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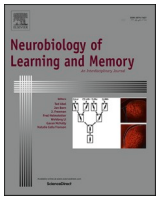

Impaired free recall of neutral but not negative material tested 105 min after cortisol administration

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ABSTRACT

Pharmacological studies have consistently shown memory retrieval impairment after administration of cortisol, particularly pronounced for emotional laboratory material (i.e. list of emotional words). However, it is unclear how pharmacological elevation of cortisol affects memory retrieval of ecologically-relevant emotional material (i.e. similar to a newspaper article about an emotional event). In the present study, we aimed to explore whether cortisol administration affects the recall of ecologically-relevant emotional and neutral material, and when memory retrieval occurs after a longer delay (105 min). In this double-blind, pseudo-randomized, placebo-control study, 79 participants learned a negative text and a neutral text. Twenty-four hours later, they were administrated either 10 mg of hydrocortisone or placebo. After 105 min, participants engaged in free recall of both texts. The group with cortisol administration showed significantly reduced free recall compared to the placebo group. Interestingly, this memory retrieval impairment was driven by significantly lower recall after cortisol vs. placebo administration for neutral texts, but not negative texts. The current finding suggests that cortisol administration impairs neutral ecologically-relevant material while leaving emotional material unaffected. These divergent findings, compared to existing literature, emphasize the necessity of employing more ecologically validated material to gain a more comprehensive understanding of the intricate interplay between cortisol administration and memory for ecological material.

1. Introduction

Animal and human studies have consistently shown differential effects of acute stress on memory depending on the memory phases (Goldfarb et al., 2019; Roozendaal, 2002). The enhancing or impairing effects of acute stress on episodic memory have been attributed to stress-induced physiological responses (Quaedflieg & Schwabe, 2018), particularly to the increase of glucocorticoid levels (cortisol in humans, corticosterone in rodents) (Lupien et al., 2007; Shields et al., 2017; Vogel & Schwabe, 2016). Findings revealed a consolidation enhancement, especially for emotionally arousing material (for a recent review Sazma et al., 2019; for a recent meta-analysis Shields et al., 2017). Conversely, studies consistently indicate detrimental effects of acute stress on memory retrieval (for a recent review Gagnon & Wagner, 2016; for a recent meta-analysis Shields et al., 2017). Studies employing a variety of stress-induction paradigms, such as pain or psychosocial stress, reliably demonstrated that acute stress impairs retrieval (Goldfarb et al., 2019; Kuhlmann et al., 2005; Schwabe & Wolf, 2009; Gagnon et al., 2019). These detrimental effects have been directly attributed to endogenous elevation of cortisol after acute stress (Lupien et al., 2007). Findings suggest that participants who exhibit a stronger cortisol response to a stressor recall fewer words during a free recall task compared to participants who do not display a similar cortisol response or control participants (Buchanan et al., 2006). It is noteworthy to observe that the majority of the studies explored a delay of 20 to 30 min between the stressor and the retrieval tasks (Quaedflieg & Schwabe, 2018; Shields et al., 2017). This delay allows to reach salivary cortisol peak levels following a stressor (Kirschbaum & Hellhammer, 1989,1994; Kumar et al., 2005; Vining et al., 1983).

Consistent with acute stress-induction studies, pharmacological

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studies of cortisol administration, inducing a rise in cortisol levels exogenously, have consistently demonstrated a memory retrieval impairment (de Quervain et al., 1998, 2000; Kuhlmann et al., 2005; Tollenaar et al., 2009). This memory retrieval impairment has typically been observed in studies where memory retrieval was tested within a time window up to 60 min following pharmacological cortisol administration (Buss et al., 2004; de Quervain et al., 2000, 2003, 2007; Kuhlmann et al., 2005; Kuhlmann & Wolf, 2005, 2006; but see Antypa et al., 2022; Tollenaar et al., 2009 for variations in delays). While there is a significant increase in cortisol levels compared to placebo administration with this delay (Buss et al., 2004; de Quervain et al., 2000; Kuhlmann et al., 2005), it appears that salivary cortisol levels peak later, i.e. after 60 min, e.g. around 75 min for a 10 mg dose in Antypa et al., 2022; around 100 min for a 10 mg dose in Tops et al., 2003. To the best of our knowledge, only one study has investigated the effects of cortisol administration after a delay longer than 60 min and expanded the observed retrieval impairment (Tops et al., 2003). Here, we decided to extend the literature on the effect of cortisol administration on memory retrieval at a longer delay than 60 min. This decision was made to ensure that salivary cortisol levels were around peak levels (for a 10 mg dose).

