GENDER	AND	EFF(	)RTFI	IL AI	Ι(	DIDANCE	
OLIDLI	I	$\perp \perp \perp \perp \setminus$	<i></i>	$\mathcal{I}$	_		

- Gender and comorbidity moderate the relationship between mood disorder
- symptoms and effortful avoidance performance

Abstract

3

We must often decide how much effort to exert or withhold to avoid undesirable outcomes or obtain rewards. In depression and anxiety, levels of avoidance tend to be excessive and reward-seeking is reduced. Yet outstanding questions remain about the links between motivated action/inhibition and anxiety and depression symptoms, and whether they differ between men and women. Here we examined the relationship between anxiety and depression symptoms and performance on effortful active and inhibitory avoidance (Study 1) and reward seeking (Study 2) in humans. Undergraduates and paid online workers  $(N_{Avoid} = 545,\, N_{Reward} = 310;\, N_{Female} = 368,\, N_{Male} = 450,\, M_{Age} = 22.58,\, Range_{Age} = 17\text{-}62)$ 11 were assessed on the Beck Depression Inventory (BDI-II) and the Beck Anxiety Inventory 12 (BAI) and performed an instructed online avoidance or reward-seeking task. Participants 13 had to make multiple presses on active trials and withhold presses on inhibitory trials to avoid an unpleasant sound (Study 1) or obtain points towards a monetary reward (Study 2). Overall, men deployed more effort than women in both avoidance and reward-seeking, and anxiety symptoms were negatively associated with active reward-seeking accuracy. Gender moderated the relationship between anxiety symptoms and inhibitory avoidance, 18 such that women with higher anxiety showed reduced inhibitory avoidance accuracy. 19 Anxiety symptoms predicted poorer active avoidance performance for those high in depression symptoms only. Our results illuminate effects of gender and symptom 21 comorbidity in the relationship between mood disorder symptoms and the motivation to

Keywords: avoidance, reward, effort, depression, anxiety 24

actively and effortfully respond to obtain positive and avoid negative outcomes.

Word count: 6824 25

22

23

27

28

39

## Gender and comorbidity moderate the relationship between mood disorder symptoms and effortful avoidance performance

#### Significance statement

We often need to take effortful action, or withhold action, to avoid unpleasant
outcomes or obtain rewards. Depression and anxiety can impact these behaviours'
effectiveness, but the role of depression in avoidance and anxiety in reward-seeking is not
well understood. Gender differences in avoidance and reward-seeking have also not been
examined. Here, we present a task in which participants had to make or withhold button
presses to avoid hearing an unpleasant sound or to obtain a reward. Men deployed more
effort than women in avoidance, and women with higher levels of anxiety symptoms had
lower inhibitory avoidance accuracy than men. Our results illuminate gender differences in
how depressive and anxiety symptoms impact our ability to avoid threats and obtain
rewards.

Introduction

#### • Avoidance and reward-seeking behaviours

Living organisms are motivated to avoid potential threats or to acquire rewards
respectively. Often achieving these goals requires action, but it can also require refraining
from action. For example, we may take action to remove a threat's potential harm through
active avoidance, or we may decide that withholding action is the best way to let the threat
pass by, as in inhibitory avoidance (Krypotos, Effting, Kindt, & Beckers, 2015; LeDoux,
Moscarello, Sears, & Campese, 2017). Alternatively, in a situation that offers the
possibility of reward, we may take action to approach the reward through active
reward-seeking or, instead, inhibit pre-potent reward seeking to wait for a larger reward
(Capuzzo & Floresco, 2020; Cools, 2008). Research suggests that the expression of similar
behavioral actions (including inhibition) is dependent on the motivational context (aversive

vs. appetitive), which influences the likelihood of selecting a specific action in a specific motivational context (Wang & Delgado, 2021). However, in neuropsychiatric research, 52 depressive disorders are often studied with regard to reward-seeking contexts, and anxiety disorders with regard to avoidance contexts, with little emphasis on the other motivational context. Symptoms of anxiety and depression have been associated with avoidance, typically operationalized via active avoidance and via questionnaires, as threats are overestimated (Bishop & Gagne, 2018; Browning, Behrens, Jocham, O'Reilly, & Bishop, 2015; Cléry-Melin et al., 2011; Mkrtchian, Aylward, Dayan, Roiser, & Robinson, 2017; Ottenbreit, Dobson, & Quigley, 2014). In depression, reward-seeking may also be impaired due to a lack of motivation to obtain rewards (Bishop & Gagne, 2018; Slaney et al., 2021). Past research has established the importance of avoidance and reward-seeking behaviours in helping us navigate our environment and stay safe (Krypotos et al., 2015; LeDoux et al., 2017). However, active vs. inhibitory subtypes of these behaviours have not typically been distinguished – especially through objective measures of observable behavior. Furthermore, anxiety and depression are often comorbid (Brown, Campbell, Lehman, Grisham, & Mancill, 2001), and this comorbidity has been linked to excessive avoidance behaviours (Ottenbreit et al., 2014). However, the role of comorbidity in affecting active vs. inhibitory avoidance, or reward-seeking, has not been examined.

Gender may also be an important variable in this relationship. For example, gender differences have been identified in the presentation and incidence of mood and anxiety disorders, such that women have higher rates of depression and present more often with depression than men (Altemus, Sarvaiya, & Neill Epperson, 2014; Kessler, 2006; Parker & Brotchie, 2010) and have rates of anxiety disorders that are twice as high as those of men (McLean, Asnaani, Litz, & Hofmann, 2011; Pittig, Treanor, LeBeau, & Craske, 2018). However, we do not know how these gender differences manifest themselves in avoidance or reward-seeking behaviours. Although mood and anxiety disorders are often comorbid, they also manifest with distinct symptoms and courses that would require distinct strategies to

treat in a clinical context (Goldstein-Piekarski, Williams, & Humphreys, 2016; McLean et al., 2011). In the present study, we ask how mood disorder symptoms impact active vs. inhibitory avoidance and reward-seeking behaviours in a population of young adults with depressive and anxiety symptoms ranging from minimal to severe.

# The role of mood disorder symptoms and gender differences in avoidance and reward-seeking

It has been proposed that mood and anxiety disorder symptoms shift the perceived value and costs of avoidance and reward-seeking in sub-optimal ways. The Altered Computations Underlying Decision Making (ACDM) framework (Bishop & Gagne, 2018) proposes that anxiety is linked to underestimation of the effort cost in avoiding an aversive 87 outcome and that depression is linked to overestimation of the effort cost in obtaining a reward. These effort costs interact with the perceived value of avoidance or reward-seeking to inform one's decision on whether or not to engage in the behaviour. Past experimental work has also identified impairments in physical effort deployment for reward in populations with depression (Pessiglione, Vinckier, Bouret, Daunizeau, & Le Bouc, 2018; Treadway, Buckholtz, Schwartzman, Lambert, & Zald, 2009; see Culbreth, Moran, & Barch, 2018 for a review) and anxiety (Wang & Delgado, 2021). However, work linking mood and anxiety disorders to impairments in adaptive avoidance and reward-seeking often focuses on these avoidance and reward-seeking behaviours as unitary processes. As such, we still do not know how shifts in perceived effort costs linked to mood and anxiety disorders manifest themselves in active or inhibitory avoidance or reward-seeking.

To better understand the degree to which depressive and anxiety symptoms
contribute to active and inhibitory forms of avoidance or reward-seeking a rigorous
assessment of effort deployment in these behaviors is needed. People with Major Depressive
Disorder (MDD) choose high-effort options less often on effort-based decision making tasks
involving reward. This behaviour is potentially symptomatic of a larger-scale motivational

deficit (Pessiglione et al., 2018; Treadway, Bossaller, Shelton, & Zald, 2012; Treadway et al., 2009). If maladaptive effort deployment is a primary characteristic of mood and anxiety disorders, then we might expect active avoidance and reward-seeking to be impaired more than inhibitory forms of these behaviours overall (Culbreth et al., 2018). Anxiety, especially in the context of depressive symptoms, has been shown to impair our sensitivity to rewards (Auerbach et al., 2022; Dillon et al., 2014), although whether anxiety's impact on reward-seeking differs for active or inhibitory behaviours is not yet clear.

