1 Assessing the influence of dopamine and mindfulness on the formation of routines in visual

2 search

3 *Kelly G. Garner[1,2], Li-Ann Leow[2], Aya Uchida[2], Christopher Nolan[1], Ole Jensen[3], Marta I.

4 Garrido[4], & Paul E. Dux[2]

5 [1] School of Psychology, University of New South Wales, Australia

6 [2] School of Psychology, University of Queensland, Australia

7 [3] School of Psychology, University of Birmingham, UK

8 [4] Melbourne School of Psychological Sciences and Graeme Clark Institute for Biomedical

9 Engineering, University of Melbourne, Australia

10 Author Note

11   *denotes corresponding author: kelly.grace.garner@unsw.edu.au

21   Correspondence concerning this article should be addressed to *Kelly G. Garner.

22 E-mail: kelly.grace.garner@unsw.edu.au

Assessing the influence of dopamine and mindfulness on the formation of routines in visual search

Data: 10.48610/a6a65c7

Task code: 10.5281/zenodo.10637597

Analysis code: 10.5281/zenodo.10637593

Abstract

Given experience in cluttered but stable visual environments, our eye-movements form stereotyped routines that sample task-relevant locations, while not mixing-up routines between similar task-settings. Both dopamine signalling and mindfulness have been posited as factors that influence the formation of such routines, yet quantification of their impact remains to be tested in healthy humans. Over two sessions, participants searched through grids of doors to find hidden targets, using a gaze-contingent display. Within each session, door scenes appeared in either one of two colours, with each colour signalling a differing set of likely target locations. We derived measures for how well target locations were learned (target-accuracy), how routine were sets of eye-movements (stereotypy), and the extent of interference between the two scenes (setting-accuracy). Participants completed two sessions, where they were administered either levodopa (dopamine precursor) or placebo (vitamin C), under double-blind counterbalanced conditions. Dopamine and trait mindfulness (assessed by questionnaire) interacted to influence both target-accuracy and stereotypy. Increasing dopamine improved accuracy and reduced stereotypy for high mindfulness scorers, but induced the opposite pattern for low mindfulness scorers. Dopamine also disrupted setting-accuracy invariant to mindfulness. Our findings show that mindfulness modulates the impact of dopamine on the target-accuracy and stereotypy of eye-movement routines, whereas increasing dopamine promotes interference between task-settings, regardless of mindfulness. These findings provide a link between non-human and human models regarding the influence of dopamine on the formation of task-relevant eye-movement routines, and provide novel insights into behaviour-trait factors that modulate the use of experience when building adaptive repertoires.

Introduction

Given stable environmental contingencies, it is adaptive for an organism to develop routine ways of performing tasks requiring multiple responses. Dopamine is assumed to play a key role in the neural computations that underlie the formation of task routines. A large body of evidence shows that dopaminergic midbrain neurons encode reward prediction errors between stimulus-outcome associations (Hollerman & Schultz, 1998; e.g. Schultz, Apicella, & Ljungberg, 1993; Waelti, Dickinson, & Schultz, 2001), and such errors are assumed to underpin the teaching signal that computes the value of actions (Sutton & Barto, 2018). A comparable signal generated in striatum marks the difference between expected and actual saccadic sequence lengths used by macaques to attain reward during visual search (Desrochers, Amemori, & Graybiel, 2015; Desrochers, Jin, Goodman, & Graybiel, 2010). This signal is assumed to reflect a cost-benefit signal that computes the value of saccadic routines. There also exists a large body of evidence from rodent and macaque models suggesting that increased striatal dopamine availability speeds the transition from goal-directed to habitual control of behaviour (Harmer & Phillips, 1998; Nadel et al., 2021, 2021; Nelson & Killcross, 2006), the latter of which is assumed to underlie performance of routines (Desrochers et al., 2015; Dezfouli & Balleine, 2012; Dezfouli, Lingawi, & Balleine, 2014; Graybiel & Grafton, 2015; Smith & Graybiel, 2016). Although this evidence implicates dopamine in the formation of task-relevant routines, whether dopamine availability modulates the formation of saccadic routines in humans remains an open question.

One way to address this question is to increase dopamine availability via administration of levodopa, a precursor to dopamine. levodopa administration in humans has been associated with increased striatal activity in response to positive reward prediction errors, assessed using blood-oxygenation-level-dependent BOLD responses (Pessiglione, Seymour, Flandin, Dolan, & Frith, 2006), and with reduction of exploratory choices during instrumental learning (Chakroun, Mathar, Wiehler, Ganzer, & Peters, 2020; Shohamy,

77 Myers, Geghman, Sage, & Gluck, 2006). This suggests that levodopa may increase the

78 perceived value of actions by inducing optimistic evaluations of outcomes (FitzGerald, Dolan,

79 & Friston, 2015), possibly by disrupting feedback processing (Shohamy et al., 2006).

80 Elevating dopamine availability via levodopa may therefore have a comparable impact on the

81 cost-benefit computations driving the formation of saccadic routines during visual search.

82 Specifically, levodopa may promote an optimistic evaluation of the performed sequence,

83 increasing the probability that it is adopted as a routine.

84   For task-oriented routines to be adaptive, it is also required that they are not mixed-up

85 between tasks, despite overlap in the situational cues and actions that mark task

86 environments. Here we define mix-ups as the performing behaviours that are relevant for the

87 task that is not currently being performed, and we refer to this as task-interference. More

88 broadly, dopamine is assumed to play a modulatory role in the activation of task-relevant

89 behaviours in response to relevant situational cues (Budzillo, Duffy, Miller, Fairhall, &

90 Perkel, 2017), as well as promoting the formation of routines. Patients with Parkinson's

91 Disease consistently show deficits switching between simple sensorimotor tasks (R. Cools,

92 Barker, Sahakian, & Robbins, 2001; Wiecki & Frank, 2010), as do healthy participants who

93 have been administered D2 antagonists (Mehta, Manes, Magnolfi, Sahakian, & Robbins,

94 2004). Such findings have been accounted for by assuming that decreased dopamine causes

95 increased uncertainty about the probability of being in a specific task-state (Friston et al.,

96 2012). These assumptions are based on evidence from constrained tasks - i.e. when single

97 correct responses are required for given stimuli. In contrast, saccadic routines are often

98 formed from a self-selected set of many possible eye-movements, and it is unclear whether

99 dopamine modulates switching between such routines. If a modulation is observed, it is

100 unclear whether the effect of increasing dopamine is opposite to that of depleted dopamine,

101 i.e. does increasing dopamine availability promote segregation of task routines? Or, does

102 increasing dopamine availability make it more difficult to switch between routines, thereby

103 increasing the probability of interference between them?

¹⁰⁴ A further but less frequently discussed component of the processes underlying task

¹⁰⁵ routine learning and deployment, is the brain's execution of task-relevant cues and actions.

¹⁰⁶ Presumably, the organism that encodes an accurate representation of cues, actions and

¹⁰⁷ outcomes is at an adaptive advantage when forming and executing task-relevant routines. A

¹⁰⁸ growing body of empirical evidence suggests that mindfulness may modulate such

¹⁰⁹ representations. Mindfulness has been defined as a mental state that emphasises current

¹¹⁰ sensory and internal inputs (Davids, 1900; Shapiro, Carlson, Astin, & Freedman, 2006), and

¹¹¹ as such is well-placed to promote accurate task-representations. In support of this,

¹¹² mindfulness practice has been associated with increased error monitoring during cognitively

¹¹³ challenging tasks (Andreu et al., 2017), and with greater sensitivity to dynamics in operant

¹¹⁴ reinforcement contingencies (Chen & Reed, 2023; Reed, 2023). This suggests that increased

¹¹⁵ mindfulness is associated with better differentiation between current and previous

¹¹⁶ contingencies of reinforcement, potentially via improved focus on the current contingencies,

¹¹⁷ thereby reducing interference from previous contingencies. Mindfulness has been shown to

¹¹⁸ vary at the trait level and is assessable using standardized questionnaires (e.g. Baer et al,

¹¹⁹ (2006)).

¹²⁰ What could be the modulatory influence of mindfulness on the formation and

¹²¹ deployment of task-relevant routines? The influence of mindfulness on routine learning and

¹²² task-switching may be opposing to the influence of dopamine: individuals low in trait

¹²³ mindfulness are faster to exploit sequential regularities in stimulus-response tasks (Stillman,

¹²⁴ Feldman, Wambach, Howard, & Howard, 2014), and exploitation of such regularities are

¹²⁵ assumed to support habitual responses (Dezfouli & Balleine, 2012; Dezfouli et al., 2014).

¹²⁶ Mindfulness may also promote task-switching; higher levels of trait mindfulness have been

¹²⁷ associated with decreased reliance on past behaviours when stimuli are conserved across

¹²⁸ tasks that carry different cognitive demands (Greenberg, Reiner, & Meiran, 2012; Kuo &

¹²⁹ Yeh, 2015). Indeed, both the reinforcement learning (RL) and active inference frameworks

¹³⁰ have been used to posit that mindfulness and dopamine engage common mechanisms;

increased mindfulness attenuates striatal reward prediction errors (Kirk & Montague, 2015; Kirk, Pagnoni, Hétu, & Montague, 2019), possibly via greater regulation from stronger cortical representations of subjective values and internal states (Kirk, Gu, Harvey, Fonagy, & Montague, 2014). In the active inference framework, both dopamine (FitzGerald et al., 2015; Friston et al., 2012) and mindfulness (Giommi et al., 2023; Laukkonen & Slagter, 2021) are assumed to increase the salience of task relevant cues, by increasing certainty of the estimates of their value. Although increasing dopamine will increase the salience of any cue present, mindfulness prioritises the salience of goal-relevant cues. These theories therefore posit that mindfulness may buffer against the influence of elevated dopamine, either by attenuating elevated reward prediction errors, or by further amplifying the salience of cues according to their goal-relevance. Despite these assumed common mechanisms of influence, it remains to be quantitatively tested whether mindfulness interacts with dopamine during the performance and execution of task-relevant visual routines.

Using a novel protocol designed to test the formation and execution of task-relevant saccadic routines in humans, we sought to test whether administration of levodopa increased suboptimal routine formation, and whether increased dopamine modulated interference between routines. We further sought to test whether higher levels of trait mindfulness provided a buffer against the impacts of increased dopamine availability. To preview the results, levodopa decreased target-accuracy and promoted routine formation in individuals with low trait-mindfulness, whereas high trait-mindfulness was associated with the opposite pattern. Regardless of mindfulness, dopamine increased task-interference.

