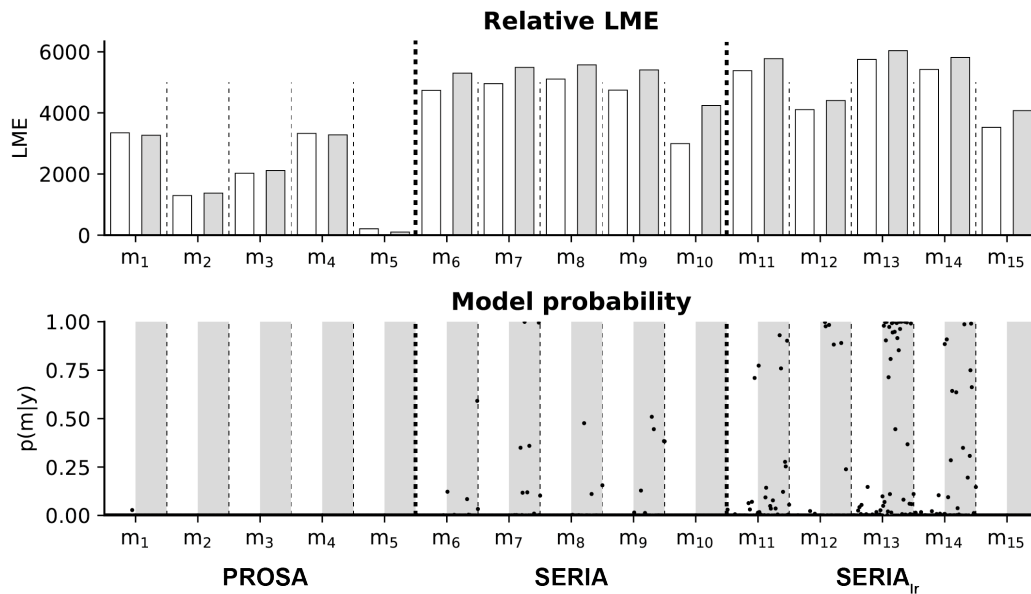
Prosaccade trials are displayed in the upper half plane and antisaccade trials in the lower (negative) half plane. Prosaccade actions are depicted in red color, whereas antisaccade actions are shown in blue. Errors in prosaccade trials are antisaccades that for this subject occurred after the first peak of early prosaccades. Errors in antisaccade trials (lower half plane) occurred at a similar latency as early prosaccades in prosaccade trials. The histograms have been normalized to have unit probability mass, i.e., the sum of the area of all bars is one.

## 516 **Modeling**

### 517 *Model comparison results*

518 Initially, we considered the models outlined in Table 2. The LME over all participants  
519 (fixed effects analysis) and the posterior probability of all models and all subjects are  
520 presented in Fig 7. Independently of the particular parametric distribution of the units,  
521 the  $SERIA_{lr}$  models had higher evidence compared to the PROSA and SERIA models. A  
522 random effects, family-wise model comparison [42] resulted in an expected frequency of  
523  $r = 87\%$  for the  $SERIA_{lr}$  family,  $r = 11\%$  for the SERIA family, and  $r = 2\%$  for the PROSA  
524 family. In addition, constraining the parameters to be equal across trial types increased  
525 the model evidence irrespective of the parametric distribution assigned to the units  
526 (Fig 7). Here, the family-wise model comparison showed that models with constrained  
527 parameters had an expected frequency of  $r = 98\%$ . Over all 30 models,  $m_{13}^c$  ( $SERIA_{lr}$  with  
528 constrained parameters, early and inhibitory increase rates gamma distributed, and late  
529 units' rate inverse gamma distributed) showed the highest LME with  $\Delta LME > 200$   
530 compared to all other models. Following [40], a difference in LME larger than 3  
531 corresponds to strong evidence.

532 To verify that the SERIA<sub>lr</sub> family was not preferred simply because the probability of early  
 533 prosaccades was fixed, we considered models in the SERIA family with the same property  
 534 (not displayed). We found that although fixing this value increased the LME of the SERIA  
 535 family, there was still a difference of  $\Delta LME > 90$  when comparing the best model of the  
 536 SERIA<sub>lr</sub> family and the best model of the SERIA family with a fix probability of early  
 537 prosaccades.

