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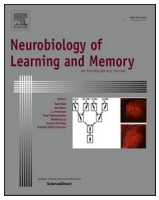

Stress effects on memory retrieval of aversive and appetitive instrumental counterconditioning in men

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ABSTRACT

Extinction training creates a second inhibitory memory trace and effectively reduces conditioned responding. However, acute stress inhibits the retrieval of this extinction memory trace. It is not known whether this also applies to other forms of associative learning such as instrumental counterconditioning, where previously learned associations are reversed and paired with the opposite valence. Therefore, the current preregistered study investigates whether stress decreases the retrieval of instrumental counterconditioning memories with aversive and appetitive consequences. Fifty-two healthy men were randomly assigned to either a stress or control group and took part in a two-day instrumental learning paradigm. During a first phase, participants learned that pressing specific buttons in response to the presentation of four neutral stimuli either leads to gaining or losing money. During a second phase, two stimuli reversed their contingencies (counterconditioning). One day later, participants were exposed to acute stress or a control condition prior to the same task, which no longer included feedback about gains or losses. Stressed participants showed more approach behavior towards appetitive and less avoidance behavior towards aversive stimuli as compared to non-stressed participants. Our findings indicate that stress effects on memory retrieval differ depending on the associative learning approach in men. These differences might be related to stress effects on decision making and different motivational systems involved.

1. Introduction

Acute stress has an impact on all phases involved in memory, such as encoding, consolidation and retrieval (Schwabe and Wolf, 2013; Shields et al., 2017). New associative learning can lead to the formation of second memory traces, for instance during extinction training (Bouton, 1993; Myers and Davis, 2007). Comparable to episodic memory retrieval, acute stress has been shown to reduce extinction memory retrieval (Meir Drexler et al., 2019; Wolf, 2017). However, second memory traces can also be acquired via other forms of associative learning, for example via counterconditioning (Bouton, 1993, 2019; Coutanche and Thompson-Schill, 2012). It remains to be shown whether findings in the field of stress and extinction are transferable to those.

Second memory traces contain a different learning content than first memory traces and compete with them due to different mechanisms such as retroactive interference, context or temporal cues (Bouton, 2019). Consequently, exhibited behavior depends on which of the associations, the first or the second memory trace, is retrieved in a given situation (Craske et al., 2018). Associative learning approaches, such as classical and instrumental conditioning, utilize different ways to establish second memory traces. In classical conditioning, on the one hand, extinction training refers to the omission of a previously associated unconditioned stimulus in the presence of a conditioned stimulus (Myers and Davis, 2007). Counterconditioning, on the other hand, refers to the repeated presentation of a conditioned stimulus with an unconditioned stimulus of the opposite valence (Keller et al., 2020). Thus, counterconditioning can be either appetitive with a subsequent rewarding unconditioned stimulus or aversive with a subsequent punishing unconditioned stimulus. In both approaches, individuals create the conflicting second memory trace that the previously learned first memory trace is no longer valid. However, counterconditioning (in contrast to extinction training) always includes two competing motivational systems, i.e., the approach and avoidance system (Bouton, 1993; Coutanche and Thompson-Schill, 2012; Nasser and McNally,

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2012). Thus, whether individuals exhibit approach or avoidance behavior towards a stimulus depends on which of the previously acquired memory traces is retrieved. Several studies have investigated the effects of counterconditioning on the reduction of previously learned behavior in fear conditioning paradigms (Kang et al., 2018; Keller and Dunsmoor, 2020; Luck and Lipp, 2018; Meulders et al., 2015; van Dis et al., 2019), learned disgust (Engelhard et al., 2014; Kerkhof et al., 2011) or phobia patients (Dour et al., 2016; de Jong et al., 2000) and yielded promising results for basic science and clinical applications (Keller et al., 2020).

Importantly, the establishment of a conflicting second memory trace can also be achieved using instrumental learning approaches (Bouton, 2019; Bouton et al., 2021). Here, a response towards a specific stimulus is reinforced with either appetitive or aversive consequences or no consequences at all. Instrumental counterconditioning, therefore, would be achieved by a subsequent pairing of a response towards a specific stimulus with a consequence of the opposite valence, thus, introducing a decision component to associative learning. Even though the investigation of instrumental learning in the laboratory is of particular importance since it resembles voluntary and adaptive behavior (Bouton, 2019), instrumental counterconditioning has not been a research focus so far.

Considering voluntary maladaptive behavior in mental disorders such as addiction or gambling disorder (e.g., Heinz et al., 2019; Luijten et al., 2020; Perandrés-Gómez et al., 2021) as well as a need for flexibility in rapidly changing environments (e.g., Perandrés-Gómez et al., 2021), adaptive retrieval of new response-outcome associations is crucial in daily life (Fellows, 2018; Heinz et al., 2019). Yet, acute stress has been shown to increase reliance on habitual over goal-directed behavior and lead to perseverative behavior after changes in contingencies (Schwabe and Wolf, 2009, Schwabe and Wolf, 2010). This effect has also been shown when stress was induced before the retrieval of previously learned behavior in a probabilistic classification learning task (Zerbes et al., 2022). However, no study so far investigated the effect of acute stress on the retrieval of reversed contingencies. Therefore, acute stress should be considered in the light of instrumental counterconditioning as well. Regarding the importance of the ability to retrieve updated contingencies outside the learning context in order to transfer them to daily life situations, it is of great value to explore stress effects explicitly on instrumental memory retrieval. For instance, whether individuals would rely on previously learned and non-adapted behavior under stress (e.g., smoking) or whether reinforced adaptive behavior learned during therapy would be exhibited (e.g., chewing gum).

In addition, the Stress Timing affects Relapse (STaR) model suggests that acute stress or the administration of cortisol improves encoding and consolidation, but interferes with retrieval of second memory traces acquired via extinction training, thus, leading to relapse (Meir Drexler et al., 2019). Cortisol is released as a result of the activation of the hypothalamus-pituitary-adrenocortical (HPA) axis in response to acute stress and has been shown to modulate learning and memory processes via acting on the amygdala, hippocampus and prefrontal cortex (de Kloet et al., 1999; Schwabe et al., 2012). Interestingly, these stress effects on extinction memory retrieval have not only been observed for classical fear conditioning (Kinner et al., 2018; Raio et al., 2014), but also for instrumental extinction of learned behavior (Hamacher-Dang et al., 2013; Kinner et al., 2016). In line with this, Bouton (1993, 2019) stated that many findings in the field of classical conditioning are transferable between associative learning approaches that work via retroactive interference by creating second memory traces (classical and instrumental conditioning). This is supported by findings showing the reliance of both classical and instrumental learning on appetitive and aversive prediction errors (PE) signaling the discrepancy between an expected and an observed reward (Abraham et al., 2014; Porcelli et al., 2012; Robinson et al., 2013; Thiele et al., 2021).

Considering the proposed similarities in underlying mechanisms as well as the theoretical transferability between associative learning approaches, the current study investigated whether predictions derived from the STaR model also apply to instrumental counterconditioning. We aimed to explore possible effects of acute stress on the retrieval of a second memory trace learned via instrumental counterconditioning. Therefore, a two-day learning paradigm with monetary reinforcement to specific button-pressing behavior was applied. Participants learned to associate button presses in response to four neutral stimuli with either (1) the loss or gain of money or (2) no changes in balance, while in a second learning phase contingencies were reversed for two stimuli requiring participants to update specific contingencies and associated motivations. After stress induction on a second experimental day, participants conducted the same instrumental task again, while reinforcements were omitted, enabling retrieval of all previously learned contingencies.

Applying the STaR model (Meir Drexler et al., 2019) for stress effects on second memory traces, we hypothesized that acute stress reduces the retrieval of the second memory trace learned via instrumental counterconditioning, leaving stressed participants to rely on non-adapted behavior of the first memory trace. Slightly deviating from our preregistered hypotheses, we added the explanation that the control group is expected to show more signs of successful retrieval of updated contingencies learned during instrumental counterconditioning, indicating goal-directed adaptive behavior to environmental changes. In addition, this effect is expected to be comparably evident for both aversive and appetitive counterconditioning, since the impact of stress on learning and memory appears to be linked to emotional arousal rather than stimulus valence (Wolf, 2009), even though other studies point towards an effect of stimulus valence on memory retrieval (Merz et al., 2019; Shields et al., 2017).

