Differential effects of dopamine and serotonin on reward and punishment processes in humans: A systematic review and meta-analysis

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Key Points

Question: Do pharmacological manipulations of dopamine and serotonin affect components of reinforcement learning in humans?

Findings: Upregulating dopamine increases reward learning/sensitivity and reward response vigor, and decreases reward discounting. Upregulation of serotonin leads to increased punishment learning/sensitivity and decreased reward discounting.

Meaning: Pharmacological manipulations of dopamine and serotonin have dissociable effects on different components of reinforcement learning. This forms a necessary basis for the development of selective markers for treatment assignment.

Abstract

Importance: To support treatment assignment, mechanistic biomarkers should be selectively sensitive to specific interventions. Here, we examine whether different components of reinforcement learning in humans satisfy this necessary precondition. We focus on pharmacological manipulations of dopamine and serotonin that form the backbone of first-line management of common mental illnesses such as depression and anxiety.

Objective: To perform a meta-analysis of pharmacological manipulations of dopamine and serotonin and examine whether they show distinct causal effects on reinforcement learning components in healthy humans.

Data Sources: Ovid MEDLINE/PubMed, Embase, and PsycInfo databases were searched for studies published between January 1, 1946 and January 19, 2023 (repeated April 9, 2024, and October 15, 2024) investigating dopaminergic or serotonergic effects on reward/punishment processes in healthy humans.

Study Selection: Studies reporting randomized, placebo-controlled, dopaminergic or serotonergic manipulations on a behavioral outcome from a reward/punishment processing task in healthy humans were included.

Data Extraction and Synthesis: Standardized mean difference (SMD) scores were calculated for the comparison between each drug (dopamine/serotonin) and placebo on a behavioral reward or punishment outcome and quantified in random-effects models for overall reward/punishment processes and four main subcategories. Study quality, moderators, heterogeneity, and publication bias were also assessed.

Main Outcome(s) and Measure(s): Performance on reward/punishment processing tasks.

Results: In total, 68 dopamine and 39 serotonin studies in healthy volunteers were included (N_{dopamine}=2452, N_{placebo}=2432; $N_{\text{serotonin}}$=1364, N_{placebo}=1393 participants). Dopamine increased overall reward (SMD=0.21; 95%CI [0.12 0.30]) but not punishment function (SMD=-0.09; 95%CI [-0.27,0.10]). Serotonin did not meaningfully affect overall punishment (SMD=0.22; 95%CI [-0.04,0.49]) or reward (SMD=0.01; 95%CI [-0.33,0.35]). Importantly, dopaminergic and serotonergic manipulations had distinct and selective effects on subcomponents. Dopamine affected reward learning/sensitivity (SMD=0.25; 95%CI [0.10,0.40]), reward discounting (SMD=-0.08; 95%CI [-0.14,-0.01]) and reward vigor (SMD=0.32; 95%CI [0.11,0.54]). By contrast, serotonin shaped punishment learning/sensitivity (SMD=0.32; 95%CI [0.05,0.59]), reward discounting (SMD=-0.35; 95%CI [-0.67,-0.02]), and aversive Pavlovian processes (within-subject studies only; SMD=0.36; 95%CI [0.20,0.53]).

Conclusions and Relevance: Pharmacological manipulations of both dopamine and serotonin have measurable effects on reinforcement learning in humans. The selective effects on different components suggests that reinforcement learning tasks could form the basis of selective, mechanistically interpretable biomarkers to support treatment assignment.

INTRODUCTION

Dopamine and serotonin are two critical neuromodulators in the brain, both playing central roles in clinical and basic neuroscience. Clinically, they are the targets of different antidepressants, which are equally effective in treating mood disorders(Cipriani et al., 2018). Yet, basic neuroscience suggests they serve distinct functions in behavior, particularly in reinforcement learning (RL). If dopamine and serotonin indeed have distinct effects in RL, as current theories predict, this could help identify new mechanisms to guide much-needed optimized treatments. Conversely, if they prove indistinguishable in humans, prevailing neuroscientific models would require substantial revision. Resolving this question in humans is therefore critical.

RL describes how rewards and losses guide behavior and is strongly related to depression. It is impaired in individuals who are currently depressed(Halahakoon et al., 2020; Pike and Robinson, 2022), and has substantial face validity as a core mechanism leading to or maintaining depression(Huys et al., 2015). RL is also intricately linked to the neuromodulator systems dopamine and serotonin as the brain appears to use these to broadcast key RL signals(Schultz et al., 1997; Kravitz et al., 2012; Eshel et al., 2015; Cardozo Pinto et al., 2024; Gershman et al., 2024).

However, a key challenge here lies in reconciling two seemingly contradictory bodies of research. On one hand, antidepressants targeting dopamine or serotonin appear similarly effective in treating depression(Cipriani et al., 2018). On the other hand, substantial neuroscience research indicate that dopamine and serotonin play distinct roles in RL(Schultz et al., 1997; Frank et al., 2004; Kravitz et al., 2012; Maier and Watkins, 2005; Dayan and Huys, 2009; Cardozo Pinto et al., 2024). One possible resolution is that different antidepressants engage different components of RL. Such a selectivity could potentially explain why individuals who do not respond to serotonergic medications may respond to more dopaminergic medications. Indeed, dopaminergic antidepressants are second-line options when first-line serotonergic treatments fail(Rush et al., 2006; Webb et al., 2019; Ang et al., 2020). As a necessary precondition for this, manipulating different neuromodulators must demonstrably affect distinct RL processes in humans—a question that remains unresolved. If validated, RL-based measures could serve as markers to guide treatment choices and inform the development of novel therapies. Thus, adopting an RL framework to clarify the cognitive roles of dopamine and serotonin represents a critical first step toward identifying candidate mechanisms driving the therapeutic effects of these antidepressants.

RL is however not a single process but a collection of mechanisms that are hypothesized to involve dopamine and serotonin in distinct ways(Husain and Roiser, 2018). Basic neuroscience highlights that dopamine is a key modulator of appetitive processes, particularly reward learning, reward discounting and reward response vigor(Schultz et al., 1997; Flagel et al., 2011; Steinberg et al., 2013; Gershman et al., 2024). Serotonin, while more complex, is often linked to aversive processes such as punishment learning, or inhibition in the face of punishments(Daw et al., 2002; Dayan and Huys, 2009). However, human studies on these neuromodulators in RL have yielded mixed and sometimes conflicting results(Rogers, 2011; Martins et al., 2017). These inconsistencies hinder our understanding of dopamine and serotonin in human behavior and the development of optimized treatments for mood and anxiety disorders. Therefore, we performed a meta-analysis of the effects of pharmacological manipulations of dopamine and serotonin on RL. Given the limited number of studies, for increased power we a) considered pharmacological manipulations broadly, not only antidepressants; and b) focused on healthy participants due

to few patient studies. Our first aim was to ask whether dopamine and serotonin alter overall reward and punishment processing. Our second aim was to identify whether they affect specific RL subcomponents. Based on theoretical frameworks and a systematic review of the literature we identified and focused the meta-analysis on the following subcomponents of RL.

Reward and punishment learning A key component of RL involves trial-and-error learning from rewards and punishments via prediction errors (the difference between expected and actual outcomes;Schultz et al. 1997). Dopamine has been extensively implicated in signaling reward prediction errors(Montague et al., 1996; Schultz et al., 1997). Some theories also postulate that dopamine dips may drive punishment learning(Collins and Frank, 2012), while computational models suggest this is under serotonin's control(Deakin and Graeff, 1991; Daw et al., 2002). Recent animal studies have however implicated serotonin in reward learning as well, firing to reward-predicting cues or contrarily, suppressing reward learning(Cohen et al., 2015; Cardozo Pinto et al., 2024). To examine these processes in humans, studies mostly employ probabilistic instrumental learning tasks.

Pavlovian bias Choices can also be driven by appetitive Pavlovian biases—automatic approach actions towards rewards—or aversive biases—reflexively action inhibition in the face of punishments—regardless of the optimal actions(Guitart-Masip et al., 2014a). Influential models propose that serotonin promotes aversive Pavlovian biases, i.e., inhibition in aversive contexts(Cools et al., 2011; Boureau and Dayan, 2011; Dayan and Huys, 2008, 2009). Human studies often use go/no-go tasks where these biases interfere with optimal actions or Pavlovian-instrumental transfer tasks(Guitart-Masip et al., 2014a; Geurts et al., 2013).

Reward discounting Decision-making also requires balancing rewards against costs. Current theories predict that dopamine signals benefits over costs, while serotonin may promote willingness to wait or exert effort for larger rewards by modulating perceived costs. Both mechanisms thus contribute to reduced reward discounting(Dalley and Roiser, 2012; Doya, 2002; Soubrié, 1986; Meyniel et al., 2016; Salamone et al., 2016). These processes are studied using tasks that contrast immediate or low effort, small rewards, with delayed or high effort, larger reward, choices.

Reward response vigor Motivation also involves deciding how vigorously actions need to be executed to obtain rewards. Dopamine is theorized to signal average reward rates, enhancing response vigor(Niv et al., 2007; Dayan, 2012). The role of serotonin is less defined, though an early computational theory suggest it may also modulate the long-term reward rates(Daw et al., 2002). Tasks in this domain assess reaction times or effort exertion relative to reward magnitude or average reward rate.

Overall, this meta-analysis aims to provide a clearer understanding of how dopamine and serotonin shape RL in humans, contributing to both theoretical and clinical advances.

Methods

Systematic review

We conducted a preregistered systematic review and meta-analysis (PROSPERO:CRD42022363747). The Ovid MEDLINE/PubMed, Embase, and PsycInfo databases were searched for articles published between January 1, 1946, and January 21, 2023. The search was repeated on April 9,

2024 and October 15, 2024 for additional articles published since 2023. Titles or abstracts were searched containing the terms (dopamine* or seroton* or tryptophan* or tyrosine*) and (reward* or motivat* or punish* or reinforce* or decision* or effort* or learn* or incentive* or volition or choice*) and (participa* or subject* or individ* or human* or healthy* or investigat* or experiment*) and restricted to articles in English and humans. Detailed description of the search strategy is described in S1.1 and Figure S1.

We included studies reporting 1) interventions manipulating either dopamine or serotonin, in 2) healthy human volunteers (18-65 years old), 3) randomized placebo-controlled studies that 4) reported a behavioral outcome from a reward and/or punishment processing task. We only included samples that 5) did not overlap with other included datasets and 6) contained sufficient information to calculate standardized mean difference (SMD) scores between placebo and drug conditions (see S1.2).

Meta-analysis

Effect sizes were calculated for behavioral outcomes relating to reward and punishment learning/sensitivity, aversive and appetitive Pavlovian bias, reward vigor, reward discounting. To evaluate overall reward and punishment processes, we consolidated the components into two main categories. The overall reward function category combined reward learning/sensitivity, appetitive Pavlovian bias, reward vigor, and reward discounting–reversing the discounting direction so that a positive SMD represents increased reward weighting. The overall punishment function combined punishment learning/sensitivity and aversive Pavlovian bias. We also identified risk attitude and model-based learning/flexibility as two additional RL subcomponents. However since these are not straightforward to combine with the other subcomponents (see S1.3), we consider them separately.

Pharmacologically, we pooled data from both agonists and antagonists, assuming symmetrical effects for drugs that upregulate or downregulate a neuromodulator. We recoded antagonist effects as if they were agonist effects. For example, if a study reported that a dopamine antagonist reduced reward vigor, we recoded this effect to represent an agonist increasing reward vigor. Some dopamine studies used low doses of agonists/antagonists intended to specifically target presynaptic autoreceptors. These effects were interpreted contrary to their typical activity profile (e.g., a low-dose agonist was coded as an antagonist), as suggested by the literature (S1.3). To assess the impact of this interpretation, we conducted sensitivity analyses using the original drug activity profiles as well.

Both within- and between-subject designs were included. The detailed procedures for calculating between- and within-subject SMDs including the conversion procedures are described in S1.4, with comparisons of different effect size conversions for within-subject studies depicted in Figure S2. Random-effects models were conducted in R (version 4.3.3) using metafor(Viechtbauer, 2010) packages to examine the effect of upregulating dopamine and serotonin compared with placebo on overall reward and punishment processes and subcomponents. Heterogeneity, publication bias, moderators and study quality were also assessed (S1.3).

Results

Data from 107 studies were included (dopamine: 2452 active vs 2432 placebo assessments; serotonin: 1364 active vs 1393 placebo assessments) (Figure 1; Table S1). Risk of bias was generally high for both randomization and allocation concealment, but low for blinding of outcome assessment (Figure S3).

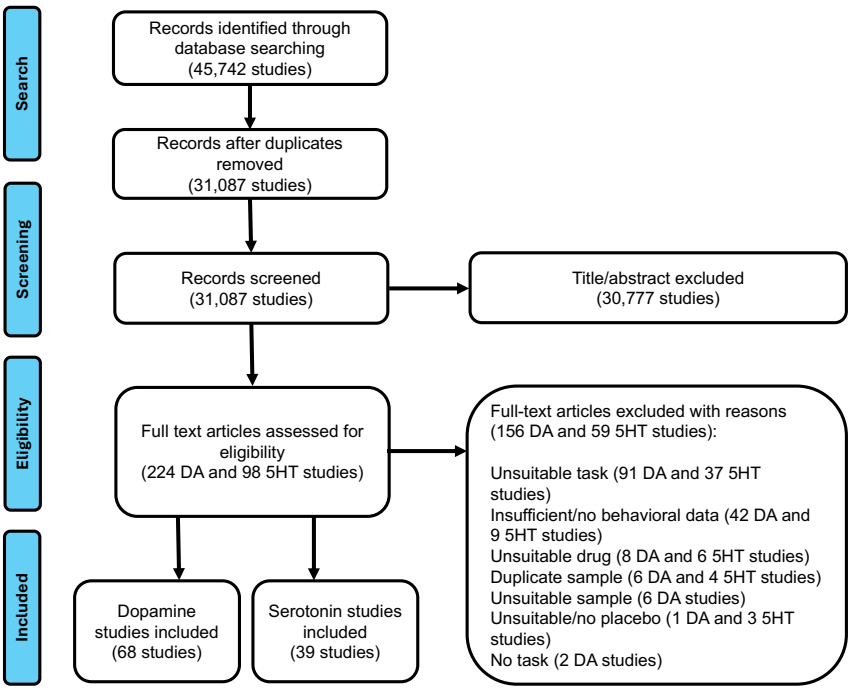


Figure 1: Flow Diagram of Study Selection and Inclusion. Abbreviations: DA: dopamine; 5HT: serotonin.

Meta-analysis Results

Dopamine

Overall, dopamine had a small positive effect on reward processes (SMD=0.21, 95%CI [0.12, 0.30]; Figure S4a) but a negligible negative effect on overall punishment processes (SMD=-0.09, 95%CI [-0.27, 0.10]; Figure S4b). Analyses according to the original drug activity profile reduced estimates but did not change inference Figure S5).

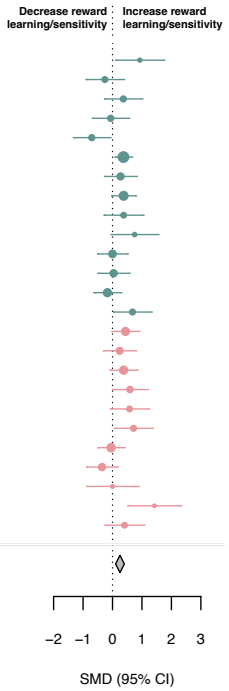
In line with theories, dopamine increased reward learning/sensitivity (Figure 2a; SMD=0.25, 95%CI [0.10, 0.40]), reward vigor (SMD=0.32, 95%CI [0.11, 0.54]; Figure 2d) and decreased reward discounting (SMD=-0.08, 95%CI [-0.14, -0.01]; Figure 2c), but did not affect appetitive Pavlovian bias (SMD=0.21, 95%CI [-0.19, 0.61]; Figure 2b) or other subcomponents (Figure 3; Figure S6). Analyses according to the original drug activity profile influenced the inference of dopamine on reward learning/sensitivity and reward discounting but no other ones (Figure S7). We also explored the effects on computational learning rate and sensitivity parameters, but there were far fewer studies reporting these and no clear pattern emerged (Figure S8).

There was low-to-moderate heterogeneity across all overall processes and main subcomponents.

Substantial heterogeneity was only found in the risk attitude and model-based/flexibility sub-components, with outlier exclusion resolving risk attitude heterogeneity, resulting in a significant positive dopamine effect (S2.2.1; Figure S9).

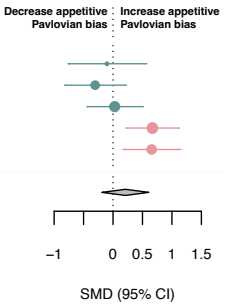
a

Study	N(Drug, Pla)	Drug, dose	SMD [95% CI]
Jocham, 2011	16	Amisulpride 200mg	0.93 [0.11, 1.75] *
Admon, 2017	20, 18	Amisulpride 50mg	−0.26 [−0.90, 0.38] *
Frank, 2006	19, 20	Haloperidol 2mg	0.37 [−0.26, 1.00] *
Walsh, 2018	20, 20	Bupropion 150mg	−0.06 [−0.68, 0.56]
Bernacer, 2013	17	Methamphetamine 0.3mg/kg	−0.70 [−1.33, −0.08]
Westbrook, 2024	95, 97	Methylphenidate 20mg	0.37 [0.09, 0.66]
Howlett, 2017	19	Methylphenidate 40mg	0.27 [−0.26, 0.81]
Addicott, 2021	22	Methylphenidate 40mg	0.38 [−0.03, 0.79]
Bellebaum, 2017	16, 20	Modafinil 200mg	0.38 [−0.29, 1.04]
Pessiglione, 2006	13, 13	L−dopa 100mg+25mg	0.75 [−0.04, 1.55]
Jansen, 2023	30, 30	L−dopa 100mg+25mg	0.00 [−0.51, 0.51]
Weis, 2012	27, 28	L−dopa 100mg+35mg	0.04 [−0.49, 0.57]
Chakroun, 2023	31	L−dopa 150mg+37.5mg	−0.17 [−0.63, 0.29]
Halahakoon, 2024	21, 19	Pramipexole 1mg/day	0.68 [0.04, 1.32]
Jocham, 2014	22	Amisulpride 400mg	0.44 [−0.02, 0.90]
Kahnt, 2015	27, 24	Amisulpride 400mg	0.24 [−0.31, 0.79]
Mikus, 2022	38, 35	Amisulpride 400mg	0.38 [−0.08, 0.84]
Cremer, 2023	23, 22	Amisulpride 400mg	0.59 [−0.00, 1.19]
Diederen, 2017	19, 19	Sulpiride 600mg	0.58 [−0.07, 1.23]
Haarsma, 2021	20, 20	Sulpiride 600mg	0.71 [0.07, 1.35]
Eisenegger, 2014	41, 35	Sulpiride 800mg	−0.05 [−0.50, 0.40]
Grob, 2012	28, 28	AMPT 40mg/kg	−0.36 [−0.88, 0.17]
Cox, 2015	10, 10	Phe / Tyr depletion 100g	0.00 [−0.88, 0.88]
Pizzagalli, 2008	11, 13	Pramipexole 0.5mg	1.42 [0.52, 2.32] *
Murray, 2019	18, 18	Pramipexole 0.5mg	0.41 [−0.25, 1.07] *
Random−effects meta−analysis:			0.25 [0.10, 0.40]



