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Experimentally-induced and real-world anxiety have no demonstrable effect on goal-directed behaviour

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Abstract:	Background Goal-directed control guides optimal decision-making and it is an important cognitive faculty that protects against developing habits. Previous studies have found some evidence of goal-directed deficits when healthy individuals are stressed, and in psychiatric conditions characterized by compulsive behaviours and anxiety. Here, we tested if goal-directed control is affected by state anxiety, which might explain the former results. Methods We carried out a causal test of this hypothesis in two experiments (between-subject N=88; within-subject N=50) that used the inhalation of hypercapnic gas (7.5% CO_2) to induce an acute state of anxiety in healthy volunteers. Results In both experiments, we induced a profoundly anxious state, both physiologically and psychologically, but this did not affect goal-directed performance. In a third experiment (N=1413), we used a correlational design to test if real-life anxiety-provoking events (panic attacks, stressful events) are associated with impaired goal-directed control. We found no evidence for this, over and above variance accounted for by trait differences in compulsivity. Conclusions In sum, three complementary experiments, two causal and one correlational, found no evidence that anxiety impairs goal-directed control.

TITLE

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Conflicts of interest

None

Ethical standards

The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008.

Data availability statement.

The datasets generated during and/or analysed during the current study are freely available on the Open Science Framework (https://osf.io/w4yfp/).

Code availability statement.

Code to reproduce results is freely available on the Open Science Framework (https://osf.io/w4yfp/).

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Abstract

Background

Goal-directed control guides optimal decision-making and it is an important cognitive faculty that protects against developing habits. Previous studies have found some evidence of goal-directed deficits when healthy individuals are stressed, and in psychiatric conditions characterized by compulsive behaviours and anxiety. Here, we tested if goal-directed control is affected by state anxiety, which might explain the former results.

Methods

We carried out a causal test of this hypothesis in two experiments (between-subject N=88; within-subject N=50) that used the inhalation of hypercapnic gas (7.5% CO_2) to induce an acute state of anxiety in healthy volunteers.

Results

In both experiments, we induced a profoundly anxious state, both physiologically and psychologically, but this did not affect goal-directed performance. In a third experiment (N=1413), we used a correlational design to test if real-life anxiety-provoking events (panic attacks, stressful events) are associated with impaired goal-directed control. We found no evidence for this, over and above variance accounted for by trait differences in compulsivity.

Conclusions

In sum, three complementary experiments, two causal and one correlational, found no evidence that anxiety impairs goal-directed control.

Background

Two well-established systems contribute to everyday decision making and behaviour, the goal-directed and the habitual system (Dickinson, 1985). Goal-directed behaviour is characterized by actions that are appropriate to the current desire for a given outcome and informed by the knowledge of the causal relationship between an action and the associated outcome (Dickinson & Balleine, 1994). More recently goal-directed control has been formalized as model-based planning, within a reinforcement learning framework (Daw, Gershman, Seymour, Dayan, & Dolan, 2011).

Though no previous study has examined whether experimentally induced state anxiety impairs goal-directed planning, a related literature on stress-induction offers a basis for this suggestion. Specifically, acute stress has been shown to induce deficits in goal-directed planning (Park, Lee, & Chey, 2017; Schwabe & Wolf, 2009, 2010), albeit inconsistently (null results: Heller, Ezie, Otto, & Timpano, 2018; Otto, Raio, Chiang, Phelps, & Daw, 2013; Radenbach et al., 2015) in healthy individuals. Acute anxiety and stress manipulations produce similar cardiovascular changes, and induce negative affect, but anxiety induction differs from stress in terms of the specific psychological experience (e.g. increased vigilance, panic, fear) and other aspects of the physiological response (Bailey, Argyropoulos, Kendrick, & Nutt, 2005; Shin & Liberzon, 2010).

Physiological and psychological stress has been likened to anxiety, and it is generally thought to impair several forms of deliberative and reflective processes, in favour of more automatic and reflexive ones (Shields, Sazma, & Yonelinas, 2016). From a neurobiological perspective, there is evidence that this mechanism is regulated by catecholamines, which act on prefrontal functioning under stress (Arnsten 1998). It has been suggested that reliance on faster, habitual mechanisms might be an evolutionary advantage in stressful situations (Arnsten 1998). Similarly, in the case of anxiety, the attentional control theory (Eysenck et al., 2007) suggests that anxiety impairs cognitive performance of top-down, executive tasks by giving greater influence to the bottom-up attentional system.

In addition, anxiety is a prominent feature of pathological manifestations characterized by an impoverished goal-directed system. For example, a fragile goal-directed system is hypothesized to lead one to get stuck in habits (C. M. Gillan, Otto, Phelps, & Daw, 2015) and typifies not only Obsessive-Compulsive Disorder (OCD) (C. M. Gillan et al., 2011; C. M. Gillan & Robbins, 2014; Vaghi et al., 2018) but also several other psychiatric conditions on the compulsivity spectrum such as eating disorder, drug abuse and alcohol addiction (Sjoerds et al., 2013; Voon et al., 2014). Accordingly, it has been suggested that goal-directed deficits constitute a trans-diagnostic trait (C. Gillan, Kosinski, Whelan, Phelps, & Daw, 2016; Robbins, Gillan, Smith, de Wit, & Ersche, 2012). One potential issue with this model is its specificity. Compulsivity is highly comorbid with anxiety (Nestadt et al., 2009), which is unsurprising, as OCD has only recently moved out of the Diagnostic and Statistical Manual category of anxiety disorders into its own classification (Stein et al., 2010). Accordingly, this raises the possibility that elevated anxiety levels in OCD might account for failures in goal-directed planning and consequent overreliance on habits.

In support of this idea, social anxiety patients appear to show similar deficits in goal-directed planning to OCD patients, despite the fact that they do not have a compulsive phenotype (Alvares, Balleine, & Guastella, 2014). Cross-sectional, correlational work has started to address this issue, finding that when a range of psychopathology measures are taken (and controlled for) within the same individuals, there is no meaningful contribution of trait anxiety to goal-directed deficits, while the association with compulsivity is robust (C. Gillan et al., 2016; Robbins et al., 2012). However, these studies are limited not just by their correlational nature, but because they assess trait anxiety, which does not speak to acute states of anxiety that are experienced by patients more transiently, often in association with their own symptoms (Mataix-Cols et al., 2003).

Here, we aimed at characterizing the relationship between increased anxiety and the functioning of the goal-directed system. We used a combination of causal and correlational approaches to investigate the role of acute anxiety on goal-directed control, in three experiments spanning laboratory and real-life settings.

Firstly, we used hypercapnic gas (i.e. with increased CO_2 level) to experimentally induce state anxiety and test its impact on goal-directed control, operationalized as sensitivity to contingency degradation (Vaghi et al., 2018). Hypercapnic gas is a well-validated method for experimentally inducing a transitory state of acute anxiety in healthy volunteers (Woods, Charney, Goodman, & Heninger, 1988). At very high doses (35% CO_2) it generates symptoms similar to those of panic disorder, with increased blood pressure and bradycardia (Argyropoulos et al., 2002; Griez, Zandbergen, Pols, & de Loof, 1990; Perna, Barbini, Cocchi, Bertani, & Gasperini, 1995), especially in subjects with panic disorder or susceptibility to it (Perna et al., 1994; Perna, Bertani, Caldirola, & Bellodi, 1996). We used lower doses (7.5% CO_2) which are reported to be sufficient to induce physiological and psychological symptoms of anxiety and sustained arousal associated with an anxiety state (Bailey et al., 2005). Subjects had profound physiological and subjective psychological responses to the anxiety induction procedure including changes in heart rate, blood pressure and self-reported anxiety, but it failed to induce deficits in goal-directed control over behaviour.

Reasoning this might be associated with study design sensitivity, we repeated this experiment using a within-subjects design and a different measure of goal-directed control – a 'model-based planning' measure derived from the two-step reinforcement learning task described above (Daw et al., 2011). Again, the procedure had substantial physiological and psychological effects consistent with the induction of an acute state of anxiety, but this had no demonstrable detrimental effect on goal-directed behaviour.

In a third and final experiment, we tested this hypothesis in a naturalistic, real-world setting using a large-scale correlational design (N=1413) (C. Gillan et al., 2016). We investigated if goal-directed (model-based) control is impaired in individuals who suffered recent 'real life' acute anxiety, specifically known to be associated with the experience of a recent panic attack (Aronson & Logue, 1988) and/or major life-stressors (Vyas, Pillai, & Chattarji, 2004). We found that the frequency of panic attacks in the past week and higher levels of stress in the past year were both modestly associated with deficits in goal-directed planning. Crucially, neither survived controlling for a correlated psychiatric trait, compulsive behaviour and intrusive

thought, which we previously showed has a strong association with goal-directed planning using these data (C. Gillan et al., 2016).

METHODS

Experiment 1

Subjects. 88 participants were recruited through university mailing lists, departmental research panels and posted flyers within the University of Cambridge and the wider community. Participants were randomly assigned to either the CO_2-induced anxiety group (n= 43, 20 females; mean age = 27.55, SD = 11.04) or the normal air 'placebo' group (n= 45, 24 females; mean age = 27.40, SD = 10.03) (Supplementary Material for further details on recruitment and inclusion and exclusion criteria).

Anxiety Manipulation. Participants were randomly assigned to two groups, one received the anxiety induction, which consisted of the inhalation of air enriched with 7.5 % CO_2 (7.5% CO_2, 20% O2, 71.5% N2, pre-mixed, BOC Special Gases, Guildford, UK) and one served as the control group, inhaling normal air. As the experimenter had to manually switch a lever to activate the delivery of one of the two air preparation, CO_2 was administered in a single-blind manner while measuring goal-directed/habit behaviour via controlled tasks, and was designed to induce a physiological state of acute anxiety in a reliable and controlled manner (Bailey et al., 2005). Participants inhaled the assigned air preparation as long as they were doing the task. To measure the effectiveness of this procedure at inducing acute anxiety, we recorded physiological measurements comprising heart rate, diastolic and systolic blood pressure and psychological measurements comprising the 17-item Acute Panic Inventory (API: Liebowitz, Fyer, Gorman, & et al., 1984), 10-item Positive and Negative Affective Scale (PANAS(Watson, Clark, & Tellegen, 1988)), and three Visual Analogue Scales assessing anxiety, fear, and happiness. Physiological measures were collected 10 minutes before, during and 15 minutes after the experimental manipulation. Psychological measures of subjective feeling due to the experimental manipulation were concomitantly collected, the only difference being that they were not interrogated during the performance of the task but immediately after and retrospectively on how they were feeling.

Contingency degradation paradigm. In a between-subjects design, subjects performed a contingency degradation task described previously and further detailed in the Supplementary Material (Vaghi et al., 2018) (Figure 1A). In short, the task was a free operant, self-paced procedure which allows testing of subjects' ability to detect action-outcome instrumental contingencies (Vaghi et al., 2018), one of the earliest operationalisations of goal-directed learning from the animal literature (Dickinson, Nicholas, & Adams, 1983).

Experienced contingency. As expected, for normal and CO_2-enriched air condition, experienced contingencies (based on experienced event frequencies, see Supplementary Material, Table S1) matched the a priori programmed ones (CO_2: r =

1.00, $p < .001$; Air: r = 1.00, $p < .001$). Therefore, programmed contingencies were used for subsequent analysis. Our findings were not confounded by between-group differences in experienced contingencies, as no main effect of group ($F_{(1, 63)} = 0.80$, $p = .37$, $\eta^2_G = 0.003$) nor interaction between group and block ($F_{(2.57, 161.61)} = 0.17$, $p = .89$, $\eta^2_G = 0.002$) was found.

Data analysis. We first performed analyses of variance (ANOVA) to determine whether there was a between-group difference in sensitivity to instrumental contingency as measured by response rate and causality judgment. Response rate was computed by dividing the number of bins for which a response was made by the total number of bins within each block. For each dependent variable, programmed contingency was used as a within-subject factor, and group was used as a between-subject factor. Analyses were conducted separately for the initial learning blocks and the test blocks. For the test blocks, we also investigated the relationship between response rate and contingency judgments, using a linear mixed-effects model. Specifically, we used contingency judgement and group as fixed effects, and we allowed the intercept and slope to vary between participants as random effects. We obtained p-values for the fixed effects using the Kenward-Roger method. Bayes factor analysis was used in case of failure to reject the null hypothesis, to examine the relative evidence for the null with default JZS priors for ANOVA (J. N. Rouder, Speckman, Sun, Morey, & Iverson, 2009) and (Rouder et al., 2012). Previous research (Schwaber et al., 2010) found a between-subjects effect size of stress on habitual performance for which default JSZ priors are suitable as specified in (J. N. Rouder et al., 2009) and (Rouder et al., 2012). Analyses were performed in R version 3.4.3 (R Foundation for Statistical Computing, Vienna, Austria; http://www.r-project.org/) using the 'afex' package for ANOVA and linear mixed models, the 'Bayes Factor' and 'brms' package for Bayes factor analysis and the 'tidyverse' packages for data organization and visualization.

