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**The impairing effect of acute stress on the intentional forgetting of future fears and its
moderation by working memory capacity**

S.M. Ashton ^a, R.G. Benoit ^b, C.W.E.M. Quaedflieg ^a

^a Faculty of Psychology and Neuroscience, Maastricht University, Maastricht, the Netherlands

^b Max Planck Research Group: Adaptive Memory, Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany

Corresponding author:

Email address: Stephanie Ashton: s.ashton@maastrichtuniversity.nl

Faculty of Psychology and Neuroscience, Maastricht University, P.O. Box 616, 6200 MD Maastricht, the Netherlands.

Abstract

Unwanted imaginations of future fears can, to some extent, be avoided. This is achieved by control mechanisms similar to those engaged to intentionally forget unwanted memories. Intentional forgetting relies on the executive control network, whose functioning is impaired after exposure to acute stress. This study investigates whether acute stress affects the ability to intentionally control future fears and, furthermore, whether individual differences in executive control predict a susceptibility to these effects. The study ran over two consecutive days. On day 1, the working memory capacity of one hundred participants was assessed. Thereafter, participants provided descriptions and details of fearful episodes that they imagined might happen in their future. On day 2, participants were exposed to either the stress or no-stress version of the Maastricht Acute Stress Test, after which participants performed the Imagine/No-Imagine task. Here, participants repeatedly imagined some future fears and suppressed imaginings of others. Results demonstrated that, in unstressed participants, suppression successfully induced forgetting of the episodes' details compared to a baseline condition. However, the observed reduction in anxiety toward these events remained unchanged. Acute stress was found to selectively impair intentional forgetting and, further, this effect was moderated by working memory capacity. Specifically, low working memory predicted a susceptibility to these detrimental effects. These findings provide novel insights into conditions under which our capacity to actively control future fears is reduced, which may have considerable implications for understanding stress-related psychopathologies and symptomatology characterized by unwanted apprehensive thoughts.

Key words: Intentional forgetting, Episodic future thinking, Anxiety, Working memory, Acute stress, Maastricht Acute Stress Test (MAST)

1. Introduction

Imaginations of our future are based on thoughts of past events (Schacter et al., 2017). However, not all imaginations are desirable. To some extent, we have the ability to choose which future thoughts we keep revisiting and which we forget. This ability can be enabled through control mechanisms similar to those engaged when we recall our past memories (Benoit et al., 2016). Intentional control of past memories comprises two distinct processes: active retrieval (positive control) and active suppression (negative control), which subsequently leads to the enhancement or impairment of memory, respectively (Anderson and Green, 2001; for meta-analyses, see Anderson and Huddleston, 2012; Stramaccia et al., 2019).

Intentional memory control serves as an adaptive emotion regulation strategy, fostering the retrieval of positive memories and inducing the forgetting of other memories that pose a threat to our integrity and well-being (e.g., fear-related memories; Nørby, 2018). The inability to control fear-related memories plays a key role in the development and maintenance of stress-related psychopathology, observable as intrusive and worrying thoughts in anxiety and mood disorders (Hertel and Gerstle, 2003; Joormann et al., 2005; Mary et al., 2020). Despite these far-reaching implications, the factors that influence our capacity to intentionally control our future fears are largely unknown.

Active suppression can be achieved via inhibitory control, an executive control function that can be engaged to stop memory retrieval (Anderson and Huddleston, 2012). Individual differences in executive control, therefore, have been suggested to account for variation in the ability to suppress unwanted memories (Anderson and Green, 2001; Levy and Anderson, 2008). Executive control is also a critical element of working memory, guiding attention to relevant and inhibiting irrelevant information (Kane et al., 2001; Marsh and Hicks, 1998). Importantly, higher working memory capacity has been found to predict an increased ability to intentionally suppress thoughts (Brewin and Beaton, 2002).

Intentional control of future fear imaginings relies on an executive control network guided by the right dorsolateral prefrontal cortex (dlPFC). This region downregulates activity in the ventromedial PFC and hippocampus (Benoit et al., 2016), regions that support the retrieval of past episodes and the simulation of future events (Benoit and Schacter, 2015; Schacter, Benoit, and Szpunar, 2017).

Moreover, stronger downregulation has been linked to successful suppression and subsequent forgetting (Benoit and Anderson, 2012; Gagnepain et al., 2014).

Acute stress alters, amongst others, functioning of frontal and temporal brain areas implicated in intentional memory control (Hermans et al., 2014). In response to an acute stressor, activation of the rapidly acting autonomic nervous system (ANS) results in the release of noradrenaline. In addition to the ANS response, activation of the hypothalamic-pituitary-adrenal (HPA) axis results in the release of the human glucocorticoid cortisol (Joels et al., 2011; Ulrich-Lai and Herman, 2009). The combined acute stress response prompts the reallocation of resources to the salience network promoting a hypervigilant state at the expense of the executive control network (Hermans et al., 2011, 2014). The dlPFC is a key neural substrate of the executive control network and activity in this region is found to reduce after acute stress exposure (McEwen and Morrison, 2013). This can result in impairments of associated higher cognitive functions such as working memory (Hermans et al., 2014; Qin et al., 2009; Schoofs et al., 2009). These effects peak during a period in which both the ANS and HPA stress response systems are activated (Elzinga and Roelofs, 2005). Furthermore, increased activation of the sympathetic stress response has been related to lower baseline working memory (Hernaes et al., 2018).

Based on these findings, the aim of the current study was three-fold. First, to replicate the original behavioural findings of Benoit et al. (2016): (i) that suppressing imaginings of future fears causes forgetting of details that are associated with the feared event and (ii) that suppressing attenuates anxiety toward that event. Second, to investigate the influence of acute stress on the active suppression of future fears. We hypothesized that acute stress would negatively affect the ability to suppress imaginations of future feared events, creating an inability to intentionally forget and attenuate anxiety. Third, to explore whether individual differences in working memory capacity influence the efficacy of active suppression after exposure to an acute stressor.