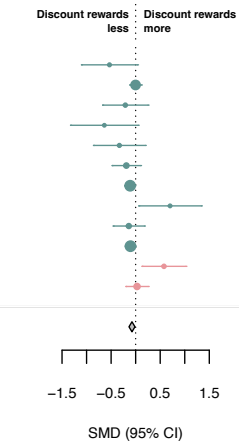
b

Study	N(Drug, Pla)	Drug, dose	SMD [95% CI]
Guitart−Masip, 2012	16, 20	L−dopa 150mg+37.5mg	−0.10 [−0.76, 0.56]
Guitart−Masip, 2014	30, 29	L−dopa 150mg+37.5mg	−0.30 [−0.82, 0.21]
Scholz, 2022	35, 35	Tolcapone 200mg	0.03 [−0.44, 0.50]
Weber, 2016	41, 40	Amisulpride 400mg	0.67 [0.22, 1.12]
Hebart, 2015	35, 34	Phe / Tyr depletion	0.65 [0.17, 1.14]
Random−effects meta−analysis:			0.21 [−0.19, 0.61]



c

Study	N(Drug, Pla)	Drug, dose	SMD [95% CI]
Wagner, 2020	23, 26	Haloperidol 2mg	−0.53 [−1.10, 0.04] *
Erfanian Abdoust, 2024	62	Haloperidol 2mg	−0.00 [−0.12, 0.12] *
de Wit, 2002	36, 36	D−amphetamine 20mg	−0.21 [−0.67, 0.25]
Wardle, 2011	17, 17	D−amphetamine 20mg	−0.64 [−1.33, 0.05]
Soder, 2021	28, 28	D−amphetamine 20mg	−0.33 [−0.86, 0.20]
Westbrook, 2020	46	Methylphenidate 20mg	−0.19 [−0.48, 0.10]
Daood, 2022	57	Methylphenidate 20mg	−0.11 [−0.21, −0.01]
Pine, 2010	13	L−dopa 150mg	0.70 [0.06, 1.34]
Smith, 2024	76, 76	L−dopa 150mg	−0.14 [−0.46, 0.18]
Kayser, 2012	23	Tolcapone 200mg	−0.11 [−0.20, −0.01]
Weber, 2016	40, 40	Amisulpride 400mg	0.58 [0.13, 1.02]
Kelm, 2013	15	Phe / Tyr depletion 68.7g	0.03 [−0.20, 0.26]
Random−effects meta−analysis:			−0.08 [−0.14, −0.01]



d

Study	N(Drug, Pla)	Drug, dose	SMD [95% CI]
Ikeda, 2019	15	Bupropion 150mg	0.30 [−0.33, 0.93]
Grimm, 2021	45	L−dopa 100mg+25mg	0.02 [−0.35, 0.39]
Michely, 2020	20	L−dopa 150mg	0.80 [0.20, 1.39]
Beierholm, 2013	30, 30	L−dopa 150mg+37.5mg	0.59 [0.07, 1.11]
Mehta, 2001	18	Bromocriptine 1.25mg	0.47 [−0.10, 1.05]
Au−Yeung, 2024	19, 18	Pramipexole 1mg/day	0.21 [−0.44, 0.86]
Graf, 2018	17	Amisulpride 200mg/day	0.21 [−0.44, 0.86]
Abler, 2007	8	Olanzapine 5mg	0.66 [−0.11, 1.42]
Mehta, 2005	14	Phe / Tyr depletion	−0.17 [−0.88, 0.54]
Random−effects meta−analysis:			0.32 [0.11, 0.54]

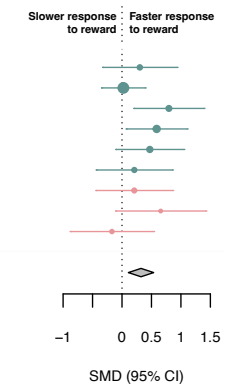


Figure 2: **Effect of upregulating dopamine on reward subcomponents.** Standardized mean differences (SMDs) of the effect of upregulating dopamine versus placebo on a) reward learning/sensitivity, b) appetitive Pavlovian bias, c) reward discounting, and d) reward vigor. Pla indicates placebo. We recoded antagonist effects as if they were agonists (pink SMD point estimates and 95% CI). Green SMD point estimates and 95% CI indicate studies that were coded as original agonists. Asterisks indicate studies that used a low dose of an agonist or antagonists. These effects were interpreted contrary to their typical activity profile (e.g., a low-dose agonist acting antagonistically), as suggested by the literature.

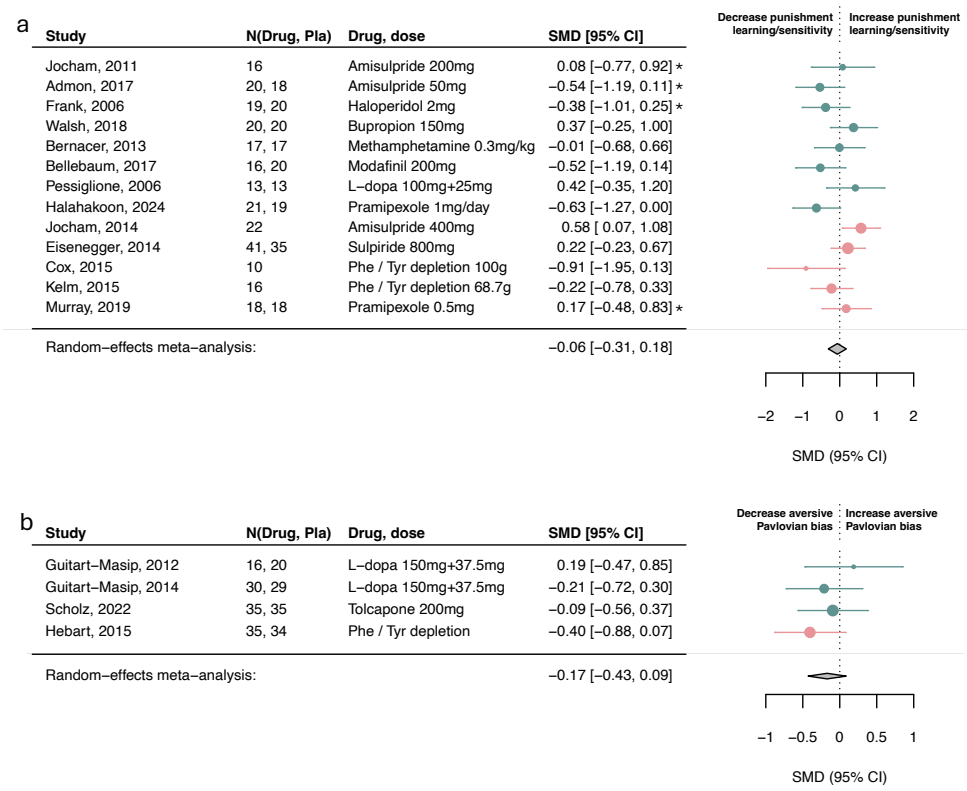


Figure 3: **Effect of upregulating dopamine on punishment subcomponents.** Standardized mean differences (SMDs) of the effect of upregulating dopamine versus placebo on a) punishment learning/sensitivity and b) aversive Pavlovian bias. We recoded antagonist effects as if they were agonists (pink SMD point estimates and 95% CI). Green SMD point estimates and 95% CI indicate studies that were coded as original agonists. Asterisks indicate studies that used a low dose of an agonist or antagonists. These effects were interpreted contrary to their typical activity profile (e.g., a low-dose agonist acting antagonistically), as suggested by the literature.

Serotonin

Overall, serotonin did not show effects on reward (SMD=0.01; 95%CI [-0.33, 0.35]; Figure S10a) or punishment processes (SMD=0.22; 95%CI [-0.04, 0.49]; Figure S10b).

Serotonin upregulation had a small-to-moderate influence on reward discounting (SMD=-0.35; 95%CI [-0.67, -0.02]; Figure 4c) and punishment learning/sensitivity (SMD=0.32; 95%CI [0.05,

0.59]; Figure 5a) but not on reward learning/sensitivity, reward vigor, Pavlovian biases (Figure 4a,b,d; Figure 5b) or other subcomponents (Figure S11).

However, three within-subject studies had to be excluded in the aversive Pavlovian domain due to missing information needed to combine with between-subject studies. Examining the six within-subject studies separately, there was a significant small-to-medium effect of serotonin on aversive Pavlovian processes (SMD=0.36; 95%CI [0.20, 0.53]; Figure S12). Exploring learning rate and sensitivity computational parameters, serotonin significantly increased punishment learning rates and decreased punishment sensitivity. Although there were few studies to pool over here (Figure S13).

There was substantial heterogeneity in overall reward/punishment categories and the reward learning/sensitivity and aversive Pavlovian subcomponents. Removing identified outliers explained some of this variance and revealed a significant increase of overall punishment processes by serotonin (SMD=0.32; 95%CI [0.10, 0.54]; S2.2.2; Figure S14).

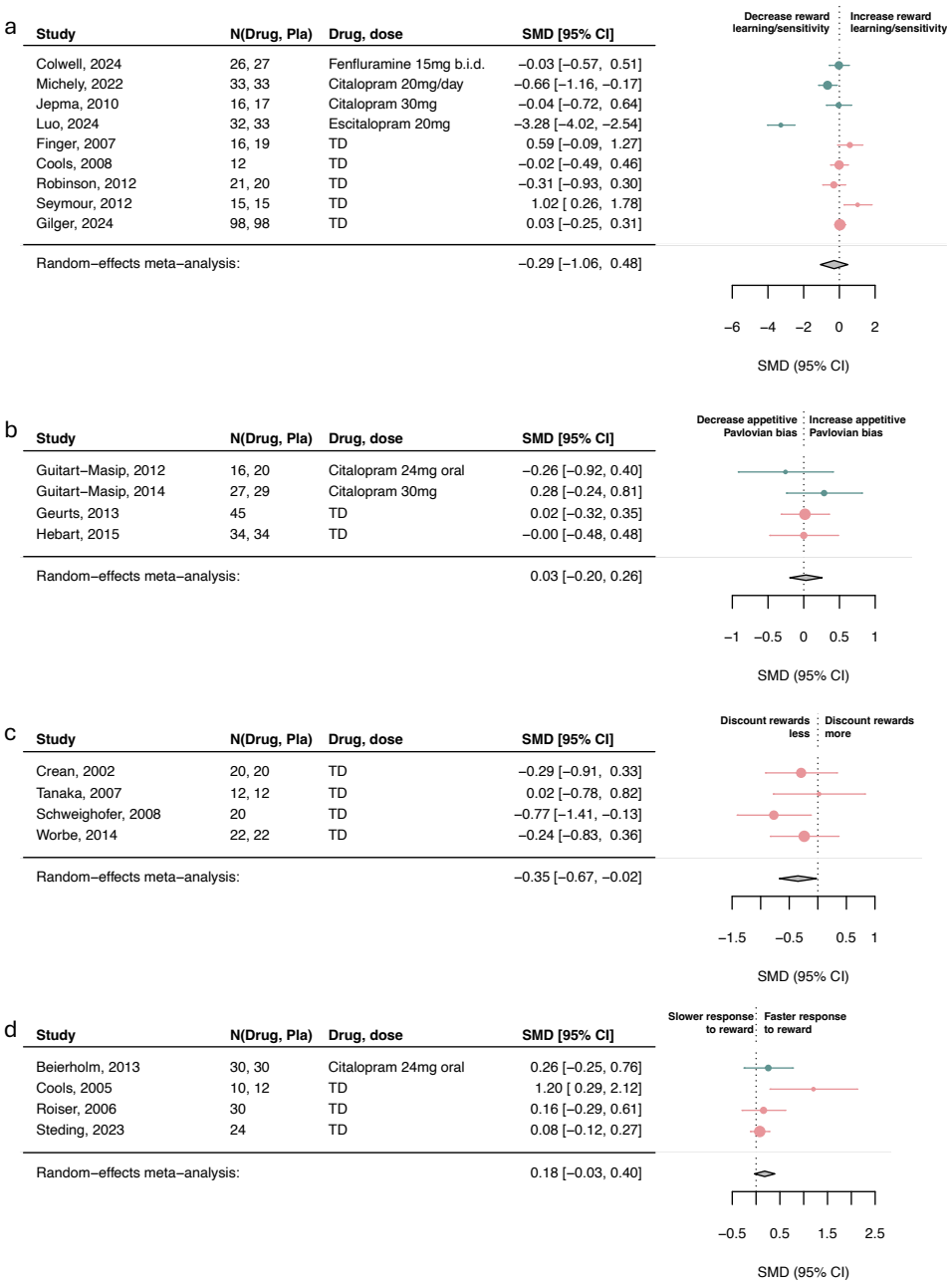


Figure 4: **Effect of upregulating serotonin on reward subcomponents.** Standardized mean differences (SMDs) of the effect of upregulating serotonin versus placebo on a) reward learning/sensitivity, b) appetitive Pavlovian bias, c) reward discounting, and d) reward vigor. Pla indicates placebo. We recoded antagonist effects as if they were agonists (pink SMD point estimates and 95% CI). Green SMD point estimates and 95% CI indicate studies that were coded as original agonists. TD: tryptophan depletion.

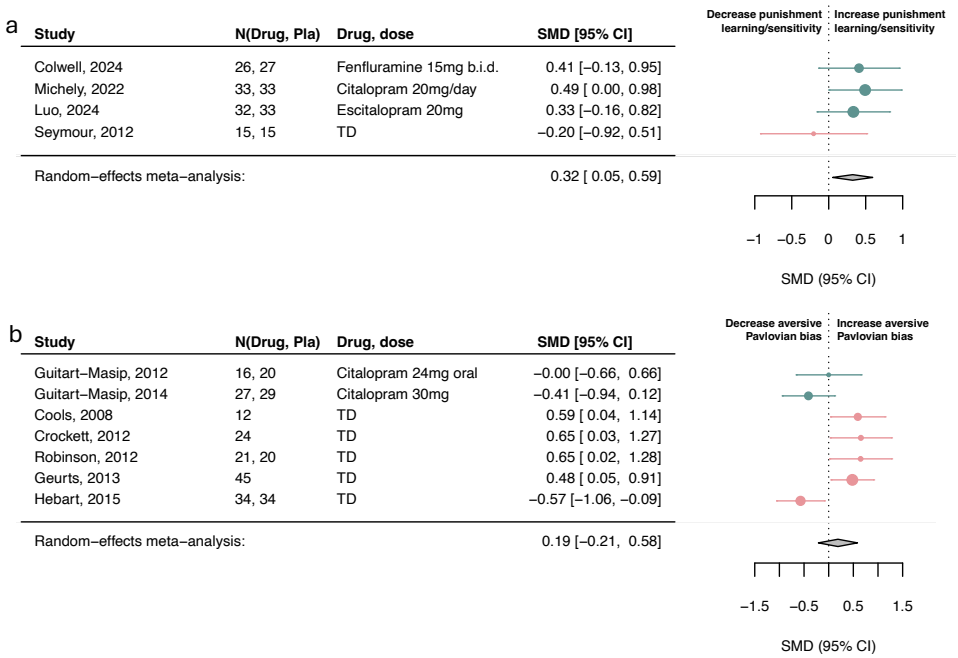


Figure 5: **Effect of upregulating serotonin on punishment subcomponents.** Standardized mean differences (SMDs) of the effect of upregulating serotonin versus placebo on a) punishment learning/sensitivity and b) aversive Pavlovian bias. We recoded antagonist effects as if they were agonists (pink SMD point estimates and 95% CI). Green SMD point estimates and 95% CI indicate studies that were coded as original agonists. TD: tryptophan depletion.

Publication Bias & moderator analyses

Egger's test suggested significant publication bias in the overall dopamine reward domain (z=2.31, p=0.02) but not in any of the other overall domains (dopamine punishment: z=-0.86, p=0.39; serotonin reward: z=0.073, p=0.94; serotonin punishment: z=-0.09, p=0.93; Figure S15).

Dopamine

Only the reward and punishment learning/sensitivity and reward discounting categories contained greater than 9 studies, allowing a test for funnel plot asymmetry(Higgins et al., 2024). None of these showed significant publication bias (reward learning/sensitivity: z=1.49, p=0.14; punishment learning/sensitivity: z=-1.49, p=0.14; reward discounting: z=0.057, p=0.95; Figure S16).

Interestingly, task type moderated the punishment learning/sensitivity results (R^2=65.47%, I^2=22.79%, p=0.01). Tasks examining choices post-learning (5 studies;Frank et al. 2004) showed a negative dopaminergic effect on punishment learning/sensitivity (SMD=-0.44; 95%CI [-0.80, -0.08]) compared to tasks examining choices during learning (8 studies;Pessiglione et al. 2006), which yielded a nonsignificant small positive effect size (SMD=0.13; 95%CI [-0.12, 0.37]).

Studies with a lower proportion of female participants were also associated with higher effect sizes in overall punishment processes (R^2=69.26%, I^2=15.44%, p=0.04, 13 studies; Figure S17). None of the other moderators had an effect (S2.3).

Serotonin

The model-based learning/flexibility subcomponent was the only one with sufficient studies to conduct a funnel plot asymmetry analysis, which revealed no significant asymmetry (z=1.45, p=0.15; Figure S18).

No meaningful moderators were identified for serotonin (S2.3).

Discussion

This meta-analysis reveals distinct roles for dopamine and serotonin in modulating RL processes in humans. Dopamine increased reward learning and sensitivity, and reward vigor. A different pattern of effects was observed for serotonin: promoting learning from punishments, and possibly amplifying aversive Pavlovian biases. Both serotonin and dopamine increased the value of rewards when contrasted with costs of time or effort. These findings contribute to two key domains: advancing neuroscience theories of dopamine and serotonin in humans, and informing clinical applications. We begin by addressing the theoretical implications and conclude with the clinical relevance.

The differing effects of dopamine and serotonin are broadly consistent with theoretical expectations(den Ouden et al., 2013; Boureau and Dayan, 2011). The most influential theory of dopamine posits that dopamine signals reward prediction errors, driving reward learning(Schultz et al., 1997; Bayer and Glimcher, 2005). Supporting this, we found that boosting dopamine promotes reward learning/sensitivity in humans. Unlike preclinical studies, however(Cohen et al., 2015; Cardozo Pinto et al., 2024), we found no serotonin effect on reward learning, reinforcing the idea that dopamine and serotonin serve dissociable functions here. Instead, serotonin selectively affected punishment learning, consistent with theories linking serotonin to aversive processing(Dayan and Huys, 2009), and highlighting an opposing role to dopamine in learning(Daw et al., 2002). Interestingly, while dopamine did not significantly impact punishment learning, task type emerged as a significant moderator. Dopamine decreased punishment learning when studies assessed behavior *post*- but not *during*-learning. This effect is in the opposite direction to serotonin, and aligns with theories suggesting dopamine dips signal negative prediction errors that facilitate punishment learning(Frank et al., 2004; Collins and Frank, 2012, 2014). The mechanisms underlying these task-specific differences remain unclear. However, post-learning generalization may be more sensitive to slow, iterative habitual learning—reflecting true trial-and-error RL(Daw et al., 2011; Doll et al., 2016)—whereas choices made during learning might reflect other dopamine-driven processes, such as working memory(Collins et al., 2014). The latter are likely to also be particularly relevant to depression given the known pattern of broad cognitive impairments(Rock et al., 2014). Future studies will need to disentangle these.

We also provide preliminary evidence for a dissociation of serotonin and dopamine in Pavlovian biases. Specifically, serotonin—but not dopamine—enhanced aversive biases in within-subject studies. This resonates with findings in depressed patients treated with serotonergic antidepressants(Malamud et al., 2024), and supports theories suggesting serotonin facilitates inhibition specifically in punishment contexts(Cools et al., 2011; Boureau and Dayan, 2011; Dayan and Huys, 2008, 2009). However, this effect is not consistently observed, potentially owing to high measurement noise in these tasks(Moutoussis et al., 2021), underscoring the need for psycho-

metrically optimized tasks(Zorowitz and Niv, 2023).

Beyond learning, it is noteworthy that we found dopamine influencing reward vigor and discounting. This aligns with animal work suggesting that dopamine encodes a unified motivational signal, influencing both how energetically actions are taken (vigor) and decisions of whether to invest in effortful activity (value-based choice;Hamid et al. 2015; Niv et al. 2007). At present, it is unclear whether the dopamine effects on vigor and discounting (especially effort-based discounting) are related in humans as well. Notably, however, our findings converge with a rodent and clinical meta-analysis, where dopaminergic agents affected both reward discounting and vigor(Costello et al., 2022; Castrellon et al., 2021).

Like dopamine, serotonin however also diminished reward discounting. Although this might suggest that both have similar functions here, a more likely explanation is that they affect reward discounting through distinct mechanisms. Prior research suggests that dopamine reduces discounting by boosting the perceived benefits while serotonin may alter the perceived costs(Westbrook et al., 2020; Meyniel et al., 2016; Miyazaki et al., 2014; Soutschek et al., 2023). Although we were unable to dissociate the precise mechanism here, it is interesting that the serotonin studies exclusively covered delay discounting tasks. This may suggest that serotonin increases the discounting factor in RL models to promote a focus on long-term over short-term outcomes(Doya, 2002; Miyazaki et al., 2014).

