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The effect of cortisol on autobiographical memory retrieval depends on remoteness and valence of memories

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ABSTRACT

There is evidence that specificity of autobiographical memory (AM) retrieval is impaired by cortisol. However, it is unknown whether glucocorticoids differentially influence the retrieval of recent versus remote AMs. Therefore, the aim of the current study was to investigate the effects of cortisol on AM retrieval, in terms of memory specificity, with respect to remoteness of the retrieved memories. A placebo controlled, double blind study was conducted. Thirty female and 24 male healthy participants (mean age 24.5, SD = 3.7) received either placebo or 10 mg hydrocortisone before completing an autobiographical memory test. Participants showed higher memory specificity for recent memories compared to remote ones. There was no main effect of cortisol on AM retrieval. However, interaction effects suggest that cortisol affects remote, but not recent memories, which seems to depend upon valence.

1. Introduction

It is well documented that cortisol has an impairing effect on memory retrieval (de Quervain, Aerni, Schelling, & Roozendaal, 2009). Most of the studies investigating this effect have used declarative memory tests, e.g. by measuring the retrieval of a previously learned word list or other recently learned stimuli. Only few studies so far investigated how cortisol affects autobiographical memory (AM) retrieval and therefore the ability to recall events from oneís own past. One test which is frequently used to investigate AM retrieval is the Autobiographical Memory Test by Williams and Broadbent (1986). In this test the most crucial outcome variable is memory specificity. An autobiographical memory is defined as specific if it includes a specific event that only happened once and which is set in place and time (for example "last Monday when I went to a colleaguesí party).

One of the first studies to investigate the influence of cortisol on memory specificity was the one of Buss, Wolf, Witt, and Hellhammer (2004). They found an impairment of AM retrieval in terms of decreased memory specificity after acute glucocorticoid administration in healthy participants as they retrieved less specific memories after hydrocortisone compared to placebo. This effect was seen mostly in neutrally valenced A Schlosser et al. (2010) replicated these findings and in another study (Wingenfeld et al., 2013) memory specificity was again reduced in response to neutral stimuli. Additionally, the intake of glucocorticoids may influence AM in a dose-dependent matter as Young, Drevets, Schulkin, and Erickson (2011) showed that AM retrieval was less specific only under high cortisol levels that were similar to those after severe psychosocial stressors.

Neuroimaging studies demonstrate that AM is based on a neuronal network of different brain areas including the medial and prefrontal cortex, the retrosplenial cortex, the hippocampus and parahippocampal gyrus, the temporal pole, the cerebellum and the amygdala (in emotional AM) (for review see Cabeza & St Jacques, 2007; Maguire, 2001; Svoboda, McKinnon, & Levine, 2006). The hippocampus is especially interesting as newer research focuses on the question whether AM becomes independent of the hippocampus and more related to the prefrontal cortex (PFC) as autobiographical memories are getting older and therefore more remote as it is supposed by Squire (1992) in the 'standard model' of memory consolidation. In fact, there is some evidence that supports this idea (Piefke, Weiss, Zilles, Markowitsch, & Fink, 2003). In contrast, the majority of imaging studies suggest that the hippocampus plays a permanent role in the retrieval of AM but activation in hippocampal

