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Research paper

Lifetime history of major depressive disorder is associated with decreased reward learning: Evidence from a novel online version of the probabilistic reward task

Shiba M. Esfand [a,1], Kaylee E. Null [a,1], Jessica M. Duda [a,2], Josh de Leeuw [b], Diego A. Pizzagalli [a,c,d,*]

[a] Center for Depression, Anxiety and Stress Research, McLean Hospital, Belmont, MA, USA
[b] Cognitive Science Department, Vassar College, USA
[c] Harvard Medical School, Boston, MA, USA
[d] McLean Imaging Center, McLean Hospital, Belmont, MA, USA

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ABSTRACT

Background: The Probabilistic Reward Task (PRT) is a signal detection task that assesses reward learning. In laboratory versions of the task, individuals with current or past major depressive disorder (MDD) were characterized by reduced response bias towards a more frequently rewarded stimuli, compared to controls. Our main goal was to develop and validate a novel online version of the PRT, and, in exploratory analyses, evaluate whether lifetime history of depression was associated with blunted reward learning.

Methods: 429 participants recruited via CloudResearch completed questionnaires assessing psychiatric history and an online PRT featuring visually appealing stimuli. 108 participants reported either current or past diagnosis of MDD (lifetime MDD group), and were compared to 321 without lifetime MDD.

Results: Participants showed overall increase in response bias, validating the online PRT. Females with lifetime MDD ($N = 43$), compared to females without prior history of MDD ($N = 173$), exhibited blunted response bias towards the more frequently rewarded stimulus (i.e., reduced reward learning).

Limitations: Participants did not undergo a structured clinical interview, thus we cannot confirm whether they met full diagnostic criteria for depression.

Conclusions: The online PRT yielded similar psychometric properties as laboratory versions of the task. In exploratory analyses, females with lifetime MDD showed a lower propensity to modulate behavior as a function of rewards, which might contribute to heightened vulnerability for developing MDD in females. Future studies should consider social, cultural, and neurobiological factors contributing to sex differences in reward responsiveness and how factors may relate to disease prognosis and treatment outcomes.

1. Introduction

Anhedonia is a core symptom of major depressive disorder (MDD) and refers to the loss of interest or pleasure in previously enjoyed activities. This symptom has been related to poorer prognosis and decreased response to psychological and pharmacological treatments (Sandman and Craske, 2022; Klein et al., 2022; Auerbach et al., 2022). Moreover, anhedonia has been associated with blunted response to rewards (Boyle et al., 2023; Pizzagalli, 2014). The Probabilistic Reward Task (PRT; (Pizzagalli et al., 2005) is a well-validated laboratory-based paradigm that assesses reward responsiveness and participants' ability to learn from rewards, and is one of the recommended tasks to probe the subdomain of "reward learning" in the NIMH's Research Domain Criteria initiative (https://www.nimh.nih.gov/about/advisory-boards-and-groups/namhc/reports/behavioral-assessment-methods-for-rdoc-constructs). During the task participants are instructed to rapidly identify stimuli that are difficult to differentiate; unbeknownst to them, correct identification of one stimulus type (i.e., the 'rich' stimulus) is rewarded more

* Corresponding author at: McLean Hospital, deMarneffe Building, 115 Mill St., Belmont, MA 02478, USA.
E-mail address: dap@mclean.harvard.edu (D.A. Pizzagalli).
[1] Current affiliation: Department of Psychology, University of California Los Angeles, Los Angeles, CA, USA.
[2] Current affiliation: Department of Psychology, Yale University, New Haven, CT, USA.

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frequently than the other. Over time, participants without depression or anhedonia develop a strong response bias towards the more frequently rewarded ('rich') stimulus, whereas individuals with depression display much smaller response bias (Pizzagalli et al., 2005; Pizzagalli et al., 2008b). Within the context of the PRT, response bias serves as a measure of reward responsiveness.

1.1. Primary aim

Following the COVID-19 pandemic, the demand and need for conducting clinical research visits remotely has dramatically increased (Bharucha et al., 2021). Moreover, remote research studies can reduce prominent barriers to participation including financial strain and travel (Peters et al., 2023). Although the PRT has been widely implemented in laboratory settings, administration of a fully online version of the PRT has yet to be assessed. In the current study, we developed a novel online version of the PRT featuring more visually complex (and appealing) stimuli (Fig. 1), and deployed it via CloudResearch – a web-based platform which utilizes Amazon Mechanical Turk, in a relatively large community sample. Extensive piloting was conducted to ensure that this online version of the PRT was psychometrically matched to the laboratory version (e.g., with respect to overall accuracy). Development and validation of an online PRT allows researchers to recruit a more heterogenous sample and promote a dimensional framework when probing reward learning. In particular, individuals with psychopathology, non-treatment seeking populations, those who wish maintain anonymity regarding their experiences, or those who face physical barriers to participation (i.e., transportation) may be more inclined to complete an online study where these concerns are no longer prevalent.

1.2. Exploratory aims

Relative to controls, individuals with a current diagnosis of MDD display blunted reward learning, evidenced by reduced response bias towards the rich stimulus (Pizzagalli et al., 2008b; Vrieze et al., 2013). Further, individuals with remitted MDD (rMDD) have also shown decreased response bias relative to controls (Pechtel et al., 2013), suggesting that blunted reward learning might be a trait-level marker of depression (but see Audrain-McGovern et al., 2014). Moreover, females, compared to males, have been found to be at heightened risk for developing MDD, with studies reporting MDD diagnosis being twice as prevalent in females (Hyde and Mezulis, 2020). Previous research has not yet found sex differences in reward learning during the PRT (Liu et al., 2011; Pechtel et al., 2013; Pizzagalli et al., 2008b), though Molokotos and colleagues found that in response to smoking cues, PRT response bias was positively correlated with left caudate activity for male smokers only (Molokotos et al., 2020).

With respect to reward sensitivity, males have been found to display heightened sensitivity and neural activation to rewards on a monetary incentive delay task (MID; Dhingra et al., 2021; Warthen et al., 2020). However, a separate study utilizing a modified MID did not find any sex differences in behavioral or neural sensitivity to both reward and punishment stimuli (Warthen et al., 2020). When completing the balloon analog risk task (BART) under stressful conditions, males displayed quicker responses and were more likely to cash in and collect rewards than females (Stanton et al., 2019). This mixed literature highlights a