Additionally, individual differences in the presentation and severity of mood and 111 anxiety disorders - beyond the mere presence or absence of the disorder - may manifest 112 with different patterns of active vs. inhibitory behaviours depending on the motivational 113 context. Among these differences, gender differences are especially prominent. Women 114 generally present with more depressive symptoms (Parker & Brotchie, 2010) and 115 experience depression comorbid with anxiety more often than men (Kessler, 2006; McLean 116 et al., 2011; Ottenbreit et al., 2014). Thus, the impact of mood and anxiety disorders on 117 our ability to avoid aversive outcomes and seek out rewarding outcomes may be linked to 118 gender differences that affect the motivational deficits these disorders present. If gender 119 differences in depressive and anxiety symptom presentation - as captured on self-report 120 scales (Beck, Steer, & Brown, 1996) - are predicted by differences in accuracy and effort 121 deployment on active and inhibitory avoidance and reward-seeking tasks, this may help 122 elucidate how observed gender differences in depressive and anxiety symptoms map on to 123 real-life behavioural changes. 124

In order to bring our understanding of mood disorder symptoms into a framework that acknowledges differences in active vs. inhibitory avoidance and reward-seeking behaviours, we must consider both anxiety and depression in a framework that directly investigates their impact on these behaviours,, and how they might interact to impair effective avoidance and reward-seeking. While the relationships between anxiety and

avoidance (Bishop & Gagne, 2018; Levita, Hoskin, & Champi, 2012; Norbury, Robbins, & 130 Seymour, 2018), and depression and reward-seeking (Rizvi, Pizzagalli, Sproule, & Kennedy, 131 2016; Slaney et al., 2021; Treadway et al., 2012) are well established, those between anxiety 132 and reward-seeking, as well as depression and avoidance, have yet to be fully characterized. 133 As depression and anxiety can be highly comorbid (Goldstein-Piekarski et al., 2016; 134 Ottenbreit et al., 2014), parsing which aspects of avoidance and reward-seeking behaviors 135 are affected uniquely by depressive symptoms, anxiety symptoms, or their common 136 pathophysiological substrates (Insel et al., 2010), would be important in informing future 137 depression and anxiety treatments. 138

#### An effortful avoidance and reward-seeking study

Despite established gender differences in the prevalence and presentation of mood 140 disorder symptoms (Kessler, 2006; Parker & Brotchie, 2010; Thompson & Bland, 2018), it 141 is not known how the relationship between mood and anxiety disorder symptoms and 142 avoidance and reward-seeking differs by gender. Gender differences in motivational deficits 143 may lead to unique patterns in active and inhibitory behaviours, but this has not been 144 examined either. As such, in this work, we ask 1) whether anxiety and depression 145 symptoms predict accuracy and effort deployment on active/inhibitory avoidance 146 vs. reward-seeking and 2) whether the relationship between mood disorder symptoms and accuracy is moderated by gender.

To address these questions, the present study examined both avoidance and reward-seeking, each with two non-clinical samples - undergraduates and online workers - with a broad distribution of mood disorder symptoms. Both studies were reverse-translated with modification from a series of rodent studies investigating deficits in active and inhibitory avoidance and reward-seeking behaviours (Capuzzo & Floresco, 2020; Piantadosi, Yeates, & Floresco, 2018). Our studies are the first to combine intermixed active and inhibitory avoidance (Levita et al., 2012) or reward-seeking trials with increasing effort

requirements throughout the task, requiring participants to switch between withholding
physical effort on inhibitory trials and deploying increasing amounts of effort on active
trials in each task. This design allows us to directly compare performance on active and
inhibitory trials in the context of increasing effort demands. Increasing effort demands may
also pull out differences in choosing an active vs. inhibitory strategy.

#### Materials and Methods

#### 162 Participants

161

We powered each study to detect a moderate-sized main effect of d=0.15 obtained with a previous study of N=217 participants using the fabs R package (Biesanz, 2020), resulting in a target sample size of N=549. Demographic information for all studies can be found in Table 1. For each study, we collected data from two samples: an undergraduate population and an online worker population. The study was approved by the research ethics board at a location which will be identified if the article is published.

#### s Study 1 (Avoidance)

We recruited undergraduate participants at a location which will be identified if the article is published. These participants received one percentage point towards their grade in a psychology course of their choosing for completing the study. Of these participants, N = 311 finished the study, of which N = 38 were excluded for not completing the pre-task survey, having below 50% accuracy on active or inhibitory avoidance trials, spending over 100 s on any given attention check, or not responding to all Beck Anxiety Inventory (BAI) questions. As such, data from N = 273 participants was used in the data analysis.

Additionally, we recruited paid online workers from around the world (N=310) on the Prolific online study platform (https://www.prolific.co/). These participants received GBP £8.07 for completing the study. Of these participants, N=294 finished the study, of which N=22 were excluded for not completing the pre-task survey, having below 50% accuracy on active or inhibitory avoidance trials, spending over 100 s on any given attention check, or not responding to all Beck Anxiety Inventory (BAI) questions. As such, data from N=272 participants was used in the data analysis.

#### 184 Study 2 (Reward-seeking)

We recruited undergraduate participants at a location which will be identified if the 185 article is published. These participants received one percentage point towards their grade in a psychology course of their choosing and a CAD \$5.00 gift card from Starbucks for 187 completing the study. Of these participants, N=83 finished the study, of which N=43188 were part of a separate analysis with different stimuli that is beyond the scope of this paper 189 and N=7 were excluded for not completing the pre-task survey, having below 50% 190 accuracy on active or inhibitory avoidance trials, spending over 100 s on any given 191 attention check, or incorrectly responding to a pre-task attention check. As such, data from 192 N=36 participants was used in the data analysis. 193

Additionally, we recruited paid online workers from around the world (N=309) on the Prolific online study platform. These participants received GBP £8.07 and a £2.69 bonus for completing the study. Of these participants, N=300 finished the study, of which N=26 were excluded for not completing the pre-task survey, having below 50% accuracy on active or inhibitory avoidance trials, spending over 100 s on any given attention check, or incorrectly responding to a pre-task attention check. As such, data from N=274 participants was used in the data analysis.

Overall, the excluded sample was 29.17% female and 70.83% male, while the analyzed sample was 45.97% female and 54.03% male.

#### Materials and Methods

#### Stimulus presentation

We used PsychoPy 2020.1.2 (RRID: SCR\_006571) via the Pavlovia online study platform (Peirce et al., 2019). Participants completed the study on their own computers; they were not allowed to complete the study on mobile devices or tablets.

#### Stimuli

208

Cues indicating active or inhibitory trials were dark blue squares and circles with a
thin black border and were generated by PsychoPy 2020.1.2 (Peirce et al., 2019) (Fig. 1);
they subtended a visual angle of about 11.5° x 11.5°. All stimuli were presented against a
grey background (RGB value [0,0,0] on a scale from -1 to 1). If participants responded
incorrectly on any trial in the avoidance studies, an aversive sound was played for 2000 ms.
The aversive sounds were randomly selected from a set of eight screeching and scraping
sounds created by our lab and ranked as highly aversive by four independent raters and in
a pilot study.

Participants completed a series of questionnaires before beginning the main task. 217 These were the State-Trait Anxiety Inventory, form Y-2 (STAI Y-2) (Spielberger, 2008); 218 the Beck Depression Inventory II (BDI-II) (Beck et al., 1996); the Beck Anxiety Inventory 219 (BAI) (Steer & Beck, 1997); the Behavioral Activation for Depression Scale (BADS) 220 (Kanter, Mulick, Busch, Berlin, & Martell, 2007); the Generalized Anxiety Disorder Scale 221 (GAD-7) (Spitzer, Kroenke, Williams, & Löwe, 2006); and the Behavioural Inhibition Scale 222 and Behavioural Activation Scale (BIS/BAS) (Carver & White, 1994). In our data 223 analysis, we looked at results from the BDI-II and BAI as these clinically validated scales most directly capture participants' levels of current depressive and anxiety symptoms. The BADS, GAD-7, and BIS/BAS capture specific behavioural facets of depression and anxiety that are less relevant to understanding overall effects of mood and anxiety disorders on avoidance and reward-seeking and were not analyzed in this study. We used the BAI as our 228 primary measure of anxiety symptoms as it is the most widely used and validated among

the anxiety scales we included (Fydrich, Dowdall, & Chambless, 1992) and as its structure parallels that of the BDI-II.

#### Procedure Procedure

233

234

#### $Avoidance\ task$

A graphical overview of the avoidance task is provided in Fig. 1A.

After calibrating their physical effort capability and the volume of the aversive stimuli in the task, participants read instructions indicating the shape to which they would have to respond with multiple spacebar presses as well as the shape to which they would have to withhold their response. They also heard an example of the aversive sound that would be played if they made an incorrect decision during the task.

Participants then began a series of practice trials in order to gain exposure to the
stimuli and types of responses they would have to make (Fig. 1A). This consisted of five
trials in which participants had to make an active avoidance response - pressing the
spacebar several times to avoid hearing an unpleasant sound; five trials in which
participants had to make an inhibitory avoidance response - not pressing the spacebar to
avoid hearing an aversive sound; and ten trials that intermixed these active and inhibitory
trials.

On each trial, participants first viewed a grey screen with a white fixation cross for
a mean duration of 2000 ms with a standard deviation (SD) of 1200 ms, jittered according
to a normal distribution with these parameters on each trial. Participants then saw a
visual cue - either a blue circle or a blue square - for 2000 ms. The cues used for active and
inhibitory trials were pseudorandomly intermixed between participants. While this cue was
on-screen, participants had to press the spacebar multiple times on active avoidance trials
or withhold pressing on inhibitory avoidance trials. On active trials, the number of presses
required was set according to the average number of presses made during the two effort

calibration trials, such that participants who pressed fewer times during the calibration
would have to press fewer times to achieve criterion during the task. The initial criterion
was 5 presses given an average of 18 or fewer presses during calibration; a criterion of 6
presses given an average of 19-33 presses inclusive during calibration; and 7 presses given
an average of 19 or more presses during calibration.