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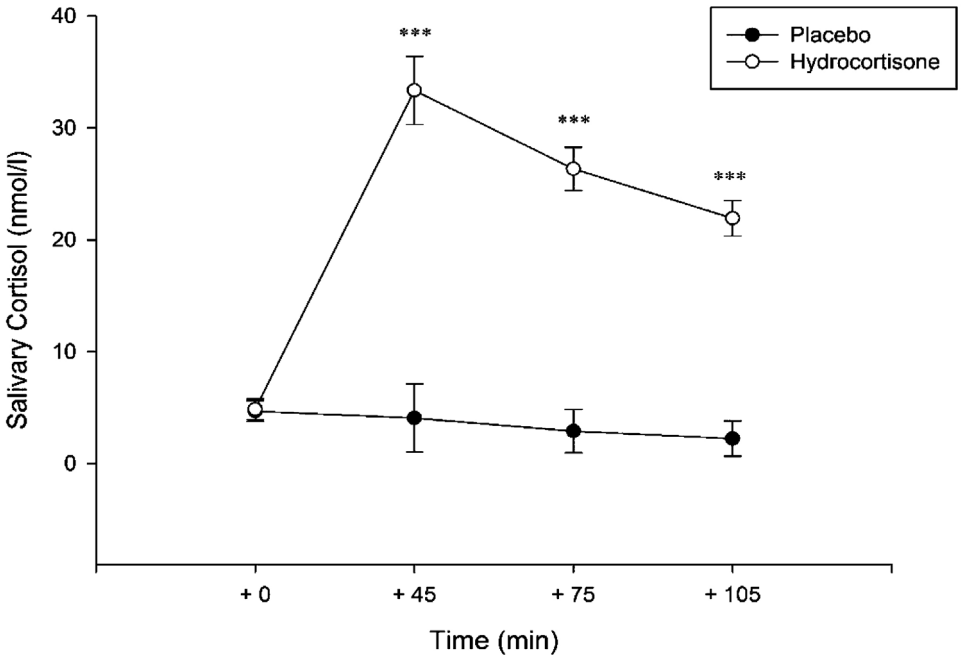

Fig. 1. Salivary cortisol concentration immediately before (+0) and 45 min, 75 min and 105 min after the intake of hydrocortisone or placebo. In the hydrocortisone condition participants showed significant higher salivary cortisol concentrations at 45 min, 75 min and 105 min after drug intake compared to participants taking placebo (*** = $p < 0.001$). All values are based on a subsample of Duesenberg et al. (2016).

subfields differs in relation to age of memories (Bonnici, Chadwick, & Maguire, 2013; Rekkas & Todd Constable, 2005). This is in accordance with the multiple trace theory by Nadel, Samsonovich, Ryan, and Moscovitch (2000). As many studies examine autobiographical memory in relation to hippocampal activation, most studies do not report on behavioral data, comparing the ability to recall specific recent or remote memories. Rekkas and Todd Constable (2005) could not find a difference between recent and remote memories regarding vividness and depth of AM whereas Piefke et al. (2003) report a tendency to better recognition of recent relative to remote memories.

In sum, there is 1) evidence that autobiographical memory retrieval is impaired by cortisol and 2) that brain activation differs between recent and remote memory. Consequently, the effect of cortisol on autobiographical memory might be mediated by the age of the retrieved memory. To this date, there is only one study, which takes remoteness of AMs into account when investigating the effect of cortisol on AM retrieval. Tollenaar, Elzinga, Spinhoven, and Everaerd (2009) investigated memory specificity after a social stressor (e.g. the TSST, Trier Social Stress Test) in healthy male subjects. They report no effect of acute stress on memory specificity but that memory specificity is affected by valence. Their results suggest that the ability to access specific neutral memories of events that happened recently is superior to the ability to recall remote neutral AM. There seems to be no difference between negative recent and remote AMs.

In conclusion, there is evidence that AM retrieval in terms of memory specificity might be impaired when cortisol levels are high, which might be mediated by valence and remoteness. Therefore, our study aims to investigate the effects of cortisol on AM retrieval with respect to memory age, i.e. recent versus remote memories, as well as valence.

First, we expect that there is a recency effect in autobiographical memory, i.e. that recent memories are more specifically recalled than remote memories as one study showed that memory specificity is higher for recent memories compared to remote ones (Piefke et al., 2003). Secondly, based on previous findings we assume that cortisol impairs AM retrieval in terms of a reduced memory specificity, but that this effect will be mostly pronounced in neutral AMs. Additionally, this study aims to investigate if the effect of cortisol on AM retrieval depends on valence and remoteness.

2. Methods

2.1. Participants

We included 30 female as well as 24 male participants (mean age = 24.5, SD = 3.7), as it is known that men and women differ regarding their autobiographical memory performance (Pillemer, Wink, DiDonato, & Sanborn, 2003; Pohl, Bender, & Lachmann, 2005; Ross & Holmberg, 1992). All participants were healthy undergraduate students and were reported on before (see (Duesenberg et al., 2016)). Only participants were included which met none of the following exclusion criteria: a former or current psychiatric diagnosis (assessed with the SCID-I-interview), a serious medical condition, especially conditions which have impact on hypothalamic-pituitary-adrenal axis (HPA axis) function, intake of oral and inhalative glucocorticoids or any other medication, pregnancy and nursing, or a body mass index over 30. Women were tested only in luteal phase due to hormonal differences between phases of menstrual cycle.