Methods

All the data from this study is available at UQ eSpace[1]. Task code[2], analysis code and code to produce the manuscript[3] are available on github.

The experiment and analysis plan were pre-registered on the Open Science Framework[4].

Participants

A total of 40 participants (mean age: 24.5, sd: 5, 30 female, 10 male) were recruited using the undergraduate and paid SONA pools administered by the University of Queensland. All procedures were cleared by the University of Queensland Human Research ethics committee [2017/HE000847], and were conducted in accordance with the National Statement on Ethical Conduct in Human Research. Participants were over 18 years old, had no known neurological or psychiatric conditions (assessed by self report), and no contraindications to levodopa, as assessed by the levodopa safety screening questionnaire. Informed consent was obtained at the start of the first session.

Procedure

Participants attended two sessions, spaced approximately one week apart. After initial blood pressure (BP) and mood assessments (Bond & Lader, 1974), participants received either placebo (vitamin C) or levodopa (Madopar 125: 100 mg levodopa and 25 mg Benserazide Hydrochloride), crushed and dispersed in orange juice, now referred to as the 'placebo' and 'dopamine' sessions respectively. The solution was prepared by an experimenter who did not administer the remaining experimental procedures. This protocol

---

was sufficient to achieve double blinding in previous work (Chowdhury, Guitart-Masip, Bunzeck, Dolan, & Düzel, 2012; Chowdhury et al., 2013). Participants then completed the Five Facet Mindfulness Questionnaire (Baer et al., 2006). This is a 15 item self-report questionnaire that measures mindfulness with regards to thoughts and experiences in daily life. It includes items such as 'I don't pay attention to what I'm doing because I'm daydreaming, worrying, or otherwise distracted' and 'I do jobs or tasks automatically without being aware of what I'm doing'. Participants also completed the Barratt Impulsivity Scale [BIS; Patton, Stanford, and Barratt (1995)], as trait impulsivity scores are associated with midbrain dopamine D2/D3 receptor availability (Buckholtz et al., 2010). Around 30 minutes after drug administration, participants completed a second BP and mood rating assessment. Participants then completed the practice stage of the task, so that the experimental stage began approximately 40 minutes after drug ingestion, within the window of peak plasma availability (Contin & Martinelli, 2010). At the end of the session, participants completed the final BP and mood rating assessment and were asked whether they thought they had been given the active or placebo drug.

Apparatus

The experimental task was run with custom code, written using Matlab 2012b (32 bit) and Psychtoolbox v3.0.14, on a Windows 7 (64-bit) on a Dell Precision T1700 desktop computer, displayed using a ASUS VG248 monitor. Gaze coordinates (x, y) were sampled at 120 Hz using a monitor-mounted iView Red-m infrared eye tracker (SensoMotoric Instruments GmbH, Teltow, Germany). Participants were seated from the monitor at an approximate viewing distance of 57 cm, and positioned on a chin-rest for the duration of the task.

Experimental Task

Each trial began with a fixation dot presented centrally on a grey screen [RGB: 200 200 200]. Participants were instructed to fixate on the dot to begin a trial. After 1000 ms of continuous correct fixation samples (within 100 pixels of fixation), a square was presented that comprised 18° visual angle along each length. The square could be one of four possible colours [RGBs: 87, 208, 169; 267, 145, 52; 167, 162, 229; 239, 91, 158]. After 1000 ms, a 4 x 4 grid of smaller squares appeared within the larger square, in a darker version of the background colour ([RGB]-50). Each square comprised 2.6°. Participants were instructed that the 4 x 4 grid represented doors, and that they were to use their eyes to open the doors to find where the target was hiding. Participants were instructed that they were to fixate on a single door to open it (see Fig 1A). When participants had fixated on a door for over 300 ms, the door either turned black [RGB: 50, 50, 50], to denote the absence of a target, or the target was displayed and the trial was terminated. If the door had turned black, it returned to its previous colour as soon as it was detected that the participant had moved their eyes from the door [see Supplemental Figure 1, for a visual depiction]. Targets were animal images drawn randomly on each trial from a pool of 100 images taken from the internet[5]. The time at which the target was available to be found varied from trial to trial, with the onset being drawn from a uniform distribution between 500-2000 ms. Once the target was available and the correct door selected, the target was displayed for 750 ms. Upon termination of the trial, the grey screen and white fixation cross were presented.

In each session, participants saw the display in two possible colours. Participants were instructed that each colour represented a world, and that the animals had different places they preferred to hide, depending on the world they were in. There were four possible target locations within each world, or from here on, each setting. For each setting, one door from each quadrant was selected as one of the four possible target locations (see Fig 1B), with the

---

[5] The folder of target images can be downloaded from here

₂₂₀ constraint that target locations could not overlap between settings. Thus each colour

₂₂₁ reflected a setting in which participants could establish a set of task-relevant eye-movements,

₂₂₂ i.e. towards the 4 possible target locations. Note that within each setting, the target was

₂₂₃ equally likely to appear behind any one of the 4 target doors (p=.25) and would never appear

₂₂₄ behind the remaining doors (p=0). Colour-target location mappings were counterbalanced

₂₂₅ across participants, as was the assignment of colours to sessions. Participants completed 80

₂₂₆ trials in each setting. Eye-movement calibration and validation was performed every 20

₂₂₇ trials. Participants were also shown the standard QWERTY keyboard and were instructed

₂₂₈ that they could press 'x' at any time to perform a new calibration and validation if they felt

₂₂₉ that their eye-movements were no longer being registered accurately.

Statistical Approach

₂₃₁   The analysis was designed to assess how well participants learned the target locations,

₂₃₂ the extent to which participants formed a routine for door selections (how stereotypical they

₂₃₃ became in their order of door-selections), and how well they disambiguated between settings.

₂₃₄ We modelled how these elements of performance were modulated by the dopamine and

₂₃₅ mindfulness factors. All custom analysis code is available online. The analysis was performed

₂₃₆ using R and RStudio v2022.07.2 (RStudio Team, 2020), and can be reproduced in the

₂₃₇ Neurodesk container environment (Renton et al., 2022).

₂₃₈   **Data cleaning.**   We asserted that a door could not be selected twice consecutively,

₂₃₉ thus any consecutive selections were classified as a single selection. As the final door

₂₄₀ selection of every trial was fixed (i.e. finding the target location ends the trial), we removed

₂₄₁ the final selection from each trial for the stereotypy (routine) analysis defined below. We

₂₄₂ excluded data from one participant whose total number of door selections was greater than 3

₂₄₃ standard deviations from the mean across both sessions. The remaining 39 datasets were

₂₄₄ retained for all of the analyses. Note that this is more inclusive than our pre-registered plan

₂₄₅ for data exclusions. Based on pilot data, we had planned to exclude participants who scored

246 $< 65\%$ accuracy over the course of a session. Analysis of the final sample suggested that this

247 was too stringent, as this resulted in the exclusion of 14 of 40 participants. We have not

248 analysed the data with the exclusion of these participants, owing to the large drop in

249 statistical power for the individual differences component of the analysis.

Target-Accuracy

251   We first sought to determine the extent to which levodopa and mindfulness influenced

252 the learning of target locations (target-accuracy). Data was grouped into blocks of 10 trials

253 per setting, and grouped across settings, resulting in 8 blocks of 20 trials. We computed for

254 each block the proportion of door selections that were target relevant (TR) given the current

255 setting (i.e. the setting presented on trial t). We assessed the influence of block, drug and

256 mindfulness on target-accuracy using Bayesian mixed-model logistic regression.

257 Target-accuracy was assumed to be drawn from a binomial distribution (1=target door,

258 0=non-target door). We then estimated the probability of drawing a target-door from the

259 total number of door selections, using a logit link function to convert probabilities to

260 log-odds. Thus the resulting regression parameter values reflect changes to the log-odds of

261 accurate door selections.

262   For this and following analyses, we identified the model that best fit the data, and

263 made inference over the resulting parameters. We report the 95% confidence intervals (CIs)

264 of the parameter posteriors, and assume a reliable effect when the 95% CIs do not include

265 zero. Models were fit using the BRMS (Bürkner, 2017) interface for Stan (Team, n.d.) and

266 RStan (Stan Development Team, 2023). We used the default weakly informative priors as

267 specified in Burkner (2017). Specifically, fixed and random effect β coefficients were given a

268 flat prior, intercept and standard deviations were assumed to be drawn from a student's t

269 distribution (df=1, location=0, scale=2.5), and the LKJ-correlation prior with parameter ζ

270 > 0 was used for the parameter covariance matrix. For each model, we checked for parameter

271 recovery using simulated data. Once fitted, we checked that the residuals showed no signs of

272 systematic error, that the chains had converged, and that $\hat{R}$ values were less than 1.01, as

273 this suggests that the model has converged.

274   To eschew an overly large model space, and in line with our pre-registration, we first fit

275 models that contained each possible combination of the block and drug regressors (and

276 associated random effects), and found the best model using leave-one-out (LOO) cross

277 validation, as implemented in Vehtari et al., (2017). Rather than re-fitting the model for

278 every sub-sample, which is computationally expensive, this algorithm instead computes

279 analytically how the predictions made by the model are influenced by each data point. The

280 relationship between this influence and the change in the posterior that would occur as a

281 consequence of holding out each data point can be used to compute the expected

282 log-pointwise predictive density (ELPD). This quantifies the error that would occur in the

283 prediction of each data point, when that data point is withheld from the model fitting

284 procedure. The resulting ELPDs are then compared between models. We report the ELPD

285 difference between the winning model and the next best models (a negative value indicates

286 preference for the winning model). As the ELPD is computed using each observed data

287 point, it is possible to estimate the standard error (SE) of the difference between models

288 (Vehtari et al, (2017)). We therefore also report the ratio of the ELPD difference to the SE,

289 as this provides a proxy for statistical significant differences between models. (Note that in

290 the pre-registration document we had proposed to compare models using the deviance

291 information criterion (DIC). As LOO is more robust than DIC to influential observations,

292 and is readily implemented for use with BRMS model objects, we opted to use LOO instead

293 of DIC).