2. Method

All methods were preregistered before data analysis. The preregistration can be retrieved under the following link: https://osf.io/7u2d8.

2.1. Participants

We used the software G*Power (Faul et al., 2009) to predetermine a sample size of 52 male participants in order to detect a medium sized effect of $d = -0.49$ based on the *meta*-analysis by Het et al. (2005). We used a significance threshold of $\alpha = 0.05$ as well as a power of $1\text{-}\beta \geq 0.95$ to find an interaction of the between-subjects factor group and the within-subjects factors valence and reversal. Furthermore, we assumed sphericity as well as a correlation of $r = 0.30$ for repeated measurements. Ultimately, we had to collect data from 60 participants in order to achieve the target sample size. Eight participants had to be excluded, because they failed to reach a preregistered task-based learning criterion (see Section 2.2). Participants were recruited via advertisements at the Ruhr University Bochum and randomly assigned to either a stress or control group (Table 1). Only male participants were recruited due to known sex hormone effects on stress reactivity and cognition (Jentsch et al., 2022; Merz & Wolf, 2017; Shields et al., 2017).

Inclusion criteria consisted of an age between 18 and 40 years, being a non-smoker with a body mass index between 18 and 28 kg/m^2, no reported somatic, endocrine, psychiatric or neurological diseases, normal or corrected-to-normal vision, no regular medication or drug intake as well as no previous participation in studies using the same stress procedure. All participants were screened for the inclusion criteria via telephone beforehand. They were asked to refrain from using dental floss, brushing their teeth, physical exercise as well as eating and drinking anything but water 90 min before the start of the experimental sessions. During both experimental days, participants were additionally asked to refrain from drinking alcohol, taking drugs or exercise excessively. Each participant was tested on two consecutive days at the same time (±1 h). All experimental sessions took place in the afternoon and started between 1 and 5 p.m. in order to control for circadian variations

Table 1
Sample characteristics split for the control and the stress group in means (±SD).

	Control group (n = 26)	Stress group (n = 26)
Age (years)	25.81 ± 4.59	24.85 ± 4.58
Body mass index (kg/m²)	23.72 ± 1.92	24.58 ± 2.56
rRST-Q		
BAS	3.00 ± 0.39	3.00 ± 0.61
BIS	2.49 ± 0.35	2.24 ± 0.53
Fight	2.64 ± 0.48	2.85 ± 0.64
Flight	2.24 ± 0.54	2.14 ± 0.65
Freeze	2.24 ± 0.40	2.05 ± 0.46
BFI-K		
Openness	3.88 ± 0.83	4.03 ± 0.70
Extraversion	3.20 ± 0.73	3.42 ± 1.11
Conscientiousness	3.36 ± 0.72	3.52 ± 0.70
Agreeableness	3.10 ± 0.76	2.75 ± 0.59
Neuroticism	2.95 ± 0.69	2.61 ± 0.94
TICS		
Work overload	10.46 ± 6.56	10.88 ± 7.42
Social overload	6.04 ± 4.30	8.00 ± 5.15
Pressure to perform	12.08 ± 5.66	14.46 ± 6.99
Work discontent	14.58 ± 7.79	12.62 ± 5.80
Excessive demands at work	6.69 ± 3.93	6.85 ± 4.74
Lack of social recognition	4.65 ± 3.14	3.88 ± 2.55
Social tension	3.96 ± 3.59	7.27 ± 4.62
Social isolation	8.35 ± 6.16	9.16 ± 5.54
Chronic worrying	6.50 ± 3.97	6.38 ± 3.53
ACQ Total win (ct)	59.23 ± 66.09	40.77 ± 64.37
Counterconditioning Total win (ct)	91.54 ± 61.75	81.54 ± 62.72

Note. Independent sample t-tests were conducted to test for group differences on each variable. All tests were Bonferroni-corrected to account for multiple testing. No significant differences emerged. rRST-Q = revised Reinforcement Sensitivity Theory Questionnaire, BAS = behavioral activation system, BIS = behavioral inhibition system, BFI-K = short version of the Big Five Inventory, TICS = Trier Inventory for the Assessment of Chronic Stress, ACQ = acquisition.

in cortisol concentrations (Shields et al., 2017; Shields, 2020).

All participants were reimbursed for participation with 20€ at the end of the second experimental session. Depending on the performance in the instrumental counterconditioning task, participants were able to additionally gain up to 4€ (see Section 2.2). The participants were informed that losing money in the instrumental counterconditioning task did not affect their reimbursement of 20€ at the end of the experiment, but only the amount of additional money. Wins during counterconditioning were cleared with losses during acquisition, but losses during counterconditioning were not cleared with wins during acquisition. Wins of the first day were not affected by task performance on the second day. The exact amount of money was calculated at the end of the experiment. The study was approved by the ethics committee of the Faculty of Psychology within the Ruhr University Bochum (application nr. 306) and conducted in agreement with the Declaration of Helsinki.

2.2. Instrumental counterconditioning task

The instrumental counterconditioning task was written in MATLAB (version 2018b) using the Psychophysics Toolbox (Brainard, 1997; Kleiner et al., 2007; Pelli, 1997) and the OTBR Toolbox (Rose et al., 2008). Four different geometrical shapes were randomly assigned to be associated with positive or negative consequences (Spos and Sneg) and whether their valence would be reversed during counterconditioning (Sposrev and Snegrev; Fig. 1a). The order of the assignments of stimuli was counterbalanced between participants.

The instrumental counterconditioning task consisted of three phases: acquisition, counterconditioning and retrieval. In each phase, stimuli were presented to the participants on a computer screen (with approximately 60 cm between computer screen and participant). During each phase, the order of stimulus presentations was pseudo-randomized in eight blocks. Each block consisted of one trial for each stimulus in order to ensure that each stimulus would be presented once before the start of a new trial. In sum, every phase consisted of 32 stimulus presentations (i.e., 8 presentations of each stimulus).

Pressing the down arrow key in response to a stimulus presentation did not lead to any changes in balance in any phase (referred to as safety key). The left arrow key led to either a gain or a loss of 20 cent, depending on the learning phase and associated contingencies (referred to as risk key). During acquisition, pressing the risk key could lead to a gain of money for Spos and Sposrev and a loss of money for Sneg and Snegrev. During counterconditioning, the risk key could lead to a gain of money for Spos and Snegrev and a loss of money for Sneg and Sposrev. Thus, contingencies reversed between both phases for Sposrev and Snegrev, but not for Spos and Sneg (Fig. 1a).

During acquisition and counterconditioning, a partial reinforcement rate was applied, leading to changes in balance after pressing the risk key in 62.5 % of trials (i.e., five out of eight stimulus presentations). The reinforcement schedule was pseudo-randomized in order to make sure that each stimulus was reinforced in the first and last block. During the remaining six blocks, each stimulus was reinforced with a rate of 50 %. During retrieval, stimuli were presented in eight blocks again, while participants did not receive reinforcements or any informative feedback upon keypresses and no money could be won or lost. However, instructions did not change for retrieval.

In every phase, each stimulus presentation was followed by a flash white square upon which participants were asked to press either the left arrow key or the down arrow key on the computer keyboard as fast as possible. Participants were not informed about the different functions of the specific keys (i.e., risk vs safety key). After pressing the risk key, participants received feedback about potential gains or losses as well as their actual balance (Fig. 1b). After pressing the safety key, participants were informed that their balance did not change. Participants were instructed to maximize their total gain. In order to make sure that participants received enough feedback on a stimulus presentation to learn the given contingencies, a preregistered task-based exclusion criterion was applied: participants were excluded in case they did not press a key at least twice per stimulus either during acquisition or counterconditioning.

