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The perfect time to be stressed: A differential modulation of human memory by stress applied in the morning or in the afternoon

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Abstract

We measured the effects of a stressful experience on memory for emotionally arousing and neutral material learned after exposure to a stressor which induces a significant increase in corticosteroid stress hormones. Because memory performance can be influenced by circadian changes in corticosteroid levels, subjects were tested either in the morning or in the afternoon. Nineteen healthy men (9 in the morning group and 10 in the afternoon group) were submitted to a psychological stress task before viewing a story composed of emotionally negative and neutral segments, while another 20 healthy males (10 in the morning group and 10 in the afternoon group) viewed the story without being exposed to the psychological stressor. Salivary cortisol levels were measured before and after the stressor. Memory performance was assessed by a one week post learning delayed recall. Results show that stress-induced increases in salivary cortisol levels impaired delayed free recall of emotionally arousing material in the morning group, but not in the afternoon group. There was no effect of stress on memory for neutral material. Altogether, these findings suggest that stressing participants in the morning, at a time of high circulating levels of corticosteroids, over stimulated the corticosteroid receptors in the brain, impairing declarative memory for emotionally arousing material unrelated to the stressor. These findings suggest that the experimental context, i.e., time of day at which the experiment occurs, the nature of the to-be-remembered material (remembering the stressful event itself or material unrelated to the stressor) and the valence of the to-be-remembered material (emotionally arousing vs. neutral), modulates the effects of stress on human declarative memory.

Keywords: Cortisol; Emotional declarative memory; Experimental context; Human; Stress

1. Introduction

Extensive animal and human research has shown that emotionally arousing and stressful experiences modulate declarative memory, which is defined as the conscious or voluntary recollection of previously learned information (McGaugh, 2000; Cahill, 2000; Kim and Diamond, 2002; Lupien and Lepage, 2001). Corticosteroid hormones (cortisol in humans, corticosterone in rodents) have been studied in relation to the memory-modulating effects of emotionally arousing and stressful experiences. The rationale for studying the impact of corticosteroids is that these hormones, when activated during emotionally arousing and stressful experiences, influence declarative memory through their interaction with corticosteroid receptors located in the frontal lobes, the amygdala and the hippocampus (Abe, 2001; Roozendaal, 2002; Kim and Diamond, 2002; Lupien and Lepage, 2001). There are two types of corticosteroid receptors in these brain regions that differ in terms of their affinity for circulating levels of corticosteroids. Mineralocorticoid receptors (MRs) have a 6- to 10-times higher affinity for corticosteroids than glucocorticoid receptors (GRs) (Reul and de Kloet, 1985). A wealth of

Abbreviations: CPS, Cold Pressure Stress; S, salivary cortisol sample; GRs, glucocorticoid receptors; TSST, Trier Social Stress Test; MRs, mineralocorticoid receptors.

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evidence now demonstrates that activation of MRs is mandatory for successful acquisition of environmental cues necessary to encode information, whereas activation of GRs is necessary for long-term memory consolidation of this information (de Kloet et al., 1999; Sandi, 1998).

1.1. Importance of time of day

In humans, endogenous corticosteroid levels follow a circadian rhythm, with higher levels in the AM phase, and lower endogenous levels in the PM phase. These endogenous variations in corticosteroid levels thus lead to a differential activation of MRs and GRs corticosteroid receptors in the AM versus PM phase. During the circadian peak of corticosteroid secretion (AM phase), MRs are saturated and there is a 67–74% occupation of GR receptors. In the PM phase, however, endogenous levels of corticosteroids occupy 90% of MRs and 10% of GRs only (de Kloet et al., 1999). Consequently, the relationship between emotionally arousing and stressful experiences, corticosteroids, and long-term declarative memory is complex, since modulation of memory by corticosteroids will be a function of both the time of testing (AM vs. PM) (Lupien et al., 2002a; Fehm-Wolfsdorf et al., 1993) and the presence or not of an emotionally arousing and stressful experience at different times of day.

