- Assessing the influence of dopamine and mindfulness on the formation of routines in visual
- search
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- Assessing the influence of dopamine and mindfulness on the formation of routines in visual search
- Data: link to go here on publication Task code: as above Analysis code: as above

26 Abstract

Given experience in cluttered but stable visual environments, our eye-movements form 27 stereotyped routines that sample task-relevant locations, while not mixing-up routines 28 between similar task-settings. Both dopamine signalling and mindfulness have been posited 29 as factors that influence the formation of such routines, yet quantification of their impact 30 remains to be tested in healthy humans. Over two sessions, participants searched through 31 grids of doors to find hidden targets, using a gaze-contingent display. Within each session, 32 door scenes appeared in either one of two colours, with each colour signalling a differing set 33 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 39 dopamine improved accuracy and reduced stereotypy for high mindfulness scorers, but 40 induced the opposite pattern for low mindfulness scorers. Dopamine also disrupted 41 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 47 building adaptive repertoires.

Introduction

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Given stable environmental contingencies, it is adaptive for an organism to develop 50 routine ways of performing tasks requiring multiple responses. Dopamine is assumed to play 51 a key role in the neural computations that underlie the formation of task routines. A large 52 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 61 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,

- Myers, Geghman, Sage, & Gluck, 2006). This suggests that levodopa may increase the perceived value of actions by inducing optimistic evaluations of outcomes (FitzGerald, Dolan, & Friston, 2015), possibly by disrupting feedback processing (Shohamy et al., 2006). Elevating dopamine availability via levodopa may therefore have a comparable impact on the cost-benefit computations driving the formation of saccadic routines during visual search. Specifically, levodopa may promote an optimistic evaluation of the performed sequence, increasing the probability that it is adopted as a routine.
- For task-oriented routines to be adaptive, it is also required that they are not mixed-up 82 between tasks, despite overlap in the situational cues and actions that mark task environments. Here we define mix-ups as the performing behaviours that are relevant for the task that is not currently being performed, and we refer to this as task-interference. More broadly, dopamine is assumed to play a modulatory role in the activation of task-relevant behaviours in response to relevant situational cues (Budzillo, Duffy, Miller, Fairhall, & Perkel, 2017), as well as promoting the formation of routines. Patients with Parkinson's Disease consistently show deficits switching between simple sensorimotor tasks (R. Cools, Barker, Sahakian, & Robbins, 2001; Wiecki & Frank, 2010), as do healthy participants who have been administered D2 antagonists (Mehta, Manes, Magnolfi, Sahakian, & Robbins, 2004). Such findings have been accounted for by assuming that decreased dopamine causes increased uncertainty about the probability of being in a specific task-state (Friston et al., 2012). These assumptions are based on evidence from constrained tasks - i.e. when single correct responses are required for given stimuli. In contrast, saccadic routines are often formed from a self-selected set of many possible eye-movements, and it is unclear whether dopamine modulates switching between such routines. If a modulation is observed, it is unclear whether the effect of increasing dopamine is opposite to that of depleted dopamine, i.e. does increasing dopamine availability promote segregation of task routines? Or, does increasing dopamine availability make it more difficult to switch between routines, thereby 100 increasing the probability of interference between them? 101

A further but less frequently discussed component of the processes underlying task 102 routine learning and deployment, is the brain's execution of task-relevant cues and actions. 103 Presumably, the organism that encodes an accurate representation of cues, actions and 104 outcomes is at an adaptive advantage when forming and executing task-relevant routines. A 105 growing body of empirical evidence suggests that mindfulness may modulate such 106 representations. Mindfulness has been defined as a mental state that emphasises current 107 sensory and internal inputs (Davids, 1900; Shapiro, Carlson, Astin, & Freedman, 2006), and 108 as such is well-placed to promote accurate task-representations. In support of this, 109 mindfulness practice has been associated with increased error monitoring during cognitively 110 challenging tasks (Andreu et al., 2017), and with greater sensitivity to dynamics in operant 111 reinforcement contingencies (Chen & Reed, 2023; Reed, 2023). This suggests that increased 112 mindfulness is associated with better differentiation between current and previous contingencies of reinforcement, potentially via improved focus on the current contingencies, 114 thereby reducing interference from previous contingencies. Mindfulness has been shown to vary at the trait level and is assessable using standardized questionnaires (e.g. Baer et al, 116 (2006)).