Clinically, perhaps the most significant finding is that dopaminergic and serotonergic pharmacological manipulations had appreciably distinct effects. They engaged different components of RL in a manner which is measurable and identifiable with simple behavioral tasks. Hence, simple RL tasks may play a useful role in measuring treatment target engagement. This contrasts with symptom markers, which do not differentiate psychiatric medications(Chekroud et al., 2024; Arnow et al., 2015). Our results thus fulfill a key precondition for future work: if different antidepressants modulate distinct RL components, then RL-based biomarkers could guide more optimized treatments. Specifically, dopaminergic agents might affect reward learning, vigor, and discounting, while serotonergic agents might target punishment learning and aspects of reward discounting. A key and important question for future work is whether individual differences in baseline RL measures could help identify individuals more likely to benefit from one or the other type of intervention. This will require studies which simultaneously measure multiple RL domains and direct head-to-head comparison of the treatments of interest.

Limitations

Several limitations warrant consideration. First, few studies reported computational RL outcomes, forcing us to rely on broad measures. While we attempted to examine learning rate and sensitivity separately, this proved challenging as few reported these. It is further hard to disentangle them (indeed, serotonin increased punishment learning but decreased punishment sensitivity; Figure S13) and both are sensitive to task designs(Eckstein et al., 2022). Despite this, meaningful variability is evident in broad measures.

Second, the lack of studies directly comparing dopamine and serotonin prevented us from examining this relationship. There is also a lack of pharmacological specificity in the dopamine domain. Some medications target both dopamine and noradrenaline, complicating interpretation.

Third, the effect of dopamine on reward learning depended on the drug-binding interpretation, shifting from negligible to meaningful when low-dose presynaptic accounts were considered. This highlights the complexities of dopaminergic research, including evidence that the direction of effects may depend on baseline dopamine levels(Cools and D'Esposito, 2011). Such complexities might therefore have added noise to the effect size estimates.

Fourth, substantial heterogeneity was observed in serotonin's effect on reward learning/sensitivity, potentially due to the lack of common tasks across studies. This suggests the meta-analytic effect may be fragile, underscoring the need for further research using established tasks.

Finally, we pooled within- and between-subject data to increase power, applying effect size corrections of within-subject studies where feasible. When not possible, inflated variance of effect sizes would be the likely consequence, reducing our power to detect significant effects. All studies were further done in healthy controls. Ultimately, however, head-to-head comparisons in patients across a broad range of tasks will be required to establish the utility of RL processes for clinical applications.

Conclusions

Despite methodological heterogeneity, there is evidence that dopamine and serotonin affect RL; and that they do so by altering specific, distinct processes. These insights are valuable as they set forth candidate mechanisms for understanding the differentiating effects of treatments targeting different neuromodulators. Critically, the selective effects are observable in highly scalable human behavioral tasks, suggesting that such assessments may provide a fertile ground for the development of differentially sensitive biomarkers.

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Additional Information

The preregistration can be found at https://www.crd.york.ac.uk/PROSPERO/display_record.php?RecordID=363747 and open data and code to replicate all analyses will be made available upon publication.

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Zorowitz, S. and Niv, Y. (2023). Improving the reliability of cognitive task measures: A narrative review. *Biological psychiatry. Cognitive neuroscience and neuroimaging*.

Supplementary Material

S1 Supplementary Methods

S1.1 Search strategy

Figure S1 displays our search strategy for each database via Ovid, including the MeSH terms. The search terms were refined on a set of 40 in-lab references(Bellebaum et al., 2017; Bernacer et al., 2013; Chakroun et al., 2020; Cook et al., 2019; Cools et al., 2009, 2008; Cox et al., 2015; Crockett et al., 2012, 2009; Deserno et al., 2021; Dodds et al., 2008; Dubois et al., 2021; Eisenegger et al., 2014; Frank and O'Reilly, 2006; Geurts et al., 2013; Guitart-Masip et al., 2012, 2014b; Hebart and Glascher, 2015; Jocham et al., 2014; Kanen et al., 2019; Kayser et al., 2015; Kroemer et al., 2019; Meyniel et al., 2016; Mikus et al., 2022; Ohmann et al., 2020; Pessiglione et al., 2006; Pizzagalli et al., 2008; Robinson et al., 2010, 2012; Rostami Kandroodi et al., 2021; Scholl et al., 2017; Scholz et al., 2022; Seymour et al., 2012; Soder et al., 2021; Tanaka et al., 2009; Vo et al., 2016; Wardle et al., 2011; Westbrook et al., 2020; Worbe et al., 2016; Wunderlich et al., 2012) to ensure they captured all relevant studies.

a

1. Dopamine/
2. exp Dopamine Agents/
3. Serotonin/
4. exp Serotonin Agents/
5. tryptophan/ or tyrosine/
6. dopamine*.ti,ab.
7. seroton*.ti,ab.
8. tryptophan*.ti,ab.
9. tyrosine*.ti,ab.
10. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9
11. learning/ or avoidance learning/ or reinforcement, psychology/ or punishment/ or reward/ or reversal learning/
12. motivation/ or exploratory behavior/ or goals/
13. decision making/ or choice behavior/ or delay discounting/ or uncertainty/
14. (reward* or motivat* or punish* or reinforce* or decision* or effort* or learn* or incentive* or choice*).ti,ab.
15. 11 or 12 or 13 or 14
16. (participa* or subject* or individ* or human* or healthy* or investigat* or experiment*).ti,ab.
17. research subjects/ or healthy volunteers/ or volunteers/
18. 16 or 17
19. 10 and 15 and 18
20. limit 19 to (english language and "humans only (removes records about animals)")

b

1. exp catecholamines/
2. exp dopamine agonists/
3. exp dopamine antagonists/
4. exp Serotonin Agonists/ or exp Serotonin/ or exp Serotonin Antagonists/
5. tryptophan/
6. tyrosine/
7. dopamine*.ti,ab.
8. seroton*.ti,ab.
9. tryptophan*.ti,ab.
10. tyrosine*.ti,ab.
11. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10
12. learning/ or reward learning/
13. behavior/ or exp approach avoidance/ or exp approach behavior/ or exp avoidance/ or exploratory behavior/
14. computational reinforcement learning/
15. exp reinforcement/
16. exp motivation/
17. exp decision making/
18. exp decision theory/
19. exp delay discounting/
20. (reward* or motivat* or punish* or reinforce* or decision* or effort* or learn* or incentive* or choice*).ti,ab.
21. 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20
22. (participa* or subject* or individ* or human* or healthy* or investigat* or experiment*).ti,ab.
23. exp experimental subjects/
24. volunteers/
25. 22 or 23 or 24
26. 11 and 21 and 25
27. limit 26 to (human and english language)

c

1. catecholamine/
2. exp *dopamine receptor stimulating agent/
3. exp *serotonin receptor affecting agent/
4. tryptophan/
5. tyrosine/
6. dopamine*.ti,ab.
7. seroton*.ti,ab.
8. tryptophan*.ti,ab.
9. tyrosine*.ti,ab.
10. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9
11. learning/ or exp *associative learning/ or exp *conditioning/ or exp **reinforcement (psychology)*/ or exp *reversal learning/ or exp **reinforcement learning (machine learning)*/
12. exp *monetary reward/ or reward seeking behavior/ or reward/
13. exp *motivation/ or exploratory behavior/
14. exp *decision making/ or exp *cognitive bias/
15. (reward* or motivat* or punish* or reinforce* or decision* or effort* or learn* or incentive* or choice*).ti,ab.
16. 11 or 12 or 13 or 14 or 15
17. (participa* or subject* or individ* or human* or healthy* or investigat* or experiment*).ti,ab.
18. research subject/ or volunteer/ or normal human/
19. 17 or 18
20. 10 and 16 and 19

Figure S1: **Complete search terms for each database.** Search and MeSH terms are listed for databases a) MEDLINE/PubMed, b) Embase, and c) PsycInfo.

S1.2 Paper selection

Data were requested from authors mainly to obtain sufficient information from within-subject studies to pool together with between-subject studies or to obtain individual data for high and no/low reward conditions in the reward vigor category. In cases where multiple drugs or dosages were reported, we chose the more commonly used drug in that category and the highest dosage,

respectively. If a study reported data from multiple tasks, we extracted data from the most commonly used task in that category. We also prioritized parameters over model-agnostic measures wherever possible, and outcome measures that were as similar to other outcome measures within the same category. We excluded studies using drugs that have unclear, complex or substantially mixed dopamine or serotonin targets and/or those that would not be considered typical neuromodulatory targets of antidepressants.

For the reward learning/sensitivity category, we only included measures that related to reward processing and could be dissociated from punishment if those were used and vice versa for the punishment learning/sensitivity category. As our initial aim was to examine RL components, we extracted computational parameters for our outcome measure where possible. For the learning/sensitivity subcomponents, we prioritized learning rate over sensitivity parameters. Sensitivity parameters are harder to interpret, as they capture both sensitivity and nonspecific noisiness. For this reason — and due to the greater number of studies using learning rates — we prioritized learning rates in our main analysis.

For the reward vigor category, we primarily included measures that compared high-reward conditions to no-reward or low-reward conditions. This approach was intended to specifically capture the influence of dopamine/serotonin on reward-induced invigoration, rather than general motor functions. If these measures were not extractable however, we included a measure of vigor on high reward only if the effect of drug on the no or low reward condition was non-significant (N=2 in the dopamine domain). Excluding these two studies slightly reduced the pooled effect size in the reward vigor subcategory (SMD=0.23; 95% CI [0.01, 0.44]) and the overall reward domain meta-analysis for dopamine (SMD=0.19; 95% CI [0.11, 0.28]) but did not change inference.

Preprints were included but abstracts or unpublished work were not. Articles were independently assessed by A.M. and either Z.Q. or T.E. Conflicts were resolved through in-person discussion with Q.J.M.H.

S1.3 Meta-analysis

Risk attitude and model-based learning/flexibility As supplementary analyses, we examined risk attitude and model-based learning/flexibility. The risk attitude component examines how risk averse or risk-seeking individuals are. This component is usually examined with gamble tasks where individuals make a choice between a gamble of some risk between winning or losing and a sure or lower risk option with lower rewards.

Model-based learning/flexibility were composed of tasks that traditionally examine model-based learning or reversal learning. Model-based learning describes how individuals need to acquire a model of the task to make goal-directed choices, in contrast to model-free learning which relies on trial-and-error learning(Daw et al., 2011). Similarly, in reversal learning tasks individuals are exposed to changes in the task rules and have to infer when the context has changed to make appropriate decisions. These tasks are thought to measure flexibility, but also model-based aspects since an understanding of the task rules are required.

Risk attitude was excluded from the main meta-analyses because, while it is categorized as a cost-benefit decision-making process and sometimes grouped with effort and temporal delay discounting, it does not necessarily integrate well with these constructs. For instance, in

risk attitude paradigms, impulsivity manifests as greater risk-seeking behavior, which however corresponds to lower reward discounting by risk. In contrast, temporal delay tasks define impulsivity as choosing smaller, sooner rewards over larger, delayed ones, which also reflects higher reward discounting by time. Given these opposing directions in reward discounting when considering impulsivity and the frequent inclusion of both rewards and punishments in gambles in risk attitude tasks, we treated risk attitude as a separate construct.

The model-based learning/flexibility subcomponent was a also considered as a separate construct as it contains measures that tap into a more complex reward processing domain and some outcome measures in this task had mixed reward and punishment features.

We also examined within-subject studies only of both of these subcomponents since a number of within-subject studies could not be combined with the between-subject studies.

Categorization of dopaminergic agents. For the primary analysis, we categorized low-dose dopamine agonists and antagonists based on their opposing pharmacological effects. This was based on a several lines of evidence suggesting that pre- or post-synaptic binding depends on dosage. For example, low dose of D2-receptor antagonists have shown to block presynaptic autoreceptors, which are inhibitory, and therefore increase instead of block dopamine transmission(Schoemaker et al., 1997; Coukell et al., 1996; Papp and Wieronska, 2000). Similarly, studies in humans have shown that a low dose antagonist increases ventral striatal response to rewards – a typical response to boosting dopamine(Jocham et al., 2011) – as well as serum prolacting levels(Frank and O'Reilly, 2006). A similar pattern has been observed for some agonists at low dosages, like pramipexole(Pizzagalli et al., 2008).

Assessment of heterogeneity and outliers. Heterogeneity was assessed with τ^2, quantifying the variance of the true effect sizes, and the I^2 statistic, representing the percentage of variability in the effect sizes not accounted for by sampling error(Higgins et al., 2003). Heterogeneity was interpreted as low (25-50%), medium (50-75%) or high (>75% I^2;(Higgins et al., 2003)). Studies were classified as outliers if their 95% confidence interval did not overlap with the pooled effect CI, using the dmetar package in R(Harrer et al., 2019). To evaluate the influence of outliers, sensitivity analyses were conducted by recalculating the pooled effect and heterogeneity after removing the outliers.

Assessment of publication bias and moderators. Small-study effects were assessed with the Egger test ($p<0.05$;Egger et al. 1997) for categories with at least 10 studies(Higgins et al., 2024). Exploratory moderator analyses (random-effects categorical or metaregression models in R using the metafor package) explored potential explanations for the between-subject variance of effect sizes. These included 1) drug type (agonist or antagonist), 2) more specific dopamine drug activity types (D2 antagonist, D2 agonist, dopamine precursor or dopamine reuptake inhibitor), 3) task type, 4) dose regimen (single or multiple), 5) mean age across the study and 6) the mean proportion of female participants included in the study. The R^2 value was used to quantify the proportion of between-study heterogeneity accounted for by the moderators.

Assessment of study quality. The quality of studies were assessed with the Cochrane Collaboration's tool for assessing risk of bias(Higgins et al., 2011) by Z.Q., Q.D., and T.S.

Assessed criteria:
1. Random sequence generation (selection bias)
2. Allocation concealment (selection bias)
3. Blinding of participants and researchers (performance bias)

4. Blinding of outcome assessment (detection bias)
5. Incomplete outcome data (attrition bias)

For each item, the risk of bias was marked as 'low' if it was explicitly mentioned, 'high' if it was not explicitly mentioned, and 'unclear' if it was not explicitly mentioned but might be true.

S1.4 Effect size calculations

The SMDs for between-subject studies were calculated using Cohen's d (S1.4.1;(Cumming, 2013; Goulet-Pelletier and Cousineau, 2018). These were extracted from papers reporting the required statistics or by using a plot digitizer (PlotDigitizer, 3.1.6, 2024). Both within- and between-subject designs were included since this design choice is irrelevant to the question and there were a substantial number of each (23 between-subject dopamine studies, 45 within-subject dopamine studies; 25 between-subject serotonin studies, 14 within-subject studies).

However, combining within- and between-subject results in one meta-analysis requires knowledge of the correlation between the drug and placebo condition from within-subject studies in order to calculate an equivalent (correlation-corrected) effect size to the between-subject design Cohen's d(Cousineau and Goulet-Pelletier, 2021; Lakens, 2013). Since none of the included studies reported this, we only included within-subject studies where we could either derive the correlation from the information provided (i.e., where the mean and SD of the drug and placebo condition, and a t-statistic or standard error of the difference were reported) or data were provided from contacted authors. For these within-subject studies, we calculated the Cohen's d_{rm} and associated variance using the (Cousineau and Goulet-Pelletier, 2021) method in the TOSTER package(Caldwell, 2022) (S1.4.1). We also compared this to alternatives in both the effect size and variance computation for within-subject studies, which made little difference (Figure S2). If a within-subject study only provided enough data for calculating between-subject Cohen's d and raw data was unavailable, we classified it as a between-subject study.

Some within-subject studies applied mixed-effects models (due to uneven subjects in each condition) or non-parametric methods to analyze the data. Since calculating Cohen's d_{rm} is not straightforward in these cases, we opted to treat these as between-subject studies or transform the raw data, respectively.

In total, out of the original within-subject studies included, 13 studies in the dopamine domain and 4 studies in the serotonin domain were treated as between-subject studies. For meta-analyses where we additionally analyzed subcomponents based on only within-subject studies (dopamine: risk-attitude, Figure S6c; model-based learning/flexibility, Figure S6d; serotonin: aversive Pavlovian bias, Figure S12), we computed Cohen's d_z (S1.4.1). These included 3 additional serotonin and 5 additional dopamine studies.

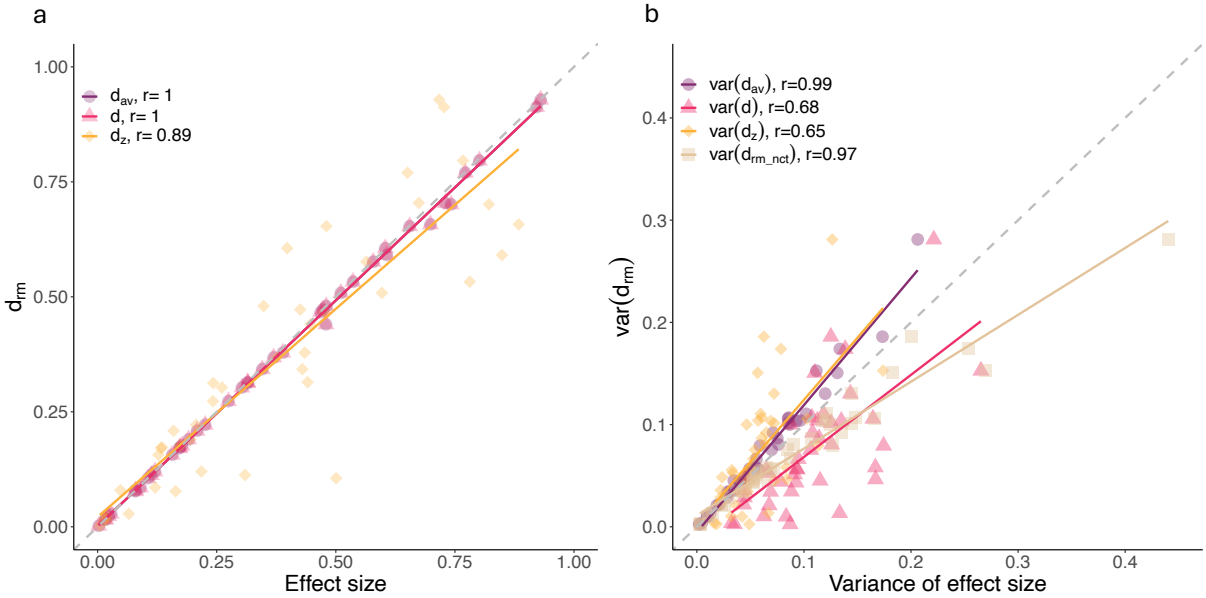


Figure S2: Comparison of a) effect size and b) variance of effect size calculations for within-subject studies that provided sufficient data to compute all variations (N=42). The y-axis represents Cohen's d_{rm} and the x-axis represents Cohen's d_{av}, d, or d_z in Figure a. $d_{av} = \frac{M_1 - M_2}{\sqrt{\frac{SD_1^2+SD_2^2}{2}}}$ (Cumming, 2013), and will equal d when the condition sample sizes are equal. In Figure b, the y-axis represents the variance of Cohen's d_{rm} (E9) and the x-axis represents four other calculations of the variance. Var(d) represents the variance of Cohen's d (E5); var(d_z) represents the variance of d_z (E15); and var(d_{av}) represents the variance of d_{av}. Vard(d_{av}) is calculated as: $var(d_{av}) = \left(\frac{CI_{up}-CI_{low}}{2\times 1.96}\right)^2$, where CI is calculated using the non-central t distribution: $CI = d_{av} \pm t\left(1-\frac{\alpha}{2}, n-1, \lambda\right) \times \sqrt{\frac{2(SD_1^2+SD_2^2-2\times r\times SD_1\times SD_2)}{N(SD_1^2+SD_2^2)}}$, $\alpha = 0.05$ and the non-centrality parameter is the observed t-value: $\lambda = d_{av} \times \sqrt{\frac{N(SD_1^2+SD_2^2)}{2(SD_1^2+SD_2^2-2\times r\times SD_1\times SD_2}}$ (Algina and Keselman, 2003). Var($d_{rm_{\text{nct}}}$) represents the variance of d_{rm} calculated with the setting "nct" for the confidence interval type in the package TOSTER(Caldwell, 2022), which uses the same equation as in (E9) but with $df = N-1$. The gray dashed diagonal line represents the reference line when y=x.