294   Upon identifying the best model, we then added the mindfulness regressor, fitting all

295 possible combinations, and once again selected the best model. Last we controlled for trait

296 impulsivity by adding BIS scores as a main effect to the winning model. Note that in no

297 cases did adding BIS scores improve the model. The full set of model comparisons are

298 presented in the supplementary materials.

Setting-Accuracy

We next sought to model the impact of levodopa and mindfulness on task interference. To measure the extent of task interference, we computed a measure of setting-accuracy. This measure indexes the total number of door selections (n) that were appropriate for the colour setting displayed on trial t (current setting, CS), relative to the number of door selections that were appropriate for the setting not displayed on trial t (i.e. the other-setting from that session, OS):

$$setting-acc = \frac{\sum CS_n}{\sum (CS_n, OS_n)}$$

We modelled the influence of levodopa and mindfulness on setting-accuracy using the Bayesian mixed-effects logistic regression approach described above (Note that in the pre-registration document we had suggested to include a regressor for context. Visual inspection of the data showed that setting-accuracy was highly comparable across contexts [see Supplemental Figure 3]. We therefore opted to simplify the model space and collapse over this factor).

Stereotypical door selections

Next, we determined the extent to which door-selections became routine over the course of the task - specifically, how much the order of door selections increased in stereotypy, and whether dopamine and mindfulness modulates the extent of stereotypy. Here we use stereotypy as a proxy for routine formation, and we define stereotypy as the tendency to choose doors in the same order, over trials (e.g. Desrochers et al., 2015).

In order to index stereotypy, we reasoned that stereotypy should result in an increase in the probability of a subset of door transitions. This stands in contrast to when making door selections in an exploratory, or non-stereotyped way, where there should be an even

321 representation of door transition probabilities. Therefore, the transition probability matrices

322 of individuals engaged in more stereotypical door selections should show higher variance

323 than those who are not engaging in stereotypical door selections. We computed trial level

324 transition probability matrices, and calculated the variance of each matrix. Variances were

325 then collapsed across settings and trials to form a stereotypy score for each participant,

326 session and block.[6]

327   The resulting stereotypy scores were subject to a comparable Bayesian mixture

328 modelling approach as described above with a few key differences; the stereotypy scores were

329 assumed to be drawn from a skewed normal distribution $\mathcal{N}(\mu, \sigma, \alpha)$ whose mean (μ) was

330 defined by the regression parameters (the distribution of stereotypy scores are presented in

331 Supplemental Figure 4). σ was assumed to be drawn from a Student's t distribution (df=3,

332 location=0, scale=2.5), the skew parameter (α) was assumed to be drawn from a normal

333 distribution $\mathcal{N}(0, 4)$. The remaining priors for the intercept, beta-coefficients and parameter

334 covariance matrix were defined in the same manner as for the accuracy data models. As the

335 log-log plot of variances vs block suggested a power function, analysis was performed on the

336 logged data. This ensured that the relationship between block and variance values was best

337 described by a straight line. Identification of the winning model proceeded as described for

338 the accuracy data above.

339 **Blinding analyses**

340   To determine whether awareness of the dopamine intervention could have contributed

341 to the findings, the probability of participant ratings were compared to the expected values

342 assuming chance guessing, using a Chi Square test. BP and mood ratings were each subject

---

[6] Note that we opted to index stereotypy using variance over transition probabilities as this measure captures consistent behaviours without over-penalizing slight variations between sequences. For example, the sequences x=[1,2,3,4,5], and y=[1,2,4,3,5] share commonalities that are captured in a transition probability matrix that would not be captured by linear measures, such as comparing triplets between trials.

to a session (dopamine vs placebo) x timepoint (pre-drug, pre-experiment, post-experiment)

Bayesian repeated measures ANOVA, implemented using the BayesFactor package for R

(Morey et al., 2023) using the default priors (Rouder, Morey, Speckman, & Province, 2012).

Results

We investigated the impact of levodopa administration and trait mindfulness on the

learning of task-relevant behaviour sets, and on the routine nature of their deployment.

Participants opened doors to search for targets in a gaze-contingent display. The colour of

the display signalled likely target locations, making some locations relevant for only that

colour. We assessed how well participants learned target locations (target-accuracy), how

routine was the order of door selections across trials (stereotypy), and how well participants

learned to segregate task-routines (setting-accuracy). Overall, mindfulness and dopamine

interacted to influence the measures of target-accuracy and stereotypy; dopamine increased

target-accuracy and reduced stereotypy for high mindfulness scorers, whereas dopamine

decreased target-accuracy and increased stereotypy for low mindfulness scorers. Dopamine

decreased setting-accuracy independent to mindfulness scores.

Target-Accuracy

Model selection. First we sought the best model in order to make subsequent

inference over the parameters. In the first stage of model selection, the experimental factors

of block (10 successive trials from each context, averaged across contexts), and drug

(dopamine vs placebo) were used in a logistic regression to model the probability of a target

door selection. We sought the combination of fixed and random effect factors that best

accounted for the data. The winning model contained fixed main effects of block and drug.

Although this model was only closely preferred to the next most complex model that

contained a block x drug interaction (ELPD diff = -0.33, ELPD:SE = -0.57), it was strongly

preferred to all other models (min ELPD diff = -958.53, ELPD:SE = -8.65).

368   We next sought to determine whether adding mindfulness scores improved the

369 predictive accuracy of the model; the winning model contained an additional main effect of

370 mindfulness, as well as block x mindfulness and drug x mindfulness interactions (ELPD diff

371 to best model without mindfulness = -3.12, ELPD:SE = -0.62). Therefore the winning

372 model to account for the data was:

373    $\hat{y} = \text{block} + \text{drug} + \text{mind} + \text{block} * \text{mind} + \text{drug} * \text{mind} + (\text{block} : \text{drug}|\text{sub})$

374   Adding BIS scores did not improve the predictive value of the model (ELPD diff =

375 -1.95, ELPD:SE = -3.77). Note that although we draw inferences over parameters from the

376 winning model, our inferences are the same as if we had used the more complex model that

377 includes the BIS scores.

378   **The effect of dopamine and mindfulness on target-accuracy.**   Having

379 established the best model to account for the data, we next determined the influence of

380 dopamine and mindfulness on target-accuracy by making inference over the resulting

381 parameters. Target-accuracy data plotted by block x drug (dopamine vs placebo) are shown

382 in Fig 2A. Target-accuracy improved over blocks, and there was a small main effect of drug.

383 These effects are described further below. However, critically, mindfulness and dopamine

384 interacted to influence target-accuracy. The drug x mindfulness parameter differed reliably

385 from zero (mean log odds = -0.08, 95% CI[-0.12, -0.03], see Fig 2E).

386   To investigate this interaction, we computed mean target-accuracy change due to the

387 drug session (μ acc[dopamine - placebo]) for each participant. Note that a positive score

388 indicates that performance was better in the dopamine session relative to placebo. Next we

389 examined the relationship between dopamine-induced target-accuracy changes and

390 mindfulness scores. As can be seen in Fig 2B, there was a positive relationship between

391 mindfulness and the influence of drug on target-accuracy. As mindfulness increased, so too

392 did target-accuracy for the dopamine relative to the placebo session. For a numeric example,

393 those scoring in the highest quartile showed mean target-accuracy scores of 0.47 (95%CI[0.44,

0.50]) during the dopamine session, relative to mean target-accuracy scores of 0.41 (95%
CI[0.38, 0.43]) during the placebo session. Individuals scoring low on mindfulness numerically
showed the opposite pattern (dopamine mean target-accuracy = 0.43, 95% CI[0.41, 0.45],
placebo mean target-accuracy = 0.44, 95%CI[0.43, 0.46]), note that Fig 2B shows the
difference between these scores). Thus the impact of dopamine on the establishment of
task-relevant eye-movements is dependent on the mindfulness state of the individual.

Participants learned the target door locations over the course of the sessions,
target-accuracy reliably increased over blocks. Mean target-accuracy in block 1 was 0.34
(95% CI[0.32, 0.37]), relative to a block 8 mean of 0.51 (95% CI[0.48, 0.53]). The model
showed that the log-odds of a target door selection increased over blocks by an average of =
0.15, (95% CI[0.08, 0.22, Fig 2C, note that the model parameters are defined in log-odds
because we used logistic regression). There was also the suggestion of a main effect of
dopamine (mean log odds = 0.08, 95% CI[0.035, 0.13, Fig 2D), however, the impact of
dopamine on target-accuracy is better explained by the drug x mindfulness interaction Fig
2E). Although the winning model contained a block x mindfulness interaction, the 95% CIs
included zero (mean log odds = 0.05, 95% CI[-0.016, 0.12], so we do not consider this
parameter any further.

Setting-Accuracy

Model selection.   We first identified the model that best accounted for the influence
of the experimental conditions on setting-accuracy. Comparable to the target-accuracy data,
the best model contained fixed effects of block and drug, with no interactions. Although this
model was only closely preferred to the next most complex model that contained a block x
drug interaction (ELPD diff = -0.66, ELPD:SE = -1.67), it was strongly preferred to all
other models (min ELPD diff = -553.79, ELPD:SE = -8.35).

Adding mindfulness scores improved the predictive accuracy of the model; the winning

419 model contained an additional main effect of mindfulness (ELPD diff = -0.13, ELPD:SE =

420 -0.12). Thus the winning model was:

421    $\hat{y} = \text{block} + \text{drug} + \text{mind} + (\text{block} : \text{drug}|\text{sub})$

422   Adding BIS scores did not improve the predictive value of the model (ELPD diff =

423 -0.02, ELPD:SE = -0.03). Note that although we draw inferences over parameters from the

424 winning model, our inferences are the same as if we had used the more complex model that

425 includes the BIS scores.

426   **Drug, and not mindfulness, impacts setting-accuracy.**   We next determined

427 the influence of dopamine and mindfulness on setting-accuracy by making inference over the

428 resulting model parameters. Dopamine reduced setting-accuracy; setting-accuracy was on

429 average 0.64 (95% CI [0.63, 0.65]) for the dopamine session, and 0.66 (95% CI [0.65, 0.68])

430 for the placebo session (see Fig 3A). The log-odds of selecting a setting-accurate target door

431 increased by a mean of 0.07 (95% CI[0.01, 0.13, Fig 3B) for the placebo session, relative to

432 the dopamine session. This suggests that dopamine caused interference between settings.