What could be the modulatory influence of mindfulness on the formation and 118 deployment of task-relevant routines? The influence of mindfulness on routine learning and 119 task-switching may be opposing to the influence of dopamine: individuals low in trait 120 mindfulness are faster to exploit sequential regularities in stimulus-response tasks (Stillman, 121 Feldman, Wambach, Howard, & Howard, 2014), and exploitation of such regularities are 122 assumed to support habitual responses (Dezfouli & Balleine, 2012; Dezfouli et al., 2014). Mindfulness may also promote task-switching; higher levels of trait mindfulness have been 124 associated with decreased reliance on past behaviours when stimuli are conserved across 125 tasks that carry different cognitive demands (Greenberg, Reiner, & Meiran, 2012; Kuo & 126 Yeh, 2015). Indeed, both the reinforcement learning (RL) and active inference frameworks 127 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 130 cortical representations of subjective values and internal states (Kirk, Gu, Harvey, Fonagy, & 131 Montague, 2014). In the active inference framework, both dopamine (FitzGerald et al., 2015; 132 Friston et al., 2012) and mindfulness (Giommi et al., 2023; Laukkonen & Slagter, 2021) are 133 assumed to increase the salience of task relevant cues, by increasing certainty of the 134 estimates of their value. Although increasing dopamine will increase the salience of any cue 135 present, mindfulness prioritises the salience of goal-relevant cues. These theories therefore 136 posit that mindfulness may buffer against the influence of elevated dopamine, either by 137 attenuating elevated reward prediction errors, or by further amplifying the salience of cues 138 according to their goal-relevance. Despite these assumed common mechanisms of influence, it 139 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.

150 Methods

All the data from this study is available at UQ eSpace. Task code¹, analysis code and code to produce the manuscript² are available on github. [Note: a link to the data will be made available once a version of this manuscript has been accepted for publication].

The experiment and analysis plan were pre-registered on the Open Science Framework³.

155 Participants

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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 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

¹ https://github.com/kel-github/variability-decision-making

² https://github.com/kel-github/DA VisRoutes/tree/master

³ (See: https://osf.io/xn6d2/?view_only=4fc3aea02fa14da79651d892db6888c9)

was sufficient to achieve double blinding in previous work (Chowdhury, Guitart-Masip, 171 Bunzeck, Dolan, & Düzel, 2012; Chowdhury et al., 2013). Participants then completed the 172 Five Facet Mindfulness Questionnaire (Baer et al., 2006). This is a 15 item self-report 173 questionnaire that measures mindfulness with regards to thoughts and experiences in daily 174 life. It includes items such as 'I don't pay attention to what I'm doing because I'm 175 daydreaming, worrying, or otherwise distracted and 'I do jobs or tasks automatically 176 without being aware of what I'm doing'. Participants also completed the Barratt Impulsivity 177 Scale [BIS; Patton, Stanford, and Barratt (1995)], as trait impulsivity scores are associated 178 with midbrain dopamine D2/D3 receptor availability (Buckholtz et al., 2010). Around 30 179 minutes after drug administration, participants completed a second BP and mood rating 180 assessment. Participants then completed the practice stage of the task, so that the 181 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, 183 participants completed the final BP and mood rating assessment and were asked whether 184 they thought they had been given the active or placebo drug. 185

186 Apparatus

The experimental task was run with custom code⁴, 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.

⁴ https://github.com/kel-github/variability-decision-making

94 Experimental Task

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Each trial began with a fixation dot presented centrally on a grey screen [RGB: 200 195 200 200. Participants were instructed to fixate on the dot to begin a trial. After 1000 ms of 196 continuous correct fixation samples (within 100 pixels of fixation), a square was presented 197 that comprised 18° visual angle along each length. The square could be one of four possible 198 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 200 background colour ([RGB]-50). Each square comprised 2.6°. Participants were instructed 201 that the 4 x 4 grid represented doors, and that they were to use their eyes to open the doors 202 to find where the target was hiding. Participants were instructed that they were to fixate on 203 a single door to open it (see Fig 1A). When participants had fixated on a door for over 300 204 ms, the door either turned black [RGB: 50, 50, 50], to denote the absence of a target, or the 205 target was displayed and the trial was terminated. If the door had turned black, it returned 206 to its previous colour as soon as it was detected that the participant had moved their eyes 207 from the door [see Supplemental Figure 1, for a visual depiction]. Targets were animal 208 images drawn randomly on each trial from a pool of 100 images taken from the internet⁵. 209 The time at which the target was available to be found varied from trial to trial, with the 210 onset being drawn from a uniform distribution between 500-2000 ms. Once the target was 211 available and the correct door selected, the target was displayed for 750 ms. Upon 212 termination of the trial, the grey screen and white fixation cross were presented. 213

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

constraint that target locations could not overlap between settings. Thus each colour 219 reflected a setting in which participants could establish a set of task-relevant eye-movements, 220 i.e. towards the 4 possible target locations. Note that within each setting, the target was 221 equally likely to appear behind any one of the 4 target doors (p=.25) and would never appear 222 behind the remaining doors (p=0). Colour-target location mappings were counterbalanced 223 across participants, as was the assignment of colours to sessions. Participants completed 80 224 trials in each setting. Eve-movement calibration and validation was performed every 20 225 trials. Participants were also shown the standard QWERTY keyboard and were instructed 226 that they could press 'x' at any time to perform a new calibration and validation if they felt 227 that their eve-movements were no longer being registered accurately. 228

229 Statistical Approach

The analysis was designed to assess how well participants learned the target locations,
the extent to which participants formed a routine for door selections (how stereotypical they
became in their order of door-selections), and how well they disambiguated between settings.
We modelled how these elements of performance were modulated by the dopamine and
mindfulness factors. All custom analysis code is available online⁶. The analysis was
performed using R and RStudio v2022.07.2 (RStudio Team, 2020), and can be reproduced in
the Neurodesk container environment (Renton et al., 2022).