Experiment 2

Subjects. 61 healthy volunteers were recruited from the local community in the same manner as described in Experiment 1. Screening and exclusion criteria were identical to Experiment 1. Further exclusion criteria were applied contingent on the experimental task employed here (Supplementary Material). The final sample size for analysis was 50 (26 female) with ages ranging from 18-62.

Reinforcement learning task (Daw, Niv, & Dayan, 2005). Participants completed a reinforcement-learning task that quantifies individual differences in goal-directed ('model-based') learning, which is operationalized as a parameter estimate from a logistic regression analysis predicting choices in the task. The task has been extensively used and described elsewhere (37) and further detailed in the Supplementary Material.

Anxiety Induction. The anxiety induction procedure as well as collection of physiological and psychological measures was identical to Experiment 1, except for the within-subjects design. Participants attended a single test session during which they completed two versions of the Reinforcement Learning Task *during* 20min inhalation of air enriched with 7.5 % CO_2 and normal air. Gas was administered in a single-blind manner and the order of CO_2 versus air was counterbalanced.

Data Analysis. Data were analysed using mixed-effects logistic regression in the *lme4* package in R 3.5.1 (http://cran.us.r-project.org). In line with previous studies (Daw et al., 2011), we tested the extent to which subjects in general tend to repeat actions performed on the previous trial or explore a new one ('Stay': coded switch= 0; stay= 1), and whether these choices were influenced by whether or not their previous action was rewarded ('Reward': coded as rewarded = 1; unrewarded = -1), was followed by a rare or common transition ('Transition': coded as common= 1, rare= -1), and their interaction ('Reward x Transition'). The intercept reflects tendencies to repeat the same action from one trial to the next, the main effect of reward reflects the contribution of model-free learning to subjects' choices, while an interaction between Reward and Transition is the hallmark of model-based (goal-directed) behaviour. We included the anxiety induction as a within-subjects factor (coded CO_2=1, Air=-1). We used Bound Optimization by Quadratic Approximation (bobyqa) with 1e5 functional evaluations. The model was specified as follows: Stay ~ Reward*Transition*CO_2 + (Reward* Transition*CO_2 + 1|Subject). Bayes factor analysis was used in case of failure to reject the null hypothesis using the anovaBF function in the BayesFactor package in R, with default JZS priors for ANOVA from (J.N. Rouder, Morey, Speckman, & Province, 2012). To avoid the issues with nested interactions from the logistic model, we extracted estimates for model-based planning separately for each subject in each condition and used these to compare an ANOVA model with a within-subjects effect of gas to an intercept-only model.

Computational Modelling. A more elaborated form of this analysis is presented in the online supplement. In brief, this method allows for analysis of a greater number of potential behavioural confounds, including separating the distinct role of learning rate and choice randomness from that of model-based, model-free and choice repetition estimates from the simpler analysis. These results largely recapitulate the main findings of the paper, with slight differences flagged as appropriate.

Experiment 3.

Participants. Data were collected online using Amazon's Mechanical Turk. Details of the experimental procedure can be found elsewhere (Gillan et al., 2016), but in brief, data were analysed from 1,413 individuals (823 female) with ages ranging from 18 to 76 (M=33, SD=11), who were based in the USA, had a history of good performance (i.e. being paid in full on at least 95% of their previous tasks) (Supplementary Material).

Reinforcement learning task. The task employed in this study was the same as that described in Experiment 2. The only difference was that subjects completed it remotely, and that a more rigorous quality control procedure was implemented appropriate to online testing (detailed in Supplement).

Panic Attacks and Life Stress. The occurrence of recent panic attacks was assessed using item 1 on the self-report version of the Panic Disorder Severity Scale (PDSS Shear et al., 1997). Life stress was assessed using the Social Readjustment Scale (Holmes & Rahe, 1967), which presents an inventory of common stressful life events to participants and asks them to select those that applied to them in the previous 12 months. The present sample had a mean score of 159 (SD=120). Scores lower than 150 are considered evidence of 'no significant stress' (N=775), while scores in excess of 300 are considered signs of major stress (N=179 in this sample)

(Figure 5B) (see also supplementary Material). Control Variables were also included as detailed in the Supplementary Material.

Data Analysis. We performed the same analysis as in Experiment 2, but here we additionally controlled for variables that have been previously linked to model-based planning, namely: IQ, age, gender and a trans-diagnostic psychiatric trait "Compulsive Behaviour and Intrusive Thought". This covariate was derived from previous published work (C. Gillan et al., 2016; Rouault, Seow, Gillan, & Fleming, 2018) which applied factor analysis to a series of questionnaires linked to self-reported measures of psychopathology. Factors were labelled based on items that loaded most strongly on each of the identified factors. Accordingly, items pertaining to the questionnaires related to 'compulsive' disorders most strongly loaded on the factor named "Compulsive Behaviour and Intrusive thought". Scores of each subject on this factor were used as a covariate in the present analysis. Bayes factor analysis was conducted on a linear model where residuals for model-based planning was the dependent measure and life stress or panic symptoms were the experimental models compared to an intercept-only model. As in experiment 2, we complemented our regression analysis with a computational model, details of which are available in the online supplement.

Results

Anxiety induction and Contingency Degradation (Experiment 1). Here we tested if experimentally induced anxiety would affect subjects' ability to detect action-outcome instrumental contingencies. In a between-subjects design, one group was assigned to inhale hypercapnic gas (7.5% CO_2) during the performance on the contingency degradation task, while the other inhaled normal air. Psychological and physiological measures confirmed that anxiety induction was successful and of a magnitude similar to that observed in prior studies (Cooper et al., 2013; Garner, Attwood, Baldwin, James, & Munafò, 2011; Garner, Attwood, Baldwin, & Munafò, 2012): participants in the CO_2 condition experienced greater self-reported anxiety ($F_{(1.97, 159.61)} = 35.57$, $p < .001$) and had a higher heart rate ($F_{(1.96, 152.92)} = 36.64$, $p < .001$) than those assigned to the Air condition (Figure 1B and 1D; Supplementary materials).

Participants learnt the contingencies in the training phase ($F_{(1, 86)} = 26.48$, $p < .001$, $\eta^2_G = 0.03$). Experimentally-induced anxiety did not affect subjects' behavioural sensitivity to instrumental contingency. Participants overall adjusted their response rate in line with the underlying contingency, as evidenced by a main effect of contingency on response rate in the test blocks ($F_{(3.73, 320.59)} = 29.95$, $p < .001$, $\eta^2_G = 0.07$). In the test blocks, there was no between-group difference ($F_{(1, 86)} = 0.22$, $p = .64$, $\eta^2_G = 0.002$) and no group by contingency interaction ($F_{(3.73, 320.59)} = 1.74$, $p = .15$, $\eta^2_G = 0.004$) (Figure 2A). Bayes Factor analysis further confirmed these findings. Specifically, the null model was strongly preferred over the alternative model with a main effect of anxiety and interaction effect of anxiety by contingency ($BF_{01} = 16.81$ and Figure S1 A).

The same was true of participants' *subjective* assessments of instrumental contingency (i.e. their explicit model of the environment). Subjects accurately tracked the underlying contingency of the task (training blocks, $F_{(1, 86)} = 30.46$, $p < .001$, $\eta^2_G = 0.12$; test blocks, $F_{(2.99, 256.89)} = 26.22$, $p < .001$, $\eta^2_G = 0.13$) and the experimental

manipulation did not affect this. There was no between-group difference ($F_{(1, 86)}$ = 0.16, p = .69, η^2_G = 0.001) and no group by contingency interaction ($F_{(2.99, 256.89)}$ = 0.33, p = .81, η^2_G = 0.002) (Figure 2B) on causality judgements. Bayes Factor analysis further confirmed these findings. Specifically, the null model was strongly preferred over the alternative model with a main effect of anxiety and interaction effect of anxiety by contingency (BF_{01} = 386.15 and Figure S1 B). Mirroring the findings on choice responses, experimentally-induced anxiety did not affect subjective judgments of instrumental contingency – adding weight to the suggestion that state anxiety may not have an appreciable effect on goal-directed control over action.

Individual Differences. Prior work showed that individual differences might be important in revealing the effect of stress on goal-directed behaviour (Heller et al., 2018; Otto et al., 2013; Radenbach et al., 2015; Schwabe & Wolf, 2010). Therefore, we tested if the detrimental effect of CO2 on goal-directed behaviour might depend on individual differences in sensitivity to the CO2 manipulation, assessed in terms of change in both self-reported and physiological measures of anxiety. For the former, we ran the model explained above with programmed contingency as a within-subject factor, introducing change in self-report anxiety as a between-subject covariate. The change in self-report anxiety was computed as the difference between VAS-anxious before inhaling the gas and after inhaling the gas. As above, there was a significant effect of programmed contingency on response rate ($F_{(3.73, 309.85)}$ = 25.42, p< .001), but there was no main effect of subjectively reported change in self-report anxiety ($F_{(1, 83)}$=0.28, p=.60) nor an interaction effect with programmed contingency ($F_{(3.73, 309.85)}$ =0.20, p=.42). Similar findings were obtained on subjective causality ratings. Accordingly, programmed contingency significantly predicted causality ratings ($F_{(3.18, 264.24)}$=33.10, p<.001) , but there was not a main effect ($F_{(1, 83)}$=0.00, p =.96) nor a significant interaction with subjectively reported change in self-report anxiety ($F_{(3.18, 264.24)}$=0.20, p =.90). Therefore, individual differences in anxiety, as self-reported by subjects upon CO_2 challenge, did not affect goal-directed planning.

We conducted the same analyses by using physiological changes in heart rate as a putatively more objective measure of change in anxiety arising from our manipulation. The physiological index for change in heart rate was computed as above, i.e. the difference between heart rate before inhaling the gas and after inhaling the gas. Changes in heart rate did not have a main effect on response rate ($F_{(1, 80)}$=0.1, p =.75), but there was a trend for an interaction between changes in heart rate and programmed contingency ($F_{(3.80, 303.94)}$=2.00, p =.10). Individuals with higher changes in heart rate tended to show slightly *greater* sensitivity to instrumental contingency, as their response rate depended more strongly on programmed contingency. Thus, if any moderating effect of anxiety sensitivity exists, it goes in the opposite direction to what has been shown in individual difference research with stress and goal-directed control (e.g. Otto *et al.*, 2013; Radenbach *et al.*, 2015). Changes in heart rate did not affect subjective causality ratings ($F_{(1, 80)}$=0.08, p =.78). Similarly there was no a significant interaction between changes in heart rate and programmed contingency ($F_{(3,29, 263.45)}$=0.44, p =.74) in predicting subjective causality ratings.

Anxiety Induction and Model-Based Planning (Experiment 2). We adopted a complementary approach to experiment 1 to test if anxiety induction would affect goal-directed planning. We employed a 'model-based' learning task (Figure 3) (Daw et al., 2011; Daw et al., 2005) in the context of a within-subjects design, which

overcomes the potential problem that individual differences in goal-directed control (e.g. associated with compulsiveness, IQ, age (C. Gillan et al., 2016)) may have hindered our ability to detect changes resulting from anxiety-induction in Experiment 1.

As in Experiment 1, the CO_2 manipulation was effective in inducing anxiety in subjects (Figure 3B and Figure 3C), with a significant increase in self-reported anxiety $F_{(1,49)}$=57.47, p<.001 and heart-rate, $F_{(1,49)}$=10.72, p=.002. However, as in Experiment 1, this did not alter goal-directed performance as CO_2 had no effect on model-based planning (β=-0.03, SE=0.04, p=.44). Bayes factor analysis indicated that there was moderate evidence in favor of the null model over the alternative model that included the acute anxiety manipulation (BF_{01} = 3.5).

The regression model overall fit subjects' behaviour as expected; 'model-free' behaviour was evident in the sample (β =.55, SE=.08, p<.001) which refers to how much subjects tend to repeat actions that were recently rewarded. Model-based learning was also overall significant (β=.28, SE=.06, p<.001), such that subjects took environmental contingency into account when deciding whether or not to repeat a rewarded choice. Finally, subjects showed an overall biased tendency to repeat choices from one trial to the next, regardless of reward or transition information (β=1.59, SE=.12, p<.001). Much like model-based learning, there was no effect of anxiety on model-free learning (β=-0.02, SE=0.03, p=.52), or action repetition (β=-0.08, SE=0.04, p=.060; Figure 4, Supplementary Table S5). Although the latter approached significance such that subjects had a slight tendency to switch choices more while under CO_2. These analyses were complemented with a full computational model (Supplementary Material), with the only difference being that the effect of CO_2 on choice switching was significant in this more comprehensive computational analysis (Supplementary Table S8). Thus, it appears there may be a modest association between acute anxiety and an increased tendency to explore new options from trial to trial.