Acute stress was elicited using the ‘Maastricht Acute Stress Test’ (MAST), a potent and reliable procedure to elicit subjective, autonomic and glucocorticoid stress responses (Quaedflieg et al., 2017; Smeets et al., 2012). To assess the intentional control of fear imaginings, the current study employed an adapted version of the ‘Imagine/No-Imagine’ task, tailored to the retrieval versus suppression of future feared events (Benoit et al., 2016).

2. Materials and Methods

2.1. Participants

The *a-priori* power calculation with G* Power ($\alpha = 0.05$, $1-\beta = 0.85$), based on the suppression effect reported in Benoit et al. 2016, indicated a required sample of 90 participants. In total, one hundred healthy participants were recruited via university subject pools and online study advertisement. All participants were aged between 18-35 and were screened for the following inclusion criteria: BMI between 17.5-28; drink less than 10 alcoholic drinks per week; smoke less than 10 cigarettes per week; no use of medication in the previous week; use drugs less than twice per month and have no history of mental illness within the past five years. All females were using hormonal contraception, to control for the known influence on the cortisol stress response (Strahler et al., 2017). Seven participants were excluded from the analysis due to missing data as a result of measurement error. The final sample consisted of 93 participants (23 male). All participants provided written informed consent and were reimbursed with University credits or monetary compensation. The test protocols were approved by the ethics committee of the Faculty of Psychology and Neuroscience, Maastricht University.

2.2. Imagine/No-Imagine paradigm

Intentional control of future fears was assessed using an adapted version of the Imagine/No-Imagine paradigm (I/NI; see Benoit et al., 2016), presented using E-Prime (Version 2.0, Psychology Software Tools, Pittsburgh, PA). The original paradigm consists of three phases, designed to be completed over one session. The current study divided the three phases over two days (see Fig. 2). To account for the 24 hour delay between sessions, an additional ‘Reminder Task’ was added and is described in the procedure.

Phase 1

On day 1, participants generated descriptions of 18 future feared events and corresponding reminder words, which act as a cue for the associated fear. Each fear had to fulfil six criteria: the event must be negative; imaginable through their own eyes; possibly occur within approximately the next two years; be a specific episode that occurs over a short time; and, importantly, it must be an event they

tend to think about. Participants also provided subjective ratings for each fear on a 5-point Likert scale (1 = not at all; 5 = extremely) based on: vividness; emotional intensity; anxiety; likelihood of occurrence; frequency of thought; and distance in the future. These subjective ratings were used to equally and randomly divide fear items into one of three stimuli categories: Imagine; No-Imagine; or baseline.

On day 2, after the reminder task, participants provided a typical detail for each of the 18 fears they had listed on day 1. These details were supposed to relate to a specific element envisioned in the participants' imagination (see Fig. 1). It could not be a word from the description, nor could it be too similar to the reminder word. Participants then provided a second subjective rating of anxiety for each fear.

Phase 2

The Imagine/No-Imagine manipulation tasked participants to actively imagine some of their future fears and to suppress imaginations of others. During this phase, we presented all six reminders of the Imagine and of the No-Imagine items. Baseline items were not cued during this phase. Each reminder was repeatedly presented (12 times each) in a random order, with the restriction that no more than three reminders of the same condition (i.e., Imagine, No-Imagine) could be shown consecutively. During Imagine trials, participants were instructed to vividly imagine the associated fear. With each repetition of the same reminder, participants were instructed to build on what they had previously imagined and develop a vivid, detailed episode. For No-Imagine trials, participants had to block out all imagination of the event until the reminder disappeared from the screen and do so without using distraction tactics, such as replacing the imagination with an alternative thought. Participants completed the task in silence and maintained their focus on the reminders. Each trial began with a centred fixation cross with a random duration of 2-2.5 seconds, followed by either an Imagine or No-Imagine cue (1.5 seconds), followed by a corresponding reminder cue (4 seconds; see Fig. 1). Imagine trials appeared in green text and No-Imagine trials appeared in red text. At the end of each trial, participants responded to the question: "How often did you imagine the future fear?" (1= never; 2 = sometimes; 3 = always). This was recorded to determine thought intrusions, classified by a 2 or 3 response during No-Imagine trials. The results are not included in this report.

Prior to the main task, participants were provided with the descriptions and reminders of 3 example fears to familiarise themselves with the Imagine/No-Imagine procedure. Two reminders were presented in the No-Imagine condition (in red font) and one reminder was presented in the Imagine condition (in green font).

Phase 3

The effects of the Imagine/No-Imagine manipulation on intentional forgetting and intentional retrieval were assessed in the cued recall phase. Here, participants recalled all typical details for each event of the Imagine, No-Imagine and baseline categories in response to their respective reminder (presented in black font). All 18 reminders were presented in a random order for 4 seconds each, during which participants had to recall the corresponding typical detail aloud. The experimenter recorded the percentage of correctly recalled typical details in the Imagine, No-Imagine and baseline categories.

The effects of the manipulation on anxiety were assessed in the final task. Participants were presented with all 18 reminders in a random order for 1 minute each. During this time, participants vividly described the future feared event aloud. At the end of each trial, participants rated their current feeling of anxiety toward the event on a 5-point Likert scale (1 = not at all; 5 = extremely).

Figure 1. Outline of the three phases of the Imagine/No-Imagine paradigm with example fears. Phase 1: participants generated descriptions, reminders and typical details of future feared events. They then recorded the first anxiety assessment. Phase 2: in response to reminders, participants intentionally retrieved (Imagine condition) or intentionally suppressed (No-Imagine conditions) imaginations of the associated fear. Phase 3: cued recall and anxiety assessment. In response to reminders, participants recalled typical details for all Imagine, No-Imagine and baseline conditions. Hereafter, the reminders were presented once more and participants freely described the associated fear before providing a final anxiety assessment with respect to that event.