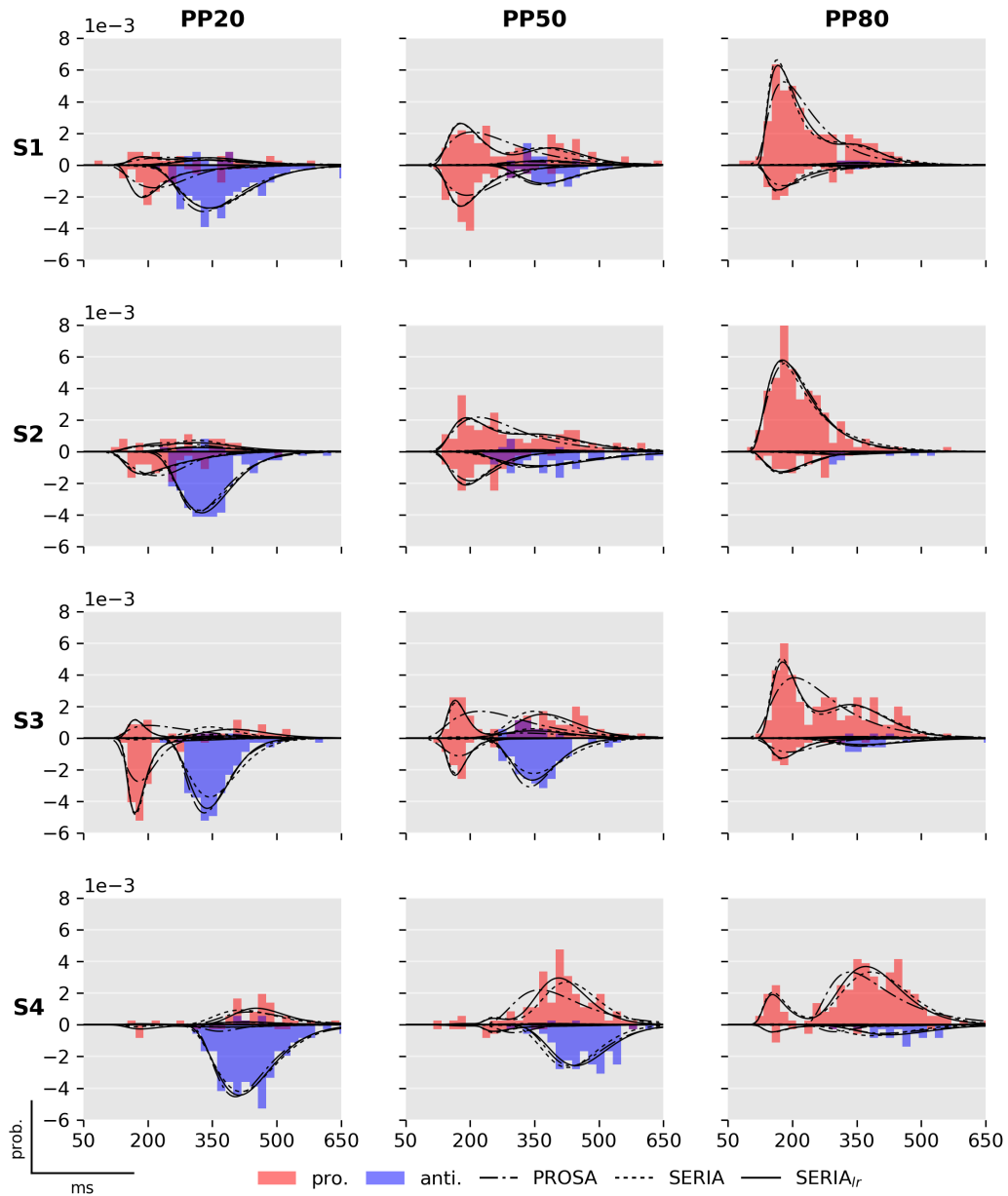


**Fig 7. Summary of model comparison.**

Top: Summed LME of all subjects for all 30 models. White bars show models with all parameters free, grey bars models with constrained parameters. LMEs are normalized by subtracting the lowest LME ( $m_5$ ). Model  $m_{13}^c$  (constrained SERIA<sub>lr</sub>) exceeded all other models ( $\Delta LME > 200$ ). Bottom: Illustration of model probability for all subjects. The posterior model probabilities for all subjects are shown as black dots. In white shading are models with all parameters free, grey bars represent models with restricted parameters. Note that in nearly all subjects, the SERIA<sub>lr</sub> models with restricted parameters showed high model probabilities.

538 Fits of four subjects using the posterior samples of the best PROSA ( $m_1$ ), SERIA ( $m_8^c$ ), and  
 539 SERIA<sub>lr</sub> ( $m_{13}^c$ ) models are depicted in Fig 8. Although model  $m_1$  was the best model in the  
 540 PROSA family, it clearly did not explain the apparent bimodality of the prosaccade RT  
 541 distributions. Instead, RTs were explained through wider distributions. No obvious  
 542 difference could be observed between the SERIA and SERIA<sub>lr</sub> models. We further  
 543 examined the model fits in Fig 9 and Fig 10 by plotting the weighted fits and cumulative  
 544 density functions of the reciprocal RT in the probit scale (reciprobit plot [22]) collapsed  
 545 across subjects for the best model of each family. The histograms of RTs clearly show a

546 large number of late prosaccades whose distribution is similar to the distribution of  
547 antisaccade RTs. The most pronounced – but still small - difference between the SERIA  
548 and SERIA<sub>lr</sub> models was visible in prosaccade trials in the PP20 condition (left panel,  
549 upper half plane), in which antisaccade errors displayed lower RT than correct late  
550 prosaccades.

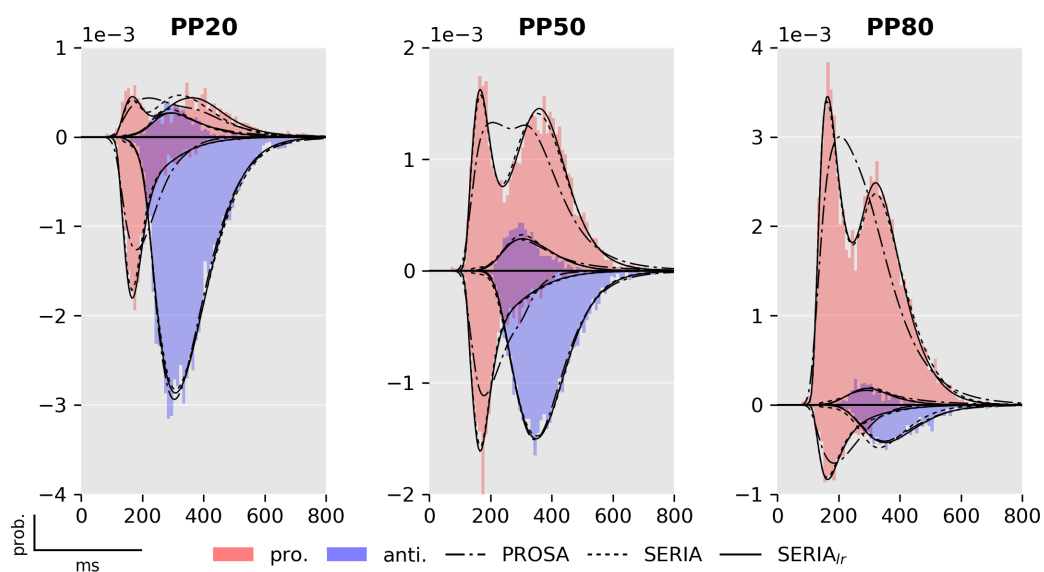


**Fig 8. Fits of best PROSA ( $m_1$ ), SERIA ( $m_8^c$ ) and SERIA<sub>r</sub> ( $m_{13}^c$ ) models**

Columns display the normalized histogram of the RTs of pro- (red) and antisaccades (blue) in each of the conditions. Rows correspond to individual subjects named S1 to S4 for display purpose. As in Fig. 6, prosaccade trials are displayed on the upper half plane, whereas antisaccade trials are displayed in the lower half plane. The predicted RT distributions based on the samples from the posterior distribution are displayed in solid (SERIA<sub>r</sub>), broken (SERIA), and dash-dotted (PROSA) lines. Note that data from subject 3 in the PP50 condition is the same as shown in Fig. 6. Early outliers are not displayed.



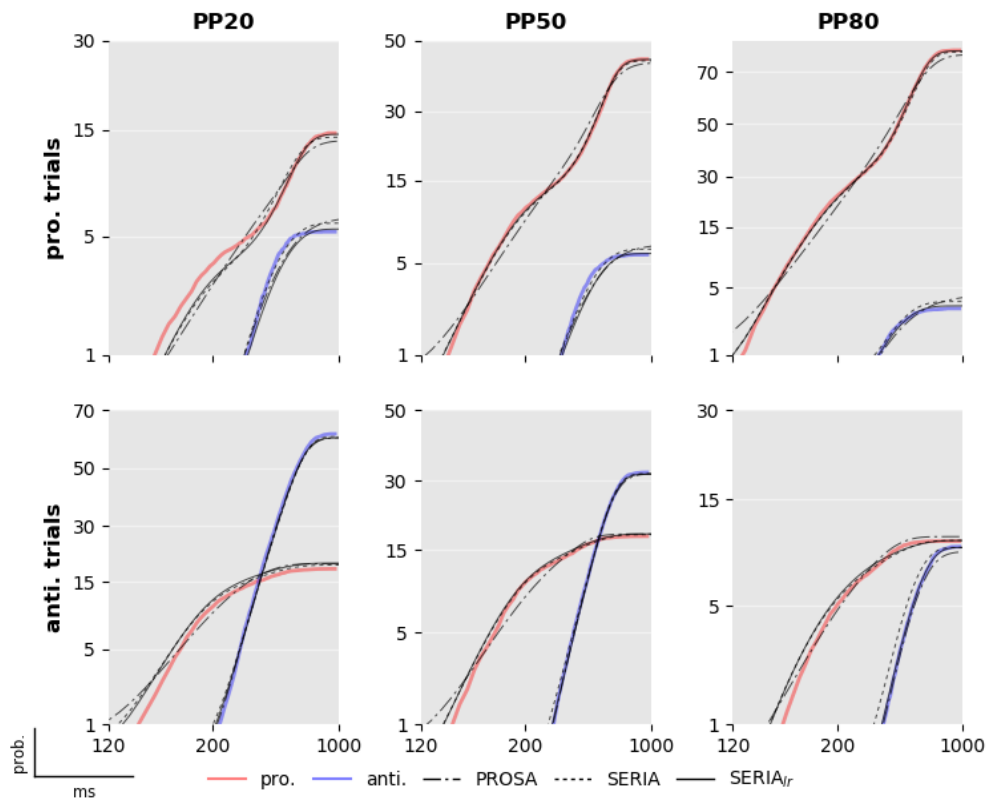
552



**Fig 9. Fits from the best models in each family ( $m_1, m_8^c, m_{13}^c$ ).**

Model fits and RT histograms for each condition collapsed across subjects. For more details see Fig. 6 and 8.