Individual Differences. Following the same logic as Experiment 1 - that individual differences in sensitivity to CO_2 might be important in revealing the effect of stress on goal-directed behaviour and switching (Otto et al., 2013; Radenbach et al., 2015; Schwabe & Wolf, 2010) - we tested if the effects of CO_2 on model-based planning might be detectible when we take into account how strongly subjects reacted to the CO_2 manipulation. As we were not powered to construct a model with a 4-way interaction (and all subordinate interactions), we extracted individual coefficients for the effect of CO_2 on model-based planning and switching and tested for correlation with subjects' change in self-reported anxiety and heart rate under CO_2. There was no significant correlation between the effect of CO_2 on model-based planning and change in anxiety, r=-.20, p=.16, but there was a marginal association with change in heart rate under CO_2, r=-.29, p=.05. The analogous analysis from the computational model provided less support, where the correlation between change in self-reported anxiety was not significant, r=-.20, p=.18, and nor was the correlation with change in heart rate, r=-.15, p=.30. Bayes factor indicated there was anecdotal evidence for the null with respect to the correlation between changes in self-reported anxiety and model-based planning (regression: BF_{01} = 1.3; computational model: BF_{01} = 1.4). For change in heart-rate, however, there was anecdotal evidence in favour of a relationship with change in model-based planning in the regression analysis (BF_{10}=1.74), but anecdotal evidence in favour of the null from the computational analysis (BF_{01} = 1.9). Nonetheless, the direction of these trends, on the whole, suggested that those subjects whose model-based planning performance declined

the most during CO_2 may have also had the biggest psychological and physiological reaction to the CO_2. However, it is notable that (i) these results go in the *opposite* direction to those in Experiment 1 and (ii) if they exist, they are *very small*. To contextualise these findings in terms of effect size, a sample of N=258 would be needed for future studies to have 90% power to detect an association between change in anxiety and changes in model-based planning under CO_2 using either the regression or computational model. For heart-rate, N=462 would be needed to have 90% power to detect an association with change in the computational modelling parameterisation of model-based planning, and N=119 to detect changes in the regression-defined model-model-based planning.

In contrast to model-based planning, there was a significant main effect of CO_2 on switching. Though not the focus of the present study, we thus repeated the individual difference analysis for switching in an exploratory fashion. We found mixed evidence. There was an association with change in self-report anxiety, where those individuals who were most anxious under CO_2 tended to switch more under CO_2 (regression: r=-.43, *p*=.001; computational model: r=-.29, p=.04). However, the same was not true for change in heart rate (regression: r=-.13, p=.37, computational model: r=-.09, p=.54). There was strong evidence that change in self-reported anxiety correlated with change in switching behaviour under CO_2 in the regression (BF_{10}=25.4), but only anecdotal evidence for this from the full computational model (BF_{10}=2.17). For heart rate, there was anecdotal evidence in favour of the *null* from both analyses (BF_{01} = 2.13 ; BF_{01} = 2.6).

Real life anxiety (Experiment 3). In two independent studies (Experiment 1 and 2) we found no effect of an acute anxiety induction on goal-directed planning. In a final experiment, we tested if anxiety in a real-life, more ecologically valid, setting might be necessary to reveal the hypothesised detrimental effect of anxiety on goal-directed behaviour. We tested 1413 subjects online using Amazon's Mechanical Turk on the model-based learning task described above. Findings relating to the association between compulsivity and model-based planning have been published elsewhere (C. Gillan et al., 2016), but in data not previously published, we enquired about whether subjects had a panic attack in the past week, which is known to induce a temporary state of acute anxiety. We chose to examine panic attacks, rather than using a questionnaire probing state anxiety, because state anxiety has an unacceptably high correlation with trait anxiety when measured in the absence of an acute stressor (e.g. r=.71 (Grös, Antony, Simms, & McCabe, 2007)). As our prior work has demonstrated that trait anxiety is not related to goal-directed planning (C. Gillan et al., 2016), we wanted to ensure that our measure of acute anxiety was not in large part confounded by trait anxiety. Measuring the occurrence of recent panic attacks is an attractive alternative (although not without limitation), because they represent an acute anxiety provoking event (Aronson & Logue, 1988) and as such is more comparable to our lab-based anxiety induction. Criteria for a panic attack were from item 1 of a validated instrument (Panic Disorder Severity Scale, PDSS (Shear et al., 1997)) and in brief required subjects to have experienced 4 of 17 symptoms (e.g. rapid or pounding heartbeat, feeling of choking, nausea, chills or hot flushes, fear of dying) and that the panic attack must have been a "sudden rush of fear or discomfort", peaking within 10 minutes. Episodes like panic attacks that have fewer than 4 symptoms were defined as limited symptom attacks, but also contributed to subjects' score. Specifically, subjects indicated the frequency of panic or limited symptom attacks in the past week on item 1 of the PDSS and this served as our measure for subsequent analyses.

Consistent with other general population samples (Barrera, Wilson, & Norton, 2010), approximately a third (N=474) of our online sample indicated they had experienced a panic or limited symptom attack in the past week (Figure 5A). The frequency of panic attacks in the past week was correlated with reductions in model-based planning (β=-.03, SE =.01, *p*=.012), but this did not survive controlling for "Compulsive Behaviour and Intrusive Thought", a transdiagnostic psychiatric dimension that is negatively correlated with model-based planning (β=-.04, SE=.01, *p*<.001; note this finding was previously published(C. Gillan et al., 2016), which was positively correlated with frequency of panic attacks (r=.42, *p*<.001). Specifically, when compulsivity was accounted for, the effect of panic attacks on model-based planning was reduced to β=-.01, SE=.01, *p*=.33 (Figure 5C). Moreover, results from the more elaborate computational model showed that the effect of panic attacks on goal-directed planning approached zero and went in the opposite direction (β=.003, SE=.01, *p*=.81) after compulsivity was controlled for (Supplementary Table S9).

We observed an association between frequency of panic attacks and choice switching (*p*=.012), mirroring our causal result from Experiment 2. However, the effect of panic attacks on increased switching did not survive inclusion of compulsivity in the model for the one-trial-back regression (*p*=.23), or in the computational model (Supplementary Table S9; *p*=.06).

Finally, we tested if life stress in the past year was associated with deficits in model-based planning. This was assessed using the Social Readjustment Scale (Holmes & Rahe, 1967), which presents an inventory of common stressful life events to participants and asks them to select those that applied to them in the previous 12 months (e.g. death of a spouse, divorce) (Figure 5B). Much like a recent panic attack, we found that life stress scores were linked to failures in model-based planning (β=-.02, SE=.01, *p*=.04). However, as was the case for panic attacks, life stress was also correlated with the compulsive factor (r=.29, *p*<.001), and indeed the relationship to model-based planning did not survive inclusion of the compulsive factor in the analysis. Specifically, the effect of life stress on model-based planning was reduced to β=-.01(SE=.01, *p*=.33; Figure 5D) in the regression analysis and β=-.01, SE=.01, *p*=.24 in the full computational model (Supplementary Table S10).

Discussion

Across three independent experiments, we found little or no evidence that anxiety has a detrimental effect on goal-directed planning. The first two studies employed an extensively validated causal manipulation for inducing an acute state of anxiety, inhalation of air enriched with CO_2 (Argyropoulos et al., 2002; Bailey et al., 2005). Using both between- and within-subject designs, and two well-validated tests for goal-directed behaviour, neither study found evidence that the causal manipulation had an effect on model-based planning. A third study took a correlational, but larger scale (N=1413), approach and tested if frequency of panic attacks in the past week, which are associated with an increase in acute state anxiety (Aronson & Logue, 1988), had poorer goal-directed performance. Unlike most clinical studies, this design incorporated a comprehensive range of clinical assessments and could thus control for clinical confounds such as trait differences in compulsivity. While we found that those who experienced more panic attacks in the past week had greater deficits in

goal-directed planning, this did not survive controlling for compulsivity, a correlated trait that has been extensively studied in the content of goal-directed control failures. Together, these data contribute to a larger literature suggesting that trait (C. Gillan et al., 2016), and now state, anxiety do not have a clear detrimental effect on goal-directed planning.

The most consistent cognitive changes that have been linked to trait anxiety are an increased attentional bias to threat or 'hypervigilance' (Mogg, Bradley, de Bono, & Painter, 1997) and the tendency to interpret ambiguous stimuli as threatening (Eysenck, Mogg, May, Richards, & Mathews, 1991). Results from studies using the 7.5% CO_2 challenge closely mirror these findings – with the manipulation increasing alerting and orienting (Garner et al., 2012), threat processing (e.g. hypervigilance) (Garner et al., 2011) and negative interpretations of neutral events (Cooper et al., 2013), thus suggesting that 7.5% hypercapnic gas manipulation in the lab can mirror cognitive changes observed in association with anxiety. While the putative role that anxiety plays in more complex forms of decision-making is of broad interest (Paulus & Yu, 2012), there is a dearth of evidence suggesting it has effects that are not explained as knock-on effects of increases in threat-sensitivity and vigilance. For example, while there is some evidence to suggest that clinically anxious individuals tend to make better long-term choices e.g. on the Iowa Gambling Task (IGT), this appears to result from a bias to avoid losses, which in the context of this task is confounded with the choice of 'advantageous' decks (Mueller, Nguyen, Ray, & Borkovec, 2010). Even this, however, has been inconsistently shown, with another study finding that high trait anxiety leads to *impaired* IGT performance (Miu, Heilman, & Houser, 2008). One potential explanation for inconsistent results in this area is that studies have been largely cross-sectional and correlational – something the design of the present investigation overcame.

Prior studies have suggested that, in the absence of a main effect, individual differences reveal that stress has some effect on goal-directed behaviour, albeit in a manner dependent on individual differences in sensitivity to the stressor itself (Otto et al., 2013; Radenbach et al., 2015). We repeated this general analytic approach here to facilitate comparison across studies, but the data were equivocal. There was no evidence that physiological sensitivity (i.e. heart rate) to CO_2 was associated with goal-directed behaviour in Experiment 1. Even if not significant the relationship showed, in contrast to previous studies, that physiological sensitivity (i.e. heart rate change) to CO_2 was associated with enhanced performance. Data from Experiment 2 hinted at an opposite trend - diminished performance in individuals that were most sensitive to the manipulation. But notably, evidence was anecdotal and often in favour of the null, depending on whether the measure was computational versus regression-based, and whether the individual difference measure was self-report or physiological. More generally, it is difficult to interpret these effects in any causal framework given the absence of a main effect, such that these associations are driven, in part, by individuals who actually performed nominally *better* under CO_2 (N=22/50 in Experiment 2). Moreover, individual differences in sensitivity to CO_2 is a somewhat problematic measure because it is itself a marker of mental health difficulties (Perna et al., 1996), presenting a confound.

Although no previous studies have examined the effect of acute experimentally-induced state anxiety on goal-directed control, several studies examined the impact of stress (Dias-Ferreira et al., 2009; Heller et al., 2018; Otto et al., 2013; Radenbach

et al., 2015; Schwabe & Wolf, 2009, 2010) in healthy volunteers. Three studies found that stress induced goal-directed deficits (Park et al., 2017; Schwabe & Wolf, 2009, 2010), mirroring findings in rodents following 21 days of unpredictable stress exposure (Dias-Ferreira et al., 2009). Three other studies, however, found no such effect (Heller et al., 2018; Otto et al., 2013; Radenbach et al., 2015). One key point of departure between studies that did and did not see an effect was the type of stressor used. Those that found significant effects used a socially-evaluated cold pressor test, and those that did not used either the cold pressor in isolation (Otto et al., 2013), or a social stress test in isolation (Heller et al., 2018; Radenbach et al., 2015). This distinction is important as the socially evaluated cold pressor test has been shown to induce a much stronger increase in cortisol, compared to cold pressor test alone (Schwabe, Haddad, & Schachinger, 2008), with the procedures otherwise eliciting similar cardiovascular and subjective stress responses. The notion that cortisol might mediate stress effects on goal-directed planning is supported by the observation that changes in cortisol were linked to deficits in performance in studies that failed to otherwise show a main effect of stress (Otto et al., 2013; Radenbach et al., 2015). In other words, the largest increases in cortisol were linked to the largest task deficits. This ties in with pharmacological evidence showing that decrements in goal-directed performance cannot be induced through noradrenergic manipulation alone; concurrent glucocorticoid stimulation is also necessary (although not sufficient) (Schwabe, Tegenthoff, Höffken, & Wolf, 2010, 2012). Differential involvement of cortisol might explain why acute stress appears to have an impact on goal-directed planning, but anxiety induction does not. While acute stress and anxiety induction result in similar cardiovascular effects (i.e. increases in heart rate and blood pressure) (Bailey et al., 2005; Schwabe et al., 2008) and noradrenergic activation (Allen, Kennedy, Cryan, Dinan, & Clarke, 2014; Bailey, Argyropoulos, Lightman, & Nutt, 2003), anxiety induction via 7.5% CO_2 does not result in a reliable increase in cortisol (Oliveira, Chagas, Garcia, Crippa, & Zuardi, 2012; Woods et al., 1988). Hypercapnia causes more pronounced and specific increases in self-reported feelings of anxiousness, fear, panic and worry, which are reduced in response to common treatments for generalized anxiety, including anxiolytics (Bailey, Kendrick, Diaper, Potokar, & Nutt, 2007; Diaper et al., 2012). Therefore, importantly, it is possible that our results are specific to this type of experimental manipulation, mostly targeting anxiety rather than stress induction.

