Dopamine alters motor learning performance in the presence and absence of feedback.

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Abstract

Skilled motor performance is essential for survival. Indeed, we often not only choose to learn motor skills because of some external reward, but also because skilled movement, in and of itself, is satisfying. While dopamine is known to drive reward-based motor learning, it remains unclear whether dopamine is implicated in motor learning under conditions ostensibly driven by intrinsic rewards/motivation (i.e., in the absence of extrinsic feedback or reward). Here, we investigated the role of dopamine in motor skill learning guided by internally determined signals of performance success, using a task where learning occurred either in the absence or presence of feedback. We found that dopamine altered performance both in the presence and in the absence of information on task success. This provides direct causal evidence for a role of dopamine in motor learning driven by internal task goals.

Learning motor skills is often driven by extrinsic reward: to play her favourite app-based game, a child quickly learns the sequence of finger-swipes needed to unlock her parent's mobile phone. Extrinsic rewards can take the form of primary (e.g., food, water) or secondary rewards (e.g., points or money) contingent upon achieving some performance criteria. The promise of reward not only drives movements to be more vigorous (e.g., Carpenter & Williams, 1995; Milstein & Dorris, 2007; Manohar *et al.*, 2015; Reuter *et al.*, 2018; Summerside *et al.*, 2018; Carroll *et al.*, 2019; Galaro *et al.*, 2019), but can also improve the acquisition (Nikooyan & Ahmed, 2015) and retention (Abe *et al.*, 2011; Galea *et al.*, 2015; Dayan *et al.*, 2016; Hamel *et al.*, 2019; Spampinato *et al.*, 2019; van der Kooij & Smeets, 2019; Sporn *et al.*, 2022; Yin *et al.*, 2023) of motor learning. A key mechanism through which reward alters behaviour is via reward prediction errors, defined as discrepancies between predicted and actual rewards (Sutton & Barto, 1998). Reward prediction errors trigger phasic firing of midbrain dopamine neurons (Schultz *et al.*, 1997), which alters the vigor of movements (Sedaghat-Nejad *et al.*, 2019) and shapes motor behaviour (Izawa & Shadmehr, 2011; Cashaback *et al.*, 2017).

Yet we also often learn for its own sake. In the absence of extrinsic rewards, a child learns how to ride a scooter not because she receives some reward, but because scooter-riding is inherently fun. The distinction between behaviour driven by intrinsic motivation and extrinsic rewards has long been recognised (Harlow, 1950; Ryan & Deci, 2000; Baldassarre & Mirolli, 2013). Although we do not fully understand the drivers of intrinsic motivation, it appears to be modulated by internal rewards associated with meeting task goals (Blain & Sharot, 2021). Information about task success might thus modulate intrinsic motivation. In experimental contexts, information about task success can alter motor learning (Schaefer *et al.*, 2012; Cashaback *et al.*, 2017; Leow *et al.*, 2018; Palidis *et al.*, 2018; Sidarta *et al.*, 2018; Kim *et al.*, 2019; Leow *et al.*, 2020; Sadaphal *et al.*, 2022; Tsay *et al.*, 2022), and its effects seem separable to extrinsic rewards contingent upon task performance (Vassiliadis *et al.*, 2021).

How does the brain learn motor skills in the absence of extrinsic rewards? Whilst an increasing body of work characterises the neural mechanisms of learning driven by extrinsic rewards, comparatively little is known about how we learn and act in the absence of extrinsic rewards (Blain & Sharot, 2021). Work in animal models implicates the dopamine system. For example, dopamine neurons in zebra finches show spontaneous activity that correlates with song performance, even in the absence of extrinsic rewards, cues, or external perturbations (Duffy *et al.*, 2022). In humans, learning and performing actions in the absence of extrinsic rewards engages midbrain dopamine-dependent reward networks that are also involved in processing primary rewards, such as the ventral striatum (Ripolles *et al.*, 2016) and the ventromedial prefrontal cortex (Chew *et al.*, 2021). This supports the view that intrinsic rewards alters behaviour mostly by co-opting existing dopamine-dependent neural circuitry used to process primary rewards (Blain & Sharot, 2021). However, intrinsic and extrinsic rewards evoke subtly different brain responses: for example, learning with and without extrinsic rewards seems to differentially implicate the dorsal and ventral striatum (Lutz *et al.*, 2012; Ripolles *et al.*, 2016), areas with substantial functional heterogeneity (Collins & Saunders, 2020). It thus remains unclear if and how processing of intrinsic and extrinsic rewards might differentially implicate brain dopamine function during learning and performance of motor skills.

Here, in a pre-registered study, we asked the following question: how does dopamine contribute to learning driven by internal goals in the absence of extrinsic rewards? We asked participants to complete an aiming task, where they were explicitly instructed to aim away from presented targets by

angles that ranged in size, where larger aiming angles are more difficult. In this target-hitting task, participants were either deprived of information about the task success (targets always disappeared mid-movement, thus precluding knowledge of target-hits/misses); or given information about task success (targets jumped mid-movement by the instructed aiming angle, such that participants were rewarded with target hits and avoided target-misses when they succeeded at the task of aiming by the instructed angle). Such feedback about task success often alters accuracy in reaching tasks (Leow *et al.*, 2020; Sadaphal *et al.*, 2022; Tsay *et al.*, 2022), and thus we expected this task feedback to also increase aiming accuracy and/or shorten reaction times. Task success information might directly affect motor performance, and/or affect motor performance indirectly, by altering intrinsic motivation to attain task goals. We assessed the role of dopamine in learning and performance in the absence or presence of task success information, by having participants consume Levodopa, a dopamine precursor which increases brain dopamine availability. We hypothesized that if dopamine contributes to performance by primarily altering the processing of extrinsic task success information, then dopamine will only alter motor performance in the presence of feedback about task success. Alternatively, if dopamine alters performance primarily by modulating intrinsic motivation, then manipulating dopamine will affect performance in a similar fashion regardless of the absence/presence of feedback about task success. Finally, if dopamine alters learning regulated by internal estimations of task performance and learning regulated by extrinsic task success information, then dopamine will alter performance both in the presence and absence of feedback about task success, but effects will differ between conditions.