If participants made an incorrect decision (pressing an insufficient number of times 260 on active trials or pressing at all on inhibitory trials), participants heard an aversive sound 261 and saw a fixation cross for 2000 ms. This aversive sound was taken from a set of ten 262 sounds created by our lab and rated as highly aversive. All sounds were scraping sounds 263 that had unpleasant psychoacoustic properties shown to reliably induce aversive responses 264 (Neumann & Waters, 2006) at a variety of frequencies. If participants made a correct 265 decision (pressing a sufficient number of times on active trials or not pressing on inhibitory trials), they saw a fixation cross surrounded by a white border on the edges of the screen 267 for 500 ms.

After completing the practice trials and viewing a final screen reminding them of 269 the instructions, participants began the main task. This consisted of up to 168 active 270 avoidance trials and 72 inhibitory avoidance trials (70% active and 30% inhibitory), 271 pseudorandomized such that no more than 6 active trials or 3 inhibitory trials appeared in 272 a row. On the 15th trial and every 40 trials thereafter, an attention check appeared asking 273 participants to press a key corresponding to the letter they heard, to ensure that they were attending to the task and able to hear auditory stimuli. Every 20 trials, the number of 275 button presses required on active trials increased by one press - this increased the effort demands on active trials across the task. The task continued until the participant responded correctly on half or less than half of the last 20 active trials - at this point, the 278 breakpoint was reached and the participant was thanked for completing the task.

#### Reward-seeking task

281

A graphical overview of the reward-seeking task is provided in Fig. 1B.

The design of the reward-seeking task was identical to that of the avoidance task, 282 with the following exceptions. First, the practice blocks were based on criterion-based 283 advancement in order to increase consistency with the design of other reward-seeking 284 studies in our lab. Participants had to achieve at least 80% accuracy in each of the active, 285 inhibitory, and intermixed reward-seeking trial blocks in order to advance; each block 286 would repeat until they achieved each criterion. Second, if the participant made a correct decision during a trial, they would see a screen indicating that they had gained 5 points along with a sum of their points thus far; if the participant made an incorrect decision during a trial, they would see a screen indicating that they had gained 0 points along with a sum of their points thus far. Both screens appeared for 1500 ms. Undergraduate 291 participants received a CAD \$5 gift card as a reward in addition to course credit for 292 completing the task; online workers received a GBP £2.69 payment as a reward in addition 293 to their payment for completing the task. Last, as this task did not incorporate audio, no 294 volume check or audio-based attention check was included. 295

#### Data analysis

All data was analyzed using R 4.1.1 "Kick Things" (R Development Core Team, 297 2011) through RStudio (Booth et al., 2018). On each behavioural task, we measured 1) 298 accuracy on active and inhibitory trials, operationalized as the proportion of correct 299 responses on each trial type; 2) effort on each trial type, operationalized as the number of presses made relative to criterion on each trial; 3) participants' depressive and anxiety symptoms, operationalized as their BDI (Beck et al., 1996) and BAI (Steer & Beck, 1997) 302 scores respectively; 4) participants' sensitivity (d') and criterion  $(\beta)$ ; and 5) breakpoint, 303 operationalized as the trial number on which the participant responded correctly on half or 304 less than half of the last 20 active trials. For each study, we combined undergraduate and 305

online worker samples to obtain a gender-balanced sample. All analyses were Bonferroni corrected for multiple comparisons. All confidence intervals were based on 1000 bootstrap replications using the confintr R package (Mayer, 2022).

Results

#### 310 Demographics

Participant's reported gender and sex heavily overlapped, with 97.53% overlap in women and 97.67% overlap in men on the avoidance tasks and 98.84% overlap in women and 97.80% overlap in men on the reward-seeking task. For this reason, the following results are expressed in terms of gender only. Women reported higher levels of depressive symptoms (t(723.12) = -3.84, p < .001, d = 0.27) and anxiety symptoms (t(706.44) = -4.71, p < .001, d = 0.34) than men across samples (Table 2, Fig. 2A, 5A). Across both studies, 20.92% of women and 15.11% of men were on medication for depression, and 19.29% of women and 14.89% of men were on medication for anxiety.

#### 19 Avoidance task

We first compared participants' accuracy on active and inhibitory avoidance trials by gender using a 2x2 within-between ANOVA (Trial Type x Gender) (Fig. 2B) (Table 3). A main effect revealed that, on average, participants were more accurate on inhibitory than on active trials  $(F(1, 522) = 405.53, p < .001, \eta^2 = 0.25; Table 4)$ . There was a main effect of gender  $(F(1, 522) = 5.85, p = .02, \eta^2 = < .01)$  as well as a gender interaction such that men had higher accuracy than women on active but not inhibitory avoidance trials  $(F(1, 522) = 4.87, p = .03, \eta^2 < .01)$ .

Depression and anxiety symptoms were not significantly associated with inhibitory or active avoidance accuracy (Table 4). However, given observed gender differences in both depression/anxiety disorder symptoms and task performance, we conducted a series of moderation analyses using the PROCESS macro (Hayes, 2017) as implemented in bruceR  $^{331}$  (Bao, 2021) to examine whether gender moderated the relationship between accuracy and  $^{332}$  anxiety and depressive symptoms (Fig. 3B). We found that gender moderated the  $^{333}$  relationship between anxiety symptoms (as measured in BAI scores) and inhibitory  $^{334}$  avoidance accuracy (F(1, 541) = 4.29, p = .04; Fig. 3A). Increased BAI scores were  $^{335}$  associated with lower inhibitory avoidance accuracy in females but not males; this  $^{336}$  relationship was not observed for BDI scores. For the full results of the moderation  $^{337}$  analysis, see Table 5.

To further examine the relationship between accuracy and anxiety and depressive symptoms, we tested whether BAI scores predicted accuracy in men and women separately. Outside of the moderation analysis after Bonferroni correction, BAI scores overall predicted inhibitory but not active avoidance performance accuracy (Fig. 3B, (t(543) = -3.01, p = .04, r = -0.13)). Additionally, higher BAI scores predicted lower inhibitory avoidance performance accuracy in women but not men (Fig. 3B; (t(260) = -3.73, p = .01, r = -0.23, 95% CI [-0.36, -0.09])).

We also conducted an interactive regression analysis to investigate whether the relationship between anxiety symptoms and active and inhibitory avoidance accuracy differed as a function of the level of depressive symptoms (Fig. 4). In active avoidance, the relationship between anxiety symptoms (BAI scores) and accuracy for all participants was a function of their level of depressive symptoms (BDI scores) (t(541) = -2.65, p = .01); however, this was not the case in inhibitory avoidance (t(541) = -0.87, p = .39). As such, only those with higher levels of depressive symptoms were impaired in active avoidance, and not those with higher levels of anxiety symptoms but lower levels of depressive symptoms.

To account for participants' bias to deploy effort and engage in active as opposed to inhibitory avoidance in general, we calculated sensitivity (d') and criterion  $(\beta)$  and repeated the moderation analyses on these alternative outcome performance measures. Sensitivity reflects participants' ability to correctly distinguish between active and inhibitory trials and deploy the required amount of effort on active trials only. Criterion reflects participants' bias towards an active or inhibitory response. Gender did not moderate the relationship between anxiety or depressive symptoms and sensitivity or criterion. However, BAI scores predicted sensitivity in women but not men (t(260) = -3.55, p = .01, r = -0.21, 95% CI [-0.36, -0.08]).

Additionally, we explored the extent to which the amount of effort that participants deployed to avoid aversive outcomes changed across the task (Fig. 8A). A a 2x2 within-between ANOVA (Block x Gender) (Table 6) revealed that participants deployed increasing amounts of effort during the task to meet increasing effort requirements (F(1, 522) = 405.53, p < .001,  $\eta^2 = 0.25$ ), and that men deployed more effort than women across the task (F(1, 522) = 5.85, p = 0.016,  $\eta^2 = < .01$ ).

Last, we examined whether participants' breakpoint in the task was explained by their levels of mood and anxiety disorder symptoms in avoidance. After Bonferroni correction, BAI and BDI scores did not predict overall active or inhibitory avoidance performance in either men or women (BAI: (t(543) = -2.44, p = .24, r = -0.10, 95% CI [-0.19, -0.02]); BDI: (t(543) = -2.15, p = .51, r = -0.09, 95% CI [-0.17, -0.01])).

#### 373 Reward-seeking task

381

We first compared participants' accuracy on active and inhibitory reward-seeking trials by gender (Fig. 6A) using a 2x2 within-between ANOVA (Trial Type x Gender) (Table 7). A main effect revealed that, on average, participants were more accurate on inhibitory than on active trials  $(F(1, 292) = 58.86, p < .001, \eta^2 = 0.07)$ . There was no main effect of gender  $(F(1, 292) = 2.61, p = .11, \eta^2 = 0.01)$  but there was a gender interaction such that men had higher accuracy than women on active but not inhibitory reward-seeking trials  $(F(1, 292) = 7.61, p = .01, \eta^2 = 0.01)$ .

Given observed gender differences in both depressive/anxiety symptoms and task

performance, we again conducted a series of moderation analyses to see whether gender moderated the relationship between accuracy and anxiety and depressive symptoms.

Anxiety was associated with reduced active reward seeking accuracy in the total sample.

However, we found no gender moderation of the relationship between anxiety or depressive symptoms and active or inhibitory reward-seeking accuracy, and BDI scores did not interact with active or inhibitory reward-seeking accuracy (Table 8, Table 9, Fig. 6A).