The extent to which more chronic forms of real-life stress impair goal-directed control is an open question and has only been partially addressed in one prior study with a relatively small sample (N=39)(Radenbach et al., 2015). Subjects with high self-reported chronic stress levels had a larger effect of acute stress on model-based planning performance, than their low stress counterparts (Radenbach et al., 2015). This might suggest that goal-directed learning is in some sense more fragile in individuals who have high levels of chronic life stress, but this is difficult to assess as the authors did not report any test for the direct association between life stress and model-based planning. We tested this using a large sample (N=1413) and did not find evidence for an association, after controlling for compulsivity. This suggests that the impact of real-life stress on goal-directed planning, if it exists, is certainly less pronounced than folk wisdom suggests. That said, here we studied goal-directed behaviour, rather than habit expression *per se*, which represents a point of departure from some of the prior research e.g. in rodents (Dias-Ferreira et al., 2009). Further work is needed in this direction as it is possible that any effect of anxiety is on habit expression, and not goal-directed control.

In experiments 2 and 3, there was a suggestion that subjects' tendency to switch their choices from one trial to the next was increased following anxiety induction and the recent occurrence of a panic attack, respectively. These findings were not hypothesised and effect sizes were somewhat inconsistent across analysis methods, but given their consistency with a prior independent study (Radenbach et al., 2015), they warrant brief discussion. One possibility is that this increase in choice switching might reflect the enhanced uncertainty characteristic of anxious states (Grupe & Nitschke, 2013) and could arise as a result of activation of the noradrenergic system (Redmond & Huang, 1979; Yu & Dayan, 2005). Evidence for this comes from work suggesting that tonic noradrenaline release is linked to an increase in task irrelevant processing and a tendency to favour exploration over exploitation (Aston-Jones & Cohen, 2005), characterised by some as a network 'reset' (Bouret & Sara, 2005). This interpretation is limited by the absence of data on cortisol and noradrenaline response and the exploratory nature of the findings. Future research will be needed to test this more directly, using a cognitive test designed to explicitly separate exploration and exploitation.

This study had limitations. Firstly, null results are difficult to draw firm conclusions from. However, the findings of Experiment 3, which benefit from the inclusion of a previously published clinical effect size comparator (the effect of compulsivity on model-based planning), help to place these null findings into a meaningful context. It is unlikely that our manipulation was not strong enough to induce a robust anxiogenic effect because previous studies have demonstrated that the 7.5% CO_2 manipulation is powerful enough to elicit robust effects on behavioural performance relating to threat sensitivity and hyper-vigilance (Cooper et al., 2013; Garner et al., 2011; Garner et al., 2012), in addition to its well-documented physiological and psychological effects (Bailey et al., 2005; Bailey et al., 2007). The magnitude of self-report and physiological changes in the present study were on-par with those observed in prior studies (Cooper et al., 2013; Garner et al., 2011; Garner et al., 2012). Finally, Bayesian analyses detail the extent to which evidence was in favour of the null, and this was in most cases in the 'very strong' range. A second limitation is that using panic attacks to measure 'real world' state anxiety is an imperfect methodology. Although panic attacks are associated with an increase in state anxiety (Aronson & Logue, 1988), they are also associated with, and defined by, a much broader cascade of physical symptoms than the experience of state anxiety. However, this approach has two advantages over measuring self-reported state anxiety (e.g. using the STAI-state scale(Spielberger, Gorsuch, Lushene, Vagg, & Jacobs, 1983)). First, in the absence of an acute event (anxiety trigger), trait and state anxiety scores tend to be highly correlated (e.g. r=.71 (Grös et al., 2007)) and the STAI-scale is thus thought to be more reflective of trait than state anxiety. Second, leveraging naturally occurring panic attacks allowed us to mirror the acute and sudden onset of anxiety that our lab-based procedure achieved.

Conclusions. Experimentally-induced state anxiety failed to produce deficits in goal-directed behaviour as measured via two independent experiments using two well-validated probes. Such lack of effect was also observed in a more ecologically valid set-up, where we used recent panic attacks as a proxy for acute anxiety. While modest decreases in goal-directed planning were seen in individuals who had recent panic attacks in the past year, these effects did not survive when controlling for compulsivity. The same was true of the occurrence of major life stressors in the past

year. In terms of clinical implications, these data suggest that state anxiety has little *specific* effect on goal-directed control, in contrast for example to compulsivity, which research has shown has a consistent association. This distinction may have important implications for the development of differential treatment approaches for patients who present with the same diagnosis, for example of OCD, but differ substantially in their levels of anxiety versus compulsivity. Dimensional approaches that seek to distinguish these dimensions and target them individually present a new frontier for psychiatry research aiming to develop more personalised treatment approaches. For future research studies more generally, these data highlight the necessity of using positive clinical control measures and causal manipulations to ascertain robust and specific associations given a deeply complex and highly inter-correlated mental health landscape.

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LEGENDS

Figure 1. Experiment 1 Study Design – Contingency Degradation Task

A. Contingency degradation task design. In each block, subjects were presented with a white triangle, signalling that they had the opportunity to press or to not press the space bar, in a free-operant, self-paced procedure (Vaghi et al., 2018). The triangle turned yellow (here in grey) when a response was recorded. Rewards (a 25 pence image) were delivered according to a probability, P(O|A), on trials when a response was made, and P(O|-A) when a response was not made.

B. Physiological response to anxiety induction. Heart rate was elevated significantly during the gas condition, $p < .001$. Error bars represent SE.

C. Programmed contingencies. Each participant completed 8 blocks where contingency was systematically varied through changes to P(O|-A). The first two blocks were considered training blocks and appeared in a fixed order as denoted in the table. The 6 remaining test blocks were presented in a counterbalanced order across subjects.

D. Psychological response to anxiety induction. Anxiety scores measures using a visual analogue scale (VAS) were also significantly elevated during the inhalation of gas compared with air, $p < .001$. Error bars represent SE. ***, p<0.001

Figure 2. Results from Experiment 1

A. There was no effect of CO_2-induced anxiety on subjects' sensitivity to instrumental contingency as measured by choice responses, $F_{(3.73,\ 320.59)} = 1.74$, $p = .15$. Error bars represent SE.

B. There was similarly no effect of group on the extent to which causality judgements scaled with instrumental contingency, $F_{(2.99,\ 256.89)} = 0.33$, $p = .81$. Error bars represent SE.

Figure 3. Experiment 2 Study Design – Model-Based Learning Task.

A. On each trial, subjects chose between two fractals, which probabilistically transition to either an orange or blue state (pictured here in greyscale) where they must make another choice. In this schematic, the fractal on the left had a 70% chance of transitioning to the blue state, what is called a 'common' transition, and a 30% chance of transitioning to the orange state, i.e. a 'rare' transition. In the second orange or blue state, subjects again chose between two fractals, each of which was associated with a probability of reward (a pound coin). Unlike the transition structure, these reward probabilities drifted slowly over time (.25 < P< .75). This meant that subjects were required to dynamically track which of the fractals in the orange and blue states were currently best. The reward probabilities depicted (34%, 68%, 72%, 67%) refer to an example trial. Model-based planning on this task is operationalised as the extent to which subjects' decision to repeat an action at the first stage, depend on (i) whether this action was rewarded on the previous trial and (ii) and whether the path from action to outcome was expected ('common').

B. Physiological response to anxiety induction. Heart rate was elevated significantly during the gas condition, $F_{(1,49)}$=10.72, p=.002. Error bars represent SE.

C. Psychological response to anxiety induction. Self-reported anxiety levels were also significantly elevated during the inhalation of gas compared with air, $F_{(1,49)}$=57.47, p<.001. Error bars represent SE. ***, p<0.001

Figure 4. Results from Experiment 2

A. Stay/switch behaviour for subjects in the Air condition as a function of whether or not the last trial was rewarded/unrewarded and followed a rare/common transition. Error bars represent SE.

B. The same plot, showing the group average behaviour under CO_2. In both plots, subjects showed the classic signatures of both model-based and model-free planning, indexed by a significant reward x transition interaction (β=.28, SE=.06, p<.001) and a main effect of reward (β =.55, SE=.08, p<.001). Error bars represent SE.

Figure 5. Results from Experiment 3

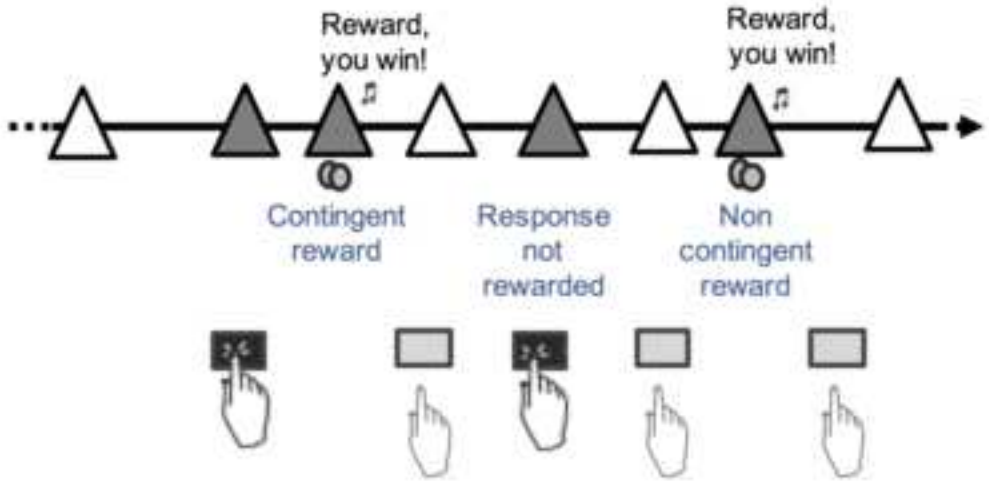
A. Histogram displaying the number of individuals endorsing the various levels of frequency and severity of panic attacks in the past week. Scores were coded as follows: none ("no panic or limited symptom attacks"), mild (no full panic attacks and no more than 1 limited symptom attack/day), moderate ("1 or 2 full panic attacks and/or multiple limited symptom attacks/day"), severe (Severe: more than 2 full attacks but not more than 1/day on average) and extreme ("full panic attacks occurred more than once a day, more days than not").

B. Histogram displaying the distribution of life stress scores in the sample.

C. There was no association between model-based planning and the occurrence of panic attacks in the past week, after controlling for age, gender, IQ and compulsive symptomatology, β=-.01, SE=.01, p=.33. Y-axis displays residuals for model-based planning after these features are taken into account.