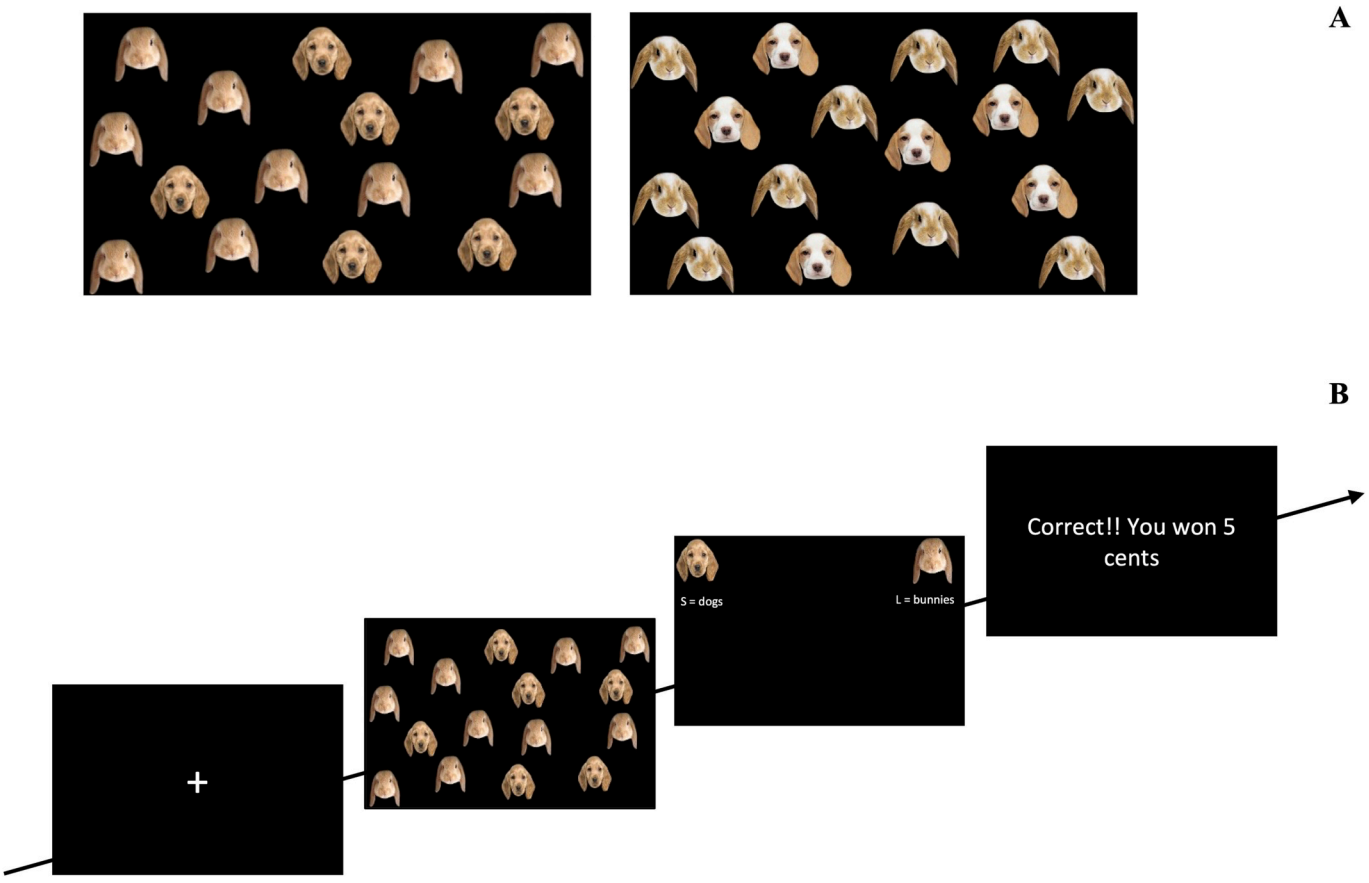

Fig. 1. Task stimuli and schematic.
Note **(A)** Example stimuli of Version 1 (left) and Version 2 (right) used in the task. **(B)** Schematic of task. For each trial participants chose whether more dogs or bunnies were presented by pressing either the 'S' or 'L' key. Reward reinforcement ratio for stimuli (i.e., bunny/dog) and key assignments were counterbalanced across participants.

need for further research to parse out potential sex differences in reward learning within the context of MDD.

Participants in our study reported on current and previous psychiatric diagnoses, current psychiatric medication use, and completed questionnaires related to current mood, anhedonia, and positive affect. We conducted exploratory analyses investigating the impact of self-reported lifetime depression, defined as either having a current or past diagnosis of MDD, on reward learning. Based on prior findings (Liu et al., 2011; Morris et al., 2015; Pechtel et al., 2013; Vrieze et al., 2013), we hypothesized that participants who reported lifetime MDD diagnosis would display blunted reward learning compared to those who did not report lifetime MDD. Given the sample size, an additional exploratory aim was to evaluate whether sex differences in reward learning would be present within the context of lifetime history of MDD.

2. Methods

2.1. Participants

Participants were recruited through CloudResearch (cloudresearch.com; Litman et al., 2017), an add-on to Amazon's Mechanical Turk (MTurk; mturk.com), which allows for additional screening procedures to ensure collection of high-quality and reliable data. Within our study we required all participants to have a minimum MTurk approval rate of 95 %, which means that at least 95 % of previously completed tasks by participants were deemed to be of acceptable quality by experimenters. Participants were also required to have completed a minimum of 100 MTurk studies prior to enrollment in our study. Meta-analyses of MTurk studies have found demographic characteristics of MTurk workers to be closely aligned with the general U.S. population (Burnham et al., 2018).

Task procedures were conducted using REDCap (Harris et al., 2009, 2019) and cognition.run (cognition.run). Participants were geographically restricted to the U.S. and at least 18 years old. Previous research studies on online platforms have utilized these qualifications and yielded good quality data (Douglas et al., 2023). Additionally, participants who completed a prior version of this task, such as during piloting, were excluded. A total of 605 participants were recruited with 537 completing the PRT across two waves of recruitment, resulting in a low (12 %) attrition rate relative to what is seen in MTurk studies (30–50 %; Aguinis et al., 2021). Only data that passed quality checks (see *Supplement* for criteria) were included, resulting in a final sample of 429.

In addition to demographic information, participants reported current and past DSM-5 diagnosis of MDD, any lifetime diagnosis of other psychiatric conditions, and any currently prescribed psychotropic medication. Sex was assessed by asking participants to report sex assigned at birth. Participants were also asked to report their gender identity (see Table 1). For current and past MDD diagnosis participants responded yes or no to the following: *'Do you have a current diagnosis of major depressive disorder?'*, *'Have you ever been diagnosed with major depressive disorder in the past?'*. The lifetime MDD group comprised of 108 participants (43 females) who reported either current ($N = 57$) or past ($N = 51$) diagnosis of MDD, including one participant who reported diagnosis of persistent depressive disorder. 321 participants (173 females) did not report any lifetime diagnosis of MDD, though 32.1 % did report other lifetime psychiatric diagnoses (Table 1). Groups did not differ with respect to age, education, race, or ethnicity, but did differ in terms of income level and psychiatric comorbidities (Table 1). Participants provided electronic informed consent and all procedures were in accordance with Mass General Brigham Human Research committee.

2.2. Task and procedures

Participants first completed the Beck Depression Inventory-II (BDI-II; (Beck et al., 1996)), the Snaith-Hamilton Pleasure Scale (SHAPS; (Snaith et al., 1995)), and the 21-item version of the Positive Valence Systems Scale (PVSS-21; (Khazanov et al., 2020)). The BDI-II is a widely used 21-

Table 1
Demographics and clinical variables.