433   Setting-accuracy improved over blocks; mean accuracy in block 1 was 0.59 (95%

434 CI[0.58, 0.61]), relative to block 8 (mean: 0.69, 95% CI[0.67, 0.71]). The model showed that

435 the probability of selecting a setting relevant target door increased by a mean log odds of

436 0.13 (95% CI[0.07, 0.19) per block (Fig 3C). In contrast to the target-accuracy data, the

437 main effect of mindfulness was not a sufficiently reliable predictor of setting-accuracy (mean

438 log odds = 0.04, 95% CI[-0.04, 0.18]).

439   *Setting-accuracy control analysis.*   Dopamine influences setting-accuracy, which

440 indexes the likelihood of door selections that are relevant for the current-setting, relative to

441 door selections that are relevant for the other-setting. As we exclude door selections for

442 locations that are never target relevant from the computation of setting-accuracy, it is

443 important to verify that setting-accuracy scores do indeed reflect interference between

444 settings, rather than a general task learning deficit. To address this in an exploratory

analysis, we reasoned that if setting-accuracy scores reflected a general deficit, then 'error'

door selections should be drawn randomly from not-target doors (other-setting = 4 & neither

= 8). A general deficit interpretation suggests that other-setting selections should be drawn

from the total set (other-setting + neither) with $p = .\overline{333}$. If setting-accuracy scores do

reflect the presence of task-interference, then it would be likely that this error would be more

common than a random door selection, therefore other-setting selections should occur at

levels higher than chance. To test this, we computed for each participant the probability of

other-setting selections, given the set of other-setting and neither door selections (p_{os}), and

performed a one-sided t-test, against a null value of $p = .333$. (Note that we opted to use an

NHST approach as we had a point null hypothesis). The p_{os} data was unlikely under the null

hypothesis (mean = 0.37, 95% CI[0.35, 0.39], $t(38) = 3.62$, $p = 0.0004$. Therefore, we reject

the hypothesis that the the dopamine induced drop in setting-accuracy reflects a general

learning deficit.

Stereotypy of door selections (routine)

Model selection.   We first sought the model that best explained the stereotypy data

using the experimental predictors of block and drug. Note that we indexed stereotypy using

the variance of transition probability matrices, where higher values indicates fewer likely

transitions, and therefore higher stereotypy. The winning model contained main fixed effects

of block and drug, and random effects for block x drug. Although this model was only

closely preferred to the next most complex model that contained a block x drug interaction

(ELPD diff = -0.26, ELPD:SE = -1.29), it was strongly preferred to all other models (min

ELPD diff = -130.14, ELPD:SE = -7.71).

Adding mindfulness scores improved the ability of the model to account for the

stereotypy data. The winning model contained an additional main effect of mindfulness and

a drug x mindfulness interaction (ELPD diff = -3.15, ELPD:SE = -0.92). The winning

model was:

471    $\hat{y} = \text{block} + \text{drug} + \text{mind} + \text{drug} * \text{mind} + (\text{block} : \text{drug}|\text{sub})$

472   Adding BIS scores did not improve the predictive accuracy of the model (ELPD diff =

473   -0.54, ELPD:SE = -1.41). Note that although we draw inferences over parameters from the

474   winning model, our inferences are the same as if we had used the more complex model that

475   includes the BIS scores.

476   **The impact of drug and mindfulness on stereotypy.**   Stereotypy scores

477   increased over blocks Fig 4A. Note that this increase is also in part due to increases in

478   target-accuracy; as fewer doors are selected in error, the variance of the transition probability

479   matrices increases. We first discuss the key results, and in the next section demonstrate their

480   relationship to target-accuracy. Critically, mindfulness and dopamine interacted to impact

481   stereotypy; we observed a reliable drug x mindfulness interaction (mean $\beta = 0.11$, 95%

482   CI[0.02, 0.21, Fig 4E). Mindfulness scores modulated the impact of dopamine on stereotypy.

483   As a numerical example, those scoring in the highest quartile showed mean stereotypy scores

484   of -8.74 (95%CI[-8.80, -8.68]) during the dopamine session, relative to mean stereotypy scores

485   of -8.68 (95% CI[-8.74, -8.62]) during the placebo session. Individuals scoring low on

486   mindfulness (lowest quartile) showed the opposite pattern (dopamine mean stereotypy =

487   -8.69, 95% CI[-8.75, -8.63], placebo mean stereotypy = -8.72, 95%CI[-8.78, -8.66]).

488   To visualise this interaction, we computed a mean variance change score between drug

489   sessions for each participant (μ stereotypy[dopamine - placebo]). Note that a positive score

490   indicates that performance was more stereotyped in the dopamine session relative to placebo.

491   As can be seen in Fig 4B, there was a negative relationship between drug-induced stereotypy

492   changes and mindfulness. Specifically, higher mindfulness scorers showed lower stereotypy in

493   the dopamine session compared to the placebo session. Low mindfulness scorers showed

494   higher sterotypy in the dopamine session compared to the placebo session. Thus the impact

495   of dopamine on the formation of eye-movement routines is dependent on the mindfulness

496   state of the individual.

⁴⁹⁷ Participants developed more stereotypical routines over the course of the experiment,

⁴⁹⁸ there was a clear main effect of block (mean increase per block: $\beta = 0.32$, 95% CI[0.20, 0.43,

⁴⁹⁹ Fig 4C). In line with the interaction of drug x mindfulness reported above, the main effect of

⁵⁰⁰ mindfulness suggested a negative relationship with stereotypy (mindfulness mean $\beta = $ -0.15,

⁵⁰¹ 95% CI[-0.26, -0.05, Fig 4D). Overall, higher mindfulness scores predicted less stereotypy in

⁵⁰² door-selection patterns relative to low mindfulness scores.

⁵⁰³ ***On the relationship between target-accuracy and stereotypy.*** Accuracy and

⁵⁰⁴ stereotypy showed opposing relationships with mindfulness and dopamine. Higher

⁵⁰⁵ mindfulness scores were associated with dopamine-induced target-accuracy increases, and

⁵⁰⁶ stereotypy decreases, relative to placebo. Individuals scoring low on mindfulness showed a

⁵⁰⁷ deleterious influence of dopamine on target-accuracy, coupled with increased stereotypy,

⁵⁰⁸ relative to placebo. As target-accuracy and stereotypy are possibly, but not necessarily

⁵⁰⁹ related, we next sought to ensure that the observed influences of dopamine and mindfulness

⁵¹⁰ on stereotypy was not driven solely driven by its correlation with target-accuracy, using an

⁵¹¹ exploratory analyses. We reasoned that such a pattern of results could be observed if the

⁵¹² measures of target-accuracy and stereotypy reflected a direct trade off; i.e. as target-accuracy

⁵¹³ goes up, stereotypy goes down. A correlation analysis ruled out this possibility. We

⁵¹⁴ computed mean target-accuracy and stereotypy scores for each participant, collapsing across

⁵¹⁵ all experimental factors, and found that target-accuracy and stereotypy were positively

⁵¹⁶ related ($r(37) = 0.81$, $p = 3.51$e-10).

⁵¹⁷ Next, to rule out the contribution of target-accuracy to the stereotypy results, we

⁵¹⁸ added mean target-accuracy, computed for each block and drug condition, as a regressor to

⁵¹⁹ the winning model. Adding target-accuracy as a regressor both clearly improved the

⁵²⁰ predictive accuracy of the model (ELPD diff = -110.26, ELPD:SE = -6.12), and served to

⁵²¹ increase certainty in the interactive influence of mindfulness and drug on stereotypy scores.

⁵²² Specifically, the estimated influence of the interaction increased from $\beta = 0.11$ to $\beta = 0.22$

⁵²³ (95% CI[0.14, 0.29]). Note that the pattern of remaining results were also consistent between

the two models. Therefore, the data support the notion that mindfulness and dopamine

interact to differently influence target-accuracy and stereotypy when participants perform

task-relevant saccadic routines. Indeed, this data suggest that mindfulness and dopamine

interacted to produce more erroneous routines. To visualise this, Fig 5 shows example door

selections from two participants, one randomly selected from the lowest quartile of

mindfulness scorers (top row), and one selected from the highest quartile of mindfulness

scorers (bottom row). As can be seen, the low mindfulness scorer had adopted a routine that

resulted in more erroneous door selections than the high mindfulness scorer. The low

mindfulness scorer appears to have developed a suboptimal task strategy of trying all doors,

regardless of task context.

Blinding check

Next we checked if participants knew whether they had received levodopa or placebo

across the two sessions. Participants were asked to report at the end of each session whether

they thought they had received levodopa or placebo. Participant responses were coded as

either correct for both sessions (cc: observed N = 7), correct for one session and incorrect for

the other (ci: N = 11), or incorrect for both sessions (ii: N = 8). The probability of the

observed guesses was not statistically unlikely given the null distribution of chance

performance (the null hypothesis specified p= .25, .5, .25 for cc, ci, ii respectively, $\chi^2(2, 26)$

$= 0.69$, $p =0.71$). Note that we were unable to include all the participants in this analysis

owing to missing data. Specifically, due to a miscommunication in the research team, the

blinding check questions contained 'Don't know' as a possible response, for which we are

unable to generate a null hypothesis. We therefore only include participants who made a

guess using the levodopa and placebo options across both sessions.

Mood and blood pressure

We also sought to determine whether dopamine influenced physiological factors such as mood and blood pressure. For mood, the winning model contained a main effect of time-point and no other fixed effects. This model was preferred relative to next best model, which contained an additional main effect of drug (BF = 3.76, ±2.14%) and was substantially preferred over the null random intercept model (BF = 514549 ±1.23%).

Mean blood pressure was computed using the formula: Mean blood volume pulse (BVP) = diastolic blood pressure (DBP) + 1/3 [systolic blood pressure (SBP) – DBP]. For mean BVP, the winning model contained main effects of both time-point and drug. This model was barely preferred to the next best model which contained a time-point x drug interaction (BF = 1.7 ±5.69%), but was strongly preferred to the random intercept model (BF = 5011975 ±3.76%). Overall, mean BVP was lower in the levodopa session (mean = 2.181.511261, 95% CI[80.3, 82.8]), relative to placebo (mean = 84.5, 95% CI[83.5, 2.185.504042]).