2.3. *The Maastricht Acute Stress Test*

The Maastricht Acute Stress Test (MAST) was used to activate the human stress system (see Smeets et al., 2012). The MAST consists of a 5 minute instruction phase, followed by a 10 minute acute stress phase alternating between two trial types: exposure to ice-cold water (4°C) and challenging mental arithmetic, in which participants count backwards in increments of 17 as fast and as accurately as possible, starting at 2043. The experimenter only provided negative feedback, addressing mistakes and speed of the arithmetic. Participants were told that they would be videotaped throughout in order to later analyse their facial expressions during the task. Unbeknownst to participants, the video camera did not record any footage and the data were not used at any point.

The no-stress control version aims to not elicit a stress response. Participants were required to immerse their hand in lukewarm water (between 35-37°C) and count continuously from 1-25 for mental arithmetic trials. Participants were not videotaped, nor provided with negative feedback.

2.4. *Physiological stress measures*

Systolic and diastolic blood pressure (SBP; DBP) were measured from the right arm at 6 time points during day 2 ($t_{\text{pre-stress}}$, t_{stress} , t_{+0} , t_{+10} , t_{+30} , t_{+50}). Blood pressure measurements were recorded using an Omron 705IT (HEM-759-E; Omron Healthcare Europe BV).

Salivary cortisol samples were obtained at 4 time points ($t_{\text{pre-stress}}$, t_{+10} , t_{+30} , t_{+50}) via synthetic Salivettes (Sarstedt1, Etten- Leur, The Netherlands). Saliva samples were stored at -20°C after collection until cortisol concentrations were determined by a commercially available chemiluminescence immunoassay with high sensitivity (IBL International, Hamburg, Germany). The intra and interassay coefficients were below 9%.

2.5. *Subjective stress*

Participants self-reported how stressful, how painful and how unpleasant they had perceived the MAST via three 100 mm Visual Analog Scales (VASs; anchors: 0 = not at all; 100 = extremely).

Mood ratings were recorded pre and post stress induction through completion of the Positive and Negative Affect Schedule (PANAS; Watson et al., 1988). The PANAS includes two 10-item mood scales relating to positive affect (PANAS-P) or negative affect (PANAS-N). Each item is rated on a 5-point Likert scale (1 = not at all; 5 = extremely) in response to how the participant feels at the present moment.

2.6. Anxiety

Changes in state anxiety were measured via the State-Trait Anxiety Inventory (STAI-S; Spielberger et al., 1983). The STAI-S consists of 20 self-report items, with scores recorded on a 4-point Likert scale in response to how anxious the participant feels at the present moment (1 = not at all; 4 = very much so). This was administered at two time points (pre-stress and post-stress).

2.7. Working memory

The Digit Span Task from the Wechsler Adult Intelligence Scale-Revised (Wechsler, 1981) was used to assess working memory capacity. Participants were read aloud a sequence of digits and asked to repeat the digits back either in the same order (forward condition) or the reverse order (backward condition). After two sequences of the same digit span length were completed successfully, the participant would proceed to the next. Each sequence increased in increments of 1 digit. If two errors were made on one sequence, the task was stopped. Scores obtained from the backward condition ($WM_{Backwards}$) were used as a measure of working memory capacity for later analysis. Performance on the backward condition has been found to correlate with activity in the right dlPFC, a key neural substrate of intentional memory control (Hoshi et al., 2000).

2.8. Procedure

Participants were randomly allocated into one of two conditions (stress: $n=50$; control: $n=50$). The study ran over two consecutive test days for a duration of approximately 1.5 and 2.5 hours, respectively. Day 1 testing ran between 08:30am-12:00pm and day 2 between 12:30-18:30pm, in order to avoid fluctuations in the circadian rhythm of cortisol. Prior to each session, participants were

instructed to refrain from eating, smoking, strenuous exercise or drinking anything but non-sparkling water for 2 hours before testing.

On test day 1 (see Fig. 2), participants were first given information regarding the experiment and thereafter provided informed consent. Next, participants completed baseline questionnaires and subsequently performed the digit span task. For the remainder of test day 1, participants generated 18 fear descriptions and corresponding reminder words (I/NI, phase 1).

On test day 2 (see Fig. 2), participants first completed the reminder task. During this task, all 18 reminder words that were created on day 1 were presented for up to 1.5 minutes. During that time, participants vividly described all imaginations of the fears aloud. After each trial, the corresponding fear description was presented as feedback. Participants then completed the remainder of phase 1, generating typical details for each fear description. Pre-stress measures of negative affect, state anxiety, blood pressure and saliva were then recorded ($t_{\text{pre-stress}}$). This was immediately followed by exposure to either the stress or no-stress version of the MAST. Blood pressure was measured once during the task (t_{stress}) and immediately after (t_{+0}). Following this, participants completed subjective stress, negative affect and state anxiety questionnaires. Ten minutes after completion of the MAST, blood pressure and the second saliva sample were taken (t_{+10}). Participants then continued to the first block of the Imagine/No-Imagine task (phase 2). At the end of block one, blood pressure and saliva samples were measured (t_{+30}) and then participants proceeded to block two under the same instructions. EEG data were recorded of each participant during phase 2. However, these results are not reported in this paper. After completion, the final blood pressure and saliva samples were measured (t_{+50}). This was followed by a cued-recall task to test memories for the typical details and a subsequent free simulation task designed to provide a final anxiety assessment (I/NI, phase 3). Participants were then debriefed, thanked and compensated for their time.

Figure 2. Overview of the study procedure. Approximate timings (T) are denoted in minutes.