Each phase of the instrumental counterconditioning task was followed by a contingency questionnaire where participants were asked to reproduce the contingencies of each stimulus ("-20ct", "+20ct" or "don't know") to add an episodic memory component. After retrieval, participants were asked to additionally reflect on the strategy used during retrieval in the form of an open question as well as a subsequent multiple-choice question ("I responded in accordance with the contingencies of the first learning phase", "I responded in accordance with the second learning phase", "I tried a new response scheme", "I did not apply a specific strategy"). Results on strategy selection can be accessed in the supplemental material (section 3.a).

2.3. Stress and control procedure

In order to induce stress, the socially evaluated cold-pressor test (SECPT) was conducted (Schwabe et al., 2008). Participants in the stress group were asked to put their dominant hand for three minutes in a basin with ice cold water (0–4 °C) while being observed by a neutral female research assistant and videotaped for later evaluation. Participants in the control group were asked to put their dominant hand for three minutes in a basin with warm water (36–37 °C). They were neither observed nor videotaped.

As an indication of the activation of the sympathetic nervous system, blood pressure and pulse were measured (Dinamap Vital Signs Monitor, Critikon, Tampa, FL, USA) three times before, three times during and three times right after the stress/control procedure. For analyses, the means of blood pressure and pulse measurements for each of the three time points were calculated.

After the procedure, participants were asked to rate their experiences

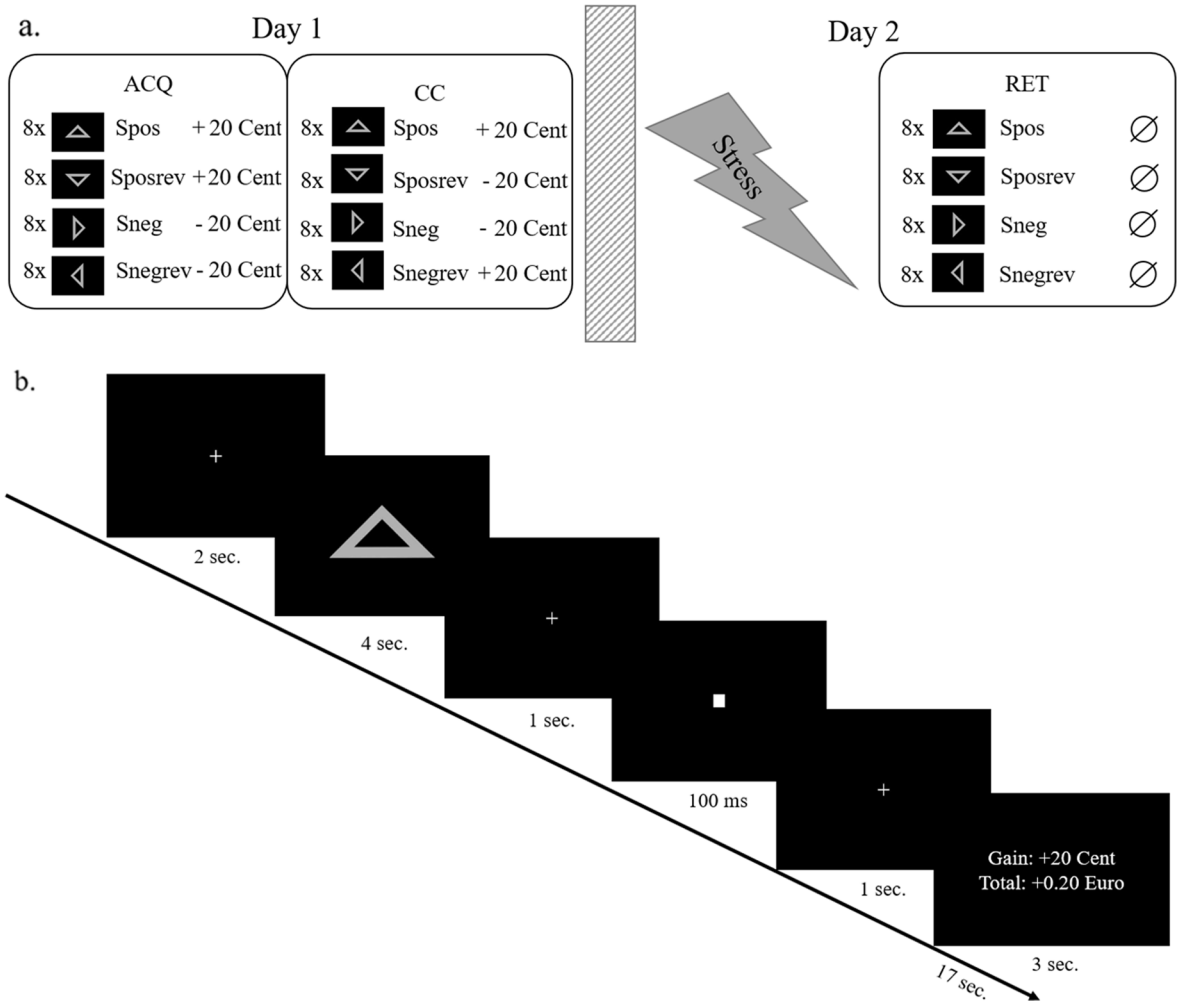

Fig. 1. Design of the instrumental counterconditioning task. a. Timeline of the experimental paradigm. The learning phases acquisition (ACQ) and counterconditioning (CC) took place on day 1. During ACQ, participants learned to associate four test stimuli with either appetitive or aversive consequences. Four gray triangles pointing to different directions (i.e., left, right, up and down) on a black background were randomly assigned as either leading to a gain of 20 cent (Spos and Sposrev) or a loss of 20 cent (Sneg and Snegrev). During CC, two stimuli reversed contingencies (Sposrev and Snegrev). On day 2, half of the participants were stressed or took part in a control condition before conducting the retrieval (RET) phase. During RET, the same stimuli were presented to the participants, however, no feedback about contingencies was given. b. Sequence of a single trial. Upon presentation of the flash white square, participants were asked to press the left or down arrow key on a computer keyboard as fast as possible. During ACQ and CC, only a left (i.e., risk) keypress could lead to changes in balance according to stimulus contingencies. Pressing the down (i.e., safety) key did not lead to any changes in balance.

in terms of difficulty, unpleasantness, stressfulness and painfulness on a scale from 0 ("not at all") to 100 ("very much"). The rating method was adopted from Schwabe et al. (2008).

2.4. Saliva sampling and analysis

In order to assess free salivary cortisol concentrations as a marker of the activation of the HPA axis as well as salivary alpha amylase (sAA) concentrations as an indirect marker of activation of the sympathetic nervous system (Ali and Nater, 2020; Nater and Rohleder, 2009), saliva was sampled using Salivette sampling devices (Sarstedt, Nümbrecht, Germany). On day 1, two saliva samples were collected (at the beginning and at the end of the experimental session). On day 2, four saliva samples were collected (5 min before the start of the stress/control procedure as well as 5, 20 and 35 min after the start of the stress/control procedure). All samples were stored at −20 °C until analyzed.

Enzyme-linked immunosorbent assays (ELISA; IBL International GmbH, Hamburg, Germany) were used on a Synergy2 plate reader (Biotek, USA) to measure free cortisol concentrations with inter- and intra-assay variations below 9 %. sAA was analyzed using colorimetric tests and 2-chloro-4-nitrophenyl-α-maltrotriosoide (CNP-G3) as a substrate reagent (Lorentz et al., 1999). Intra- and inter-assay variabilities were below 8 %.

2.5. Questionnaires

Assuming that certain personality traits might influence task performance, three additional questionnaires were given to the participants and used for a randomization check (Table 1).

The German version of the revised Reinforcement Sensitivity Theory Questionnaire (rRST-Q; Reuter et al., 2015) assesses behavioral activation (8 items), behavioral inhibition (11 items) as well as fight, flight and freeze responses (12 items) on a four-point Likert scale ranging from "strongly disagree" to "strongly agree".