1.2. The nature of the to-be-remembered material

Some research data suggest that the effects of emotionally arousing/stressful events and corticosteroids on declarative memory also vary according to the nature of the to-be-remembered material (Akirav and Richter-Levin, 1999; Kim and Diamond, 2002; Sandi, 1998). Hence, an emotionally arousing and stressful experience produces a retrograde enhancement of memory for *that* experience (remembering the stressful event itself), and corticosteroid hormones are involved in the memory-enhancing effects of emotionally arousing and stressful events. For instance, in rodents, post-training stimulation of the corticosteroid system enhances, and pre-training corticosterone synthesis inhibition impairs, expression of conditioned fear and inhibitory avoidance in animals (Cordero et al., 2002; Liu et al., 1999; Roozendaal, 2002; Roozendaal et al., 1996; Sandi, 1998). In humans, prelearning inhibition of corticosteroid synthesis impairs declarative memory for emotionally arousing and stressful material (Maheu et al., 2004), whereas prelearning stimulation of the corticosteroid system enhances it (Buchanan and Lovallo, 2001; Abercrombie et al., 2003).

In contrast, more discrepant data emerge from studies measuring the effects of emotionally arousing and stressful experiences on subsequent declarative memory for material *unrelated* to the source of the stressor. Rodent studies have shown that, when a laboratory stressor (e.g., tailshocks, water immersion or restraint stress) is administered at various time-points before or after learning, as well as before recall, stress-induced elevations in corticosteroid levels modulate declarative memory according to an inverted U-shaped function. Optimal declarative memory for material unrelated to the stressor (e.g., inhibitory avoidance protocols or spatial water-maze tasks) occur at moderate levels of stress and stress-induced increases in circulating corticosteroid levels, whereas lower (i.e., boredom or drowsiness) or higher stress levels and stress-induced increases in circulating corticosteroid levels are less effective or may even impair declarative memory performance on these tasks (Kim et al., 2001; Park et al., 2001; Akirav et al., 2004; Klenerova et al., 2002, 2003; de Quervain et al., 1998; for a review, see de Kloet et al., 1999; Kim and Diamond, 2002; Roozendaal, 2002; Sauro et al., 2003; Shors, 2004). Similar findings were found in humans, as high corticosteroid levels following acute psychological stress (e.g., public speaking task), with the exception of Domes et al. (2002) and Wolf et al. (2002), were associated with memory impairments for material unrelated to the stressor such as neutral words lists (Kirschbaum et al., 1996; Lupien et al., 1997; Wolf et al., 2001; see Lupien and Lepage, 2001; Sauro et al., 2003).

1.3. The valence of the to-be-remembered material

When evaluating the effects of emotionally arousing and stressful experiences on memory for information unrelated to the stressor, practically all human studies performed to this day measured the impact of stress on memory for material that was neutral in nature. So far, only one human study has measured the effects of stress and high cortisol levels on declarative memory for material that is emotionally arousing in nature. Cahill et al. (2003) presented emotionally arousing or neutral slides to their subjects and, after viewing the slides, participants were submitted to the cold pressor stress (CPS; immersion of forearm in ice-cold (0°–3 °C) water) or to a control situation (immersion of forearm in warm (37°–40 °C) water). Results showed that, in contrast to the control situation, CPS significantly elevated salivary cortisol levels. Furthermore, CPS, as compared to the control situation, enhanced post-stress long-term (1 week delayed recall) declarative memory for emotionally arousing slides, without influencing memory for the neutral slides. These results suggest that, in humans, high stress-induced increases in corticosteroids may enhance memory for previously learned material that is emotionally arousing in nature, even if this material is not related to the stressor.

However, many of the studies that have measured the impact of stress and emotionally arousing events on memory for material unrelated to the stressor in humans have not taken into account the time at which the emotionally arousing and stressful situation was applied. As we have underlined above, endogenous levels of corticosteroids (and thus, activation of MRs and GRs) significantly vary across the day, with higher endogenous levels of corticosteroids in the AM phase compared to the PM phase. Consequently, the addition of a stressful and emotionally arousing event, which by itself will trigger a significant increase in endogenous levels of corticosteroids, should have a differential impact on activation of MRs and GRs as a function of time of day. In the AM phase, most of the MRs and about half of the GRs are activated, while in the