2.9. Statistical Analysis

The data were checked for normality using Q-Q plots and Shapiro-Wilk tests. Two participants were identified as outliers for recall of baseline items or anxiety ratings more than 3 SDs below the mean. These participants were excluded from further analyses. Therefore, the final sample size was 91 (stress: $n=47$; control: $n=44$).

A log-transformation was performed to account for skewed cortisol data, the values of which were used in subsequent analyses. Subjective stress was determined via the mean score of the three VASs for each participant. To determine the change in anxiety ratings from the Imagine/No-Imagine manipulation, the difference score between the baseline rating (phase 1) and the final anxiety rating (phase 3) was used for analysis. The baseline rating was calculated via the mean score of the two anxiety ratings produced during phase 1.

In cases of violated normality or sphericity, adjusted Welch's F ratios and Greenhouse-Geisser corrected values are reported, respectively. All post-hoc analyses were performed using Bonferroni corrections for multiple comparisons. Two-tailed p -values are reported for the interaction analysis and moderation analysis of working memory. One-tailed p -values are reported for planned directed comparisons for the stress and Imagine/No-Imagine manipulations. ANOVA results are supplemented with Partial Eta Squared values (η_p^2) as a measure of effect size (η_p^2 of 0.01 indicate small effects, η_p^2 of 0.06 medium effects, and η_p^2 of 0.14 large effects; Fritz, Morris, and Richler, 2012).

3. Results

3.1. Acute stress induction

3.1.1. Physiological stress responses

Significant increases in blood pressure and cortisol confirmed the success of the acute stress induction. One participant had missing data for blood pressure. To assess the difference in noradrenergic response between groups before, during and repeatedly after the MAST, a repeated-measures ANOVA was performed on blood pressure recordings (SBP and DBP) with Time (6 levels: $t_{\text{pre-stress}}$, t_{stress} , t_{+0} , t_{+10} , t_{+30} , t_{+50}) as the within-subjects (WS) factor and Condition (2 levels: stress vs. control) as the between-subject (BS) factor. Results revealed that systolic and diastolic blood pressure were elevated in response to the stress-version of the MAST, but not in response to the control manipulation (Time*Condition; SBP: $F_{(2.98,263.05)}=27.76$, $p<.001$, $\eta_p^2 = 0.24$; DBP: $F_{(2.59,227.96)}= 47.86$, $p<.001$, $\eta_p^2 = 0.35$; see Fig. 3). Follow-up tests demonstrated that, prior to the MAST, the conditions did not differ significantly in blood pressure (both p 's $>.18$). Commencing the MAST, the conditions differed significantly at t_{stress} (SBP: $F_{(1,88)}=46.31$, $p<.001$, $\eta_p^2 = 0.35$; DBP: $F_{(1,88)}=57.45$, $p<.001$, $\eta_p^2 = 0.40$), t_{+0} (SBP: $F_{(1,88)}=30.57$, $p<.001$, $\eta_p^2 = 0.26$; DBP: $F_{(1,88)}=50.28$, $p<.001$, $\eta_p^2 = 0.36$) and t_{+10} (SBP: $F_{(1,88)}=5.61$, $p=.01$, $\eta_p^2 = 0.06$; DBP: $F_{(1,88)}=10.87$, $p<.001$, $\eta_p^2 = 0.11$) and t_{+30} (SBP: $F_{(1,88)}=3.65$, $p=.03$, $\eta_p^2 = 0.04$). No significant differences were observed at t_{+30} for DBP and t_{+50} for both SBP and DBP (all p 's $>.058$).

To assess the effects of the MAST on the neuroendocrine measures, we performed a repeated-measures ANOVA on the cortisol concentrations at different time points (WS; Time, 4 levels: $t_{\text{pre-stress}}$, t_{+10} , t_{+30} , t_{+50}) for each condition (BS; 2 levels: stress vs. control). The analysis revealed elevated concentrations in the stress condition compared to controls (Time*Condition: $F_{(1.72,153.003)}=23.14$ $p<.001$, $\eta_p^2=0.21$; see Fig. 3). Follow-up tests identified differences between groups at pre-stress ($F_{(1,89)}=10.07$, $p=.001$, $\eta_p^2=0.102$), t_{+10} ($F_{(1,89)}=72.63$, $p<.001$, $\eta_p^2=0.45$), t_{+30} ($F_{(1,89)}=63.38$, $p<.001$, $\eta_p^2=0.42$) and t_{+50} ($F_{(1,89)}=50.13$, $p<.001$, $\eta_p^2=0.36$).

Figure 3. Physiological and neuroendocrine stress response. Systolic and diastolic blood pressure (SBP; DBP; Panel A) and untransformed salivary cortisol concentrations (Panel B) in response to the MAST. Significant differences between groups are indicated (** $p < .001$; * $p < .05$). Graphs display means ($\pm$ SE).

3.1.2. Subjective stress responses

Participants reported higher subjective stress in the stress condition compared to control. The univariate ANOVA revealed that participants in the stress condition experienced the experimental manipulation as significantly more stressful than participants in the control condition (VAS; $F_{(1,89)} = 502.42$, $p < .001$, $\eta_p^2 = 0.85$; see table 1). Furthermore, negative affect and state anxiety increased significantly in the stress condition compared to control (PANAS-N; Time*Condition: $F_{(1,89)} = 165.82$, $p < .001$, $\eta_p^2 = 0.34$; STAI-S: Time*Condition: $F_{(1,89)} = 94.67$, $p < .001$, $\eta_p^2 = 0.52$). Follow up tests revealed no significant difference between the conditions at the pre-stress measure (both p 's $> .13$) and a significant difference at the post-stress measure (PANAS-N; $F_{(1,89)} = 51.57$, $p < .001$, $\eta_p^2 = 0.37$; STAI-S: $F_{(1,89)} = 101.54$, $p < .001$, $\eta_p^2 = 0.53$).