Considering human studies with pharmacological cortisol administration, the majority have focused on investigating the effects of elevated cortisol levels on episodic memory using controlled laboratory material such as words (i.e. list of words, pairs of words) or pictures (Antypa et al., 2022; de Quervain et al., 2000; Kuhlmann et al., 2005; Kuhlmann & Wolf, 2006; Roozendaal et al., 2003; Schilling et al., 2013; Tollenaar et al., 2009; Tops et al., 2003). However, the retrieval of real-world-like events is notably more intricate and complex than retrieval of simpler material used in the laboratory. Therefore, it is of utmost importance to investigate the impact of cortisol administration on the retrieval of ecologically-relevant material.

In addition, the nature of retrieval tasks (e.g. free recall, cued recall or recognition) appears to influence the findings regarding memory retrieval following cortisol administration (Gagnon & Wagner, 2016). After cortisol administration, free recall is consistently impaired (de Quervain et al., 2000; Kuhlmann & Wolf, 2005; Tops et al., 2003), while findings on cued recall and recognition are inconsistent with either impairing effects or no impact (Antypa et al., 2022; Buss et al., 2004; de Quervain et al., 2003; Tops et al., 2003). These inconsistencies may be directly associated with the complexity of the tasks, where recognition, being less demanding, is less susceptible to the influence of cortisol (Buchanan et al., 2006; Gagnon & Wagner, 2016). Concerning cued recall, the administration of different doses of cortisol has highlighted an inverted U-shape between cued recall and cortisol levels, indicating a performance-dose relationship (Schilling et al., 2013). Moreover, a concurrent noradrenergic activation might be necessary to induce memory retrieval impairment across all type of tasks (Gagnon & Wagner, 2016; Roozendaal et al., 2004). Given these discrepancies observed depending on the memory task type, it is vital to incorporate various memory tasks within the same study to explore whether cortisol administration impacts them in similar ways.

Additionally, this retrieval impairment upon increased cortisol levels appears to be more pronounced when the material (i.e. list of words) is emotional compared to neutral (studies on cortisol administration: Antypa et al., 2022; de Quervain et al., 2007; Kuhlmann et al., 2005, but see Buss et al., 2004; studies on acute stress induction: Buchanan et al., 2006; Kuhlmann et al., 2005; Smeets, 2011; Smeets et al., 2008). This retrieval impairment has been attributed to the time-dependent neuromodulatory response exerted by cortisol (de Quervain et al., 1998; Roozendaal et al., 2003), in conjunction with the activation of the noradrenergic system (Roozendaal, 2002; Roozendaal et al., 2004).

At the neural level, brain regions like the hippocampus, amygdala and prefrontal cortex (PFC) are particularly rich in cortisol receptors (Groeneweg et al., 2011; Reul & de Kloet, 1985). Altogether, these brain regions also support encoding, consolidation and retrieval processes (Cahill et al., 1995; Eichenbaum et al., 2007; Rubin et al., 2017), making cortisol level elevation influential in modulating episodic memory. Noteworthy, the amygdala exerts influences upon the hippocampus and the PFC, eliciting significant modulatory effects for emotionally laden content (Arnsten, 2009; McGaugh, 2004). Recent findings suggest that increased cortisol levels heighten neural excitability in the hippocampus and the amygdala (de Kloet et al., 1993; Groeneweg et al., 2011; Karst et al., 2005, 2010), enhancing consolidation (Cahill et al., 2003; Goldfarb et al., 2019; Roozendaal, 2002; van Marle et al., 2013), but impairing retrieval (de Quervain et al., 2000; Goldfarb et al., 2019; Roozendaal, 2002).

