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Beta-blocker propranolol modulates decision urgency during sequential information gathering

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Beta-blocker propranolol modulates decision urgency during sequential information gathering

Abbreviated title: Propranolol modulates information gathering

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45 **Abstract**

46 Arbitrating between timely choice and extended information gathering is critical for
47 effective decision making. Aberrant information gathering behaviour is thought to be a
48 feature of psychiatric disorders, such as schizophrenia and obsessive-compulsive disorder,
49 but we know little about the underlying neurocognitive control mechanisms. In a double-
50 blind placebo-controlled drug study involving 60 healthy human subjects (30 female), we
51 examined the effects of noradrenaline and dopamine antagonism on information gathering
52 during performance of an information sampling task. We show that modulating noradrenaline
53 function with 40 mg of the beta-blocker propranolol leads to decreased information gathering
54 behaviour. Modulating dopamine function via a single dose of 400 mg amisulpride revealed
55 some effects that were intermediate between those of propranolol and placebo. Using a
56 Bayesian computational model, we show sampling behaviour is best explained by inclusion
57 of a nonlinear urgency signal that promotes commitment to an early decision. Noradrenaline
58 blockade promotes the expression of this decision-related urgency signal during information
59 gathering. We discuss the findings with respect to psychopathological conditions that are
60 linked to aberrant information gathering.

61
62 **Significance Statement**

63 Knowing when to stop gathering information and commit to a choice option is non-
64 trivial. This is an important element in arbitrating between information gain and energy
65 conservation. In this double-blind, placebo-controlled drug study, we investigated the role of
66 catecholamines noradrenaline and dopamine on sequential information gathering. We found
67 that blockade of noradrenaline led to a decrease in information gathering. Dopamine
68 blockade showed an intermediate, but non-significant, effect. Using a Bayesian

69 computational model, we show that this noradrenaline effect is driven by an increased
70 decision urgency, a signal that reflects an escalating subjective cost of sampling. The
71 observation that noradrenaline modulates decision urgency suggests new avenues for treating
72 patients that show information gathering deficits.

73 **Introduction**

74 A precipitous decision without the benefit of sufficient information is often
 75 detrimental especially if the outcome has non-trivial consequences (e.g., buying a house). By
 76 contrast, excess information gathering for trivial decisions (e.g., which toothpaste to buy)
 77 wastes both time and energy. A dilemma posed by arbitrating between extended information
 78 gathering versus more time-efficient, albeit less well informed, choice is often referred to as a
 79 speed-accuracy trade-off (Martin and Müller, 1899; Henmon, 1911).

80 A speed-accuracy tradeoff is well captured in sequential information gathering tasks
 81 (Huq et al., 1988; Chamberlain et al., 2007). Several psychiatric disorders, including
 82 schizophrenia, are consistently associated with a reduced propensity to gather information,
 83 often termed as ‘jumping-to-conclusions’. Such behaviour is found in patients (e.g., Fear and
 84 Healy, 1997; Moutoussis et al., 2011; Dudley et al., 2016) but is also a feature of prodromal
 85 states (Rausch et al., 2016) and first-degree relatives (Van Dael et al., 2006). This contrasts
 86 with patients diagnosed as having obsessive-compulsive disorder (OCD) who tend to gather
 87 more information (Volans, 1976; Fear and Healy, 1997; Pélissier and O’Connor, 2002; Voon
 88 et al., 2016; Hauser et al., 2017c, 2017b), although not ubiquitously so (Chamberlain et al.,
 89 2007; Jacobsen et al., 2012; Grassi et al., 2015).

90 The neurocognitive control mechanisms that drive these effects are unknown. Using
 91 Bayesian computational modelling, we recently showed that one key contributor is a decision
 92 urgency signal that promotes timely decisions (Hauser et al., 2017c, 2017b). The neural
 93 processes that modulate urgency signals in sequential information gathering remain
 94 unknown. In this study, we examine the role of catecholaminergic neuromodulators in
 95 information gathering. Dopamine is implicated in the genesis of schizophrenia (Laruelle,
 96 2013), but previous studies found inconsistent results about its role in jumping to conclusions
 97 (Menon et al., 2008; So et al., 2010; Ersche et al., 2011; So et al., 2012; Andreou et al., 2013;

98 Ermakova et al., 2014; Andreou et al., 2015). Other evidence points to a critical role for
99 noradrenaline, including the role in signalling uncertainty (Aston-Jones and Cohen, 2005; Yu
100 and Dayan, 2005; Dayan and Yu, 2006), suggesting this neuromodulator might play a role
101 during information gathering.

102 Here, we assessed the contributions of both dopamine and noradrenaline to
103 information gathering in 60 healthy subjects. Using a double-blind placebo-controlled design,
104 we examined the effects of catecholaminergic antagonists with a high specificity for either
105 dopamine (amisulpride) or noradrenaline (propranolol). We show that blocking noradrenaline
106 by means of propranolol modulates information gathering in an information sampling task,
107 whereas dopamine antagonism by means of amisulpride did not cause a significant change in
108 behaviour. Using computational modelling, we demonstrate that the effect of propranolol is
109 best accounted for via alteration of an urgency signal.

110 **Materials and Methods**

111 *Subjects*

112 We conducted a double-blind, placebo-controlled, between-subjects study involving
 113 three groups of 20 subjects each. Subjects were randomly allocated to one of the three groups
 114 (ensuring an equal gender balance) after excluding those who met the following exclusion
 115 criteria: a history of psychiatric or neurological disorder, regular medication (except
 116 contraceptives), current health issues, any drug allergies. The groups did not differ in their
 117 mood (PANAS) (Watson et al., 1988), intellectual ability (WASI abbreviated version)
 118 (Wechsler, 1999) or age (Table 1). Data from the same sample has been reported previously
 119 (Hauser et al., 2017a) that addressed a different topic. UCL research ethics approved this
 120 study and all subjects provided written informed consent.

121

122 *Drug groups*

123 To assess the effects of neurotransmitters dopamine and noradrenaline on information
 124 gathering, we used three different drug conditions. The noradrenaline group received 40 mg
 125 of propranolol (β -adrenoceptor antagonist). The dopamine group received 400 mg of the
 126 D2/3 antagonist amisulpride. We selected these drugs because they have an affinity for the
 127 targeted neurotransmitter with a high specificity. The dopamine group received the active
 128 drug 120 minutes prior to the task and an additional placebo 30 minutes after the first drug.
 129 The noradrenaline group first received a placebo, and after 30 minutes the active drug. A
 130 third, placebo group received placebo at both time points. This schedule aligned with
 131 procedures used in previous studies investigating the effects of dopamine or noradrenaline on
 132 cognition (e.g., Silver et al., 2004; Gibbs et al., 2007; De Martino et al., 2008; Hauser et al.,
 133 2017a; Kahnt and Tobler, 2017).