Table 1

Means ($\pm$ SE) of subjective stress, negative affect and state anxiety scores before and after the MAST for the stress and control conditions.

	VAS	PANAS-N		STAI-S	
		Pre	Post	Pre	Post
Stress	70.57 (2.49)	7.28 (0.39)	9.91 (0.57)	37.77 (1.45)	49.47 (1.48)
Control	6.50 (1.29)	6.71 (0.31)	5.52 (0.16)	35.86 (1.31)	31.55 (0.94)

3.2. Intentional control of future fears: forgetting of typical details

To analyse the effects of acute stress on intentional forgetting and intentional retrieval, two separate repeated-measures ANOVAs were used with recall scores for each Stimulus Type (2 levels: No-Imagine vs. baseline; Imagine vs. baseline, respectively) and Condition (2 levels: stress vs. control). There was a trend for acute stress to influence intentional forgetting (Stimulus Type*Condition: $F_{(1,89)} = 3.38$, $p = .07$, $\eta_p^2 = 0.04$; see Fig. 4). Follow-up tests revealed that, replicating Benoit et al. (2016), the unstressed participants forgot more typical details of No-Imagine than baseline items ($F_{(1,43)} = 3.09$, $p = .043$, $\eta_p^2 = 0.067$). By comparison, the stressed participants demonstrated an inability to forget typical details, as reflected by a non-significant difference between the recall of No-Imagine and baseline items ($F_{(1,46)} = 0.57$, $p = .23$, $\eta_p^2 = 0.012$). No significant interaction or main effect was observed for Imagine versus baseline items (both p 's $> .43$), suggesting that acute stress did not influence the intentional retrieval of fear details.

3.3. Intentional control of future fears: attenuation of anxiety

To analyse the effects of the Imagine/No-Imagine manipulation on anxiety toward future feared events, we first compared anxiety difference scores (post-baseline) within the control condition in order to replicate the findings of Benoit et al. (2016). Though suppression lead to numerically lower anxiety for No-Imagine compared to baseline items, this effect was not significant ($F_{(1,43)} = 0.69$, $p = .21$, $\eta_p^2 = 0.016$; see Fig. 4). In contrast, a significant difference was observed between Imagine and baseline

items, demonstrating that the retrieval of fears lead to an increase in anxiety ($F_{(1,43)} = 5.05$, $p = .015$, $\eta_p^2 = 0.11$).

To next analyse the effects of acute stress on anxiety toward future fears, two separate repeated-measures ANOVAs were used with anxiety difference scores for each Stimulus Type (2 levels: No-Imagine vs. baseline; Imagine vs. baseline, respectively) and Condition (2 levels: stress vs. control). Acute stress did not significantly interact with the effect of No-Imagine versus baseline on anxiety (Stimulus Type*Condition: $F_{(1,89)} = 1.94$, $p = .17$, $\eta_p^2 = 0.021$). However, direct comparisons yielded a trend for suppressed items ($F_{(1,89)} = 2.44$, $p = .061$, $\eta_p^2 = 0.027$) with unstressed participants showing a decrease in anxiety while stressed participants demonstrating an increase in anxiety. There was no such effect for baseline items ($F_{(1,89)} = 0.73$, $p = .39$, $\eta_p^2 = 0.001$). Finally, there was no interaction between acute stress and the effect of Imagine versus baseline (Stimulus Type*Condition: $F_{(1,89)} = 2.77$, $p = .099$, $\eta_p^2 = 0.03$). A direct comparison of the intentionally retrieved items also showed no significant difference between conditions ($F_{(1,89)} = 0.18$, $p = .34$, $\eta_p^2 = 0.002$).

Figure 4. Behavioural results from phase 3 of the Imagine/No-Imagine paradigm. Panel A: Scores obtained during the cued-recall phase for both conditions. Effects are denoted for the interaction between condition and stimulus type (# $p = .07$), the within group difference for the control condition between the percentage of recalled No-Imagine and baseline items (* $p < .05$). Panel B: Difference scores of anxiety ratings (post – baseline scores) for both conditions. Effects are denoted for planned comparisons within the control condition (* $p < .05$) and between the conditions for No-Imagine items (¥ $p = .061$). Graphs display means ($\pm$ SE).

3.4. Moderation of the effect of acute stress on intentional control by working memory capacity

Two separate multiple regression analyses using the PROCESS tool for SPSS (Model 1 with 1000 bootstrapping) were carried out to investigate the moderating effect of working memory on the stress-induced impairment of the intentional control of fears. The models analysed both intentional forgetting (No-Imagine – baseline) and intentional retrieval (Imagine – baseline). Scores from the backward condition ($WM_{Backwards}$) of the digit span task were added as a moderator.

For the intentional forgetting of fears details, the overall model including condition was significant ($WM_{Backwards}$: $F_{(3,87)}=4.26$, $p=.007$, $R^2=0.13$). Supporting the trend result for our prior repeated-measures ANOVA, condition significantly predicted differences in intentional forgetting ($b=73.86$, $t_{(87)}=3.37$, $p=.001$, CI [30.30, 117.41]). Furthermore, a significant interaction between condition and working memory was observed ($b=-12.34$, $t_{(87)}=-3.02$, $p=.003$, CI [-20.45, -4.22]). To explore this effect, further simple slope analyses on the conditional effects of condition were tested at two levels of working memory: low (-1SD) and high (+1SD). Low working memory capacity significantly contributed to the effect of stress on intentional forgetting ($WM_{Backwards(low)}$: $b=24.17$, $t_{(87)}=3.49$, $p=.001$, CI [10.39, 37.95]). High working memory capacity did not contribute significantly ($p=.41$). This indicates that the intentional forgetting of low capacity individuals was influenced by acute stress; in contrast, this effect was absent in high capacity individuals.

