CHAPTER 5

THE DELAYED EFFECTS OF A CORTICOSTERONE ADMINISTRATION ON ANXIETY STATE IMPAIR MEMORY ON A HIGH-AROUSING BUT NOT ON A LOW-AROUSING LEARNING TASK

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Manuscript in preparation
ABSTRACT

There is extensive evidence that glucocorticoids through their actions in the basolateral amygdala (BLA) modulate memory functions. Glucocorticoids also modulate anxiety behavior and it is hypothesized that this effect may be caused by the alteration of BLA neuron morphology. But it is not known whether memory functions and anxiety behavior are modulated by the same glucocorticoids-induced mechanisms. We recently demonstrated that a single injection of corticosterone could induce a delayed anxiolytic effect in male Wistar rats. To determine whether this anxiolytic treatment can also alter memory functions, we examined the effects of the treatment on the performance in high- and low-arousing memory tasks (inhibitory avoidance and object recognition). We showed that a single injection of corticosterone could impair performance in the inhibitory avoidance memory task 10 days after its administration. Interestingly, the same treatment did not alter the performance in the object recognition task 10 days later. Data from the object recognition task experiment showed that the animals were able to learn, indicating that corticosterone may only affect emotional memory. The present findings demonstrate that a single injection of corticosterone not only has a delayed anxiolytic effect but also impairs learning and memory performance in a highly arousing task like the inhibitory avoidance paradigm. This suggests that glucocorticoids-induced mechanisms may simultaneously modulate anxiety behavior and processing of emotional information.
INTRODUCTION

Extensive evidence has shown that corticosteroid hormones released shortly after an emotionally arousing experience influence learning and memory processing of these types of stressful events while they have little effects on neutral experiences (Abercrombie et al., 2006; Bohannon, 1988; Cahill and McGaugh, 1998; Neisser et al., 1996). The impact of glucocorticoid release on memory functions is dose-dependent, but also differs with respect to the phase of memory processing (encoding of information, consolidation or retrieval) that is being observed (Lupien and McEwen, 1997; Roozendaal, 2000 and 2002). For instance, moderate doses of glucocorticoids administered acutely after a training experience can enhance the memory consolidation of the event (Cottrell and Nakajima, 1977; Okuda et al., 2004; Zorawski and Killcross, 2002). In contrast, acute administration of glucocorticoids before a retention test will impair the memory retrieval (de Quervain et al., 1998 and 2000; Wolkowitz et al., 1990). Similarly stress levels of glucocorticoids impair working memory retrieval (Lupien et al., 1999; Arnsten, 2000; Roozendaal, 2002). It was demonstrated that all the aforementioned actions of corticosteroid hormones require arousal-induced noradrenergic activity within the basolateral amygdala (BLA) (Quirarte et al., 1997; Roozendaal and McGaugh, 1997a; Roozendaal et al., 2004a and 2009). Besides, the BLA works in concert with other brain structures of the limbic system, such as the hippocampus and the prefrontal cortex, to modulate the different memory functions (Nathan et al., 2004; Roozendaal et al., 2004b; Roozendaal and McGaugh, 1997b and 2011).

Arousal- or stress-induced glucocorticoid release also affects emotional states, particularly anxiety (Kalueff, 2007; McEwen et al., 2012; Smythe et al., 1997). The deleterious consequences of chronic administration of corticosteroids and exposure to very high levels of these hormones on emotional states have been clearly established (Corodimas et al., 1994; Korte et al., 1996; Lee et al., 1994). For instance, chronic corticosterone administration increases anxiety-like behavior in rats, while adrenalectomy tends to reduce this type of behavior (Stone et al., 1988). On the other hand, both increased and decreased anxiety levels have been observed after acute glucocorticoid treatment (Buchanan et al., 2001; File et al., 1979; Grillon et al., 2011; Mitra and Sapolsky, 2008; Putman et al., 2007; Sandi et al., 1996; Wirth et al., 2011). Similar to its role in learning and memory processes, the amygdala is also critically involved in the expression of anxiety (Davis et al., 1994; Etkin et al., 2004; LeDoux, 2003). Anxiety-like behaviors are correlated with specific neuronal activity within the amygdala, particularly in the BLA (Sajdyk and Shekhar, 1997; Truitt et al., 2009; Tye et al., 2011; Wang et al., 2011). On the other hand, lesions of the amygdala prevent the expression of anxious behavioral and physiological responses (Feldman et al., 1994; Kopchia et al., 1992; Möller et al., 1997). Glucocorticoid signaling within the BLA plays an essential role in anxiogenesis (Shepard et al., 2000 and 2003). Recent evidence suggests that corticosteroid hormones modulate anxiety behavior by altering the dendritic morphology of the principal neurons of the BLA (Vyas et al., 2002 and 2004; Mitra et al., 2005; Mitra and Sapolsky, 2008). Indeed, BLA dendritic hypertrophy
is correlated with high levels of anxiety whereas reduction of dendritic trees has been associated to reduction of anxiety levels (Adamec et al., 2012; Mitra et al., 2009a). In addition, manipulations that prevent hormone-induced changes in BLA morphology also could reinstate normal anxiety levels (Mitra et al., 2009b; Mitra and Sapolsky, 2010).