2. Method

2.1. Participants

Participants were recruited from The University of Queensland community and were reimbursed for participation (AUD$20/hour). Participants were screened for neurological and psychiatric conditions, contraindications for Levodopa, and injury preventing the use of their right-arm and provided written informed consent. In accordance with the National Health and Medical Research Council's guidelines, this experiment was approved by the human ethics committee at The University of Queensland. No datasets were excluded from the study.

To the best of our knowledge, there are no equivalent studies examining how dopamine alters motor performance on a visuomotor mental rotation task in the presence or absence of extrinsically defined task errors. We used a Bayesian stopping rule to optimize sample sizes, as stated in our preregistration (https://osf.io/m7a3g/). Specifically, we intended to stop data collection either upon obtaining moderate evidence for including or excluding an effect of dopamine ($BF_{incl} > 3$ or $BF_{excl} > 3$) for aiming accuracy or reaction times, or upon collecting 80 complete datasets (20 participants for each of the 4 conditions), in line with previous studies which examine effects of Levodopa on motor performance in neurotypical young adults. We reached our stopping rule of $BF_{incl} > 3$ upon collecting the minimum of 15 participants per group.

2.1. Study design

In this 2 x 2 between-subjects design manipulating drug (placebo, levodopa) and feedback about task success (no feedback, feedback), participants were randomly assigned to complete one of the following four study conditions: (1) placebo + feedback (n=15), (2) levodopa + feedback (n=17), (3) placebo + no-feedback (n=15), and (4) levodopa + target disappear (n=16). Randomisation of study

conditions to each participant was performed using https://www.random.org/. The feedback manipulation is detailed later. Briefly, in the task feedback condition, targets "jumped" mid-movement by the instructed aiming angle, such that target-hits were contingent upon successful aiming. In the no-feedback condition, targets disappeared mid-movement, removing the possibility of target hits regardless of aiming success: participants thus had no feedback about their task success.

2.3. Drug manipulation

Participants ingested either Madopar 125 tablet (100mg Levodopa and 28.5mg benserazide hydrochloride) or a vitamin C tablet (Placebo). Tablets were crushed and dispersed in orange juice to achieve participant blinding. Drug administration was completed by an experimenter uninvolved in data collection, out of view of the experimenter responsible for data collection, to achieve experimenter blinding. This method is effective for double-blinding (Beierholm *et al.*, 2013; Leow *et al.*, 2023; Leow *et al.*, 2024). We chose Levodopa as it increases brain dopamine levels without affecting norepinephrine levels (Everett & Borcherding, 1970), and achieves peak plasma levels within approximately 45 minutes of ingestion. Participants waited 45 minutes after drug ingestion to complete the aiming task. During this wait period, we assessed participants trait impulsivity by asking participants to complete the Barratt Impulsivity Scale, and assessed working memory capacity by asking participants to complete either the memory updating task or the operation span task (Lewandowsky *et al.*, 2010); the other task was completed at the end of the session). These measures were taken as proxy measures of individual baseline dopamine function, which has previously been found to be partly predicted by impulsivity (Buckholtz *et al.*, 2010) and working memory (Cools *et al.*, 2008). Some studies find such measures can partly predict effects of pharmacological manipulations of dopamine (Clatworthy *et al.*, 2009; Broadway *et al.*, 2018; Fallon *et al.*, 2019): thus, we intended to include these measures as covariates of no interest in our analyses.

To assess for changes in arousal, heart rate, blood pressure, and mood were measured at three timepoints (1) before drug ingestion, (2) approx. 15-20 minutes post-ingestion, and (3) post-study completion (approx. 150 minutes post-ingestion). Mood was assessed using the Mood Rating Scale (Bond & Lader, 1974) which includes sixteen items separated in following factors: alertness, contentedness and calmness.

2.4. Apparatus

We used a vBot planar robotic manipulandum (Howard *et al.*, 2009), which has a low-mass, two-link carbon fiber arm and measures position with optical encoders sampled at 1,000 Hz. Participants completed the aiming task while seated on a height-adjustable chair at their ideal height for viewing the screen. Visual feedback was presented on a horizontal plane on a 27" LCD computer monitor (ASUS, VG278H, set at 60-Hz refresh rate) mounted above the vBOT and projected to the subject via a mirror in a darkened room. Participants had no direct vision of their hand. Hand position was represented by a red cursor (0.25 cm radius circle) on a black background. The mirror also allowed visual feedback of the target (a 0.5 cm-radius circle) and the start location (a 0.35 cm radius circle), which was aligned 10 cm to the right of the participant's midsagittal plane at approximately mid-sternum level.