553



**Fig 10. Reciprobit of best models.**

Predicted and empirical cumulative density function of the reciprocal RT in the probit scale for each condition and model collapsed across all subjects. The data shown are the same as in Fig 9, but split for trial types and illustrated as cumulative distributions. Note that the y-axis is in the probit scale and that nearly all differences between the model and the data occur at very small probability values of 5% or below.

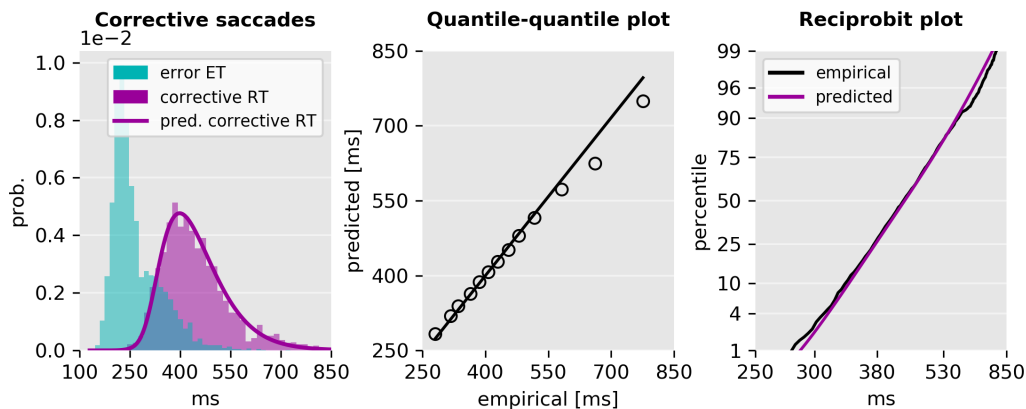
554 *Corrective antisaccades*

555 The RTs of antisaccades that follow an error prosaccade were not directly modeled.  
 556 However, we hypothesized that corrective antisaccades are delayed late antisaccade  
 557 actions, whose distribution is given by the *response time* distribution of late antisaccades

$$\frac{1}{p(U_a < U_p)} \int_0^{\infty} p(U_a = t)p(U_p > t)dt. \quad (36)$$

558 A total of 2989 corrective antisaccades were included in the analysis. The mean ( $\pm$ std)  
 559 end time of the erroneous prosaccades was 268( $\pm$ 63)ms. The mean RT of corrective  
 560 antisaccades was 447( $\pm$ 103)ms, and the weighted mean arrival time of the late  
 561 antisaccade unit was 367ms. Fig 11 displays the histogram of the end time of all  
 562 prosaccade errors, the RT of all corrective antisaccades and the time shifted (+80ms)

563 predicted response time of late antisaccades. Since we did not have a strong hypothesis  
 564 regarding the magnitude of the delay of the corrective antisaccades, we selected the time  
 565 shift to be the difference between the mean corrective antisaccade RT and the mean  
 566 predicted response time of late antisaccades. Visual inspection strongly suggests that the  
 567 distribution of corrective antisaccade RTs is well approximated by the distribution of the  
 568 late responses. The short difference between corrective antisaccades' RT and the  
 569 expected response time of the late antisaccade unit (80ms) favors the hypothesis that the  
 570 plan for a corrective antisaccade is initiated before the incorrect prosaccade had finished.



**Fig 11. Empirical and predicted RT of corrective antisaccades.**

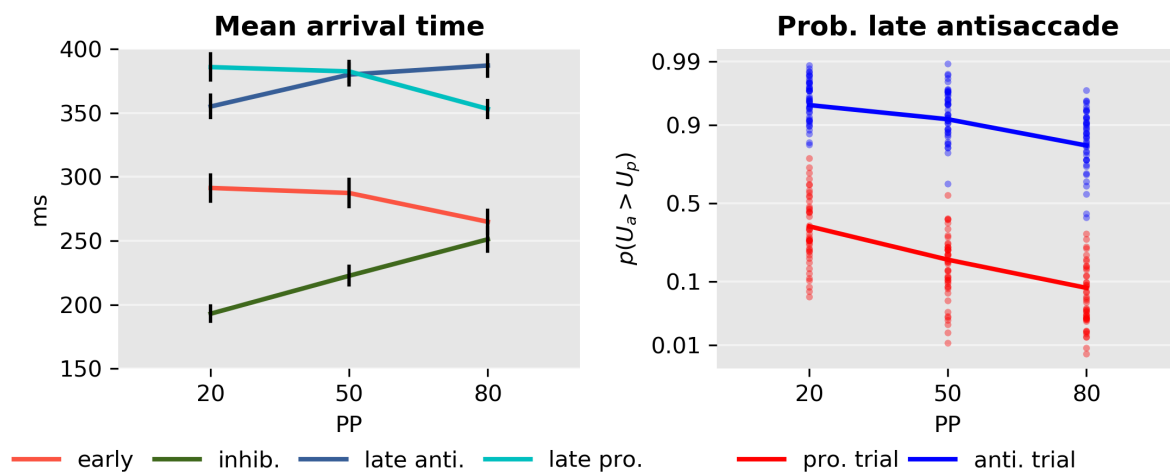
Left: End time of erroneous prosaccades, RTs of corrective antisaccades, and time shifted predicted response time distribution of late antisaccades. The time shift was selected to be the difference between the empirical and predicted mean response time. Center: Quantile-quantile plot of the predicted and empirical distribution of corrective antisaccades, and a linear fit to the central 98% quantiles. There is a small deviation only at the tail of the distribution. Right: Reciprobit plot of the empirical and predicted cumulative density functions of the RT of corrective antisaccades. The scale of the horizontal axis is proportional to the reciprocal RT. The vertical axis is in the probit scale.