It is already known that learning and memory processes and anxiety levels influence each other; and since they share common neuroanatomical and neurochemical substrates, they may also be modulated by common mechanisms (Kalueff 2007; McNaughton, 1997; Ribeiro et al., 1999; Salomons et al., 2012; Uzun et al., 2010). Given that corticosteroids are involved in both learning and memory and anxiety, and can modulate the functioning of the underlying neuroanatomical substrates, common corticosteroid-mediated mechanisms are possible candidates for simultaneous modulation of anxiety and memory.

We recently demonstrated that a single injection of corticosterone (of 3 or 10 mg/kg) could cause a delayed anxiolytic effect in naïve rats. This effect was dependent on simultaneous noradrenergic activity. This is similar to what previously has been demonstrated for the corticosterone-induced effects on memory functions and accordingly supports the hypothesis that anxiety and memory are modulated by identical glucocorticoid-induced mechanisms.

In order to determine whether learning and memory processes are also altered similarly to anxiety by an early corticosterone treatment, we decided to examine the learning and memory performance at the time when the anxiolytic effect of corticosterone is observed in male Wistar rats. We also examined whether a potential modification of learning and memory functions would be dependent on the emotional component of the learning task, as it is well known that the effects of glucocorticoids on memory are influenced by the emotional context (Conrad, 2005; de Kloet et al., 1999). For this purpose, two different learning tasks, with different levels of arousal, were chosen; the low-arousing object recognition task and the high arousing inhibitory avoidance task. The animals received the highest dose of corticosterone (10 mg/kg) and were randomized for participation in the two different tasks. Ten days after the injection, the animals were trained in the assigned learning task, and learning and retention abilities were studied.

MATERIALS AND METHODS

Animals
Male adult Wistar rats (340-450 g at the time of drug treatment) from Charles River Breeding Laboratories (Germany) were group-housed (3 rats per cages) and maintained on a 12-h/12-h light/dark cycle (lights on: 07:00-19:00 h) with ad libitum access to food and water. Rats assigned to the vehicle, corticosterone and undisturbed home cage conditions were housed in separate cages and placed on different shelves within the animal colony room. Behavioral training and testing were performed during the
light phase of the cycle between 10:00 and 16:00 h. All experimental procedures were in compliance with the European Communities Council Directive of 24 November 1986 (86/609/EEC) and were approved by the Institutional Animal Care and Use Committee of the University of Groningen, The Netherlands.

**Drug Treatment**

After a 1-week habituation period to the housing conditions, the rats were handled 1 min per day for 4 consecutive days. On the following day, they received a single injection of corticosterone or vehicle. Other rats were assigned to a home cage control group and were left undisturbed. Drug administration was administered between 10:00 and 11:00 h. The dose of corticosterone (10 mg/kg; Sigma-Aldrich) was selected on the basis of our prior data indicating that it reduces anxiety-like behavior on an elevated plus maze 10 days later (Messanvi et al., unpublished observation). Corticosterone was first dissolved in 100% ethanol and subsequently diluted in peanut oil (Sigma-Aldrich) to reach the appropriate concentration. The final ethanol concentration was 5%. The vehicle solution contained 5% ethanol in peanut oil only. Vehicle or corticosterone was administered subcutaneously in a volume of 2.0 ml/kg. Vehicle and drug solutions were prepared freshly before each experiment. After the injection, rats were placed back into their home cage and left undisturbed until behavioral training 10 days later. Rats were pseudo-randomly assigned to either the inhibitory avoidance or object recognition task. Rats housed together in the same cage were always assigned to the same learning and memory task.