Participants were recruited via local advertising. The study was approved by the ethics committee of the German Psychological Society. All procedures were carried out with full understanding of the participant and written informed consent was obtained prior to testing. Participants received a 20 € allowance.

2.2. Procedures

A placebo controlled, double blind study was conducted. Each participant was tested once and was assigned to either placebo or hydrocortisone (10 mg) condition in a randomized order. 75 min after drug intake participants completed an autobiographical mem-

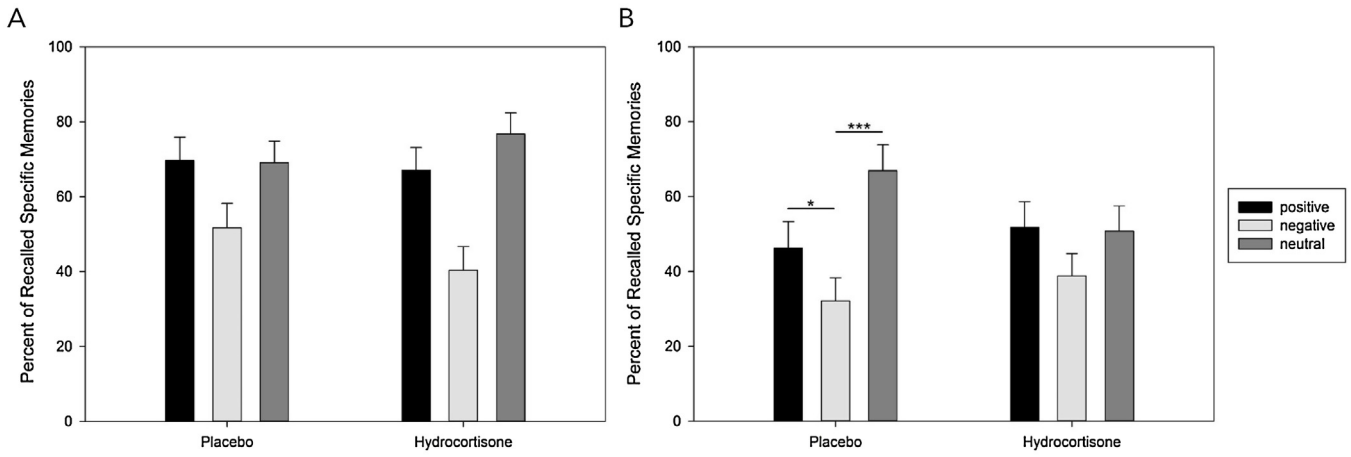

Fig. 2. Percentage of recalled specific A) recent and B) remote memories after the intake of placebo and hydrocortisone, displayed for each valence separately. In remote memories (B), we found a significant difference between positive and negative memories, and neutral and negative memories after the intake of placebo, but not hydrocortisone. In recent memories (A), we could not find an interaction between treatment and valence. (* $p < 0.05$, *** $p < 0.001$).

Table 1
Sample Characteristics.

	Hydrocortisone Condition ($N = 28$)	Placebo Condition ($N = 26$)	Statistical Analyses
age	24.6 (3.7)	24.3 (3.7)	$t(52) = -0.33$, $p > 0.05$
Sex (female, %)	14 (53.8)	16 (57.1)	$\chi^2(1) = 0.06$, $p > 0.05$
Body Mass Index	22.7 (2.4)	22.1 (2.3)	$t(52) = -1.08$, $p > 0.05$
smoking (yes)	7 (25)	25 (26.9)	$\chi^2(2) = 0.953$, $p > 0.05$
oral contraceptives (only women, %)	10 (62.5)	7 (50)	$\chi^2(1) = 0.475$, $p > 0.05$

Note: Unless otherwise specified, all data reported in means and standard deviations.