### 571 *Effects of prosaccade probability on model parameters*

572 The effect of PP on the parameters of the model was investigated by examining the  
 573 expected value of the parameters of the best scoring model ( $m_{13}^c$ ). Initially, we considered  
 574 the question of whether the mean arrival or response time of each of the units changed  
 575 as a function of PP. For arrival times, this corresponds to

$$\frac{1}{N} \sum_{j=1}^N (E[U_i | k_j^i, \theta_j^i] + \delta_j^i) \quad (37)$$

576 where  $i$  is an index over the units,  $j$  is an index over  $N$  samples collected using MCMC, and  
 577  $\delta_j^i$  is the estimated delay. In the case of the late units, we considered only the response  
 578 time of correct actions. Fig 12 left displays the mean arrival and response times. These  
 579 were submitted to four separate ANOVA tests, which revealed that PP had a significant  
 580 effect on all four units: early unit ( $F_{2,138} = 9.2, p < 10^{-3}$ ), late antisaccade ( $F_{2,138} =$   
 581  $26.6, p < 10^{-3}$ ), late prosaccade ( $F_{2,138} = 19.6, p < 10^{-3}$ ), and inhibitory unit ( $F_{2,138} =$   
 582  $30.9, p < 10^{-3}$ ). We then explored the differences across conditions through planned  
 583 post hoc tests on each condition for each of the units (Table 6). The arrival times of the  
 584 early unit did not change significantly between condition PP20 and PP50, but decreased  
 585 significantly in the PP80 condition as compared to the PP50 block. The response times of  
 586 late antisaccades increased significantly between the PP20 and the PP50 conditions but  
 587 not so between the PP50 and PP80. Late prosaccades followed the opposite pattern,  
 588 showing only a significant decrease in response time between the PP50 and PP80  
 589 conditions. Finally, the inhibitory unit changed significantly across all conditions.



**Fig 12. Model parameters.**

Left: Mean arrival or response time and standard error of the early and inhibition units and late pro- and antisaccades. Right: Probability of a late antisaccade  $p(U_a > U_p)$  in prosaccade (red) and antisaccade (blue) trials in each condition in the probit scale.

590

**Table 6. Post hoc comparison of the effect of PP.**

	Early			Inhib.			Late pro.			Late anti.		
	Mean [ms]	$t_{138}$	p	Mean [ms]	$t_{138}$	p	Mean [ms]	$t_{138}$	p	Mean [ms]	$t_{138}$	p
PP20- PP50	4	0.6	0.50	-30	-4.0	<0.001*	3	0.5	0.55	-24	-36	<0.001*
PP20- PP80	26	3.9	<0.001*	-58	-7.8	<0.001*	32	5.7	<0.001*	-32	-5.4	<0.001*
PP50- PP80	22	3.3	0.001*	-28	-3.8	<0.001*	29	5.1	<0.001*	-7	-1.5	0.13

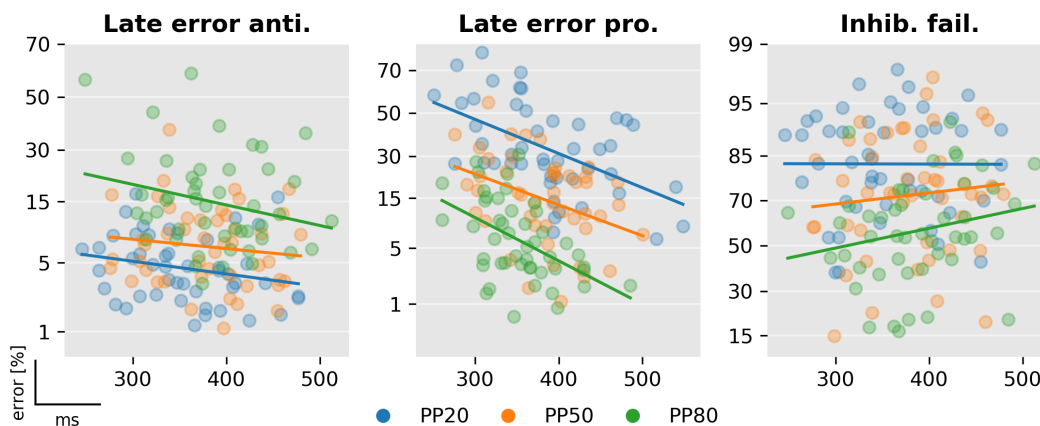
Effect of PP on the mean arrival time for each of the early, inhibitory units, and the late pro and antisaccade units in the corresponding trial type.

591 Finally, we examined how the probability of a late antisaccade  $p(U_a > U_p)$  (Fig 12, right)  
 592 depended on PP and TT. The estimated parameters for both pro- and antisaccade trials  
 593 were analyzed with a model with factors SUBJECT, TT, PP and the interaction between  
 594 TT and PP. An ANOVA test demonstrated that both PP ( $F_{2,276} = 51.2, p < 10^{-3}$ ) and TT  
 595 ( $F_{1,276} = 985.0, p < 10^{-3}$ ) had a significant effect, but there was no evidence for an  
 596 interaction between the two factors ( $F_{2,276} = 1.5, p = 0.23$ ), suggesting that PP affected  
 597 the probability of a late antisaccade equally in pro- and antisaccade trials.

### 598 **Subject specific parameters**

599 Finally, we investigated how some of the parameters of the model were related to each  
 600 other across subjects. Because it has been commonly reported that schizophrenia is  
 601 related with higher ER, but also with increased antisaccade RT, an interesting question is  
 602 whether higher late-action response times are correlated with the percentage of late  
 603 errors and inhibition failures, i.e., early saccades that are not stopped. We found that the  
 604 response time of late pro ( $F_{1,135} = 13.6, p < 0.001$ ) and antisaccades ( $F_{1,135} = 7.1, p <$   
 605  $0.01$ ) was negatively correlated with the probability of a late error (Fig 13), but no  
 606 significant interaction between PP and response time was found (pro:  $F_{2,135} = 1.7, p =$   
 607  $0.19$ ; anti  $F_{2,135} = 0.3, p = 0.76$ ). Hence, late responders tended to make fewer late  
 608 errors, suggesting a speed/accuracy trade-off in addition to the main effect of PP. We  
 609 further considered the question whether the percentage of inhibition failures was  
 610 correlated with the expected arrival time of the late antisaccade unit in antisaccade trials  
 611 (Fig. 13 right). Note that the number of inhibition failures is the same in both trial types

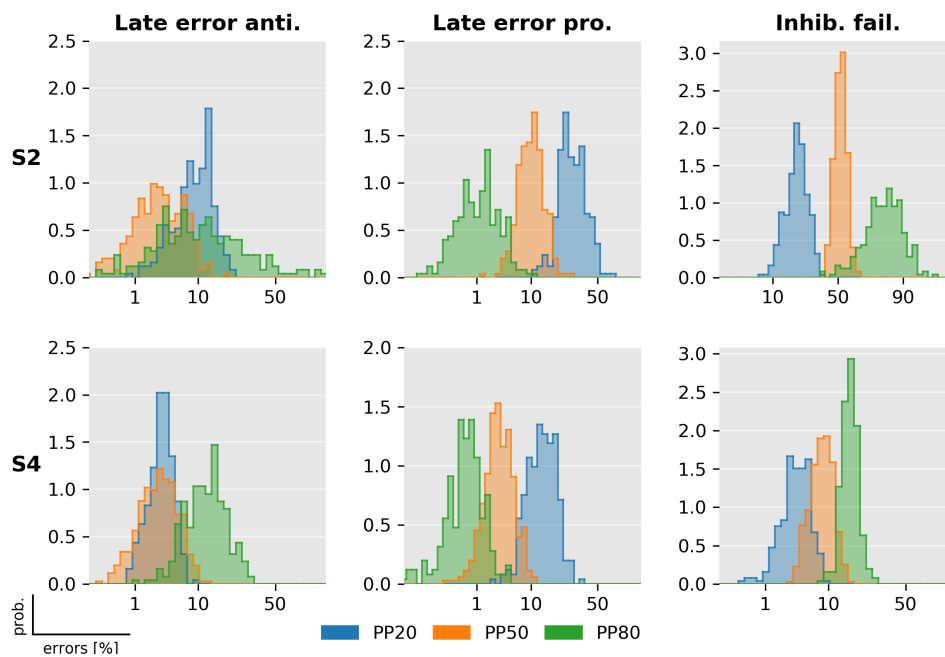
612 in a constrained model, but inhibition failures are errors in antisaccade trials and correct  
613 early reactions in prosaccade trials. We found that these parameters were not  
614 significantly correlated ( $F_{2,135} = 1.2, p = 0.26$ ). This was also the case when we  
615 considered the expected response time of late prosaccades in prosaccade trials (not  
616 displayed;  $F_{2,135} = 0.0, p = 0.98$ ).