On this background, for this study, we aimed to examine the effects of cortisol administration on the retrieval of ecologically-relevant material. Participants learned neutral and emotional texts and twenty-four hours after, were orally administered 10 mg of hydrocortisone. Around 100 min after administration (in order to reach peak salivary cortisol levels, based on previous studies of 10 mg cortisol administration), participants engaged in a free recall, recognition and temporal sequential order tasks.

In light of the existing body of research demonstrating memory retrieval impairment after cortisol administration, we expected to see lower memory performance after cortisol administration compared to placebo administration in the free recall, recognition and sequential order tasks. Moreover, for emotional material, we hypothesized that memory retrieval of the emotional text will be more impaired than the retrieval of neutral text following cortisol administration compared to placebo administration.

2. Methods

2.1. Participants

94 healthy volunteers (48 females; $M = 21.92$, $SD = 2.49$; age range: 18–30 years old) took part in the study, the majority of them students from the University of Geneva. All participants were French speaking. In order to minimize variations in circadian rhythms, we did not include people who travelled across several time zones recently, worked during the night or had sleeping disorders. People with somatic, psychiatric or neurologic disorders as well as pregnant participants were also not included. Depression symptoms were checked using the Beck Depression Inventory II (BDI-II). Participants were asked to have a good night of sleep before the experiment, and to avoid eating, drinking (except water) or doing physical exercise two hours before participation and alcohol 24 h before the experiment. Participants were pseudo-randomly assigned to the cortisol or placebo group in a double-blind procedure. 15 participants were excluded because of missing data ($n = 5$); BDI score higher than 13 ($n = 1$); low levels of free recall of texts at encoding (1.5*interquartile range (IQR) under the 1st quartile; $n = 2$), low percentage of free recall performance (see section 2.5 Memory performance; 1.5*IQR under the 1st quartile; $n = 3$) and high cortisol levels across the entire experiment (1.5* IQR under the 1st quartile; $n = 4$). For the recognition test, 3 additional participants were excluded due to experimenter errors. Similarly, 5 additional participants were excluded due to experimenter errors for the sequential temporal order test. The final analysis comprised 79 participants (39 in the placebo group (20 women) and 40 participants in the cortisol group (21 women)). The two groups did not differ in age, body mass index (BMI) (kg/m^2) or BDI-II scores (all $p > .091$, see Table 1). All subjects gave their written informed consent before participation and were compensated for their participation. The study was approved by the local ethic committee.

2.2. Design

The study was designed as a double-blind, pseudo-randomized, placebo-controlled, between-subjects experiment. 40 participants were administered 10 mg of hydrocortisone orally (Gelapharm) named cortisol group, 39 participants a placebo pill (placebo group). The dose

Table 1
Demographics and control variables.

	Cortisol group (n = 40; 21 females) Mean ± SD	Placebo group (n = 39, 20 females) Mean ± SD
Age	22.63 ± 3.16	21.64 ± 1.75
BMI (kg/m^2)	21.94 ± 2.72	21.28 ± 3.30
BDI-II	4.45 ± 3.94	3.81 ± 2.80

There were no difference between the groups in the demographics or control variables. All p >.091.

of hydrocortisone was chosen based on previous studies showing that 10 mg of hydrocortisone lead to an increase in cortisol levels and modulate memory performance in a time-dependent manner (Henckens et al., 2011; Tops et al., 2003; van Ast et al., 2013).

2.3. Material

The material consisted of an emotional and a neutral text (emotional: "Murderer" and neutral: "Fashion") presented in French. Murderer described the killing of children in detail. Fashion described clothes during a fashion show (Schürer-Necker, 1994; Wagner et al., 2001; Wilhelm et al., 2011). Texts were shown to differ in emotionality by subjective feelings and physiological measures (Schürer-Necker, 1994).

2.4. Procedure

Fig. 1 shows the experimental procedure. The experiment took place on two consecutive sessions (24 h apart), starting either at 13:00 or 15:00 in order to avoid high basal cortisol levels observed in the morning (Kirschbaum & Hellhammer, 1989). For the Learning Session on Day 1, participants were instructed to memorize as many details as possible for a later recall of the emotional and the neutral text. First, they read the emotion text (4 min) and recall it. Subsequently, they ready the neutral text (4 min) and recalled it. After reading of each text, they engaged in an immediate free recall with no time limit to obtain an estimate of initial Learning performance. Participants were explicitly instructed to recall the texts with as much detail as possible and to write them down verbatim.