**Inhibitory Avoidance Task**

The inhibitory avoidance apparatus consisted of a trough-shaped alley (91 cm long, 15 cm deep, 20 cm wide at the top, and 6.4 cm wide at the bottom) divided into two compartments, separated by a sliding door that opened by retracting into the floor (McGaugh et al., 1988). The starting compartment (30 cm) was made of opaque white plastic and was well lit; the shock compartment (60 cm) was made of dark, electrifiable metal plates and was not illuminated. Training and testing were conducted in a sound- and light-attenuated room.

During the training trial, the rats were placed in the starting compartment of the apparatus, facing away from the door, and allowed to enter the dark (shock) compartment. After the rat stepped completely into the dark compartment, the sliding door was closed and a single inescapable footshock (0.45 mA; 1 s) was delivered. The animal’s individual reaction to the shock was scored using an arbitrary scale ranging from 0 to 4 (0 = no visible reaction; 1 = flinch reaction; 2 = walk/run; 3 = jump reaction; 4 = jumps accompanied by vocalizations). The rats were removed from the shock compartment 20 s later and placed back in their home cages until testing. On the retention test, 48 h after training, the rat was placed again in the starting compartment of the apparatus and the latency to re-enter the former shock compartment with all four paws (maximum latency of 600 s) was measured. Longer latencies were interpreted...
as indicating better retention. Shock was not administered on the retention test trial.

**Object Recognition Task**
Separate groups of rats were trained on the mildly arousing object recognition task 10 days after drug treatment. The experimental apparatus consisted of a gray open-field box (40 cm x 40 cm x 40 cm) with a saw-dust covered floor, placed in a dimly illuminated room. The objects to be discriminated were white glass light bulbs (6 cm diameter by 11 cm length) and transparent glass vials (5.5 cm diameter by 5 cm height). The rats were not habituated to the experimental apparatus prior to the training session. On the training trial, the rat was placed in the experimental apparatus and allowed to explore two identical objects (A1 and A2) for 5 min. Rat’s behavior was recorded by using a video camera positioned above the experimental apparatus. To avoid the presence of olfactory trails, sawdust was stirred and the objects were thoroughly cleaned with 70% ethanol between rats. Retention was tested 24 h after the training session. One copy of the familiar object (A3) and a new object (B) were placed in the same location as stimuli during the training trial. All combinations and locations of objects were counterbalanced to reduce potential biases because of preference for particular locations or objects. The rat was placed in the experimental apparatus for 3 min and the time spent exploring each object and the total time spent exploring both objects were recorded. Exploration of an object was defined as pointing the nose to the object at a distance of 1 cm and or touching it with the nose. Turning around, climbing or sitting on an object was not considered as exploration. A discrimination index was calculated as the difference in time exploring the novel and familiar objects, expressed as the ratio of the total time spent exploring both objects (Okuda et al., 2004). Rats showing a total exploration time <10 s on either training or testing were excluded as prior data has indicated that these rats do not acquire the task (Okuda et al., 2004).

**Statistics**
Inhibitory avoidance training and retention latencies are expressed as median and interquartile range (IQR). Non-parametric Kruskal-Wallis and two-tailed Mann-Whitney U tests were used to analyze the training latencies and retention latencies. Non-parametric statistics were used because the retention latencies were restricted by the maximum score of 600 s causing the results to be non-Gaussian. To determine whether learning has occurred, paired t-tests were used to compare the training and retention latencies. Data of the object recognition task are expressed as mean ± SEM. Object exploration training and object discrimination index were analyzed with one-way ANOVAs, followed by Fisher’s LSD post-hoc comparison tests to determine the source of detected significances, when appropriate. For all comparisons, a probability level of p < 0.05 was accepted as statistical significance.
RESULTS

Effect of a single corticosterone administration on performance in the high arousing inhibitory avoidance task 10 days later
The aim of this experiment was to investigate whether an acute corticosterone injection, shown to cause an anxiolytic effect 10 days later, can also affect learning and memory on a high-arousing task.

We first examined whether the corticosterone treatment affected training performance. Average step-through latencies for all groups during training, before footshock, were 30.9 ± 3.0 s (mean ± SEM). Kruskal-Wallis test for entrance latencies of the training trial revealed no significant differences between groups \( H(2) = 1.8, p = 0.4 \) as shown in Fig. 2A. The reactivity to the electric shock was similar among the different groups (data not shown). These findings indicate that the drug treatment did not influence general motor behavior or footshock sensitivity during the training trial.