The German version of the short version of the Big Five Inventory (BFI-K; Rammstedt and John, 2005) assesses the personality traits openness to experience (5 items), conscientiousness (4 items), extraversion (4 items), agreeableness (4 items) as well as neuroticism (4 items) on a five-point Likert scale ranging from "strongly disagree" to "strongly agree".

The Trier Inventory for the Assessment of Chronic Stress (TICS; Schulz and Schlotz, 1999) consists of 57 items assessing how often specific stressful experiences occurred within the last three months on a five-point Likert scale ranging from "never" to "very often". Nine aspects of chronic stress are assessed: work overload, social overload, pressure to perform, work discontent, excessive demands at work, lack of social recognition, social tension, social isolation and chronic worrying.

Exploratory correlation analyses of these questionnaire data with task performance did not reveal any significant associations.

2.6. General procedure

Upon arrival, participants were seated in a chamber in front of a computer screen, informed about the experimental procedure and asked to give written informed consent. Afterwards, participants filled in a demographic questionnaire as well as the rRST-Q and gave the first saliva sample. Then, they were instructed on the acquisition and counterconditioning phases in one task instruction stating that contingencies might change between learning phases. After each phase, participants filled in contingency questionnaires. The second saliva sample was collected after counterconditioning.

On day 2, the first saliva sample and the first three measurements of blood pressure and pulse were taken upon arrival. Afterwards, participants were informed about either the following stress or control procedure. For the stress procedure, participants gave written informed consent about being videotaped during the SECPT for later evaluation. Then, participants were guided into a neighboring chamber. For the stress group, a female research assistant entered and conducted the stress procedure. For the control group, no additional research assistant was present. Afterwards, participants were guided back to the first chamber in front of the computer screen where they rated the stress/control condition and gave the second saliva sample of day 2. Then, they filled in the BFI-K and TICS. 20 min after the stress/control procedure, they were asked to give the third saliva sample and instructed on the retrieval phase. After finishing retrieval, participants again filled in the contingency questionnaire, gave the fourth saliva sample and were reimbursed for participation.

2.7. Statistical analyses

For all statistical tests, significance levels were set to $\alpha = 0.05$. In case of violations of the normality assumption, non-parametric alternatives were applied. Greenhouse-Geisser corrections for violations of sphericity were applied where appropriate. In addition, Bonferroni correction was used to account for multiple testing were applicable. The following packages were applied in R (R Core Team, 2021) version 4.1.0: "tidyverse" (Wickham et al., 2019), "haven" (Wickham and Miller, 2021), "jtools" (Long, 2020), "sandwich" (Zeileis et al., 2020), "lmtest" (Zeileist and Hothorn, 2002), "sjPlot" (Lüdecke, 2021), "MASS" (Venables and Ripley, 2002), "car" and "effects" (Fox and Weisberg, 2019), "afex" (Singmann et al., 2021), "DescTools" (Signorell, A. e. a., 2021), "Rmisc" (Hope, 2013), "rstatix" (Kassambara, 2021), "describedata" (McGowan, 2019), "psych" (Revelle, 2021) and "nparLD" (Noguchi et al., 2012).

Questionnaire data was scored as indicated in the manuals. Independent samples t-tests were conducted to test for successful randomization on age, body mass index, BIS, BAS, FFFS, TICS and BFI-K scores (Table 1).

Due to violations of the normality assumption, salivary cortisol and sAA concentrations were analyzed using a non-parametric alternative to a mixed ANOVA (Noguchi et al., 2012). All preregistered analyses of the stress response can be accessed in the supplemental material (section 1.a). Time (day 1: before vs after the learning phases; day 2: 5 min before as well as 5, 20 vs 35 min after the SECPT) was included as a within-subjects factor and group (stress vs control group) as between-subjects factor. Blood pressure and pulse measures were averaged for each time point and analyzed using mixed ANOVA or a non-parametric alternative, in which case ANOVA-type statistics (ATS) are reported, with the within-subjects factor time (before, during vs after the SECPT) and the between-subjects factor group.

Independent samples t-tests or Mann-Whitney-U-Tests for each time of measurement were conducted as post-hoc analyses of salivary cortisol and sAA as well as blood pressure and pulse.

Stress ratings on difficulty, painfulness, stressfulness and unpleasantness were analyzed using the Mann-Whitney-U-Test due to non-normal distributions.

For the analysis of the instrumental counterconditioning task, all preregistered analyses were run and can be accessed in the supplementary material (section 1.b-1.d). In the preregistered analyses, the dependent variable was treated as a continuous variable, while actually the participants only had the options to press the risk or safety key in each trial, which constitutes a binary dependent variable. Therefore, statistical analyses were adapted to account for the binomial data distribution.

The dependent variable was defined as risk keypress (1) or not (0) in each trial. Logistic regressions with cluster robust standard errors for participants and trials (Mansournia et al., 2021) were calculated to investigate changes in risk keypresses over trials and simultaneously account for repeated measures. For the first trial of retrieval, a separate logistic regression model was calculated clustered for participants to investigate spontaneous retrieval of previously learned information without the influence of additional retrieval trials without feedback information. In order to explore possible confounding by other variables, each logistic regression was calculated including all three predictors: valence (positive vs negative), reversal (not reversed vs reversed) and stress (control vs stress group). For all analyses, valence was coded 0 = positive and 1 = negative, reversal as 0 = not reversed and 1 = reversed as well as stress as 0 = control group and 1 = stress group. All models were improved using stepwise backwards exclusion on the basis of the Akaike information criterion (AIC) in order to estimate the prediction error of the models until the best fit for the data was found (Field, 2018; Ranganathan et al., 2017).

All analyses of the instrumental counterconditioning task were repeated with the safety keypresses or no responses (1 = yes, 0 = no) as dependent variable (see supplemental material section 2). Analyses of the retrieval phase only were repeated restricted to cortisol responders in the stress group and non-responders in the control group (see supplemental material section 1.e).

3. Results

3.1. Stress induction

According to endocrine, physiological as well as subjective data, stress induction via the SECPT was successful (Table 2). On day 1, cortisol concentrations declined from the beginning to the end of the experiment (main effect time: $ATS_{(1)} = 10.30$, $p < .01$), reflecting the circadian cortisol rhythm. On day 2, stress led to increased cortisol concentrations over time (main effect group: $ATS_{(1)} = 6.49$, $p = .01$; main effect time: $ATS_{(1.79)} = 8.81$, $p < .001$; time*group interaction: $ATS_{(1.79)} = 13.48$, $p < .001$). In particular, stress led to higher cortisol concentrations 20 min ($W = 147, p < .001$) as well as 35 min ($W = 141, p < .001$) after the stress/control procedure, but not at baseline or 5 min after stress onset ($p > .3$).

sAA concentrations decreased from the beginning to the end of the experiment on day 1 (main effect time: $ATS_{(1)} = 10.45, p < .01$) as well as on day 2 ($ATS_{(2.26)} = 12.25$, $p < .001$). However, post-hoc paired Wilcoxon tests did not reveal significant differences regarding which sAA concentrations were different from each other over time on day 2 (all $p > .1$).

Stress also led to both increased systolic and diastolic blood pressure as compared to the control procedure (systolic blood pressure: main

Table 2
Stress measures split for the control and the stress group in means (±SD).