**Fig 13. Correlation between late arrival times and errors**

Left: Percentage of late errors against late antisaccades' response times in antisaccade trials. Center: Percentage of late errors against late prosaccades' response time in prosaccade trials. Left: Percentage of inhibitory failures against late antisaccades' response time in antisaccade trials. The horizontal axis is in the probit scale.

617 Fig 14 illustrates the posterior distribution of late errors and inhibition failures of two  
618 representative subjects as estimated using MCMC. Clearly, PP induced strong differences  
619 in the percentage of inhibition failures and late errors in prosaccade trials in both  
620 subjects. The effect of PP is less pronounced in late errors in antisaccade trials. The  
621 posterior distributions also illustrate how the  $SERIA_{lr}$  model can capture individual  
622 differences: For example, the percentage of late prosaccade errors in the PP80 condition  
623 and the percentage of inhibition failures across all conditions are clearly different in each  
624 subject.



**Fig 14. Posterior distribution of late errors and inhibition failures**

The posterior distribution of the percentage of late and inhibitory failures of two exemplary subjects (see Fig 8 and 13). Samples from the posterior distribution were obtained using MCMC. Histograms display the distributions of the samples in the probit scale (horizontal axis). For these two subjects, the posterior distribution of late prosaccade and inhibitory failures clearly discriminates between the three PP conditions.

625

## 626 **Discussion**

627 In this study, we provided a formal treatment of error rates (ER) and reaction times (RT)  
628 in the antisaccade task using probabilistic models. We applied these models to data from  
629 an experiment consisting of 3 mixed blocks with different probabilities of pro- and  
630 antisaccades trials. Model comparison showed that a novel model that allows for late pro-  
631 and antisaccades explains our experimental findings better than a model in which all late  
632 responses are assumed to be antisaccades. The parameter estimates of the hidden units  
633 of the model showed that changes in the inhibition unit and a late decision process  
634 explained most of the overt changes in behavior caused by our experimental  
635 manipulation, i.e., differences in trial type probability. Moreover, we found that all units  
636 were sensitive to the PP in a block, although late responses tended to plateau when the  
637 corresponding trial type was not highly frequent.

638 Our main finding is that two decision processes are necessary to properly model the  
639 antisaccade task: on one hand, an early race between a prepotent response towards a  
640 target and an endogenously generated signal to cancel this action, and, on the other hand,  
641 a secondary late race between two units encoding the cue-action mapping. Although the  
642 late decision process can be closely approximated by assuming that RT and actions are  
643 independent (at least in our experimental design), Bayesian model comparison  
644 demonstrated that late decisions are more accurately described by a race between two  
645 units representing different actions. The two decision processes are the sources of early  
646 errors –fast prosaccades in antisaccade trials- and late errors –late actions incongruent  
647 with the cue presented. The late decision process displays a speed/accuracy tradeoff and  
648 is biased by the probability of a trial type in a block. Moreover, this decision process  
649 predicts the RT distribution of corrective antisaccades that follow early errors. Because  
650 the extra latency of these corrective antisaccades (80ms) is much lower than the average  
651 time by which the erroneous prosaccade is terminated, it is unlikely that corrective  
652 antisaccades are due to a restart in the decision process, but rather these are late actions  
653 that overwrite early errors.

### 654 **Influence of trial type probability on reaction times and error rates**

655 Our results show that both RT and ER depend on PP. While this was a highly significant  
656 factor in our study, there are mixed findings in previous reports. ER in antisaccade trials  
657 was found to be correlated with TT probability in several studies [29,46,47]. However,



658 this effect might depend on the exact implementation of the task [47,48]. Changes in  
659 prosaccade ER similar to our study have been reported by [29] and [48]. Studies in which  
660 the type of saccade was signaled at fixation prior to the presentation of the peripheral cue  
661 do not always show this effect [47]. The results on RTs are less consistent in the literature.  
662 Our findings of increased anti- and decreased prosaccade RTs with higher PP are in line  
663 with the overall trend in [29], and with studies in which the cue was presented centrally  
664 [29,47]. Often, there is an additional increase in RT in the PP50 condition [29,47], which  
665 was visible in our data as a slight increase in RT in the PP50 condition on top of the linear  
666 effect of PP. Overall, RTs in our study were relatively slow compared to studies in which  
667 the TT cue was separated from the spatial cue [46,47]. However, a study with a similar  
668 design and added visual search reported even slower RTs in both pro- and antisaccades  
669 [29].

## 670 **Interpretation of model comparison results**

671 Formal comparison of generative models can offer insight into the mechanisms  
672 underlying eye movement behavior [11] and might be relevant in translational  
673 neuromodeling applications, such as computational psychiatry [49-53]. Here, we have  
674 presented what is, to our knowledge, the first formal statistical comparison of models of  
675 the antisaccade task. For this, we formalized the model introduced in [17] and proceeded  
676 to develop a novel model that relaxes the one-to-one association of early and late  
677 responses with pro- and antisaccades, respectively. All models and estimation techniques  
678 presented here are openly available under the GPLv3.0 license as part of the open source  
679 package TAPAS ([www.translationalneuromodeling.org/tapas](http://www.translationalneuromodeling.org/tapas)).

680 Bayesian model comparison yielded four conclusions at the family level. First, the SERIA  
681 models were clearly favored when compared to the PROSA models. Second, including a  
682 late race between actions representing late pro- and antisaccades (SERIA<sub>lr</sub>) resulted in an  
683 increase in model evidence, compared to a model not including a late race (SERIA). Third,  
684 models in which the race parameters of the early and inhibitory unit were constrained to  
685 be equal across TT had a higher LME than models in which all parameters were free.  
686 Hence, the effect of the cue in a single trial was limited to the late action, and did not affect  
687 the race between an early and inhibitory process. This constitutes an important external  
688 validation, as it means that model comparison does favor a model which respects the  
689 temporal order of the experiment: Information about TT is only available after the

690 stimulus was presented and, thus, it is unlikely to have an impact of the fast reactive  
691 responses. Fourth, early responses were nearly always prosaccades. Crucially, these four  
692 conclusions are based on family-wise comparison across all parametric distribution of  
693 the increase rate of the units.