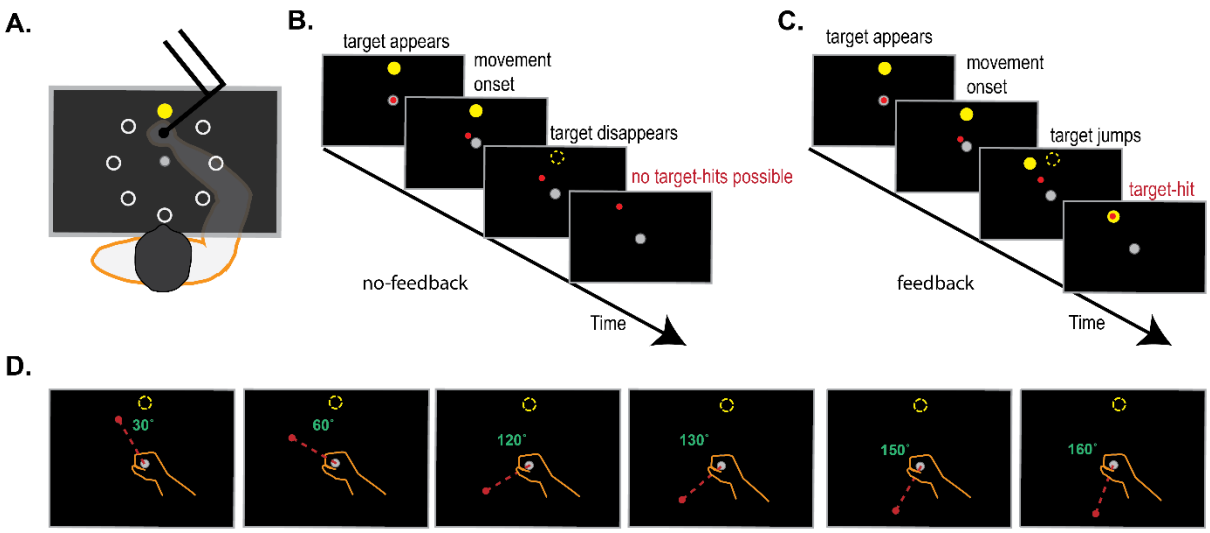

Figure 1. A. Participants completed the aiming task by aiming away from one of eight possible targets (each 1 of the 8 target positions appeared in random order in every bin, where 1 bin= 1 visit to each of the 8 targets). This task resembles those of (Georgopoulos & Massey, 1987; Neely & Heath, 2010) B. In the no-feedback condition, participants did not know whether they successfully hit the target, as the targets would disappear mid-movement, making target-hits impossible. C. In the feedback condition, as the target would "jump" mid-movement by the instructed aiming angle, successful aiming by the instructed aiming angle would result in target hits. D. During training, participants aimed away from the presented targets by the instructed angles (30°, 60°, 120°, 130°, 150°, 160°), for 10 bins, under either the no-feedback or the feedback condition. The order of the aiming angle was the same for all participants: 130°, 30°, 0°, 150°, 60°, 160°, 120°.

2.5. Aiming task

2.5.1. Trial structure

In the aiming task, participants were asked to aim towards targets by an instructed aiming angle. At the start of each trial, participants saw a grey start position (0.35cm radius circle) aligned approximately 10cm to the right of participant's midsagittal plane, mid-sternum level, and a red virtual circular cursor (a 0.25cm radius circle) representing robot handle position against a black background. With their right hand holding the robot handle, participants first positioned the cursor in the start circle. Once the cursor stayed within the start circle for 2 seconds, a yellow target (0.5cm radius circle), accompanied by an auditory signal, appeared at one of eight possible target directions, in random order (0°, 45°, 90°, 135°, 180°, 225°, 270°, or 315°), 9cm away from the start. Target directions were pseudorandomised such that each of the 8 possible targets directions occurred once every 8 trials (every 8 trials was 1 bin). Once a trial was initiated, if no initiation of arm movement was detected within 6 seconds, the trial was terminated. Similarly, in instances where the participant failed to achieve the required movement extent (the 9cm start-target distance), the trial was terminated. Terminated trials were replaced at the end of each 8-trial bin.

2.5.2. Block structure

First, participants received a familiarisation block where they were acquainted with the task of aiming away from the presented target by 90° clockwise. Then, participants were asked to aim away from the presented target by 7 prespecified angles: 30°, 60°, 120°, 130°, 150°, and 160°, clockwise. Block order

was the same for all participants: 130°, 30°, 0°, 150°, 60°, 160°, 120°. For each aiming angle, participant completed sets of the following blocks.

(1) **Instruction**: 3 bins (24 trials). To explicitly instruct participants on the aiming task, a ring of landmarks (letters and numbers) were displayed around the target positions, and participants were asked to aim directly towards the letter 'A' which was positioned at the instructed aiming angle relative to the current target.
(2) **Training:** 10 bins (80 trials). Depending on assigned condition, participants either received feedback about task success/task failure, or no feedback. In the **feedback condition**, feedback on task success was given by having the target "jump" mid-movement by the instructed aiming angle (0°, 30°, 60°, 120°, 130°, 150°): successful aiming resulted in a target-hit, unsuccessful aiming resulted in a target miss. This "jump" was achieved by extinguishing the target once the movement extent exceeds 4cm (start-target distance = 9cm), and immediately re-displaying the target at the ideal aiming direction. In the **no-feedback condition**, targets were extinguished once the movement extent exceeded 4cm: preventing the experience of target hits or target misses.
(3) **Post-training probe**: 5 bins (40 trials). To assess for persistent effects of feedback during training, aiming behaviour was assessed in probe trials, which provide no feedback (i.e., targets disappeared mid-movement).
(4) **Washout:** 5 bins (40 trials). To return behaviour to baseline, participants were asked to aim directly towards the presented target. The target remained visible throughout the trial.

To reduce task duration, we did not include the landmark, probe, or washout trials for the straight ahead (0°) aiming angle. Participants completed a total of 1368 trials.

2.6. Data analysis

Our analyses followed our preregistration analysis plan (https://osf.io/m7a3g/). As our task instructions emphasized accurate aiming, our primary dependent variable of interest was aiming accuracy, which was estimated from absolute directional error: the unsigned difference between the ideal aiming angle and the absolute values of the actual reach direction, where reach direction was measured at 20% of the start-target distance (i.e., 1.8 cm into the 9cm start-target distance). We note that this differs from our recent study **(Leow *et al.*, 2024)**, where we estimated signed directional errors (signed difference between unsigned reach directions and the ideal aiming angle, which allows us to distinguish between under-aiming and over-aiming, e.g., reach angles of less than or greater than the aiming angle). Here we were not interested in distinguishing between under-aiming and over-aiming: instead, we were interested in absolute unsigned errors in reaching to the target. We also assessed the number of target-hits (i.e., the number of trials where participants 0.25cm radius cursor was in contact of the 0.5cm radius target).