Discussion

We investigated the impact of levodopa administration and trait mindfulness on the learning of task-relevant behaviour sets, and on the routine nature of their deployment. Participants opened doors to search for targets in a gaze-contingent display. The colour of the display signalled likely target locations, making some locations relevant for only that colour. We assessed how well participants learned target locations (target-accuracy), how routine was the order of door selections across trials (stereotypy), and how well participants learned to segregate task-routines (setting-accuracy). levodopa impacted target-accuracy, stereotypy and setting-accuracy, but in the case of the former two, this impact was modulated by trait mindfulness. High trait mindfulness corresponded to increased target-accuracy and decreased stereotypy, for levodopa relative to placebo, whereas low trait

mindfulness was associated with decreased target-accuracy and increased stereotypy (for levodopa relative to placebo). These results quantify, for the first time, that increasing systemic dopamine availability induces an increase in stereotypy, that may come at the cost of target-accuracy, that is modulated by trait-mindfulness, and that increased dopamine availability increases routine confusion. These findings carry implications for our theoretical understanding of how the brain establishes and switches between task-relevant behavioural routines, which we outline below.

The current findings offer insight into the relationship between dopamine and mindfulness. Dopamine and mindfulness have been indirectly related in both the reinforcement learning (RL) (Kirk et al., 2014, 2019) and active inference frameworks (FitzGerald et al., 2015; Friston et al., 2012; Giommi et al., 2023; Laukkonen & Slagter, 2021), yet there exists no other study to-date that assesses their joint impact on behaviour. Here we find that levodopa and mindfulness jointly modulate learning and stereotypy, with levodopa yielding conditions of decreased target-accuracy and increased stereotypy in low trait mindfulness scorers. We hypothesise that low mindfulness results in poorer sensory-action representations which renders the individual more susceptible to error when estimating the reward value of actions, which is compounded by over-optimistic estimations induced by elevated dopamine availability. The result is a failure to differentiate between the actions that do and do not lead to reward, and an increased probability of reliance on past behaviours. This could be manifest via impoverished top-down, cortical regulation of positive prediction errors in striatum (Kirk et al., 2014), as has been predicted within an RL framework. The same result could also be accounted for by a decrease in certainty regarding sensory prediction errors occurring with low mindfulness (Giommi et al., 2023; Laukkonen & Slagter, 2021), in tandem with dopamine inducing inflated certainty regarding reward outcomes (FitzGerald et al., 2015), as has been suggested via the active inference framework.

Note that the two accounts predict comparable outcomes so we are unable to differentiate between them with the current data. However, the current findings do constrain

these accounts regarding the extent of overlap between the actions of dopamine availability and mindfulness. Increased dopamine availability increased routine confusion, regardless of trait mindfulness. Therefore, there are limitations to the modulatory influence of mindfulness on the actions of dopamine. The establishment and maintenance of a task-set is assumed to reflect a superordinate representation of a goal and the set of actions required to attain that goal (Desrochers, Burk, Badre, & Sheinberg, 2016; Lee, Hazeltine, & Jiang, 2022; Schumacher & Hazeltine, 2016; Sutton & Barto, 2018; Vaidya, Jones, Castillo, & Badre, 2021). The current data suggest that while dopamine and trait mindfulness can jointly modulate the learning and execution of subordinate representations, i.e. the set of actions used, mindfulness does not modulate the impact of dopamine on superordinate task representations, at least under the current task conditions. Future work should determine whether these observed limits in the modulatory influence of mindfulness are due to a limited locus of effect, or are due to increased vulnerability to the impacts of dopamine at superordinate levels of representation.

The finding that levodopa increased interference between settings extends previous work showing that dopamine impacts switching between simple sensorimotor tasks that require only one response (R. Cools et al., 2001; Mehta et al., 2004; Wiecki & Frank, 2010). Collectively, these findings point to a U-shaped function linking dopamine levels and task-switching impairments, in that depleted and inflated levels of dopamine result in poorer task switching. This observation informs theoretical accounts of the relationship between dopamine and an agent's ability to infer the current task state, which have previously only considered the impacts of depleted dopamine (Friston et al., 2012). These findings do support previously postulated hypotheses that there should be a U shaped relationship between dopamine levels and task-performance, that is in part dependent on task demands (R. Cools & D'Esposito, 2011). As the currently studied behaviours are more complex than the constrained sensorimotor tasks that are typically used in task-switching studies, future work should verify whether levodopa administration comparably impacts task-switching in

simple sensorimotor tasks, and whether depleted dopamine impacts switching between tasks requiring multiple responses. This will determine whether the relationship between dopamine and task-switching is comparable across tasks or depends upon task demands.

To minimise task interference, an agent must maintain a representation of the actions required to achieve the task goal, and must associate this representation to the correct task cues. We found that levodopa increased the probability that actions from a non-relevant task-set would be selected during current task performance invariant to mindfulness, whereas the probability that an erroneous action was selected varied across individuals according to their trait mindfulness. Therefore, the most consistent locus of task-set confusion is between actions that have been credited as successful in either task-context. What remains to be determined is whether levodopa caused task-interference, or attenuated the ability to associate successful actions with the appropriate situational cues. If the latter is true, then levodopa would have caused individuals to learn one task, that did not incorporate the colour cue as a relevant disambiguating signal. We seek to arbitrate between these possibilities in future work.

In contrast to expectations, levodopa led to an overall reduction in stereotypy in door selections, suggesting that increased dopamine availability reduces the probability of forming a routine when performing multiple responses. This is in contrast to previous findings showing that increased dopamine speeds the transition to habit formation (Harmer & Phillips, 1998; Nadel et al., 2021, 2021; Nelson & Killcross, 2006). As with task-switching studies, such findings are largely based on rodent models using tasks comprising one or two stimulus-response associations. Our findings show that in the case of sets of task-relevant saccades, increasing dopamine does not necessarily lead to increased habit formation. Moreover, levodopa did not improve target-accuracy overall, suggesting that our results cannot be solely attributed to levodopa increasing model-based control (Deserno et al., 2021; Kroemer et al., 2019; Wunderlich, Smittenaar, & Dolan, 2012), or adjusting the balance between exploitation and exploration (Chakroun et al., 2020; Kayser, Mitchell, Weinstein, &

Frank, 2015).

What then is the influence of dopamine on the cost/benefit computations that drive routine formation? In accordance with previous work with non-human primates (Desrochers et al., 2015; Desrochers et al., 2010), the current data suggest that dopamine is a modulator of the computations that drive routines in humans. However, the current data also show that the modulatory influence of dopamine is dependent on the behaviour-trait state of the individual. Specifically, increased dopamine appears to drive individuals low in mindfulness towards a stereotypical solution that is suboptimal in terms of target-accuracy, suggesting a poor evaluation of sequence costs relative to benefits. In contrast, individuals high in trait mindfulness show increased target-accuracy but reduced stereotypy, suggesting an appropriate crediting of successful actions, but also suggesting either some volatility in their execution, or better learning that the probability of a target was uniform across target-relevant locations. While the current data demonstrate the applicability of dopamine signalling to the computations that underlie the formation of routines, the data also show further work is required to determine the internal state variables that determine whether increased dopamine availability will have a positive or negative impact on performance.

One possibility that remains unexplored in the current study is that working memory capacity may be a moderating factor in the relationship between mindfulness and stereotypy. Individuals low in mindfulness may also show low working memory capacity (Ruocco & Wonders, 2013). This may result in a reliance on strategies that avoid taxation of working memory, such as adhering to a routine that will lead to the target, despite the potential delay in reward. Indeed, the delay in reward may be less costly than the effort of retaining the relevant target locations in working memory. It has been proposed that dopaminergic projections to the prefrontal cortex (see Cools & D'Esposito, (2011), and perhaps beyond (Froudist-Walsh et al., 2021), are critical for the gating of sensory information into working memory (Chatham & Badre, 2015; Gruber, Dayan, Gutkin, & Solla, 2006), and such projections may well have been modulated by the levodopa manipulation. Evidence

regarding the relationship between mindfulness and working memory is mixed (Im et al., 2021; Jha et al., 2019), and larger, systematic studies are warranted to pin down the nature of this relationship. Future investigations should focus on the potential moderating role of working memory when mindfulness and dopamine interact to influence stereotypy, in order to pin down causal links between these factors.

The current work is not without limitations. A difference was found in mean BVP between the levodopa and placebo sessions, suggesting more general physiological differences between the sessions. However, the effect of levodopa on blood-pressure is well characterised, and depends partly on the effective dose (dose per kilogram, Goldberg et al (Goldberg & Whitsett, 1971)). It is unlikely that low and high mindfulness individuals differed systematically in terms of effective dose. Participants were also not able to detect whether they had received levodopa or placebo above what would be expected by chance. Therefore, the physiological changes appeared to not be subjectively detectable, lowering the likelihood that discernible subjective differences impacted the results. Note that although the power of our blinding test was lowered owing to missing data, the remaining N was comparable to sample sizes from previous investigations into the impact of dopaminergic pharmacological intervention on decision-making, that employed comparable blinding tests (Leow, Bernheine, Carroll, Dux, & Filmer, 2023; Pine, Shiner, Seymour, & Dolan, 2010; Vo, Seergobin, & MacDonald, 2018; Vo, Seergobin, Morrow, & MacDonald, 2016; Wunderlich et al., 2012).

Although target-accuracy and stereotypy theoretically need not be correlated, we did find a moderate positive correlation between the two measures. Critically, the modulatory influence of mindfulness and dopamine on stereotypy was found to be larger after accounting for target-accuracy. Furthermore, target-accuracy and stereotypy were at antithesis to each other with regard to the demonstrated impacts of mindfulness and levodopa. Nonetheless, further work should be done to confirm the dissociable impact of dopamine and mindfulness on these two aspects of performance. We shall seek to achieve this in future studies by controlling task parameters to maintain target-accuracy, while examining modulations to

stereotypy.

It could also be anticipated that participants who received levodopa administration in the first session may show carry-over effects to the subsequent session, e.g. levodopa may modulate the extent to which the individual learns that there are two settings, and this may affect how they approach the task in the second placebo session. Our double-blind, counter balanced design renders it unlikely that the current findings are due to session order effects, and our statistical power is such that we are not well placed to detect them in the current data. However, it would be very interesting to determine how levodopa influences carryover of task formation and routine execution to new situations. Future work should include conditions that allow us to tease out order effects, for example by including DA-DA and placebo-placebo conditions.