At the Retrieval session on Day 2, participants were administered 10 mg hydrocortisone or placebo. At + 105 min after pill intake, participants were asked to freely recall the texts as they had done the previous day. Thereafter, they were presented with 12 pairs of words (content word of negative and neutral text separately and a synonym). In the recognition memory test, they should indicate which word of the pair appeared in the texts (see Rimmele et al., 2010). Then, as a temporal

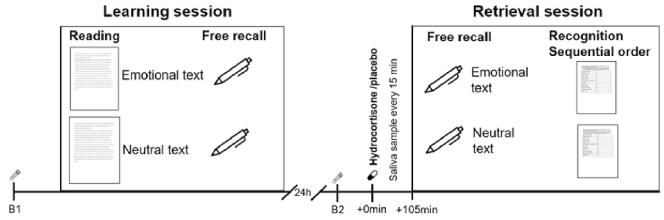

Fig. 1. Experimental procedure. At the Learning Session, participants read the emotional text first and then the neutral text (each for four min) and immediately recalled each text. Twenty-four hours later, they were administered either hydrocortisone (10 mg) or placebo, and 105 min later recalled the texts, engaged in a recognition task and a sequential order task. At Retrieval Session, there was no instruction given concerning the order of recall of the texts (i.e. participants could recall the emotional or the neutral text first). Saliva samples were taken at baseline on both days (B1 at Learning Session and B2 at Retrieval Session). After pill administration (+0 min), saliva samples (total of seven) were taken every fifteen minutes until the free recall to assess salivary cortisol levels.

order task, they arranged the 12 selected words in their respective order of appearance in the texts (Wilhelm et al., 2011). Participants were not given any restriction concerning the order of recall of the texts. At the end of the experiment, participants were asked whether they thought they had been administered hydrocortisone or placebo. Participants were not able to correctly identify whether they had received hydrocortisone or placebo [$\chi^2(1) = 0.203$, p =.653].

2.5. Memory performance

Memory performance was assessed with a free recall, recognition and temporal order task separately for the emotional and the neutral text. Free recall performance was calculated as the free recall percentage of target words (i.e. number of words recalled at Retrieval Session on Day 2 divided by number of words recalled at Learning Session on Day 1). The words counted as correct included exact encoded words, as well as words derived from the same word stem, especially in word type transition (e.g. from noun to adjective) (Schürer-Necker, 1994; Wagner et al., 2005). Recognition performance was calculated as the number of correctly identified target words (compared to synonym words) for both emotional and neutral texts. Temporal sequential order performance was calculated as a deviation score (distance between the position where the subject placed the word and the absolute position in the text (Krug et al., 2006)).

2.6. Saliva samples

To assess salivary cortisol levels, nine saliva samples were in total taken during the two days. To assess basal salivary cortisol levels at the Learning Session on Day 1, one saliva sample was taken on Day 1 (prior Learning session, see Fig. 1). At the Retrieval session on Day 2, a saliva sample was taken as baseline prior to cortisol/placebo administration (prior Retrieval session, see Fig. 1). After pill ingestion another seven saliva samples were taken, each fifteen minutes apart. Salivary cortisol samples were collected with Sarstedt salivette tubes (Sarstedt, Rommelsdorf Germany) and were stored at −25C° until analysis. Cortisol levels were analyzed using luminescence immunoassay for the in vitro diagnostic quantitative determination of cortisol in human saliva (IBL, International), with functional sensitivity of 0.011 µg/dl. Inter- and intra-assay coefficients of variation across all cortisol concentrations were equal or below 5 %.

2.7. Data analyses

Salivary cortisol levels were log-transformed to account for non-normal distribution. Salivary cortisol levels at Learning Session on Day 1 were compared with independent sample *t*-test between cortisol and placebo group. Salivary cortisol levels at Retrieval Session on Day 2 were analyzed with mixed-design ANOVAs with Substance (cortisol vs. placebo) as a between-subjects factor and Time (8 time-points saliva sample on Day 2) as a within-subjects factor. Follow-up t-tests were run if appropriate and considered as significant if p <.05.