Experimental design: information gathering task

We examined sequential information gathering using a modified version of an information sampling task (Clark et al., 2006; Hauser et al., 2017c, 2017b). In each game, subjects saw 25 covered cards (depicted by gray squares, Fig. 1A) and had to decide whether the majority of cards comprised yellow or blue (colours varied across games). Using a computer mouse, the subjects were allowed to open as many cards as they wished before committing to one of the two colours.

The first 15 games belonged to a ‘fixed’ condition, in which there was no external cost for sampling more information. Subjects received 100 points for correct decisions and lost 100 points for incorrect decisions, independent of the number of cards opened or the time spent on task prior to decision. The second 15 games belonged to a ‘decreasing’ condition, in which information gathering was accompanied by a reduction in potential wins: starting from a potential win of 250 points, opening each card led to a 10-point reduction in wins (e.g. win after 5 opened cards: $250 - 5 * 10 = 200$ points). Incorrect decisions were punished with -100 points irrespective of the amount of prior sampling.

Before the first game, subjects performed a single practice game to familiarise themselves with the task. After each decision, subjects were informed about their winnings and then directly moved to the next game. The game sequences were selected so that 10 games in each condition were relatively difficult with a generative probability close to 50% (similar to that in the original information sampling task; (Clark et al., 2006)). An additional 5 sequences were easier with a clearer majority (generative probabilities of a binomial process $p \sim .7$) to allow for a broader variability in information gathering (order of sequences was randomised).

158

159 *Statistical analysis*

160 In this study we tested whether blockade of dopamine or noradrenaline function
 161 impacted on information gathering behaviour. The number of draws before a decision is a
 162 good indicator for the amount of information that a subject opts to collect before making a
 163 decision. We thus analysed this behavioural metric using a repeated-measures ANOVA with
 164 the between-subject factor group (propranolol, amisulpride, placebo) and the within-subject
 165 factor condition (fixed, decreasing). Effects were further assessed using independent-sample
 166 t-tests. Effects sizes are indicated using partial eta-squared and Cohen's d. As secondary
 167 measures, we also assessed whether a group won more points or was less accurate in their
 168 decision making (i.e. how often subjects decided for a current minority of cards) using the
 169 same statistical procedures.

170

171 *Computational modelling*

172 To understand cognitive mechanisms of how decisions arise, and to probe deeper into
 173 how drugs impact these cognitive processes, we used a Bayesian computational model that
 174 we previously developed and validated for this task (Hauser et al., 2017c, 2017b). In brief,
 175 the winning model assumes that at each state of the game subjects arbitrate between three
 176 actions: deciding for yellow, deciding for blue, continuing with sampling (non-deciding).
 177 This arbitration is based on a decision policy, which in turn is based state-action Q-values
 178 (Watkins, 1989) of each option. The Q-values for deciding in favour of either colour are
 179 computed as the outcome of a correct/incorrect decision, weighted by their inferred
 180 likelihood (i.e. 'how likely am I to win if I decide for yellow now, given the cards I have
 181 opened so far?'). The action-value for continuing sampling indexes the value of future states

182 (using backwards induction), plus a subjective cost per step. Notably the latter captures an
 183 urgency to decide that arises as sampling continues.

184 Here, we reiterate the key equations of the winning model for completeness. Please
 185 see Hauser et al. (2017c) for a more detailed description and discussion (also cf Moutoussis et
 186 al., 2011; Hauser et al., 2017b). Our model assumes that subjects try to infer the colour that
 187 forms the majority of cards, based on the cards seen so far. This means that the subjects infer
 188 the probability that the majority of cards belongs to a particular colour (e.g. yellow (y))
 189 $P(MY | n_y, N)$, where MY depicts a majority of yellow cards, n_y the number of opened
 190 yellow cards, and N the total number of opened cards.

191 $P(MY)$ is fully determined as soon as 13 or more of the opened cards belong to one
 192 colour (of a total number of cards: $N_{tot}=25$). Otherwise, it can be inferred by calculating the
 193 probability of the majority of cards being yellow, given a specific generative probability q
 194 (proportion of yellow and blue cards in the machinery that produces the sequence), weighted
 195 by the likelihood of this generative probability based on the currently seen cards:

$$\begin{aligned}
 P(MY | n_y, N) &= \int_0^1 P(MY | q, n_y, N) P(q | n_y, N) dq \\
 &= \sum_{Y > N_{tot}/2}^{N_{tot} - (N - n_y)} \int_0^1 \text{Bin}(Y - n_y | q, N_{tot} - N) P(q | n_y, N) dq
 \end{aligned}
 \tag{1.1}$$

197 The first expression is a binomial of getting $Y - n_y$ yellow draws out of $N_{tot} - N$, given
 198 generative probability q . The second expression is the probability of the q being the
 199 generative probability. This can be calculated using Bayes rule:

$$dq P(q | n_y, N) = \frac{P(n_y | q, N) P_0(q)}{\int P(n_y | q', N) P_0(q') dq'} dq \tag{1.2}$$

203 We assume that the probability of n yellow draws of N total draws follows a binomial
 204 distribution and that the prior belief about the generating q follows a beta distribution with
 205 the parameters α and β (here $\alpha=1, \beta=1$).

206 The beliefs about the majority of cards are subsequently translated into action-values.
 207 The action value of choosing Y , ($Q(Y)$), is the product of reward/cost of choosing the right or
 208 wrong option (R_{cor} , R_{inc}) and the success-probabilities of these actions. $Q(B)$ is calculated
 209 analogously.

$$210 \quad Q(Y | n_y, N) = R_{cor} P(MY | n_y, N) + R_{inc} P(MB | n_b, N) \quad (1.3)$$

211 The rewards of correctly (R_{cor}) and incorrectly declaring (R_{inc}) can be cast in different
 212 ways. According to the objective instructions, in the fixed condition R_{cor} is set to 100 and R_{inc}
 213 to -100. For the decreasing condition, we compared two different formulations. In our main
 214 model ('subjective'), we also kept R_{cor} constant in the decreasing condition. This was done so
 215 that the subjective costs (c_s , cf below) soak up the subjectively perceived overall costs, i.e. a
 216 combination of externally imposed and internally generated costs. This way, we can
 217 investigate the subjectively perceived total costs. Alternatively, we formulated an 'objective'
 218 costs model, where R_{cor} changes as a function of step (250, 240, 230, ...), as set up in the
 219 task. This 'objective' model only differed in the decreasing, but not in the fixed condition.
 220 Additionally, R_{inc} was kept at -100 for all models and conditions (as per instructions). For the
 221 simulation of an optimal model (green diamonds in Fig. 1), we used the objective model and
 222 assumed no additional costs-per-step.