For intentional retrieval, the overall model did not prove significant ($p=.92$); therefore, there was no evidence that working memory capacity moderated effects of the intentional retrieval of fears.

4. Discussion

Accumulating evidence points to the fascinating possibility that we can, to some degree, intentionally control our fears and thoughts by actively retrieving and imagining some experiences while suppressing others. The current results, in part, replicate the original behavioural findings of Benoit et al. (2016). Active suppression of future fear imaginings resulted in intentional forgetting of details associated with the event. Furthermore, retrieval of fears resulted in an increase in anxiety toward these events. However, we did not replicate the finding that suppression contrastingly attenuates anxiety.

The current study further investigated the effects of acute stress on the intentional control of future fears and examined whether individual differences in executive control would moderate these effects. Due to the known impairing effects of stress on executive control, we predicted that exposure to an acute stressor would impair the active suppression of future fear details. This should thus hinder the ability to intentionally forget. The data were consistent with the hypothesis, with no significant reduction in recall of the No-Imagine item details compared with the baseline items by participants in the stress condition. Although we did not find evidence for this effect on anxiety, there was a trend for unstressed participants to show a decrease in anxiety toward suppressed future feared events, whereas stressed participants showed an increase.

Acute stress and individual differences in neuroendocrine responses seem to alter the functioning of the neural circuits connected to the intentional control of fears. On the one hand, forebrain circuits are involved in regulating the HPA axis response and stress integrative functions (Ulrich-Lai and Herman, 2009). On the other hand, non-genomic glucocorticoids switch the network balance in the brain, reducing activity in the executive network, including the dlPFC (Hermans et al., 2011, 2014; Qin et al., 2009). Moreover, individual differences in cortisol levels during stress recovery have been found to moderate the dlPFC–amygdala connectivity during rest (Quaedflieg et al., 2015). The dlPFC facilitates successful intentional forgetting of future fears by affecting activity in the vmPFC and hippocampus, i.e. structures that are key to facilitate the retrieval of past memories and the construction of future feared events (Benoit et al, 2016). A stress-induced down-regulation of the dlPFC may thus prevent the top-down inhibitory control signal to these regions (McEwen et al., 2016).

Results further revealed that individuals with low working memory capacity were more susceptible to the negative effects of acute stress on intentional forgetting. In contrast, individuals with high working memory were unaffected and their ability to intentionally forget did not differ from their counterparts in the control condition. This emphasizes the critical role executive control serves for actively suppressing imaginations of future fears under acute stress. Furthermore, working memory capacity selectively moderated the effects of acute stress on intentional forgetting as opposed to intentional retrieval.

Previous research has found that, in the absence of noradrenergic activation, (genomic) glucocorticoid actions interfere with inhibitory processing (Shields et al., 2015). This concurs with present findings, supporting the notion that inhibitory control is critical for suppressing unwanted thoughts or memories (Levy and Anderson, 2008; Benoit et al., 2016). Furthermore, the fact that our data showed an effect that was specific to No-Imagine items speaks against the view that our findings represent another example for the well-known stress-induced retrieval changes (de Quervain et al., 2000; Gagnon and Wagner, 2016). If acute stress had merely affected retrieval *per se*, one would have expected that memory for baseline and Imagine fear details would also have been affected. This was, however, not the case.

The current study assessed working memory capacity as a measure of executive control (McCabe et al., 2010). Levy and Anderson (2008) suggested that individual differences in executive control are able to predict the success of intentional memory control. They further suggest that, as such, factors that influence the ability to engage efficient executive control should therefore also affect the latter. When observing intentional memory control effects in the absence of further manipulation, baseline working memory capacity has not been found to predict the outcome of intentional forgetting (Waldhauser et al., 2011). However, when the demand of working memory is manipulated to a high load during memory control, the ability to intentionally forget has been found to decrease (Noreen and de Fockert, 2017). Furthermore, individuals with low working memory capacity have been found to be more susceptible to the detrimental effects of stress on other forms of higher cognitive functioning, such as goal-directed behaviour (Otto et al., 2013; Quaedflieg et al., 2019). Combined, these past and current findings suggest that a reduced working memory capacity negatively affects intentional forgetting and, furthermore, creates a vulnerability to the detrimental effects of stress.

The physiological and subjective data provide evidence that the MAST successfully induced acute stress. In line with previous studies (e.g. Quaedflieg et al., 2017; Smeets et al., 2012), participants in the stress condition showed an increase in subjective stress, systolic and diastolic blood pressure and cortisol concentrations when compared to control. Expanding on findings from previous studies, participants in the stress condition reported increased state anxiety following the MAST. It has previously been shown that individuals with higher trait anxiety are less able to reduce feelings of

anxiety toward future fears via intentional suppression (Benoit et al., 2016). As such, an increase in state anxiety could, in part, influence the subsequent outcome of attempts to suppress imaginings of future fears.

It should be noted that the sample consisted of predominately female participants ($n=71$), all of which were using hormonal contraception. Hormonal alterations throughout the menstrual cycle have been related to the variability in cortisol responses after acute stress in women (Kudielka et al., 2009). The use of hormonal contraceptives has also been found to alter the learning and memory of emotional content under response to stress (Nielsen et al., 2014). As such, these findings may not generalize to naturally cycling women.

The current study expands on previous findings by showing how active suppression of fear imaginings can be deficient under acute stress and that this is moderated by individual differences in executive control. Specifically, a low working memory capacity seems to predict a susceptibility to the detrimental effects of acute stress. Working memory can, to some extent, be improved. Working memory training has shown promising results, reducing symptomatology of anxiety and depression in vulnerable individuals (Beloe and Derakshan, 2019; Sari et al., 2016). However, it has been argued that, despite the benefits of working memory training, these learned skills do not transfer to other tasks (Gathercole et al., 2019). It would be of interest for future research to explore whether working memory training could be developed specifically to enhance intentional forgetting.