694 A further consequence of our findings is that two independent and qualitatively different  
695 decision processes lead to an antisaccade: the race process between early and inhibitory  
696 units, and the secondary decision process that generates late responses. A separation of  
697 decisions into a ‘where’ and a ‘when’ component has been proposed by [54], but mainly  
698 in conceptual terms. However, model comparison showed that these two components  
699 (‘where’ and ‘when’) cannot be completely dissociated and that time plays a role in the  
700 late decision. Nevertheless, the assumption that action type and arrival time of late  
701 responses were independent yielded a good fit to this particular data set, suggesting that  
702 it is, in many cases, an acceptable approximation to assume a time-independent late  
703 decision process. The most obvious difference between the SERIA and SERIA<sub>lr</sub> can be  
704 observed in prosaccade trials in the PP20 condition (left panel, upper half plane Fig. 9),  
705 in which late prosaccades are slower than antisaccades. We discuss this point in more  
706 detail later.

#### 707 *Parametric distribution of reaction times*

708 The parametric distribution of oculomotor RTs has been discussed in great detail in the  
709 literature (e.g., [13,55]). Here, we did not aim at determining the most suitable  
710 distribution, but rather opted for a practical approach by evaluating different models  
711 with a reduced number of parametric distributions. We then based our conclusions on  
712 the model with the highest LME. Nevertheless, one can consider the connection of the  
713 models presented here with other families of parametric distributions. In particular, the  
714 linear relationship

$$\frac{S_i}{r_i} = t \quad (38)$$

715 could be seen as to be formally inconsistent with the observation that RT are likely to be  
716 explained by stochastic accumulation processes (see for example [56,57], but [58]). This  
717 is a weaker constraint than one would expect, because under low noise conditions, for  
718 example, the linear relationship can be a good approximation of neural activity. Even if

719 the relationship is not linear, for any continuous function  $\phi$  with an inverse function  $\phi^{-1}$ ,  
 720 the model can be recasted as [59]:

$$s_i = \phi(tr_i), \quad (39)$$

$$\phi^{-1}(s_i)/r_i = t. \quad (40)$$

721 In any case, linear accumulation models have been shown to yield similar conclusions to  
 722 stochastic accumulation models [58].

723 More generally, it can be shown that if RTs follow a generalized inverse normal  
 724 distribution (GIN) of the form

$$GIN(t; \lambda, \kappa, \psi) = \frac{(\psi/\kappa)^\lambda}{2K_\lambda(\sqrt{\kappa\psi})} t^{\lambda-1} \exp\left(-\frac{1}{2}(\kappa t^{-1} + \psi t)\right) \quad (41)$$

725 where  $\lambda \leq 0$ , and  $K_\lambda$  is a modified Bessel function of the second kind, there exists a  
 726 continuous diffusion process whose first hit distribution (FHD) follows the GIN [60]. A  
 727 particular case of this distribution is the Wald distribution for which  $\lambda = -\frac{1}{2}$ ,  $\kappa = 0$ . It is  
 728 the FHD of the Brownian diffusion process with drift

$$X_t = -\sqrt{\sigma}\psi t + \sigma W_t \quad (42)$$

729 where  $W_t$  denotes a Wiener process,  $x_0 > 0$ , and the absorbing boundary  $a$  is zero. More  
 730 relevant here, when  $\psi = 0$  the distribution reduces to an inverse gamma distribution, the  
 731 FHD of the process

$$X_t = \sqrt{\sigma}(2\lambda - 1) t^{-1} + \sigma W_t \quad (43)$$

732 with  $x_0 > 0$  and boundary  $a = 0$  (for a detailed mathematical treatment see [60]). Thus,  
 733 if the rates of a ballistic, linear processes are assumed to be gamma distributed, the RTs  
 734 follow a distribution that is formally equivalent to a first hit model with stochastic  
 735 updates and fixed rates. While the model presented here can be seen as a ballistic  
 736 accumulation model, this equivalence suggests that it is *compatible* with a diffusion  
 737 process with infinitesimal mean change proportional to  $t^{-1}$ .

738 *Other antisaccade models*

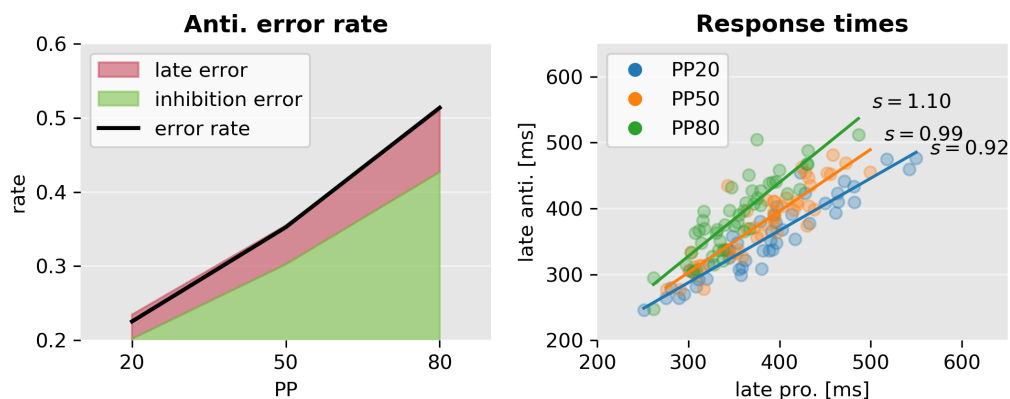
739 In broad terms, three families of antisaccade models can be distinguished (reviewed in  
740 [61]). The first set of models is based on a race process with independent saccadic and  
741 stop units. These models build on the seminal work of [16] on the stop-signal paradigm.  
742 According to this model, a 'GO' signal triggers a stochastic 'race' process that generates a  
743 response once it reaches threshold. Critically, a stop signal triggers a second process that  
744 inhibits the first 'GO' response if it is the first to reach threshold. Importantly, the pace of  
745 both units is mutually independent. This model was further extended for the antisaccade  
746 task by [17] (but see [14,21], and the review in [20]), who included a third unit such that  
747 an antisaccade is generated when a reflexive prosaccade is inhibited by an endogenously-  
748 triggered stop process. Note that the original 'horse-race' model has also been modified  
749 [62] to account for different competing response actions, similarly as in the antisaccade  
750 task. The models proposed here belong to this family.

751 A second type of model relies on lateral or mutual inhibition of competing pro- and  
752 antisaccade units. In this direction, Cutsuridis and colleagues [61,63,64] proposed that  
753 lateral inhibition is implemented by inhibitory connections in the intermediate layers of  
754 the superior colliculus. Thus, saccades are the result of accumulation processes, but these  
755 are not independent of each other. Crucially, no veto-like stop signal is required. Although  
756 no formal model-fitting has been proposed for this model, qualitative agreement with  
757 data suggests that it might capture behavioral patterns relevant in translational  
758 applications [64,65]. Since no probabilistic version of this model is available, it is not yet  
759 possible to decide on the grounds of model comparison whether mutually dependent or  
760 independent race processes best explain current behavioral findings.

761 Finally, several models that incorporate detailed physiological mechanisms have been  
762 proposed [23,66-68]. These models cannot be easily assigned to one of the above  
763 categories, as they often employ both an inhibitory mechanism that stops or withholds  
764 the reactive responses as well as competition between actions. In addition, while more  
765 realistic models possess a more fine-grained representation of the underlying  
766 neurobiology, they rely on a large number of parameters and for this reason, it is difficult  
767 to fit them to behavioral data (for discussion, see [11]).