Whilst our instructions and task structure emphasised aiming accuracy, we were also interested in evaluating changes in the speed of movement planning. To this end, we also quantified reaction time, defined as the interval from target appearance to movement onset, where movement onset was the time at which the hand speed first exceeded 2 cm/s.

In accordance to our preregistered analysis plan, to test the effect of the drug and target-jump manipulations on aiming performance, we ran Bayesian Repeated-Measures ANOVAs with within-subjects variables Angle (0°, 30°, 60°, 120°, 130°, 150°, 160°) and Bin (1….10) and between-subjects

variables Drug (Placebo, Levodopa) and Condition (Target Jump, Target Disappear) on dependent variables of interest, for the instruction block, training block and the post-training probe block. To evaluate how the task feedback manipulations altered performance and training-related performance gains in the absence and presence of levodopa, we ran follow-up Feedback x Angle x Bin ANOVAs, separately for the placebo and levodopa groups. To evaluate how levodopa altered performance and training-related performance gains with and without task feedback, we ran follow-up Drug x Angle x Bin ANOVAs, separately for groups with and without task feedback. Statistical analyses were run using JAMOVI 2.3.28.

In our preregistration, we stated that we would enter impulsivity and working memory capacity as covariates of no interest, following previous work that use such measures as a proxy of striatal dopamine synthesis capacity, as they are thought to predict responsivity to dopamine drug manipulations. However, new evidence shows evidence against the use of impulsivity or working memory capacity as a proxy of striatal dopamine synthesis capacity (van den Bosch *et al.*, 2023). Furthermore, because our Bayesian stopping rule stipulated that we stopped data collection upon showing moderate evidence for an effect of drug, we stopped data collection at a relatively small sample size that precludes strong inferences about these covariates. Results were not meaningfully altered by including the covariates. We thus decided against entering impulsivity and working memory capacity as covariates in our analyses.

3. Results

3.1. Manipulation checks

We first evaluated learning effects by testing whether our explicit instructions, given in the pre-training instruction block, improved task performance, and then asessing whether performance improved across bins during the training block.

3.1.1. Explicit task instructions improved performance.

In each instruction block, prior to each training block, participants were given 24 trials (3 bins) with the same explicit task instructions and aiming landmarks across all conditions, to help participants learn to aim at the required aiming angles. Aiming performance improved across bins during the instruction blocks, as reaction times reduced from the first bin to subsequent bins (main effect of bin for reaction time BF_{incl} = 4.70E+29), whilst accuracy was maintained across bins (no evidence for main effect of bin for error, BF_{incl} = 0.504). Levodopa did not alter reaction times nor accuracy in the instruction blocks (moderate strong evidence for excluding the main effect of drug and interactions with drug, BF_{excl} ranging from 2.89 to 14.196).

3.1.2. Training improved performance across bins

Training improved performance across the 10 training bins, as evidenced in reduced errors across bins (error, BF_{incl} = 5.351; see Figure 4), as shown by moderate to strong evidence for the main effect of training bin for reaction time (BF_{incl} = 1479.072). Hit rates were maintained across bins, as shown by moderate to strong evidence for excluding a main effect of bin (BF_{excl} = 5039) and all interactions with bin (BF_{excl} > 7).