We sought to determine the modulatory influence of dopamine availability and trait-mindfulness on the formation and deployment of task-relevant saccadic routines. We found evidence for theoretical assertions that dopamine and mindfulness share overlap in their locus of influence, but also demonstrated boundaries in that overlap. Mindfulness modulated the impact of dopamine on task-learning and routine development, with levodopa administration resulting in low mindfulness individuals being more likely to show impaired learning and increased stereotypy. Invariant to trait-mindfulness, levodopa increased the likelihood of task-interference between settings, suggesting that dopamine either hampers the binding of actions to situational cues, or promotes confusion between task-states. Collectively, these data suggest that the fidelity of situational representations interact with reinforcement learning systems to drive the formation of behavioural routines.

References

Andreu, C. I., Moënne-Loccoz, C., López, V., Slagter, H. A., Franken, I. H. A., & Cosmelli, D. (2017). Behavioral and Electrophysiological Evidence of Enhanced Performance Monitoring in Meditators. *Mindfulness*, *8*(6), 1603–1614.

733   https://doi.org/10.1007/s12671-017-0732-z

734 Baer, R. A., Smith, G. T., Hopkins, J., Krietemeyer, J., & Toney, L. (2006). Using

735   Self-Report Assessment Methods to Explore Facets of Mindfulness. *Assessment*, *13*(1),

736   27–45. https://doi.org/10.1177/1073191105283504

737 Bond, A., & Lader, M. (1974). The use of analogue scales in rating subjective feelings.

738   *British Journal of Medical Psychology*, *47*(3), 211–218.

739   https://doi.org/10.1111/j.2044-8341.1974.tb02285.x

740 Buckholtz, J. W., Treadway, M. T., Cowan, R. L., Woodward, N. D., Li, R., Ansari, M. S.,

741   . . . Zald, D. H. (2010). Dopaminergic network differences in human impulsivity. *Science*

742   *(New York, N.Y.)*, *329*(5991), 532. https://doi.org/10.1126/science.1185778

743 Budzillo, A., Duffy, A., Miller, K. E., Fairhall, A. L., & Perkel, D. J. (2017). Dopaminergic

744   modulation of basal ganglia output through coupled excitation–inhibition. *Proceedings of*

745   *the National Academy of Sciences*, *114*(22), 5713–5718.

746   https://doi.org/10.1073/pnas.1611146114

747 Bürkner, P.-C. (2017). Brms: An R package for Bayesian multilevel models using Stan.

748   *Journal of Statistical Software*, *80*, 1–28.

749 Chakroun, K., Mathar, D., Wiehler, A., Ganzer, F., & Peters, J. (2020). Dopaminergic

750   modulation of the exploration/exploitation trade-off in human decision-making. *eLife*, *9*,

751   e51260. https://doi.org/10.7554/eLife.51260

752 Chatham, C. H., & Badre, D. (2015). Multiple gates on working memory. *Current Opinion*

753   *in Behavioral Sciences*, *1*, 23–31. https://doi.org/10.1016/j.cobeha.2014.08.001

754 Chen, X., & Reed, P. (2023). The effect of brief mindfulness training on the micro-structure

755   of human free-operant responding: Mindfulness affects stimulus-driven responding.

756   *Journal of Behavior Therapy and Experimental Psychiatry*, *79*, 101821.

757   https://doi.org/10.1016/j.jbtep.2022.101821

758 Chowdhury, R., Guitart-Masip, M., Bunzeck, N., Dolan, R. J., & Düzel, E. (2012).

759   Dopamine modulates episodic memory persistence in old age. *The Journal of*

Neuroscience: The Official Journal of the Society for Neuroscience, *32*(41), 14193–14204.

https://doi.org/10.1523/JNEUROSCI.1278-12.2012

Chowdhury, R., Guitart-Masip, M., Lambert, C., Dayan, P., Huys, Q., Düzel, E., & Dolan,

R. J. (2013). Dopamine restores reward prediction errors in old age. *Nature*

Neuroscience, *16*(5), 648–653. https://doi.org/10.1038/nn.3364

Contin, M., & Martinelli, P. (2010). Pharmacokinetics of levodopa. *Journal of Neurology*,

257(Suppl 2), S253–261. https://doi.org/10.1007/s00415-010-5728-8

Cools, R., Barker, R. A., Sahakian, B. J., & Robbins, T. W. (2001). Enhanced or impaired

cognitive function in Parkinson's disease as a function of dopaminergic medication and

task demands. *Cerebral Cortex (New York, N.Y.: 1991)*, *11*(12), 1136–1143.

https://doi.org/10.1093/cercor/11.12.1136

Cools, R., & D'Esposito, M. (2011). Inverted-U shaped dopamine actions on human working

memory and cognitive control. *Biological Psychiatry*, *69*(12), e113–e125.

https://doi.org/10.1016/j.biopsych.2011.03.028

Davids, T. W. R. (1900). *Buddhist suttas* (Vol. 11). Clarendon Press.

Deserno, L., Moran, R., Michely, J., Lee, Y., Dayan, P., & Dolan, R. J. (2021). Dopamine

enhances model-free credit assignment through boosting of retrospective model-based

inference. *eLife*, *10*, e67778. https://doi.org/10.7554/eLife.67778

Desrochers, T. M., Amemori, K., & Graybiel, A. M. (2015). Habit Learning by Naive

Macaques Is Marked by Response Sharpening of Striatal Neurons Representing the Cost

and Outcome of Acquired Action Sequences. *Neuron*, *87*(4), 853–868.

https://doi.org/10.1016/j.neuron.2015.07.019

Desrochers, T. M., Burk, D. C., Badre, D., & Sheinberg, D. L. (2016). The Monitoring and

Control of Task Sequences in Human and Non-Human Primates. *Frontiers in Systems*

Neuroscience, *9*.

Desrochers, T. M., Jin, D. Z., Goodman, N. D., & Graybiel, A. M. (2010). Optimal habits

can develop spontaneously through sensitivity to local cost. *Proceedings of the National*

Academy of Sciences, *107*(47), 20512–20517. https://doi.org/10.1073/pnas.1013470107

Dezfouli, A., & Balleine, B. W. (2012). Habits, action sequences and reinforcement learning. *European Journal of Neuroscience*, *35*(7), 1036–1051. https://doi.org/10.1111/j.1460-9568.2012.08050.x

Dezfouli, A., Lingawi, N. W., & Balleine, B. W. (2014). Habits as action sequences: Hierarchical action control and changes in outcome value. *Philosophical Transactions of the Royal Society B: Biological Sciences*, *369*(1655), 20130482. https://doi.org/10.1098/rstb.2013.0482

FitzGerald, T. H. B., Dolan, R. J., & Friston, K. (2015). Dopamine, reward learning, and active inference. *Frontiers in Computational Neuroscience*, *9*.

Friston, K. J., Shiner, T., FitzGerald, T., Galea, J. M., Adams, R., Brown, H., . . . Bestmann, S. (2012). Dopamine, Affordance and Active Inference. *PLOS Computational Biology*, *8*(1), e1002327. https://doi.org/10.1371/journal.pcbi.1002327

Froudist-Walsh, S., Bliss, D. P., Ding, X., Rapan, L., Niu, M., Knoblauch, K., . . . Wang, X.-J. (2021). A dopamine gradient controls access to distributed working memory in the large-scale monkey cortex. *Neuron*, *109*(21), 3500–3520.e13. https://doi.org/10.1016/j.neuron.2021.08.024

Giommi, F., Bauer, P. R., Berkovich-Ohana, A., Barendregt, H., Brown, K. W., Gallagher, S., . . . Vago, D. R. (2023). The (In)flexible self: Psychopathology, mindfulness, and neuroscience. *International Journal of Clinical and Health Psychology*, *23*(4), 100381. https://doi.org/10.1016/j.ijchp.2023.100381

Goldberg, L. I., & Whitsett, T. L. (1971). Cardiovascular effects of levodopa. *Clinical Pharmacology & Therapeutics*, *12*(2part2), 376–382. https://doi.org/10.1002/cpt1971122part2376

Graybiel, A. M., & Grafton, S. T. (2015). The Striatum: Where Skills and Habits Meet. *Cold Spring Harbor Perspectives in Biology*, *7*(8), a021691. https://doi.org/10.1101/cshperspect.a021691

814 Greenberg, J., Reiner, K., & Meiran, N. (2012). "Mind the Trap": Mindfulness Practice

815 Reduces Cognitive Rigidity. *PLOS ONE*, *7*(5), e36206.

816 https://doi.org/10.1371/journal.pone.0036206

817 Gruber, A. J., Dayan, P., Gutkin, B. S., & Solla, S. A. (2006). Dopamine modulation in the

818 basal ganglia locks the gate to working memory. *Journal of Computational Neuroscience*,

819 *20*(2), 153–166. https://doi.org/10.1007/s10827-005-5705-x

820 Harmer, C. J., & Phillips, G. D. (1998). Enhanced appetitive conditioning following

821 repeated pretreatment with d-amphetamine. *Behavioural Pharmacology*, *9*(4), 299–308.

822 https://doi.org/10.1097/00008877-199807000-00001

823 Hollerman, J. R., & Schultz, W. (1998). Dopamine neurons report an error in the temporal

824 prediction of reward during learning. *Nature Neuroscience*, *1*(4), 304–309.

825 https://doi.org/10.1038/1124

826 Im, S., Stavas, J., Lee, J., Mir, Z., Hazlett-Stevens, H., & Caplovitz, G. (2021). Does

827 mindfulness-based intervention improve cognitive function?: A meta-analysis of

828 controlled studies. *Clinical Psychology Review*, *84*, 101972.

829 https://doi.org/10.1016/j.cpr.2021.101972

830 Jha, A. P., Denkova, E., Zanesco, A. P., Witkin, J. E., Rooks, J., & Rogers, S. L. (2019).

831 Does mindfulness training help working memory "work" better? *Current Opinion in*

832 *Psychology*, *28*, 273–278. https://doi.org/10.1016/j.copsyc.2019.02.012

833 Kayser, A. S., Mitchell, J. M., Weinstein, D., & Frank, M. J. (2015). Dopamine, Locus of

834 Control, and the Exploration-Exploitation Tradeoff. *Neuropsychopharmacology*, *40*(2),

835 454–462. https://doi.org/10.1038/npp.2014.193

836 Kirk, U., Gu, X., Harvey, A. H., Fonagy, P., & Montague, P. R. (2014). Mindfulness training

837 modulates value signals in ventromedial prefrontal cortex through input from insular

838 cortex. *NeuroImage*, *100*, 254–262. https://doi.org/10.1016/j.neuroimage.2014.06.035

839 Kirk, U., & Montague, P. R. (2015). Mindfulness meditation modulates reward prediction

840 errors in a passive conditioning task. *Frontiers in Psychology*, *6*.