In the presence of stress-related psychopathology, it has been shown that the efficacy in suppressing unwanted memories is reduced (Hertel and Gerstle, 2003; Joorman et al., 2005; Mary et al., 2020; Nørby, 2018). Moreover, meta-analytical evidence indicates, more generally, that individuals with problems of controlling intrusive thoughts are deficient in suppressing memories (Stramaccia et al., 2019). Here, we demonstrate that exposure to acute stress negatively affects the ability to intentionally forget. Furthermore, individual differences in working memory moderate this effect. The current findings serve as an insightful step toward understanding the causes of failure in the intentional control of future fear imaginings.

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References

1. Anderson, M.C., Green, C., 2001. Suppressing unwanted memories by executive control. *Nature* 410, 336-339.
2. Anderson, M. C., Huddleston, E., 2012. Towards a cognitive and neurobiological model of motivated forgetting, in: Belli, R. (Eds.) *True and false recovered memories*. Springer New York, NY, pp. 53-120.
3. Anderson, M.C., Ochsner, K., Kuhl, B., Cooper, J., Robertson, E., Gabrieli, S.W., Glover, G., Gabrieli, J.D.E., 2004. Neural systems underlying the suppression of unwanted memories. *Science* 303, 232–235.
4. Beloe, P., Derakshan, N., 2019. Adaptive working memory training can reduce anxiety and depression vulnerability in adolescents. *Dev. Sci.* 1–13.
5. Benoit, R.G., Davies, D.J., Anderson, M.C. 2016. Reducing future fears by suppressing the brain mechanisms underlying episodic simulation. *PNAS* 113, 1–10.
6. Benoit, R.G., Schacter, D.L., 2015. Specifying the core network supporting episodic simulation and episodic memory by activation likelihood estimation. *Neuropsychologia* 75, 450-457.
7. Brewin, C.R., Beaton, A., 2002. Thought suppression, intelligence, and working memory capacity. *Behav. Res. Ther.* 40, 923-930,
8. Conway, A., & Engle, R., 1994. Working memory and retrieval: A resource-dependent inhibition model. *J. Exp. Psychol. Gen.* 123, 354-373

9. De Quervain, D.J.F., Roozendaal, B., Nitsch, R.M., McGaugh, J.L., Hock, C., 2000. Acute cortisone administration impairs retrieval of long-term declarative memory in humans. *Nat. Neurosci.* 3, 313–314.
10. Elzinga, B.M., Roelofs, K. 2005. Cortisol-induced impairments of working memory require acute sympathetic activation. *Behav. Neurosci.* 119, 98–103.
11. Fritz, C.O., Morris, P.E., Richler, J.J. 2012. Effect size estimates: Current use, calculations, and interpretation. *J. Exp.* 141, 2–18.
12. Gagnepain, P., Henson, R. N., & Anderson, M. C. (2014). Suppressing unwanted memories reduces their unconscious influence via targeted cortical inhibition. *PNAS*, 111, E1310-E1319.
13. Gagnepain, P., Hulbert, J., Anderson, M.C., 2017. Parallel Regulation of Memory and Emotion Supports the Suppression of Intrusive Memories. *J. Neurosci.* 37, 6423–6441.
14. Gagnon, S.A., Wagner, A.D., 2016. Acute stress and episodic memory retrieval: Neurobiological mechanisms and behavioral consequences. *Ann. N. Y. Acad. Sci.* 1369, 55–75.
15. Gathercole, S. E., Dunning, D. L., Holmes, J., & Norris, D. (2019). Working memory training involves learning new skills. *J. Mem. Lang.* 105, 19–42.
16. Hermans, E.J., Marle, H.J.F. van, Ossewaarde, L., Henckens, M.J.A.G., Qin, S., Kesteren, M.T.R. van, Fernández, G., 2011. Stress-Related Noradrenergic Activity Prompts Large-Scale Neural Network Reconfiguration. *Science* 334, 1151–1154.
17. Hermans, E.J., Henckens, M.J., Joels, M., Fernandez, G., 2014. Dynamic adaptation of large-scale brain networks in response to acute stressors. *Trends Neurosci.* 37, 304-314.
18. Hernaes, D., Quaedflieg, C.W.E.M., Offermann, J.S., Santa, M.M.C., van Amelsvoort, T., 2018. Neuroendocrine stress responses predict catecholamine-dependent working memory-related dorsolateral prefrontal cortex activity. *Soc. Cogn. Affect Neurosci.* 13, 114–123.
19. Hertel, P. T., & Gerstle, M., 2003. Depressive deficits in forgetting. *Psychol. Sci.* 14, 573–578.
20. Hoshi, Y., Oda, I., Wada, Y., Yamashita, Y., Oda, M., & Ohta, K. et al., 2000. Visuospatial imagery is a fruitful strategy for the digitspan backward task: A study with near-infrared optical tomography. *Brain Res. Cogn. Brain Res.* 9, 339–342.