Free recall at Learning Session on Day 1 was calculated as the total amount of content words correctly recalled separately for emotional and neutral text. An identical score was obtained for free recall at Retrieval Session on day 2. Free recall percentage at the Retrieval Session with respect to initial Learning was calculated as the percentage ratio between the content words recalled during the Retrieval session on Day 2 and content words recalled at the Learning session on Day 1 independently for emotional and neutral text (Wilhelm et al., 2011). Recognition was calculated as the addition of all correctly recognized words in the recognition test distinctly for emotional and neutral text. Temporal order was calculated as the deviation position between the assigned position and the absolute position of the word within the texts separately for emotional and neutral text (Wilhelm et al., 2011). Given that we expected memory retrieval to be particularly more impaired for

emotional than neutral material after cortisol vs. placebo administration, we analyzed free recall performance, recognition performance and sequential order performance with mixed-design ANOVAs with Substance (cortisol vs. placebo) as a between-subjects factor and Emotion (emotional text vs. neutral text) as a within-subjects factor. When appropriate, Green-House corrections of degrees of freedom were used. Follow-up t-tests were run if appropriate and considered significant if p <.05.

3. Results

3.1. Hormonal measures

As expected, salivary cortisol levels were significantly lower in the placebo group than in the cortisol group after the substance administration (Substance X Time interaction, [F(2.949, 162.201) = 30.32, p <.001]; main effect of Substance, [F(1, 55) = 98.11, p <.001]; main effect of Time, [F(2.949, 162.201) = 8.18, p <.001]; Fig. 2). Baseline salivary cortisol levels did not differ between groups at the Learning session on Day 1 and at the Retrieval session on Day 2 (all p >.670). After pill intake, for all other measurement times, cortisol levels were higher in the cortisol compared to the placebo group (all p <.001).

3.2. Memory performance

3.2.1. Free recall

At the Learning Session on Day 1, free recall (total number of content words) of the emotional text (M = 39.03, SD = 10.57) was higher than free recall of the neutral text (M = 21.35, SD = 9.56; main effect of Emotion, [F(1, 77) = 269.23, p <.001, η^2 = 0.778]). As expected, free recall at the Learning Session did not differ between placebo and cortisol groups (see Table 2, main effect of Substance, [F(1, 77) = 3.44, p =.067, η^2 = 0.043]; Emotion X Substance interaction, [F(1, 77) = 0.11, p =.746, η^2 = 0.001]).

At the Retrieval session on Day 2, free recall of the emotional text (M = 31.72, SD = 11.13) was again better than free recall of the neutral text (M = 16.66, SD = 9.47; main effect of Emotion, [F(1,77) = 269.90, p <.001, η^2 = 0.778). In addition, a trend towards a main effect of Substance [F(1, 77) = 3.872, p =.053, η^2 = 0.048] was found with better free recall for placebo group (M = 52.56, SD = 19.50) compared to cortisol group (M = 44.30, SD = 17.81). No Emotion by Substance interaction effects were observed [F(1, 77) = 0.233, p =.631, η^2 = 0.003]. Exploratory analyses, conducted on free recall of emotional and neutral text separately by substance group, showed better free recall of neutral text for placebo group (M = 18.97, SD = 9.08) compared to cortisol group (M = 14.40, SD = 9.40; [t(77) = 2.20, p =.031, d = 0.495], but no difference between groups for the emotional texts.

Table 2
Free recall memory performance.

	Cortisol group Mean ± SD	Placebo group Mean ± SD
Emotional text		
Content words recalled on Day 1	37.05 ± 10.39	41.05 ± 10.50
Content words recalled on Day 2	29.90 ± 10.33	33.59 ± 11.73
Recall percentage (Day 2 to Day 1)	80.57 ± 15.27	80.81 ± 15.00
Recognition	7.41 ± 2.00	7.97 ± 1.76
Temporal Order	38.74 ± 11.02	37.05 ± 13.05
Neutral text		
Content words recalled on Day 1	19.73 ± 9.27	23.03 ± 9.69
Content words recalled on Day 2	14.40 ± 9.40	18.97 ± 9.08*
Recall percentage (Day 2 to Day 1)	70.22 ± 19.10	83.34 ± 17.61**
Recognition	7.81 ± 2.41	7.83 ± 2.48
Temporal Order	36.78 ± 14.49	35.88 ± 15.42