To further elucidate the relationship between accuracy and anxiety and depressive 388 symptoms, we evaluated whether BAI and BDI scores predicted accuracy in men and 380 women separately. After Bonferroni correction, BAI and BDI scores did not predict overall 390 active or inhibitory reward-seeking performance in either men or women (Fig. 6B). We also 391 conducted an interactive regression analysis to investigate whether the relationship 392 between anxiety symptoms and active and inhibitory reward-seeking accuracy differed as a 393 function of their level of depressive symptoms (Fig. 7). In active reward-seeking, the relationship between anxiety symptoms (BAI scores) and accuracy for all participants was 395 not a function of their level of depressive symptoms (BDI scores) (t(306) = 0.45, p = .66); this was also not the case in inhibitory reward-seeking (t(306) = -0.78, p = .44).

To evaluate participants' bias to deploy effort and engage in active as opposed to inhibitory reward-seeking, we again calculated sensitivity (d') and criterion  $(\beta)$  and performed the moderation analysis using these alternative outcome measures of performance. Gender did not moderate the relationship between anxiety or depressive symptoms and sensitivity or criterion.

Additionally, we explored how the effort that participants deployed to obtain reward changed across the task (Fig. 8B). A a 2x2 within-between ANOVA (Block x Gender)

(Table 10) revealed that participants deployed increasing amounts of effort during the task to meet increasing effort requirements (F(1, 292) = 58.86, p = <.001,  $\eta^2 = 0.07$ ), and revealed no gender differences in effort deployment (F(1, 292) = 2.61, p = .11,  $\eta^2 = 0.01$ ).

Last, we examined whether participants' breakpoint in the task was explained by their levels of mood and anxiety disorder symptoms in reward-seeking. After Bonferroni correction, BAI and BDI scores did not predict overall active or inhibitory reward-seeking performance in either men or women (BAI: (t(308) = -0.31, p = 1.00, r = -0.02, 95% CI [-0.12, 0.04]); BDI: (t(308) = -0.75, p = 1.00, r = -0.04, 95% CI [-0.12, 0.04])).

413 Discussion

#### 414 Summary

In the present study, we investigated gender differences in active and inhibitory 415 avoidance behaviours. Additionally, we explored how mood and anxiety disorder symptoms 416 negatively impact active vs. inhibitory avoidance and reward-seeking behaviours. Lastly, 417 we examined whether accuracy and effort deployment in avoidance and reward-seeking are 418 associated with depressive and anxiety symptoms, and whether the relationship between 419 accuracy and mood disorder symptoms is moderated by gender. Anxiety symptoms 420 interacted with participants' depressive symptoms level in active avoidance but not in 421 active reward-seeking or in inhibitory avoidance or reward-seeking, such that participants' 422 anxiety symptoms negatively impacted their accuracy more if they also had a high level of 423 depressive symptoms. Compared to men, women showed higher levels of self-reported 424 depression and anxiety. Throughout active avoidance and reward-seeking trials, men made 425 more effortful responses than women. Gender moderated the relationship between anxiety 426 symptoms and inhibitory avoidance. Women showed lower performance in inhibitory avoidance than men as a function of higher levels of anxiety symptoms, with no 428 corresponding effect for depressive symptoms. In contrast, higher levels of anxiety were 429 associated with lower active reward-seeking performance in both men and women. Our 430 findings illuminate gender differences in active and inhibitory subtypes of avoidance and 431 reward-seeking behaviours where effort was required to obtain the desired outcome. 432

#### Interpretation of results

Based on previous findings, we can speculate that the gender differences are driven 434 at least in part by mood and anxiety disorder symptoms. In particular, the observed 435 gender difference in inhibitory avoidance performance could reflect more general gender 436 differences in stress tolerance. Parker and Brotchie (2010) argued that women have a 437 higher predisposition (diathesis) to stress than men and, in our study, women reported 438 higher anxiety symptoms than men. In our avoidance task, it is advantageous to act to 439 avoid an aversive outcome - especially given high levels of anxiety symptoms (Bishop & Gagne, 2018). As such, inhibiting responding may be especially difficult given a combination of high anxiety symptoms and a decreased tolerance for stress in women compared to men. Furthermore, this gender difference in diathesis could drive a reduced ability to inhibit effort when needed - an impairment in shifting from an active to an inhibitory strategy given higher levels of anxiety symptoms (Gustavson, Altamirano, Johnson, Whisman, & Miyake, 2017). Given the observed interaction of lower accuracy at higher depressive and anxiety symptom levels in active avoidance, increased comorbidity of 447 depressive and anxiety symptoms in women could also partly explain these results -448 although this interaction was not significantly observed in the presence of gender 449 differences in inhibitory avoidance.

Beyond inhibitory avoidance, the observed gender differences in effort and accuracy
on active avoidance and reward-seeking trials could reflect gender differences in effort
deployment. Men made more effortful responses relative to criterion than women on active
avoidance trials. This could be caused by women having smaller wrists with which to
generate physical force than men (Morse, Jung, Bashford, & Hallbeck, 2006), as well as
increased testosterone in men - which is associated with increased physical effort
deployment during competitions (Losecaat Vermeer, Riečanský, & Eisenegger, 2016).
Although our tasks did not have competitive elements, participants may still have

completed the task with an eye towards maximizing performance. Since deploying more
effort in the task would increase one's chance of staying above criterion, this increased
effort deployment could explain the increased active trial accuracy for men across the
avoidance and reward-seeking tasks. It is important to qualify that gender has a significant
cultural component, and cultural factors could also play a role in gender differences in
effort deployment - perhaps via effects of a lower tolerance for stress on effort deployment
(Parker & Brotchie, 2010).

We also found that the effects of anxiety symptoms on active avoidance accuracy 466 depended on an interaction between anxiety symptoms and depressive symptom level, such 467 that only those with higher levels of depression symptoms who were also high in anxiety 468 were impaired. This suggests a role for comorbidity between anxiety and depressive 469 symptoms in people's ability to deploy effort to actively avoid an unpleasant outcome 470 (Brown et al., 2001). As such, when those with mood disorder symptoms attempt to avoid 471 aversive outcomes, impairments to effort deployment necessary for avoidance may be 472 driven by features of anxiety symptoms and depressive symptoms together, as opposed to 473 one mood disorder or another independently. Past work has only predicted increases in 474 effort deployment in avoidance given anxiety and decreases in effort deployment in general 475 given depression (Bishop & Gagne, 2018). As such, the observed impairment given 476 symptoms of both mood disorders sheds light on how comorbid mood disorder symptoms 477 can impact avoidance behaviours. Importantly, this relationship was not observed in 478 inhibitory avoidance or in active or inhibitory reward-seeking. In inhibitory avoidance, 479 mood disorder effects were specific to anxiety symptoms in women only, and only anxiety symptoms significantly impacted active reward-seeking accuracy. As such, it may be that an anxious subtype of depressive symptoms uniquely impacts our ability to deploy effort to avoid an unpleasant outcome. This is inconsistent with previous findings by Wurst et al. 483 (2021) suggesting that there were no significant differences in fear learning – which may be 484 a process involved in avoidance – between those with anxious and non-anxious depression. 485

However, as our task's difficulty is bound by increasing effort and not learning, and as we were looking at a non-clinical sample, such effects of comorbidity may not have come out in the context of our study.

The relationship between higher anxiety symptoms and reduced active 480 reward-seeking performance is novel, as past work has primarily focused on the relationship between depressive symptoms and reward-seeking and has not focused on subtypes of 491 avoidance (Bishop & Gagne, 2018). The ways in which depressive symptoms drive reduced 492 reward sensitivity are well-established (Slaney et al., 2021), but it was previously not clear whether anxiety symptoms would drive greater success in obtaining rewards (through underestimation of the effort required to obtain a reward) or reduced reward-seeking performance (through inefficient allocation of effort that results in increased fatigue). In our 496 task, participants' performance on effortful active trials was reduced given higher anxiety 497 symptoms, suggesting that the form of anxiety symptoms participants faced may not have 498 driven increased effort deployment or reduced effort costs. This finding runs counter to past 499 work suggesting that trait anxiety is associated with impairments in shifting away from an 500 effortful task (Gustavson et al., 2017). As we evaluate participants' current as opposed to 501 trait anxiety, this pattern of results could be explained by anxiety-related impairments to 502 effort deployment that are reflected in measures of anxiety as a personality trait. 503

Similarly, the relationship between higher anxiety symptoms and reduced inhibitory avoidance performance differs from previous predictions of improved avoidance given anxiety symptoms, such as those of Bishop and Gagne (2018). However, Bishop and Gagne framed this relationship in terms of active and not inhibitory avoidance, as they predicted that underestimations of effort cost would drive excessive avoidance behaviours. Anxiety symptoms may be associated with impairments to inhibitory avoidance precisely because of this bias towards action given the possibility of aversive outcomes, an effect that could be driven by a perceived lack of control over outcomes in the task (Wang & Delgado, 2021).

Additionally, we did not observe a relationship between depressive symptoms and accuracy or effort deployment in reward-seeking, as has previously been observed (Bishop & Gagne, 2018). The effort demands of the task may not have deterred people with high depressive symptoms from working for a reward, which could be explained by the depressive symptoms experienced by participants not impacting effort deployment.