21. Joel, M., Fernandez, G., Roozendaal, B., 2011. Stress and emotional memory: a matter of timing. *Trends Cogn. Sci.* 15, 280-288.
22. Joormann, J., Hertel, P.T., Brozovich, F., Gotlib, I.H., 2005. Remembering the Good, Forgetting the Bad : Intentional Forgetting of Emotional Material in Depression. *Nat. Neurosci.* 114, 640–648.
23. Kane, M., Bleckley, M., Conway, A., & Engle, R., 2001. A controlled-attention view of working-memory capacity. *J. Exp. Psychol. Gen.* 130, 169-83.
24. Kudielka, B.M., Hellhammer, D.H., Wust, S., 2009. Why do we respond so differently? Reviewing determinants of human salivary cortisol responses to challenge. *Psychoneuroendocrinology* 34, 2–18.
25. Levy, B.J., Anderson, M.C., 2008. Individual differences in suppressing unwanted memories: The executive deficit hypothesis. *Acta Psychologica* 127, 623–635.
26. Marsh, R.L., Hicks, J.L., 1998. Event-based prospective memory and executive control of working memory. *J. Exp. Psychol. Learn. Mem. Cogn.* 24, 336-349.
27. Mary, A., Dayan, J., Leone, G., Postel, C., Fraisse, F., Malle, C., ... Gagnepain, P. (2020). Resilience after trauma: The role of memory suppression. *Science*, 367(6479).
28. McCabe, D.P., Roediger, H.L, McDaniel, M.A., Balota, D.A., Hambrick, D.Z., 2010. The relationship between working memory capacity and executive functioning: evidence for a common executive attention construct. *Neuropsychology* 24, 222-243.
29. McEwen, B.S., Nasca, C., Gray, J.D., 2016. Stress Effects on Neuronal Structure: Hippocampus, Amygdala, and Prefrontal Cortex. *Neuropsychopharmacology* 41, 3–23.
30. McEwen, B.S., Morrison, J.H., 2013. The Brain on Stress: Vulnerability and Plasticity of the Prefrontal Cortex over the Life Course. *Neuron* 79, 16-29.
31. Nielsen, S.E., Ahmed, I., Cahill, L., 2014. Postlearning stress differentially affects memory for emotional gist and detail in naturally cycling women and women on hormonal contraceptives. *Behav. Neurosci.* 128, 482–493.

32. Noreen, S., de Fockert, J.W., 2017. The Role of Cognitive Load in Intentional Forgetting Using the Think/No-Think Task. *Exp. Psychol.* 64, 14–26.
33. Nørby, S. 2018. Forgetting and emotion regulation in mental health, anxiety and depression. *Memory* 26, 342-363.
34. Otto, A.R., Raio, C.M., Chiang, A., Phelps, E.A., Daw, N.D. 2013., Working-memory capacity protects model-based learning from stress. *PNAS*, 110, 20941–20946.
35. Qin, S., Hermans, E.J., van Marle, H.J.F., Luo, J., Fernández, G., 2009. Acute Psychological Stress Reduces Working Memory-Related Activity in the Dorsolateral Prefrontal Cortex. *Biol. Psychiatry* 66, 25–32.
36. Quaedflieg, C.W.E.M., Meyer, T., van Ruitenbeek, S., Smeets, T., 2017. Examining habituation and sensitization across repetitive laboratory stress inductions using the MAST. *Psychoneuroendocrinology*, 77, 175-181.
37. Quaedflieg, C.W.E.M., Stoffregen, H., Sebalo, I., Smeets, T., 2019. Stress-induced impairment in goal-directed instrumental behaviour is moderated by baseline working memory. *Neurobiol. Learn. Mem.* 158, 42–49.
38. Quaedflieg, C.W.E.M., van de Ven, V., Meyer, T., Siep, N., Smeets, T., 2015. Temporal dynamics of stress-induced alternations of intrinsic amygdala connectivity and neuroendocrine levels. *PLoS ONE* 10, e0124141
39. Sari, B.A., Koster, E.H.W., Pourtois, G., Derakshan, N., 2016. Training working memory to improve attentional control in anxiety: A proof-of-principle study using behavioral and electrophysiological measures. *Biol. Psychol.* 121, 203–212.
40. Schacter, D.L., Benoit, R.G., Szpunar, K.K. 2017. Episodic Future Thinking: Mechanisms and Functions. *Curr. Opin. Behav. Sci.* 17, 41-50.
41. Schoofs, D., Wolf, O.T., Smeets, T., 2009. Cold pressor stress impairs performance on working memory tasks requiring executive functions in healthy young men. *Behav. Neurosci.* 123, 1066–1075.

42. Shields, G.S., Bonner, J.C., Moons, W.G., 2015. Does cortisol influence core executive functions? A meta-analysis of acute cortisol administration effects on working memory, inhibition, and set-shifting. *Psychoneuroendocrinology* 58, 91–103.
43. Smeets, T., Cornelisse, S., Quaedflieg, C.W.E.M., Meyer, T., Jelicic, M., Merckelbach, H., 2012. Introducing the Maastricht Acute Stress Test (MAST): A quick and non-invasive approach to elicit robust autonomic and glucocorticoid stress responses. *Psychoneuroendocrinology* 37, 1998-2008.
44. Spielberger, C. D., Gorsuch, R. L., Lushene, R., Vagg, P. R., & Jacobs, G. A. (1983). *Manual for the state-Trait anxiety inventory*. Palo Alto, AC: Consulting Psychologist Press.
45. Strahler, J., Skoluda, N., Kappert, M.B., Nater, U.M., 2017. Simultaneous measurement of salivary cortisol and alpha-amylase: Application and recommendations. *Neurosci. Biobehav. Rev.* 83, 657-677.
46. Stramaccia, D. F., Rischer, K. M., Fawcett, J., & Benoit, R. G., 2019. Memory suppression and its deficiency in psychological disorders: A focused meta-analysis. *PsyArXiv*. doi:10.31234/osf.io/5wynm.
47. Ulrich-Lai, Y.M., Herman, J.P., 2009. Neural regulation of endocrine and autonomic stress responses. *Nat.* 10, 397- 409.
48. Waldhauser, G.T., Johansson, M., Bäckström, M., Mecklinger, A., 2011. Trait anxiety, working memory capacity, and the effectiveness of memory suppression. *Scand. J. Psychol.* 52, 21–27.
49. Watson, D., Clark, L., Tellegen, A., 1988. Development and validation of brief measures of positive and negative affect: The panas scales. *J. Pers. Soc. Psychol.* 54, 1063-70.
50. Wechsler, D., 1981. *Wechsler adult intelligence scale-revised*. New York: Harcourt Brace Jovanovich.