Data cleaning. We asserted that a door could not be selected twice consecutively,
thus any consecutive selections were classified as a single selection. As the final door
selection of every trial was fixed (i.e. finding the target location ends the trial), we removed
the final selection from each trial for the stereotypy (routine) analysis defined below. We
excluded data from one participant whose total number of door selections was greater than 3
standard deviations from the mean across both sessions. The remaining 39 datasets were

⁶ https://github.com/kel-github/DA VisRoutes

retained for all of the analyses. Note that this is more inclusive than our pre-registered plan for data exclusions⁷. Based on pilot data, we had planned to exclude participants who scored < 65% accuracy over the course of a session. Analysis of the final sample suggested that this was too stringent, as this resulted in the exclusion of 14 of 40 participants. We have not analysed the data with the exclusion of these participants, owing to the large drop in statistical power for the individual differences component of the analysis.

249 Target-Accuracy

We first sought to determine the extent to which levodopa and mindfulness influenced 250 the learning of target locations (target-accuracy). Data was grouped into blocks of 10 trials 251 per setting, and grouped across settings, resulting in 8 blocks of 20 trials. We computed for 252 each block the proportion of door selections that were target relevant (TR) given the current 253 setting (i.e. the setting presented on trial t). We assessed the influence of block, drug and 254 mindfulness on target-accuracy using Bayesian mixed-model logistic regression. 255 Target-accuracy was assumed to be drawn from a binomial distribution (1=target door, 0=non-target door). We then estimated the probability of drawing a target-door from the total number of door selections, using a logit link function to convert probabilities to log-odds. Thus the resulting regression parameter values reflect changes to the log-odds of 259 accurate door selections. 260

For this and following analyses, we identified the model that best fit the data, and made inference over the resulting parameters. We report the 95% confidence intervals (CIs) of the parameter posteriors, and assume a reliable effect when the 95% CIs do not include zero. Models were fit using the BRMS (Bürkner, 2017) interface for Stan (Team, n.d.) and RStan (Stan Development Team, 2023). We used the default weakly informative priors as specified in Burkner (2017). Specifically, fixed and random effect β coefficients were given a

⁷ https://osf.io/2y6pk

flat prior, intercept and standard deviations were assumed to be drawn from a student's t distribution (df=1, location=0, scale=2.5), and the LKJ-correlation prior with parameter ζ > 0 was used for the parameter covariance matrix. For each model, we checked for parameter recovery using simulated data. Once fitted, we checked that the residuals showed no signs of systematic error, that the chains had converged, and that \hat{R} values were less than 1.01, as this suggests that the model has converged.

To eschew an overly large model space, and in line with our pre-registration, we first fit 273 models that contained each possible combination of the block and drug regressors (and 274 associated random effects), and found the best model using leave-one-out (LOO) cross 275 validation, as implemented in Vehtari et al., (2017). Rather than re-fitting the model for 276 every sub-sample, which is computationally expensive, this algorithm instead computes 277 analytically how the predictions made by the model are influenced by each data point. The 278 relationship between this influence and the change in the posterior that would occur as a 279 consequence of holding out each data point can be used to compute the expected 280 log-pointwise predictive density (ELPD). This quantifies the error that would occur in the 281 prediction of each data point, when that data point is withheld from the model fitting 282 procedure. The resulting ELPDs are then compared between models. We report the ELPD difference between the winning model and the next best models (a negative value indicates preference for the winning model). As the ELPD is computed using each observed data point, it is possible to estimate the standard error (SE) of the difference between models 286 (Vehtari et al., (2017)). We therefore also report the ratio of the ELPD difference to the SE, 287 as this provides a proxy for statistical significant differences between models. (Note that in 288 the pre-registration document we had proposed to compare models using the deviance 289 information criterion (DIC). As LOO is more robust than DIC to influential observations, 290 and is readily implemented for use with BRMS model objects, we opted to use LOO instead 291 of DIC). 292

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

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possible combinations, and once again selected the best model. Last we controlled for trait impulsivity by adding BIS scores as a main effect to the winning model. Note that in no cases did adding BIS scores improve the model. The full set of model comparisons are presented in the supplementary materials.

298 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).