Kirk, U., Pagnoni, G., Hétu, S., & Montague, R. (2019). Short-term mindfulness practice attenuates reward prediction errors signals in the brain. *Scientific Reports*, *9*(1), 6964. https://doi.org/10.1038/s41598-019-43474-2

Kroemer, N. B., Lee, Y., Pooseh, S., Eppinger, B., Goschke, T., & Smolka, M. N. (2019). L-DOPA reduces model-free control of behavior by attenuating the transfer of value to action. *NeuroImage*, *186*, 113–125. https://doi.org/10.1016/j.neuroimage.2018.10.075

Kuo, C.-Y., & Yeh, Y.-Y. (2015). Reset a task set after five minutes of mindfulness practice. *Consciousness and Cognition*, *35*, 98–109. https://doi.org/10.1016/j.concog.2015.04.023

Laukkonen, R. E., & Slagter, H. A. (2021). From many to (n)one: Meditation and the plasticity of the predictive mind. *Neuroscience & Biobehavioral Reviews*, *128*, 199–217. https://doi.org/10.1016/j.neubiorev.2021.06.021

Lee, W.-T., Hazeltine, E., & Jiang, J. (2022). Interference and integration in hierarchical task learning. *Journal of Experimental Psychology: General*, *151*(12), 3028–3044. https://doi.org/10.1037/xge0001246

Leow, L.-A., Bernheine, L., Carroll, T. J., Dux, P. E., & Filmer, H. L. (2023). *Dopamine increases accuracy and lengthens deliberation time in explicit motor skill learning.* bioRxiv. https://doi.org/10.1101/2023.01.31.526542

Mehta, M. A., Manes, F. F., Magnolfi, G., Sahakian, B. J., & Robbins, T. W. (2004). Impaired set-shifting and dissociable effects on tests of spatial working memory following the dopamine D2 receptor antagonist sulpiride in human volunteers. *Psychopharmacology*, *176*(3), 331–342. https://doi.org/10.1007/s00213-004-1899-2

Morey, R. D., Rouder, J. N., Jamil, T., Urbanek, S., Forner, K., & Ly, A. (2023). *BayesFactor: Computation of Bayes Factors for Common Designs.*

Nadel, J. A., Pawelko, S. S., Scott, J. R., McLaughlin, R., Fox, M., Ghanem, M., . . . Howard, C. D. (2021). Optogenetic stimulation of striatal patches modifies habit formation and inhibits dopamine release. *Scientific Reports*, *11*(1), 19847. https://doi.org/10.1038/s41598-021-99350-5

Nelson, A., & Killcross, S. (2006). Amphetamine exposure enhances habit formation. *The Journal of Neuroscience: The Official Journal of the Society for Neuroscience*, *26*(14), 3805–3812. https://doi.org/10.1523/JNEUROSCI.4305-05.2006

Patton, J. H., Stanford, M. S., & Barratt, E. S. (1995). Factor structure of the Barratt impulsiveness scale. *Journal of Clinical Psychology*, *51*(6), 768–774. https://doi.org/10.1002/1097-4679(199511)51:6%3C768::aid-jclp2270510607%3E3.0.co;2-1

Pessiglione, M., Seymour, B., Flandin, G., Dolan, R. J., & Frith, C. D. (2006). Dopamine-dependent prediction errors underpin reward-seeking behaviour in humans. *Nature*, *442*(7106), 1042–1045. https://doi.org/10.1038/nature05051

Pine, A., Shiner, T., Seymour, B., & Dolan, R. J. (2010). Dopamine, Time, and Impulsivity in Humans. *Journal of Neuroscience*, *30*(26), 8888–8896. https://doi.org/10.1523/JNEUROSCI.6028-09.2010

Reed, P. (2023). Focused-attention mindfulness increases sensitivity to current schedules of reinforcement. *Journal of Experimental Psychology: Animal Learning and Cognition*, *49*, 127–137. https://doi.org/10.1037/xan0000352

Renton, A. I., Dao, T. T., Abbott, D. F., Bollmann, S., Campbell, M. E., Chang, J., . . . Evas, S. (2022). Neurodesk: An accessible, flexible, and portable data analysis environment for reproducible neuroimaging. *bioRxiv*, 2022–2012.

Rouder, J. N., Morey, R. D., Speckman, P. L., & Province, J. M. (2012). Default Bayes factors for ANOVA designs. *Journal of Mathematical Psychology*, *56*(5), 356–374. https://doi.org/10.1016/j.jmp.2012.08.001

RStudio Team. (2020). *RStudio: Integrated development environment for r* [Manual]. Boston, MA: RStudio, PBC.

Ruocco, A. C., & Wonders, E. (2013). Delineating the contributions of sustained attention and working memory to individual differences in mindfulness. *Personality and Individual Differences*, *54*(2), 226–230. https://doi.org/10.1016/j.paid.2012.08.037

Schultz, W., Apicella, P., & Ljungberg, T. (1993). Responses of monkey dopamine neurons

to reward and conditioned stimuli during successive steps of learning a delayed response task. *The Journal of Neuroscience: The Official Journal of the Society for Neuroscience*, *13*(3), 900–913. https://doi.org/10.1523/JNEUROSCI.13-03-00900.1993

Schumacher, E. H., & Hazeltine, E. (2016). Hierarchical Task Representation: Task Files and Response Selection. *Current Directions in Psychological Science*, *25*(6), 449–454. https://doi.org/10.1177/0963721416665085

Shapiro, S. L., Carlson, L. E., Astin, J. A., & Freedman, B. (2006). Mechanisms of mindfulness. *Journal of Clinical Psychology*, *62*(3), 373–386. https://doi.org/10.1002/jclp.20237

Shohamy, D., Myers, C. E., Geghman, K. D., Sage, J., & Gluck, M. A. (2006). L-dopa impairs learning, but spares generalization, in Parkinson's disease. *Neuropsychologia*, *44*(5), 774–784. https://doi.org/10.1016/j.neuropsychologia.2005.07.013

Smith, K. S., & Graybiel, A. M. (2016). Habit formation. *Dialogues in Clinical Neuroscience*, *18*(1), 33–43.

Stan Development Team. (2023). *RStan: The R interface to Stan.*

Stillman, C. M., Feldman, H., Wambach, C. G., Howard, J. H., & Howard, D. V. (2014). Dispositional mindfulness is associated with reduced implicit learning. *Consciousness and Cognition*, *28*, 141–150. https://doi.org/10.1016/j.concog.2014.07.002

Sutton, R. S., & Barto, A. G. (2018). *Reinforcement learning: An introduction*. MIT press.

Team, S. D. (n.d.). *Stan Modeling Language Users Guide and Reference Manual.*

Vaidya, A. R., Jones, H. M., Castillo, J., & Badre, D. (2021). Neural representation of abstract task structure during generalization. *eLife*, *10*, e63226. https://doi.org/10.7554/eLife.63226

Vehtari, A., Gelman, A., & Gabry, J. (2017). Practical Bayesian model evaluation using leave-one-out cross-validation and WAIC. *Statistics and Computing*, *27*(5), 1413–1432. https://doi.org/10.1007/s11222-016-9696-4

Vo, A., Seergobin, K. N., & MacDonald, P. A. (2018). Independent effects of age and

levodopa on reversal learning in healthy volunteers. *Neurobiology of Aging, 69*, 129–139. https://doi.org/10.1016/j.neurobiolaging.2018.05.014

Vo, A., Seergobin, K. N., Morrow, S. A., & MacDonald, P. A. (2016). Levodopa impairs probabilistic reversal learning in healthy young adults. *Psychopharmacology, 233*(14), 2753–2763. https://doi.org/10.1007/s00213-016-4322-x

Waelti, P., Dickinson, A., & Schultz, W. (2001). Dopamine responses comply with basic assumptions of formal learning theory. *Nature, 412*(6842), 43–48. https://doi.org/10.1038/35083500

Wiecki, T. V., & Frank, M. J. (2010). Neurocomputational models of motor and cognitive deficits in Parkinson's disease. *Progress in Brain Research, 183*, 275–297. https://doi.org/10.1016/S0079-6123(10)83014-6