Memory performances for each text and each group. Text recall at the Learning Session on Day 1 (all p >.093) and at the Retrieval session on Day 2 (total number of content words freely recalled). On Day 2, the cortisol group showed lower free recall of neutral text compared to the placebo group in both measures, i.e. lower number of content words of neutral texts and lower recall percentage of neutral texts (number of words freely recalled at the Retrieval session divided by number of words freely recalled at the Learning Session). * p <.05. ** p <.01.

Most importantly and in accordance with our hypothesis, when adjusting free recall on Day 2 for initial Learning performance on Day 1, the cortisol group (M = 75.40 %, SD = 14.20 %) showed lower free recall (percentage ratio between content words at Retrieval session on Day 2 with respect to Learning session on Day 1) compared to the placebo group (M = 82.07 %, SD = 13.35 %) (main effect of Group, [F(1, 77) = 4.63, p =.035, η^2 = 0.057]). In addition, contrary to our hypothesis, we found an interaction between the emotionality of the texts and the substance (interaction Emotion X Substance, [F(1, 77) = 8.79, p <.01, η^2 = 0.102]; Fig. 3): the cortisol group recalled significantly less of the neutral text (M = 70.22 %, SD = 19.10 %) compared to placebo group (M = 83.34 %, SD = 17.61 %; [t(77) = 3.17, p =.002, d = 0.714]). In contrast, free recall percentage of the emotional text did not differ

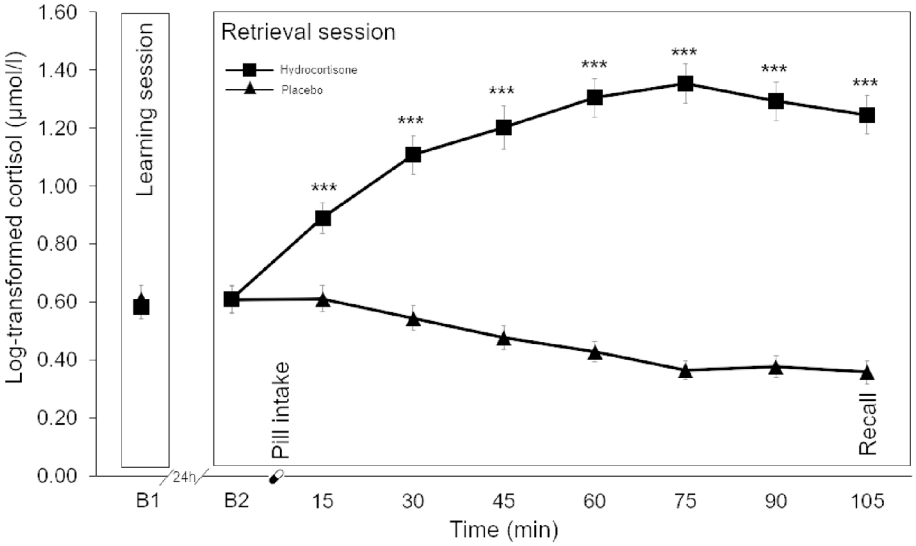

Fig. 2. Baseline cortisol levels at the Learning session on Day 1 (B1) and at the Retrieval session on Day 2 (B2). After the pill intake (either 10 mg of hydrocortisone or placebo), the cortisol levels were significantly different between cortisol group (squares) and place group (triangles). The levels still differ at the time of memory recall of the texts (+105 min). There were no differences between the groups at encoding or before pill administration at retrieval. ***p <.001.