S1.4.1 Conversion of outcome measures into effect sizes and associated variances

For between-subject studies and studies treated as between-subject studies, the following equations were used:

- **Cohen's d from Means and Standard Deviations of 2 samples.**

$$d = \frac{M_1 - M_2}{SD_{pooled}} \tag{E1}$$

where d is Cohen's d, M_1 is the mean of one sample, M_2 is the mean of the other sample, SD_{pooled} is the pooled standard deviation of the two samples.

- **Pooled standard deviation of 2 samples.**

$$SD_{pooled} = \sqrt{\frac{(N_1 - 1)SD_1^2 + (N_2 - 1)SD_2^2}{N_1 + N_2 - 2}} \tag{E2}$$

where N_1 is the size of one sample, N_2 is the size of the other sample, SD_1 is the standard deviation of one sample, SD_2 is the standard deviation of the other sample.

- **Cohen's d from t-statistic.**

$$d = \frac{t}{\sqrt{\frac{1}{N_1} + \frac{1}{N_2}}} \tag{E3}$$

where t is the independent t-statistic reported.

- **Cohen's d from F-statistic.**

$$d = \sqrt{\frac{F}{\frac{1}{N_1} + \frac{1}{N_2}}} \tag{E4}$$

where F is the F-statistic reported.

- **Variance on Cohen's d.**

$$Var(d) = \frac{N_1 + N_2}{N_1 \times N_2} + \frac{d^2}{2(N_1 + N_2)} \tag{E5}$$

For within-subject studies, Cohen's d_{rm} was computed, taking into account the correlation between measures, using the Cousineau and Goulet-Pelletier (2021) method. This is useful for when effect sizes are being compared for studies that involve between and within subjects designs(Goulet-Pelletier and Cousineau, 2018). The TOSTER package in R was used, which uses the following equations(Caldwell, 2022):

- **Cohen's d_{rm} from Means, Standard Deviations and Correlation Coefficient of paired samples.**

$$d_{rm} = \frac{M_1 - M_2}{S_{diff}} \times \sqrt{\frac{2}{(1 - r)}} \tag{E6}$$

where d_{rm} is Cohen's d_{rm}, M_1 is the mean of one condition (drug), M_2 is the mean of the other condition (placebo), S_{diff} is the standard deviation of the difference scores, and r is the correlation between the drug and placebo conditions.

- **The standard deviation of the difference scores.**

$$S_{diff} = \sqrt{SD_1^2 + SD_2^2 - 2 \times r \times SD_1 \times SD_2} \tag{E7}$$

where S_{diff} is the standard deviation of the difference scores of the two samples, SD_1 is the standard deviation of one condition, and SD_2 is the standard deviation of the other condition.

- **The degrees of freedom for Cohen's d_{rm} under the Cousineau and Goulet-Pelletier (2021) method.**

$$df = 2(N-1) \tag{E8}$$

where N represents the sample size.

- **The variance of Cohen's d_{rm}**

$$Var(d_{rm}) = \frac{df}{df-2} \times \frac{2(1-r)}{N} \times \left(1 + d_{rm}^2 \times \frac{N}{2(1-r)}\right) - \frac{d_{rm}^2}{1} \tag{E9}$$

For within-subject studies where we had M_1, M_2, SD_1, SD_2 and the paired t-statistic, we estimated the correlation coefficient r between conditions with the following procedure:

1. Compute standard error of the difference:

$$SED = \frac{|M_1 - M_2|}{t} \tag{E10}$$

2. Compute the standard deviation of the difference scores:

$$S_{diff} = SED \times \sqrt{N} \tag{E11}$$

3. Calculate covariance:

$$\text{Cov} = \frac{SD_1^2 + SD_2^2 - SD_d^2}{2} \tag{E12}$$

4. The correlation coefficient r is:

$$r = \frac{\text{Cov}}{SD_1 \times SD_2} \tag{E13}$$

For supplemental meta-analyses where we only included within-subject studies, we first computed a paired t-test if one was not already provided in the study and then computed Cohen's d_z with the following equation:

- **Cohen's d_z based on the t-statistic, t:**

$$d_z = \frac{t}{\sqrt{N}} \tag{E14}$$

- **The variance of Cohen's d_z:**

$$Var(d_z) = \frac{1}{N} + \frac{d_z^2}{2 \times N} \tag{E15}$$

S2 Supplementary Results

	Dopamine			Serotonin		
Category	No. of studies	Placebo N	Drug N	No. of studies	Placebo N	Drug N
Overall reward	50	1358	1362	21	572	559
Overall punishment	17	362	365	11	292	285
Reward learning/sensitivity	25	616	623	9	274	269
Reward discounting	12	439	436	4	74	74
Reward vigour	9	185	186	4	96	94
Appetitive Pavlovian	5	158	157	4	128	122
Punishment learning/sensitivity	13	244	249	4	108	106
Aversive Pavlovian	4	118	116	7	184	179
Model-based learning/flexibility	8	236	239	10	306	300
Risk attitude	5	155	152	6	105	104
Aversive Pavlovian within-subjects	-	-	-	6	145	
Risk attitude within-subjects	5	127		-	-	-
Model-based learning/flexibility within-subjects	8	198		-	-	-

Table S1: Number of studies and participants (N) for each condition for each assessed category.

S2.1 Assessment of study quality

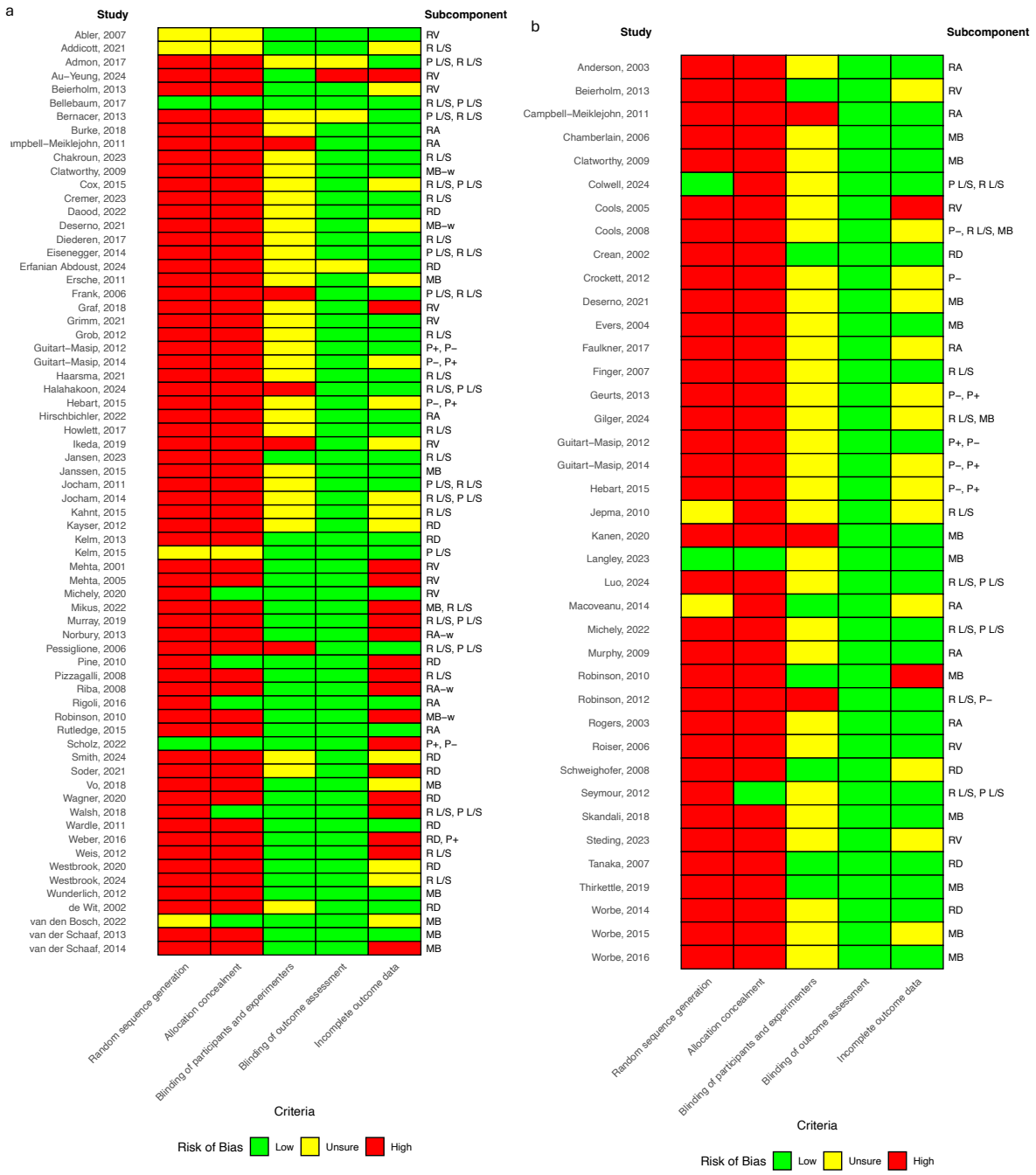


Figure S3: **Risk of bias assessment.** Abbreviations: R L/S: reward learning sensitivity; P L/S: punishment learning/sensitivity; P+: appetitive Pavlovian; P-: aversive Pavlovian; RD: reward discounting; RV: reward vigor; MB: model-based learning/flexibility; RA: risk attitude: -w: within-subjects study

S2.2 Heterogeneity

S2.2.1 Dopamine

There was low heterogeneity in overall reward (τ^2=0.04, I^2=46.7%) and overall punishment processes (τ^2=0.05, I^2=36.7%). Excluding four identified outlier studies(Erfanian Abdoust et al., 2024; Bernacer et al., 2013; Pizzagalli et al., 2008; Pine et al., 2010) reduced heterogeneity in overall reward processes (τ^2=0.018; I^2=33.15%), but did not substantially affect the pooled effect size (SMD=0.23, 95% CI [0.15, 0.31]).

There was also low heterogeneity in the reward learning/sensitivity subcomponent (τ^2=0.06, I^2=42.87%; removing two identified outliers(Bernacer et al., 2013; Pizzagalli et al., 2008) reduced this heterogeneity further τ^2=0.02, I^2=18.21%, which did not significantly affect the pooled effect size (SMD=0.26, 95% CI [0.13, 0.38]). There was moderate-to-substantial heterogeneity in the appetitive Pavlovian (τ^2=0.14, I^2=67.66%), risk attitude (τ^2=0.22, I^2=88.22%), and model-based learning/flexibility subcomponent (τ^2=0.31, I^2=84.76%). Removing an identified outlier in the risk attitude subcomponent(Burke et al., 2018) reduced heterogeneity to τ^2=0.01, I^2=32.98%, which resulted in a significant SMD estimate (SMD=0.27, 95% CI [0.08, 0.47]; Figure S9). There was no-to-low heterogeneity in the punishment learning/sensitivity, (τ^2=0.089, I^2=46.03%), reward vigor (τ^2=0.02, I^2=19.18%), reward discounting (τ^2=0.0009, I^2=7.35%), and aversive Pavlovian (τ^2 <0, I^2=0%) subcomponent. No other outliers were detected in either the subcategories or overall sample.

S2.2.2 Serotonin

Between-subject heterogeneity in overall reward (τ^2= 0.55, I^2 = 81.7%) and punishment (τ^2= 0.12, I^2= 61.7%) processes were moderate-to-substantial. Removing one outlier study(Luo et al., 2024) in the overall reward category reduced heterogeneity to low, explaining a substantial part of the heterogeneity (τ^2= 0.02, I^2= 28.77%), resulting in a small positive but non-significant pooled effect size (SMD=0.11; 95% CI, [-0.03, 0.24]). Removing one outlier(Hebart and Glascher, 2015) in overall punishment function reduced the heterogeneity to low (τ^2 = 0.05, I^2= 37.02%), which increased the overall effect size and made it significant (SMD=0.32; 95% CI, [0.10, 0.54]; Figure S14).

There was no heterogeneity in the punishment learning/sensitivity (τ^2 <0, I^2= 0.01%), appetitive Pavlovian (τ^2 < 0, I^2= 0%), reward vigor (τ^2 = 0.01, I^2= 17.37%) and reward discounting (τ^2 <0, I^2= 0%) subcomponent. There was low-to-moderate heterogeneity in the model-based learning/flexibility (τ^2= 0.032, I^2= 33.40%) and risk attitude subcomponent (τ^2= 0.13, I^2= 55.67%) and substantial heterogeneity in the reward learning/sensitivity (τ^2 = 1.30, I^2 = 94.68%) and aversive Pavlovian category (τ^2= 0.21, I^2= 72.66%). Removing one identified outlier(Luo et al., 2024) in the reward learning/sensitivity subcomponent reduced the heterogeneity somewhat (τ^2= 0.13, I^2= 64.92%) but did not affect the pooled effect size (SMD=0.03; 95% CI [-0.29, 0.34]). No other outliers were detected.

S2.3 Moderator analyses

Several moderators were used to assess potential sources of bias in overall reward and punishment processing and subcomponents with sufficient number of studies (N>9) and substantial heterogeneity. These included reward and punishment learning/sensitivity subcomponents in

the dopamine domain and the model-based learning/flexibility subcomponent in the serotonin domain. Task type was only assessed for the subcomponents since these would likely just recapitulate the subcomponents in the overall reward/punishment domains.

S2.3.1 Dopamine

Table S2 lists the number of studies included for all the DA moderator analyses.

Lower proportion of female participants in the overall punishment category was associated with higher effect sizes (R^2=69.26%, I^2=15.44%, p=0.04, Figure S17), but did not significantly moderate overall reward function (p=0.71). None of the other moderators were significant predictors in the overall reward/punishment categories (drug regimen - single vs. multiple drug administrations: reward p=0.47; punishment p=0.42; drug type - agonist vs. antagonist: reward p=0.12; punishment p=0.48; more fine-grained drug activity classifications: reward p=0.27; punishment p=0.35; overall study age: reward p=0.83; punishment p=0.46).

Task type was a significant predictor in the punishment learning/sensitivity subcomponent (R^2 = 65.47%, I^2=22.79%, p=0.01). Studies using the Probabilistic Selection Task (5 studies; Frank et al. 2004) had a moderate and significant negative impact on punishment learning/sensitivity processes (SMD=-0.44, 95% CI [-0.80, -0.08]) compared with studies that used other tasks (8 studies; all but one comprised of the Probabilistic Instrumental Learning task(Pessiglione et al., 2006)), which yielded a nonsignificant small positive effect size (SMD=0.13, 95% CI [-0.12, 0.37]). Task type did not moderate reward learning/sensitivity (p=0.47). Drug type (reward: p=0.32; punishment: p=0.26), more fine-grained drug type (reward: p=0.54; punishment: p=0.52), age (reward: p=0.81; too few punishment studies to assess) or proportion of female participants (reward: p=0.42; punishment: p=0.06) did not moderate the reward/punishment learning/sensitivity results. There was only one study in the reward and punishment learning/sensitivity subcomponents that used multiple drug administrations and this moderator was therefore not evaluated here.

As an additional exploratory analysis, we examined if the results in the reward discounting category might differ depending on the task type. This was explored based on previous reviews suggesting that dopamine might have a predominant role in effort but not temporal discounting (Soutschek et al., 2023). Although effort versus temporal delay discounting studies were not significantly different from each other (p=0.09), the effect of dopamine on reward discounting was only significant in the effort discounting paradigms (SMD=-0.28, 95% CI [-0.52, -0.03]; 3 studies) but not in the temporal delay discounting tasks (SMD=-0.06, 95% CI [-0.13, 0.02]; 9 studies). However, there were too few studies to reliably test this and due to the lack of significant difference of dopamine between these tasks, we do not interpret this further but suggest this as an area for future research to resolve.

S2.3.2 Serotonin

Table S3 describes the number of studies included for all the serotonin moderator analyses.

A subgroup analysis indicated that drug type significantly moderated the effect sizes in overall reward processing (R^2=18.45%, I^2=88.42%, p=0.03). However, further analysis showed that the individual effect sizes for both the antagonist (SMD=0.26, 95% CI [-0.12, 0.65]) and agonist (SMD=-0.49, 95% CI [-1.04, 0.05]) subgroups were not significant, indicating that the overall significant moderation effect is driven by differences in directionality rather than by significant effects within each group. This effect is likely driven by the previously identified outlier(Luo

et al., 2024). Removing this outlier, drug activity is no longer a significant predictor (p=0.11).

The same was true for drug type moderating effect sizes in the model-based/flexibility subcategory (R^2=39.04%, I^2=22.92%, p=0.046), with neither the agonist (SMD=-0.19, 95% CI [-0.49, 0.11]) or antagonist (SMD=0.19, 95% CI [-0.03, 0.42]) subgroup having a significant overall effect on model-based learning. Drug type was not a significant moderator of the effect of serotonin on overall punishment function (p=0.76). Subgroup analyses with more fine-grained drug activity was not conducted since these included virtually the same groupings as the agonist/antagonist subgroup analysis. Drug regimen (single vs multiple drug administrations) did not significantly moderate the overall reward (p=0.50) or punishment (p=0.42) processes. There was only one study with multiple drug administrations in the model-based/flexibility subcomponent and thus this moderator was not assessed here. Neither age nor proportion of female participants were significant predictors in the overall reward category (age: p=0.82, %female participants: p=0.32) or in the model-based/flexibility subcomponent (too few studies to examine age; %female participants: p=0.27). There were too few studies to examine age and %female participants in the overall punishment category. Task type was not a significant moderator of model-based learning/flexibility (p=0.11).

		Category			
	Moderator	overall reward	overall punishment	reward learning/sensitivity	punishment learning/sensitivity
1	Drug type	DA+=33, DA-=17	DA+=11, DA-=6	DA+=14, DA-=11	DA+=8, DA-=5
2	specific drug type	D2-=15, DAP=11, DARI=12, O=12	D2-=5, O=12	D2-=10, DAP=4, DARI=6, O=5	D2-=5, other=8
3	Task type	-	-	PILT=10, PST=5, O=10	PILT/O=8, PST=5
4	Drug regimen	multiple=3, single=47	multiple=1, single=16	multiple=1, single=24	multiple=1, single=12
5	Age	N=36	N=10	N=16	N=8
6	%Female	N=41	N=13	N=20	N=11

Table S2: Number of studies for each moderator in the dopamine (DA) domain. DA+: agonist, DA-: antagonist, D2-: D2-receptor antagonist, DAP: DA precursor, DARI: DA reuptake inhibitor, PILT: Probabilistic instrumental learning task, PST: Probabilistic selection task, O: other.

		Category		
	Moderator	overall reward	overall punishment	model-based learning/flexibility
1	Drug type	5HT+=7, 5HT-=14	5HT+=5, 5HT-=6	5HT+=4, 5HT-=6
2	Task type			Two-step=3, O=1, reversal=6
3	Drug regimen	multiple=2, single=19	multiple=2, single=9	multiple=1, single=9
4	Age	N=15	N=7	N=9
5	%Female	N=17	N=6	N=10

Table S3: Number of studies for each moderator in the serotonin (5HT) domain. 5HT+: agonist, 5HT-: antagonist, O: other.