PM phase, most of the MRs and about a tenth of the GRs are activated. If one applies a stressor in the AM phase, the endogenous increase in corticosteroid levels will act by saturating GRs, while the same stressor applied in the PM phase will act by activating about half of the GRs. Since stress-induced elevations in corticosteroid levels have been shown to modulate declarative memory for material unrelated to the stressor according to an inverted U-shaped function, the differential activation of MRs and GRs at different times of the day thus imply that a stressor applied in the morning should impair memory function (right hand-side of the inverted U-shaped curve), while the same stressor applied in the PM phase should increase or have no impact on memory (left hand-side or top of the inverted U-shaped curve; see Lupien et al., 2002a; Lupien and Lepage, 2001). Given the differential effects of stress on emotionally arousing versus neutral information (Cahill et al., 2003), it can also be suggested that the application of a stressor in the AM versus PM phase should have a different effect on the recall of emotionally arousing or neutral information unrelated to the source of the stressor.

Accordingly, the goal of this study was to assess, in humans, the effects of a stressor applied in the AM versus PM phase on long-term declarative memory for emotionally arousing and neutral material learned after the stressor. In order to do so, participants were submitted to a psychological stress task or to a control condition in the morning or in the afternoon, and all subjects then viewed a story composed of emotionally arousing and neutral segments. Salivary cortisol samples were taken to assess corticosteroids' stress reactivity. Post-stress long-term (one week delayed recall) declarative memory for the story unrelated to the stressor was compared to post-stress long-term declarative memory measured under the control condition.

2. Methods

2.1. Experimental subjects

Forty healthy English- and French-speaking men, aged between 18 and 33 years (mean age: 22.5 ± 3.6 years), were recruited from the university community. The study was approved by the Douglas Hospital Research Ethics Board and informed consent was obtained from all participants, who were compensated for taking part in the study. Twenty participants were submitted to a stress condition, while twenty other subjects were submitted to a no stress condition. In both the stress and no stress conditions, half the subjects (stress condition: $n = 10$; no stress condition: $n = 10$) were tested in the morning (from 9 to 11 h), while the other half of the subjects (stress condition: $n = 10$; no stress condition: $n = 10$) were tested in the afternoon (from 14 to 16 h). All participants were medication free and reported no active medical illness, as well as no past or present psychiatric disorders. Care was taken not to evaluate participants during stressful periods (such as exam periods). Individuals working night shifts, or participants who had undergone major life changes (e.g., death of a close family member in the past year) were excluded from the study. Females were excluded from the study to avoid any confounding effects of the different phases of the menstrual cycle on memory (Hampson, 1990) and on cortisol reactivity during the stress condition (Kirschbaum et al., 1999).

2.2. Declarative memory task

In both the stress and no stress conditions, participants viewed a narrated series of 11 colored pictures presenting a story composed of emotionally arousing and neutral segments. The story presented was similar as the one used by Maheu et al. (2004), which has proven efficient in measuring emotional memory. In this story, a young girl engaged in a woodworking activity with her grandfather is injured and subsequently rushed to the hospital. The series of pictures was separated into three phases: Phase 1 (pictures 1 to 4) presented neutral information, Phase 2 (pictures 5–8) presented emotionally negative information, and Phase 3 (pictures 9–11) presented neutral information. Narratives accompanying phases 1 and 3 were neutral, whereas narratives accompanying phase 2 were emotionally negative.

Given the incidental nature of the declarative memory task (i.e., participants were not aware of the later memory evaluation; see Maheu et al., 2004), participants in the stress condition were told that we were interested in their physiological reactions (i.e., salivary cortisol levels) to the stimuli, while participants submitted to the no stress condition were told that we were interested in their subjective emotional reactions to the stimuli. Participants were instructed, before the viewing of the story, to relax and simply watch the story presented as if they were at the movies. Long-term memory for the story was assessed one week after the series of pictures were presented (i.e., second experimental session; see Psychoneuroendocrine procedure). Indeed, at the end of the first experimental session (during which the emotionally arousing story was viewed), participants in both the stress and no stress conditions were given a phone call meeting, to occur one week later, in order to complete a questionnaire on emotions. When called back, subjects were informed that no questionnaire needed to be completed, and were instead asked to recall as much information as possible about the story viewed a week earlier. At the end of the phone call meeting, the experimenter asked the subjects whether they anticipated the long-term declarative memory test; all reported that the long-term declarative memory test was unsuspected. All subjects were debriefed with respect to the real goal of the study at the end of the phone call meeting.