Forty-eight-hour retention test latencies of rats from the home cage group were significantly longer than their step-through latencies during the training trial \( (p < 0.01) \), indicating that the rats retained memory of the shock experience. Kruskal-Wallis test revealed a significant group effect on retention test latencies \( H(2) = 7.2, p = 0.03 \) as shown in Fig. 2B. Mann-Whitney U test comparison of groups revealed that retention latencies of the corticosterone group were significantly shorter than those of the home cage control \( (Z = -2.3; p = 0.02) \) and vehicle groups \( (Z = -2.1; p = 0.04) \). Retention test latencies of the vehicle and home cage controls did not differ significantly \( (Z = -0.6; p = 0.57) \).

These findings indicate that a single dose of corticosterone has long-lasting effects and can impair performance on a highly arousing inhibitory avoidance task 10 days later.

![Figure 1](image_url)

**Figure 1. Early corticosterone administration impairs performance in the inhibitory avoidance task.** Ten days after the injection of corticosterone the animals were trained in the inhibitory avoidance apparatus. Retention was tested, for 48h later. Step-through latencies and retention latencies are expressed as median ± interquartile range. (A) Step-through latencies of the home-cage animals \((n = 11)\), the vehicle-treated animals \((n = 14)\) and the corticosterone-treated animals \((n = 13)\) during the training session. (B) Retention latencies of the different groups during the testing session 48h later. * \( p < 0.05 \) as compared with the home-cage and vehicle-treated animals.
Effect of a single corticosterone administration on performance in the mildly arousing object recognition task 10 days later

To investigate whether the corticosterone injection can induce general memory impairment or whether this effect is limited to more arousing tasks, in the next experiment we examined whether similar corticosterone treatment could influence object recognition performance.

On the training day, the average time spent exploring the two identical objects for all the animals was 26.7 ± 1.5 s (mean ± SEM). One-way ANOVA for object exploration during the training trial revealed no significant difference between the three groups (home cage: 24.2 ± 3.9 s; vehicle: 26.1 ± 1.9 s; CORT: 29.1 ± 2.4 s) [F(2,43) = 0.86; p = 0.43]. These findings indicate that the drug injection 10 days earlier did not influence general object exploration of the animals during the training.

As shown in Fig. 2, one-way ANOVA for discrimination index revealed no difference between groups (home cage: 25.9 ± 9.3%; vehicle: 24.0 ± 10.5%; CORT: 28.4 ± 9.9%) [F(2,43) = 0.51; p = 0.95]. Furthermore, one-sample t tests revealed that the discrimination index of all groups was significantly different from zero [home cage: t(12) = 2.80, p < 0.05; vehicle: t(15) = 2.29, p < 0.05; CORT: t(16) = 2.88, p < 0.05], indicating that all groups readily discriminated the novel object from the familiar object during the retention test. Total exploration of the two objects on the retention test also did not differ between groups (ANOVA).

Taken together, the findings indicate that a single dose of corticosterone, given 10 days before training, does not affect learning or memory on a low-arousing task.

Figure 2. Early corticosterone administration does not affect performance in the object recognition task.

Ten days after the injection of corticosterone, the rats underwent a 5-min object recognition training session in which they could explore two identical objects. Retention was tested, for 24h later by placing the animals, for 3 min, into the apparatus containing a similar object as in the training and a novel object. Total exploration time and discrimination index are expressed as mean ± SEM. (A) Total exploration time of the objects during the training session of the home-cage animals (n = 13), the vehicle-treated animals (n = 16) and the corticosterone-treated animals (n = 17). (B) Discrimination index of the animal during the testing session 24h later.
DISCUSSION