311 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 317 in the probability of a subset of door transitions. This stands in contrast to when making 318 door selections in an exploratory, or non-stereotyped way, where there should be an even 319 representation of door transition probabilities. Therefore, the transition probability matrices 320 of individuals engaged in more stereotypical door selections should show higher variance 321 than those who are not engaging in stereotypical door selections. We computed trial level 322 transition probability matrices, and calculated the variance of each matrix. Variances were then collapsed across settings and trials to form a stereotypy score for each participant, session and block.8 325

The resulting stereotypy scores were subject to a comparable Bayesian mixture 326 modelling approach as described above with a few key differences; the stereotypy scores were 327 assumed to be drawn from a skewed normal distribution $\mathcal{N}(\mu, \sigma, \alpha)$ whose mean (μ) was 328 defined by the regression parameters (the distribution of stereotypy scores are presented in 329 Supplemental Figure 4). σ was assumed to be drawn from a Student's t distribution (df=3, 330 location=0, scale=2.5), the skew parameter (α) was assumed to be drawn from a normal 331 distribution $\mathcal{N}(0,4)$. The remaining priors for the intercept, beta-coefficients and parameter 332 covariance matrix were defined in the same manner as for the accuracy data models. As the 333 log-log plot of variances vs block suggested a power function, analysis was performed on the 334 logged data. This ensured that the relationship between block and variance values was best 335 described by a straight line. Identification of the winning model proceeded as described for 336 the accuracy data above. 337

⁸ 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.

Blinding analyses

To determine whether awareness of the dopamine intervention could have contributed to the findings, the probability of participant ratings were compared to the expected values assuming chance guessing, using a Chi Square test. BP and mood ratings were each subject 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 346 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 351 learned to segregate task-routines (setting-accuracy). Overall, mindfulness and dopamine 352 interacted to influence the measures of target-accuracy and stereotypy; dopamine increased 353 target-accuracy and reduced stereotypy for high mindfulness scorers, whereas dopamine 354 decreased target-accuracy and increased stereotypy for low mindfulness scorers. Dopamine 355 decreased setting-accuracy independent to mindfulness scores. 356

357 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).

We next sought to determine whether adding mindfulness scores improved the predictive accuracy of the model; the winning model contained an additional main effect of mindfulness, as well as block x mindfulness and drug x mindfulness interactions (ELPD diff to best model without mindfulness = -3.12, ELPD:SE = -0.62). Therefore the winning model to account for the data was:

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

Adding BIS scores did not improve the predictive value of the model (ELPD diff = -1.95, ELPD:SE = -3.77). Note that although we draw inferences over parameters from the winning model, our inferences are the same as if we had used the more complex model that includes the BIS scores.

The effect of dopamine and mindfulness on target-accuracy. Having
established the best model to account for the data, we next determined the influence of
dopamine and mindfulness on target-accuracy by making inference over the resulting
parameters. Target-accuracy data plotted by block x drug (dopamine vs placebo) are shown
in Fig 2A. Target-accuracy improved over blocks, and there was a small main effect of drug.
These effects are described further below. However, critically, mindfulness and dopamine
interacted to influence target-accuracy. The drug x mindfulness parameter differed reliably
from zero (mean log odds = -0.08, 95% CI[-0.12, -0.03], see Fig 2E).

To investigate this interaction, we computed mean target-accuracy change due to the drug session (μ acc[dopamine - placebo]) for each participant. Note that a positive score indicates that performance was better in the dopamine session relative to placebo. Next we

examined the relationship between dopamine-induced target-accuracy changes and 388 mindfulness scores. As can be seen in Fig 2B, there was a positive relationship between 389 mindfulness and the influence of drug on target-accuracy. As mindfulness increased, so too 390 did target-accuracy for the dopamine relative to the placebo session. For a numeric example, 391 those scoring in the highest quartile showed mean target-accuracy scores of 0.47 (95%CI[0.44, 392 0.50) during the dopamine session, relative to mean target-accuracy scores of 0.41 (95%) 393 CI[0.38, 0.43]) during the placebo session. Individuals scoring low on mindfulness numerically 394 showed the opposite pattern (dopamine mean target-accuracy = 0.43, 95% CI[0.41, 0.45], 395 placebo mean target-accuracy = 0.44, 95%CI[0.43, 0.46]), note that Fig 2B shows the 396 difference between these scores). Thus the impact of dopamine on the establishment of 397 task-relevant eye-movements is dependent on the mindfulness state of the individual. 398 Participants learned the target door locations over the course of the sessions, 399 target-accuracy reliably increased over blocks. Mean target-accuracy in block 1 was 0.34 400 (95% CI[0.32, 0.37]), relative to a block 8 mean of 0.51 (95% CI[0.48, 0.53]). The model 401 showed that the log-odds of a target door selection increased over blocks by an average of = 402 0.15, (95% CI[0.08, 0.22, Fig 2C, note that the model parameters are defined in log-odds 403 because we used logistic regression). There was also the suggestion of a main effect of 404 dopamine (mean log odds = 0.08, 95% CI[0.035, 0.13, Fig 2D), however, the impact of 405 dopamine on target-accuracy is better explained by the drug x mindfulness interaction Fig 406 2E). Although the winning model contained a block x mindfulness interaction, the 95% CIs 407

410 Setting-Accuracy

parameter any further.