768 Regarding neurobiologically realistic models, the model proposed by [23] is the most  
769 similar to the SERIA model. It posits two different mechanisms that interact in the

770 generation of antisaccades: an action-selection module and a remapping module that  
771 controls the cue-action mapping. As a consequence, this model allows for the generation  
772 of late errors that follow a similar RT distribution as correct antisaccades. Consistent with  
773 this observation, the SERIA model can quantitatively distinguish between inhibition and  
774 late cue-action mapping errors (Fig 15, left panel). A less obvious similarity between the  
775 SERIA model and [23] is that different cues do not lead *directly* to different dynamics in  
776 the action module, but only in the so-called ‘remapping’ module. Furthermore, the  
777 incorporation of a late race is conceptually close to the approach proposed by [23], which  
778 includes a winner take all competition in what we have referred here as late responses.  
779 Similarly, our model comparison results show that different cues (i.e., trial types) do not  
780 affect the GO/NO-GO process but only the late cue-action mapping.



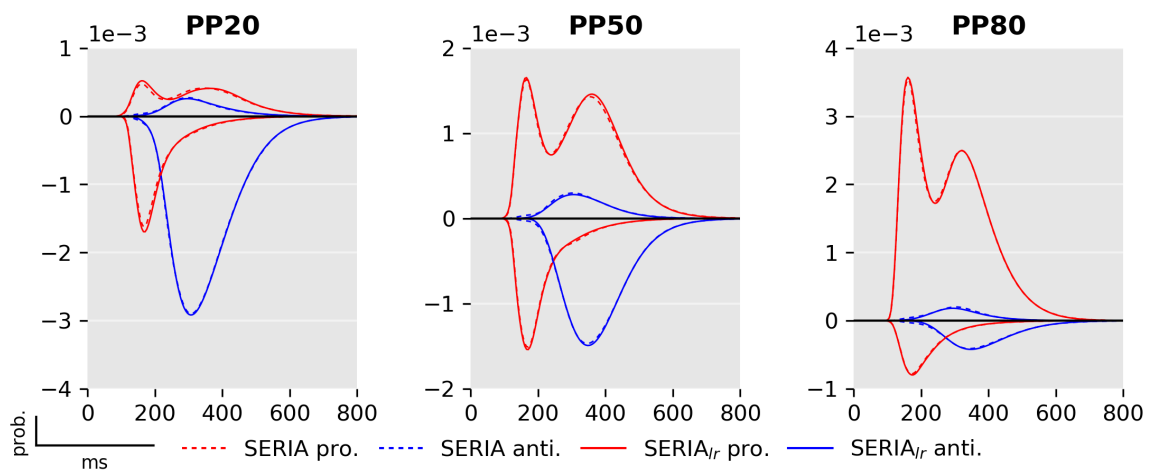
**Fig 15. Error sources and the correlation of response times**

Left: Error rate (black line) split into the two causes predicted by the model. Inhibition errors are early actions that always trigger prosaccades. Similarly as described by [23], late errors occur when a late response leads to a prosaccade. Right: Correlation between correct antisaccade and late prosaccades response times according to the best SERIA<sub>lc</sub> model. The best linear fit is depicted as a solid line. The mean ratio of pro- and antisaccade response times ( $s$ ) is displayed on the right. Although late pro- and antisaccade response times are highly correlated, their ratio is different in each condition (interaction PP and late prosaccade response time  $F = 9.2, p < 0.001$ ).

## 781 **Parameter changes across trial types**

782 One of the most salient results presented here is that models in which the parameters of  
783 the units were constrained to be equal across trial types had a larger LME than models in  
784 which all the parameters were free, suggesting that the early and inhibitory race units  
785 were not affected by the cue presented on a single trial. While visual inspection of the  
786 predicted likelihood under the posterior parameters showed that most of the prominent

787 characteristics of the data were explained correctly, some more subtle effects were not  
788 captured accurately by the SERIA model. This is particularly clear in the PP20 condition,  
789 in which the SERIA model displays a large bias in prosaccades trials in the PP20 condition.  
790 One possible explanation is that restricting the parameters across trial types made the  
791 model too rigid to capture this effect. Fig 16 compares the fitted RT distributions for  
792 models  $m_8$  (SERIA) and  $m_{13}$  (SERIA<sub>lr</sub>), in which no constraint on the parameters was  
793 imposed. Both models are qualitatively almost identical, although as shown in Fig 7, the  
794 LME favored the SERIA<sub>lr</sub> model. Thereby, the qualitative similarity between both models  
795 indicates that, in our experiment, the RT of late decisions is only weakly dependent on  
796 time. In conclusion, although removing the constraint on the parameters did improve the  
797 fit, the differences are marginal and, thus did not justify the additional model complexity.  
798 As mentioned above this is consistent with the notion that the information about trial  
799 type is only available to the subject once the peripheral stimulus (green bar) has been  
800 processed. Presumably tens of milliseconds after the stimulus onset. In fact, this example  
801 illustrates the protection against overfitting provided by the LME, as this is a case in  
802 which simpler models were preferred over more complex models despite of slightly less  
803 accurate fits.



**Fig 16: Comparison between unconstrained SERIA and SERIA<sub>lr</sub> models.**

Comparison between models  $m_8$  (broken lines; SERIA model) and  $m_{13}$  (solid lines; late race SERIA<sub>lr</sub> model.).

804 Arguably, the constrained SERIA model fails to fully capture the RT of late prosaccade in  
805 the PP20 and PP50 conditions because of the assumption that late prosaccades have the  
806 same arrival time as late antisaccades. As shown in Fig 15, although the response time of

807 late pro- and antisaccades are strongly correlated, the average ratio of the response times  
808 changes across conditions.

### 809 **The effect of trial type probability**

810 It is far from obvious why TT probability affects RT and ER in the antisaccade task. One  
811 possible explanation is that increased probability leads to higher preparedness for either  
812 pro- or antisaccades. Such a theory posits an intrinsic trade-off between preparations for  
813 one of the two action types that leads to higher RTs and ERs in low probability trials.  
814 Thus, a trade-off theory predicts that the arrival times of early and late responses should  
815 be negatively correlated. Although this hypothesis can explain our behavioral findings in  
816 terms of summary statistics, our model suggests a more complicated picture.

817 The main explanation of our results is the effect of TT probability on the inhibitory unit  
818 and the probability of a late prosaccade. A higher probability of antisaccade trials leads  
819 to faster inhibition and to a higher number of late prosaccades. This resulted in higher  
820 mean RT in prosaccade trials when PP is low. In the case of antisaccades, although the  
821 mean arrival times of the late unit increased in the PP50 condition, the increased arrival  
822 time of the inhibitory unit on the PP80 condition skewed the antisaccade distribution  
823 towards higher RTs. Nevertheless, the  $SERIA_{lf}$  implies the anticorrelation of late pro- and  
824 antisaccades in a single trial type, as these are the results of a GO-GO race.