	Control group (n = 26)	Stress group (n = 26)
Salivary cortisol (nmol/l)		
Day 1		
Baseline 1	3.92 ± 2.55	4.41 ± 2.12
Baseline 2	3.21 ± 1.85	3.83 ± 2.36
Day 2		
Baseline	2.90 ± 1.31	3.45 ± 1.97
+ 5 min.	2.92 ± 1.29	3.22 ± 1.54
+ 20 min.	2.87 ± 1.27	7.22 ± 5.90 ***
+ 35 min.	2.53 ± 1.07	6.25 ± 5.45 ***
Salivary alpha amylase		
Day 1		
Baseline 1	150.38 ± 83.75	185.00 ± 164.65
Baseline 2	128.61 ± 73.67	157.43 ± 131.40
Day 2		
Baseline	165.66 ± 104.41	170.29 ± 112.24
+ 5 min.	136.03 ± 79.56	161.37 ± 110.19
+ 20 min.	118.78 ± 75.80	143.04 ± 92.60
+ 35 min.	123.75 ± 68.61	136.38 ± 77.22
Systolic blood pressure (mmHg)		
Baseline	115.49 ± 10.87	122.01 ± 13.98
During procedure	111.25 ± 9.93	139.09 ± 14.32 ***
After procedure	112.87 ± 10.95	126.05 ± 14.34 ***
Diastolic blood pressure (mmHg)		
Baseline	63.12 ± 8.32	66.58 ± 8.23
During procedure	60.57 ± 9.26	79.87 ± 9.74 ***
After procedure	60.95 ± 8.07	67.18 ± 9.60 *
Pulse		
Baseline	72.73 ± 8.71	71.46 ± 10.43
During procedure	71.87 ± 9.60	74.22 ± 11.15
After procedure	71.84 ± 8.42	67.59 ± 8.65
Ratings after procedure		
Difficulty	1.54 ± 4.64	60.38 ± 28.77 ***
Unpleasantness	2.69 ± 5.33	58.46 ± 27.81 ***
Stress	1.92 ± 4.91	46.54 ± 27.41 ***
Pain	0.77 ± 2.72	65.77 ± 26.41 ***

Note. *$p < 0.05$, ***$p \leq 0.001$.

effect group: $F_{(1.49)} = 22.65$, $p < .001$; main effect time: $F_{(1.97,96.53)} = 25.10$, $p < .001$; time*group interaction: $F_{(1.97,96.53)} = 60.33$, $p < .001$; diastolic blood pressure: main effect group: $ATS_{(1)} = 16.63$, $p < .001$; main effect time: $ATS_{(1.84)} = 21.92$, $p < .001$; time*group interaction: $ATS_{(1.84)} = 36.73$, $p < .001$). In particular, groups differed during and after the SECPT procedure both for systolic (during: $t_{(49)} = 8.04$, $p < .001$; after: $t_{(49)} = 3.68$, $p < .001$) and diastolic blood pressure (during: $W = 48$, $p < .001$; after: $W = 197$, $p = .02$), but not before stress induction (all $p > .06$).

With regard to pulse, a significant main effect time ($F_{(1.75,85.62)} = 8.32$, $p < .001$) as well as a significant time*group interaction ($F_{(1.75,85.62)} = 7.73$, $p < .001$) emerged. Post-hoc tests revealed a significant decline in pulse from before to after the procedure ($t_{(25)} = 3.79$, $p < .01$) as well as from during to after the procedure ($t_{(25)} = 4.50$, $p < .001$) only for the stress group. In the control group, no significant differences between time points emerged ($p > .45$).

In addition, participants in the stress group rated the procedure as being significantly more difficult ($W = 33.5$, $p < .001$), unpleasant ($W = 33$, $p < .001$), stressful ($W = 36$, $p < .001$) and painful ($W = 15$, $p < .001$) as compared to participants in the control group.

3.2. Instrumental counterconditioning task

3.2.1. Acquisition

An overall logistic regression model clustered for both participants and trials with valence, stress and their interaction as predictors yielded the best fit of the data (Table 3). Compared to the saturated model including all predictors and interactions (AIC = 2151.43), the best fitting model yielded a considerably smaller AIC (indicating a smaller prediction error) while still giving a significant model of the data. The overarching model predicted for the control group a probability of 68.27 % to press the risk key for Spos and Sposrev and 32.69 % for Sneg and Snegrev. In the stress group, the predicted probability of pressing the risk key in response to Spos and Sposrev was 59.38 % and 33.41 % in response to Sneg and Snegrev. Even though the stress group was overall significantly less likely to press the risk key for Spos and Sposrev as compared to the control group, the probability was still significantly above chance ($b = 0.38$, $z = 3.54$, $p < .001$, $OR = 1.46$, $CI = [1.18,1.81]$), indicating successful learning in both groups (Fig. 2; see Fig. S1 in the supplemental material for an illustration subdivided for the groups).

3.2.2. Counterconditioning

A significant model including valence, reversal and their interaction as predictors yielded the best model fit (Table 3). Compared to the saturated model including all predictors and interactions (AIC = 1878.22), the AIC was considerably smaller. During counterconditioning, the predicted probabilities were 75 % for Spos, 24.52 for Sposrev, 20.91 % for Sneg and 70.43 % for Snegrev. In sum, predicted probabilities by the model indicated successful counterconditioning, thus, reversed probabilities for reversed stimuli as compared to acquisition. Moreover, counterconditioning was successful in both the control and the stress group, as no significant group differences emerged (all effects with stress: $b < 0.15$, $z < 0.45$, $p > .65$; Fig. 2; see Fig. S2 in the supplemental material for an illustration subdivided for the groups).

3.2.3. Retrieval

3.2.3.1. First retrieval trial. For the first trial of retrieval, the best model fit included an intercept indicating keypresses to Spos (b = 0.72, z = 2.42, p = .02, OR = 2.06, CI = [1.14, 3.72]), valence (b = -1.63, z = -3.77, p < .001, OR = 0.2, CI = [0.08,0.46]), reversal (b = -0.49, z = -1.17, p = .24, OR = 0.61, CI = [0.27,1.40]) and the valence × reversal interaction ($b = 1.39$, $z = 2.29$, $p = .02$, $OR = 4.03$, $CI = [1.21,13.41]$) as predictors. In addition, reversed stimuli did not differ between each other (b = -0.23, z = -0.59, p = .55, OR = 0.79, CI = [0.37,1.71]). Compared to the saturated model including all predictors and interactions ($AIC = 284.84$), the best fitting model yielded a smaller AIC of 279.69 with a model $\chi^2_{(3)} = 16.64$, $p < .001$. For the single stimuli, the predicted probabilities for risk keypresses were: 67.31 % for Spos, 55.77 % for Sposrev, 28.85 % for Sneg and 50 % for Snegrev. In sum, the analysis of spontaneous retrieval of contingencies only showed specific keypresses for valence-consistent positive and negative stimuli. Regarding both reversed stimuli, keypresses were at chance level. In addition, spontaneous retrieval did not differ between groups (all effects with stress in the saturated model: $b < 1.32$, $z < 1.57$, $p > .11$).

3.2.3.2. All retrieval trials. An overall logistic regression model including valence, reversal, stress, valence*reversal and reversal*stress yielded the best model fit (Table 3). The AIC was a bit smaller as compared to a saturated model including all predictors and interactions (AIC = 2155.98; results of both models were identical). Overall predicted probabilities for a risk keypress for each stimulus in the control group were 58.18 % for Spos, 51.45 % for Sposrev, 19.70 % for Sneg and 47.10 % for Snegrev. In the stress group, the predicted probabilities for each stimulus were 70.66 % for Spos, 47.10 % for Sposrev, 29.82 % for Sneg and 42.80 % for Snegrev (Fig. 3).

In order to investigate these group differences more closely, we had a look at the effects of stress on each stimulus separately over all retrieval trials. For **Spos**, both the control ($b = 0.33$, $z = 2.34$, $p = .02$, $OR = 1.39$, $CI = [1.05,1.83]$) and the stress ($b = 0.87$, $z = 5.77$, $p < .01$, $OR = 2.41$, $CI = [1.79,3.25]$) group pressed the risk key significantly above chance.

