INTRODUCTION

- Patients with post-traumatic stress disorder (PTSD) exhibit a combination of memory intensification (or extinction impairment) and memory deficits.
- Glucocorticoids have a role in memory formation, and they may contribute to memory changes in PTSD.
- Glucocorticoids have an important role in aversive memory (Roozendal et al., 2006).
- Small pilot study (n=3 patients with PTSD) showed that a small daily dose of cortisol could reduce the frequency or intensity of feelings associated with a traumatic event (Aerni et al., 2004).
- Cortisol acts through mineralocorticoid (MRs) or glucocorticoid receptors (GRs).

OBJECTIVES

Thus, the objective of the present study was to evaluate the effect of
- Spironolactone (an MR antagonist)
- Mifepristone (a GR antagonist)
- Dexamethasone (a GR agonist)

on the extinction of contextually conditioned fear, an animal model of PTSD. Propranolol was used as a positive control.

METHODS

- Adult male Wistar rats, from our own breeding colony, under controlled conditions.

GENERAL PROCEDURE

day 1 Conditioning day 2 Test 1 day 3 Test 2 day 4 Test 3

CONDITIONING PROCEDURE
day 1 Contextual fear conditioning (training session)

Habituation in the conditioning chamber for 3 min ⇒ foot shock (1 seg, 1.5 mA) ⇒ remain in the chamber ⇒ 1 min after shock

Pamplona et al. 2006

EXTINCTION (TEST) PROCEDURE
day 2 ⇒ day 4

Memory index ⇒ freezing behaviour in non-reinforced re-exposures to the context (test sessions). An animal was considered frozen when it presented a stereotypical crouching position with complete immobility, except for breathing movements.

RESULTS

PRE-TEST: PROPRANOLOL

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Fig. 1 Effect of propranolol (10 mg/kg, s.c., 20 minutes before each extinction test) on the extinction of contextual fear memory in rats (n=10/group). * P<0.05 and ** P<0.01 as compared to the vehicle (veh) in the same test session.

POST-TEST: SPIRONOLACTONE

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Fig. 2 Effect of post-session spironolactone administration (10 mg/kg, s.c., administered immediately after the 1st and 2nd extinction tests) on the extinction of contextual fear memory in rats (n=10/group). ** P<0.01 as compared to the 1st session with the same treatment.

CONCLUSIONS

The results showed that:
- Spironolactone increased the extinction of an aversive memory (but only when administered before extinction sessions) ⇒ this can indicate an impairment in memory retrieval and not an increase of a new learning (association between context and shock absence).
- neither Dexamethasone nor Mifepristone treatment had any effect.
- as expected, Propranolol (positive control) administered before a test session increased memory extinction.

These results indicate that MR antagonists may be an option for the treatment of PTSD.

REFERENCES