### 825 **Action inhibition**

826 The biological implementation of action inhibition in the antisaccade and other  
827 countermanding tasks has received a lot of attention and is still debated [69-73]. Our  
828 work adds evidence to the theory that the antisaccade task requires a process that  
829 inhibits prepotent responses and is independent of the initiation of a late action [20].  
830 Recent evidence from electrophysiological recordings in the rat brain ([74] reviewed by  
831 [71]) suggests that the hypothesized race between go and inhibitory responses might be  
832 implemented by different pathways in the basal ganglia [68]. In addition to the basal  
833 ganglia, microstimulation of the supplementary eye fields tends to facilitate inhibition of  
834 saccades in the countermanding task [75].

### 835 **Corrective antisaccades**

836 Although not a primary goal of our model, we considered the question of predicting  
837 corrective antisaccades. This problem has received some attention recently



838 [18,61,65,76], as more sophisticated models of the antisaccade task have been developed.  
839 We speculated that corrective antisaccades are generated by the same mechanism as late  
840 responses. Thus, their RT distribution should follow a similar distribution. Our results  
841 strongly suggest that this is the case (see Fig 11). Moreover, the time delay of the  
842 corrective antisaccades indicates that, on average, these actions are not the result of the  
843 late unit being restarted at the end time of the erroneous prosaccade, as this would lead  
844 to much higher RTs. Rather, the planning of a corrective antisaccade might be started  
845 much before the end of the execution of an erroneous prosaccade, in accordance with the  
846 parallel planning model of the antisaccade task [46] and the 'GO - STOP+GO' model in  
847 [21].

### 848 **Translational applications**

849 Despite the large number of studies of clinical patients using the antisaccade task, an  
850 important question remains open: What are the causes of the errors in different  
851 neurological and psychiatric conditions? For example [77,78] argued that errors in  
852 schizophrenia might be explained, at least partially, by a failure to generate a secondary  
853 late action based on several modifications of the antisaccade task. However, it was also  
854 proposed that the increased ER in schizophrenia is due to high tonic dopamine levels in  
855 the basal ganglia, that lead to decreased inhibition of early responses [68]. More  
856 generally, different neurological and psychiatric diseases, or even patients with the same  
857 condition, might be characterized by a different source of errors. For example, there is  
858 intriguing evidence [79] that patients with different diseases such as attention deficits  
859 disorders [80], Parkinsons' disease [81], and amyotrophic lateral sclerosis [82] might be  
860 characterized by different ratios of early and late errors. An interesting experimental  
861 finding in our study related to this is the considerable amount of erroneous antisaccades  
862 in prosaccade trials. An increased number of such errors could be caused by reduced  
863 cognitive flexibility leading to impaired shifting between tasks as observed for example  
864 in obsessive compulsive disorder [83]. The ability to quantify different types of errors  
865 through computational modeling might help to further characterize these diseases.

### 866 **Summary**

867 Here we have presented a novel model of the antisaccade task. While the basic structure  
868 of the model follows the layout of a previous model [17], we have introduced two crucial  
869 advancements. First, we postulated that late responses could trigger both pro- and



870 antisaccades, which are selected by an independent decision process. Second, the  
871 generative nature of our model allows for Bayesian model inversion, which enables the  
872 comparison of different models and families of models on formal grounds. To our  
873 knowledge this has not been done for any of the previous models of the antisaccade task,  
874 which is of relevance for translational applications that aim at better understanding  
875 psychiatric diseases by means of computational modeling.

876 The application of the model to a large data set yielded several novel results. First, the  
877 early and inhibitory race processes triggered by different cues are almost identical.  
878 Moreover, different PP had very different effects on the individual units, which was not  
879 obvious from the linear analysis of the mean RT and ER.-Crucially, our modeling approach  
880 allowed us to look at a mechanistic explanation or the effects of PP by examining the  
881 individual units. In future work we aim to disentangle the mechanisms of behavioral  
882 differences caused by neuromodulatory drugs and psychiatric illnesses using formal  
883 Bayesian inference.

884

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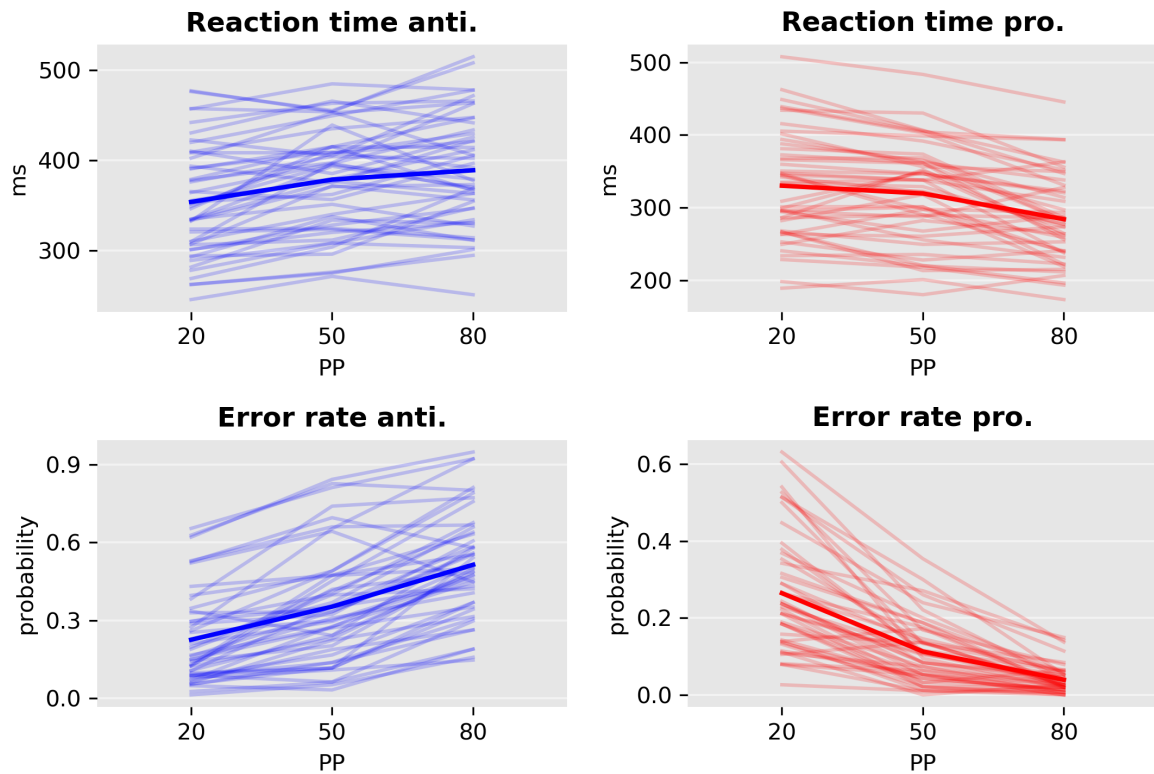
887 for their helpful comments on an earlier version of this manuscript.

## 888 **Supporting Information**

### 889 **Supporting information 1**

890 **S1\_Dataset.zip. Table of Data.** Spreadsheet including all reaction times, actions and  
891 errors that entered the analysis. More details are included directly in the file.

### 892 **Supporting information 2**



#### **S2: Reaction time and error rate in all conditions for each subject.**

Mean reaction times and error rates are displayed as solid lines.

893

894

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