The present study investigated whether anxiety behavior and learning and memory functions which share common neurochemical and neuroanatomical substrates, are simultaneously modulated by glucocorticoids. For this purpose, male Wistar rats received a single injection of a high dose of corticosterone (10 mg/kg) that has been shown to have an anxiolytic effect 10 days after (Messanvi et al., unpublished observations). In the present study, 10 days after the injection, the learning and memory capabilities were assessed in low- and high-arousing conditions, respectively the object recognition task and the inhibitory avoidance task. Our findings indicate that the corticosterone treatment can impair performance in the inhibitory avoidance memory task 10 days later, as shown by the low retention latencies of the corticosterone-treated animals compared to the control animals (home cage and vehicle groups). The latency to enter the dark compartment and the reactivity to the footshock during the training session were similar in all the groups. These results indicate that the probably low levels of anxiety in the corticosterone-treated rats did not influence the training of those animals. Interestingly, the same treatment does not alter the performance in the object recognition task. The mean total exploration time during training and testing, as well as the mean discrimination index during testing are similar among the different treatment groups. Besides, the discrimination indexes indicate that the animals are able to learn and recall information that is not emotionally arousing. The present findings demonstrate that an acute administration of corticosterone having a delayed anxiolytic effect, as shown previously, can also impair learning and memory performance in a task that is highly arousing like the inhibitory avoidance paradigm. Our findings that acute administration of corticosterone decreases performance in high-arousing memory task but not in a low-arousing memory task are in line with previous studies indicating that anxiolytic compounds also affect learning and memory functions that have strong emotional components (Beuzen and Belzung, 1995; Ribeiro et al., 1999). For instance, agonists of the serotonin 5-HT$_{1A}$ receptor, which are anxiolytic agents, have also impairing effects on memory consolidation (Leong et al., 2012; McEntee and Crook, 1991; Quartermain et al., 1993). The frequently prescribed benzodiazepines are also well known for impairing different types and stages of memory (Beracochea, 2006; Thiebot, 1985; Uzun et al., 2010). We have recently demonstrated the delayed anxiolytic properties of an acute corticosterone administration in a previous series of experiments (Messenvi et al., unpublished observations). Ten days (but not one day) after the injection, the rats displayed an increased exploration of the open arms of the elevated plus maze. In the present study, animals trained 10 days after corticosterone treatment displayed reduced performance in the inhibitory avoidance task during the testing session. The present data indicate that when corticosterone has anxiolytic effects, it also affects memory performance in high-arousing conditions. This provides further evidence that memory processing of emotional information and anxiety behavior partly share common corticosterone-induced mechanisms. There is evidence from animal studies that the actions of benzodiazepines are mediated by GABAergic mechanisms within the BLA (Izquierdo et al., 1990; Silva and Tomaz,
1995; Tomaz et al., 1992 and 1993). Given that both enhanced GABA transmission within the BLA and intra-amygdala infusion of benzodiazepines reduced anxiety, it was suggested that the anxiolytic and amnestic effects of benzodiazepines are mediated by the same mechanisms within the BLA (Delgado et al., 2005; Graeff, 1990; cf Tomaz 1993). Similarly to benzodiazepine effects, the BLA could be one of the regions where corticosterone-induced mechanisms simultaneously modulate learning and memory functions and anxiety behavior. Extensive evidence has already demonstrated the role of the BLA in mediating glucocorticoids influence on learning and memory (Abercrombie et al., 2006; Roozendaal et al., 2009). There is also strong evidence that glucocorticoid hormones induce changes in anxiety behavior that are correlated with alteration of the morphology of BLA principal neurons (Mitra et al., 2009; Mitra and Sapolsky, 2008). Indeed, high anxiety levels are accompanied by increased numbers of dendritic branches and/or dendritic spine density (Adamec et al., 2012; Mitra and Sapolsky, 2008). We did not assess the neuromorphology in our experiments, but we can hypothesize that the corticosterone-induced anxiolytic effects would be accompanied of a reduced complexity of the dendritic arbors of BLA principal neurons. Remodeling of neuron morphology, particularly at the level of the dendritic arborization, is concomitant to changes in synaptic networks, which will alter the circuitry (Alfarez et al., 2008; Engert and Bonhoeffer, 1999; Maletic-Savatic et al., 1999). In the BLA, which harbors circuits involved in memory and anxiety, these corticosterone-induced morphological changes might ultimately alter the two functions simultaneously. In follow-up experiments we will determine the effects of our treatment on BLA neuromorphology, in parallel to their effects on learning and memory performance.