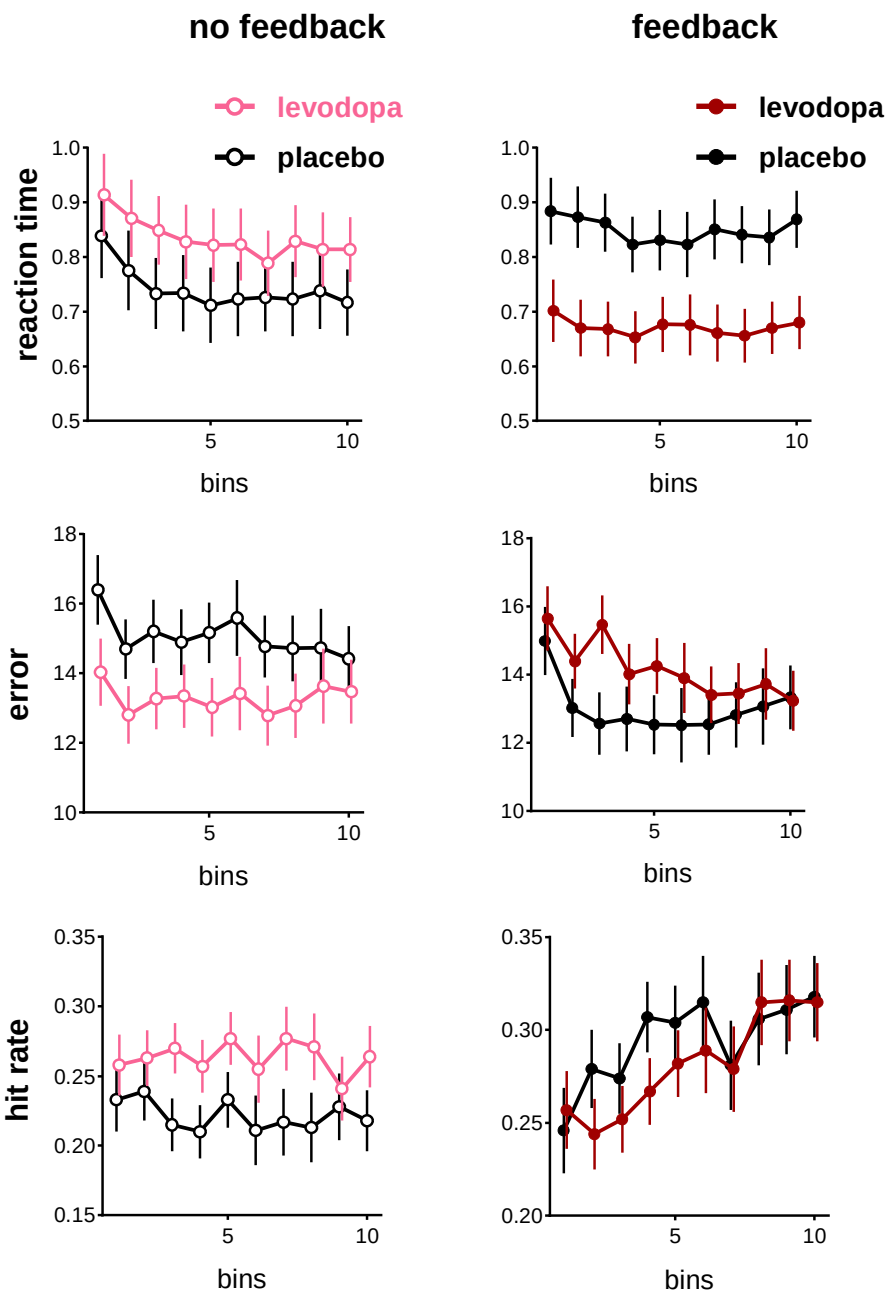

Figure 2. Bin-by-bin target hit rates, errors, and reaction times, averaged across all aiming angles (except for 0°). Without task feedback, levodopa augmented the tendency to trade speed for accuracy, resulting in overall lengthier reaction times, smaller errors, and higher hit rates. With task feedback, levodopa shortened reaction times and slightly increased errors, whilst still maintaining similar hit rates.

3.2. Dopamine altered performance both with and without task feedback.

Dopamine differentially altered performance depending on the presence of task feedback (see Figure 3), although the effects of dopamine depended on aiming angle (hit rate: angle x drug interaction, BF_{incl} = 2.221 e+7) and feedback condition [angle x dopamine x feedback interactions for error (BF_{incl} = 25.226) and reaction time (BF_{incl} = 6.71e+9)].

In the absence of task feedback, levodopa (relative to placebo) augmented the tendency to trade speed for accuracy, resulting in overall longer reaction times (angle x drug interaction, BF_{incl} = 7.332, post-hoc t-tests for effect of drug: $BF_{10, U}$ = 392303), smaller errors ($BF_{10, U}$ = 10549), and higher hit rates ($BF_{10, U}$ = 50741). Indeed, levodopa reduced errors even when aiming straight at the target ($BF_{10, U}$ = 4164). This effect of levodopa in trading-off speed for accuracy persisted into the post-training probe block, with moderate to strong evidence that dopamine improved accuracy ($BF_{10, U}$ = 5.148) and hit rates ($BF_{10, U}$ = 399.473) and lengthened reaction times ($BF_{10, U}$ = 27.301).

In the presence of task feedback, dopamine sped up reaction times whilst maintaining achievement of the task goal (hitting the target), at a small cost of reduced aiming accuracy. Specifically, while levodopa (relative to placebo) had no effect on hit rates (moderate evidence for the null hypothesis for the main effect of Drug $BF_{01, U}$ = 7.451), it shortened reaction times (main effect of drug, BF_{incl} = 2.73, angle x drug interaction, BF_{incl} = 6.53e+16, post-hoc t-tests on effect of drug, $BF_{10, U}$ = 3.35e+26). For the largest aiming angles (130, 150, 160), these faster reaction times under levodopa conditions were accompanied by a small overall mean increase in errors of 2.159° (see Figure 3 bottom panel). Follow-up Angle x Bin ANOVAs and post-hoc tests for these three large angles yielded strong evidence for the effect of drug [$BF_{10, U}$ = 2413], although the main effect of drug was indeterminate [BF_{incl} = 0.597]. Effects persisted into the post-training probe block where the task feedback was removed, as dopamine sped up reaction times ($BF_{10, U}$ = 3.834e+17) whilst maintaining accuracy (strong evidence for the null hypothesis, $BF_{01, U}$ = 13.469) and hit rates (moderate evidence for the null hypothesis, $BF_{01, U}$ = 7.792).

Note that similar to our previous work (Leow *et al.*, 2024), the 130° aiming direction resulted in lower errors, possibly because participants could use the strategy of aiming by 50° counterclockwise, and because 50° is similar to the familiar angle of 45°: familiar angles tend to require in shorter movement planning times (Neely & Heath, 2010).