Overall, participants had lower accuracy in avoidance compared to reward-seeking; 517 this could be a function of differences in motivation to engage in avoidance or 518 reward-seeking. Motivation to complete the tasks can be driven in part by participants' 519 valuations of task-relevant stimuli (Bishop & Gagne, 2018). A major difference between our 520 tasks arises in the outcome of an incorrect decision. In avoidance, an incorrect decision is 521 associated with an aversive sound; in reward-seeking, it is associated with not receiving points. Although the salience of an aversive sound may suggest that it is more motivating and would therefore be associated with increased accuracy, hearing it may also be more demotivating - especially for participants with mood disorder symptoms. Hearing the 525 aversive sound repeatedly could be a salient indicator of a lack of control over task outcomes (Wang & Delgado, 2021).

#### 28 Limitations

There are some limitations to our interpretation of our findings. First, since the
dichotomy of the task demands is between effortful active trials and inhibitory trials that
require no effort, we cannot compare the effects of high vs. low effort demands on inhibitory
avoidance or reward-seeking behaviours. As such, our interpretation of the relationship
between effort deployment and mood disorder symptoms only extends to active trials.
Accuracy in the task was likely tied to participants' effort capabilities, as increased effort
deployment was required throughout the task on active trials to meet the criterion level of
effort and make the correct response on the trial. However, we calibrated the criterion to
participants' effort ability and considered accuracy on inhibitory as well as active trials to

reduce the reliance of task outcomes on individual differences in effort deployment. 538 Additionally, as the proportion of active trials was greater than that of inhibitory trials, 539 participants may have become fatigued on the majority of trials in the task, increasing over 540 time. This fatigue from effort deployment, combined with boredom (from the task being 541 repetitive) could be difficult to disentangle from other shifts in motivation to deploy effort 542 throughout the task (e.g. those related to the value of avoidance or reward-seeking). 543 However, as fatigue is likely to arise in most physically effortful tasks, our tasks still reflect real-world physical effort demands. Furthermore, as this study took place online, the study had to use repeated keyboard presses instead of other, more continuous or better-controlled measures of physical effort such as a grip squeeze (Aridan, Malecek, Poldrack, & Schonberg, 2019). However, repeated button presses have been validated as being physically effortful and have been used in in-person contexts (Gold et al., 2013).

#### Future work

Future studies could build on our findings by investigating how patterns of 551 information about specific aspects of effortful avoidance and reward-seeking are 552 instantiated in key brain regions. The posterior anterior cingulate cortex (pACC) and 553 ventral striatum encode information about prospective gains given physical effort 554 requirements (Aridan et al., 2019). These regions - and their homologues in rodents - have 555 been shown to be differentially necessary for active vs. inhibitory avoidance (Piantadosi et 556 al., 2018) and reward-seeking (Capuzzo & Floresco, 2020). Investigating how these regions 557 represent information on prospective gains and losses relative to effort costs could illuminate how we weigh the benefits and costs of deploying effort to obtain rewards and avoid aversive outcomes. Additionally, separating out different factors contributing to effort deployment through a computational modelling approach would be important to 561 understand the individual contributions of various factors to participants' performance. 562 These factors could include action biases (Mkrtchian et al., 2017), perceived value of

avoidance or reward (Bishop & Gagne, 2018); or fatigue (Pessiglione et al., 2018).

Furthermore, it would be helpful to evaluate whether subscales of mood disorder symptoms

- potentially linked to subtypes such as anxious depression (Wurst et al., 2021) - pull out

factors that drive participants' behaviours in avoidance and reward seeking. This analysis

could further illuminate our observed gender differences - for example, to evaluate whether

reduced inhibitory avoidance performance in women given increased anxiety symptoms is

reflective of an anxious subtype of depression (Wurst et al., 2021).

#### 1 Conclusion

Our studies address outstanding questions of whether accuracy and effort 572 deployment on avoidance and reward-seeking predict mood disorder symptoms, and 573 whether the relationship between accuracy and mood disorder symptoms is moderated by 574 gender. We separate out active and inhibitory avoidance and reward-seeking behaviours in 575 a context that allows for direct comparisons between them, instead of considering 576 avoidance and reward-seeking behaviours as unitary wholes. We highlight gender 577 differences in each of these subtypes of avoidance and reward-seeking given varying levels 578 of mood disorder symptoms, contextualizing past work on gender differences in these 579 symptoms (Parker & Brotchie, 2010). In particular, we are the first to examine these 580 proposed gender differences in an active and inhibitory avoidance and reward-seeking 581 context. These findings could inform clinical interventions to address maladaptive 582 deployment of avoidance and lack of motivation for reward-seeking, targeted by gender. Additionally, we link active avoidance and reward-seeking to motivation for physical effort deployment given varying levels of mood and anxiety disorders. As many tasks in life require physical effort deployment, understanding where it can be impaired is an important 586 pursuit. Our findings underscore the importance of considering individual differences in the 587 ways in which avoidance and reward-seeking can be impaired in life. 588

### Data and code availability

The data and materials for all experiments, as well as the code used to generate this manuscript and conduct all analyses, are available at [URL redacted for double-blind review].

References

Altemus, M., Sarvaiya, N., & Neill Epperson, C. (2014). Sex differences in anxiety 594 and depression clinical perspectives. Frontiers in Neuroendocrinology, 35(3), 595 320–330. https://doi.org/10.1016/j.yfrne.2014.05.004 596 Aridan, N., Malecek, N. J., Poldrack, R. A., & Schonberg, T. (2019). Neural correlates of effort-based valuation with prospective choices. NeuroImage, 598 185(July 2018), 446–454. https://doi.org/10.1016/j.neuroimage.2018.10.051 599 Auerbach, R. P., Pagliaccio, D., Hubbard, N. A., Frosch, I., Kremens, R., Cosby, E., 600 ... Pizzagalli, D. A. (2022). Reward-Related Neural Circuitry in Depressed and 601 Anxious Adolescents: A Human Connectome Project. Journal of the American 602 Academy of Child & Adolescent Psychiatry, 61(2), 308-320. 603 https://doi.org/10.1016/j.jaac.2021.04.014 604 Bao, H.-W.-S. (2021). bruceR: Broadly useful convenient and efficient r functions. 605 Retrieved from https://CRAN.R-project.org/package=bruceR 606 Beck, A. T., Steer, R. A., & Brown, G. K. (1996). Manual for the beck depression 607 inventory-II. San Antonio, TX: Psychological Corporation. 608 Biesanz, J. (2020). Fabs: Functions for applied behavioural sciences in r. Retrieved 609 from https://github.com/jbiesanz/fabs%0ACitation%20Key:%20Biesanz2020 610 Bishop, S. J., & Gagne, C. (2018). Anxiety, depression, and decision making: A 611 computational perspective. Annual Review of Neuroscience, 41(1), 371–388. 612 https://doi.org/10.1146/annurev-neuro-080317-062007 613 Booth, D. S., Szmidt-Middleton, H., King, N., Westbrook, M. J., Young, S. L., Kuo, 614 A., ... Rstudio Team. (2018). RStudio: Integrated development for r. Nature. 615 https://doi.org/10.1108/eb003648 616 Brown, T. A., Campbell, L. A., Lehman, C. L., Grisham, J. R., & Mancill, R. B. 617 (2001). Current and lifetime comorbidity of the DSM-IV anxiety and mood 618 disorders in a large clinical sample. Journal of Abnormal Psychology, 110(4), 619

```
585–599. https://doi.org/10.1037/0021-843X.110.4.585
620
           Browning, M., Behrens, T. E., Jocham, G., O'Reilly, J. X., & Bishop, S. J. (2015).
621
              Anxious individuals have difficulty learning the causal statistics of aversive
622
              environments. Nature Neuroscience, 18(4), 590–596.
623
              https://doi.org/10.1038/nn.3961
624
           Capuzzo, G., & Floresco, S. B. (2020). Prelimbic and infralimbic prefrontal
625
              regulation of active and inhibitory avoidance and reward-seeking. Journal of
626
              Neuroscience, 40(24), 4773-4787.
627
              https://doi.org/10.1523/JNEUROSCI.0414-20.2020
628
           Carver, C. S., & White, T. L. (1994). Behavioral inhibition, behavioral activation,
629
              and affective responses to impending reward and punishment: The BIS/BAS
630
              scales. Journal of Personality and Social Psychology.
631
              https://doi.org/10.1037/0022-3514.67.2.319
632
           Cléry-Melin, M. L., Schmidt, L., Lafargue, G., Baup, N., Fossati, P., & Pessiglione,
633
              M. (2011). Why don't you try harder? An investigation of effort production in
634
              major depression. PLoS \ ONE, \ 6(8).
635
              https://doi.org/10.1371/journal.pone.0023178
636
           Cools, R. (2008). Role of Dopamine in the Motivational and Cognitive Control of
637
              Behavior. The Neuroscientist, 14(4), 381-395.
638
              https://doi.org/10.1177/1073858408317009
639
           Culbreth, A. J., Moran, E. K., & Barch, D. M. (2018). Effort-cost decision-making
640
              in psychosis and depression: Could a similar behavioral deficit arise from
641
              disparate psychological and neural mechanisms? Psychological Medicine, 48(6),
642
              889–904. https://doi.org/10.1017/S0033291717002525
643
           Dillon, D. G., Rosso, I. M., Pechtel, P., Killgore, W. D. S., Rauch, S. L., &
644
              Pizzagalli, D. A. (2014). Peril and pleasure: An RDOC-inspired examination of
645
              threat responses and reward processing in anxiety and depression. Depression
646
```

```
and Anxiety, 31(3), 233–249. https://doi.org/10.1002/da.22202
647
           Fydrich, T., Dowdall, D., & Chambless, D. L. (1992). Reliability and validity of the
648
              beck anxiety inventory. Journal of Anxiety Disorders, 6(1), 55–61.
649
              https://doi.org/10.1016/0887-6185(92)90026-4
650
           Gold, J. M., Strauss, G. P., Waltz, J. A., Robinson, B. M., Brown, J. K., & Frank,
651
              M. J. (2013). Negative symptoms of schizophrenia are associated with abnormal
652
              effort-cost computations. Biological Psychiatry, 74(2), 130–136.
653
              https://doi.org/10.1016/j.biopsych.2012.12.022
654
           Goldstein-Piekarski, A. N., Williams, L. M., & Humphreys, K. (2016). A
655
              trans-diagnostic review of anxiety disorder comorbidity and the impact of
656
              multiple exclusion criteria on studying clinical outcomes in anxiety disorders.
657
              Translational Psychiatry, 6(6), e847–e847. https://doi.org/10.1038/tp.2016.108
658
           Gustavson, D. E., Altamirano, L. J., Johnson, D. P., Whisman, M. A., & Miyake, A.
659
              (2017). Is set shifting really impaired in trait anxiety? Only when switching
660
              away from an effortfully established task set. Emotion, 17(1), 88–101.
661
              https://doi.org/10.1037/emo0000212
662
           Hayes, A. F. (2017). Introduction to mediation, moderation, and conditional process
663
              analysis: A regression-based approach. Guilford publications.
664
           Insel, T., Cuthbert, B., Garvey, M., Heinssen, R., Pine, D. S., Quinn, K., ... Wang,
665
              P. (2010). Research Domain Criteria (RDoC): Toward a New Classification
666
              Framework for Research on Mental Disorders. American Journal of Psychiatry,
667
              167(7), 748–751. https://doi.org/10.1176/appi.ajp.2010.09091379
668
           Kanter, J. W., Mulick, P. S., Busch, A. M., Berlin, K. S., & Martell, C. R. (2007).
669
              The Behavioral Activation for Depression Scale (BADS): Psychometric
670
              Properties and Factor Structure. Journal of Psychopathology and Behavioral
671
              Assessment, 29(3), 191–202. https://doi.org/10.1007/s10862-006-9038-5
672
```