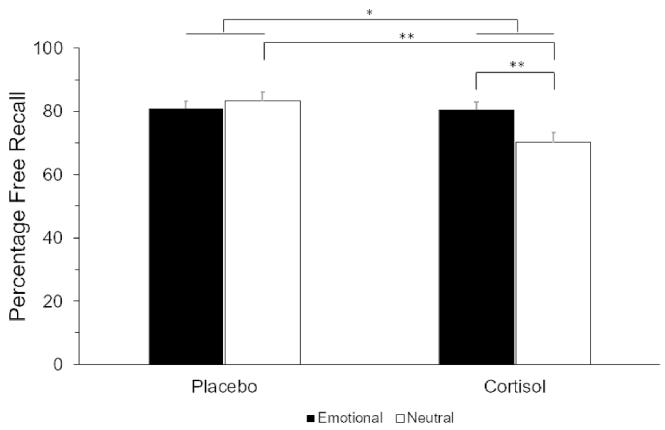

Fig. 3. Cortisol decreased memory recall of the neutral texts assessed by memory percentage (words freely recalled at the Retrieval session on Day 2 divided by words freely recalled at the Learning session on Day 1, SE). In the cortisol group, the emotional text was better remembered than the neutral text. * p <.05. ** p <.01.

between the cortisol and the placebo group (p >.945). Last, the emotionality of the texts did not influence free recall percentage in both groups (main effect of Emotion, [F(1, 77) = 3.24, p =.076, η^2 = 0.040].

3.2.2. Recognition

Contrary to our expectations, cortisol administration did not influence recognition of the texts (main effect of Substance, [F(1, 71) = 0.87, p =.353, η^2 = 0.012]). Recognition was also not impacted by the emotionality of the texts (main effect of Emotion, [F(1, 71) = 0.145, p =.704, η^2 = 0.002]; interaction Emotion X Substance, [F(1, 71) = 0.334, p =.565, η^2 = 0.005]).

3.2.3. Temporal order

Opposite to our hypothesis, temporal order was not impacted by cortisol administration (main effect of Substance, [F(1, 69) = 0.229, p =.634, η^2 = 0.003]) or by the emotionality of the texts (main effect of Emotion, [F(1, 69) = 0.351, p =.555, η^2 = 0.005] and interaction, [F(1, 69) = 0.003, p =.959, η^2 = 0.000]).

4. Discussion

The present study aimed at exploring the effects of a long delay (+105 min) after cortisol administration on memory recall for ecologically-relevant neutral and negative material using a free recall, a recognition memory and a sequential temporal memory test. Consistent with the literature, we expected memory retrieval to be impaired after cortisol compared to placebo administration. Moreover, we expected to observe a greater impairment for emotional negative material compared to neutral material after cortisol administration. Here, we show that testing memory after a longer delay (105–125 min) after administration of 10 mg of hydrocortisone impaired free recall of neutral texts, while leaving free recall of emotional texts as well as recognition and sequential temporal memory unaffected.

Our finding of impaired recall of neutral memories in the cortisol vs. placebo group is in line with previous research showing that administration of 25 mg of cortisone 60 min before testing impairs memory recall of neutral material (de Quervain et al., 2000, 2003). Similarly, administration of 10 mg of hydrocortisone 60 min before testing impairs recall of neutral autobiographic memories (Buss et al., 2004). Similar impairments in memory recall have also been found in studies after stress induction ranging from 20 min to 90 min of delay. The present study extends the memory retrieval impairment of glucocorticoids at a longer delay, i.e. 105–125 min after cortisol administration.