223 The action value of not deciding ($Q(ND)$) computes the value of future states in terms
 224 of the future action values and their probabilities. Additionally, a cost per step is imposed that
 225 assumes that there are internal (and external) costs that emerge when continuing with
 226 sampling (urgency signal). $Q(ND)$ is calculated using backward induction to solve the
 227 Bellman equation, using state values $V(s')$ and a cost per step c_s :

$$V(s') = \sum_{\text{all available } a \text{ in } s'} \pi(a, s') Q(a, s') \quad (1.4)$$

$$Q(ND | n_y, N) = -c_s + \sum_{s'=\left\{\begin{smallmatrix} n_y+i \\ N+1 \end{smallmatrix}\right\}}^{i=[0,1]} P(s' | n_y, N) V(s') \quad (1.5)$$

The probability of reaching state s' and seeing i new yellow items is based on the current belief state, which in turn is mainly determined by the current evidence n_y, N . Thus:

$$P(s' | n_y, N) = \int_{\text{all } q} \text{Bin}(i | 1, q) P(q | n_y, N) dq \quad (1.6)$$

The choice policy π for the state-action space is specified as the following softmax function with decision temperature parameter τ and irreducible noise (lapse rate) parameter ξ (cf Guitart-Masip et al., 2012):

$$\pi(ND | n_y, N) = \frac{e^{Q(ND|n_y, N)/\tau}}{e^{Q(Y|n_y, N)/\tau} + e^{Q(B|n_y, N)/\tau} + e^{Q(ND|n_y, N)/\tau}} (1 - \xi) + \frac{\xi}{3} \quad (1.7)$$

Decision urgency: nonlinear sigmoidal cost function

We compared two different possible cost functions: fixed cost per sample ('linear') vs a model in which the costs per sample increased according to a sigmoid function ('nonlinear', cf below). The latter could capture the possibility that subjects felt an increasing urgency (Cisek et al., 2009) to decide, for instance if it becomes increasingly annoying to gather more samples with potentially little informational content and waste time, similar to previous reports that show that costs increase nonlinearly (Drugowitsch et al., 2012; Murphy et al., 2016).

We implemented the nonlinear cost function as a sigmoid, where the cost per step c_s (eq. (1.5)) changes on each step n (1, ..., 25):

$$c_s = \frac{10}{1 + e^{-10(n-p)}} \quad (1.8)$$

250 The free impatience parameter p describes the indifference point, i.e. at what stage in
 251 the game the agent becomes impatient. We set the scaling factor as well as the slope
 252 parameter to 10. Model comparison revealed that fixing these parameters led to an equal
 253 performance in terms of model fit, and thus outperformed other, more complex models that
 254 had these parameters as free parameters. Parameter p was independently modelled in the two
 255 conditions, allowing for different urgency trajectories.

256 Studies investigating urgency in perceptual decision making have used different forms
 257 of nonlinear urgency signals, such as exponentials (e.g., Drugowitsch et al., 2012). In our
 258 task, these urgency signals are different in that they influence the planning (value of non-
 259 deciding) rather than a decision threshold directly. This means that the actual costs for
 260 continuing sampling are weighted sums of the future costs, and consequently, even if c_s itself
 261 plateaus, the adversarial effects can still grow (ultimately linearly). We lack sufficient data
 262 for determining exact form of the nonlinearly escalating urgency.

263

264 *Model fitting and model comparison*

265 We optimized the parameters to maximise a LogLikelihood for each participant
 266 individually. We used a genetic algorithm implemented in Matlab (Goldberg, 1989) (300
 267 generations, crossover-heuristic for generation of children, 4 individuals to survive in next
 268 generation). Initial population/parameter for all subjects was based on results from a previous
 269 study (Hauser et al., 2017b) and we bounded the parameter space based on these previous
 270 studies, their definitions within the model and their psychological meaning (p : [0 25], τ : [1
 271 10], ξ : [0 .5]). In every case, we ensured the best fitting parameters each fell within these
 272 boundaries.

273 For model comparison, we used summed AIC (Akaike, 1973) and BIC (Schwarz,
274 1978). The best fitting model was then used for further analyses as reported in the results
275 section.

276 Similar to our previous findings (Hauser et al., 2017c, 2017b), a subjective costs
277 model (AIC: 13079, BIC: 13333) clearly outperformed an objective model that incorporates
278 the explicit external costs (AIC: 17875, BIC: 18129). Further, we found that a model with a
279 nonlinear cost-function outperformed a linear cost model (AIC: 9709, BIC: 10133). This
280 means that decision urgency arises in a nonlinear, sigmoidal fashion, escalating as sampling
281 continues. This model also outperformed a logistic regression model recently proposed by
282 Malhotra et al. (2017), where choice was predicted by evidence difference and time (AIC:
283 17582, BIC: 17920). Thus, our findings accord with the sort of nonlinear urgency-signals
284 considered to influence a class of perceptual decision making problems (e.g., Churchland et
285 al., 2008; Cisek et al., 2009; Drugowitsch et al., 2012; Murphy et al., 2016).

286 Further model comparison revealed that a model with only one free parameter p (mid-
287 point of a sigmoid) per condition in the cost function achieved the same model fits as more
288 complex versions with additional free parameters, and thus outperformed these models in
289 terms of AIC and BIC (AIC: 9331, BIC: 9585). Simulations using this winning model
290 revealed similar behavioural patterns as seen in subjects' actual behaviour (Fig. 2A-C). The
291 significant difference for sampling under propranolol, the similar number of draws before
292 decision, and the total points won suggests that our winning model captures subjects' actual
293 task behaviour, as well as it describes group differences accurately. This means we can
294 investigate the model to better understand whether there are meaningful computational
295 differences between groups. Moreover, we performed a parameter recovery analysis of the
296 winning model and found that we are well able to recover the parameters (Fig. 2D).

297 To assess how noradrenaline modulated the computational mechanisms underlying
298 information gathering, we focused on a comparison between placebo and propranolol and
299 whether the decision urgency arose at different time points. To do this we derived the model
300 parameter p that modulates the emergence of the urgency signals as well as the model-
301 derived urgency signal itself. A group difference for the latter was assessed using cluster-
302 extent permutation tests (Nichols and Hayasaka, 2003), similar to that used in our previous
303 studies (Hauser et al., 2017b, 2017c). Because of the non-independence between samples, we
304 computed the cluster size of the true effect and compared it against a null distribution of
305 cluster sizes from randomly permuted data ($p < .05$, height threshold $t=1$, 1000 permutations).
306 This is a common approach in neuroimaging data analyses, for which the data show similar
307 features (e.g., Hunt et al., 2013; Hauser et al., 2015).
308