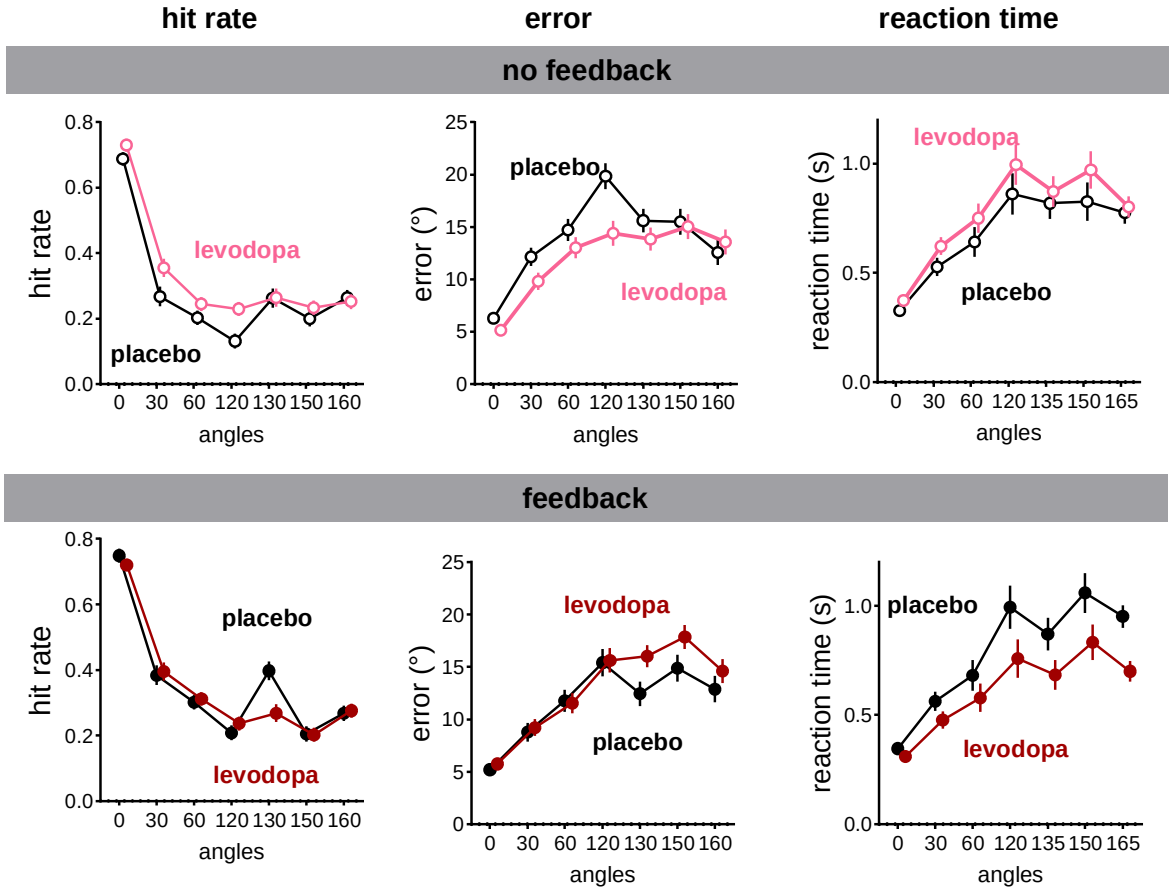

Figure 3. Without task feedback, levodopa increased the tendency to trade speed for accuracy, increasing hit rates and reducing errors whilst lengthening reaction times. Task feedback seemed to reduce this tendency to trade speed for accuracy: with task feedback, levodopa sped-up reaction times at a small cost to accuracy for larger angles, whilst mostly maintaining hit rates (except for the 130 angle).

3.3. Levodopa renders performance resilient to detrimental effects of feedback absence.

The effect of feedback on performance depended on whether participants received levodopa or placebo. In contrast to their placebo group counterparts, who showed lower hit rates and larger errors in the absence of task feedback (see Figure 4 top left panels), levodopa group participants maintained high hit rates and accuracy with and without task feedback (see Figure 4 bottom left panels), possibly by trading off speed in movement planning for accuracy in the absence of task feedback (Figure 4 bottom right panel). This was illustrated by a Drug x Feedback x Angle interactions for error (BF_{incl} = 25.226) and reaction time, (BF_{incl} = 6.71e+9). To evaluate the effect of task feedback on training performance, with and without exogenous dopamine, we ran separate Feedback x Angle ANOVAs for the placebo and levodopa groups.

In the absence of exogenous dopamine (i.e., in the placebo groups), task feedback increased accuracy at the cost of slower reaction times for larger, more difficult aiming angles, as the task-feedback group showed higher hit rates ($BF_{10, U}$ = 2.065e+13) and reduced errors ($BF_{10, U}$ = 1.698e+8), (see Figure 4 top

panels), but this greater accuracy came at the cost of lengthier reaction times for larger aiming angles of 120 and above ($BF_{10, U}$ = 4.491e+13).

In the presence of exogenous dopamine (i.e., the levodopa groups), task accuracy was not influenced by task feedback - see Figure 4 bottom left panels, moderate evidence for null effect of task feedback for hit rate (BF_{incl} = 5.376), inconclusive effect of task feedback for error (BF_{incl} = 1.136). This maintenance of accuracy despite an absence of task feedback co-occurred with lengthened reaction times (angle x feedback interaction, BF_{incl} = 24.036, effect of feedback: $BF_{10, U}$ = 4.219e+21).