Kessler, R. C. (2006). The epidemiology of depression among women. Women and

673

Depression: A Handbook for the Social, Behavioral, and Biomedical Sciences, 74, 674 22–38. https://doi.org/10.1017/CBO9780511841262.004 675 Krypotos, A. M., Effting, M., Kindt, M., & Beckers, T. (2015). Avoidance learning: 676 A review of theoretical models and recent developments. Frontiers in Behavioral 677 Neuroscience, 9(July). https://doi.org/10.3389/fnbeh.2015.00189 678 LeDoux, J. E., Moscarello, J., Sears, R., & Campese, V. (2017). The birth, death 679 and resurrection of avoidance: A reconceptualization of a troubled paradigm. 680 Molecular Psychiatry, 22(1), 24–36. https://doi.org/10.1038/mp.2016.166 681 Levita, L., Hoskin, R., & Champi, S. (2012). Avoidance of harm and anxiety: A role 682 for the nucleus accumbens. NeuroImage, 62(1), 189–198. 683 https://doi.org/10.1016/j.neuroimage.2012.04.059 684 Losecaat Vermeer, A. B., Riečanský, I., & Eisenegger, C. (2016). Competition, 685 testosterone, and adult neurobehavioral plasticity (Vol. 229, pp. 213–238). 686 Elsevier. https://doi.org/10.1016/bs.pbr.2016.05.004 687 Mayer, M. (2022). Confintr: Confidence intervals. Retrieved from 688 https://CRAN.R-project.org/package=confintr 689 McLean, C. P., Asnaani, A., Litz, B. T., & Hofmann, S. G. (2011). Gender 690 differences in anxiety disorders: Prevalence, course of illness, comorbidity and 691 burden of illness. Journal of Psychiatric Research, 45(8), 1027–1035. 692 https://doi.org/10.1016/j.jpsychires.2011.03.006 693 Mkrtchian, A., Aylward, J., Dayan, P., Roiser, J. P., & Robinson, O. J. (2017). 694 Modeling avoidance in mood and anxiety disorders using reinforcement learning. 695 Biological Psychiatry, 82(7), 532–539. 696 https://doi.org/10.1016/j.biopsych.2017.01.017 697 Morse, J. L., Jung, M.-C., Bashford, G. R., & Hallbeck, M. S. (2006). Maximal 698 dynamic grip force and wrist torque: The effects of gender, exertion direction, 699 angular velocity, and wrist angle. Applied Ergonomics, 37(6), 737–742. 700

```
https://doi.org/10.1016/j.apergo.2005.11.008
701
           Neumann, D. L., & Waters, A. M. (2006). The use of an unpleasant sound as an
702
              unconditional stimulus in a human aversive pavlovian conditioning procedure.
703
              Biological Psychology, 73(2), 175–185.
704
              https://doi.org/10.1016/j.biopsycho.2006.03.004
705
           Norbury, A., Robbins, T. W., & Seymour, B. (2018). Value generalization in human
706
              avoidance learning. eLife, 7(66). https://doi.org/10.7554/eLife.34779
707
           Ottenbreit, N. D., Dobson, K. S., & Quigley, L. (2014). An examination of
708
              avoidance in major depression in comparison to social anxiety disorder.
709
              Behaviour Research and Therapy, 56(1), 82–90.
710
              https://doi.org/10.1016/j.brat.2014.03.005
711
           Parker, G., & Brotchie, H. (2010). Gender differences in depression. International
712
              Review of Psychiatry, 22(5), 429–436.
713
              https://doi.org/10.3109/09540261.2010.492391
714
           Peirce, J., Gray, J. R., Simpson, S., MacAskill, M., Höchenberger, R., Sogo, H., ...
715
              Lindeløy, J. K. (2019). PsychoPy2: Experiments in behavior made easy.
716
              Behavior Research Methods, 51(1), 195–203.
717
              https://doi.org/10.3758/s13428-018-01193-y
718
           Pessiglione, M., Vinckier, F., Bouret, S., Daunizeau, J., & Le Bouc, R. (2018). Why
719
              not try harder? Computational approach to motivation deficits in
720
              neuro-psychiatric diseases. Brain, 141(3), 629–650.
721
              https://doi.org/10.1093/brain/awx278
722
           Piantadosi, P. T., Yeates, D. C. M., & Floresco, S. B. (2018). Cooperative and
723
              dissociable involvement of the nucleus accumbens core and shell in the
724
              promotion and inhibition of actions during active and inhibitory avoidance.
725
              Neuropharmacology, 138, 57–71.
726
              https://doi.org/10.1016/j.neuropharm.2018.05.028
727
```

Pittig, A., Treanor, M., LeBeau, R. T., & Craske, M. G. (2018). The role of 728 associative fear and avoidance learning in anxiety disorders: Gaps and directions 729 for future research. Neuroscience & Biobehavioral Reviews, 88, 117–140. 730 https://doi.org/10.1016/j.neubiorev.2018.03.015 731 R Development Core Team, R. (2011). R: A language and environment for 732 statistical computing. 733 Rizvi, S. J., Pizzagalli, D. A., Sproule, B. A., & Kennedy, S. H. (2016). Assessing 734 anhedonia in depression: Potentials and pitfalls. Neuroscience and Biobehavioral 735 Reviews, 65, 21–35. https://doi.org/10.1016/j.neubiorev.2016.03.004 736 Slaney, C., Perkins, A. M., Davis, R., Penton-Voak, I., Munafò, M. R., Houghton, C. 737 J., & Robinson, E. S. J. (2021). Objective measures of reward sensitivity and 738 motivation in people with high vs low anhedonia. 739 https://doi.org/10.1101/2021.10.21.21265287 740 Spielberger, C. (2008). State-trait anxiety inventory for adults. Garden. Spitzer, R. L., Kroenke, K., Williams, J. B. W., & Löwe, B. (2006). A Brief 742 Measure for Assessing Generalized Anxiety Disorder: The GAD-7. Archives of 743 Internal Medicine, 166(10), 1092. https://doi.org/10.1001/archinte.166.10.1092 744 Steer, R. A., & Beck, A. T. (1997). Beck anxiety inventory. (pp. 23–40). Lanham, 745 MD, US: Scarecrow Education. 746 Thompson, A. H., & Bland, R. C. (2018). Gender similarities in somatic depression 747 and in DSM depression secondary symptom profiles within the context of 748 severity and bereavement. Journal of Affective Disorders, 227 (November 2017), 749 770–776. https://doi.org/10.1016/j.jad.2017.11.052 750 Treadway, M. T., Bossaller, N. A., Shelton, R. C., & Zald, D. H. (2012). 751 Effort-based decision-making in major depressive disorder: A translational 752 model of motivational anhedonia. Journal of Abnormal Psychology, 121(3), 753

553–558. https://doi.org/10.1037/a0028813

754

Treadway, M. T., Buckholtz, J. W., Schwartzman, A. N., Lambert, W. E., & Zald, 755 D. H. (2009). Worth the 'EEfRT'? The effort expenditure for rewards task as an 756 objective measure of motivation and anhedonia. PLoS ONE, 4(8), 1–9. 757 https://doi.org/10.1371/journal.pone.0006598 758 Wang, K. S., & Delgado, M. R. (2021). The Protective Effects of Perceived Control 759 During Repeated Exposure to Aversive Stimuli. Frontiers in Neuroscience, 15, 760 625816. https://doi.org/10.3389/fnins.2021.625816 761 Wurst, C., Schiele, M. A., Stonawski, S., Weiß, C., Nitschke, F., Hommers, L., ... 762 Menke, A. (2021). Impaired fear learning and extinction, but not generalization, 763 in anxious and non-anxious depression. Journal of Psychiatric Research, 135, 764 294–301. https://doi.org/10.1016/j.jpsychires.2021.01.034 765

## GENDER AND EFFORTFUL AVOIDANCE

Table 1
Demographic information for all participants.