Table 3
Best model fits per phase.

	b (S.E.)	Z	Lower CI	Odds ratio	Upper CI	Model estimation
Acquisition						
Intercept	0.77 (0.11)***	6.96	1.73	2.15	2.67	$\chi^2_{(3)} = 167.48$***
Valence	−1.49 (0.16)***	−9.35	0.17	0.23	0.31	
Stress	−0.39 (0.15)*	−2.51	0.50	0.68	0.92	*AIC* = 2145.69
Interaction	0.42 (0.23)	1.83	0.97	1.52	2.39	
Counter-conditioning						
Intercept	1.10 (0.11)***	9.69	2.40	3.00	3.75	$\chi^2_{(3)} = 440.23$***
Valence	−2.43 (0.17)***	−14.26	0.06	0.09	0.12	*AIC* = 1871.09
Reversal	−2.22 (0.17)***	−12.90	0.08	0.11	0.15	
Interaction	4.42 (0.26)***	17.13	50.13	83.19	138.05	
Retrieval						
Intercept	0.33 (0.12)**	2.76	1.10	1.39	1.76	$\chi^2_{(5)} = 153.44$***
Valence	−1.74 (0.17)***	−10.28	0.13	0.18	0.25	
Reversal	−0.27 (0.17)	−1.61	0.55	0.76	1.06	*AIC* = 2153.90
Stress	0.55 (0.14)***	3.94	1.32	1.73	2.28	
Valence*Reversal	1.56 (0.24)***	6.55	2.98	4.76	7.61	
Reversal*Stress	−0.72 (0.19)***	−3.82	0.33	0.49	0.70	

Note. Standard errors in all models are cluster-robust for both participants and trials. Valence is coded as 0 = positive and 1 = negative, reversal is coded as 0 = not reversed and 1 = reversed, stress is coded as 0 = control group and 1 = stress group. *p <.05, **$p \leq 0.01$, ***$p \leq 0.001$.

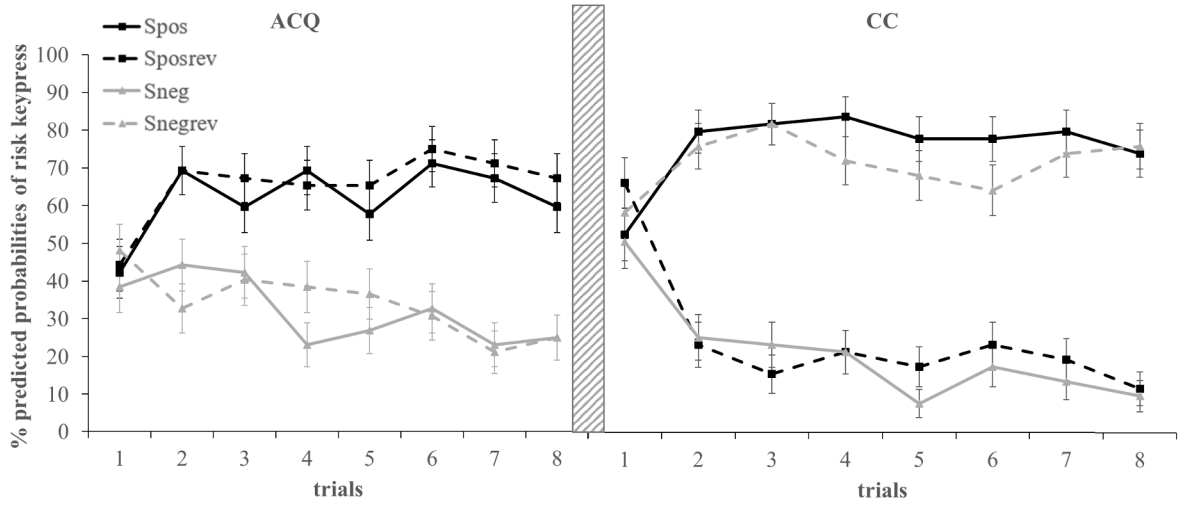

Fig. 2. Predicted probabilities per trial during acquisition (ACQ) and counterconditioning (CC) for all participants. Predicted probabilities are based on the separate logistic regression models for each trial with valence and reversal as predictors. Error bars represent standard errors of the respective predicted probability. Standard errors are cluster-robust for participants. Spos = non-reversed positive stimulus, Sposrev = reversed positive stimulus, Sneg = non-reversed negative stimulus, Snegrev = reversed negative stimulus. Stimulus names regarding valence are based on the respective contingencies during acquisition.
Successful learning during acquisition is indicated by increasing predicted probabilities for risk keypresses for Spos and Sposrev and decreasing predicted probabilities for risk keypresses for Sneg and Snegrev. Successful learning during counterconditioning is indicated by increasing predicted probabilities for risk keypresses for Spos and Snegrev and decreasing predicted probabilities for risk keypresses for Sneg and Sposrev.

However, the probability of the stress group to press the risk key was significantly higher as compared to the control group (b = 0.55, z = 2.65, p <.01, OR = 1.73, CI = [1.15,2.61]). For **Sposrev**, neither the control nor the stress group pressed the risk key over chance level and the difference between groups was not significant (all p >.05). While the overall significant reversal*stress interaction as indicated in the best model fit was not reflected here, there was a trend towards less risk keypresses in the stress group as compared to the control group that failed to reach significance (b = -0.37, z = -1.86, p =.06, OR = 0.69, CI = [0.47,1.02]). With regard to **Sneg**, both the control (b = -1.4, z = -8.05, p <.001, OR = 0.25, CI = [0.17,0.35]) and stress group (b = -0.86, z = -5.64, p <.001, OR = 0.42, CI = [0.32,0.57]) pressed the risk key significantly below chance level. However, the stress group was more likely to press the risk key as compared to the control group (b = 0.55, z = 2.37, p =.02, OR = 1.73, CI = [1.10,2.73]). Lastly, with regard to **Snegrev**, both groups did not differ from each other or with regard to chance level in the probability for risk keypresses (all p >.1).

In sum, the stress group generally pressed the risk key significantly more often in response to valence-consistent stimuli. Groups did not differ significantly regarding reversed stimuli. Both groups pressed the risk key at chance level for reversed stimuli (Fig. 4).

4. Discussion

The current study focused on stress effects on the retrieval of instrumental counterconditioning memories. We expected that non-stressed participants would retrieve updated contingencies, indicating adaptive behavior to environmental changes. Furthermore, stress should reduce retrieval of updated contingencies and increase reliance on contingencies learned during the first learning phase. Despite successful contingency learning and updating as indicated by keypresses in both learning phases (cf. Fig. 2) and a successful stress induction as revealed in physiological and endocrine measures (cf. Table 2), both hypotheses were not confirmed by the data. Rather, both stressed and non-stressed men only showed specific response patterns with regard to valence-consistent information, i.e., approach behavior towards stimuli with

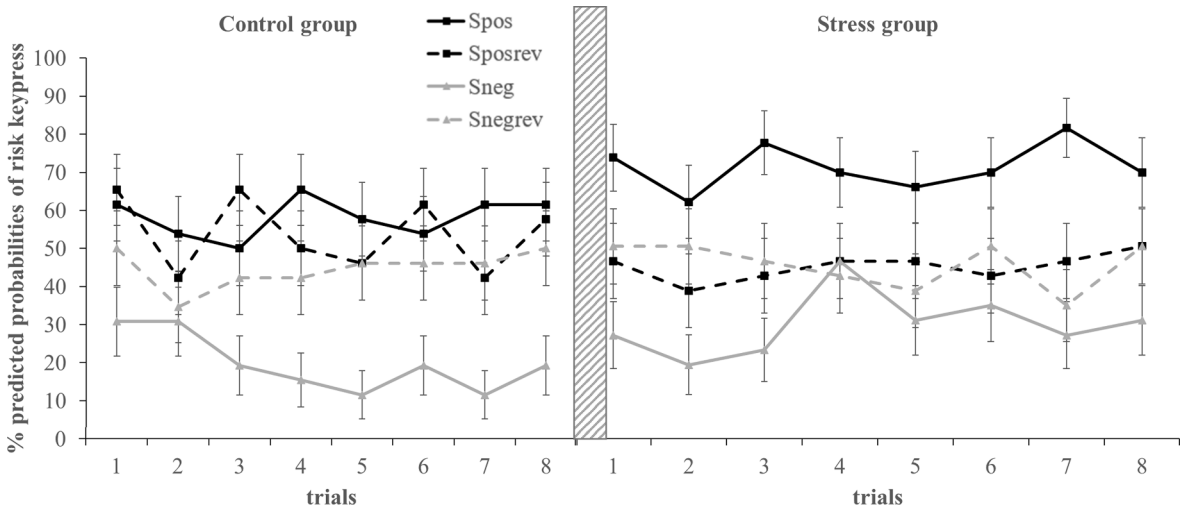

Fig. 3. Predicted probabilities per trial during retrieval separated for the control and stress group. Predicted probabilities are based on separate logistic regression models for each retrieval trial with valence, reversal and stress as predictors. Error bars represent standard errors of the respective predicted probabilities. Standard errors are cluster-robust for participants. Spos = non-reversed positive stimulus, Sposrev = reversed positive stimulus, Sneg = non-reversed negative stimulus, Snegrev = reversed negative stimulus. Stimulus names regarding valence are based on the respective contingencies during acquisition.
Overall, the stress group pressed the risk key significantly more often than the control group for both Spos and Sneg during retrieval. Keypresses for reversed stimuli did not differ between groups and were at chance level.