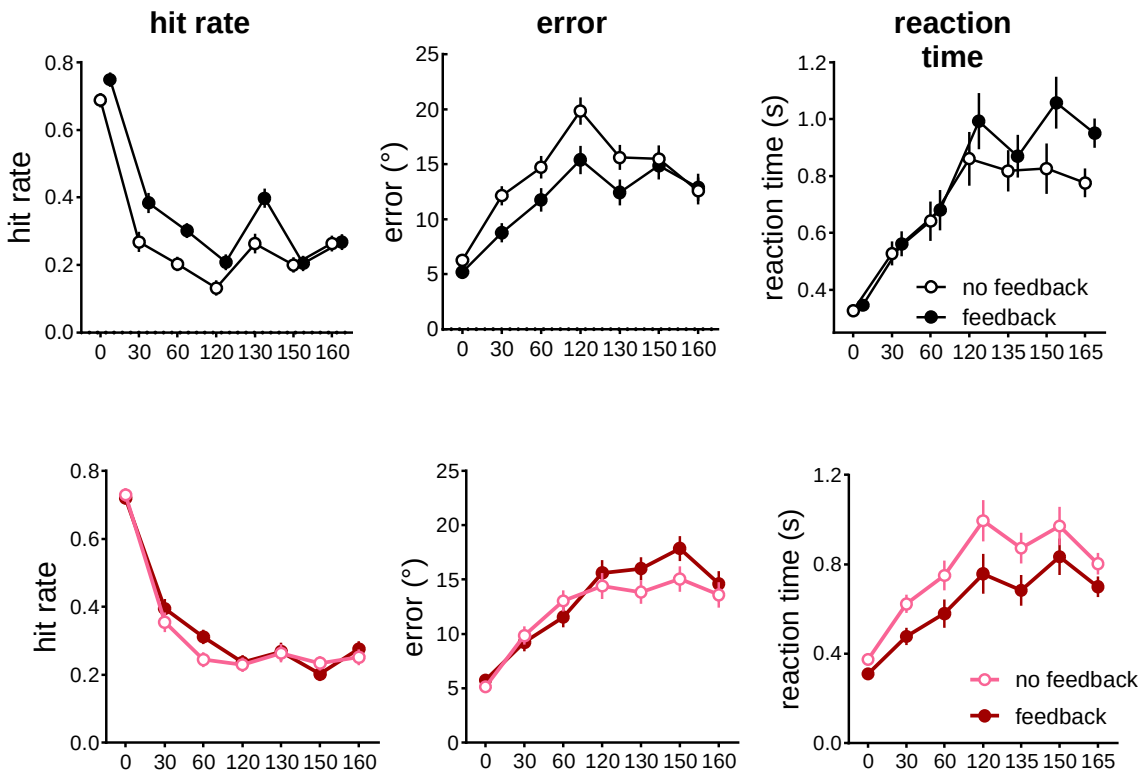

Figure 4. For the placebo groups, removing task feedback reduced hit rates, increased errors (left panel), and lengthened reaction times for the larger aiming angles (right panel). For the levodopa groups, hit rates and accuracy where comparable with/without task feedback (left/middle panels) in contrast to the placebo group (Figure 2). Also, in contrast to the placebo group, the levodopa group showed longer reaction times in the absence of feedback (right panel).

3.4. Feedback manipulations at training resulted in persistent post-training effects.

After the training block, all participants were asked to re-aim in post-training probe blocks without any feedback manipulations. We assessed how previous training with/without feedback altered subsequent aiming performance in the probe block. Probe block aiming performance in the placebo groups depended on feedback presence at training: placebo groups who trained without feedback showed fewer hits ($BF_{10, U}$ = 768705.885) and larger errors ($BF_{10, U}$ = 80865484477.445), and shorter reaction times ($BF_{10, U}$ = 2.81e+19) than their counterparts who trained with feedback. Thus, for the placebo groups, post-training performance was impaired by the absence of feedback at training. In contrast, the levodopa groups appeared to maintain the accuracy of their aiming regardless of whether they trained with or without feedback. Levodopa groups who trained without feedback showed similar hits and accuracy (moderate-strong evidence for the null hypothesis, hits: $BF_{01, U}$= 5.263; errors: $BF_{01, U}$ = 11.848) but lengthier reaction times ($BF_{01, U}$= 9.37) at post-training probe trials than their counterparts who trained with feedback. Thus, the Levodopa group participants maintained accuracy despite prior training without feedback, via a strategy of trading speed for accuracy.

3.5. Control measurements

Pharmacological manipulations of dopamine, particularly at larger doses than used here, can elicit undesired side effects such as nausea (for example, see Thirugnanasambandam *et al.*, 2011; Chen *et al.*, 2020). However, none of our participants reported this. Exogenous dopamine can also change mood state (Vo *et al.*, 2018), however, here, we did not find evidence that levodopa altered our participants mood state as indicated by inconclusive evidence for a change in mood state on the Bond Larder Scale (BF_{excl} = 1.288). Blood pressure and heart rate was also unaltered, as Time (before drug administration, 30 minutes after drug administration, 2 hours after drug administration) x Drug ANOVAs yielded moderate evidence for the null hypothesis for Time x Drug interactions for blood pressure (diastole: BF_{excl} = 4.149, systole: BF_{excl} = 8.547) and mood (BF_{excl} = 3.681), and heart rate (BF_{excl} = 3.731). In addition, participants were not above chance at accurately guessing the drug condition, as shown by Bayesian binomial tests (BF0+ = 4.685). Neither experimenters nor participants were above chance at accurately guessing the drug condition, as shown by moderate evidence for the null hypothesis from Bayesian binomial tests (participant: BF0+ =6.181, experimenter: BF0+ = 4.603).

Discussion

Here, in a preregistered, double-blind, placebo-controlled study, we examined how task feedback altered explicit motor skill learning, and whether the effect of task feedback on skill learning depended on dopamine. Participants were either provided with salient information on their task success/failure, or deprived of task success information about their performance. In a task that prioritised accuracy, not speed, exogenous dopamine appeared to help participants optimise task success. When deprived of task success information: levodopa increased the number of target-hits and increased accuracy: and this was achieved by participants varying the speed accuracy trade-off, as shown by a increase in reaction times. When feedback about task success was provided, levodopa sped-up reaction times whilst maintaining overall task success (target-hits). Our results provide direct evidence for a role of dopamine in distinct processes that shape performance in motor skill learning: one driven by internally generated estimations of performance, and another driven by external information about performance.