For the long-term free recall, participants in both the stress and no stress conditions were encouraged to remember as much as they could about the main story line, as well as any details that came to mind. The long-term free recall was tape-recorded to be analyzed later. Participants were credited with the recall of a picture (for a total of one point per picture) if they remembered elements that could only have been seen in that particular picture and not in any other picture or mentioned in the narration. Because the number of pictures per phase varied, the total scores per story phase were calculated as percentages of correct responses. French and English versions of the story

were used, and there were no differences in the long-term free recall with regard to the language in which the story was presented in ($p > 0.10$).

2.3. Psychological stress protocol

Subjects in the stress condition were submitted to a psychological stress task, the Trier Social Stress Test (TSST), developed by Kirschbaum et al. (1993). This laboratory stressor consists of a free speech and a mental arithmetic task performed in front of an audience. The total procedure, including preliminary instructions and a preparation period, takes 20 min. A wealth of findings demonstrated the efficacy of the TSST in substantially increasing free salivary cortisol levels (Kirschbaum et al., 1993, 1996; Wolf et al., 2001, 2002; Schommer et al., 2003).

2.4. Psychoneuroendocrine procedure

Subjects in both the stress and no stress conditions were tested individually on two separate occasions. For the first experimental session, participants in the stress condition were asked to have a light breakfast or a light lunch no later than 7 h (morning stress group) or 11h30 (afternoon stress group), during which they were asked not to have any citrus products, coffee, tea and sweets (e.g., hot chocolate). They were also asked to avoid exercising the day of the experimental session, and were asked not to eat and drink anything but water 1 h before the start of the experiment. A small percentage of participants in the stress condition ($n = 4$) were social smokers (<eight cigarettes/week), and they were asked not to smoke before attending the experimental session. Subjects in the stress condition arrived at the laboratory at 8h30 (morning stress group) or 13h30 (afternoon stress group). After a resting period of 30 min, a baseline free salivary cortisol sample (S1) was taken at 9 h (morning stress group) or 14 h (afternoon stress group). Subjects in the stress condition were submitted to the psychological stress task (TSST) 5 min after the baseline salivary cortisol sample was taken. Further saliva samples (S2–3) were then taken at 9h15 (morning stress group) or 14h15 (afternoon stress group), 9h30 (morning stress group) or 14h30 (afternoon stress group), and every 10 min (S4–12) from 9h40 (morning stress group) or 14h40 (afternoon stress group) until 11 h (morning stress group) or 16 h (afternoon stress group). Ten minutes after the psychological stress task ended, i.e., at 9h40 (morning stress group) and 14h40 (afternoon stress group), subjects viewed the emotionally arousing story. Participants left the laboratory at 11 h (morning stress group) or 16 h (afternoon stress group).

For the first experimental session, subjects in the no stress condition were submitted to the viewing of the emotionally arousing story only. Participants in the no stress condition were all tested between 9 and 11 h (morning no stress condition) or between 14 and 16 h (afternoon no stress condition). In both the stress and no stress condition, the memory task procedure was identical. The second experimental session occurred a week later, at which time participants in both the stress and no stress conditions were called over the phone and asked to recall the story (see earlier Declarative memory task description).

2.5. Salivary cortisol assays

Salivary cortisol samples were collected using Sarstedt salivette device (Sarstedt, Germany) and stored at −20 °C until assayed. Samples were thawed and spun at 3000 rpm and 4 °C for 20 min and cortisol concentrations were determined by radioimmunoassay using a kit from DSL (Diagnostic Systems Laboratories, Inc., Texas, USA). Salivary samples of cortisol were mixed with 500 μL of ^{125}I-labelled cortisol reagent and 500 μL of cortisol antiserum complex reagent. Total binding and non-specific binding typically ranged between 47–63% and 0.5–1.5%, respectively. The separation of bound antigens was obtained by using a pre-reacted double antibody system. When using this technique, cross-reactivity of the antigen is less than 4% with 11-deoxycortisol and less than 1% with any other naturally occurring steroids. The intra- and inter-assay coefficients of variation were 4.6% and 5%, respectively. The limit of detection of the assay was 0.01 μg/dl. All samples were assayed in duplicates.