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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

included zero (mean log odds = 0.05, 95\% CI[-0.016, 0.12], so we do not consider 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 model contained an additional main effect of mindfulness (ELPD diff = -0.13, ELPD:SE = -0.12). Thus the winning model was:

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

Adding BIS scores did not improve the predictive value of the model (ELPD diff = -0.02, ELPD:SE = -0.03). Note that although we draw inferences over parameters from the winning model, our inferences are the same as if we had used the more complex model that includes the BIS scores.

Drug, and not mindfulness, impacts setting-accuracy. We next determined
the influence of dopamine and mindfulness on setting-accuracy by making inference over the
resulting model parameters. Dopamine reduced setting-accuracy; setting-accuracy was on
average 0.64 (95% CI [0.63, 0.65]) for the dopamine session, and 0.66 (95% CI [0.65, 0.68])
for the placebo session (see Fig 3A). The log-odds of selecting a setting-accurate target door
increased by a mean of 0.07 (95% CI[0.01, 0.13, Fig 3B) for the placebo session, relative to
the dopamine session. This suggests that dopamine caused interference between settings.

Setting-accuracy improved over blocks; mean accuracy in block 1 was 0.59 (95% CI[0.58, 0.61]), relative to block 8 (mean: 0.69, 95% CI[0.67, 0.71]). The model showed that the probability of selecting a setting relevant target door increased by a mean log odds of 0.13 (95% CI[0.07, 0.19) per block (Fig 3C). In contrast to the target-accuracy data, the main effect of mindfulness was not a sufficiently reliable predictor of setting-accuracy (mean log odds = 0.04, 95% CI[-0.04, 0.18]).

Setting-accuracy control analysis. Dopamine influences setting-accuracy, which indexes the likelihood of door selections that are relevant for the current-setting, relative to

door selections that are relevant for the other-setting. As we exclude door selections for locations that are never target relevant from the computation of setting-accuracy, it is 441 important to verify that setting-accuracy scores do indeed reflect interference between 442 settings, rather than a general task learning deficit. To address this in an exploratory 443 analysis, we reasoned that if setting-accuracy scores reflected a general deficit, then 'error' 444 door selections should be drawn randomly from not-target doors (other-setting = 4 & neither 445 = 8). A general deficit interpretation suggests that other-setting selections should be drawn 446 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 448 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 450 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 454 the hypothesis that the dopamine induced drop in setting-accuracy reflects a general 455 learning deficit.

457 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:

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

Adding BIS scores did not improve the predictive accuracy of the model (ELPD diff = -0.54, ELPD:SE = -1.41). Note that although we draw inferences over parameters from the winning model, our inferences are the same as if we had used the more complex model that includes the BIS scores.

The impact of drug and mindfulness on stereotypy. Stereotypy scores 475 increased over blocks Fig 4A. Note that this increase is also in part due to increases in 476 target-accuracy; as fewer doors are selected in error, the variance of the transition probability 477 matrices increases. We first discuss the key results, and in the next section demonstrate their relationship to target-accuracy. Critically, mindfulness and dopamine interacted to impact 479 stereotypy; we observed a reliable drug x mindfulness interaction (mean $\beta = 0.11, 95\%$ 480 CI[0.02, 0.21, Fig 4E). Mindfulness scores modulated the impact of dopamine on stereotypy. 481 As a numerical example, those scoring in the highest quartile showed mean stereotypy scores 482 of -8.74 (95%CI[-8.80, -8.68]) during the dopamine session, relative to mean stereotypy scores 483 of -8.68 (95% CI[-8.74, -8.62]) during the placebo session. Individuals scoring low on 484 mindfulness (lowest quartile) showed the opposite pattern (dopamine mean stereotypy = 485 -8.69, 95% CI[-8.75, -8.63], placebo mean stereotypy = -8.72, 95%CI[-8.78, -8.66]). 486

To visualise this interaction, we computed a mean variance change score between drug sessions for each participant (μ stereotypy[dopamine - placebo]). Note that a positive score indicates that performance was more stereotyped in the dopamine session relative to placebo. As can be seen in Fig 4B, there was a negative relationship between drug-induced stereotypy changes and mindfulness. Specifically, higher mindfulness scorers showed lower stereotypy in

the dopamine session compared to the placebo session. Low mindfulness scorers showed higher sterotypy in the dopamine session compared to the placebo session. Thus the impact of dopamine on the formation of eye-movement routines is dependent on the mindfulness state of the individual.

Participants developed more stereotypical routines over the course of the experiment, there was a clear main effect of block (mean increase per block: $\beta = 0.32$, 95% CI[0.20, 0.43, Fig 4C). In line with the interaction of drug x mindfulness reported above, the main effect of mindfulness suggested a negative relationship with stereotypy (mindfulness mean $\beta = -0.15$, 95% CI[-0.26, -0.05, Fig 4D). Overall, higher mindfulness scores predicted less stereotypy in door-selection patterns relative to low mindfulness scores.