Wunderlich, K., Smittenaar, P., & Dolan, R. J. (2012). Dopamine Enhances Model-Based over Model-Free Choice Behavior. *Neuron, 75*(3-4), 418–424. https://doi.org/10.1016/j.neuron.2012.03.042
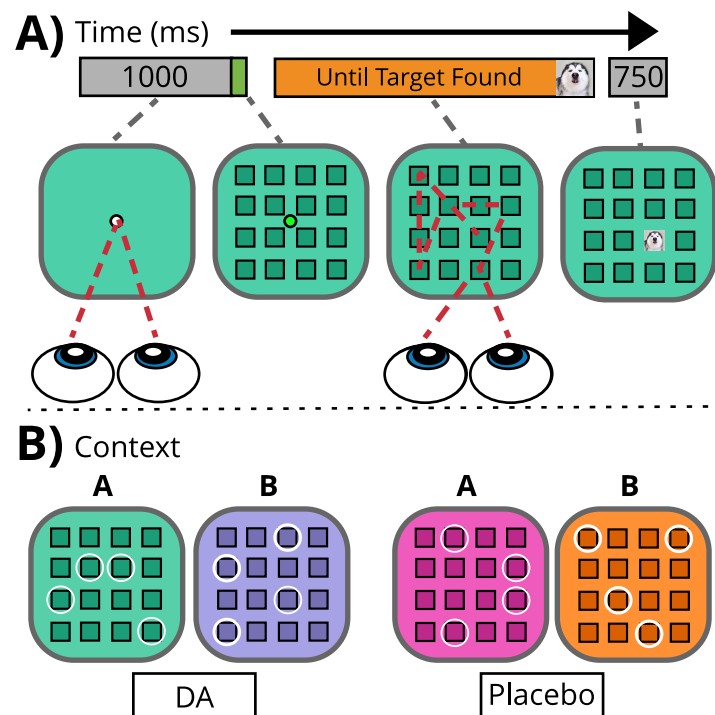
Figure 1. Experimental Task. A) A single trial where participants use their eyes to open doors to locate an animal image target. B) Contexts and sessions: in each session, participants are exposed to two colour contexts each with 4 unique and equiprobable target locations. Colours and target locations were counterbalanced across participants and sessions. In each session, levodopa (DA) or placebo is administered under double blind conditions.
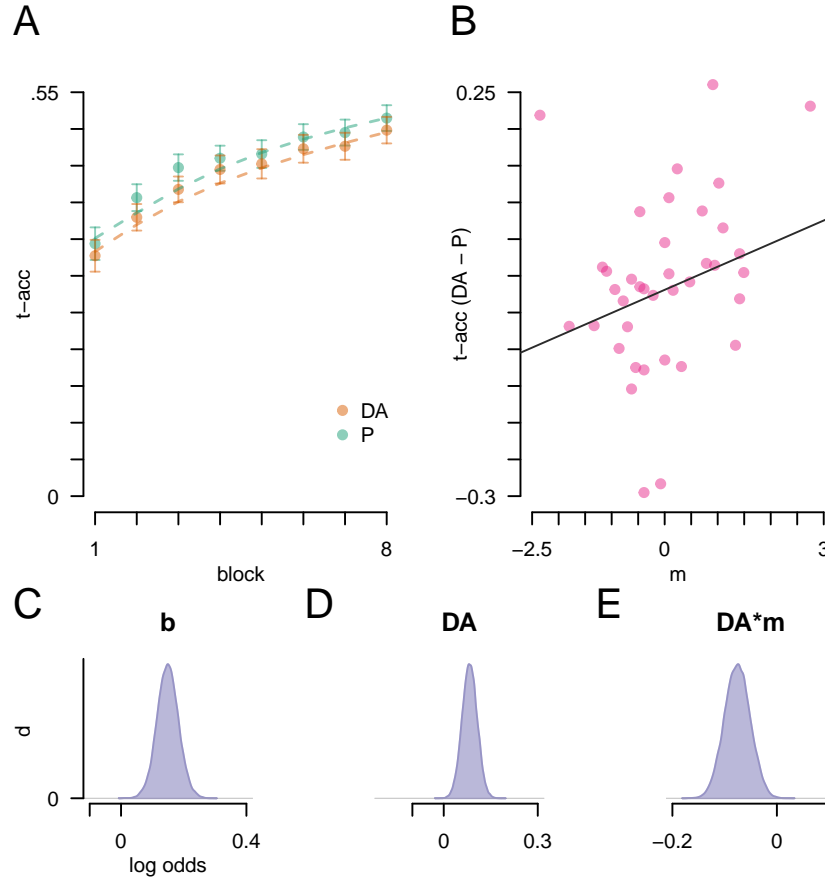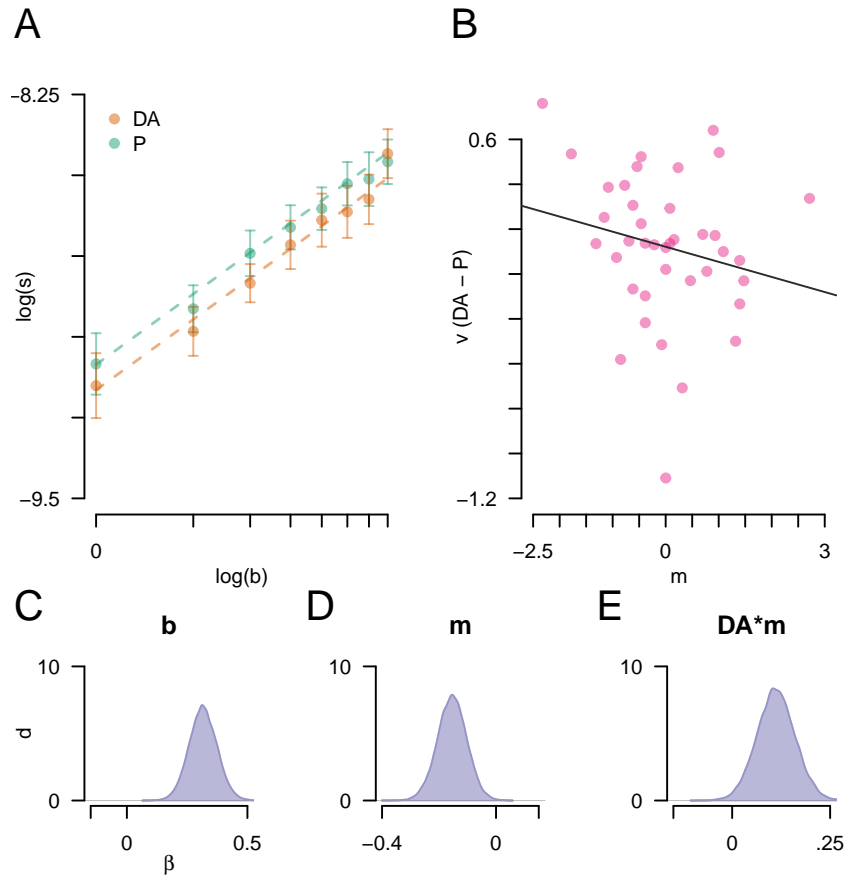
Figure 2. The influence of dopamine and mindfulness on target-accuracy. A) Target-accuracy (t-acc) data by block and drug. Circles reflect observed average target-accuracy, dotted lines reflect the fit of the winning model. B) The association between trait mindfulness (x-axis) and the impact of drug on accuracy [dopamine-placebo]. The bottom row shows posterior densities (in log odds) estimated for C) the main effect of block (b), D) the main effect of dopamine, and E) the drug x mindfulness (m) interaction. DA = dopamine, P = placebo, d = density. Error bars reflect within-subject standard error of the mean [SE].
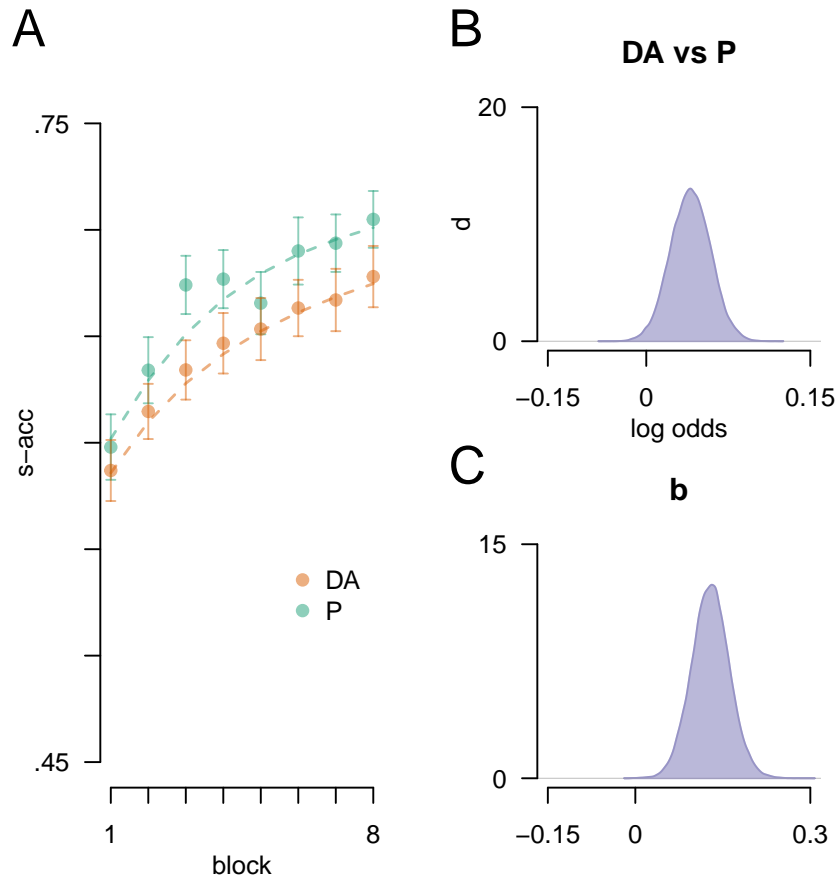
Figure 3. The influence of dopamine and mindfulness on setting-accuracy. A) Setting-Accuracy (s-acc) data by block and drug. Circles reflect observed average setting accuracy, dotted lines show the fit of the winning model. B) Estimated posterior density (in log odds) for the main effect of drug (dopamine vs placebo), D) same as in B, but for the main effect of block. DA = dopamine, P = placebo, b = block, d = density. Error bars reflect within-subject standard error of the mean [SE].

Figure 4. The influence of dopamine and mindfulness on door selection stereotypy. A) Log stereotypy scores by log block and drug. Circles reflect observed average variance (of the transition matrices), dotted lines show the fit of the winning model. B) The association between trait mindfulness (x-axis) and the impact of drug on variance [DA-P]. The bottom row shows posterior densities (in log odds) estimated for C) the main effect of block (b), D) the main effect of dopamine, and E) the drug x mindfulness (m) interaction. log(s) = log stereotypy scores, log(b) = block, DA = dopamine, P = placebo, b = block, m = mindfulness, DA*m = drug x mindfulness interaction, d = density. Error bars reflect within-subject standard error of the mean [SE].
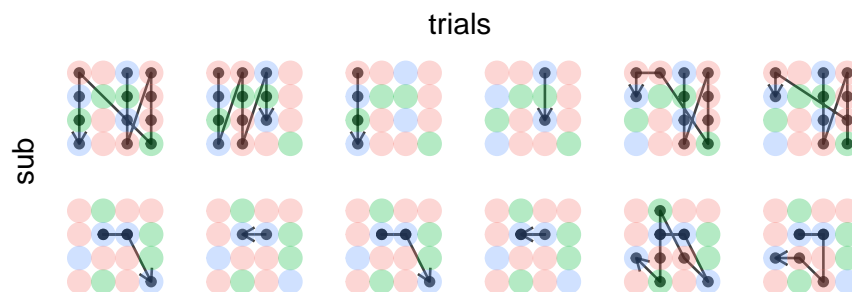
Figure 5. Example door selection routines for two participants (rows) over 6 consecutive trials from the last block of the dopamine session. Door selections follow the order indicated by the arrow. Blue circles reflect target doors for that setting, and green doors are target doors for the other setting. Red doors are erroneous doors in that a target was never found there.