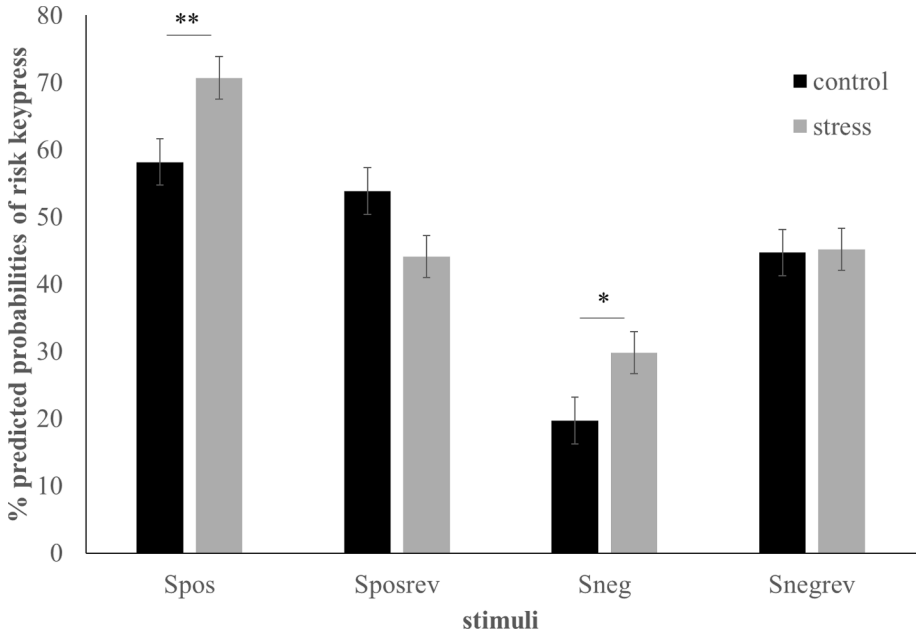

Fig. 4. Predicted probabilities per stimulus during retrieval. Predicted probabilies per stimulus are based on separate logistic regression models per stimulus combination with stress as single predictor. Error bars represent standard errors of the respective predicted probabilities. Standard errors are cluster-robust for participants and trials. Spos = non-reversed positive stimulus, Sposrev = reversed positive stimulus, Sneg = non-reversed negative stimulus, Snegrev = reversed negative stimulus. Stimulus names regarding valence are based on the respective contingencies during acquisition.
The stress group was significantly more likely to press the risk key for Spos and Sneg as compared to the control group. No significant difference emerged for reversed stimuli. $*p < .05$, $**p \leq 0.01$.

appetitive consequences (Spos) and avoidance behavior towards stimuli with aversive consequences (Sneg). Regarding reversed contingencies neither stressed nor non-stressed men showed any response preferences and the exhibition of approach and avoidance behavior was at chance level. However, while general response patterns did not differ between groups, stressed men showed more approach behavior towards valence-consistent stimuli (Spos and Sneg) in an uncertain situation (i.e., retrieval without feedback) as compared to non-stressed men (cf. Fig. 3 + Fig. 4). This indicates an effect of stimulus valence in stressed men, as retrieval of valence-consistent positive information was increased, while retrieval of valence-consistent negative information was decreased.

The current findings were not predicted on the basis of the STaR model (Meir Drexler et al., 2019). Importantly, the STaR model focuses on the influence of stress or cortisol on extinction learning and retrieval. However, in the learning phases of the current study, feedback about performance and contingencies was always provided. Therefore, behavior was not extinguished or reduced, but rather reversed. In addition, the retrieval phase was not designed to reduce behavior, as no informative feedback was provided. This is also reflected in the data, where an "extinction-like" reduction of behavior was not shown during retrieval, even though no behavioral reinforcement was applied anymore. Rather, participants generally stuck to their response patterns over the course of retrieval trials (cf. Fig. 3).

In contrast to extinction as well as classical counterconditioning studies, the current study adds a decision making and risk-taking component by employing an instrumental task with potential wins and losses which might be related to difference in neural processing. Stress effects on extinction memory processing are related to the influence of cortisol on the hippocampus, prefrontal cortex and amygdala (Sandi and Pinelo-Nava, 2007). Studies comparing appetitive counterconditioning

and extinction, however, point towards an increased deactivation of the amygdala during counterconditioning as well as increased activity in the nucleus accumbens as compared to extinction training (Houtekamer et al., 2021; Keller et al., 2022). Moreover, decision making as well as rewarding and punishing feedback processing has rather been related to dopaminergic activity in the striatum and orbitofrontal cortex (OFC) in order to associate hedonic value and salience to stimuli and to make informed decisions (Fellows, 2018; Frank et al., 2004). Interestingly, the OFC is especially involved in top-down control of decision making and is supposed to lead to rather risk averse decisions under uncertainty in non-stressed participants (Frank and Claus, 2006). However, stress has been related to a failure of the OFC to exert this top-down control (Sequeira and Gourley, 2021), leading to decreased risk aversion and increased reward sensitivity (Pabst et al., 2013; Starcke and Brand, 2016) as well as impaired reversal learning (Frank and Claus, 2006). Accordingly, studies employing probabilistic learning tasks indicate that acute stress improves learning of cues predicting positive outcomes (Lighthall et al., 2013) and reduces learning from negative outcomes (Petzold et al., 2010). Thus, when interpreting the current findings, the interactive effects of cortisol and dopamine and their influence on the processing of rewards and punishments associated with actions should be considered.

Accordingly, increased cortisol levels have consistently been associated with increases in extracellular dopamine levels in the mesolimbic pathway as well as in the striatum (Pruessner et al., 2004; Ungless et al., 2010). Considering the dopaminergic PE as the basis of contingency learning, some studies found an association between increases in dopamine and better learning from positive outcomes at the cost of learning from negative outcomes (Byrne et al., 2019; Frank et al., 2004; Lighthall et al., 2013). In addition, previous studies showed that stress leads to a failure in the differentiation between rewards and punishments during contingency learning. For instance, Porcelli et al. (2012) found that the striatum and OFC that are presumably involved in dopaminergic processing and differentiation of rewards and punishments fail to show differentiating activity during encoding under stress. This finding might hint towards a failure of those areas to successfully update contingencies associated with specific stimuli and, thus, impair the ability to apply previously learned information to current decisions. However, no study so far investigated whether this impairment is also present during the retrieval of previously learned contingencies.

Considering those previous studies, the current results are filling the knowledge gap between stress effects on contingency learning and stress effects on contingency retrieval. Taking the interactive effects of cortisol and dopamine into account, the STARS (Stress Triggers Additional Reward Salience) model (Mather and Lighthall, 2012) states that stress promotes reward-related and disrupts punishment-related behavior, leading to increased approach and impaired avoidance learning. Thus, according to the STARS model stress hormones should facilitate risky and disadvantageous decisions and this effect has been shown to be especially pronounced in men (Deuter et al., 2017). Consequently, increases in approach behavior in stressed men as evident in the current study might be related to dopamine-related increases in reward sensitivity at the cost of avoidance behavior (Frank and Claus, 2006; Starcke and Brand, 2016). Our study, thus, expands previous findings regarding stress-induced changes in contingency learning by showing similar effects when it comes to the retrieval of previously learned contingencies.