D. There was no association between model-based planning and life stress experienced over the past year, after controlling for age, gender, IQ and compulsive symptomatology, β=-.01, SE=.01, p=.33. As above, Y-axis displays residuals for model-based planning

A



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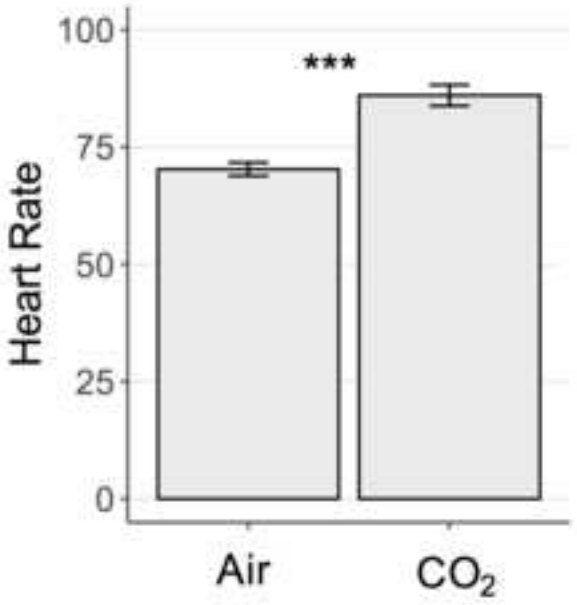
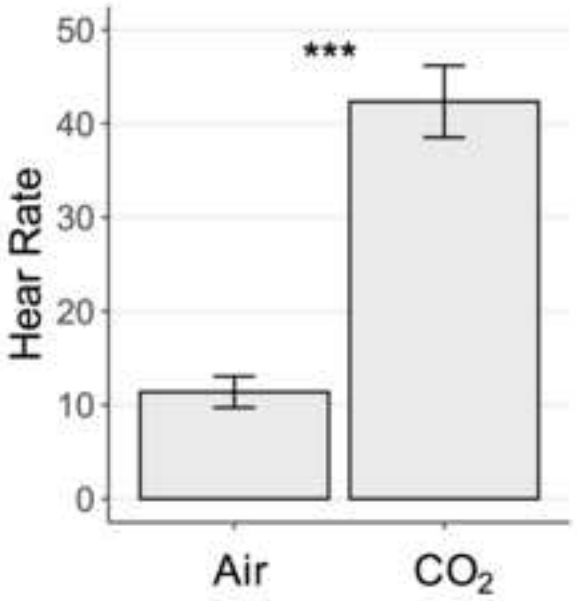
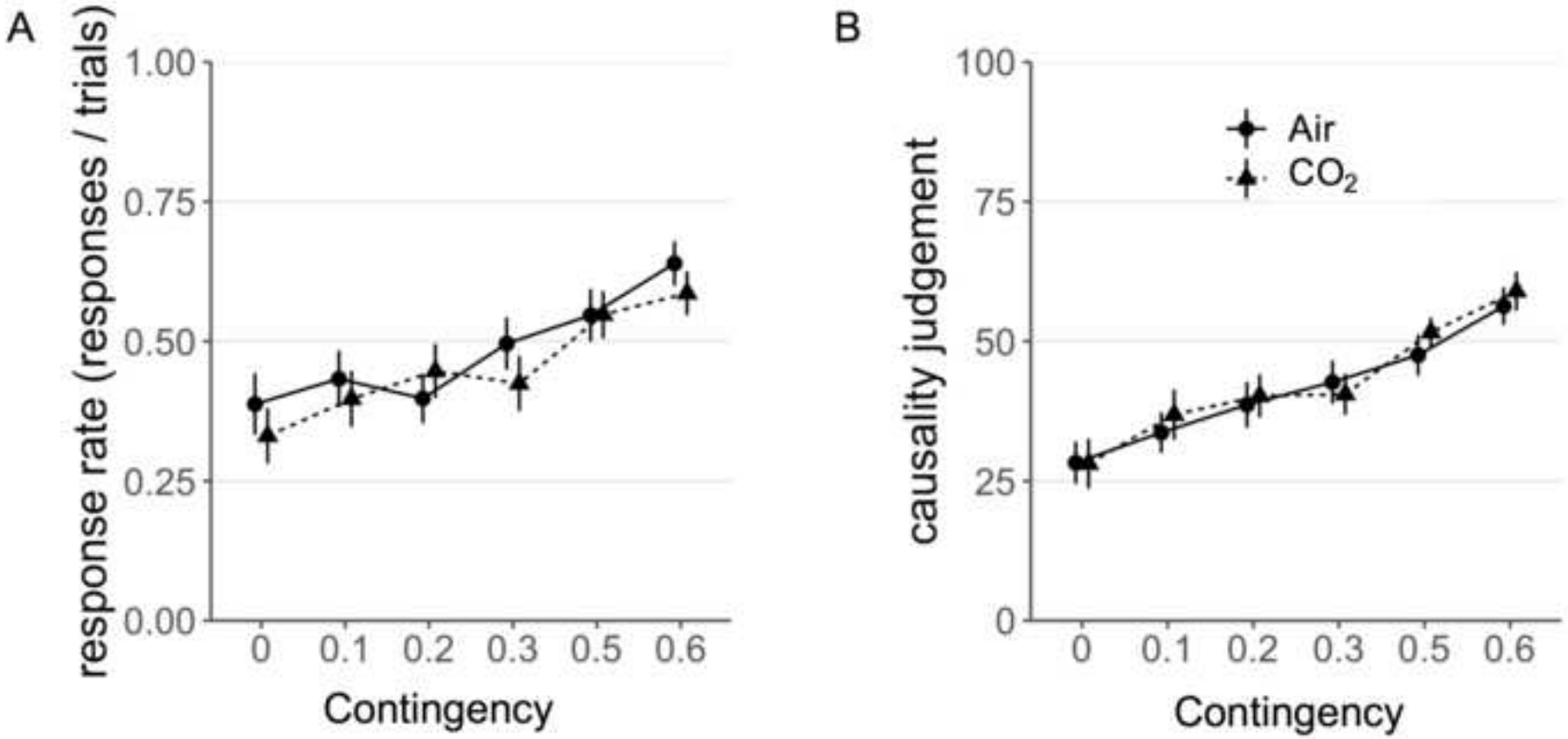


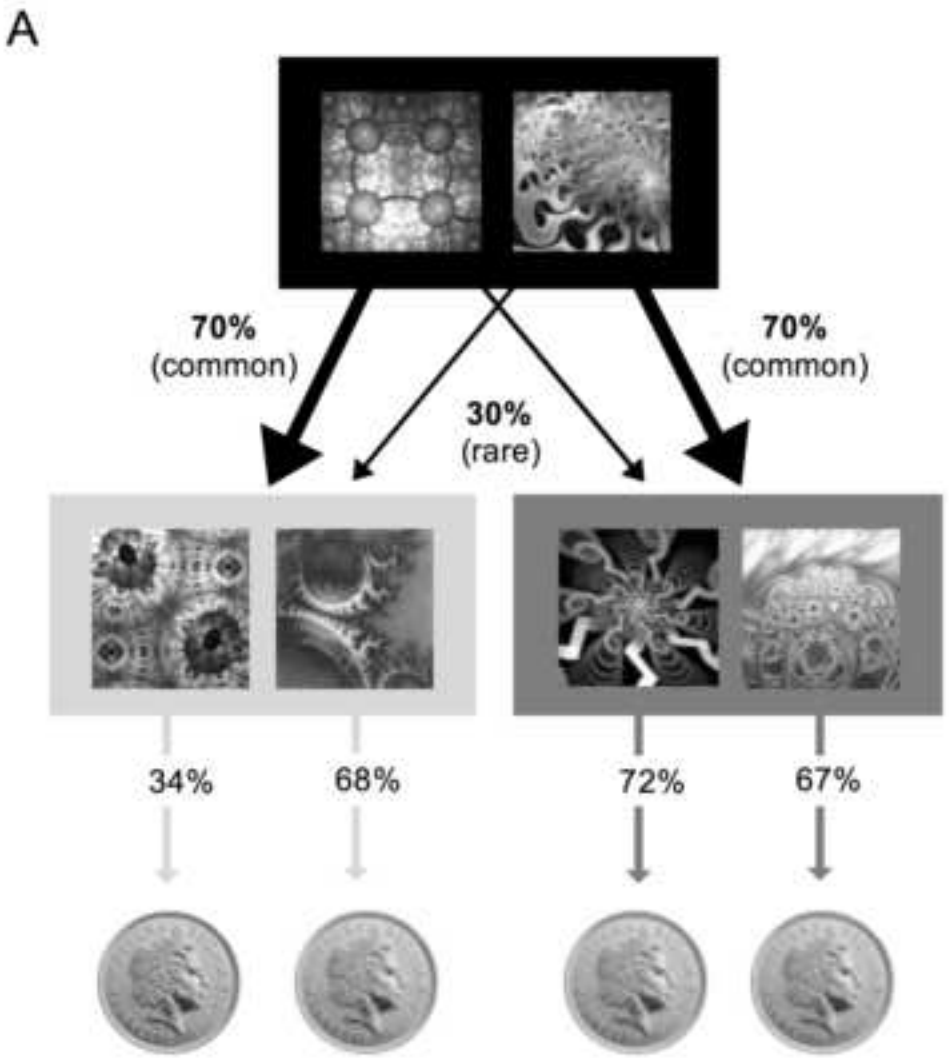
C

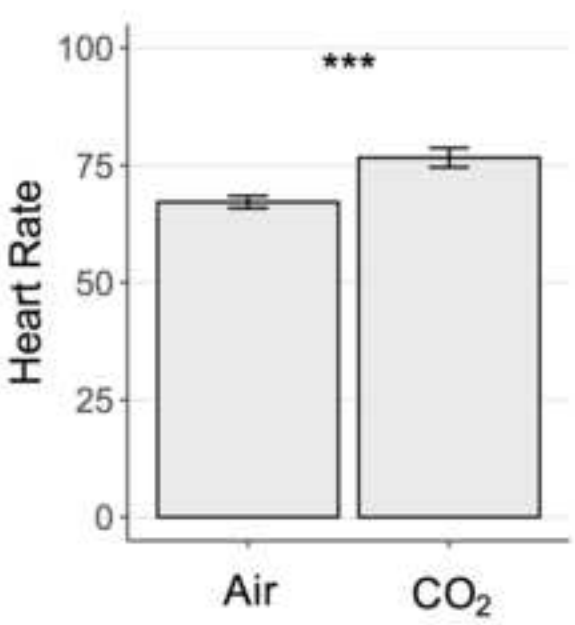
		Programmed contingency		
	Block	**P(O|A)**	**P(O|-A)**	**ΔP**
Fixed Order	1	0.60	0.00	0.60
	2	0.60	0.30	0.30
Shuffled in a Latin square	3	0.60	0.00	0.60
	4	0.60	0.10	0.50
	5	0.60	0.30	0.30
	6	0.60	0.40	0.20
	7	0.60	0.50	0.10
	8	0.60	0.60	0.0

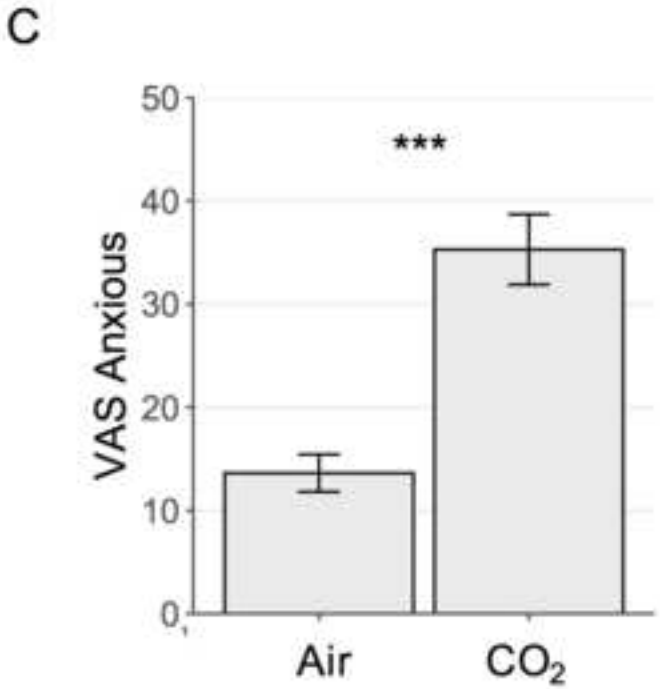
D

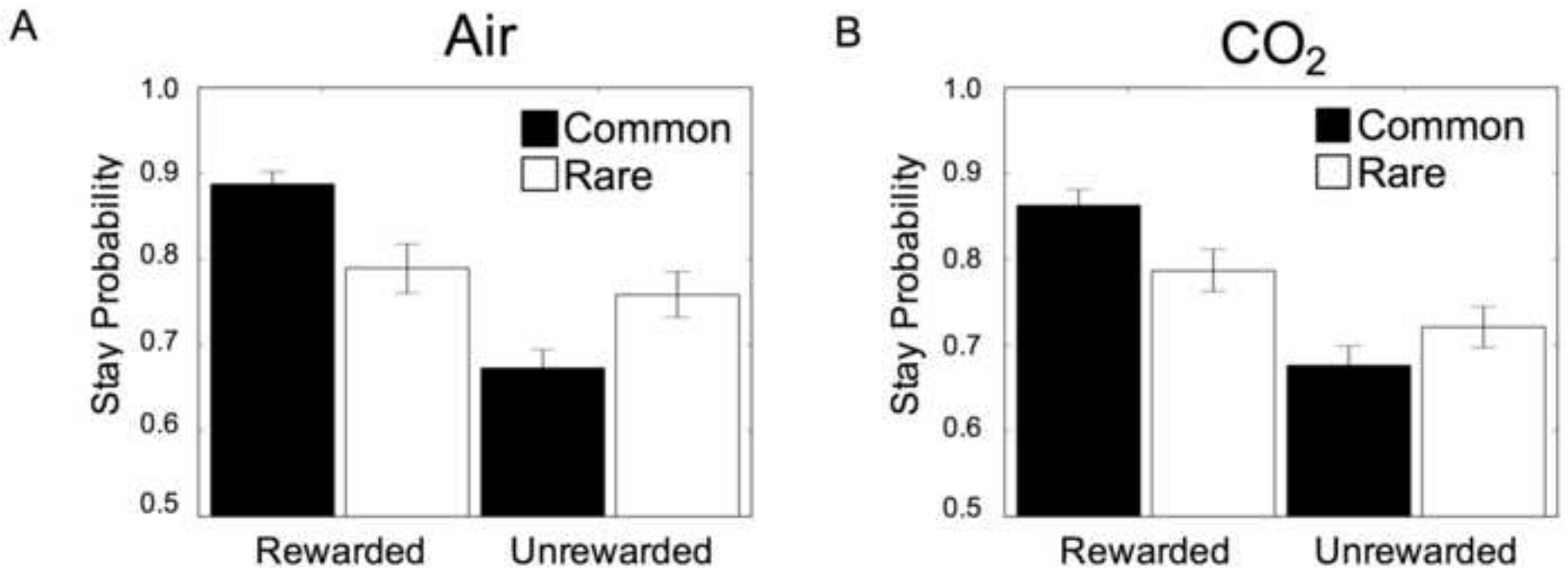












Figure(s)