To the best of our knowledge, our study is the first to provide causal evidence for a role of dopamine in motor performance when skill learning was driven by internally generated estimations of performance in neurotypical humans. We built upon our previous study (Leow *et al.*, 2024), which provided extrinsic task feedback information throughout the task. In that work, we showed that increasing dopamine availability improved task performance by increasing a propensity to better adhere to task goals, suggesting engagement of instrumental motivation to optimize adherence to task goals (Leow *et al.*, 2024). However, because task feedback was always present, it was unclear whether the effects of dopamine in that study resulted from effects of dopamine on intrinsic motivational processes that operates in the absence of task feedback, and/or extrinsic motivational processes that rely on task feedback. Here, by explicitly manipulating the presence and absence of task feedback, we provide direct evidence for a role of dopamine in process(es) driven by internally generated estimations of performance. Whilst neuroimaging evidence indirectly implicates the striatal mesolimbic areas when learning in the absence of extrinsic feedback (Daniel & Pollmann, 2012; Guggenmos *et al.*, 2016; Ripolles *et al.*, 2016), and pharmacological manipulations of dopamine show a role of dopamine in modulating motor or cognitive task performance in exchange for rewards (De Vries *et al.*, 2010; Chong *et al.*, 2015; McGuigan *et al.*, 2019; Michely *et al.*, 2020), there is a surprising dearth of direct evidence for a role of dopamine in motor performance in the *absence* of extrinsic task or reward feedback. Whilst one previous study showed that modulating dopamine availability via levodopa or a dopamine antagonist altered language learning in the absence of external task feedback (Ripollés *et al.*, 2018), that study lacked a placebo control, and thus it is unclear if effects were driven by levodopa improving learning or by the dopamine antagonist impairing learning. Here, in our placebo-controlled design, we show that exogenous dopamine improved motor performance, both in the absence of task feedback, and in the presence of task feedback. By directly contrasting effects of dopamine on a design utilizing only minimal differences between conditions with and without feedback about task success, we demonstrated separable effects of levodopa on performance with and without task feedback.

Exactly how did levodopa alter performance with and without task feedback in our study? Compared to the placebo group, participants in the levodopa group seemed better able to leverage task feedback to optimise performance, speeding-up reaction times without incurring a cost to task success. The finding that exogenous dopamine improves feedback-based performance is consistent with previous findings of improved motor and cognitive task performance with levodopa in the presence of feedback (De Vries *et al.*, 2010; Chowdhury *et al.*, 2013; Shellshear *et al.*, 2015). This effect seems most prominent with larger, more difficult aiming angles, which may partly explain why previous work using somewhat subtler manipulations do not show effects of dopamine manipulations (Quattrocchi *et al.*, 2018; Palidis *et al.*, 2021). The picture differed somewhat in the absence of task feedback. Whilst accuracy suffered in the absence of feedback about task success in the placebo group (Schaefer *et al.*, 2012; Kim *et al.*, 2018; Leow *et al.*, 2018; 2020; Oza *et al.*, 2020; Tsay *et al.*, 2022), exogenous dopamine here appeared to help maintain accurate performance, such that accuracy was similar regardless of whether feedback about task success was present. This improved capacity to maintain task performance seems consistent with an increasing body of work showing that exogenous dopamine tends to blunt the effect of manipulations of task-related information on performance, such as the valence of potential task outcomes (e.g.,Guitart-Masip *et al.*, 2014; Vellani *et al.*, 2020). In summary, our findings suggest that dopamine influences motivation, both to improve internally determined task performance, and to improve performance shaped by extrinsic task feedback.

How might levodopa have changed motor performance in the absence of extrinsic information about task success during skill learning? Levodopa is a precursor to dopamine, which increases brain dopamine availability. Animal studies show that levodopa increases phasic firing of striatal dopamine cells (Willuhn *et al.*, 2014). We speculate that levodopa increased the amplitude of dopamine signalling in response to internal evaluations of task performance. This interpretation is in line with recent findings in animals which demonstrate a key role of dopamine in internal evaluations of performance (Guggenmos *et al.*, 2016; Duffy *et al.*, 2022). For example, spontaneous dopamine activity in songbirds correlate with self-evaluation of performance quality in the absence of external rewards, cues, or perturbation (Duffy *et al.*, 2022). Similarly, Markowitz *et al.* (2023) showed that in rats acting in the absence of explicit reward (i.e., in darkness), dopamine release was followed by an increase in spontaneous actions, and that increased dopamine release after such actions was associated with an increased probability of repeating such actions. In a similar vein, one fMRI study in humans has suggested that activation of the striatum in response to reward, traditionally interpreted as a neural representation of the value of that reward, might instead be better interpreted as a representation of how well those rewards align with one's internal representation of a task goal (Frömer *et al.*, 2019). In a task where participants were asked to choose the best option or the worse option, neural activity in value-related regions were better accounted for by how well the reward aligned with the task goal, rather than how rewarding each option was (Frömer *et al.*, 2019). These results, as well as ours, are broadly supportive of the view that dopamine in the striatum is instrumental to internal estimations of task performance relative to some goal (Ptasczynski *et al.*, 2022), consistent with the idea that dopamine has a generalised role in prediction (Gardner *et al.*, 2018).

Summary

The role of intrinsic motivation has long been recognised within the context of motor skill learning (Wulf & Lewthwaite, 2016), and theories have broadly implicated brain dopamine in driving intrinsic motivation during skill learning (Lewthwaite & Wulf, 2017). However, to date, such theories have yet to be substantiated by evidence in healthy humans. Our findings provide this missing evidence. We show that exogenous dopamine alters performance during skill learning, both in the absence and in the presence of extrinsic feedback, demonstrating a key role of dopamine in optimising motor performance during skill learning, even in the absence of external task feedback. Our study thus provides direct evidence for the role of dopamine in performance guided by internal estimations of performance in humans. This work not only has implications for implementation of skill learning in rehabilitation contexts in populations with changes in brain dopamine function (e.g., healthy ageing; (Bäckman *et al.*, 2006), but will also improve future implementation of dopamine pharmacotherapy as an adjunct strategy to optimise motor rehabilitation (Scheidtmann et al., 2001; Rosser et al., 2008).

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