309 Results

310 *Noradrenaline blockade decreases information gathering*

311 An analysis of the number of draws before declaring a choice, as an index for
 312 information gathering, revealed a main effect of group, supporting a significant drug effect on
 313 information gathering (Fig. 1B, $F(2,57)=4.29$, $p=.018$, $\eta^2=.131$). Follow-up analysis showed
 314 this effect was driven by a reduction in information gathering in the noradrenaline compared
 315 to a placebo group in both conditions (fixed condition: $t(38)=2.55$, $p=.015$, $d=.81$; decreasing
 316 condition: $t(38)=2.71$, $p=.010$, $d=.86$). The dopamine group showed an intermediate effect
 317 but did not significantly differ from either group (fixed condition: vs placebo: $t(38)=1.53$,
 318 $p=.134$, $d=.48$; vs noradrenaline: $t(38)=1.08$, $p=.286$, $d=.34$; decreasing condition: vs placebo:
 319 $t(38)=1.47$, $p=.150$, $d=.47$; vs noradrenaline: $t(38)=1.47$, $p=.149$, $d=.46$). A split-half between
 320 early and later trials replicated the propranolol effect for each half, and did not reveal any
 321 additional amisulpride effect, arguing against drug-induced learning differences. A main
 322 effect of condition, but no interaction with group, indicated that subjects across placebo and
 323 drug conditions gathered more information in the fixed compared to the decreasing condition
 324 (condition main effect: $F(1,57)=145.92$, $p<.001$, $\eta^2=.719$; interaction: $F(2,57)=.528$, $p=.592$,
 325 $\eta^2=.018$).

326

327 *No significant drug effects on winnings or accuracy*

328 To test whether the noradrenaline or dopamine drug affected other aspects of
 329 performance, we compared the total points won as well as accuracy of decisions. There was
 330 no group effect on winnings (Fig. 1C, $F(2,57)=.04$, $p=.961$, $\eta^2=.001$) or an interaction
 331 ($F(2,57)=1.67$, $p=.198$, $\eta^2=.055$), suggesting that the reduced information gathering in
 332 noradrenaline was not large enough to impact subjects' winnings. This absence of a

333 difference in winnings (placebo vs propranolol: fixed condition: $t(38)=1.32$, $p=.195$, $d=.42$;
 334 decreasing: $t(38)=-1.06$, $p=.294$, $d=.33$) reflects the fact that most sequences had a generative
 335 probability close to 50%. Therefore, a decrease in information/decrease in costs under
 336 propranolol were not large enough to percolate through to actual winnings. The groups did
 337 not differ in choice accuracy (Fig. 1D, evident in a lack of main effect of group:
 338 $F(2,57)=1.90$, $p=.159$, $\eta^2=.063$; the absence of an interaction: $F(2,57)=.86$, $p=.428$, $\eta^2=.029$).
 339 This indicates the drug manipulation did not impact on general motivation to solve the task
 340 correctly.

341

342 *Propranolol promotes urgency-to-decide*

343 To understand the cognitive processes that drive a lowered information gathering
 344 disposition in the noradrenaline group, we fitted a Bayesian computational model (cf. Hauser
 345 et al., 2017c, 2017b) to individual subjects' data. Decision policy of the best fitting model as
 346 a function of evidence and sampling is depicted in Fig. 3.

347 In the model, the speed with which subjects make a decision is modulated by two
 348 separate processes: a finite horizon and subjective urgency. The former arises because there is
 349 a limit on the number of cards such that whenever 13 cards of the same colour are opened,
 350 opening more cards does not provide further information. The latter, however, is not build
 351 into the task explicitly (especially in the fixed condition), but is based on a finding that
 352 subjects apparently become more liberal in their decision criterion as sampling progresses
 353 (Cisek et al., 2009; Drugowitsch et al., 2012; Thura and Cisek, 2014; Murphy et al., 2016;
 354 Malhotra et al., 2017). In the model, urgency is captured by a subjective cost for each sample,
 355 and we found that it arises in a nonlinear fashion (being low in the beginning but escalates
 356 over the course of sampling). The cost arose significantly earlier in the noradrenaline

357 compared to placebo condition in both conditions (Fig. 4, fixed: $p=.003$, decreasing $p=.029$)
 358 reflecting their lower number of draws.

359 We compared the individually fitted model parameters between groups and found a
 360 group effect in the repeated-measures ANOVA ($F(2,57)=4.42$, $p=.016$, $\eta^2=.134$) for the
 361 parameter p . This describes the mid-point of an escalating urgency signal. Subsequent t-tests
 362 revealed that the noradrenaline group expressed significantly lower parameter values in both
 363 conditions (Table 2; p_{fixed} : $t(38)=2.60$, $p=.013$, $d=.82$; $p_{decreasing}$: $t(38)=2.94$, $p=.006$, $d=.93$),
 364 meaning subjective costs/urgency arise significantly earlier in the sampling process. The
 365 dopamine group, again, did not differ from other groups (p_{fixed} : vs placebo: $t(38)=-1.30$,
 366 $p=.201$, $d=.41$; vs noradrenaline: $t(38)=1.21$, $p=.232$, $d=.38$; $p_{decreasing}$: vs placebo: $t(38)=-$
 367 1.10 , $p=.279$, $d=.35$; vs noradrenaline: $t(38)=1.54$, $p=.132$, $d=.48$). The choice stochasticity
 368 parameter τ ($F(2,57)=.25$, $p=.783$, $\eta^2=.009$) as well as the lapse rate parameter ζ
 369 ($F(2,59)=1.10$, $p=.340$, $\eta^2=.037$) did not yield significant group differences.

370 A similar effect was found when analysing a (worse-fitting) logistic regression (as
 371 suggested in Malhotra et al., 2017), where a time-dependent predictor was significantly
 372 increased in the propranolol group (fixed condition: placebo $\beta=0.858\pm0.576$; propranolol:
 373 $\beta=1.189\pm0.431$; $t(38)=-2.05$, $p=.047$; decreasing condition: placebo: $\beta=1.375\pm0.672$;
 374 propranolol: $\beta=1.987\pm0.914$; $t(38)=-2.41$, $p=.021$), with no difference in the intercept (fixed
 375 condition: placebo $\beta=-3.941\pm0.962$; propranolol: $\beta=-3.561\pm0.906$; $t(38)=-1.28$, $p=.207$;
 376 decreasing condition: placebo: $\beta=-3.440\pm1.302$; propranolol: $\beta=-3.603\pm1.337$; $t(38)=.39$,
 377 $p=.698$), which hints towards a stronger collapse of a decision threshold rather than a lowered
 378 initial threshold. However, we caution that the insights afforded by the simplicity of this
 379 analysis does not compensate for its limited accuracy in capturing the data, compared to the
 380 cognitive model (in terms of fit quality or BIC).

381

382 Discussion

383 An arbitration between gathering more information and time-efficiency is a non-
 384 trivial aspect of decision making, and it is thought to go awry in a range of psychiatric
 385 disorders such as schizophrenia or OCD (Fear and Healy, 1997; Moutoussis et al., 2011;
 386 Hauser et al., 2017c, 2017b). We show that inhibiting noradrenergic function by means of a
 387 noradrenergic beta-adrenoceptor blockade leads to decreased information gathering. Using
 388 computational modelling we show that noradrenaline blockade has a primary effect on a
 389 component of the decision process that reflects an ‘urgency to decide’. Urgency signals
 390 facilitate decision making, and have primarily been described in perceptual decision making
 391 (Cisek et al., 2009; Drugowitsch et al., 2012; Thura and Cisek, 2014; Murphy et al., 2016).
 392 Our results demonstrate that a similar urgency signal plays a role in sequential information
 393 gathering, where a decision urgency arises nonlinearly.