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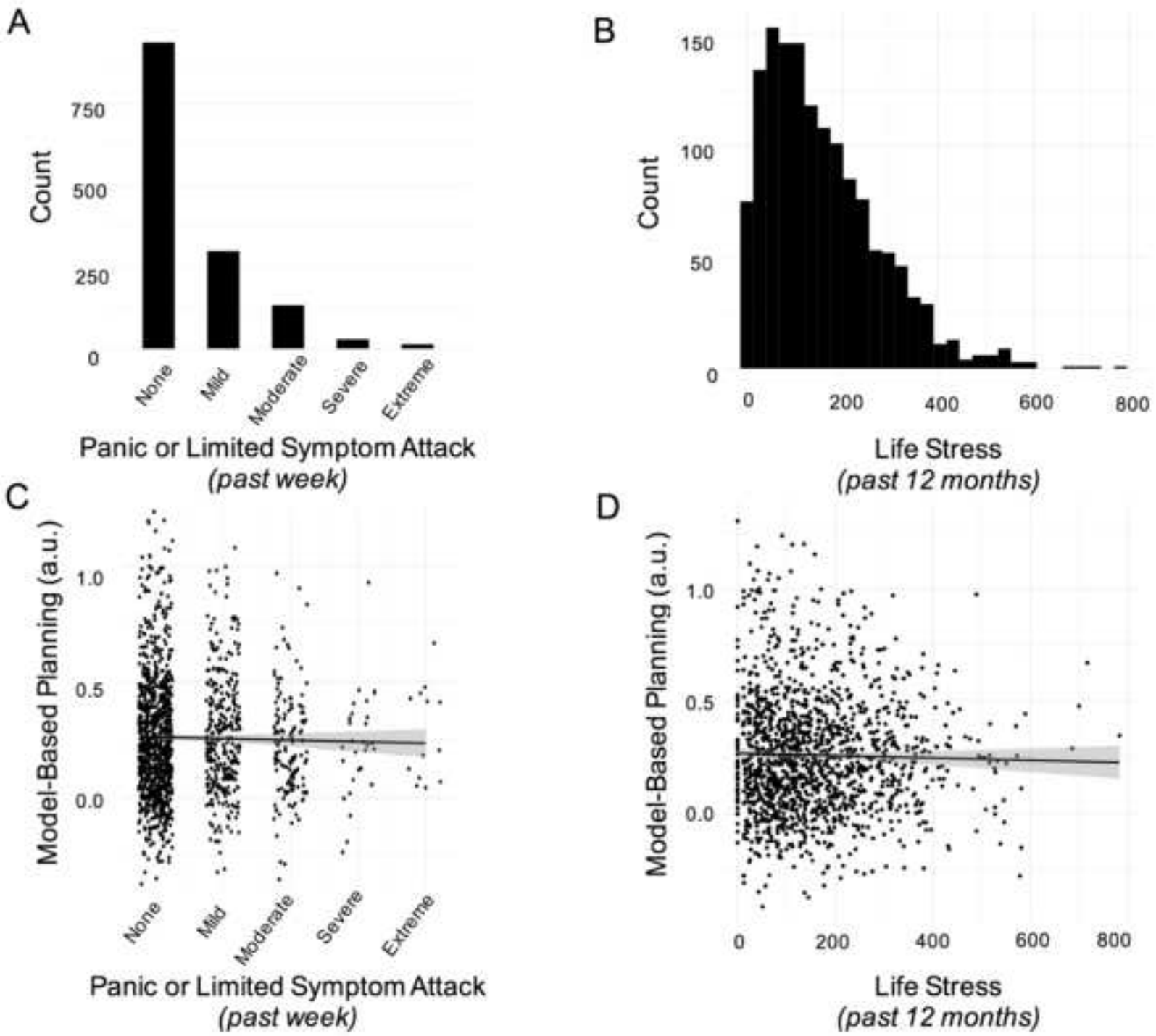

Supplementary Materials for:

Experimentally-induced and real-world anxiety have no demonstrable effect on goal-directed behaviour.

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Experiment 1

Subjects. Recruitment and experimental procedures were approved by the Ethics Committee of the University of Cambridge, School of the Biological Sciences. For subjects included in the experiment, exclusion criteria were screened by a structured telephone interview and were as follows: current or past diagnosis of cardiovascular disease, respiratory disease, thyroid disease, or diabetes; lifetime history of DSM-VI Axis I disorders (Mini International Neuropsychiatric Interview: MINI (Sheehan *et al.*, 1998)); having a first-degree relative diagnosed with panic disorder; (history of) migraine or epilepsy; pregnancy; excessive weekly consumption of alcohol (28 units for males, 21 units for females), excessive daily consumption of caffeine (more than 8 caffeinated drinks per day); current (illegal) drug use; recent history of smoking on a daily basis. Participants were free of regular medication intake, with the exception of oral contraceptives. Invited participants were asked to abstain from alcohol consumption 24 hours prior to the experiment, as well as caffeinated drinks from the midnight before the experiment. Sample size was determined based on a previous study (Schwabe and Wolf, 2010) that found a between-subjects effect of stress on habitual performance with partial eta squared = .07. 88 subjects were required to reproduce an effect of this size with 80% power. Participants were reimbursed for their time and informed consent was obtained prior to participation.

Contingency degradation manipulation. Participants were tested on the ability to detect action-outcome instrumental contingency via the experimental manipulation of contingency degradation. Our index of contingency was the standard ΔP measure indexing the action-outcome instrumental relationship (Dickinson and Balleine, 1994). ΔP was the difference between the conditional probability of outcome given an action [P(O|A)], i.e., the probability of response-contingent outcome; and the probability of receiving an outcome given the absence of an action [P(O|-A)], i.e., the probability of a non-contingent outcome, such that ΔP = P(O|A) - P(O|-A). By increasing non-contingent outcomes, the contingency (i.e., the causal action-outcome association) is degraded. Under these circumstances, individuals who are making decisions in a goal-directed manner should stop or reduce responding in line with the reduction in instrumental contingency.

Contingency degradation paradigm. In a free-operant, self-paced procedure, a white triangle on the screen signalled that the participant was free to press, or not to press, the space bar. On each response, the triangle turned yellow until the end of the *a priori* specified bin to signal that a response has been recorded and to prevent multiple responses within the same 1-second bin. When a reward was delivered, following a key press or not, an image of a 25 pence coin was shown at the end of the bin for 500 milliseconds with the text “Reward, you win!” and a sound. If no outcome was delivered, no feedback was given and the next bin started. Each participant completed 8 blocks where ΔP was

systematically varied (Figure 1B). A running total of money earned within the block was displayed in the corner of the screen and reset to 0 at the beginning of each block. Causality judgments regarding the relationship between pressing the key and receiving the reward were collected at the end of each block. Each block included 140 un-signalled bins, each lasting 1 second. If a response occurred during a given bin, the outcome was delivered with probability P(O|A) defined a priori for that block; if no response occurred, the outcome was delivered with probability P(O|-A) defined a priori for that block. Only the first space-bar press within the bin had any programmed consequences. By varying P(O|A) and P(O|-A), different levels of instrumental contingency were established in each block. In the first 2 blocks, all participants inhaled normal air and the associated programmed contingencies were always presented in the same order (high contingency 0.6, followed by degradation of the contingency to 0.3), providing an implicit training phase. The remaining blocks (test phase) were presented according to a Latin square design for participants in each of the two experimental groups.

Prior to the experiment, the instructions informed the participants that they could earn 25 pence whilst pressing the space bar on a keyboard, and that they were free to press the key as often as they liked. They were further instructed that the relationship between pressing the space bar and receiving the 25p reward would vary during the experiment, and that pressing the space bar might earn a reward, a reward might also arrive on its own, or pressing the space bar might prevent a reward from arriving. Lastly, they were informed that occasionally they would be asked to rate the degree to which pressing the space bar caused the occurrence of the reward.

Table S1: Programmed contingency, experienced contingency, response rate, and causality judgement for each experimental block.

		Programmed contingency			Experienced contingency		Response Rate		Causality judgment	
	Block	**P(O|A)**	**P(O|-A)**	**ΔP**	**Air**	**CO_2**	**Air**	**CO_2**	**Air**	**CO_2**
Fixed Order	1	0.60	0.00	0.60	0.61	0.60	0.54	0.57	58.79	63.19
	2	0.60	0.30	0.30	0.36	0.35	0.42	0.46	40.15	43.84
Shuffled in a Latin square	3	0.60	0.00	0.60	0.60	0.59	0.64	0.59	56.29	58.97
	4	0.60	0.10	0.50	0.52	0.51	0.55	0.55	47.53	51.61
	5	0.60	0.30	0.30	0.30	0.31	0.50	0.42	42.68	40.53
	6	0.60	0.40	0.20	0.21	0.19	0.40	0.45	38.65	40.22
	7	0.60	0.50	0.10	0.07	0.06	0.43	0.40	33.66	36.87
	8	0.60	0.60	0.0	-0.02	-0.03	0.39	0.33	28.27	28.10

P(O|A), probability of the outcome given the action; P(O|-A), probability of the outcome in the absence of the action; ΔP =contingency. Dependent variables are given as mean.

Blocks 1-2 were presented in a fixed order; Block 4-8 were presented according to a Latin square design. Programmed contingency refers to the a priori experimentally programmed contingency resulting from the a priori programmed conditional probabilities. Experienced contingency was computed on the basis of experienced event frequencies.

Psychological and physiological response to stress. Psychological and physiological measures confirmed that participants in the CO_2 condition experienced greater anxiety and stress than those assigned to the Air condition (Figure 1B and 1D). Group means and standard deviations are presented in Table S2 and S3, respectively. Subjective ratings of negative affect increased under CO_2; there were significant group by time interaction effects (all $p < .001$) for the API, the PANAS negative affect subscale, as well as the "fearful" and "anxious" visual analogue scales (Figure 1D). The results for positive affect were mixed; happiness decreased under CO_2 ($p = .004$), but there was no significant difference for the (more extensive) PANAS positive affect subscale ($p = .84$). In terms of autonomic measures of arousal, there were significant group by time interaction effects (all $p < .001$) for heart rate, systolic blood pressure and diastolic blood pressure. As shown in Figure 1B, heart rate and blood pressure significantly increased under inhalation of CO_2 compared to normal air.

Relationship between response rate and causality judgments. As goal-directed control involves the implementation of contingency knowledge into flexible action, we lastly tested the extent to which causality judgments predicted response rate, and whether that might be affected by CO_2-induced anxiety. Overall, response rate was linearly predicted by causality ratings ($F_{(1,\ 96.44)} = 78.18$, $p < .001$), but the slope of this relationship was not significantly different between groups (group by causality judgement interaction effect: $F_{(1,\ 96.44)} = 0.05$, $p = .83$) (Figure 2B). This analysis thus indicated that the linear relationship between subjectively detected instrumental contingency and response rate remained intact in face of an acute anxiety induction. To examine the relative evidence for the null we used Bayes analysis from the 'bmrs' package in R. For this specific model (i.e., mixed models) there is no "default" and we had to set our own priors. We standardized the data and used relatively wide (i.e., 'weakly informative') priors, following recommendations from the 'brms' package documentation (Bürkner ,2017). Specifically, we used normal priors with mean=0 and standard deviation=10 for the fixed effect parameters; half student-t priors with degrees of freedom=3, location=0 and scale=10 for the standard deviation of the random effects; and an LKJ prior with shape=1 for the correlation between random effects. The null model (including only causality judgements) was very strongly preferred over the alternative model with fixed effect of anxiety and anxiety by causality judgement interaction ($BF_{01} = 5882.35$).