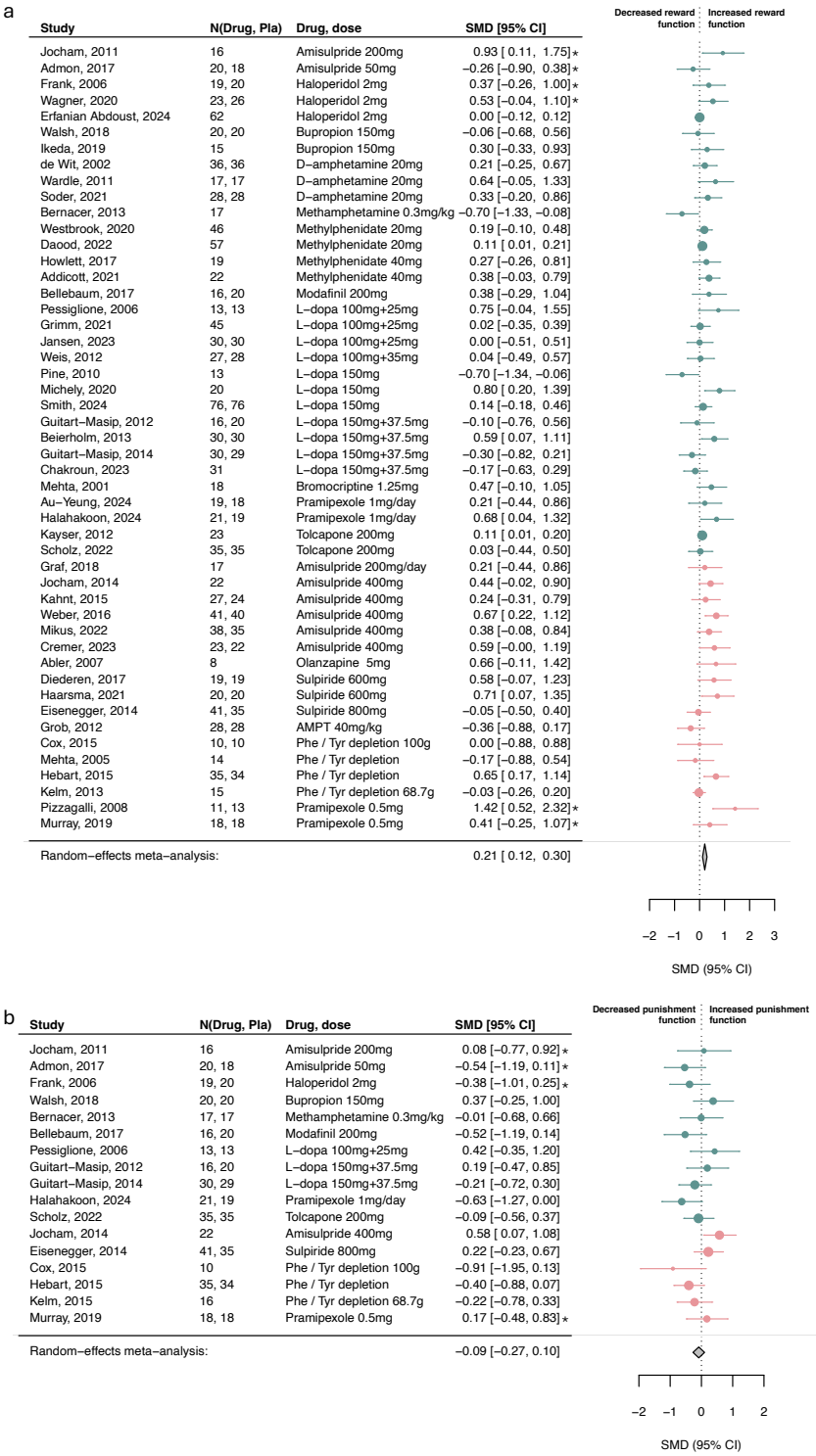


Figure S4: **The effect of upregulating dopamine on overall reward and punishment.** Standardized mean differences (SMDs) between the effect of upregulating dopamine versus placebo on a) overall reward reward function, and b) overall punishment function. Pla indicates placebo. We recoded antagonist effects as if they were agonists (pink SMD point estimates and 95% CI). Green SMD point estimates and 95% CI indicate studies that were coded as original agonists. Asterisks indicate studies that used a low dose of an agonist or antagonists. These effects were interpreted contrary to their typical activity profile (e.g., a low-dose agonist acting antagonistically), as suggested by the literature.

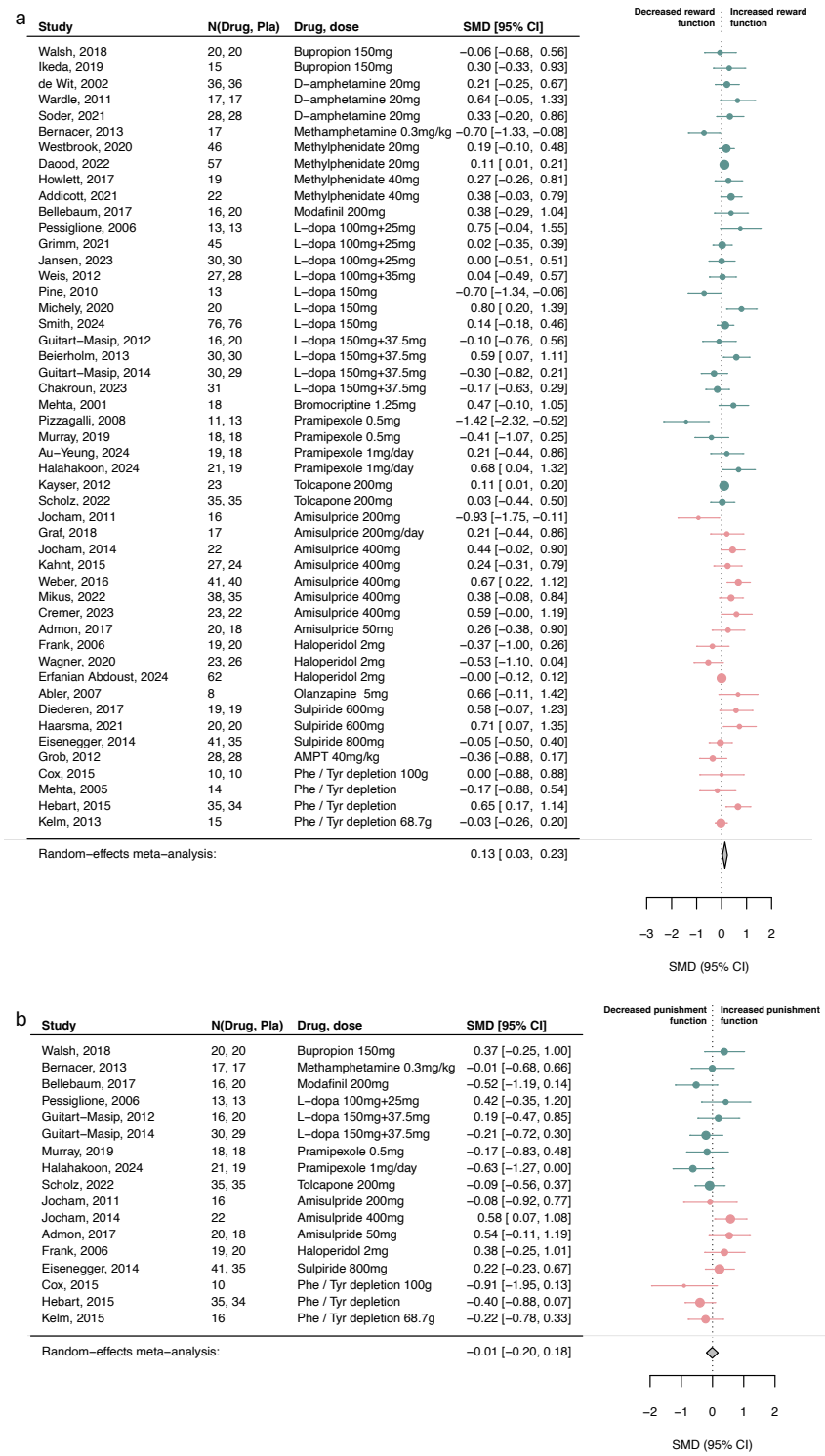


Figure S5: **The effect of upregulating dopamine on overall reward and punishment according to original drug profile.** Standardized mean differences (SMDs) between the effect of upregulating dopamine versus placebo on a) overall reward reward function, and b) overall punishment function according to the original drug activity profile. Pla indicates placebo. We recoded antagonist effects as if they were agonists (pink SMD point estimates and 95% CI). Green SMD point estimates and 95% CI indicate studies that were coded as original agonists.

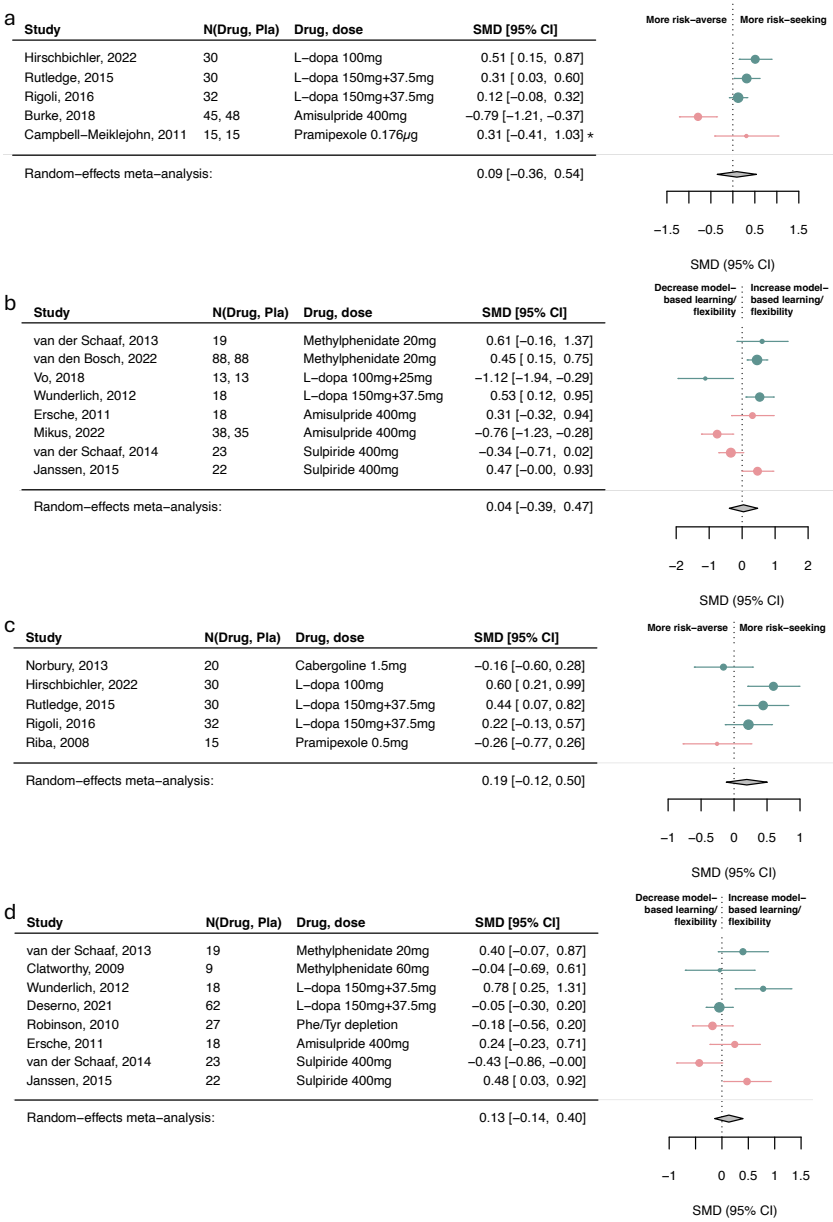
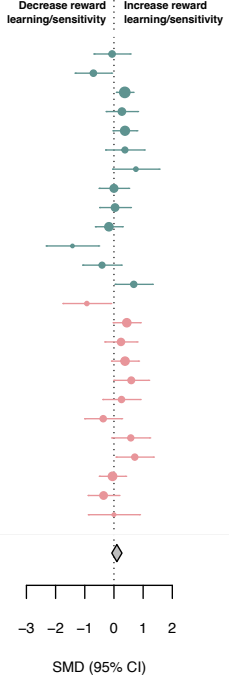


Figure S6: **The effect of upregulating dopamine on risk and model-based learning/flexibility.** Standardized mean differences (SMDs) between the effect of upregulating dopamine versus placebo on a) risk attitude, b) model-based learning/flexibility, c) risk attitude in within-subject studies only, and d) model-based learning/flexibility in within-subjects only. Pla indicates placebo. We recoded antagonist effects as if they were agonists (pink SMD point estimates and 95% CI). Green SMD point estimates and 95% CI indicate studies that were coded as original agonists. Asterisks indicate studies that used a low dose of an agonist or antagonists. These effects were interpreted contrary to their typical activity profile (e.g., a low-dose agonist acting antagonistically), as suggested by the literature.

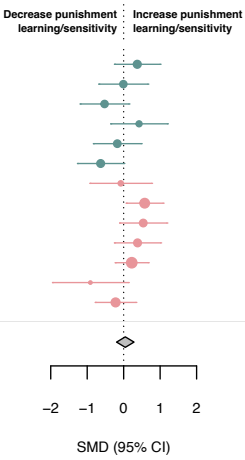
a

Study	N(Drug, Pla)	Drug, dose	SMD [95% CI]
Walsh, 2018	20, 20	Bupropion 150mg	−0.06 [−0.68, 0.56]
Bernacer, 2013	17	Methamphetamine 0.3mg/kg	−0.70 [−1.33, −0.08]
Westbrook, 2024	95, 97	Methylphenidate 20mg	0.37 [0.09, 0.66]
Howlett, 2017	19	Methylphenidate 40mg	0.27 [−0.26, 0.81]
Addicott, 2021	22	Methylphenidate 40mg	0.38 [−0.03, 0.79]
Bellebaum, 2017	16, 20	Modafinil 200mg	0.38 [−0.29, 1.04]
Pessiglione, 2006	13, 13	L−dopa 100mg+25mg	0.75 [−0.04, 1.55]
Jansen, 2023	30, 30	L−dopa 100mg+25mg	0.00 [−0.51, 0.51]
Weis, 2012	27, 28	L−dopa 100mg+35mg	0.04 [−0.49, 0.57]
Chakroun, 2023	31	L−dopa 150mg+37.5mg	−0.17 [−0.63, 0.29]
Pizzagalli, 2008	11, 13	Pramipexole 0.5mg	−1.42 [−2.32, −0.52]
Murray, 2019	18, 18	Pramipexole 0.5mg	−0.41 [−1.07, 0.25]
Halahakoon, 2024	21, 19	Pramipexole 1mg/day	0.68 [0.04, 1.32]
Jocham, 2011	16	Amisulpride 200mg	−0.93 [−1.75, −0.11]
Jocham, 2014	22	Amisulpride 400mg	0.44 [−0.02, 0.90]
Kahnt, 2015	27, 24	Amisulpride 400mg	0.24 [−0.31, 0.79]
Mikus, 2022	38, 35	Amisulpride 400mg	0.38 [−0.08, 0.84]
Cremer, 2023	23, 22	Amisulpride 400mg	0.59 [−0.00, 1.19]
Admon, 2017	20, 18	Amisulpride 50mg	0.26 [−0.38, 0.90]
Frank, 2006	19, 20	Haloperidol 2mg	−0.37 [−1.00, 0.26]
Diederen, 2017	19, 19	Sulpiride 600mg	0.58 [−0.07, 1.23]
Haarsma, 2021	20, 20	Sulpiride 600mg	0.71 [0.07, 1.35]
Eisenegger, 2014	41, 35	Sulpiride 800mg	−0.05 [−0.50, 0.40]
Grob, 2012	28, 28	AMPT 40mg/kg	−0.36 [−0.88, 0.17]
Cox, 2015	10, 10	Phe / Tyr depletion 100g	0.00 [−0.88, 0.88]
Random−effects meta−analysis:			0.10 [−0.07, 0.28]



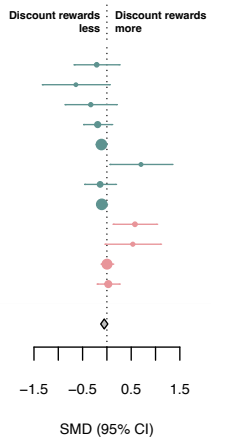
b

Study	N(Drug, Pla)	Drug, dose	SMD [95% CI]
Walsh, 2018	20, 20	Bupropion 150mg	0.37 [−0.25, 1.00]
Bernacer, 2013	17, 17	Methamphetamine 0.3mg/kg	−0.01 [−0.68, 0.66]
Bellebaum, 2017	16, 20	Modafinil 200mg	−0.52 [−1.19, 0.14]
Pessiglione, 2006	13, 13	L−dopa 100mg+25mg	0.42 [−0.35, 1.20]
Murray, 2019	18, 18	Pramipexole 0.5mg	−0.17 [−0.83, 0.48]
Halahakoon, 2024	21, 19	Pramipexole 1mg/day	−0.63 [−1.27, 0.00]
Jocham, 2011	16	Amisulpride 200mg	−0.08 [−0.92, 0.77]
Jocham, 2014	22	Amisulpride 400mg	0.58 [0.07, 1.08]
Admon, 2017	20, 18	Amisulpride 50mg	0.54 [−0.11, 1.19]
Frank, 2006	19, 20	Haloperidol 2mg	0.38 [−0.25, 1.01]
Eisenegger, 2014	41, 35	Sulpiride 800mg	0.22 [−0.23, 0.67]
Cox, 2015	10	Phe / Tyr depletion 100g	−0.91 [−1.95, 0.13]
Kelm, 2015	16	Phe / Tyr depletion 68.7g	−0.22 [−0.78, 0.33]
Random−effects meta−analysis:			0.04 [−0.19, 0.28]



c

Study	N(Drug, Pla)	Drug, dose	SMD [95% CI]
de Wit, 2002	36, 36	D−amphetamine 20mg	−0.21 [−0.67, 0.25]
Wardle, 2011	17, 17	D−amphetamine 20mg	−0.64 [−1.33, 0.05]
Soder, 2021	28, 28	D−amphetamine 20mg	−0.33 [−0.86, 0.20]
Westbrook, 2020	46	Methylphenidate 20mg	−0.19 [−0.48, 0.10]
Daood, 2022	57	Methylphenidate 20mg	−0.11 [−0.21, −0.01]
Pine, 2010	13	L−dopa 150mg	0.70 [0.06, 1.34]
Smith, 2024	76, 76	L−dopa 150mg	−0.14 [−0.46, 0.18]
Kayser, 2012	23	Tolcapone 200mg	−0.11 [−0.20, −0.01]
Weber, 2016	40, 40	Amisulpride 400mg	0.58 [0.13, 1.02]
Wagner, 2020	23, 26	Haloperidol 2mg	0.53 [−0.04, 1.10]
Erfanian Abdoust, 2024	62	Haloperidol 2mg	0.00 [−0.12, 0.12]
Kelm, 2013	15	Phe / Tyr depletion 68.7g	0.03 [−0.20, 0.26]
Random−effects meta−analysis:			−0.05 [−0.13, 0.02]



d

Study	N(Drug, Pla)	Drug, dose	SMD [95% CI]
Hirschbichler, 2022	30	L−dopa 100mg	0.51 [0.15, 0.87]
Rutledge, 2015	30	L−dopa 150mg+37.5mg	0.31 [0.03, 0.60]
Rigoli, 2016	32	L−dopa 150mg+37.5mg	0.12 [−0.08, 0.32]
Campbell−Meiklejohn, 2011	15, 15	Pramipexole 0.176μg	−0.31 [−1.03, 0.41]
Burke, 2018	45, 48	Amisulpride 400mg	−0.79 [−1.21, −0.37]
Random−effects meta−analysis:			−0.00 [−0.46, 0.46]

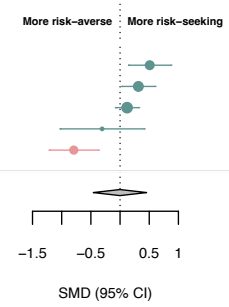


Figure S7: **The effect of upregulating dopamine on subcomponents according to original drug profile.** The figure shows standardized mean differences (SMDs) between the effect of upregulating dopamine versus placebo on a) reward learning/sensitivity, b) punishment learning/sensitivity, d) reward discounting and d) risk attitude according to the original drug activity profile. Pla indicates placebo. Forest plots c and d display SMDs that reflect Cohen's d_z. We recoded antagonist effects as if they were agonists (pink SMD point estimates and 95% CI indicate studies that were coded as original agonists.