394 Our computational modelling showed that noradrenaline directly modulates how
 395 quickly an urgency signal arises. Inhibiting noradrenaline function led to an earlier
 396 emergence of this urgency signal. Theories of noradrenaline functioning suggest that it
 397 influences cognition at different timescales, with tonic and phasic noradrenaline expressing
 398 distinct functional roles (Aston-Jones and Cohen, 2005; Yu and Dayan, 2005; Dayan and Yu,
 399 2006). Because our manipulation is likely to influence both tonic and phasic noradrenaline, a
 400 specific contribution of one, or other, cannot be inferred from our data. We note a recent
 401 perceptual decision making study (Murphy et al., 2016) supports the idea that phasic
 402 noradrenaline might be critical for decision urgency. The authors showed that phasic pupil
 403 response, a potential indicator for phasic noradrenaline (Joshi et al., 2016), is linked to longer
 404 decision times possibly signalling a delayed emergence of an urgency signal. Whether such
 405 phasic noradrenaline promotes urgency directly, or whether it is mediated indirectly by

406 signalling unexpected uncertainty (Dayan and Yu, 2006), which in turn delays an arising
 407 urgency, can be addressed in future studies.

408 Our findings suggest that manipulating noradrenaline could benefit patients whose
 409 information gathering is aberrant. In particular, we showed previously that compulsive
 410 subjects and patients with OCD gather information excessively and that this is due to a
 411 delayed emergence of decision urgency (Hauser et al., 2017c, 2017b). The antagonistic effect
 412 of propranolol on this urgency signal raises the theoretical possibility that this agent might
 413 alleviate an indecisiveness found in OCD patients. We are not aware of any study that has
 414 investigated the role of noradrenergic beta-receptor blockade in the treatment of OCD.
 415 Indirect evidence for the viability of this mode of intervention comes from observation with
 416 the therapeutic agent clomipramine. This is a first-line treatment for OCD (Koran et al.,
 417 2007) whose mode of action comprises complex noradrenergic effects including a down-
 418 regulation of beta-adrenoceptor density (Asakura et al., 1982), that might attenuate the impact
 419 of endogenous noradrenaline on beta-adrenoceptor related functions. Additionally,
 420 augmenting clomipramine with pindolol, a beta-blocker, is reported to have positive effects
 421 on OCD symptoms (Koran et al., 2007; Sassano-Higgins and Pato, 2015). These findings
 422 would support a more systematic examination of whether propranolol has beneficial effects
 423 for OCD patients in general, or more specifically patients where there is evidence for
 424 prepotent excessive information gathering behaviour.

425 Previous studies on the effects of dopaminergic drugs on sequential information
 426 gathering have produced mixed results. In schizophrenia, anti-psychotic medication does not
 427 directly alleviate jumping-to-conclusion behaviour (Menon et al., 2008; So et al., 2010,
 428 2012), and even remitted patients express intermediate levels of information gathering
 429 (Moutoussis et al., 2011). In healthy subjects, only one study found a more cautious decision
 430 making after dopamine D2/3 agonist administration (Ersche et al., 2011), while several other

431 studies did not find an effect of either dopamine enhancing or reducing medications (Andreou
 432 et al., 2013; Ermakova et al., 2014; Andreou et al., 2015). Using amisulpride, we found no
 433 significant effect on information gathering. However, in almost all analysis, the effects of
 434 amisulpride were intermediate between placebo and propranolol, and non-significantly
 435 different from propranolol. These results suggest that amisulpride induces a similar, albeit
 436 weaker, effect than our noradrenaline manipulation. Whether this is due to a less direct
 437 influence of dopamine on information gathering, or whether it might be due to a lower
 438 effective dose of amisulpride (as compared to propranolol) remains unclear. We believe the
 439 latter is less likely as there have been several studies showing significant effects of such a
 440 dose on cognition (e.g., Ramaekers et al., 1999; Kahnt and Tobler, 2017), but multiple
 441 administrations of amisulpride, as in patient treatment, might reveal a different effect.

442 A limitation of this study is that although we selected drugs that preferentially target
 443 dopamine or noradrenaline function, these agents have known effects on other systems. In
 444 particular, although propranolol has a high affinity for beta-adrenoceptors (Fraundorfer et al.,
 445 1994), it also has a lesser affinity for serotonin receptors (Hamon et al., 1990). Moreover,
 446 similar to other studies which have investigated the effect of amisulpride on cognitive
 447 functioning, we used only a single dose of this agent (e.g., Burke et al., 2017; Kahnt and
 448 Tobler, 2017). However, this single dose is not comparable to the impact of long-term
 449 antipsychotic treatment, where the therapeutic dosage of amisulpride is often higher and
 450 where there are likely to be complex effects on dopamine transmission. In addition, so as to
 451 be comparable with the clinical studies, we decided to use a relatively brief task. Although
 452 the length of this task provides consistent behavioural findings regarding when subjects
 453 decide on average, a more extended task would allow us also to compute other measures,
 454 such as behavioural decision thresholds. Future, more extended studies could provide

455 additional insight about when and how an urgency signal affects a decision threshold and
456 whether it purely affects the collapse or also its plateau.

457 In conclusion, we show that information gathering is modulated by noradrenergic
458 beta-adrenoceptor blockade. Our computational modelling shows this is mediated via a
459 modulation of a subjective, nonlinear urgency-to-respond signal. The effect of dopaminergic
460 receptor blockade remained inconclusive, with a much weaker effect than that seen for
461 propranolol. An involvement of noradrenaline in this aspect of decision making opens
462 potential avenues for therapy in psychiatric conditions where there is aberrant information
463 gathering.