Table S2: Means and standard deviations for positive and negative affect by group and time

	Pretest		Test		Post-test	
	Air	CO_2	Air	CO_2	Air	CO_2
API	1.80 ± 2.00	2.88 ± 3.28	2.98 ± 3.69	16.5 ± 8.17	3.10 ± 3.99	4.35 ± 6.05
VAS						
Anxious	17.49± 16.95	18.19± 18.10	11.39± 11.77	42.34± 27.08	13.22± 14.05	16.83± 19.82
Fearful	14.48± 19.15	12.88± 16.22	10.23± 15.12	35.59± 27.52	11.84± 17.76	14.16± 19.70
Happy	63.23± 18.20	53.66± 19.96	54.26± 19.98	34.11± 19.62	59.05± 21.93	52.70± 22.69
PANAS						
Negative	12.67 ± 3.27	12.71 ± 3.23	11.41 ± 2.24	17.28 ± 6.42	12.19 ± 3.48	12.65 ± 4.62
Positive	27.60 ± 7.76	26.95 ± 8.35	22.14 ± 8.30	20.67 ± 7.92	24.43 ± 9.29	23.47 ± 8.64

API, Acute Panic Inventory; VAS, Visual Analogue Scale; PANAS, Positive and Negative Affective Scale. Data show mean and standard deviation.

Table S3: Means and standard deviations for autonomic arousal by group and time

	Pretest		Test		Post-test	
	Air	CO_2	Air	CO_2	Air	CO_2
HR	70.0± 10.4	70.1± 10.5	70.3± 10.0	86.0± 15.8	68.1± 11.1	68.0± 13.2
BP systolic	116.0±13.6	117.7±16.3	115.0±12.3	140.4±22.8	115.2±20.1	123.3±16.7
BP diastolic	69.2± 8.2	71.6± 10.4	70.5 ± 9.9	83.7± 15.8	72.2 ± 9.7	78.5± 11.7

HR, rate rate; BP, blood pressure. Data show mean and standard deviation.

Figure S1

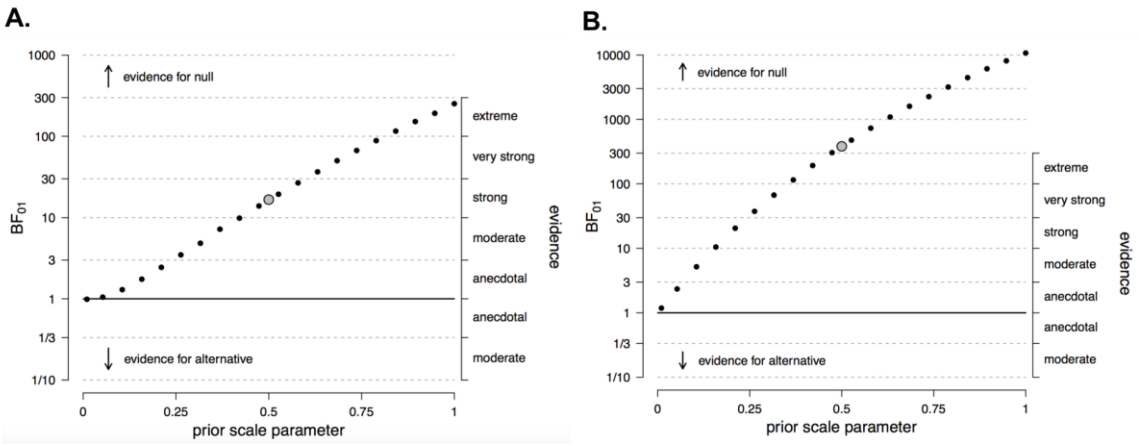

Figure S1. Bayes Factor as a function of the scale parameter of the Cauchy prior for the fixed effects under the alternative hypothesis. The grey dot indicates the result from the default prior (scale parameter = 0.5). As the scale parameter increases (i.e. the prior becomes wider), the Bayes Factor increasingly favors the null hypothesis. Even under the prior setting that most favors the alternative hypothesis (i.e. scale parameter close to zero), the Bayes Factor remains in favor of the null hypothesis, both in the case of response rate (**A**) and subjective causality ratings (**B**).

Supplementary Information for Experiment 2

Subjects. Four subjects aborted the experiment and data were lost from an additional 3. Because of the nature of the analyses, subjects were excluded if their stay/switch behaviour showed such little variation as to preclude a hierarchical model-fit (choosing same response >90% of trials, N=3) or conversely, deviated substantially (>3 SDs) from the mean in the opposite direction (N=1). Sample size was determined based on a previous study (Schwabe and Wolf, 2010) that found a between-subjects effect of stress on habitual performance with partial eta squared = .07. Using a within-subject design, and assuming a .5 correlation across within-subject conditions, we determined that 47 subjects were required to reproduce an effect of this size with 95% power. The study was approved by the same ethics committee as Experiment 1. Participants were reimbursed for their time and informed consent was obtained prior participation.

Reinforcement learning task. On each trial, participants were presented with a choice between two fractals, each of which commonly (70%; see Figure 3A) led to a particular second state displaying another two fractals. These second-state fractals each had some probability (between .25 and .75) of being rewarded with a pound coin. On 30 % of trials ("rare" transition trials; Figure 3A), choices uncharacteristically led to the other state. A purely model-free learner makes choices irrespective of these contingencies (i.e. which action is most strongly linked to which second stage state), and instead focuses on repeating actions that were followed by reward. A model-based strategy, in contrast, is characterized by sensitivity to both reward and the transition structure (contingency) within the task. This means that when a stage 1 action is ultimately rewarded at the end of a trial, a model-based learner will repeat that stage 1 action again, only if the path to reward they took was likely (i.e. involved a common transition). If the path they took to reward was unlikely (involving a rare transition), a model-based subject switches their stage 1 action to promote their chances of returning to that valuable second stage state. The chances that a second stage fractal would be rewarded drifted slowly over time, such that in order to perform optimally, subjects needed to update action preferences dynamically throughout the task.

Before starting the task, participants completed a training session, which comprised written instructions, the viewing of 20 trials demonstrating the probabilistic association between the second stage fractals and coin rewards, and completion of 20 trials of active practice with the probabilistic transition structure of the task. Subjects were then tested for their comprehension of the task with a short quiz (Gillan *et al.*, 2016a) and if they answered any questions incorrectly, these comprehension issues were clarified on-screen. The task consisted of 200 trials in which participants had 2.5 s in which to make a response using the left and right keys following presentation of the first-state choice. If no response was made on time, "no response" were presented on the screen, and the next trial started. If a choice was made, the selected fractal

moved to the top centre of the screen and shrunk in size. A new, second-state fractal appeared in the centre of the screen and was followed by an image of a pound coin or a zero. Subjects completed two counterbalanced versions of the task, with different fractal stimuli and reward drifts. Model-based planning has been previously shown to correlate with sensitivity to outcome devaluation (Gillan *et al.*, 2015), OCD diagnosis (Voon *et al.*, 2014), symptoms (Gillan *et al.*, 2016a), and has been successfully modified using pharmacological manipulations (Wunderlich, Smittenaar and Dolan, 2012; Worbe *et al.*, 2015). As such, it represents an established test of goal-directed planning.

Psychological and physiological response to stress. Under acute CO_2 administration, subjects were more anxious, fearful, and less happy (all p<.001, Table 2). Subjects' scores on the acute panic index (API) also increased (p<.001) under CO_2, as did their heart-rate (p<.001) and blood pressure (p<.001). Subjects also reported more negative affect (p<.001) and less positive affect (p=.029) on the PANAS.

Table S4. Self-report within-subject changes associated with acute CO_2 administration

	Air	**CO_2**	**F**	***p***
	Mean (SD)	*Mean (SD)*		
API	3.6 (4.0)	13.4 (9.0)	64.86	< .001***
PANAS PA	24.6 (8.4)	22.4 (8.9)	5.16	= .03*
PANAS NA	11.5 (2.7)	15.9 (5.1)	55.1	< .001***
VAS anxious	13.6 (12.6)	35.3 (24.0)	57.47	< .001***
VAS fearful	9.4 (9.8)	25.6 (24.1)	35.44	< .001***
VAS happy	51.5 (20.7)	41.6 (22.2)	15.72	< .001***
BP-systolic^	114.8 (15.2)	133.9 (22.2)	74.17	< .001***
BP-diastolic^	73.1(12.0)	81.1(15.3)	15.7	< .001***
HR^	67.2 (9.0)	76.6 (14.4)	25.28	<.001***

SD= standard deviation; API = acute panic index; PANAS= positive and negative affect schedule; PA= positive affect; NA= negative affect' VAS= visual analogue scale; BP= blood pressure; HR= heart rate.
^BP data were missing for 1 subject and HR was missing for 2 subjects.
**** p<.05; **p<.01, ***p<.001***

Detailed Results for Model-Based Task. The regression model fit subjects' behavior as expected, based on the prior literature; there was a significant main effect of Reward (β =.55, SE=.08, p<.001) and a significant Reward x Transition interaction (β=.28, SE=.06, p<.001), providing evidence that, overall, subjects' choices showed signatures of both model-free and model-based processes. The intercept was significant; subjects had an overall tendency to repeat choices from one trial to the next, β=1.59, SE=.12, p<.001) (Table S5). Importantly, CO_2 had

no effect on subjects' tendency to exhibit model-based (β=-0.03, SE=0.04, *p*=.44) or model-free (β=-0.02, SE=0.03, *p*=.52) behavior. There was a non-significant trend for subjects to switch more under CO_2 (main effect of CO_2 condition, β=-0.08, SE=0.04, *p*=.060; Table S5).

Table S5. Results from regression model for Experiment 1

Coefficient	**β (SE)**	***z*-value**	***p*-value**
(Intercept)	1.59(0.12)	12.88	<.001 ***
Reward	0.55(0.08)	6.74	<.001 ***
Transition	0.08(0.04)	1.96	0.05 *
CO_2	-0.08(0.04)	-1.85	0.06
Reward:Transition	0.28(0.06)	4.48	<.001 ***
Reward:CO_2	-0.02(0.03)	-0.65	0.52
Transition:CO_2	0.04(0.03)	1.48	0.14
Reward:Transition:CO_2	-0.03(0.04)	-0.76	0.44

***p*<.05 ** *p*<.01 ***p*<.001**
SE=standard error

Computational Modeling Method

Reinforcement Learning (RL) Model

We used a reinforcement-learning (RL) model based on a hybrid of model-free $Q_{MF}(s_A, a)$ and model-based $Q_{MB}(s_A, a)$, as utilized in previous studies (Sharp *et al.*, 2016; Daw *et al.*, 2011). This model consists of separate model-based and model-free subcomponents, both of which estimate a state-action value function, which maps each possible action to its expected future reward. On trial t, we denote the first-stage state (always s_A) by $s_{1,t}$, the second-stage states by $s_{2,t}$, the chosen first-stage action by a_t, and the second-stage rewards as r_t .

For the model-free algorithm, we used temporal difference (TD) learning (Rummery and Niranjan, 1994), which updates the value for the visited state-action pair at $s_{1,t}$ according to: $Q_{MF}(s_{1,t}, a_t) = Q_{MF}(s_{1,t}, a_t) + \alpha\delta_{1,t}$

where α is a learning rate parameter and $\delta_{1,t}$ is the reward prediction error (RPE) at state 1, trial t:$\delta_{1,t} = Q_{MF}(s_{2,t}) - Q_{MF}(s_{1,t}, a_t)$

The RPE is based on the second-stage value, $Q_{MF}(S_{2,t})$. Second-stage values are themselves updated according to: $Q_{MF}(s_{2,t}) = Q_{MF}(s_{2,t}) + \alpha\delta_{2,t}$

where the RPE at the second stage state, trial t ($\delta_{2,t}$) is determined by whether or not the trial was rewarded, r_t:$\delta_{2,t} = r_t - Q_{MF}(s_{2,t})$

The model assumes that the eligibility trace =1 for all subjects (Sharp *et al.*, 2016), thus propagating second-stage reward information to the first-stage values. At the end of each trial, we decayed the Q values for all of the non-selected actions by multiplying them by 1 − α (Lau and Glimcher, 2005; Ito and Doya, 2009).