On the relationship between target-accuracy and stereotypy. Accuracy and 502 stereotypy showed opposing relationships with mindfulness and dopamine. Higher 503 mindfulness scores were associated with dopamine-induced target-accuracy increases, and 504 stereotypy decreases, relative to placebo. Individuals scoring low on mindfulness showed a 505 deleterious influence of dopamine on target-accuracy, coupled with increased stereotypy, 506 relative to placebo. As target-accuracy and stereotypy are possibly, but not necessarily 507 related, we next sought to ensure that the observed influences of dopamine and mindfulness 508 on stereotypy was not driven solely driven by its correlation with target-accuracy, using an 509 exploratory analyses. We reasoned that such a pattern of results could be observed if the 510 measures of target-accuracy and stereotypy reflected a direct trade off; i.e. as target-accuracy goes up, stereotypy goes down. A correlation analysis ruled out this possibility. We 512 computed mean target-accuracy and stereotypy scores for each participant, collapsing across all experimental factors, and found that target-accuracy and stereotypy were positively related (r(37) = 0.81, p = 3.51e-10). 515

Next, to rule out the contribution of target-accuracy to the stereotypy results, we
added mean target-accuracy, computed for each block and drug condition, as a regressor to
the winning model. Adding target-accuracy as a regressor both clearly improved the

predictive accuracy of the model (ELPD diff = -110.26, ELPD:SE = -6.12), and served to 519 increase certainty in the interactive influence of mindfulness and drug on stereotypy scores. 520 Specifically, the estimated influence of the interaction increased from $\beta = 0.11$ to $\beta = 0.22$ 521 (95% CI[0.14, 0.29]). Note that the pattern of remaining results were also consistent between 522 the two models. Therefore, the data support the notion that mindfulness and dopamine 523 interact to differently influence target-accuracy and stereotypy when participants perform 524 task-relevant saccadic routines. Indeed, this data suggest that mindfulness and dopamine 525 interacted to produce more erroneous routines. To visualise this, Fig 5 shows example door 526 selections from two participants, one randomly selected from the lowest quartile of 527 mindfulness scorers (top row), and one selected from the highest quartile of mindfulness 528 scorers (bottom row). As can be seen, the low mindfulness scorer had adopted a routine that 529 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. 532

533 Blinding check

Next we checked if participants knew whether they had received levodopa or placebo 534 across the two sessions. Participants were asked to report at the end of each session whether 535 they thought they had received levodopa or placebo. Participant responses were coded as 536 either correct for both sessions (cc. observed N = 7), correct for one session and incorrect for 537 the other (ci: N = 11), or incorrect for both sessions (ii: N = 8). The probability of the 538 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 543 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 547 mood and blood pressure. For mood, the winning model contained a main effect of 548 time-point and no other fixed effects. This model was preferred relative to next best model, 549 which contained an additional main effect of drug (BF = 3.76, $\pm 2.14\%$) and was 550 substantially preferred over the null random intercept model (BF = $514549 \pm 1.23\%$). 551 Mean blood pressure was computed using the formula: Mean blood volume pulse 552 (BVP) = diastolic blood pressure (DBP) + 1/3 [systolic blood pressure (SBP) - DBP]. For 553 mean BVP, the winning model contained main effects of both time-point and drug. This 554 model was barely preferred to the next best model which contained a time-point x drug 555 interaction (BF = $1.7 \pm 5.69\%$), but was strongly preferred to the random intercept model 556 $(BF = 5011975 \pm 3.76\%)$. Overall, mean BVP was lower in the levodopa session (mean = 557 2.181.511261, 95% CI[80.3, 82.8]), relative to placebo (mean = 84.5, 95% CI[83.5,

560 Discussion

2.185.504042]).

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 569 target-accuracy and decreased stereotypy, for levodopa relative to placebo, whereas low trait 570 mindfulness was associated with decreased target-accuracy and increased stereotypy (for 571 levodopa relative to placebo). These results quantify, for the first time, that increasing 572 systemic dopamine availability induces an increase in stereotypy, that may come at the cost 573 of target-accuracy, that is modulated by trait-mindfulness, and that increased dopamine 574 availability increases routine confusion. These findings carry implications for our theoretical 575 understanding of how the brain establishes and switches between task-relevant behavioural 576 routines, which we outline below. 577

The current findings offer insight into the relationship between dopamine and 578 mindfulness. Dopamine and mindfulness have been indirectly related in both the 579 reinforcement learning (RL) (Kirk et al., 2014, 2019) and active inference frameworks 580 (FitzGerald et al., 2015; Friston et al., 2012; Giommi et al., 2023; Laukkonen & Slagter, 581 2021), yet there exists no other study to-date that assesses their joint impact on behaviour. 582 Here we find that levodopa and mindfulness jointly modulate learning and stereotypy, with 583 levodopa yielding conditions of decreased target-accuracy and increased stereotypy in low 584 trait mindfulness scorers. We hypothesise that low mindfulness results in poorer 585 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 587 induced by elevated dopamine availability. The result is a failure to differentiate between the 588 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 & 593 Slagter, 2021), in tandem with dopamine inducing inflated certainty regarding reward 594 outcomes (FitzGerald et al., 2015), as has been suggested via the active inference framework. 595