ory test (AMT), which is described below. All test sessions started at 1 pm in order to benefit from stable endogenous cortisol level during afternoon. Saliva samples were collected immediately before drug intake (0 min) and 45, 75 and 105 min afterwards, using Salivette devices (Sarstedt). After collection, which took place at room temperature, saliva samples were stored at −80 °C until biochemical analysis. Cortisol concentration was determined in the Neurobiology Laboratory of the Dept. of Psychiatry, Charité University Berlin. Free cortisol was analyzed using a commercially available TR-FRET-based, in-house adopted immunoassay (Cisbio International, Codolet, France), which was performed in principle according to the manufacturer's instructions. Intraassay coefficients of variation were below 8%, interassay coefficients of variation were below 10%.

A modified version of the *autobiographic memory test* (AMT) was used (Buss et al., 2004; Schlosser et al., 2010; Williams & Broadbent, 1986; Wingenfeld et al., 2012). The participants were instructed to write down a specific event from their past in response to emotional adjectives which were consecutively presented on cards. Specificity of answers was evaluated by two trained raters separately. An answer was considered specific when at least three of the following criteria were met: description of the location, time, and persons involved and activities carried out. It was also recorded if they could not produce any memory at all. Before completing the test participants practiced on an additional cue word. In the current study, we presented in total 20 emotional adjectives separated into two parts each consisting of 10 words (3 positive, 4 negative, 3 neutral). In part 1 (recent), participants were instructed to recall a specific event what happened during the last week as a recent memory. In part 2 (remote), participants were asked to write down a specific event they experienced around one year before testing as a remote memory. Both lists were presented to each participant in a randomized order.

2.3. Statistical procedures

To compare sociodemographic characteristics we conducted independent samples *t*-tests for continuous variables and Pearsonís Chi-Square tests for categorical variables. Regarding cortisol levels, we conducted a 4×2 repeated measures-ANOVA with time (0, +45, +75, +105) as within-subject factor and treatment (hydrocortisone vs. placebo) as between-subject factor. Following, the analysis for specific memories are described in detail. For statistical analyses and detailed results regarding categoric, extended, and non-memories please see the provided supplementary material. Regarding number of recalled specific memories, we conducted a $2 \times 3 \times 2 \times 2$ repeated measures-ANOVA with recency (recent vs. remote) and valence (positive, negative, neutral) as within-subject factors and treatment (hydrocortisone vs. placebo) and sex (male vs. female) as between subject factors. All post hoc *t*-tests were performed with Bonferroni correction. All means are reported as percentage of specifically recalled autobiographical memories for better comparisons as there are different numbers of items in each valence category. All analyses are reported with a significance level of $p < 0.05$.

3. Results

3.1. Sociodemographic variables

Both groups, the hydrocortisone versus placebo condition, did not differ regarding sociodemographic variables like age, sex, body mass index, smoking habits and in case of female participants intake of oral contraceptives. All means and standard deviations are given in Table 1. As only undergraduate students were included, all participants had the same level of education.

3.2. Salivary cortisol levels

Rm-ANOVA revealed a significant main effect for time ($F(1.9,97.4) = 26.13$, $p < 0.001$), a significant main effect for drug ($F(1,50) = 76.61$, $p < 0.001$) and a significant interaction between time and drug ($F(1.9,97.4) = 30.25$, $p < 0.001$). Post hoc t-tests indicated that both drug groups did not differ at baseline cortisol levels ($t(52) = -0.35$, $p > 0.05$), but there was a significant increase in cortisol levels after hydrocortisone compared to placebo at the subsequent measurement points (all $p$ís < 0.001, see Fig. 1).

3.3. Autobiographic memory test

Rm-ANOVA revealed no significant main effect of drug ($F(1,50) = 0.064$, $p > 0.05$) or sex ($F(1,50) = 1.922$, $p > 0.05$).

There was a significant main effect of recency ($F(1,50) = 24.4$, $p < 0.001$). Post hoc t-test ($t(53) = 4.93$, $p < 0.001$) indicated that participants recalled significantly more specific events which happened during the last week (recent memories, $M = 61.3$, $SD = 24.9$) than when they were asked to recall an event from a year ago (remote memories, $M = 47.2$, $SD = 28.4$).