2.6. Data analysis

One participant in the morning stress group was withdrawn from all analyses (physiological and cognitive analyses) because of cortisol data loss (19 participants in the stress condition, 9 in the morning stress condition and 10 in the afternoon stress condition). Physiological and cognitive data were verified for assumptions of normality and sphericity, and logarithmic transformations or Greenhousse-Geiser (1959) corrections were applied when normality or sphericity was not met. Consequently, although the salivary cortisol data were logged, to allow proper statistical analyses, salivary cortisol results are presented as untransformed results in μg/dl units for the sake of comparison between studies. Mixed analyses of variance (ANOVAs) were performed to measure the impact of stress on salivary cortisol levels and memory performance. Simple effects and, when appropriate, Tukey honestly significant difference analyses were conducted on all significant physiological and cognitive findings. Preliminary analyses revealed that there were no interaction between morning (stress vs. no stress) and afternoon (stress vs. no stress) conditions and Neutral Story Phases 1 and 3 (Ps > 0.01). As a result, recall scores on phases 1 and 3 were averaged, and the factor of valence (emotionally arousing vs. neutral) was entered in the mixed ANOVAs assessing morning and afternoon condition's effects on long-term declarative memory performance.

A mixed analysis of variance (ANOVA) using time of stress (morning stress vs. afternoon stress) as the between-subjects factor and salivary cortisol samples (S1–12) as the within-subjects factor was performed to distinguish the effects of morning versus afternoon stress on cortisol levels. The effects of the morning stressor on memory were analyzed by comparing performance of the morning stress versus no stress group using an ANOVA with Condition (stress vs. no stress) as

the between-subjects factor, and Valence (emotionally arousing vs. neutral) as the within-subjects factors. The effects of the afternoon stressor on memory were analyzed by comparing performance of the afternoon stress versus no stress group using an ANOVA with Condition (stress vs. no stress) as the between-subjects factor, and Valence (emotionally arousing vs. neutral) as the within-subjects factors. Inclusion of all four conditions [Time of day (AM vs. PM), and Condition (stress vs. no stress)] in a single omnibus F test was precluded for one main reason. Indeed, the stress conditions applied in the morning vs. the afternoon were not orthogonally independent (i.e. cognitive performance after stress in the morning versus the afternoon totally depended upon different endogenous levels of corticosteroids before the stressor). Consequently, the stressor was applied in two populations which did not start the experiment at the same level of endogenous circulating levels of cortisol. Given this later fact, any modulatory actions of stress on memory function would be obscured by these baseline differences between groups (Winer, 1986).

3. Results

3.1. Physiological measures

The ANOVA measuring the effects of time of stress on salivary cortisol samples revealed that there was a significant two-way interaction between time of stress and salivary cortisol samples [$F(11,187)=1.81$, $p<0.05$]. As shown in Fig. 1, post hoc comparisons of free salivary cortisol levels between groups demonstrated that the morning stress group had significantly higher baseline cortisol levels (S1) than the afternoon stress group ($p<0.05$). There were, however, no group differences in cortisol stress reactivity (S2–12) to the psychological stress task (Ps>0.1).

3.2. Memory results

When comparing the effects of morning condition (morning stress vs. no stress) on long-term memory for emotionally arousing and neutral material, we found a significant two-way interaction between morning condition and valence [$F(1,17)=5.6$, $p<0.03$]. As shown in Fig. 2A, post hoc comparisons demonstrated that long-term memory for emotionally arousing material was impaired by stress, while long-term memory for neutral information was not ($p<0.03$). The ANOVA measuring the effects of afternoon condition (afternoon stress vs. no stress) on long-term memory for the emotionally arousing story revealed a main effect of valence [$F(1,18)=0.16$, $p<0.01$], but no main effect of afternoon condition and no interaction between afternoon condition and valence (Ps>0.1). Fig. 2B shows that emotionally arousing material was better remembered than neutral material by both the afternoon stress and no stress groups ($p<0.01$).