Note that the two accounts predict comparable outcomes so we are unable to 596 differentiate between them with the current data. However, the current findings do constrain 597 these accounts regarding the extent of overlap between the actions of dopamine availability 598 and mindfulness. Increased dopamine availability increased routine confusion, regardless of 599 trait mindfulness. Therefore, there are limitations to the modulatory influence of 600 mindfulness on the actions of dopamine. The establishment and maintenance of a task-set is 601 assumed to reflect a superordinate representation of a goal and the set of actions required to 602 attain that goal (Desrochers, Burk, Badre, & Sheinberg, 2016; Lee, Hazeltine, & Jiang, 2022; 603 Schumacher & Hazeltine, 2016; Sutton & Barto, 2018; Vaidya, Jones, Castillo, & Badre, 604 2021). The current data suggest that while dopamine and trait mindfulness can jointly 605 modulate the learning and execution of subordinate representations, i.e. the set of actions 606 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 610 superordinate levels of representation. 611

The finding that levodopa increased interference between settings extends previous 612 work showing that dopamine impacts switching between simple sensorimotor tasks that 613 require only one response (R. Cools et al., 2001; Mehta et al., 2004; Wiecki & Frank, 2010). 614 Collectively, these findings point to a U-shaped function linking dopamine levels and 615 task-switching impairments, in that depleted and inflated levels of dopamine result in poorer 616 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 618 considered the impacts of depleted dopamine (Friston et al., 2012). These findings do 619 support previously postulated hypotheses that there should be a U shaped relationship 620 between dopamine levels and task-performance, that is in part dependent on task demands 621 (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 628 required to achieve the task goal, and must associate this representation to the correct task 629 cues. We found that levodopa increased the probability that actions from a non-relevant 630 task-set would be selected during current task performance invariant to mindfulness, whereas 631 the probability that an erroneous action was selected varied across individuals according to 632 their trait mindfulness. Therefore, the most consistent locus of task-set confusion is between 633 actions that have been credited as successful in either task-context. What remains to be 634 determined is whether levodopa caused task-interference, or attenuated the ability to 635 associate successful actions with the appropriate situational cues. If the latter is true, then 636 levodopa would have caused individuals to learn one task, that did not incorporate the 637 colour cue as a relevant disambiguating signal. We seek to arbitrate between these 638 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 653 routine formation? In accordance with previous work with non-human primates (Desrochers 654 et al., 2015; Desrochers et al., 2010), the current data suggest that dopamine is a modulator 655 of the computations that drive routines in humans. However, the current data also show that 656 the modulatory influence of dopamine is dependent on the behaviour-trait state of the 657 individual. Specifically, increased dopamine appears to drive individuals low in mindfulness 658 towards a stereotypical solution that is suboptimal in terms of target-accuracy, suggesting a 659 poor evaluation of sequence costs relative to benefits. In contrast, individuals high in trait 660 mindfulness show increased target-accuracy but reduced stereotypy, suggesting an 661 appropriate crediting of successful actions, but also suggesting either some volatility in their 662 execution, or better learning that the probability of a target was uniform across 663 target-relevant locations. While the current data demonstrate the applicability of dopamine 664 signalling to the computations that underlie the formation of routines, the data also show 665 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 684 between the levodopa and placebo sessions, suggesting more general physiological differences 685 between the sessions. However, the effect of levodopa on blood-pressure is well characterised, 686 and depends partly on the effective dose (dose per kilogram, Goldberg et al (Goldberg & 687 Whitsett, 1971)). It is unlikely that low and high mindfulness individuals differed 688 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, 690 the physiological changes appeared to not be subjectively detectable, lowering the likelihood 691 that discernible subjective differences impacted the results. Note that although the power of 692 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, & 696 MacDonald, 2018; Vo, Seergobin, Morrow, & MacDonald, 2016; Wunderlich et al., 2012). 697

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 707 the first session may show carry-over effects to the subsequent session, e.g. levodopa may 708 modulate the extent to which the individual learns that there are two settings, and this may 709 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 714 conditions that allow us to tease out order effects, for example by including DA-DA and 715 placebo-placebo conditions. 716

We sought to determine the modulatory influence of dopamine availability and 717 trait-mindfulness on the formation and deployment of task-relevant saccadic routines. We 718 found evidence for theoretical assertions that dopamine and mindfulness share overlap in 719 their locus of influence, but also demonstrated boundaries in that overlap. Mindfulness 720 modulated the impact of dopamine on task-learning and routine development, with levodopa 721 administration resulting in low mindfulness individuals being more likely to show impaired learning and increased stereotypy. Invariant to trait-mindfulness, levodopa increased the 723 likelihood of task-interference between settings, suggesting that dopamine either hampers the binding of actions to situational cues, or promotes confusion between task-states. 725 Collectively, these data suggest that the fidelity of situational representations interact with 726 reinforcement learning systems to drive the formation of behavioural routines. 727