There was also a significant main effect of valence ($F(2, 100) = 32.8$, $p < 0.001$). Contrasts revealed that the number of specific memories after positive cue words ($M = 58.65$, $SE = 4.21$; $F(1,50) = 5.17$, $p = 0.027$) and negative cue words ($M = 40.74$, $SE = 3.77$; $F(1,50) = 6.98$, $p = 0.011$) was significantly less than after neutral ones ($M = 65.84$, $SE = 3.5$).

A 4-way interaction between recency, drug, sex and valence failed to reach significance ($F(2, 100) = 0.886$, $p > 0.05$). There was a significant interaction effect between recency, drug and sex ($F(1,50) = 6.847$, $p = 0.012$) and a significant interaction effect between recency, drug and valence, $F(2,100) = 5.14$, $p = 0.008$). To disentangle these interactions, we conducted post hoc ANOVAs for recent and remote AM, separately, with valence as within-subject factor and drug and sex as between-subject factors, as before.

Regarding recent memories (see Fig. 2a), ANOVA again revealed a significant main effect valence ($F(2,100) = 19.17$, $p < 0.001$), but no significant main effect of drug ($F(1,50) = 0.09$, $p > 0.05$) and sex ($F(1,50) = 2.57$, $p > 0.05$), nor a significant interactions (all $p$ís > 0.05).

Regarding remote memories (see Fig. 2b), ANOVA revealed a significant main effect of valence ($F(2,100) = 12.433$, $p < 0.001$) and a significant interaction between valence and drug ($F(2,100) = 3.75$, $p = 0.027$; see Fig. 2). All other main effects or interactions failed to reach statistical significance (all $p$ís > 0.05). Post hoc t-tests indicated that in the placebo condition there was a significant difference between positive and negative remote memories ($t(25) = 3.14$, $p = 0.036$) and between neutral and negative memories ($t(25) = 2.95$, $p = 0.001$). The difference between neutral and positive remote memories marginally failed to reach statistical significance ($t(25) = -5.55$, $p = 0.063$). After the intake of hydrocortisone all comparisons of the valence categories were non-significant ($p$ís > 0.05). Additionally, there was no significant difference between hydrocortisone and placebo in any of the three valence categories ($p$ís > 0.05).

Additional analyses regarding categoric and extended memories, and non-memories are reported in detail in the supplementary material. In sum, participants reported higher numbers of categoric and extended memories for remote events, whereas they exhibited more non-memories for recent compared to remote events. Additionally, we found a main effect of valence for categoric memories and non-memories, with a higher number of memories for negative cue-words compared to positive and negative ones. Finally, there was no significant main effect for drug in categoric, extended and non-memories. However, post hoc ANOVA indicated that hydrocortisone had an effect on the number of retrieved non-memories depending upon valence, as the administration of hydrocortisone only lead to a significant increase in the number of non-memories for negative cue-words.

4. Discussion

Aim of this study was to investigate whether the effect of hydrocortisone on autobiographical memory (AM) depends on recency of memories and valence. We did not find an overall effect of hydrocortisone on AM retrieval, but there were significant main effects of recency and valence.

In our study, memory retrieval was more specific for recent compared to remote AMs as we could show that the number of specific memories was higher for recent compared to remote events. Additionally, participants retrieved less categoric or extended recent memories compared to remote ones. This adds to findings from Piefke et al. (2003) that recent memories are not only easier to recognize but also retrieved more specifically than remote ones, indicating that recent AMs are easier to access. Interestingly, Tollenaar et al. (2009) found a recency effect only for neutral but not for negative AMs. The authors suggest that emotional memories are often accompanied by higher arousal and, thus, are better recalled even if they are remote. However, we did not control for arousal, but future studies should include assessments of arousal and vividness of the recalled memory. It is to note, that the study of Tollenaar et al. (2009) and ours show important methodological differences which limit comparison. We defined a recent memory as an event that happened within the past week (in contrast to an event from the last 2 years as in Tollenaar et al. (2009). That might have led to the recency effect independent of valence, as these events might still be very present. Our results regarding recency in non-memories are somewhat suprising. Following the previous results from this study and by Tollenaar et al. (2009) someone would expect more non-memories for remote AM than for recent AM. Actually, it is vice versa as the number of non-memories was higher for recent AM compared to remote ones. Taken together, there seems to be a recency effect in terms of reduced memory specificity, whereas in recent AM participants tend to have more non-memories.