Considering emotionality, our study showed no effect of cortisol administration on memory recall for an emotional text. This finding contrasts with previous findings of cortisol administration and stress induction in humans. Previous studies have consistently shown impaired retrieval of emotional material after cortisol administration when recall was tested 8 min to 60 min after administration (Antypa et al., 2022; Kuhlmann et al., 2005; Kuhlmann & Wolf, 2005, 2006; de Quervain et al., 2007; Schilling et al., 2013) and after acute stress induction when recall was tested 20–30 min after the stressor, i.e. when cortisol levels typically peak due to stress induction (Buchanan et al., 2006; Domes et al., 2004; Goldfarb et al., 2019; Kuhlmann et al., 2005; Shields et al., 2017). However, some findings suggest an impairment undifferentiated of valence (Hidalgo et al., 2015; Smeets, 2011; Tollenaar et al., 2009). Nevertheless, most of these studies used material such as word lists (de Quervain et al., 2003; Kuhlmann et al., 2005). In contrast, we used more complex ecologically-relevant material, i.e. validated emotional text material, which is similar to everyday material, e.g. articles in a newspaper. As such, not only the difference in the delay between cortisol administration and memory testing, but also the difference in the type of material may contribute to the discrepant findings, as previous studies showed emotional recall impairment under increased cortisol levels with simpler test material (e.g. word lists) and shorter delays after cortisol administration. In contrast, the higher complexity of our material and the longer delay between cortisol administration and testing in our study may explain that we found no difference in emotional memory recall in the cortisol vs. the placebo group in our study. This explanation is in line with a previous study that tested more complex autobiographical memory and found that cortisol administration 60 min before retrieval impaired recall for neutral events in an autobiographic test while leaving memory recall for emotional events intact (Buss et al., 2004). Moreover, this emotional impact could be ascribed to the amygdala's role during encoding, likely resulting in a more robust consolidation of emotional memories in comparison to neutral memories, consequently leading to a weaker retrieval (Buss et al., 2004). This relationship was observed in an fMRI study, indicating a positive correlation between the activity of the amygdala during encoding and the subsequent recognition of emotional pictures (Cahill et al., 2003). These findings suggest that when encoding and consolidation are more robust, the impairing effects of cortisol administration may not manifest. Such observations align with mnemonic strategies like the testing effect, which demonstrates protective effects against stress (Smith et al., 2016). Concerning retrieval per se, our findings may be explained by the fact that the elevation of cortisol, without concurrent activation of noradrenergic system as seen during acute stress, may not be sufficient to induce a memory retrieval impairment of emotional material. Future neuro-imaging studies examining the effect of cortisol administration on memory recall are imperative to deepen our understanding of how cortisol administration (without noradrenergic activation) affects brain functioning and memory retrieval.

Considering recognition, here we show that administration of 10 mg hydrocortisone has no impact on recognition memory. This finding is consistent with numerous findings that showed that cortisol administration does not affect recognition memory (de Quervain et al., 2000, 2003; Oei et al., 2007). This finding is also in line with literature of showing no impact of a stress-induced glucocorticoid increase on recognition memory (Buchanan et al., 2006; Schwabe & Wolf, 2014). In fact, recognition is an easier task which is less cognitively demanding in which glucocorticoids may not exert their impairing effects (Gagnon & Wagner, 2016).

Considering temporal memory, we found no differences on recall of temporal order after cortisol administration. Temporal sequence memory has been linked to associative memory (binding of different single items) and shown to be improved when cortisol is administered post-learning (Wilhelm et al., 2011). This finding has been attributed to cortisol possibly influencing cerebral structures, such as the hippocampus which is thought to be involved in relational binding of between items of an episode. Compared to cortisol's influence on memory

consolidation, here we found no effect of cortisol administration on temporal sequence memory when cortisol was administered at retrieval. Possibly, cortisol exerts differential effects on temporal sequence memory depending on the memory phase that its levels are increased.

As expected, in this study, 10 mg of hydrocortisone increased salivary cortisol levels from 15 min to 105 min after oral administration. This finding is in line with previous findings that report salivary cortisol increase in this time window using a 10 mg dose (van Ast et al., 2013; Fleischer et al., 2019; Tops et al., 2003). At the time of recall testing at 105 min at the Retrieval Session on Day 2, cortisol levels were still significantly elevated in the cortisol group compared to the placebo group. Cortisol levels were similar to awakening morning response or moderate psychosocial stressor at time of recall (Rimmele et al., 2015; van Ast et al., 2014). These findings suggest that cortisol rise directly impacts memory retrieval of neutral but not emotional material.

In conclusion, the present findings show that free recall of memory tested 105 min after cortisol administration is impaired for free recall of neutral texts, but not for emotional texts. These findings advance understanding of cortisol induced memory impairment of ecologically-relevant material.

CRediT authorship contribution statement

Daniela Barros Rodrigues: Data curation, Formal analysis, Investigation, Visualization, Writing – original draft, Writing – review & editing. **Despina Antypa:** Methodology, Supervision, Writing – review & editing. **Ulrike Rimmele:** Conceptualization, Funding acquisition, Methodology, Project administration, Resources, Supervision, Writing – original draft, Writing – review & editing.

Data availability

Data will be made available on request.

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