	No MDD history ($N = 321$)	Lifetime MDD ($N = 108$)	Statistic	*p*-value
Current age (years)				
Mean (*SD*)	39.7 (11.1)	37.8 (10.4)	–	0.108
Median [Min, Max]	37.0 [20.0, 77.0]	35.0 [22.0, 73.0]		
Sex assigned at birth				
Male	147 (45.8 %)	64 (59.3 %)	–	0.014
Female	173 (53.9 %)	43 (39.8 %)		
Missing	1 (0.3 %)	1 (0.9 %)		
Gender				
Cisgender Man	168 (52.3 %)	38 (35.2 %)	–	<0.001
Cisgender Woman	144 (44.9 %)	63 (58.3 %)		
Non-Binary/ Genderqueer/Gender Fluid	3 (0.9 %)	2 (1.9 %)		
Prefer Not to Say	3 (0.9 %)	0 (0 %)		
Prefer to Self-Describe	2 (0.6 %)	0 (0 %)		
Transgender Man/ Trans Masculine	0 (0 %)	1 (0.9 %)		
Transgender Woman/ Trans Feminine	0 (0 %)	4 (3.7 %)		
Missing	1 (0.3 %)	0 (0 %)		
Education (years)				
Mean (SD)	14.9 (2.03)	15.3 (2.42)	–	0.506
Median [Min, Max]	16.0 [9.00, 20.0]	16.0 [12.0, 25.0]		
Missing	40 (12.5 %)	6 (5.6 %)		
Income				
Less than $10,000	11 (3.4 %)	8 (7.4 %)		
$10,000–$25,000	34 (10.6 %)	21 (19.4 %)	–	0.038
$25,000–$50,000	105 (32.7 %)	28 (25.9 %)		
$50,000–$75,000	84 (26.2 %)	19 (17.6 %)		
$75,000–$100,000	42 (13.1 %)	15 (13.9 %)		
More than $100,000	43 (13.4 %)	17 (15.7 %)		
Missing	2 (0.6 %)	0 (0 %)		
Race				
American Indian or Alaska Native	1 (0.3 %)	2 (1.9 %)	–	0.413
Asian	16 (5.0 %)	5 (4.6 %)		
Black or African American	37 (11.5 %)	8 (7.4 %)		
More Than One Race	10 (3.1 %)	6 (5.6 %)		
Native Hawaiian or Pacific Islander	2 (0.6 %)	0 (0 %)		
Prefer to Self-Describe	4 (1.2 %)	1 (0.9 %)		
White	246 (76.6 %)	86 (79.6 %)		
Missing	5 (1.6 %)	0 (0 %)		
Ethnicity				
Hispanic or Latinx	26 (8.1 %)	8 (7.4 %)	–	1
Not Hispanic or Latinx	286 (89.1 %)	96 (88.9 %)		
Missing	9 (2.8 %)	4 (3.7 %)		
Current medication				
Anticonvulsant	1 (0.3 %)	0 (0 %)	–	<0.001
Antipsychotics	1 (0.3 %)	1 (0.9 %)		
Benzodiazepines	2 (0.6 %)	4 (3.7 %)		
Beta Blockers	4 (1.2 %)	1 (0.9 %)		
Buspirone	3 (0.9 %)	2 (1.9 %)		
More than one type of medication	8 (2.5 %)	26 (24 %)		
None	285 (88.8 %)	54 (50 %)		
SNRIs	2 (0.6 %)	3 (2.8 %)		
SSRIs	8 (2.5 %)	17 (15.7 %)		
Stimulants	6 (1.9 %)	0 (0 %)		
Tricyclics	0 (0 %)	1 (0.9 %)		

(*continued on next page*)

Table 1 (*continued*)

	No MDD history (*N* = 321)	Lifetime MDD (*N* = 108)	Statistic	*p*-value
Additional psychiatric diagnosis (MDD not included)				
Anorexia Nervosa	1 (0.3 %)	1 (0.9 %)	–	<0.001
Bipolar Disorder	2 (0.6 %)	1 (0.9 %)		
GAD	26 (8.1 %)	10 (9.3 %)		
Multiple dx (MDD not included)	41 (12.8 %)	74 (68.5 %)		
None	218 (67.9 %)	5 (4.6 %)		
OCD	3 (0.9 %)	0 (0 %)		
Other	4 (1.2 %)	1 (0.9 %)		
PTSD	3 (0.9 %)	1 (0.9 %)		
SAD	12 (3.7 %)	5 (4.6 %)		
SUD	3 (0.9 %)	0 (0 %)		
Binge Eating Disorder	0 (0 %)	1 (0.9 %)		
PDD	0 (0 %)	7 (6.5 %)		
Specific Phobia	0 (0 %)	1 (0.9 %)		
Missing	8 (2.5 %)	1 (0.9 %)		
BDI-II total				
Mean (*SD*)	9.94 (10.9)	20.5 (13.3)	t(384) = −7.67	<0.001
Median [Min, Max]	5.75 [0, 49.0]	19.5 [0, 54.0]		
Missing	33 (10.3 %)	10 (9.3 %)		
BDI-II anhedonic subscore				
Mean (*SD*)	2.13 (2.63)	4.50 (3.06)	t(417) = −7.70	<0.001
Median [Min, Max]	1.00 [0, 12.0]	5.00 [0, 10.0]		
Missing	8 (2.5 %)	2 (1.9 %)		
SHAPS total				
Mean (*SD*)	24.6 (6.14)	29.4 (6.84)	t(400) = −6.50	<0.001
Median [Min, Max]	25.0 [14.0, 47.0]	29.0 [15.0, 47.0]		
Missing	20 (6.2 %)	7 (6.5 %)		
PVSS-21 total				
Mean (*SD*)	137 (27.4)	123 (32.3)	t(388) = 4.24	<0.001
Median [Min, Max]	139 [65.0, 189]	125 [55.0, 189]		
Missing	28 (8.7 %)	11 (10.2 %)		

Note. MDD, major depressive disorder, PDD, persistent depressive disorder, GAD, generalized anxiety disorder, OCD, obsessive compulsive disorder, PTSD, post-traumatic stress disorder, SAD, social anxiety disorder, SUD, substance use disorder. The table above depicts mean and standard deviation (SD) of self-reported demographics and total scores on various clinical measures by group. Education is reported in years, with 12 years being equivalent to completion of a high school diploma.

item scale to assess severity of depressive symptoms. We administered a modified version of the BDI-II, which did not include the suicidality item; to account for the missing item, the individual scores for each item were averaged and then added to the total score (Gale and Hawley, 2001). The SHAPS is among the most widely used self-report scales of hedonic capacity (see *Supplement* for BDI-II and SHAPS cutoffs; Franken et al., 2007). Finally, the PVSS-21 assesses several reward-related subdomains, including desire for rewards, expectations of receiving rewards, willingness to expend effort to obtain rewards, anticipation of future rewards, and immediate and delayed response to rewards. The short version of the PVSS includes 21 items (PVSS-21). For the current online sample, the internal reliability (Cronbach's alpha) was excellent for all scales (BDI-II: $\alpha = 0.95$; SHAPS: $\alpha = 0.90$; PVSS-21 total score: $\alpha = 0.95$). Results correlating clinical measures and PRT variables can be found in the *Supplement*.