Study	$N_{recruited}$	$N_{analyzed}$	$N_{\text{female}}$	$N_{\rm male}$	$N_{\rm other}$	${\rm M_{age}}$	$\mathrm{Range}_{\mathrm{age}}$
1 (Avoidance, undergraduate)	357	273	175	86	12	20.42	17-32
2 (Avoidance, paid global)	310	272	87	176	9	24.06	18-57
3 (Reward-seeking, undergraduate)	114	36	28	8	0	20.67	18-26
4 (Reward-seeking, paid global)	309	274	78	180	16	25.18	18-62

33

Table 2
Mean and SD Beck Depression Inventory II (BDI) and Beck Anxiety Inventory (BAI) proportion scores (score divided by total possible score).

Task	Gender	$\rm M_{BDIprop}$	$\mathrm{SD}_{\mathrm{BDIprop}}$	$\rm M_{\rm BAIprop}$	$SD_{BAIprop}$
Avoidance	Female	0.30	0.19	0.30	0.22
	Male	0.23	0.16	0.23	0.19
Reward-seeking	Female	0.29	0.19	0.28	0.21
	Male	0.26	0.17	0.22	0.17

## GENDER AND EFFORTFUL AVOIDANCE

Table 3
ANOVA of accuracy on active and inhibitory avoidance trials.

Effect	$\mathrm{df_n}$	$\mathrm{df_d}$	F	p	sig.	$\eta^2$
Gender	1	522	5.85	0.016	*	< .01
Trial Type	1	522	405.53	< .001	***	0.25
Gender:Trial Type	1	522	4.87	0.028	*	< .01

35

Table 4
Relationship between accuracy and mood disorder symptoms on active and inhibitory avoidance trials.

Trial Type	Comparison	df	t	p	sig.
Active avoidance	BDI~accuracy	541	-0.32	0.75	
	BAI~accuracy	541	-1.37	0.17	
Inhibitory avoidance	BDI~accuracy	541	-0.87	0.38	
	BAI~accuracy	541	-0.73	0.47	

**Table 5**Gender moderation of relationship between accuracy and mood disorder symptoms on active and inhibitory avoidance trials.

Trial Type	Comparison	$\mathrm{df_n}$	$\mathrm{df_d}$	t	p	sig.
Active avoidance	Gender moderation of BDI~accuracy	1	541	0.01	0.92	
	Gender moderation of BAI~accuracy	1	541	0.28	0.59	
Inhibitory avoidance	Gender moderation of BDI~accuracy	1	541	1.04	0.31	
	Gender moderation of BAI~accuracy	1	541	4.29	0.04	*

Table 6
ANOVA of effort deployment on active avoidance trials by gender.

Effect	$\mathrm{df_n}$	$\mathrm{df_d}$	F	p	sig.	$\eta^2$
Gender	3.00	516.00	7.08	< .001	***	0.03
Block	3.37	1740.44	294.38	< .001	***	0.1
Gender:Block	10.12	1740.44	0.77	0.659		< .001

Table 7
ANOVA of accuracy on active and inhibitory reward-seeking trials.

Effect	$\mathrm{df_n}$	$\mathrm{df_d}$	F	p	sig.	$\eta^2$
Gender	1	292	2.61	0.107		0.01
Trial Type	1	292	58.86	< .001	***	0.07
Gender:Trial Type	1	292	7.61	0.006	**	0.01

Table 8
Relationship between accuracy and mood disorder symptoms on active and inhibitory reward-seeking trials.

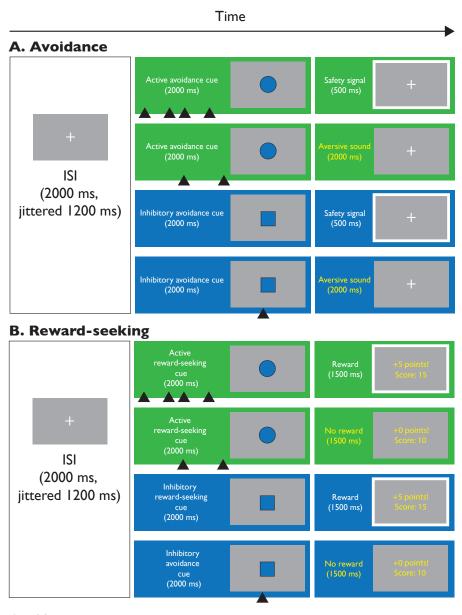
Trial Type	Comparison	df	t	p	sig.
Active reward-seeking	BDI~accuracy	306	-0.52	0.61	
	BAI~accuracy	306	-2.56	0.01	*
Inhibitory reward-seeking	BDI~accuracy	306	-0.54	0.59	
	BAI~accuracy	306	-0.83	0.41	

**Table 9**Gender moderation of relationship between accuracy and mood disorder symptoms on active and inhibitory reward-seeking trials.

Trial Type	Comparison	$\mathrm{d}f_{n}$	$\mathrm{d}f_{\mathrm{d}}$	t	p	sig.
Active reward-seeking	Gender moderation of BDI~accuracy	1	306	0.56	0.46	
	Gender moderation of BAI~accuracy	1	306	3.30	0.07	
Inhibitory reward-seeking	Gender moderation of BDI~accuracy	1	306	0.12	0.73	
	Gender moderation of BAI~accuracy	1	306	0.00	0.96	

Table 10
ANOVA of effort deployment on active reward-seeking trials by gender.

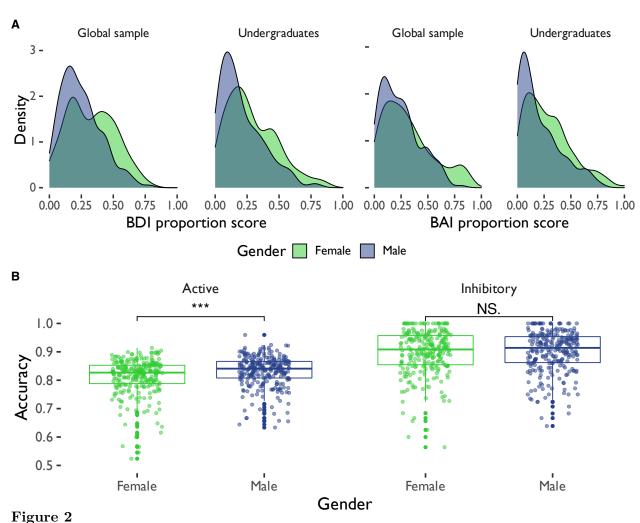
Effect	$\mathrm{df_n}$	$\mathrm{df_d}$	F	p	sig.	$\eta^2$
Gender	3.00	379.00	2.03	0.11		0.01
Block	3.39	1283.92	387.02	< .001	***	0.16
Gender:Block	10.16	1283.92	0.43	0.936		< .001



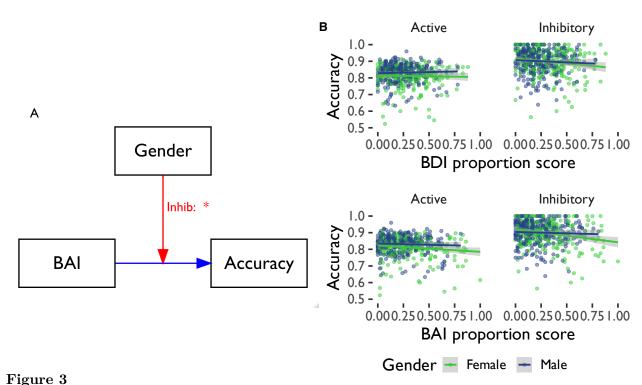
= I key press

#### Figure 1

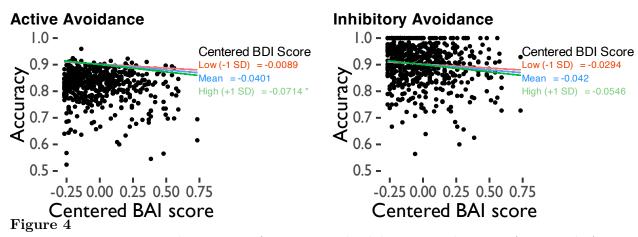
A diagram of the active and inhibitory avoidance and reward-seeking tasks. In the avoidance task (A), after an inter-stimulus interval (ISI) with a fixation cross onscreen, participants were presented with a cue associated with active or inhibitory avoidance. For the active avoidance cue, participants had to respond with repeated spacebar presses to avoid hearing an aversive sound. For the inhibitory avoidance cue, participants had to withhold responding to avoid hearing an aversive sound. In the reward-seeking task (B), after the ISI, participants were presented with a cue associated with active or inhibitory reward-seeking. For the active reward-seeking cue, participants had to respond with repeated spacebar presses to obtain points towards a monetary reward. For the inhibitory reward-seeking cue, participants had to withhold responding to obtain points towards a monetary reward. ISI = Inter-stimulus interval.