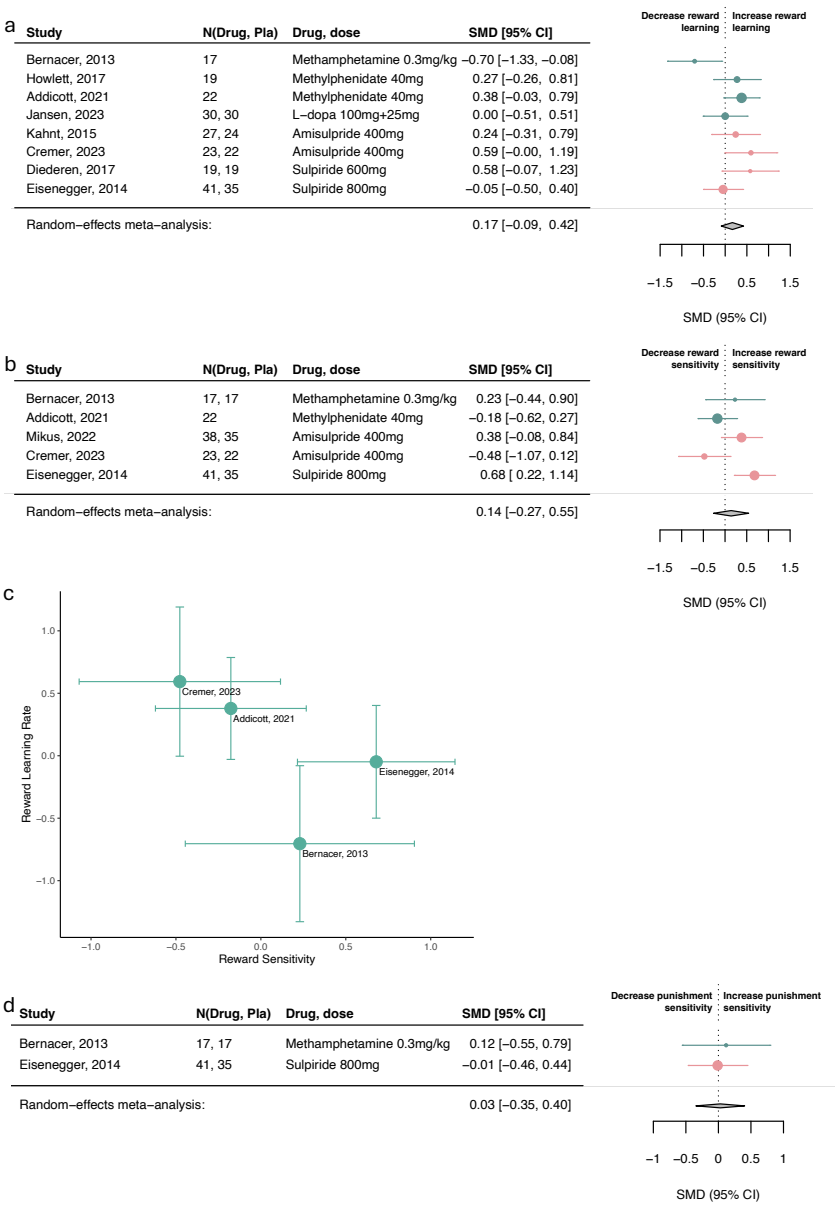


Figure S8: **The effect of upregulating dopamine on learning rate and sensitivity parameters.** Standardized mean differences (SMDs) between the effect of upregulating dopamine versus placebo on a) reward learning rates, b) reward sensitivity, c) scatter plot of reward learning rate and reward sensitivity SMDs for studies that reported both - error bars represent 95% CI, and d) punishment sensitivity. Pla indicates placebo. We recoded antagonist effects as if they were agonists (pink SMD point estimates and 95% CI). Green SMD point estimates and 95% CI indicate studies that were coded as original agonists.

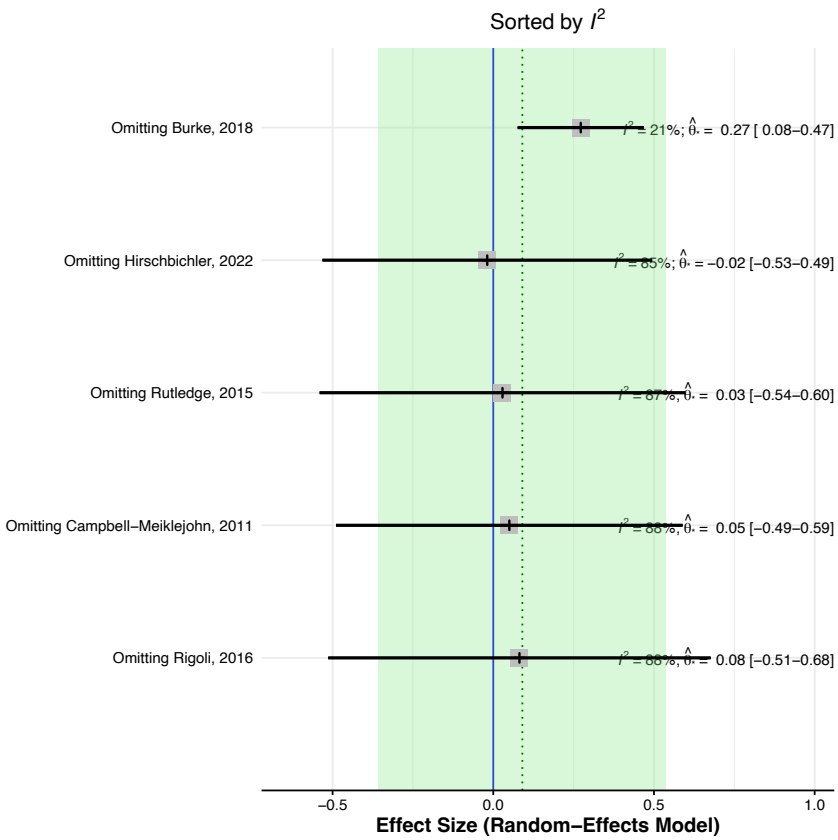


Figure S9: **Leave-one-out meta-analysis for the effect of dopamine on risk attitude.** It is ordered by heterogeneity (low to high), displaying the recalculated pooled effect size and 95% confidence interval with one study omitted each time. The shaded area represents the 95% confidence interval of the original pooled effect size, and the dotted line represents the original estimated pooled effect size.

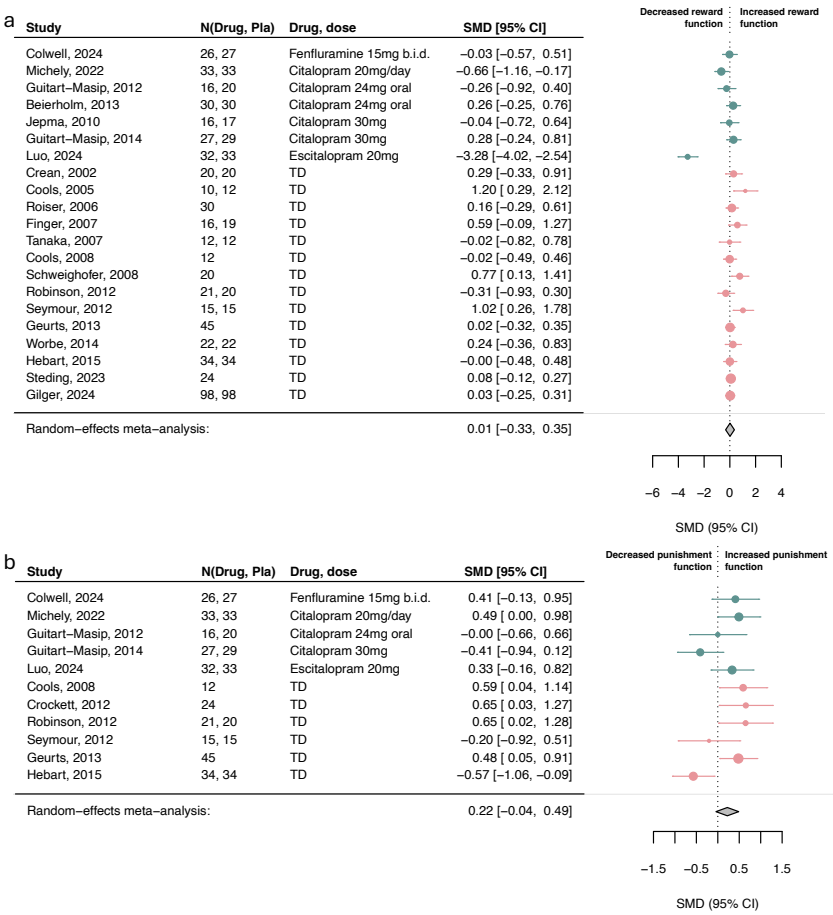


Figure S10: **The effect of upregulating serotonin on overall reward and punishment.** Standardized mean differences (SMDs) between the effect of upregulating serotonin versus placebo on a) overall reward function, and b) overall punishment function. Pla indicates placebo. We recoded antagonist effects as if they were agonists (pink SMD point estimates and 95% CI). Green SMD point estimates and 95% CI indicate studies that were coded as original agonists. TD: tryptophan depletion.

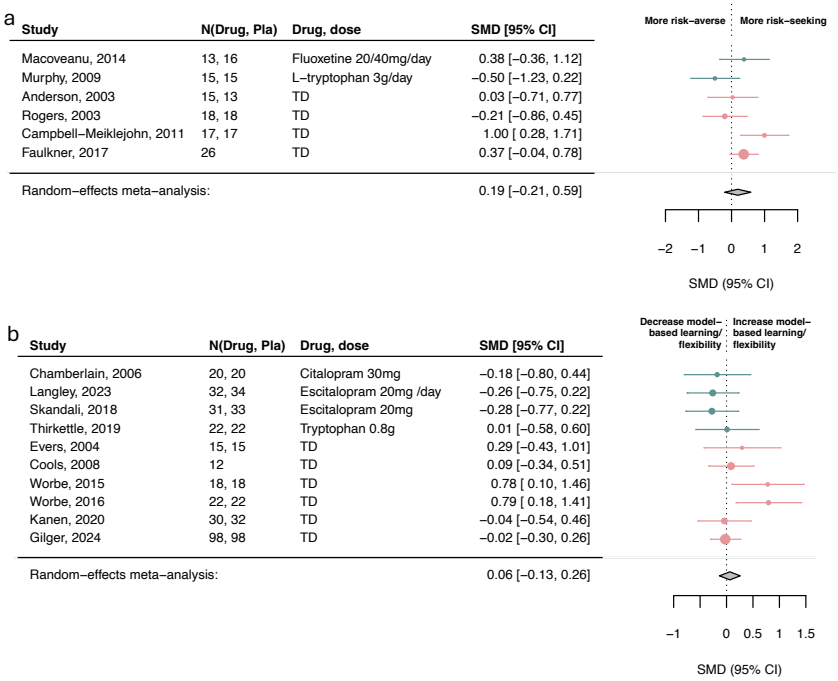


Figure S11: **The effect of upregulating serotonin on risk attitude and model-based learning/flexibility.** Standardized mean differences (SMDs) between the effect of upregulating serotonin versus placebo on a) risk attitude, and b) model-based learning/flexibility. Pla indicates placebo. We recoded antagonist effects as if they were agonists (pink SMD point estimates and 95% CI). Green SMD point estimates and 95% CI indicate studies that were coded as original agonists. TD: tryptophan depletion.

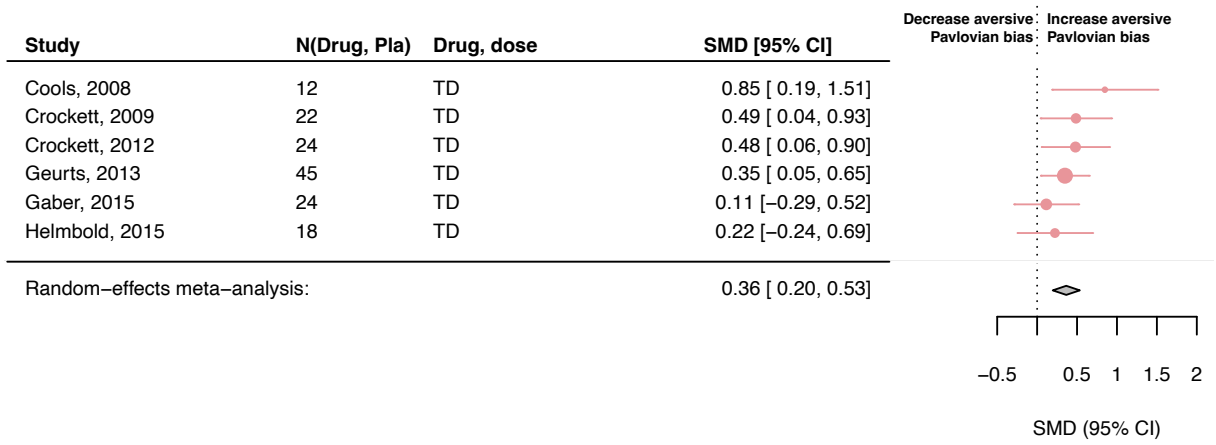


Figure S12: **The effect of upregulating serotonin on aversive Pavlovian biases in within-subject studies.** Standardized mean differences (SMDs) between the effect of upregulating serotonin versus placebo on aversive Pavlovian bias, only including within-subject studies. These SMDs reflect Cohen's d_z. Pla indicates placebo. We recoded antagonist effects as if they were agonists (pink SMD point estimates and 95% CI). TD: tryptophan depletion.

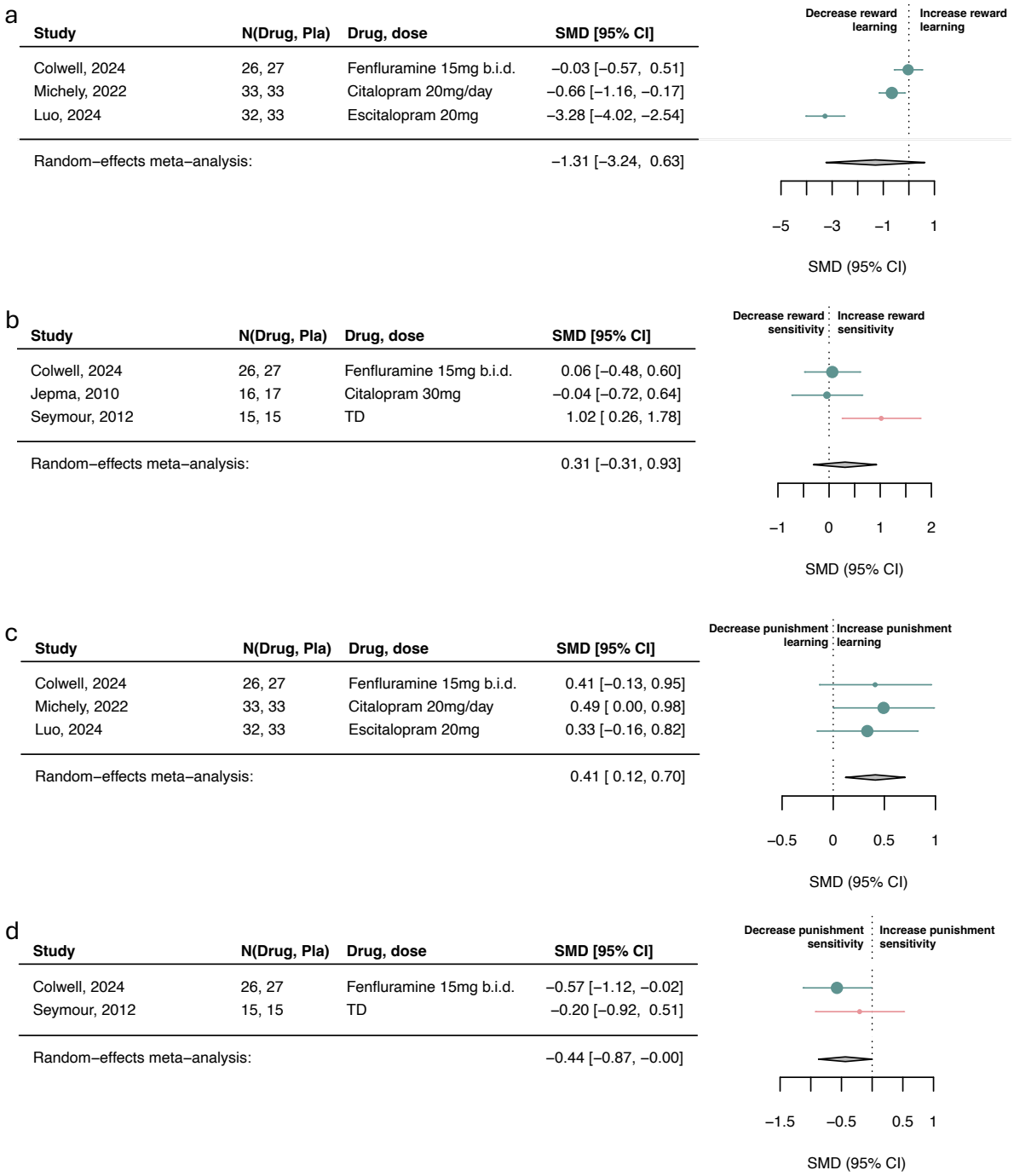


Figure S13: **The effect of upregulating serotonin on learning rate and sensitivity parameters.** Standardized mean differences (SMDs) between the effect of upregulating serotonin versus placebo on a) reward learning rates, b) reward sensitivity, c) punishment learning rates, and d) punishment sensitivity. Pla indicates placebo. We recoded antagonist effects as if they were agonists (pink SMD point estimates and 95% CI). Green SMD point estimates and 95% CI indicate studies that were coded as original agonists. TD: tryptophan depletion.

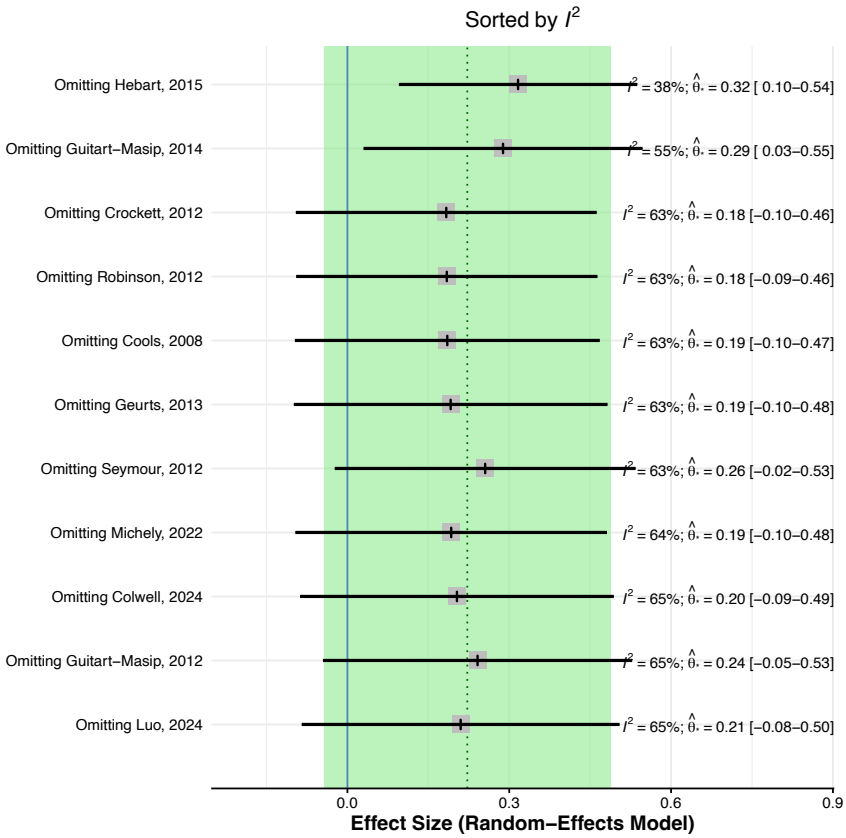


Figure S14: **Leave-one-out meta-analysis for the effect of serotonin on overall punishment function.** It is ordered by heterogeneity (low to high), displaying the recalculated pooled effect size and 95% confidence interval with one study omitted each time. The shaded area represents the 95% confidence interval of the original pooled effect size, and the dotted line represents the original estimated pooled effect size.