After surveys, participants completed the online PRT, developed using jsPsych version 6 (de Leeuw et al., 2023); task code and stimuli are available upon request. Participants were instructed to sit 50 cm from the screen and completed a series of practice trials prior to engaging in the task. During the practice participants were presented with various difficult-to-differentiate stimuli consisting of images of dogs and bunnies in ratios of 6:10 (Fig. 1A) and were instructed to identify whether more dogs or bunnies were present by pressing the correct key ('S' or 'L'; Fig. 1B). Note that laboratory versions of the PRT use black-and-white cartoon faces, whereas we opted to use colorful images of animals with the idea that this would increase engagement during the online task. Participants were informed that correct identification on some trials would result in monetary reward of 5 cents, with the goal of collecting as many rewards as possible; they were also instructed that not all correct responses would receive a reward. Correct identification of one stimulus type (e.g., more dogs) was rewarded more frequently (i.e., "rich stimulus") than the other (i.e., "lean stimulus"). Specifically, rewards were administered in a ratio of 4:1 (32 rich vs. 8 lean rewards per block), which differed from original versions of the task which implemented a 3:1 ratio (Pizzagalli et al., 2005; Pizzagalli et al., 2008a; Pizzagalli et al., 2008b). This reward ratio was chosen as cross-species administration of the task indicated that a more asymmetric reward ratio resulted in greater response bias towards rich stimuli (Kangas et al., 2020). Further as this task was administered online, we chose to utilize a 4:1 reward ratio to ensure a response bias would be elicited.

The online PRT consisted of 3 blocks of 100 trials, with a 30 s break in-between blocks. Each trial began with a fixation cross (500 ms) followed by stimulus image (Fig. 1B). Two versions of the task were administered with differing dog/bunny stimuli (see Fig. 1A). We utilized different versions of the task in order to assess whether differences in stimuli impacted results. If no differences in discriminability between the two versions emerged, then they were deemed comparable with respect to task difficulty and could be used for future studies involving repeated administrations. Stimulus exposure for the first round of data collection was chosen after pilot testing to ensure psychometric properties comparable to previously validated versions of the task (Pizzagalli et al., 2005; Pizzagalli et al., 2008a; Pizzagalli et al., 2008b). To further improve the psychometric properties of the task, we later increased stimulus duration in a second round of data collection. An initial group of participants completed either Version 1 or Version 2 the task where stimuli were presented for 400 ms ($N = 233$) or 450 ms ($N = 34$), respectively. A second group of participants were later recruited and completed either Version 1 ($N = 83$) or Version 2 of the task ($N = 81$) at an increased stimulus duration (425 ms and 500 ms, respectively).

2.3. Data reduction

Task performance was analyzed with respect to response bias, discriminability, accuracy (% correct), and reaction time (RT). Response bias – the main variable of interest – provides an index of participants' implicit preference towards the more frequently rewarded (i.e., 'rich') stimuli by considering the number of correct trials for the rich stimulus compared to the lean stimulus. For example, a participant with a high response bias would likely have achieved greater accuracy on rich trials compared to lean trials. Discriminability – an important control variable – serves as an index of task difficulty as it is primarily influenced by ability to differentiate between stimuli, see *Supplement* for response bias and discriminability computations and additional quality assessment cutoffs.

2.4. Statistical analyses

2.4.1. Online PRT validation

All analyses were conducted in IBM SPSS Statistics Version 28 (IBM Corp, 2020). We first assessed whether response bias, discriminability, RT, and accuracy differed between task versions; accordingly, ANOVAs with *Task Version* (Version 1: 400 ms, Version 1: 425 ms, Version 2: 450 ms, Version 2: 500 ms) × *Block* (1, 2, 3) were conducted for each

variable. For accuracy and reaction time, the ANOVA included an additional factor of *Stimulus Type* (Rich, Lean). No significant main effect of *Task Version* on response bias, discriminability, or any interactions were found (see *Supplement,* all $F < 2.38$, and $ps > 0.07$); thus, data from all versions of the task were aggregated. Significant main effects of task version on reaction time and accuracy were found (see *Supplement* for more information). Validation of the online PRT was assessed based on whether the following psychometric properties, seen in laboratory based versions of the task were found (see Table 2 for summary): 1) a significant increase in response bias across blocks, 2) significantly greater accuracy for rich (vs lean) stimuli, and 3) significantly faster reaction time when identifying rich (vs lean) stimuli. Specific tests used to assess these properties are detailed more below.

2.4.2. Sex and lifetime MDD analyses

Independent *t*-tests and Fisher's exact tests were conducted to assess possible differences in clinical measures and demographic variables between individuals with no MDD history and participants with lifetime MDD (Table 1). In the context of this paper any references to 'sex' are strictly referring to sex assigned at birth and not gender identity; information on gender identity can also be found in Table 1. Fisher's exact tests revealed significant association between sex and lifetime MDD (no MDD history$_{females}$ = 53.9 %, lifetime MDD$_{females}$ = 39.8 %, $p = 0.014$), and a significant association between gender and lifetime MDD (no MDD history$_{cisgender\ women}$ = 44.9 %, lifetime MDD$_{cisgender\ women}$ = 58.3 %, $p < 0.001$). For analyses, we chose to focus on sex differences, over gender, due to the limited variability in reported gender identities (i.e., non-binary and transgender identities) within our sample. Additionally, groups differed significantly based on income level (Table 1). Thus, separate ANCOVAs with *Sex* (female, male) and *Group* (no MDD history, lifetime MDD) as between factors, *Block* (1, 2, 3) as within factor, and *Income* entered as covariate were conducted to assess possible differences for response bias and discriminability. For accuracy and reaction time, the ANCOVA included an additional factor of *Stimulus Type* (Rich, Lean). Moreover, for accuracy, and reaction time, *Task Version* was entered as an additional covariate. Greenhouse-Geisser corrections were used when relevant, and post-hoc Bonferroni-corrected simple tests were performed in cases of significant ANCOVA findings.

Participants who did not report sex or lifetime MDD diagnosis were removed from the analyses. Independent *t*-test and Fisher's exact tests were run to evaluate whether participants with vs. without missing data differed in any demographic or clinical variables. No differences were found with respect to gender, race, ethnicity, income, BDI-II, and SHAPS (all $ps > 0.053$; see *Supplement* for details).

3. Results

3.1. Response bias

A *Sex* × *Group* × *Block* ANCOVA (covariate: Income) predicting response bias revealed a significant main effect of *Block* (Fig. 2A; $F(2, 804) = 6.35$, $p = 0.002$, partial $\eta^2 = 0.016$), with Bonferroni-corrected simple tests revealing greater response bias in Blocks 2 (95 % CI [0.164, 0.207], $p < 0.001$) and 3 (95 % CI [0.209,0.250] $p < 0.001$) compared to Block 1 (95 % CI [0.087,0.121], $p < 0.001$), and greater response bias in Block 3 than Block 2. These findings indicate that the task successfully elicited development of response bias.