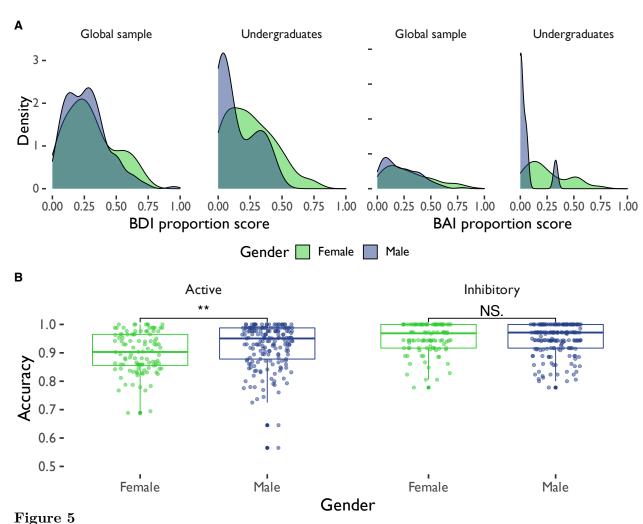
(A) Distribution of anxiety (BAI) and depressive symptom (BDI) proportion scores (score divided by total possible score) by gender and sample. (B) Accuracy by gender on active and inhibitory avoidance, and moderation of the relationship between accuracy and anxiety (BAI) scores by gender. Dots represent average accuracy on each trial type by participant. BAI = Beck Anxiety Inventory, BDI = Beck Depression Inventory.



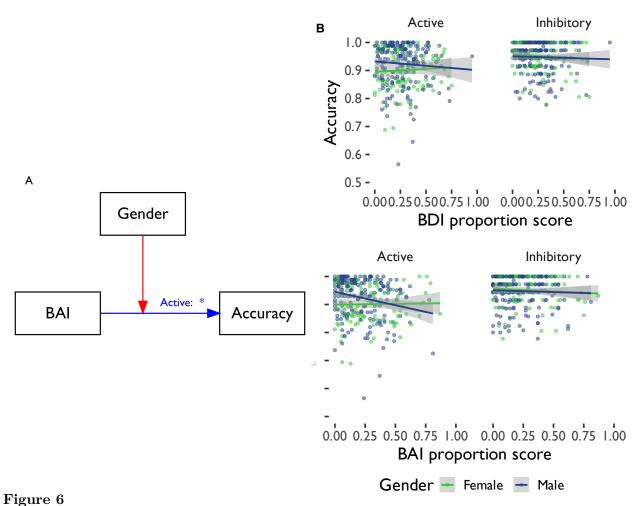
(A) Moderation of the relationship between accuracy and anxiety (BAI) proportion scores by gender in active and inhibitory avoidance. Gender significantly moderated the relationship between anxiety symptoms (BAI proportion scores) and inhibitory avoidance accuracy. (B) Accuracy by gender on active and inhibitory avoidance. BAI = Beck Anxiety Inventory. Proportion scores are scores divided by total possible score.



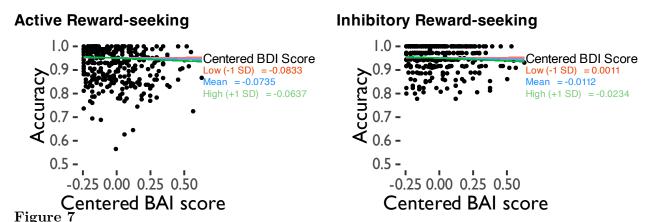
Interactive regression analysis output for active and inhibitory avoidance. BAI = Beck Anxiety Inventory, BDI = Beck Depression Inventory. Numbers on right indicate coefficients for regression lines at each level of BDI score (centred 1 standard deviation below the mean, at the mean, and 1 standard deviation above the mean).



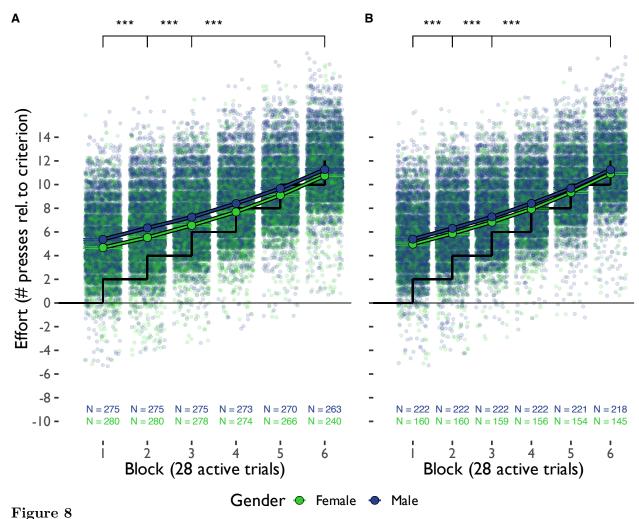
(A) Distribution of anxiety (BAI) and depressive symptom (BDI) scores by gender and sample. (B) Accuracy by gender on active and inhibitory reward-seeking, and moderation of the relationship between accuracy and anxiety (BAI) scores by gender. Proportion scores are scores divided by total possible score. BAI = Beck Anxiety Inventory, BDI = Beck Depression Inventory.



(A) Moderation of the relationship between accuracy and anxiety (BAI) proportion scores by gender on active and inhibitory reward-seeking. Anxiety symptoms (BAI proportion scores) were significantly associated with active reward-seeking accuracy. (B) Accuracy by gender on active and inhibitory reward-seeking. BAI = Beck Anxiety Inventory. Proportion scores are scores divided by total possible score.

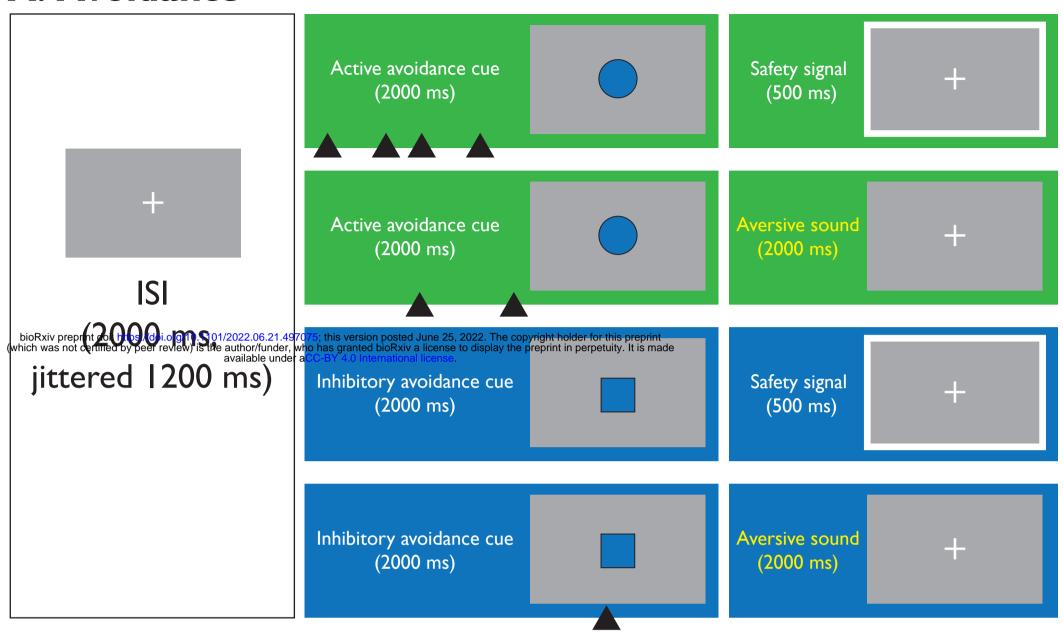


Interactive regression analysis output for active and inhibitory reward-seeking. BAI = Beck Anxiety Inventory, BDI = Beck Depression Inventory. Numbers on right indicate coefficients for regression lines at each level of BDI score (centred 1 standard deviation below the mean, at the mean, and 1 standard deviation above the mean).



Effort deployment across active avoidance (A) and reward-seeking (B) trials relative to the criterion effort deployment required to avoid an aversive outcome or obtain reward (black line). Each point represents one trial. N values represent number of participants of each gender who completed the task during that block of trials.

## A. Avoidance



# **B.** Reward-seeking