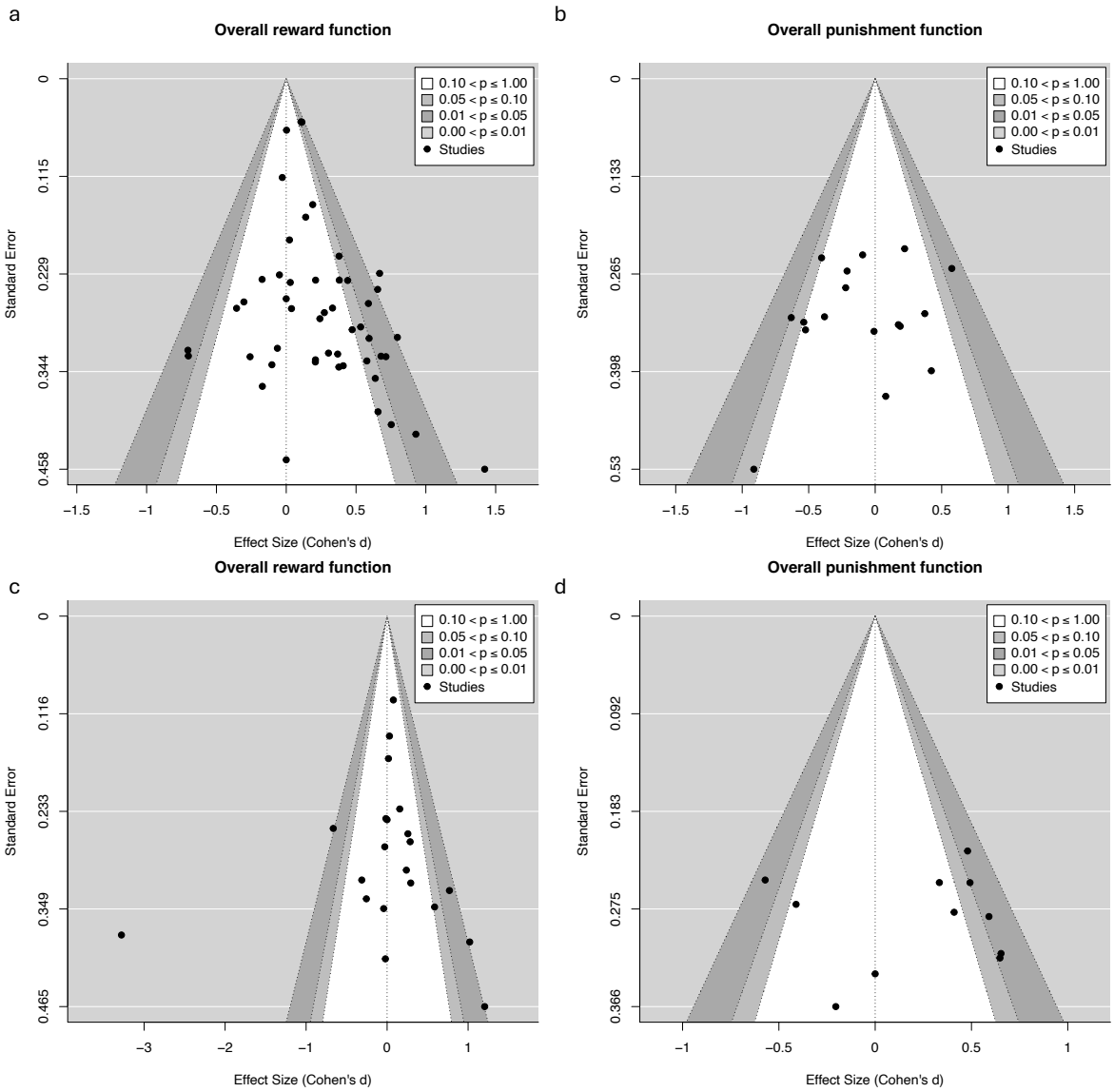


Figure S15: Funnel plots of dopamine on reward components: a) overall reward function, b) overall punishment function, and funnel plots of serotonin on c) overall reward function, and d) overall punishment function.

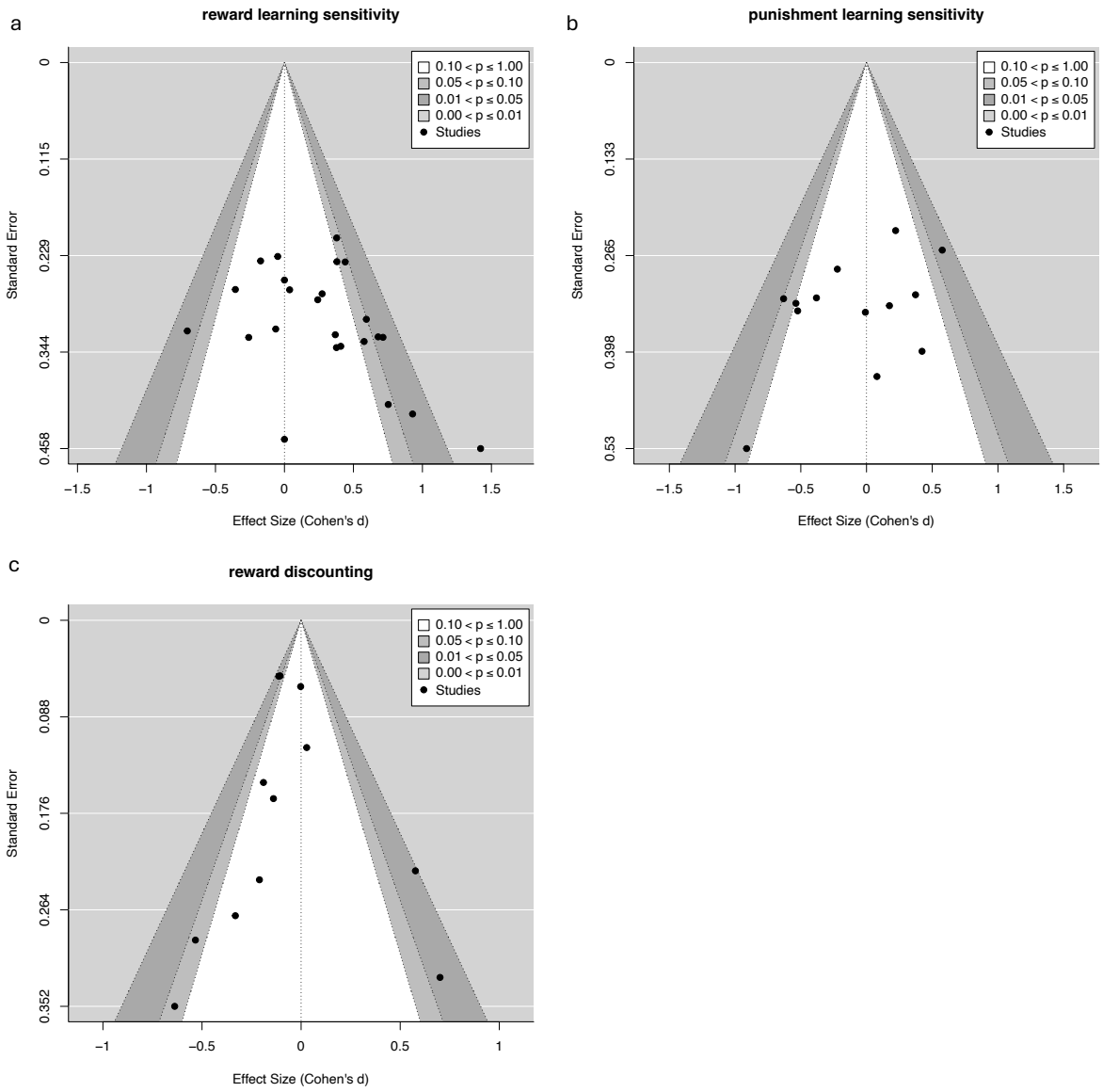


Figure S16: Funnel plots of dopamine on a) reward learning/sensitivity, b) punishment learning/sensitivity, and c) reward discounting.

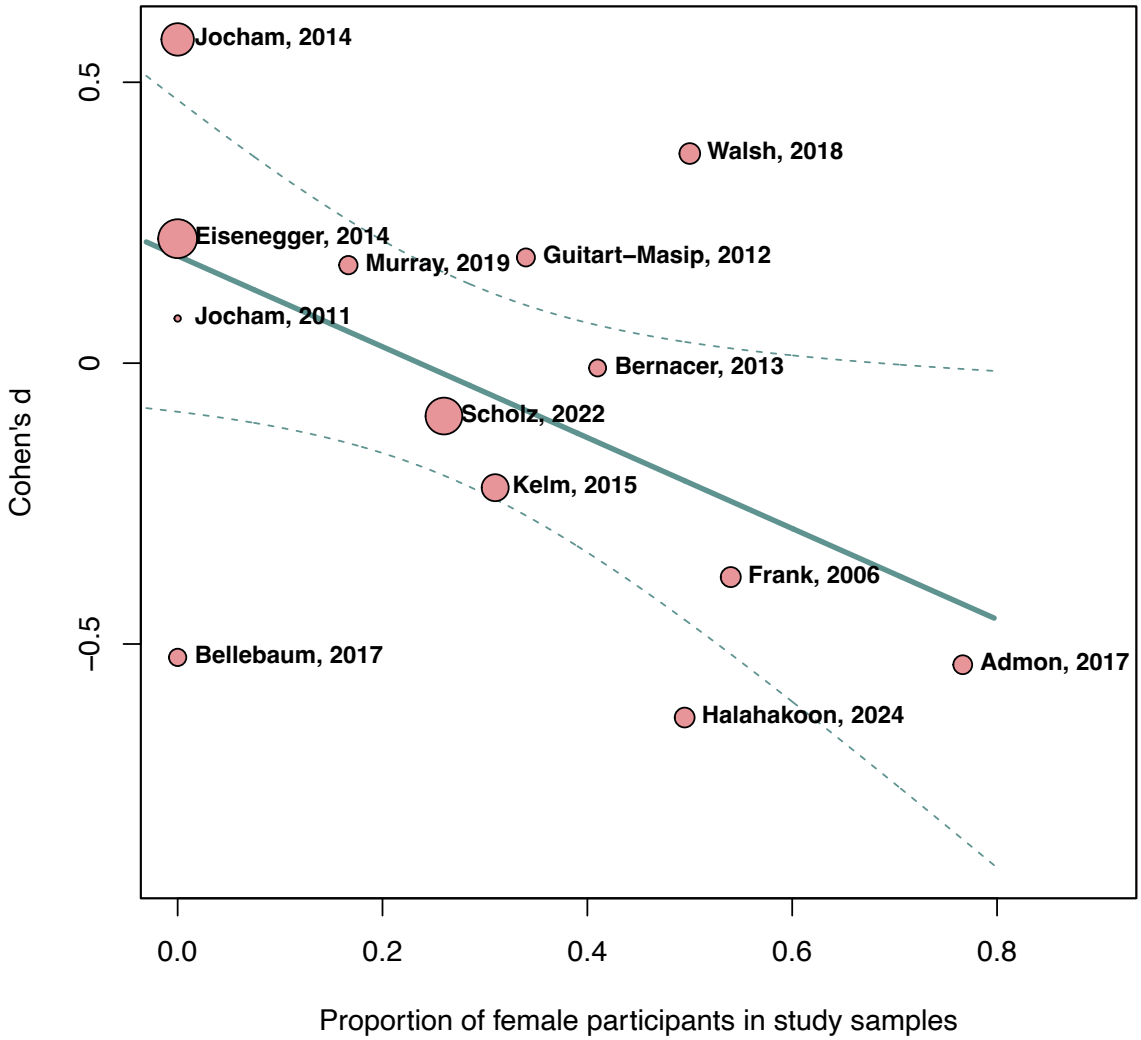


Figure S17: Bubble plot of the moderating effect of female participant proportion on the effect of dopamine on overall punishment processes. The size of the circle represents the weight the studies received in the meta-analysis analysis - with larger circles being more influential.

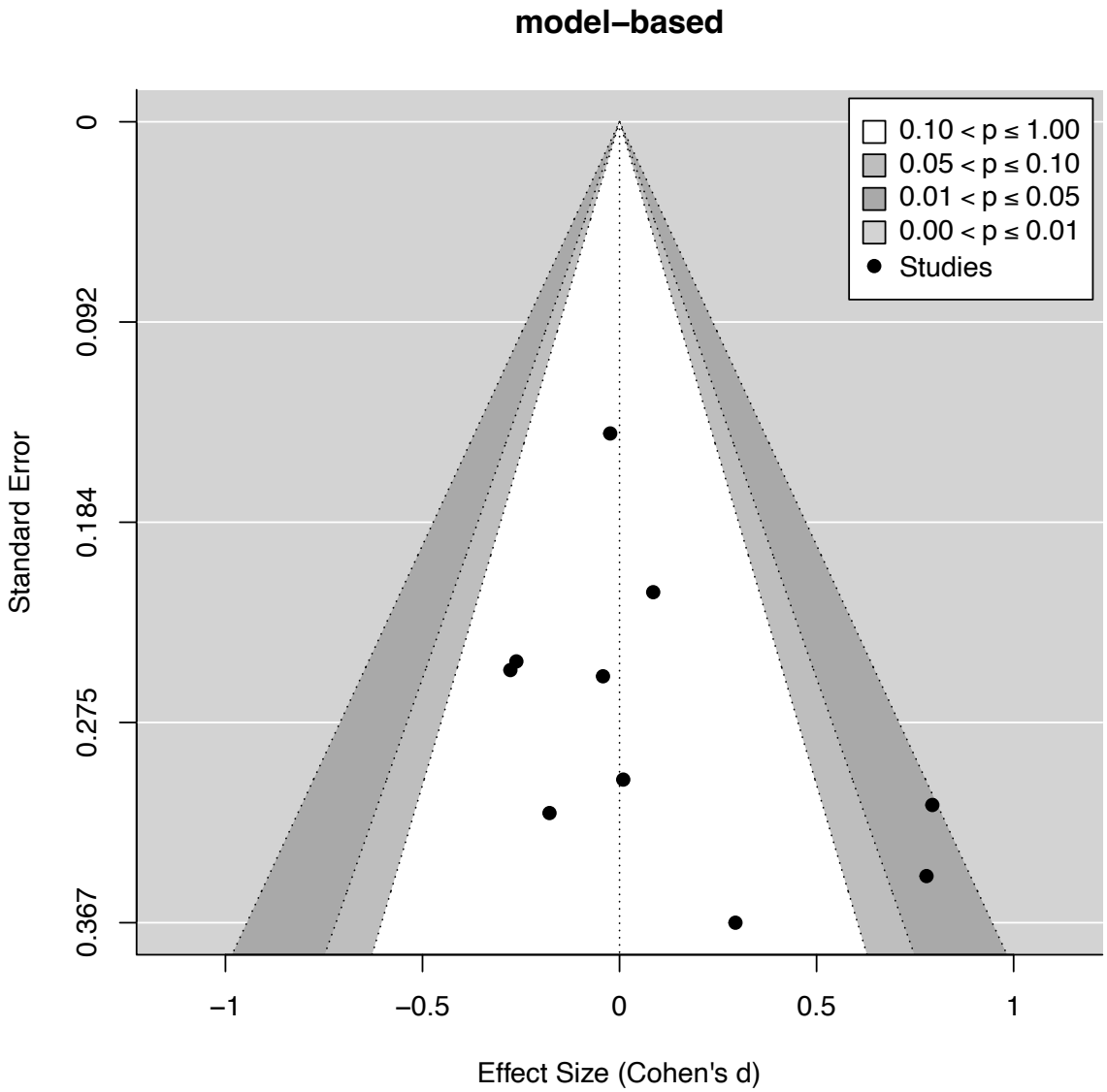


Figure S18: Funnel plot of serotonin on model-based learning/flexibility.