Moreover, a significant main effect of *Sex* (Fig. 2B; $F(1, 402) = 4.12$, $p = 0.043$, partial $\eta^2 = 0.010$), driven by males (95 % CI [0.166, 0.212]) displaying greater overall response bias than females (95 % CI [0.138, 0.177]) was found. In an exploratory analysis, a significant *Sex* × *Group* interaction emerged (Fig. 2B; F(1, 402) = 3.91, $p = 0.049$, partial $\eta^2 = 0.010$). Post-hoc tests revealed that among female participants, a lifetime history of MDD (95 % CI [0.105, 0.171]) was associated with a significantly lower response bias compared with no depression history (95 % CI [0.155, 0.199] (Fig. 2B; $p = 0.0497$). Among those with lifetime MDD, females displayed a lower response bias than males (95 % CI [0.158, 0.241]; $p = 0.043$). Finally, there was no main effect of *Group* on response bias (Fig. 2B; $F(1, 402) = 0.35$, $p = 0.556$, partial eta$^2 = 0.001$, 95 % CI$_{Controls}$ [0.163, 0.192], 95 % CI$_{LifetimeMDD}$ [0.142,0.195]), and there was no significant effect of the covariate *Income* on response bias $F(1,402) = 0.37$, $p = 0.546$, partial eta$^2 = 0.001$).

3.2. Discriminability

No significant effects of *Block* ($F(2,740.99) = 0.83$, $p = 0.429$, partial $\eta^2 = 0.002$, 95 % CI$_{Block1}$ [0.312,0.373], 95 % CI$_{Block2}$ [0.322,0.394], 95 % CI$_{Block3}$ [0.362,0.440]), *Sex* ($F(2,397) = 0.26$, $p = 0.612$, partial $\eta^2 = 0.001$, 95 % CI$_{Males}$ [0.309,0.408], 95 % CI$_{Females}$ [0.333,0.418]), or *Group* ($F(1,397) = 0.17$, $p = 0.677$, partial $\eta^2 = 0.000$, 95 % CI$_{Controls}$

Table 2
Findings from laboratory PRT studies.

Study	Response bias	Accuracy	Reaction Time	Discriminability
Pizzagalli et al., 2005	Increase in response bias between Block 1 and Block 2. No changes in response bias between Block 2 and 3	Greater accuracy for rich (vs lean) stimuli. Accuracy for rich stimuli increased between Blocks 1 and 2, and 1 and 3. No changes in lean accuracy between blocks.	Shorter reaction time to rich (vs lean) stimuli in all three blocks. Reduced overall reaction time from Blocks 1 to 2 and 1 to 3.	No significant change in discriminability between blocks.
Bogdan and Pizzagalli, 2006	Main effect of Block with increase in response bias between Blocks 1 and 2 and Blocks 1 and 3.	Rich accuracy was greater in no-stress (vs when exposed to stress) condition. Overall accuracy was greater for rich (vs lean) stimuli.	Not reported	Greater discriminability in Block 2 compared to Block 1. No differences between Blocks 1 and 3 or 2 and 3.
Pizzagalli et al., 2008b	No main effect of Block on response bias. MDD subjects showed lower overall response bias scores.	Greater overall accuracy for rich (vs lean) stimuli. MDDs (compared to controls) showed lower accuracy for rich stimuli.	Shorter reaction time to rich (vs lean) stimuli in all three blocks. Reduced overall reaction time from Blocks 1 to 2 and 1 to 3.	No significant change in discriminability between blocks.
Pechtel et al., *2013*	Increase in response Bias between Block 1 and Block 2, and no change in response bias between Block 2 and 3 for controls. No changes in response bias for rMDDs across blocks. Reduced Block 2 response bias in rMDDs compared to controls.	Greater overall accuracy for rich (vs lean) stimuli. Controls showed greater rich accuracy than rMDDs. No group differences for lean accuracy.	Shorter overall reaction time to rich (vs lean) stimuli.	Controls displayed greater discriminability than rMDDs in Block 1 and 2, but not Block 3.
Audrain-McGovern et al., 2014	No effect of depression group (i.e., history of depression vs no history) or smoking status on response bias.	Not reported		

Note. MDD, major depressive disorder, rMDD, remitted major depressive disorder. Pizzagalli et al., 2005 and Bogdan and Pizzagalli, 2006 tested PRT performance among healthy control subjects only. Pizzagalli et al., 2008b compared MDD and healthy control participants, Pechtel et al., 2013 compared rMDD and healthy controls, and Audrain-McGovern compared smokers with history of depression to smokers without such history.

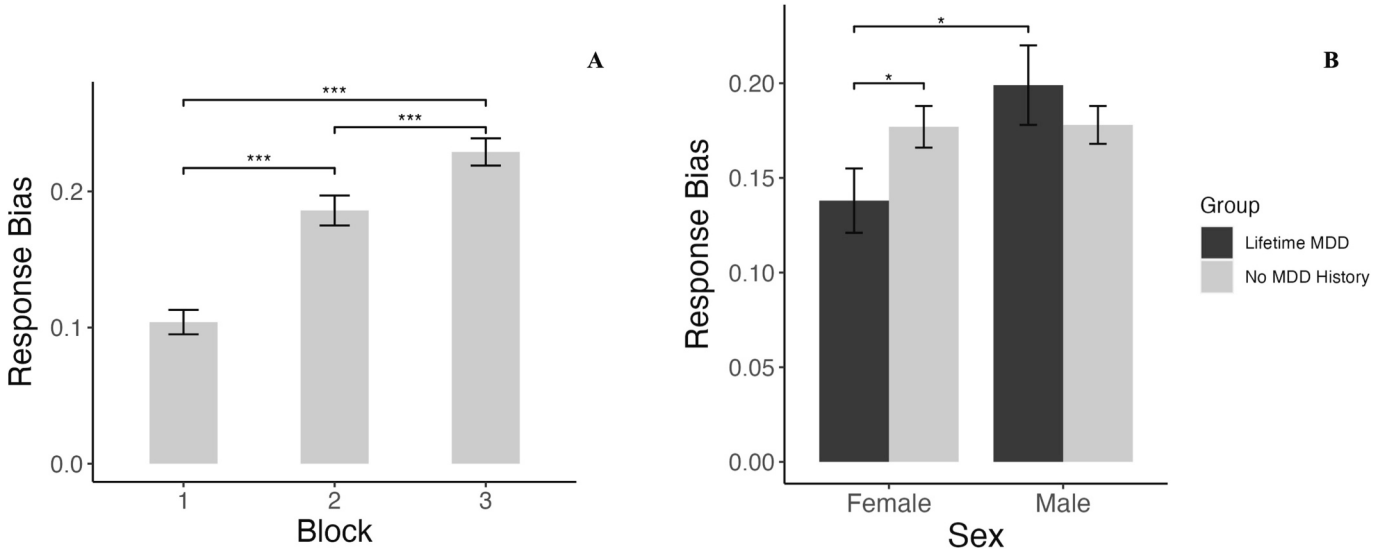

Fig. 2. Response bias by block and group.
Note. **(A)** Response bias by block. Across all participants an increase in response bias towards the more frequently rewarded stimuli emerged, which confirms the online PRT elicited the desired performance outcome. **(B)** Overall response bias, averaged across three blocks, for participants with lifetime MDD and those with no MDD history and by sex. Females with history of MDD were characterized by reduced response bias compared to females without such history and males with MDD.