The finding that only performance in the highly emotionally arousing memory task is reduced by the early corticosterone treatment is consistent with the fact that glucocorticoids modulate memory of emotionally arousing information and have little effects on consolidation and retrieval of neutral events (Abercrombie et al., 2006; Bohannon, 1988; Cahill et al., 2003; Cahill and McGaugh, 1998; Neisser et al., 1996). We used two different tasks in order to determine the influence of arousal on the delayed effects of corticosterone on learning and memory performance. Inhibitory avoidance is an aversive task, and the electric shock, even of mild intensity, provokes a considerable release of norepinephrine in the BLA, that correlates with a strong memory for the event (Galvez et al., 1996; McIntyre et al., 2002). In contrast, an object recognition task is only mildly arousing (Roozendaal et al. Castello, 2008), but 5 minutes of training are sufficient to induce a relatively good memory for all the groups as we demonstrated here. In our experiments, corticosterone was administered 10 days before training and testing when the circulating corticosterone levels are normal physiological range as shown previously (Messanvi et al., unpublished observation; Mitra and Sapolsky, 2008). Therefore, the influence of glucocorticoids on memory performance observed here is not conveyed by the same mechanisms as when the hormones are delivered around the training or testing session. It is still interesting to observe that, either directly or indirectly, and on short or long-term, corticosteroid hormones selectively affect emotional memory through different types of mechanisms. Few studies have
investigated the long-term effects of acute elevation of glucocorticoids on memory function. Delayed impairing effects of glucocorticoids on memory performance have been reported by studies in which the hormone had been administered several days in a row (Newcomer et al., 1994 and 1999; Wolkowitz et al., 1990). In one of these studies, the authors also tested the delayed effects of an acute administration of dexamethasone, and found no modification in memory performance (Wolkowitz et al., 1990). To our knowledge, there is no previous study concerning the long-term consequence of single exposure to glucocorticoids. The mechanisms by which corticosterone can induce a long term decrease of performance in the high-arousing task have to be investigated. Here again, it would be interesting to examine morphological changes in the BLA circuitry. For corticosterone-induced alteration of the neuronal network could impair the processing of memories, particularly those with a strong emotional component. Evidence indicates that the integrity of the amygdala is crucial for encoding, memory consolidation and retrieval of emotionally-arousing information, whereas it would be less important for low arousing information (Adolphs et al., 1994 and 1997; Aggleton et al., 1992; Anderson and Phelps, 2001; Kensinger and Corkin, 2004; LaBar and Cabeza, 2006; Mumby and Pinel, 1994; Murray and Mishkin, 1998; Richardson et al., 2004; Vuilleumier et al., 2004). This could explain why corticosterone-treated animals perform less than the controls animals in the inhibitory avoidance task, and why there is no difference in the object recognition task.

It is important to notice that the present experimental setting does not allow us to ascertain whether the impaired performance observed in the inhibitory avoidance task reflect a real memory impairment. The object recognition task experiment demonstrated that the animals were able to learn a task. Therefore, there is a possibility that the animals remember the shock experience and actually associated the dark compartment with this aversive experience. However, because of their low levels of anxiety, they may be less frightened of a potential new shock and would be less inhibited to go in the dark compartment than control animals. Indeed in a review, Beuzen and Belzung discussed the fact that less anxious animals may process and recall information normally but that their preference for dark places may not be as much inhibited (Beuzen and Belzung, 1995).

Posttraumatic disorder (PTSD), a common anxiety disorder, develops after an experience of severe trauma and is characterized by three groups of symptoms: hyperarousal, avoidance and re-experiencing of the traumatic event (American Psychiatric Association, 2000; Parsons and Ressler; 2013; Yehuda, 2004). There is evidence that dysregulation of the HPA axis, reflected by a low level of cortisol at the time of the trauma, is a risk factor to develop the disease (Yehuda, 2009). Consistent with this view, studies have shown that administration of exogenous cortisol to patients could either reduce the incidence of PTSD if done early, or reduce the re-experiencing symptoms in patients suffering from chronic PTSD (Aerni et al., 2004; Schelling 2004; Weis et al., 2006). At the moment of the trauma, low cortisol levels fail to shut down the stress response and therefore allow enhanced consolidation of the event. In chronic PTSD, elevation of cortisol concentration is thought to weaken
the traumatic memories by impairing their retrieval, and ultimately improves the mood of the patients (De Quervain and Margraf, 2008). Our findings are interesting in that respect, because the present anxiolytic glucocorticoids treatment can impair performance of aversive memory task while having no effect on the neutral task. This dual action of a single corticosterone administration, both on anxiety-like behavior and aversive memories, if confirmed, would be interesting to test in animal models of PTSD symptoms, and could constitute a path to explore in terms of defining the therapeutic actions of glucocorticoids.
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