Study	Category	Drug, Dose	N drug	N placebo	Original Design	Design	Task	Outcome	Study Age	Study Female Proportion	Drug Regimen
Addicott, 2021(Addicott et al., 2021)	R L/S	methylphenidate 40mg	22	22	w	w	restless bandit	learning rate	27.7	0.57	1
Admon, 2017*(Admon et al., 2017)	R L/S	amisulpride 50mg	20	18	bw	bw	PST	choose A	25.9	0.77	1
Bellebaum, 2017(Bellebaum et al., 2017)	R L/S	modafinil 200mg	16	20	bw	bw	PST	choose A	24.85	0	1
Bernacer, 2013(Bernacer et al., 2013)	R L/S	methamphetamine 0.3mg/kg	17	17	w	w	PILT	learning rate	25.3	0.41	1
Chakroun, 2023(Chakroun et al., 2023)	R L/S	L-dopa 150mg+37.5mg	31	31	w	w	PILT	accuracy	26.85	0	1
Cox, 2015(Cox et al., 2015)	R L/S	Phe / Tyr depletion 100g	10	10	w†	bw	PST	choose A/C	NA	NA	1
Cremer, 2023(Cremer et al., 2023)	R L/S	amisulpride 400mg	23	22	bw	bw	foraging	learning rate	NA	0.47	1
Diederen, 2017(Diederen et al., 2017)	R L/S	sulpiride 600mg	19	19	bw	bw	observational reversal	learning rate	24.4	0.47	1
Eisenegger, 2014(Eisenegger et al., 2014)	R L/S	sulpiride 800mg	41	35	bw	bw	PILT	learning rate	NA	0	1
Frank, 2006*(Frank and O'Reilly, 2006)	R L/S	haloperidol 2mg	19	20	w†	bw	PST	choose A	21	0.54	1
Grob, 2012(Grob et al., 2012)	R L/S	AMPT 40mg/kg	28	28	w†	bw	PRT	response bias block 3	25.8	1	1
Haarsma, 2021(Haarsma et al., 2021)	R L/S	sulpiride 600mg	20	20	bw	bw	observational reversal	accuracy	24.35	0.42	1
Halahakoon, 2024(Halahakoon et al., 2024)	R L/S	pramipexole 1mg/day	21	19	bw	bw	PILT	accuracy change pre-post intervention	23.5	0.5	0
Howlett, 2017(Howlett et al., 2017)	R L/S	methylphenidate 40mg	19	19	w	w	random dot based PILT	learning rate	NA	0	1
Jansen, 2023 (Jansen et al., 2023)	R L/S	L-dopa 100mg+25mg	30	30	w†	bw	PILT	learning rate	22.8	0	1
Jocham, 2011*(Jocham et al., 2011)	R L/S	amisulpride 200mg	16	16	w	w	PST	p(correct) win-win	26.13	0	1
Jocham, 2014(Jocham et al., 2014)	R L/S	amisulpride 400mg	22	22	w	w	PILT	final accuracy	NA	0	1
Kahnt, 2015(Kahnt et al., 2015)	R L/S	amisulpride 400mg	27	24	bw	bw	noninstrumental outcome prediction	learning rate	22.4	0	1
Mikus, 2022(Mikus et al., 2022)	R L/S	amisulpride 400mg	38	35	bw	bw	Two-step task	inverse temperature	NA	NA	1
Murray, 2019*(Murray et al., 2019)	R L/S	pramipexole 0.5mg	18	18	w†	bw	PILT	accuracy	32.1	0.17	1
Pessiglione, 2006(Pessiglione et al., 2006)	R L/S	L-dopa 100mg+25mg	13	13	bw	bw	PILT	accuracy	NA	NA	1
Pizzagalli, 2008*(Pizzagalli et al., 2008)	R L/S	pramipexole 0.5mg	11	13	bw	bw	PRT	response bias block 3-1	NA	NA	1
Walsh, 2018(Walsh et al., 2018)	R L/S	bupropion 150mg	20	20	bw	bw	PILT	points won	23.825	0.5	1
Weis, 2012(Weis et al., 2012)	R L/S	L-dopa 100mg+35mg	27	28	bw	bw	appetitive instrumental conditioning	accuracy learning	28.5	0.31	1
Westbrook, 2024(Westbrook et al., 2020)	R L/S	methylphenidate 20mg	95	97	w†	bw	PILT WM	late accuracy	NA	NA	1
Addicott, 2021(Addicott et al., 2021)	R S	methylphenidate 40mg	22	22	w	w	restless bandit	inverse temperature	27.7	0.57	1
Bernacer, 2013(Bernacer et al., 2013)	R S	methamphetamine 0.3mg/kg	17	17	w†	bw	PILT	temperature	25.3	0.41	1
Cremer, 2023(Cremer et al., 2023)	R S	amisulpride 400mg	23	22	bw	bw	foraging	inverse temperature	NA	0.47	1
Eisenegger, 2014(Eisenegger et al., 2014)	R S	sulpiride 800mg	41	35	bw	bw	PILT	temperature	NA	0	1
Admon, 2017*(Admon et al., 2017)	P L/S	amisulpride 50mg	20	18	bw	bw	PST	avoid B	25.9	0.77	1
Bellebaum, 2017(Bellebaum et al., 2017)	P L/S	modafinil 200mg	16	20	bw	bw	PST	avoid B	24.85	0	1
Bernacer, 2013(Bernacer et al., 2013)	P L/S	methamphetamine 0.3mg/kg	17	17	w†	bw	PILT	learning rate	25.3	0.41	1
Cox, 2015(Cox et al., 2015)	P L/S	Phe / Tyr depletion 100g	10	10	w	w	PST	avoid B/D	NA	NA	1
Eisenegger, 2014(Eisenegger et al., 2014)	P L/S	sulpiride 800mg	41	35	bw	bw	PILT	learning rate	NA	0	1
Frank, 2006*(Frank and O'Reilly, 2006)	P L/S	haloperidol 2mg	19	20	w†	bw	PST	avoid B	21	0.54	1
Halahakoon, 2024(Halahakoon et al., 2024)	P L/S	pramipexole 1mg/day	21	19	bw	bw	PILT	accuracy change pre-post intervention	23.5	0.5	0
Jocham, 2011*(Jocham et al., 2011)	P L/S	amisulpride 200mg	16	16	w	w	PST	p(correct) lose-lose	26.13	0	1
Jocham, 2014(Jocham et al., 2014)	P L/S	amisulpride 400mg	22	22	w	w	PILT	final accuracy	NA	0	1
Kelm, 2015(Kelm and Boettiger, 2015)	P L/S	Phe / Tyr depletion 68.7g	16	16	w	w	PAL	passive avoidance errors	NA	0.31	1
Murray, 2019*(Murray et al., 2019)	P L/S	pramipexole 0.5mg	18	18	w†	bw	PILT	accuracy	32.1	0.17	1
Pessiglione, 2006(Pessiglione et al., 2006)	P L/S	L-dopa 100mg+25mg	13	13	bw	bw	PILT	accuracy	NA	NA	1
Walsh, 2018(Walsh et al., 2018)	P L/S	bupropion 150mg	20	20	bw	bw	PILT	points lost	23.825	0.5	1
Bernacer, 2013(Bernacer et al., 2013)	P S	methamphetamine 0.3mg/kg	17	17	w†	bw	PILT	temperature	25.3	0.41	1
Eisenegger, 2014(Eisenegger et al., 2014)	P S	sulpiride 800mg	41	35	bw	bw	PILT	temperature	NA	0	1
Guitart-Masip, 2012(Guitart-Masip et al., 2012)	P+	L-dopa 150mg+37.5mg	16	20	bw	bw	go/nogo	nogo to win	23.15	0.34	1
Guitart-Masip, 2014(Guitart-Masip et al., 2014b)	P+	L-dopa 150mg+37.5mg	30	29	bw	bw	go/nogo	nogo to win	NA	NA	1
Hebart, 2015(Hebart and Glascher, 2015)	P+	Phe / Tyr depletion	35	34	bw	bw	PIT	appetative PIT	NA	NA	1
Scholz, 2022(Scholz et al., 2022)	P+	tolcapone 200mg	35	35	w†	bw	go/nogo	nogo to win	31.3	0.26	1
Weber, 2016(Weber et al., 2016)	P+	amisulpride 400mg	41	40	bw	bw	PIT	button press rew-unrew CS	21.805	NA	1
Guitart-Masip, 2012(Guitart-Masip et al., 2012)	P-	L-dopa 150mg+37.5mg	16	20	bw	bw	go/nogo	go to avoid	23.15	0.34	1
Guitart-Masip, 2014(Guitart-Masip et al., 2014b)	P-	L-dopa 150mg+37.5mg	30	29	bw	bw	go/nogo	go to avoid	NA	NA	1
Hebart, 2015(Hebart and Glascher, 2015)	P-	Phe / Tyr depletion	35	34	bw	bw	PIT	aversive PIT	NA	NA	1
Scholz, 2022(Scholz et al., 2022)	P-	tolcapone 200mg	35	35	w†	bw	go/nogo	go to avoid	31.3	0.26	1
Daood, 2022(Daood et al., 2022)	RD	methylphenidate 20mg	57	57	w	w	DD	p(choose now)	26.42	0.6	1
Erfanian Abdoust, 2024*(Erfanian Abdoust et al., 2024)	RD	haloperidol 2mg	62	62	w	w	DD	p(high cost option)	22.79	0.52	1
Kayser, 2012(Kayser et al., 2012)	RD	tolcapone 200mg	23	23	w	w	DD	p(choose now)	NA	0.56	1
Kelm, 2013(Kelm and Boettiger, 2013)	RD	Phe / Tyr depletion 68.7g	15	15	w	w	DD	p(choose now)	NA	0	1
Pine, 2010(Pine et al., 2010)	RD	L-dopa 150mg	13	13	w	w	DD	k parameter	21	0.57	1
Smith, 2024(Smith et al., 2024)	RD	L-dopa 150mg	76	76	w†	bw	DD	Larger-but-later choices	28.26	0.42	1
Soder, 2021(Soder et al., 2021)	RD	d-amphetamine 20mg	28	28	w†	bw	physical effort	p(hard task)	24.07	0.5	1
Wagner, 2020*(Wagner et al., 2020)	RD	haloperidol 2mg	23	26	bw	bw	DD	p(delay)	23.85	0.74	1
Wardle, 2011(Wardle et al., 2011)	RD	d-amphetamine 20mg	17	17	w†	bw	physical effort	p(hard task)	22.7	0.65	1
Weber, 2016(Weber et al., 2016)	RD	amisulpride 400mg	40	40	bw	bw	DD	p(choose now)	NA	NA	1
Westbrook, 2020(Westbrook et al., 2020)	RD	methylphenidate 20mg	46	46	w	w	cognitive effort	subjective value(hard task)	NA	NA	1
de Wit, 2002(de Wit et al., 2002)	RD	d-amphetamine 20mg	36	36	w†	bw	DD	k parameter	24	0.5	1
Abler, 2007(Abler et al., 2007)	RV	olanzapine 5mg	8	8	w	w	MID	RT high reward	31.3	0.5	1
Au-Yeung, 2024(Au-Yeung et al., 2024)	RV	pramipexole 1mg/day	19	18	bw	bw	eye-tracking vigour	Velocity residuals	23.59	0.48	0
Beierholm, 2013(Beierholm et al., 2013)	RV	L-dopa 150mg+37.5mg	30	30	bw	bw	odd-ball discrimination	average reward rate on RTs	24.15	0.43	1
Graf, 2018(Graf et al., 2018)	RV	amisulpride 200mg/day	17	17	w	w	MID	RT 100-0	23.8	0	0
Grimm, 2021(Grimm et al., 2021)	RV	L-dopa 100mg+25mg	45	45	w	w	MID	RT high-neutral reward	22.81	0.51	1
Ikeda, 2019(Ikeda et al., 2019)	RV	bupropion 150mg	15	15	w	w	MID	RT high-neutral reward	31.7	0.53	1
Mehta, 2001(Mehta et al., 2001)	RV	bromocriptine 1.25mg	18	18	w	w	Reward-responsivity	No. cards sorted in sort 3 - No. cards sorted in sorts 2/4	24.15	0	1
Mehta, 2005(Mehta et al., 2005)	RV	Phe / Tyr depletion	14	14	w	w	Reward-responsivity	No. extra cards correctly sorted	33.9	0.14	1
Michely, 2020(Michely et al., 2020)	RV	L-dopa 150mg	20	20	w	w	dynamic effort	grip force high reward	25.6	0.45	1
Clatworthy, 2009(Clatworthy et al., 2009)	MB/F	methylphenidate 60mg	9	9	w	w	reversal	reversal learning	NA	0	1
Deserno, 2021(Deserno et al., 2021)	MB/F	L-dopa 150mg+37.5mg	62	62	w	w	model-based bandit	model-based choice	NA	NA	1
Ersche, 2011(Ersche et al., 2011)	MB/F	amisulpride 400mg	18	18	w	w	probabilistic reversal	perseverative errors	32.7	0.2	1
Janssen, 2015(Janssen et al., 2015)	MB/F	sulpiride 400mg	22	22	w	w	observational reversal	reversal errors	32.2	0	1
Mikus, 2022(Mikus et al., 2022)	MB/F	amisulpride 400mg	38	35	bw	bw	Two-step task	omega parameter	NA	NA	1
Robinson, 2010(Robinson et al., 2010)	MB/F	Phe/Tyr depletion	27	27	w	w	observational reversal	reversal errors	NA	0.48	1
Vo, 2018(Vo et al., 2018)	MB/F	L-dopa 100mg+25mg	13	13	bw	bw	probabilistic reversal	reversal errors	NA	NA	1
Wunderlich, 2012(Wunderlich et al., 2012)	MB/F	L-dopa 150mg+37.5mg	18	18	w	w	Two-step task	omega parameter	23.3	0	1
van den Bosch, 2022(van den Bosch et al., 2022)	MB/F	methylphenidate 20mg	88	88	w†	bw	observational reversal	accuracy reversal	NA	NA	1
van der Schaaf, 2013(van der Schaaf et al., 2013)	MB/F	methylphenidate 20mg	19	19	w	w	observational reversal	accuracy reversal	20.9	0.52	1
van der Schaaf, 2014(van der Schaaf et al., 2014)	MB/F	sulpiride 400mg	23	23	w	w	observational reversal	accuracy reversal	NA	0.5	1
Burke, 2018(Burke et al., 2018)	RA	amisulpride 400mg	45	48	bw	bw	gambling	utility curvature	NA	NA	1
Campbell-Meiklejohn, 2011*(Campbell-Meiklejohn et al., 2011)	RA	pramipexole 0.176μg	15	15	bw	bw	gambling	p(gamble)	24.9	0.53	1
Hirschbichler, 2022(Hirschbichler et al., 2022)	RA	L-dopa 100mg	30	30	w	w	gambling	p(gamble)	31.67	0.53	1
Norbury, 2013(Norbury et al., 2013)	RA	cabergoline 1.5mg	20	20	w	w	gambling	p(gamble)	26.7	NA	1
Riba, 2008*(Riba et al., 2008)	RA	pramipexole 0.5mg	15	15	w	w	gambling	p(risky choice)	24.4	NA	1
Rigoli, 2016(Rigoli et al., 2016)	RA	L-dopa 150mg+37.5mg	32	32	w	w	gambling	p(gamble)	23.4	0.5	1
Rutledge, 2015(Rutledge et al., 2015)	RA	L-dopa 150mg+37.5mg	30	30	w	w	gambling	p(gamble) gain	23.4	0.63	1

Table S4: **Characteristics of all dopamine studies.** Asterisks indicate studies that used a low dose of an agonist or antagonists. These effects were interpreted contrary to their typical activity profile (e.g., a low-dose agonist acting as an antagonist), as suggested by the literature. Daggers indicate studies that were originally within-subject studies (in column 'original design') but we could only calculate a between-subjects Cohen's d (indicated in column 'design'). In drug regimen, 1 indicates a single drug administration and 0 indicates multiple drug administrations. Abbreviations: R L/S: reward learning/sensitivity; R S: reward sensitivity; P L/S: punishment learning/sensitivity; P S: punishment sensitivity; P+: appetitive Pavlovian; P-: aversive Pavlovian; RD: reward discounting; RV: reward vigor: MB/F: model-based learning/flexibility; RA: risk attitude; w: within-subject studies; bw: between-subject studies; PST: probabilistic selection task; PILT: probabilistic instrumental learning task; WM: working memory; PAL: passive avoidance learning; PIT: Pavlovian instrumental task; DD: delay discounting; MID: monetary incentive delay.

Study	Category	Drug, Dose	N drug	N placebo	Original Design	Design	Task	Outcome	Study Age	Study Female Proportion	Drug Regimen
Colwell, 2024(Colwell et al., 2024)	R L/S	fenfluramine 15mg b.i.d.	26	27	bw	bw	PILT	learning rate	20.17	0.6	0
Cools, 2008(Cools et al., 2008)	R L/S	TD	12	12	w	w	observational reversal	non-reversal errors	22.4	0.67	1
Finger, 2007(Finger et al., 2007)	R L/S	TD	16	19	bw	bw	PAL	omission errors	27.94	0.52	1
Gilger, 2024(Gilger et al., 2024)	R L/S	TD	98	98	w†	bw	Two-step	main effect reward	32.2	0.38	1
Jepma, 2010(Jepma et al., 2010)	R L/S	citalopram 30mg	16	17	bw	bw	restless bandit	inverse temperature	21.55	0.49	1
Luo, 2024(Luo et al., 2024)	R L/S	escitalopram 20mg	32	33	bw	bw	probabilistic reversal	learning rate	26	0.49	1
Michely, 2022(Michely et al., 2022)	R L/S	citalopram 20mg/day	33	33	bw	bw	gambling card	learning rate	24.65	0.39	0
Robinson, 2012(Robinson et al., 2012)	R L/S	TD	21	20	bw	bw	observational reversal	non-reversal errors	27.6	1	1
Seymour, 2012(Seymour et al., 2012)	R L/S	TD	15	15	bw	bw	restless bandit	sensitivity	NA	NA	1
Colwell, 2024(Colwell et al., 2024)	R S	fenfluramine 15mg b.i.d.	26	27	bw	bw	PILT	outcome sensitivity	20.17	0.6	0
Colwell, 2024(Colwell et al., 2024)	P L/S	fenfluramine 15mg b.i.d.	26	27	bw	bw	PILT	learning rate	20.17	0.6	0
Luo, 2024(Luo et al., 2024)	P L/S	escitalopram 20mg	32	33	bw	bw	probabilistic reversal	learning rate	26	0.49	1
Michely, 2022(Michely et al., 2022)	P L/S	citalopram 20mg/day	33	33	bw	bw	gambling card	learning rate	24.65	0.39	0
Seymour, 2012(Seymour et al., 2012)	P L/S	TD	15	15	bw	bw	restless bandit	sensitivity	NA	NA	1
Colwell, 2024(Colwell et al., 2024)	P S	fenfluramine 15mg b.i.d.	26	27	bw	bw	PILT	outcome sensitivity	20.17	0.6	0
Geurts, 2013(Geurts et al., 2013)	P+	TD	45	45	w	w	PIT	appetitive PIT	23.8	NA	1
Guitart-Masip, 2012(Guitart-Masip et al., 2012)	P+	citalopram 24mg oral	16	20	bw	bw	go/nogo	nogo to win	23.3	0.49	1
Guitart-Masip, 2014(Guitart-Masip et al., 2014b)	P+	citalopram 30mg	27	29	bw	bw	go/nogo	nogo to win	NA	NA	1
Hebart, 2015(Hebart and Glascher, 2015)	P+	TD	34	34	bw	bw	PIT	appetative PIT	NA	NA	1
Cools, 2008(Cools et al., 2008)	P-	TD	12	12	w	w	observational reversal	non-reversal errors	22.4	0.67	1
Crockett, 2009(Crockett et al., 2009)	P-	TD	22	22	w	w	go/nogo RT	punishment-induced slowing	NA	NA	1
Crockett, 2012(Crockett et al., 2012)	P-	TD	24	24	w	w	go/nogo RT	punishment-induced slowing	NA	NA	1
Gaber, 2015(Gaber et al., 2015)	P-	TD	24	24	w	w	go/nogo RT	punishment-induced slowing	25.34	NA	1
Geurts, 2013(Geurts et al., 2013)	P-	TD	45	45	w	w	PIT	aversive PIT	23.8	NA	1
Guitart-Masip, 2012(Guitart-Masip et al., 2012)	P-	citalopram 24mg oral	16	20	bw	bw	go/nogo	go to avoid	23.3	0.49	1
Guitart-Masip, 2014(Guitart-Masip et al., 2014b)	P-	citalopram 30mg	27	29	bw	bw	go/nogo	go to avoid	NA	NA	1
Hebart, 2015(Hebart and Glascher, 2015)	P-	TD	34	34	bw	bw	PIT	aversive PIT	NA	NA	1
Helmbold, 2015(Helmbold et al., 2015)	P-	TD	18	18	w	w	go/nogo RT	punishment-induced slowing	24.22	NA	1
Robinson, 2012(Robinson et al., 2012)	P-	TD	21	20	bw	bw	observational reversal	non-reversal errors	27.6	1	1
Crean, 2002(Crean et al., 2002)	RD	TD	20	20	w†	bw	DD	k parameter	21.5	0	1
Schweighofer, 2008(Schweighofer et al., 2008)	RD	TD	20	20	w	w	DD dynamic	discount factor gamma	NA	0	1
Tanaka, 2007(Tanaka et al., 2007)	RD	TD	12	12	w†	bw	multi-step DD	p(large reward choices)	NA	0	1
Worbe, 2014(Worbe et al., 2014)	RD	TD	22	22	bw	bw	DD	k parameter	28.97	0.61	1
Beierholm, 2013(Beierholm et al., 2013)	RV	citalopram 24mg oral	30	30	bw	bw	odd-ball discrimination	average reward rate on RTs	23.92	0.5	1
Cools, 2005(Cools et al., 2005)	RV	TD	10	12	bw	bw	CRRT	RT 90-10	23.55	0	1
Roiser, 2006(Roiser et al., 2006)	RV	TD	30	30	w	w	CRRT	RT 90-10	26.75	0.43	1
Steding, 2023(Steding et al., 2023)	RV	TD	24	24	w	w	physical effort	button press high-low	NA	1	1
Chamberlain, 2006(Chamberlain et al., 2006)	MB/F	citalopram 30mg	20	20	bw	bw	reversal	perseverative errors	25.83	0.5	1
Cools, 2008(Cools et al., 2008)	MB/F	TD	12	12	w	w	observational reversal	switch errors	22.4	0.67	1
Evers, 2004(Evers et al., 2004)	MB/F	TD	15	15	w†	bw	probabilistic reversal	perseverative errors	21.8	0.8	1
Gilger, 2024(Gilger et al., 2024)	MB/F	TD	98	98	w†	bw	Two-step	omega parameter	32.2	0.38	1
Kanen, 2020(Kanen et al., 2020)	MB/F	TD	30	32	bw	bw	probabilistic reversal	perseveration	NA	0.47	1
Langley, 2023(Langley et al., 2023)	MB/F	escitalopram 20mg /day	32	34	bw	bw	Two-step task	Reward × Transition	25.01	65.17	0
Skandali, 2018(Skandali et al., 2018)	MB/F	escitalopram 20mg	31	33	bw	bw	Probabilistic reversal	reversal errors	26	0.49	1
Thirkettle, 2019(Thirkettle et al., 2019)	MB/F	Tryptophan 0.8g	22	22	bw	bw	probabilistic reversal	reversal errors	21.1	0.64	1
Worbe, 2015(Worbe et al., 2015)	MB/F	TD	18	18	bw	bw	3-stage instrumental learning	devalued choices	26.33	0.56	1
Worbe, 2016(Worbe et al., 2016)	MB/F	TD	22	22	bw	bw	Two-step task	omega parameter	29.14	0.52	1
Anderson, 2003(Anderson et al., 2003)	RA	TD	15	13	bw	bw	gambling	mean indifference odds against win	23	0.39	1
Campbell-Meiklejohn, 2011(Campbell-Meiklejohn et al., 2011)	RA	TD	17	17	bw	bw	gambling	p(gamble)	24.18	0.53	1
Faulkner, 2017(Faulkner et al., 2017)	RA	TD	26	26	w	w	gambling	p(gamble)	29.45	0.54	1
Macoveanu, 2014(Macoveanu, 2014)	RA	fluoxetine 20/40mg/day	13	16	bw	bw	gambling	p(risky choice)	NA	0	0
Murphy, 2009(Murphy et al., 2009)	RA	l-tryptophan 3g/day	15	15	bw	bw	gambling	p(gamble)	25.54	0.53	0
Rogers, 2003(Rogers et al., 2003)	RA	TD	18	18	bw	bw	gambling	p(gamble)	23.8	0.5	1

Table S5: **Characteristics of all serotonin studies.** Daggers indicate studies that were originally within-subject studies (in column 'original design') but we could only calculate a between-subjects Cohen's d (indicated in column 'design'). In drug regimen, 1 indicates a single drug administration and 0 indicates multiple drug administrations. Abbreviations: R L/S: reward learning/sensitivity; R S: reward sensitivity; P L/S: punishment learning/sensitivity; P S: punishment sensitivity; P+: appetitive Pavlovian; P-: aversive Pavlovian; RD: reward discounting; RV: reward vigor: MB/F: model-based learning/flexibility; RA: risk attitude; w: within-subject studies; bw: between-subject studies; PST: probabilistic selection task; PILT: probabilistic instrumental learning task; WM: working memory; PAL: passive avoidance learning; PIT: Pavlovian instrumental task; DD: delay discounting; MID: monetary incentive delay.