[0.328,0.392], 95 % $CI_{LifetimeMDD}$ [0.317,0.431]) (see Supplemental Fig. 1), nor *Sex* × *Group* $F(2,397) = 0.06$, $p = 0.800$, partial $\eta^2 = 0.000$ interaction emerged. Moreover, the covariate of *Income* had no significant effect on discriminability ($F(1,397) = 0.02$, $p = 0.967$, partial $\eta^2 = 0.001$). Thus, response bias findings were not confounded by differences in task difficulty.

3.3. Accuracy

The *Sex* × *Group* × *Block* × *Stimulus Type* ANCOVA (controlling for *Income* and *Task Version*) predicting accuracy revealed that the effect of the covariate *Task Version* was significant ($F(1, 419) = 6.01$, $p = 0.015$, partial $eta^2 = 0.014$). Additionally, a significant interaction of *Block* × *Stimulus Type* ($F(2,838) = 3.32$, $p = 0.037$, partial $\eta^2 = 0.008$) was found. Post-hoc tests revealed greater accuracy for rich (vs lean) stimuli in all three blocks (95 % $CI_{RichBlock1}$ [0.718,0.748], 95 % $CI_{RichBlock2}$ [0.754,0.784], 95 % $CI_{RichBlock3}$ [0.783,0.812]). Accuracy for rich stimuli increased from Block 1 to Block 2 ($p < 0.001$), Block 1 to Block 3 ($p < 0.001$), and Block 2 to Block 3 ($p < 0.001$). Conversely, accuracy for lean stimuli decreased between Block 1 (95 % $CI_{LeanBlock1}$ [0.617,0.654]) to Block 2 (95 % $CI_{LeanBlock2}$ [0.576,0.621]; $p < 0.001$) and Block 1 to 3 (95 % $CI_{LeanBlock3}$ [0.571,0.616]; $p < 0.001$) no difference in lean accuracy was found between Block 2 and 3 ($p = 0.10$). These accuracy patterns indicate that the task elicited the intended effects (Supplemental Fig. 2). Finally, in an exploratory analysis, a significant interaction between *Sex*, *Group*, and *Stimulus Type* emerged ($F(1,419) = 4.57$, $p = 0.033$, partial $\eta^2 = 0.011$; Fig. 3).

To unpack the *Sex* × *Group* × *Stimulus Type* interaction, a *Sex* × *Stimulus Type* ANCOVA was run separately for participants with no MDD history and those with lifetime MDD. Among participants with no MDD history, there was no main effect of *Sex* ($F(1,314) = 0.01$, $p = 0.938$, partial $\eta^2 = 0.000$, 95 % CI_{Males} [0.665,0.704], 95 % $CI_{Females}$ [0.664,0.707]) or *Sex* × *Stimulus Type* interaction ($F(1,314) = 0.22$, $p = 0.643$, partial $\eta^2 = 0.001$, 95 % $CI_{FemalesRich}$ [0.743,0.781], 95 % $CI_{FemalesLean}$ [0.581,0.637], 95 % $CI_{MalesRich}$ [0.747,0.782], 95 % $CI_{MalesLean}$ [0.578,0.630]) predicting accuracy; however, there was a main effect of the covariate *Task Version* ($F(1, 314) = 4.10$, $p = 0.044$, partial $\eta^2 = 0.013$) and *Stimulus Type* ($F(1, 314) = 28.90$, $p < 0.001$, partial $\eta^2 = 0.084$, 95 % CI_{Rich} [0.750,0.776], 95 % CI_{Lean} [0.587,0.626]). Post-hoc tests for *Stimulus Type* revealed greater accuracy for identifying rich (vs lean) stimuli ($p < 0.001$).

For participants with lifetime MDD, a significant *Sex* × *Stimulus Type* interaction emerged ($F(1,103) = 7.24$, $p = 0.008$, partial $\eta^2 = 0.066$); however, post-hoc tests comparing rich (95 % $CI_{RichMales}$ [0.755,0.826], 95 % $CI_{RichFemales}$ [0.720,0.778], $p = 0.077$) and lean accuracy (95 % $CI_{LeanMales}$ [0.541,0.652], 95 % $CI_{LeanFemales}$ [0.582,0.672], $p = 0.398$) for males and females were not significant (Fig. 3). A main effect of *Stimulus Type* was again found ($F(1,103) = 16.80$, $p < 0.001$, partial $\eta^2 = 0.14$) with post-hoc tests showing greater accuracy for rich (vs lean) stimuli (95 % CI_{Rich} [0.747,0.793], 95 % CI_{Lean} [0.576,0.647], $p < 0.001$). Neither the covariate of *Income* ($F(1,103) = 0.39$, $p = 0.553$, partial $\eta^2 = 0.004$) nor *Task Version* ($F(1,103) = 2.02$, $p = 0.158$, partial $\eta^2 = 0.019$) displayed a significant effect on accuracy.

3.4. Reaction time

An analogous *Sex* × *Group* × *Block* × *Stimulus Type* ANCOVA (controlling for Income and Task Version) predicting reaction time revealed significant main effects of *Block* ($F(1.57, 646.68) = 14.55$, $p < 0.001$, partial $eta^2 = 0.034$) and *Stimulus Type* ($F(1,411) = 22.43$, $p < 0.001$, partial $\eta^2 = 0.052$). Post hoc tests revealed greater reaction time in Block 1 compared to Block 2 ($p < 0.001$, 95 % CI_{Block1} [734.094,784.899], 95 % CI_{Block2} [611.425,656.597]) and Block 3 ($p < 0.001$, 95 % CI_{Block3}: [584.019,626.149]), and greater reaction time in Block 2 compared to Block 3 ($p < 0.001$) (Supplemental Fig. 3 A). Further, post hoc tests showed participants displayed slower reaction time to lean (95 % CI_{Lean}: [657.420, 702.014]), compared to rich (95 % CI_{Rich}: [631.718, 673.637]), stimuli ($p < 0.001$) (Supplemental Fig. 3B). No main effects of *Group* ($F(1,411) = 0.69$, $p = 0.407$, partial $\eta^2 = 0.002$, 95 % $CI_{Controls}$: [635.798, 678.401], 95 % $CI_{LifetimeMDD}$: [637.841, 712.749]) or *Sex* ($F(1,411) = 1.69$, $p = 0.194$, partial $\eta^2 = 0.004$, 95 % CI_{Males}: [647.960, 712.972], $CI_{Females}$: [623.626, 680.231]) emerged, nor effects of either covariate *Income* ($F(1,411) = 0.14$, $p = 0.705$, partial $\eta^2 = 0.000$) and *Task Version* ($F(1,411) = 0.16$, $p = 0.688$, partial $\eta^2 = 0.000$).