The model-based RL algorithm works by learning the transition structure of the task (the state most often visited previously after each top-stage choice) and immediate reward values for each second stage state, then computing cumulative state-action values by iterative expectation over these. At the second stage (where immediate rewards were offered), the problem of learning immediate rewards is equivalent to that for TD above, because $Q_{MF}(s_{2t})$ is just an estimate of the immediate reward r_t; with no further stages to anticipate, and the SARSA learning rule reduces to a delta rule for predicting the immediate reward. Thus, the two approaches coincide at the second stage, and we define $Q_{MB} = Q_{MF}$ at those states. Critically, the top level model-based values are defined from both the transition and reward estimates using the Bellman Equation (Bellman, 1957):

$$Q_{MB}\left(s_A, a_{A_j}\right) = P\left(s_B|s_A, a_j\right) Q_{MF}(s_B) + P\left(s_C|s_A, a_j\right) Q_{MF}(s_C)$$

where we have assumed these are recomputed on each trial from the current estimates of the transition probabilities and rewards. To connect the model-based and model-free values to choices, we use a softmax choice rule, which assigns a probability to each action based on a weighted sum of model-based and model free values (Otto *et al.*, 2013). The probability of each choice at the first stage is calculated, accordingly, as

$$P\left(a_t = a|s_{1,t}\right) = \frac{\exp[\beta_{MB} \cdot Q_{MB}\left(s_{1,t}, a\right) + \beta_{MF} \cdot Q_{MF}\left(s_{1,t}, a\right) + p \cdot rep(a)]}{\Sigma_{a'} \exp[\beta_{MB} \cdot Q_{MB}\left(s_{1,t}, a'\right) + \beta_{MF} \cdot Q_{MF}\left(s_{1,t}, a'\right) + p \cdot rep(a')]}$$

The indicator function rep(a) is defined as 1 if a is the same one as was chosen on the previous trial, zero otherwise. Together with the “stickiness” parameter p, this captures first-order perseveration (p > 0) or switching (p < 0) in the first-stage choices (Lau and Glimcher, 2005). Second-stage choices are modeled with only a single value term$Q_{MF}(s_{1,t}, a)$ with its an inverse temperature β and no stickiness parameter.

This model was embedded within a multi-level random effects model of the population variation in its parameters to estimate it for all subjects simultaneously and to estimate the effect of condition on these parameters, i.e. CO_2 (on/off). This was done identically to Sharp and colleagues (2016), in that the within-subjects effect of CO_2 is a subject-specific latent variable with its own population-level mean and variance, which are themselves inferred. All of the parameters of the model were taken as random effects, instantiated separately for each subject *s* from a common group level distribution. We estimated the parameters of the group level distributions using uninformative priors: for all parameters, the prior means and SDs were the heavy-tailed *Cauchy*(0,2), with the exception of α, where we selected narrower prior distributions so that the sigmoid-transformed parameters were roughly uniform in [0,1] a priori; prior mean and SD were *Normal*(0,1).

We estimated the joint distribution of the parameters of the model, conditional on all subjects' observed choices and rewards. For this, we used Markov Chain Monte Carlo (MCMC) techniques (specifically the No-U-Turn variant of Hamiltonian Monte Carlo) as implemented in the Stan modeling language (v2.5, 2014). Given a probabilistic generative model (the above equations) and a subset of observed variables, MCMC techniques provide samples from the conditional joint distribution over the remaining latent variables. We ran four chains of 4,000 samples each, discarding the first 2,000 samples of each chain for burn-in. We examined the time-series plots of the chains visually for convergence and also computed Gelman and Rubin's (1992) potential scale reduction factors. For this, large values indicate convergence problems, whereas values near 1 are consistent with convergence. We ensured that these diagnostics were less than 1.02 for all variables.

Computational Modeling Results for Experiment 2

Using the complementary computational analysis detailed above, we estimated learning rates and choice stochasticity, in addition to model-based, model-free and exploratory behaviour. This allowed us to test if changes in learning rates and/or choice randomness might explain our findings of increased exploration under CO2. Consistent with the one-trial back regression analysis, CO_2 had a significant effect on stay/switch behaviour only, such that subjects were more likely to switch to a new action under acute CO_2 (Table S7). This does not correspond to more randomness in choice, which is captured by the stochasticity parameter.

Table S6. Group-level estimates of the effect of CO_2(on/off) on each free parameter in the computational model.

Influence of CO_2 (ON/OFF) on Model Parameter Estimates					
	αCO_2	pCO_2	$mbCO_2$	$mfCO_2$	$beta2CO_2$
Upper 95%	0.29	**-0.04**	0.07	0.23	0.12
Median	-0.21	**-0.16**	-0.05	0.08	-0.11
Lower 95%	-0.60	**-0.27**	-0.17	-0.06	-0.35

***α* = learning rate; *p* = perseveration; *mb* = model-based; *mf* = model-free; *beta2* = choice stochasticity.**
For the effect of CO_2 on each parameter, the median posterior estimate is given, together with the 95% confidence intervals. Only the slope of pCO_2 (i.e. the effect of CO_2 on perseveration) is significantly different from zero, such that subjects were more likely to switch choices from trial to trial (i.e. perseverate less) under CO_2.

Experiment 3Subjects. Participants were paid a base rate of $2.50, in addition to a bonus based on their earnings during the reinforcement-learning task (M=$0.54, SD=0.04). This study was approved by the New York University Committee on Activities Involving Human Subjects. These participants are the same as those in a previously published article (Gillan *et al.*, 2016a). Participants provided their consent online after reading the study information in agreement with the requirements of the relevant research committee. Sample size was determined using pilot data N=548 from a prior study (Gillan *et al.*, 2016a) suggesting that to achieve 80-90% power to detect an association between OCD symptoms and model-based planning in an online sample, using a two-tailed test with a significance level of $p<.05$, the sample size should range between N=1223-1637.

Exclusion criteria for online task data. In line with suggestions made for conducting experiments online using Amazon's Mechanical Turk (AMT), *a priori* exclusion criteria were applied to ensure data quality (Crump, McDonnell and Gureckis, 2013). Subjects were excluded if they missed more than 10% of trials (n=62), responded on the same key on more than 95% of trials on which they registered a response (n=85) or had implausibly fast reaction times, i.e. ±2 standard deviations from the mean (n=18). *Clinical Questionnaires Exclusion Criterion:* In an effort to identify participants who were not reading the questions prior to selecting their responses, we included one catch item: "If you are paying attention to these questions, please select "A little" as your answer". Very few subjects failed to select the appropriate response to this catch question; those that did were excluded (n=6). *IQ Test Exclusion Criterion:* Participants who did not answer correctly to any of the IQ questions were excluded from further analysis (n=87). The adaptive character of the test meant that participants

responding incorrectly received increasingly easy items; consistently failing to respond correctly indicates that given participants might have been inattentive or dishonest. In total, 258/1671 (15%) were excluded from this experiment, in line with a previously published report using this dataset. Note that in this dataset, it was also established that the results did not change regardless of the application of these criteria (Gillan *et al.*, 2016b). In addition to these criteria, we also required subjects to score 100% on a brief test that queried their comprehension of the task instructions. If they failed this test, they were required to restart the instructions (and repeat the practice trials) until the 100% criterion was reached.

Panic Attacks and Life Stress. The occurrence of recent panic attacks was assessed using item 1 on the self-report version of the Panic Disorder Severity Scale (PDSS): "How many panic and limited symptoms attacks did you have during the week?". Subjects were provided with a definition of a panic attack: a "sudden rush of fear or discomfort", peaking within 10 minutes accompanied by 4 of 17 symptoms (e.g. rapid or pounding heartbeat, feeling of choking, nausea, chills or hot flushes, fear of dying). Subjects were told that episodes that have fewer than 4 symptoms are 'limited symptom attacks'. Panic attack frequency scores ranged from none ("no panic or limited symptom attacks"), mild (no full panic attacks and no more than 1 limited symptom attack/day), moderate ("1 or 2 full panic attacks and/or multiple limited symptom attacks/day"), severe (Severe: more than 2 full attacks but not more than 1/day on average) and extreme ("full panic attacks occurred more than once a day, more days than not").
In the Social Readjustment Scale, events are weighted in a manner that reflects the relative amount of stress that event causes, with the death of a spouse and divorce being the most stressful and minor violations of the law, major holidays and vacations being the least.

Control Variables. As detailed in a prior report, subjects completed a range of self-report questionnaires that were the topic of a factor analysis in a previously published study (Gillan *et al.*, 2016a), which was subsequently validated in an independent dataset (Rouault *et al.*, 2018). One factor, titled "Compulsive Behaviour and Intrusive Thought", was shown to be highly associated with model-based planning failures in this sample. Scores on this factor were thus controlled, along with IQ, age and gender.

Detailed Results for Model-Based Task and Panic Attacks (past week). Basic results from this task, and its association to compulsivity, age and IQ, have been published in detail elsewhere (Gillan *et al.*, 2016a). The novel results relevant to this study are as follows: one-trial-back regression analysis controlling for IQ, age and gender only, revealed that the frequency of panic attacks in the past week was associated with reductions in model-based planning (p=.012), and also increase in switch behavior (p=.04), but no effect on model-free learning (p=.80). Neither of these significant effects survived inclusion of compulsivity in the model (panic_attack*model-based, p=.33; panic_attack*switching, p=.24).

Table S7. Results from Regression Analysis with Anxiety Attacks

Coefficient	β	SE	*z*-value	*p*-value
model-based * panic attack	**-0.03**	**0.01**	**-2.52**	**.012***
controlling for compulsivity	-0.01	0.01	-0.97	.33
model-free * panic attack	-.005	0.02	-0.25	.80
controlling for compulsivity	.004	0.02	0.223	.82
repetition * panic attack	**-0.07**	**0.04**	**-2.09**	**.04***
controlling for compulsivity	-.04	0.04	-1.19	.23

Detailed Results for Model-Based Task and Life Stress (12 months).

Table S8. Results from Regression Analysis with Life Stress (12 month)

Coefficient	β	SE	*z*-value	*p*-value
model-based * life stress	**-.02**	**.01**	**-2.02**	**.04***
controlling for compulsivity	-.01	.01	-.98	.33
model-free * life stress	-.01	.02	-.74	.46
controlling for compulsivity	-.01	.02	-.46	.65
repetition * life stress	-.02	.03	-.87	.38
controlling for compulsivity	-.01	.03	-.22	.83

Computational Modeling Method for Experiment 3

The computational model proceeded exactly in Experiment 2, except that the within-subject manipulation was absent. We estimated each subject's learning rate, model-based, model-free, perseveration and choice stochasticity parameters and then tested the extent to which these parameters were associated with panic attacks and life stress, after controlling for age, gender, IQ and the compulsive dimension in secondary regression analyses. The general

pattern from the simpler analysis was reproduced with a couple of slight differences. First, the effect of panic attacks on model-based planning was not significant, even without controlling for compulsivity (Table S10). Second, the effect of panic attacks on choice switching (*p*) was significant both when compulsivity was and was-not controlled for (Table S10).

Table S9. Association between having a recent panic attack (Item 1 on PDSS) and parameters in the computational model.

Coefficient	**β**	**SE**	***z*-value**	***p*-value**
learning rate * panic attack	.00	.01	0.25	.81
controlling for compulsivity	.01	.01	0.88	.38
perseveration * panic attack	**-0.05**	**0.02**	**-2.55**	**.01****
controlling for compulsivity	-0.04	0.02	-1.87	.06
model-based * panic attack	-0.02	0.01	-1.62	.10
controlling for compulsivity	-0.00	0.01	0.25	.81
model-free * panic attack	-0.01	0.03	-0.32	.75
controlling for compulsivity	0.01	0.03	0.30	.76
stochasticity * panic attack	-0.03	0.04	-0.66	.51
controlling for compulsivity	-0.04	0.04	0.90	.37

Table S10. Association between Life Stress (12 months) on parameters in the computational model

Coefficient	β	SE	*z*-value	*p*-value
learning rate * panic attack	-0.00	.01	-.02	.98
controlling for compulsivity	0.00	.01	.36	.72
perseveration * panic attack	-0.00	.02	-.18	.86
controlling for compulsivity	0.01	.02	.38	.70
model-based * panic attack	**-0.02**	**.01**	**-2.33**	**.02***
controlling for compulsivity	-0.01	.01	-1.17	.24
model-free * panic attack	-0.02	.02	-0.61	.54
controlling for compulsivity	-0.01	.03	-0.22	.82
stochasticity * panic attack	**-0.08**	**.03**	**-2.43**	**.02***
controlling for compulsivity	-0.05	.03	-1.52	.13

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