464

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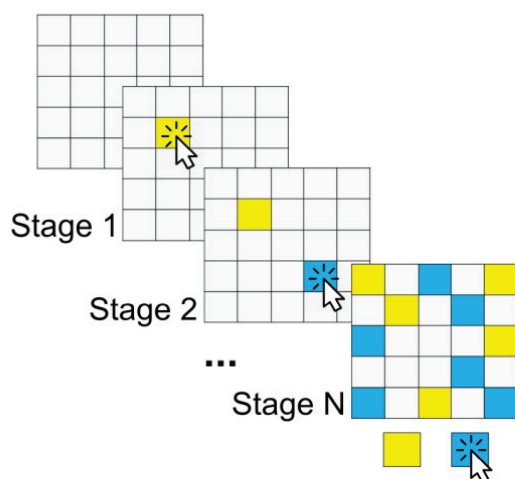
Figure 1. Noradrenaline blockade diminished information gathering. (A) Starting from a fully covered deck of cards, subjects were allowed to open as many cards until they felt ‘certain enough’ to indicate whether they believed the majority of the 25 cards was yellow or blue. In a ‘fixed’ condition, no external costs for sampling applied, but in the ‘decreasing’ condition, a potential win of 250 points reduced by 10 points per uncovered card. (B) Information gathering is decreased consequent on noradrenaline blockade (propranolol), but not consequent on a dopamine perturbation (amisulpride). This increase in impulsivity is consistently observed across both conditions, rendering the statistics of choices in the noradrenaline group closer to those of an optimal model (green diamonds) in the decreasing condition, but further away in the fixed condition. The drug manipulation did not lead to a statistically significant difference in points earned (C), and did not affect choice accuracy (D, the probability of choosing the colour that currently forms the majority of cards at time of decision). * $p < .05$; $\text{mean} \pm 1 \text{ s.e.m.}$

Figure 2. Best-fitting model reproduced behaviour. The model with a nonlinear urgency reproduced subjects’ observed behaviour. We simulated agents with the individual parameters associated with subjects, recovering the differences between placebo and propranolol in the sampling (A), and showing similar patterns in performance (B) and accuracy (C). (D) Parameter recovery analyses were reassuring, especially for the urgency parameters p . * $p < .05$; $\text{mean} \pm 1 \text{ s.e.m.}$

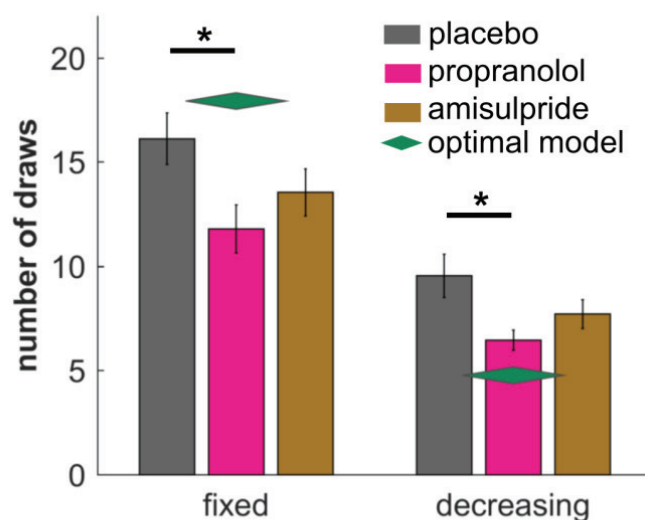
Figure 3. Model policy. The model policy reflects the choice probability for choosing yellow, blue or continuing sampling (pink), depending on the evidence difference (y-axis) and the information gathering stage (x-axis). This depiction shows that subjects are less likely to sample in the decreasing condition in general (less pinkish areas). Also, one can clearly see how a non-decision area is diminished in the propranolol group (middle panels) compared to the placebo group (left panels).

Figure 4. Premature urgency drives noradrenaline-modulated decreases in information gathering. A cost per step signal reflects an emerging urgency to commit to a decision as sampling progresses. This urgency signal arises nonlinearly, escalating significantly earlier in the noradrenaline group in the fixed (A) and the decreasing (B) condition. The group mean of the urgency signal ($\pm 1 \text{ s.e.m.}$) is derived from a sigmoidal model function for subjective costs, which outperformed linear models.