3.5. Follow-up analyses

ANCOVAs detailed above were rerun excluding any controls that reported either current use of psychiatric medication or additional psychiatric diagnoses. In these control analyses the lifetime MDD group

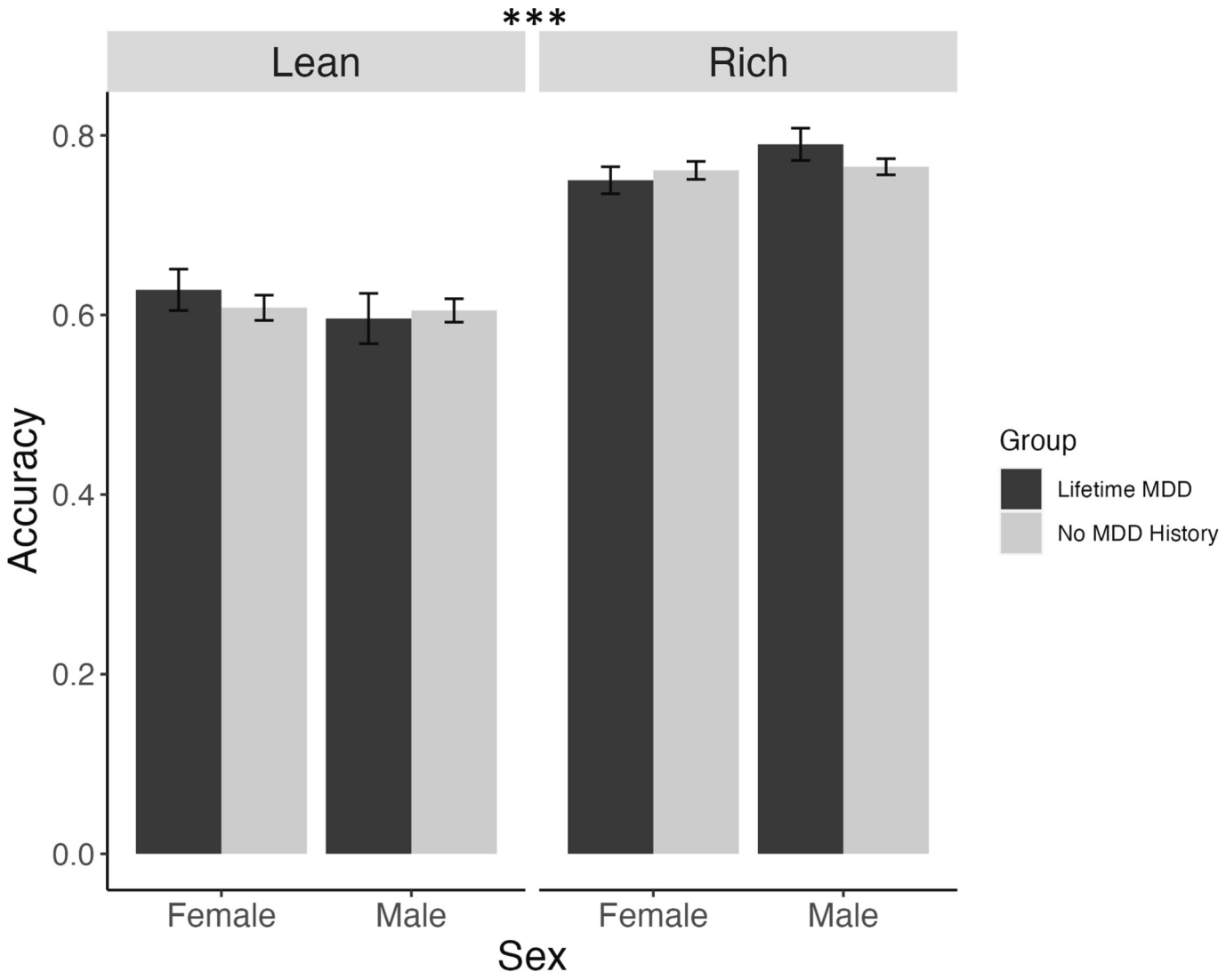

Fig. 3. Accuracy by stimulus type and group.
Note. Lean and rich accuracy for females and males with no MDD history and participants with lifetime MDD.

included individuals who reported comorbidities (a majority of lifetime MDDs reported additional psychiatric diagnoses) as well as psychiatric medication use as current medication use likely indicates current depressive symptoms. With respect to response bias, the main effect of *Block* remained $F(2, 600) = 4.78$, $p = 0.009$, partial $\eta^2 = 0.015$, with greater response bias seen in Blocks 2 (95 % CI [0.165, 0.212]) and 3 (95 % CI [0.211,0.254]) compared to Block 1 (95 % CI [0.084,0.120]), and greater response bias in Block 3 than Block 2, all $p < 0.001$. The main effect of *Sex* was also unaffected, ($F(1, 300) = 4.82$, $p = 0.029$, partial $\eta^2 = 0.016$, 95 % CI_{Males} [0.168, 0.217], 95 % $CI_{Females}$ [0.135, 0.178]); however, the *Sex* × *Group* interaction was no longer significant ($F(1, 300) = 2.52$, $p = 0.113$, partial $\eta^2 = 0.008$, 95 % $CI_{FemaleControl}$ [0.148, 0.202], 95 % $CI_{FemaleLifetimeMDD}$ [0.104, 0.171], 95 % $CI_{Male\text{-}Control}$ [0.160, 0.210], 95 % $CI_{MaleLifetimeMDD}$ [0.158, 0.241]). Results for discriminability and reaction time were unaffected by removing controls with current medication/psychiatric diagnosis (see *Supplement*). For accuracy, the *Block* × *Stimulus Type* interaction was no longer significant ($F(2,624) = 1.99$, $p = 0.138$, partial $\eta^2 = 0.006$), but the main effect of *Stimulus Type* remained ($F(1,312) = 34.22$, $p < 0.001$, partial $\eta^2 = 0.099$, 95 % CI_{Rich} [0.757,0.785], 95 % CI_{Lean} [0.593,0.634]). Overall these results indicate that the task elicited the intended effects (see *Supplement* for full details regarding follow-up analyses).

4. Discussion

The current study developed and validated a novel online version of the PRT with new stimuli. Our primary goal was to develop a novel online PRT that would be psychometrically matched to the laboratory-based task. In both versions of our online PRT, participants exhibited a significant increase in response bias towards the more frequently rewarded stimuli across three blocks. We did not find any differences in discriminability, between groups or task versions, indicating that response bias findings were not confounded by task difficulty or differences in stimuli. Similar to the laboratory-based task, participants were more accurate in identifying the 'rich' (i.e., more frequently rewarded) stimuli than the 'lean' (i.e., less frequently rewarded) stimuli, and showed an increase in rich accuracy across the three task blocks. Relatedly, participants showed decreased reaction time across blocks, and in particular in response to 'rich' stimuli. Together, these patterns suggest that the current online version of the PRT elicited the intended effects, and participants responded in similar patterns as seen in laboratory-based administrations of the task. The validation of this online PRT task may allow for future research using this paradigm to assess clinical populations remotely. The utilization of remote methods in our research is important as it reduces several barriers to participation, and may increase participant retention.