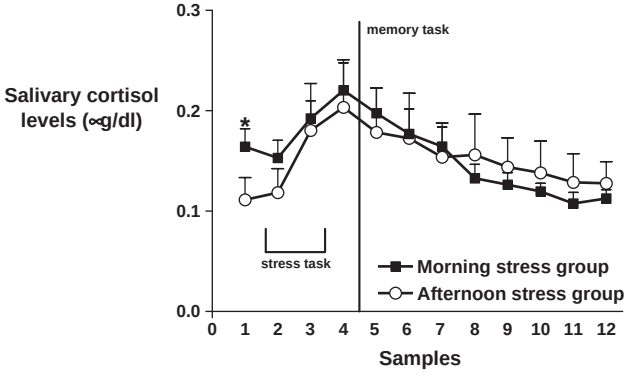

Fig. 1. Comparison of mean salivary cortisol levels between groups. *, baseline cortisol levels were significantly elevated in the morning stress group as compared to baseline cortisol levels in the afternoon stress group ($p<0.05$). Error bars represent standard errors of the mean (SEM).

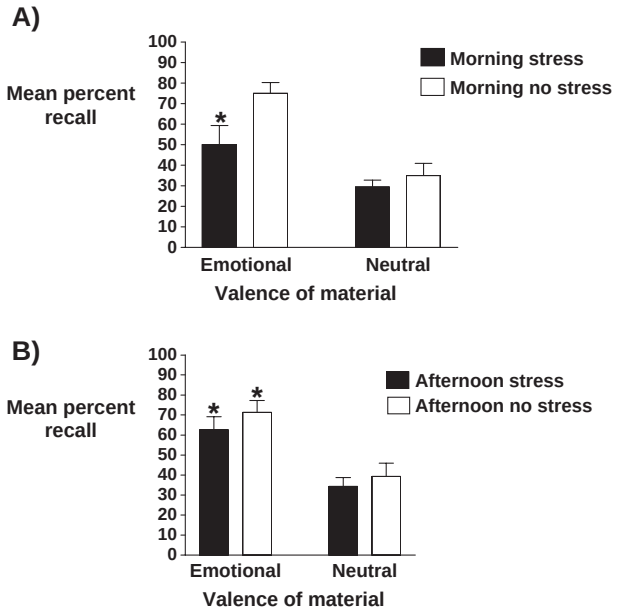

Fig. 2. Comparison of long-term memory performance (in mean percent recall) between groups. (A) Morning condition: *, significant differences between recall of the stress vs. no stress group (B) afternoon condition: *, significant differences between recall of emotionally arousing vs. neutral material across all groups.

4. Discussion

The results of this study provide new evidence in a young human population that the time at which a stress is applied has a different impact on memory for emotionally arousing and neutral events learned after the stressor. Indeed, when participants were submitted to a stressful experience at a time of high circulating levels of corticosteroids (i.e., in the morning), stress and stress-induced elevations in corticosteroids impaired memory for emotionally arousing information, without influencing memory for neutral information. However, when participants were submitted to a stressful experience at a time of low circulating levels of corticosteroids (i.e., in the afternoon), stress and stress-induced elevations in corticosteroids had no impact on memory for emotionally arousing and neutral information. The findings of this study are in line with animal and human research

suggesting that corticosteroids modulate memory according to an inverted U-shaped function, with highly elevated levels of corticosteroids triggering memory impairments and optimal corticosteroid levels preventing memory deficits (Park et al., 2001; Lupien et al., 2002a,b; Abercrombie et al., 2003; see Sandi, 1998; Lupien and Lepage, 2001; de Kloet et al., 1999, 2002; Kim and Diamond, 2002; Roozendaal, 2002; Shors, 2004).