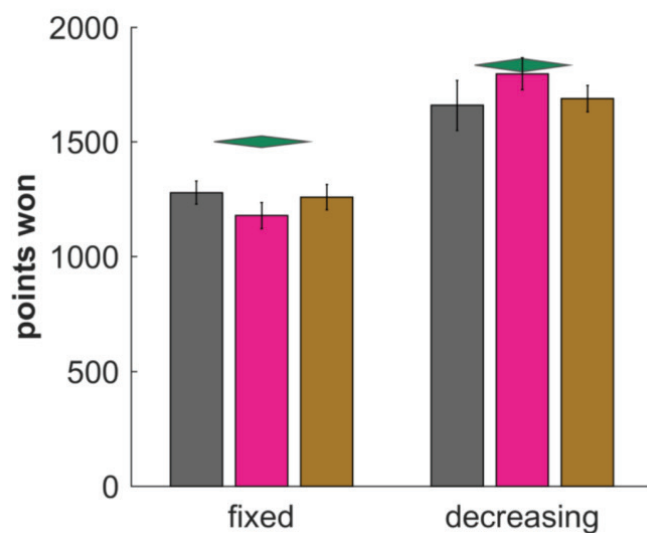
A information gathering task



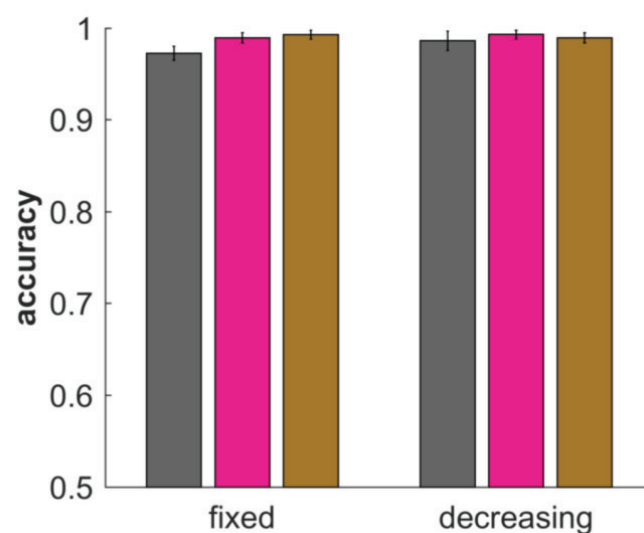
B draws to decision

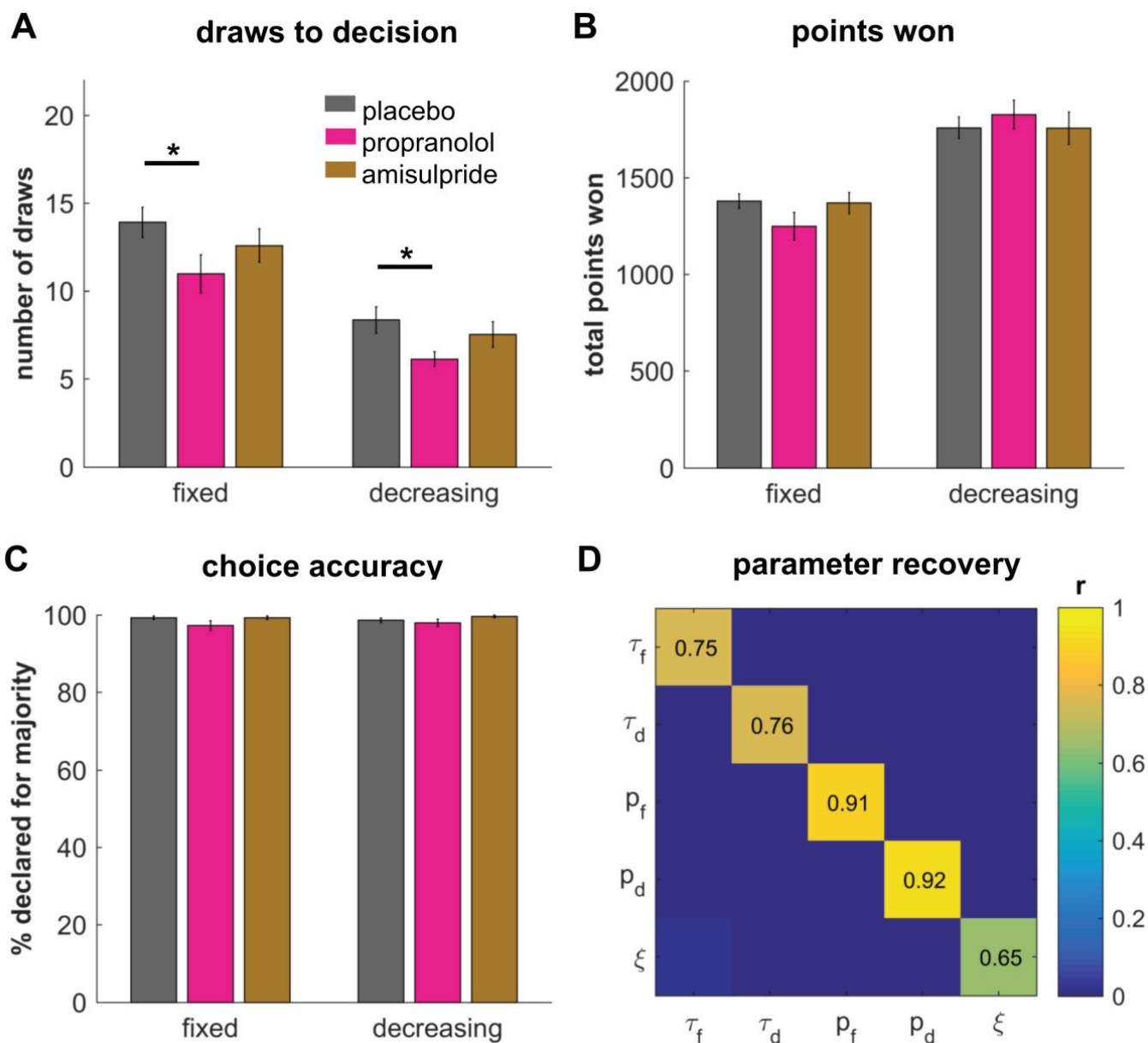


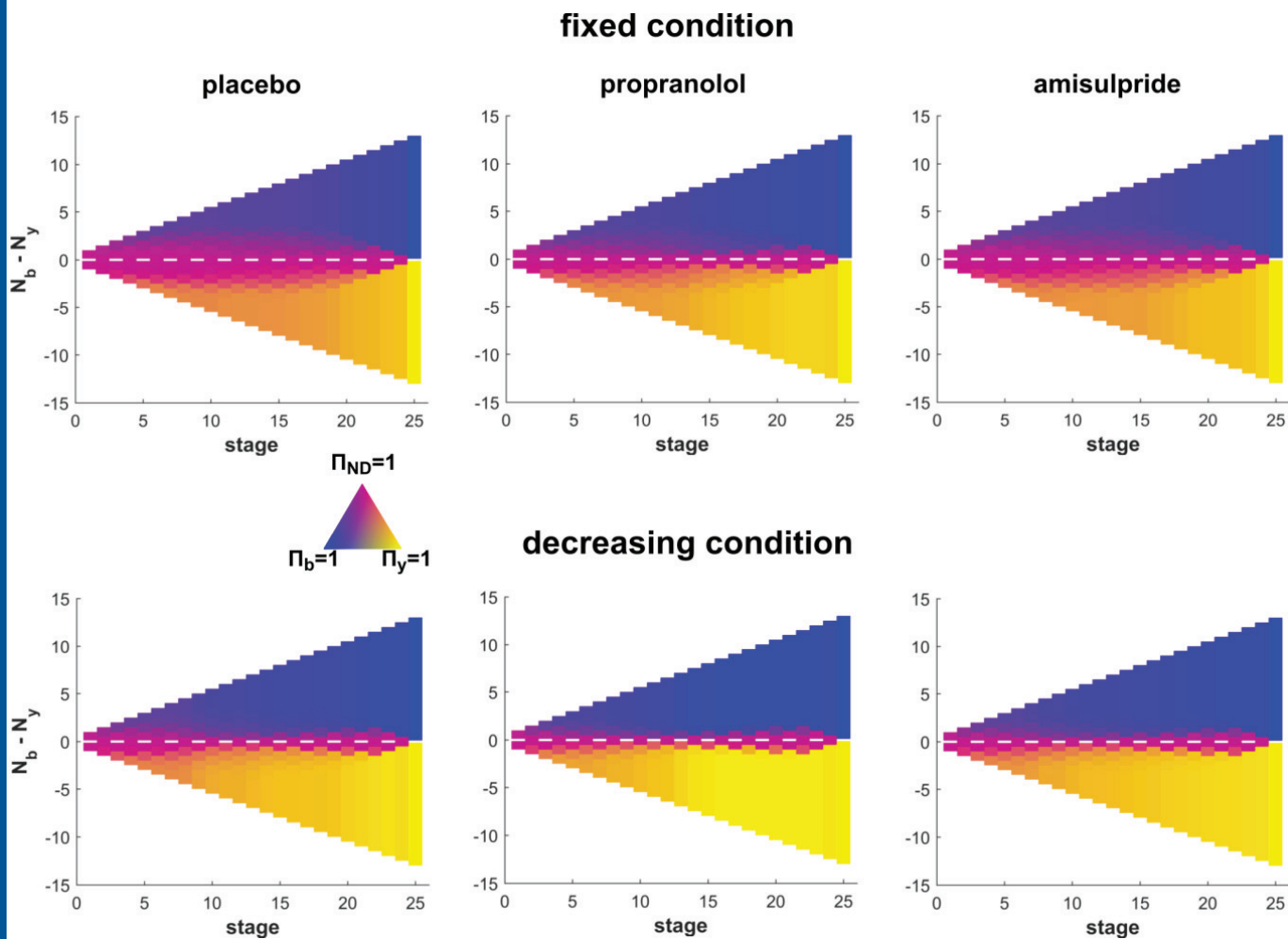
C points won



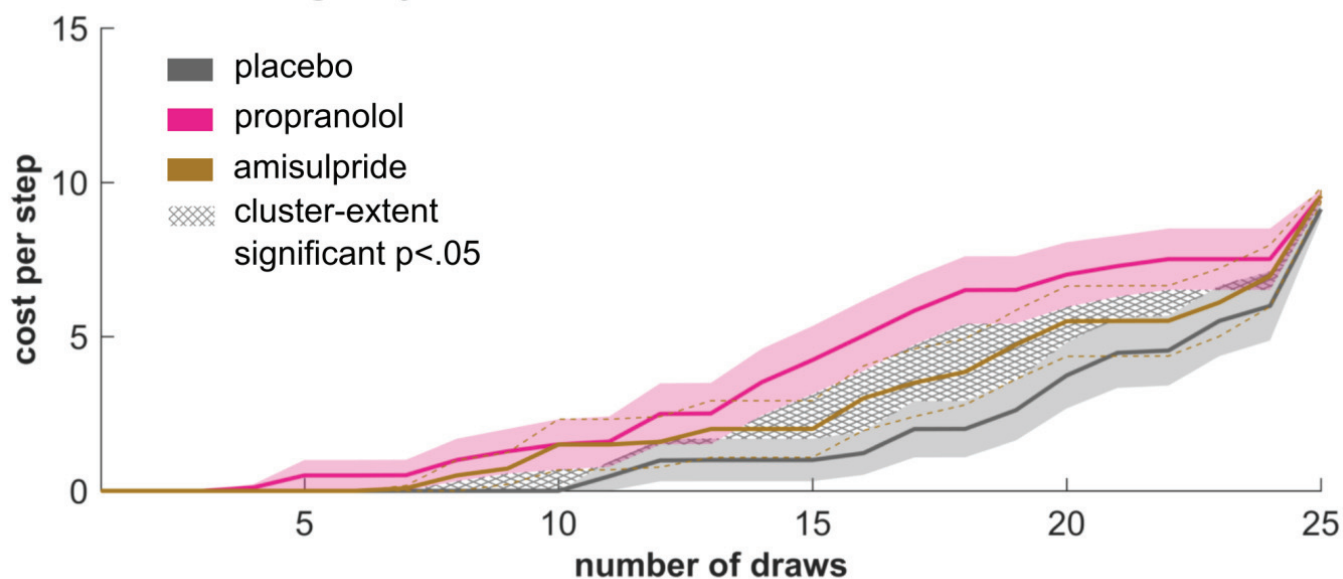
D choice accuracy







A decision urgency, fixed condition



B decision urgency, decreasing condition

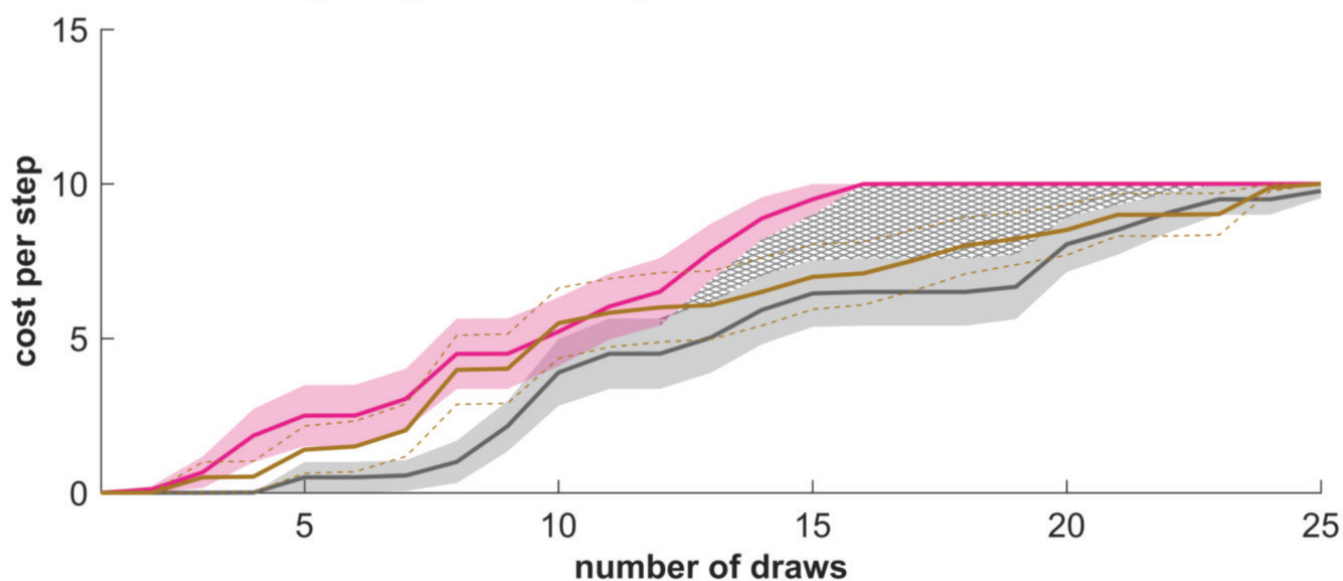


Table 1. Drug group characteristics. The drug groups were matched for an equal gender balance and did not differ in their age, intellectual abilities (WASI) or their affect (PANAS). mean $\pm$ SD.

	placebo	propranolol	amisulpride	
gender (m/f)	10/10	10/10	10/10	
IQ	112.45 $\pm$ 12.22	118.75 $\pm$ 8.55	114.60 $\pm$ 11.77	F(2,57)=1.70 , p=.191
age	24.50 $\pm$ 4.16	23.15 $\pm$ 4.31	22.35 $\pm$ 2.21	F(2,57)=1.74 , p=.185
positive affect	29.22 $\pm$ 10.47	27.15 $\pm$ 7.75	27.80 $\pm$ 8.12	F(2,57)=.286 , p=.752