A core feature of MDD is blunted response to rewards and rewarding stimuli (Boyle et al., 2023; Halahakoon et al., 2020; Pizzagalli, 2014). Accordingly, a secondary aim of our study was to examine whether adults with lifetime diagnosis of MDD would display blunted reward learning, compared to individuals with no MDD history. Extending prior findings (Pizzagalli et al., 2008b; Vrieze et al., 2013; Pechtel et al., 2013), individuals with lifetime MDD were characterized by reduced reward learning, albeit only among females and only when including the full sample. These results could be due to differences in sample characteristics between the current online sample and those evaluated in the laboratory (Liu et al., 2011; Pechtel et al., 2013; Pizzagalli et al., 2008b), such that in our sample participants with lifetime MDD reported current use of psychiatric medication and comorbid psychiatric disorders. While some PRT studies have allowed for comorbid anxiety disorders within their depressed sample (Audrain-McGovern et al., 2014; Pizzagalli et al., 2008b; Vrieze et al., 2013), they typically excluded any other psychiatric comorbidities and prescription medication use, and did not allow any current psychiatric diagnosis, or medication use, among controls. In fact when we excluded for medications and comorbidities in our control group, we no longer saw differences in reward learning between females with lifetime MDD and females with no such history. However, the heterogeneity of our lifetime MDD sample may be more representative of typical presentations of depression, which often include comorbidities as well as medication use, relative to laboratory samples.

While an overall effect of lifetime depression on reward learning did not emerge, we did find sex-specific differences between participants with lifetime MDD and those with no history of MDD. Specifically, *females* with self-reported lifetime MDD diagnosis displayed blunted reward learning, compared to females who did not report current or past MDD and males with lifetime MDD. A main effect of sex, such that males displayed greater reward learning, remained even when excluding controls with current psychiatric diagnoses or medication use. To our knowledge, no prior research utilizing the PRT has found sex differences in baseline reward learning (Cunningham et al., 2021; Liu et al., 2011; Pechtel et al., 2013; Pizzagalli et al., 2008b); however, Cunningham and colleagues found, under stress, that males displayed greater response bias on the PRT (Cunningham et al., 2021). Additionally, during a monetary incentive task males, compared to females, displayed heightened arousal, greater behavioral accuracy, and increased neural activation in the nucleus accumbens a critical region in the brain's reward system (Warthen et al., 2020). Thus, future research assessing sex differences in reward responsivity within the context of MDD should consider environmental and neurobiological factors as well as recruit larger sample sizes to evaluate possible sex-specific effects.

4.1. Limitations

This study has several limitations. First, participants did not undergo a structured clinical interview to confirm clinical diagnoses and instead provided self-report of lifetime psychiatric disorders. It is possible that some participants who reported current MDD diagnosis had subthreshold symptoms at the time of data collection. Relatedly, individuals who reported only past MDD diagnosis may not have been fully remitted. It is also a possibility that participants reporting a current or past diagnosis, or even no diagnosis, of any psychiatric condition were incorrect in their reporting as we did not assess where the diagnosis originated from. Further the stigma surrounding mental health may have prevented individuals from reporting diagnosis, seeking care, or diagnostic assessment.

Additionally, questionnaires and task completion were conducted without the presence of an experimenter. Though in-depth instructions were provided to encourage sitting the correct distance from the screen, finding a distraction-free environment to complete the task, using index fingers to respond, and implementing other Wi-Fi/set-up requirements, we cannot know for certain whether participants followed these instructions. However, we note that the internal reliability for all mood-related scales (BDI-II, SHAPS, and PVSS-21) was excellent (range: 0.90–0.95), suggesting that participants reliably completed these scales. Moreover, we included attention checks during the questionnaires, and conducted quality checks of the PRT data; participants who failed either attention or a priori data quality checks were excluded from analyses. Nevertheless, future research should implement the online PRT in laboratory settings to ensure proper task administration as well as to allow for direct recruitment of participants with MDD. Moreover, our study implemented a cross-sectional design, so we are unable to infer causal relationships between sex, lifetime depression, and reward learning.

4.2. Conclusions

A novel online version of the PRT was developed and deployed to assess reward learning among a nationally representative community sample of participants. Our task was successfully validated as participants displayed an increase in response bias across blocks, greater accuracy and decreased reaction time when identifying the 'rich' stimulus. To our knowledge, this study is the first to identify sex differences in response bias (a measure of reward learning) towards a more frequently rewarded stimulus, which is possibly due to the relatively large sample size. Specifically, females with lifetime MDD, compared to females with no MDD history and males with lifetime MDD, displayed blunted reward learning. Sex at birth and gender identity are often conflated despite being separate constructs (Bates et al., 2022), thus future directions should aim to recruit more non-binary and transgender participants. Additionally, future studies should consider environmental and neurological impacts, as well as gender-identity differences when assessing reward responsivity within the context of depression.

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CRediT authorship contribution statement

Shiba M. Esfand: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Project administration, Visualization, Writing – original draft, Writing – review & editing. **Kaylee E. Null:** Conceptualization, Investigation, Methodology, Project administration, Writing – review & editing. **Jessica M. Duda:** Conceptualization, Investigation, Methodology, Project administration, Writing – review & editing. **Josh de Leeuw:** Methodology, Software, Writing – review & editing. **Diego A. Pizzagalli:** Conceptualization, Formal analysis, Investigation, Project administration, Resources, Supervision, Writing – review & editing.

Declaration of competing interest

Over the past 3 years, Dr. Pizzagalli has received consulting fees from Boehringer Ingelheim, Compass Pathways, Engrail Therapeutics, Neumora Therapeutics (formerly BlackThorn Therapeutics), Neurocrine Biosciences, Neuroscience Software, Otsuka Pharmaceutical, Sage Therapeutics, Sama Therapeutics, Sunovion Pharmaceuticals, and Takeda; he has received honoraria from the American Psychological Association, Psychonomic Society and Springer (for editorial work) and from Alkermes; he has received research funding from the Brain and Behavior Research Foundation, the Dana Foundation, Millennium Pharmaceuticals, Wellcome Leap MCPsych, and NIMH; he has received stock options from Compass Pathways, Engrail Therapeutics, Neumora Therapeutics, and Neuroscience Software; he has a financial interest in Neumora Therapeutics, which has licensed the copyright to the probabilistic reward task through Harvard University. Dr. Pizzagalli's interests were reviewed and are managed by McLean Hospital and Partners HealthCare in accordance with their conflict-of-interest policies. No

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jad.2024.01.133.

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