We did not find a main effect for cortisol-treatment as AM performance did not differ between the placebo and the hydrocortisone condition. Our result is – in part – in line with the study by Young et al. (2011) who could show that autobiographical memory is only impaired after a high dosage (mean 31.8 mg) of hydrocortisone whereas a low dose (mean 10.9) did not affect AM performance. As the dosage administered in our study is similar to the low dose in their study, it is conceivable that the increase in salivary cortisol was still in a range where AM performance is not affected. Additionally, after a psychosocial stressor, which leads to a moderate increase in cortisol compared to pharmacological approaches, AM performance was not altered compared to a non-stress situation (Tollenaar et al., 2009). However, some studies do report impairment in memory specificity after hydrocortisone (Buss et al., 2004; Schlosser et al., 2010; Wingenfeld et al., 2013). This impairing effect is only found for neutral, but not for valenced autobiographical memories and is therefore not generalizable to AM in general. As stated before, the influence of cortisol on AM also depends on remoteness of the recalled memory. None of the former studies controlled for remoteness, therefore it is not comprehensible if the reported cortisol effect is perhaps due to participants recalling more remote memories. This is of importance, as our results suggest that cortisol only affects remote, but not recent AM. In the placebo condition, retrieval of positive and neutral remote autobiographical memories was superior to the retrieval of negative remote AM. This reflects the main effect of valence we found. In comparison, there was no difference between positive, neutral or negative remote AMs in the hydrocortisone condition. Thus, it

seems that cortisol alters the effect of valence in remote specific memories.

We also found that the valence of autobiographical memories was associated with the specificity of the recalled memories. Overall, participants had more memories that were rated as specific in response to neutral cue words compared to emotional words. This is surprising as in declarative memory tasks the retrieval for emotional memories is more pronounced than for neutral ones (Matt, Vázquez, & Campbell, 1992). Additionally, we found that participants exhibited more non-memories and categoric memories for negative cue-words compared to positive and neutral ones. Comparisons to previous studies are difficult as most of the studies using a similar AMT do not provide statistics on valence effects. Only two studies investigating cortisol and autobiographical memory report on valence as a main factor (Schlosser et al., 2010; Wingenfeld et al., 2013) whereas in both studies valence did not have a significant effect on memory specificity. As both studies use a short version of the AMT including only six adjectives in total, this absence of valence effects might reflect insufficient statistical power. Therefore, future studies on the effects of valence on AM should include more cue words per valence category to provide sufficient statistical power for analyses of valence.

There are some limitations to mention. We used a modified version of the AMT as this test was originally designed to look at memory specificity and not to differentiate between remote versus recent memories. Therefore, this new version of the AMT has not been validated yet. To distinguish between recent and remote memories, we asked participants to recall events that happened either one week or one year before the test session. It is to note that these categories are somewhat arbitrary. For future studies, it might be of interest to ask for even more remote memories (for example from their youth) or to include even more recency categories (for example childhood, youth, 1 year or 1 week ago).

Additionally, the current study did not have a crossover design. All participants were tested only once and received either placebo or hydrocortisone. Therefore, we did not investigate intra-individual differences, but group differences. It is to mention, that we report on autobiographical memory specificity. To rate a reported memory as specific participants had to meet certain criteria. Therefore, we cannot make a statement whether cortisol affects other variables of AM like memory vividness or easiness to access these memories. Additionally, there is no control whether the retrieved memories are accurate or fabricated. This is a general methodological issue with this type of autobiographical memory test. It rather assesses retrieval style than memory accuracy."

Taken together, this study investigated systematically the influence of recency on autobiographical memory. Our results indicate that there is a recency effect in autobiographical memory as it is easier to retrieve specific recent memories than remote ones. Moreover, cortisol does not affect recent, but remote autobiographical memories depending on valence.

Declaration of interest

There were no conflicts of interest, financial or otherwise, to declare.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.biopsycho.2016.12.010.

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