The memory impairing effects of stress in the morning group can be explained by the differential involvement of the two corticosteroid receptors. Indeed, a closer look at the findings depicted in Fig. 1 shows that the morning group presented higher baseline salivary cortisol levels when compared to the afternoon group. This is to be expected since, in humans, circadian corticosteroid levels reach their maximum peak in the morning, before slowly declining during the day to reach a nocturnal through. After participants were submitted to the psychological stress task (the TSST), however, group differences disappeared; this is attributable to a higher magnitude in cortisol elevation in the afternoon group (Fig. 1).

Therefore, in this study, it is most probable that an over stimulation of the corticosteroid system occurred in the participants submitted to the stressor in the morning, leading to a complete saturation of both the MRs and GRs (extreme right-end of the inverted U-shaped function). Such saturation of both corticosteroid receptors might have impaired subsequent frontal lobes, amygdala and hippocampal processing, which led to the observed deficits in declarative memory (de Kloet et al., 1999; Lupien and Lepage, 2001; Kim and Diamond, 2002). In contrast, the corticosteroid system was also stimulated in participants submitted to the stressor in the afternoon, but towards an optimal level (towards the top of the inverted U-shaped function). Such stimulation was clear enough to prevent learning and declarative memory impairments, but not enough to enhance memory function.

Furthermore, in this study, stress applied in the morning impaired memory for the emotionally arousing material, without influencing memory for the neutral information. Interestingly enough, we are not the only ones to report impairing effects of high corticosteroids on memory for emotionally arousing material specifically, as some previous human studies also demonstrated that elevated salivary cortisol levels predicted poorer free recall of emotionally arousing material, but not of neutral information (Abercrombie et al., 2003; Rimmele et al., 2003). The absence of stress' effects on memory for neutral material, in this experiment, could be attributable to the memory task used in our protocol. Indeed, as shown in Fig. 2, there is a floor effect for the recall of neutral information, i.e., memory performance for neutral material was lower than memory performance for emotionally arousing material, in both the stress and no stress groups. Therefore, it is difficult to detect an effect of stress on memory for neutral information because memory performance for such information is already low in normal conditions (no stress groups). Memory performance for emotionally arousing material, however, was very high in normal conditions (no stress groups), thus leaving leeway for stress-induced memory impairments to be observed for emotionally arousing material.

Stress applied in the afternoon did not trigger any memory deficits (see above). Rather, a main effect of valence was detected: emotionally arousing material was significantly better recalled than neutral information for both the stress and no stress afternoon groups. These results extend previous human findings showing that emotionally arousing material is better remembered than neutral information (Christianson, 1992; LaBar and Phelps, 1997; Maheu and Lupien, 2003). Memory enhancement for emotionally arousing material could be attributed to the fact that emotionally salient events trigger attention, learning and memory processes, thus optimizing encoding and memory consolidation of the event (see Christianson, 1992; Maheu and Lupien, 2003).

5. Conclusion

Altogether, the results of the present study show that the experimental context plays a major role in modulating the effects of stress on human declarative memory. Indeed, the time of day at which the experiment takes place and thus, the endogenous levels of corticosteroids measured at the time of the experiment, are clearly important methodological factors to consider when measuring the effects of emotion and stress on human declarative memory. The nature of the to-be-remembered stimuli, i.e., the emotionally arousing and stressful event itself or material unrelated to the source of the stressor, as well as the valence of the information to memorize, i.e., emotionally arousing or neutral, are also capable of influencing human memory processes. Recent animal and human studies have demonstrated that genetics, personality, gender, life experience, as well as other methodological factors such as synthetic doses of hormones administered, memory task difficulty and stages of memory processes evaluated (encoding vs. consolidation vs. retrieval) can all influence the direction of the effects of emotion and stress on memory (Meaney, 2001; Lupien and Lepage, 2001; Kim and Diamond, 2002; de Kloet et al., 2002; Wolf, 2003; Roozendaal, 2002; Cahill, 2003; Hamann and Canli, 2004). Clearly, the time of day at which the experiment occurs, as well as the nature and the valence of the to-be-remembered material, are further factors to add to this list. Future studies considering and controlling for all the above mentioned factors should prove highly valuable to our understanding of the effects of emotionally arousing and stressful experiences on human declarative memory processes.

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