With regard to valence-inconsistent stimuli (Sposrev and Snegrev), the similar findings in both groups and the random response patterns do not necessarily indicate that the design was not able to detect any group differences at all. Chance level performance rather reflects equally likely deviations in both directions with no possible problems due to ceiling or floor effects. Additionally, random response patterns might be related to different predictive values associated with reversed stimuli (O'Doherty, 2014). Trapp et al. (2015) found that humans prefer stimuli with high predictive values over those with low predictive values when making decisions. During retrieval, the ambiguity associated with reversed stimuli might have been too high to allow an informed decision on the basis of previously learned information, leading to guessing and inconsistent keypresses over all retrieval trials and in both groups. In contrast to the findings regarding valence-consistent stimuli, the random response pattern during retrieval of reversed stimuli occurred independently of stimulus valence.

Investigating stress effects on learning and memory retrieval in different settings is of high clinical importance. Considering the utilization of extinction training in the treatment of mental disorders (Abramowitz, 2013; Craske et al., 2014; Craske et al., 2018; Zlomuzica et al., 2020), studies showing the limited long-term effectiveness of this treatment in daily life stressful situations challenge current therapeutic approaches (Loerinc et al., 2015). Consequently, finding ways to improve the stress resistance and stability of newly learned behavior in daily life is highly recommended. Moreover, Bouton (2019) stated that the investigation of instrumentally learned behavior and its retrieval is a controlled way of studying voluntary behavior. With regard to mental disorders such as addiction or gambling disorder, it is important to explore how decisions are made and which contingencies are retrieved, especially under stress (Heinz et al., 2019; Perales et al., 2017; Sinha, 2007; Thomas et al., 2011). Our findings suggest consistently increased approach behavior under stress even without any informative feedback both for positive and negative stimuli, indicating a possible route for relapses. Furthermore, the instrumental counterconditioning paradigm employed in this study does not point towards a facilitation of memory retrieval of a second memory trace over the original memory trace. Rather, it appears that counterconditioning leads to increased ambiguity associated with stimuli and thereby decreases the predictive value leading to guessing behavior.

Additionally, considering the specific association in classical counterconditioning, where a conditioned stimulus is associated with an unconditioned stimulus of the opposite valence, it has been suggested that ambiguity is increased, since the same conditioned stimulus is paired with two incompatible unconditioned stimuli (Holmes et al., 2016; van Dis et al., 2019). The current findings suggesting guessing of contingencies in both stressed and non-stressed men support this interpretation also in instrumental counterconditioning, pointing towards increased ambiguity that, in turn, increases uncertainty and disrupts goal-directed strategy use. However, considering previous findings suggesting improved counterconditioning memory retrieval over extinction memory retrieval (Engelhard et al., 2014; Kaag et al., 2016; Kang et al., 2018; Keller and Dunsmoor, 2020; Raes and de Raedt, 2012), it would be interesting to investigate stress effects when other forms of reinforcement are applied, such as electric shocks and food. This might reduce the gambling quality of the current task. Recent studies already explore the so-called "rewarded extinction", employing a counterconditioning paradigm to overcome previously acquired fear memories and yield promising results (Keller et al., 2022).

Notably, group differences already occurred during acquisition (but not during counterconditioning): the stress group was overall significantly less likely to press the risk key for stimuli coupled with positive consequences (Spos and Sposrev) as compared to the control group. Still, the probability of risk keypresses was significantly above chance leading to the assumption that overall successful learning emerged in both groups. During retrieval, the stress group had a higher tendency of pressing the risk key for valence-consistent stimuli (Spos and Sneg) compared to the control group, whereas no group differences occurred for valence-inconsistent stimuli (Sposrev and Snegrev). Taking the acquisition results into account, the observed stress effect for Spos during retrieval might have been even larger than reported, if groups had not differed during acquisition. For Sposrev, the trend towards less risk keypresses in the stress compared to the control group could simply reflect the result pattern during acquisition and might disappear in the case of absent initial group differences.

When further interpreting the current findings, some limitations should be considered. Firstly, the counterconditioning phase

immediately followed the acquisition phase. However, the immediate extinction effect suggests that extinction learning is impaired if it occurs too soon after acquisition training (Maren, 2014). Therefore, the learning of the counterconditioning memory trace might have been impaired by a too short time interval between acquisition and counterconditioning. The current results point towards a commingling between both learning phases (as indicated by guessing of reversed stimuli). A longer interval between acquisition and counterconditioning (e.g., 24 h apart) might have led to a clearer separation between both phases, a consolidation of the initial memory trace and prevention of retroactive interference, however at the cost of differentially old memories during retrieval (24 h vs 48 h) in such a three-day design. Please note that an "event boundary" between acquisition and counterconditioning was realized in the current study, in which participants filled in contingency questionnaires. Thus, these phases were clearly separated for the participants (also referred to as first and second phase in the instructions) and not realized in one run without any break. This procedure should have led to "event segmentation" which organizes events into unique memories to be selectively consolidated and reduces retroactive interference (e.g., Clewett & Davachi, 2017; Dunsmoor et al., 2018; Ezzyat and Davachi, 2014; Kurby and Zacks, 2008; Radvansky and Zacks, 2017). A replication of the current results with a three-day design should be realized in the future.

Secondly, even though we predetermined our sample size with a preregistered power analysis, the assumed effect size of $d = -0.49$ might overestimate the underlying effect. In particular in light of the null results during retrieval concerning stimuli undergoing contingency reversal (Sposrev and Snegrev), a larger sample size might have been necessary to avoid Type II errors. Thus, our findings are in need of replication. Thirdly, participants achieved higher gains during counterconditioning as compared to acquisition (cf. Table 1). However, the amount of gained money in either phase did not correlate significantly with keypresses during retrieval and, therefore, might not have influenced strategy use (see supplemental material section 3.b). Fourthly, money served as a secondary reinforcer in this study. Considering different neural correlates associated with aversive and appetitive primary as compared to secondary reinforcements (Beck et al., 2010; Delgado et al., 2011), it would be interesting to see the stress effects on the retrieval of instrumentally learned contingencies using primary reinforcers (e.g., shocks and food). Finally, the generalizability of the current findings is limited since no female participants were included in the study. Of note, acute stress and stress hormones have in part differential effects on memory retrieval in male and female participants (Merz and Wolf, 2017). Moreover, stress has been shown to influence decision making differentially for men and women (Mather and Lighthall, 2012). This research showed that stress hormones increase risk taking in men, but decrease risk taking in women. Thus, the current results might be completely reversed in women, which needs to be tested in future studies. Importantly, when investigating stress effects on cognitive performance in women, the use of hormonal contraceptives as well as the current phase in the menstrual cycle should always be considered (Jentsch et al., 2022; Merz & Wolf, 2017; Shields et al., 2017).

5. Conclusion

The current study showed that stress increases approach behavior towards unambiguous stimuli, regardless of stimulus valence in healthy men. Even without continuous contingency feedback, stressed men exhibited increased approach behavior towards stimuli that were consistently associated with appetitive consequences as well as decreased avoidance behavior towards stimuli that were always associated with aversive consequences. The results bear important implications for behavioral disorders indicating an increased probability to repeat maladaptive behavior under stress, even if it does not lead to the expected consequence(s) or if it was consistently punished before. Moreover, it adds to an understanding how stress could lead to relapses in gambling disorder, as reward sensitivity and risk-taking appear to not only be increased during learning under stress, but also during retrieval.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

The data that were used in this study are openly available in the homepage of the Open Science Framework (OSF) and can be accessed via the following link: https://osf.io/bdfu6/

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Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.nlm.2022.107697.

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