negative affect	11.45 $\pm$ 2.37	11.95 $\pm$ 4.87	11.25 $\pm$ 1.92	F(2,57)=.236 , p=.790

Table 2. Model parameter comparison. Group comparison reveals that the propranolol group has significantly lower indifference point parameters for both the fixed (p_f) and the decreasing (p_d) condition. This means that their urgency arises earlier in an information gathering process and thus drives them to make more hasty decisions. None of the other parameters were significantly different. mean $\pm$ SD.

	placebo	propranolol	amisulpride	placebo vs propranolol
p_f	21.01 $\pm$ 4.47	16.52 $\pm$ 6.27	18.86 $\pm$ 5.88	t(38)=2.60, p=.013
p_d	13.90 $\pm$ 5.89	9.14 $\pm$ 4.23	11.77 $\pm$ 6.38	t(38)=2.94, p=.006
τ_f	2.85 $\pm$ 2.23	3.30 $\pm$ 2.47	3.26 $\pm$ 2.58	t(38)=-.60, p=.550
τ_d	5.10 $\pm$ 2.74	4.73 $\pm$ 2.35	5.52 $\pm$ 2.68	t(38)=.45, p=.653
ξ	0.004 $\pm$ 0.009	0.007 $\pm$ 0.008	0.004 $\pm$ 0.007	t(38)=-1.21, p=.234