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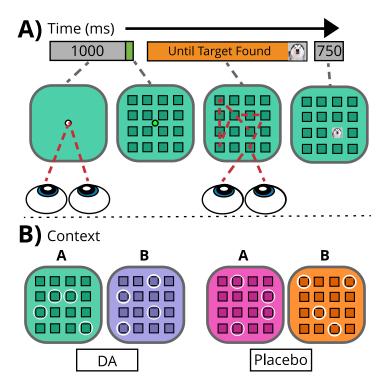


Figure 1. Experimental Task. A) A single trial where participants use their eyes to open doors to locate an animal image target. B) Contexts and sessions: in each session, participants are exposed to two colour contexts each with 4 unique and equiprobable target locations. Colours and target locations were counterbalanced across participants and sessions. In each session, levodopa (DA) or placebo is administered under double blind conditions.

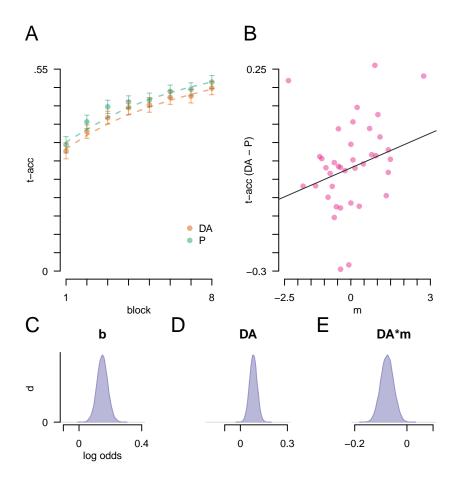


Figure 2. The influence of dopamine and mindfulness on target-accuracy. A) Target-accuracy (t-acc) data by block and drug. Circles reflect observed average target-accuracy, dotted lines reflect the fit of the winning model. B) The association between trait mindfulness (x-axis) and the impact of drug 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].

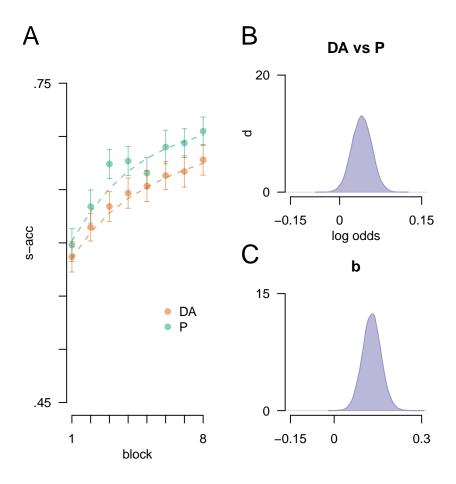


Figure 3. The influence of dopamine and mindfulness on setting-accuracy. A) Setting-Accuracy (s-acc) data by block and drug. Circles reflect observed average setting accuracy, dotted lines show the fit of the winning model. B) Estimated posterior density (in log odds) for the main effect of drug (dopamine 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].

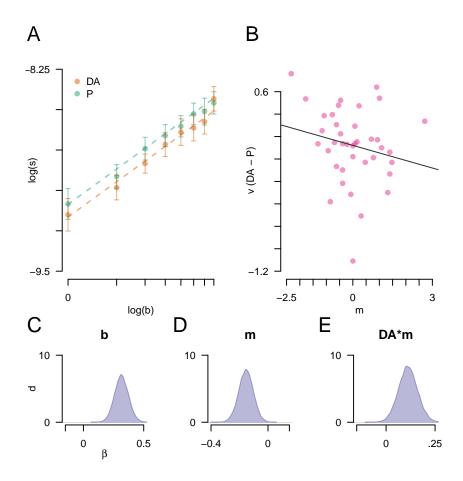


Figure 4. The influence of dopamine and mindfulness on door selection stereotypy. A) Log stereotypy scores by log block and drug. Circles reflect observed average variance (of the transition matrices), dotted lines show the fit of the winning model. B) The association between trait mindfulness (x-axis) 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, $\log(b) = \operatorname{block}$, $\operatorname{DA} = \operatorname{dopamine}$, $\operatorname{P} = \operatorname{placebo}$, $\operatorname{b} = \operatorname{block}$, $\operatorname{m} = \operatorname{mindfulness}$, $\operatorname{DA}^* = \operatorname{drug} \times \operatorname{mindfulness}$ interaction, $\operatorname{d} = \operatorname{density}$. Error bars reflect within-subject standard error of the mean [SE].

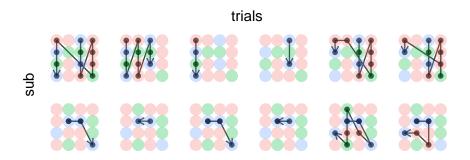


Figure 5. Example door selection routines for two participants (rows) over 6 consecutive trials from the last block of the dopamine session. Door selections follow the order indicated by the arrow. Blue circles reflect target doors for that setting, and green doors are target doors for the other setting. Red doors are erroneous doors in that a target was never found there.