FACILITATION OF THE LABILIZATION/RECONSOLIDATION PROCESS OF A RESISTANT FEAR MEMORY

Espejo PJ, Giachero M, Bustos SG, Molina VA.

INTRODUCTION
The memory consolidation theory propose that recent learning can be transiently modified, however once this process is complete, this trace is consolidated and insensitive to further modifications, including pharmacological intervention (1). In the last years, numerous studies have proposed that recalling a previously consolidated memory can render this trace vulnerable to interference (2-5), for instance to benzodiazepine ligands such as Midazolam (MDZ) (6), this process is followed by a stable phase termed memory reconsolidation (4,7). There are, however boundary conditions that place constraints on the onset of the labile phase after retrieval (8). For instance, memory age, the duration of the reactivation period and the interaction between these factors have a crucial influence on retrieval-induced lability (9-11). In addition, activation of NMDA sites seems to be a prerequisite for the emergence of memory reconsolidation (12). It is known that exposure to a stressful event prior to fear learning induces resistance to the emergence of the unstable phase after recall (13).

The main goal of this study was to evaluate the vulnerability to MDZ after the retrieval of consolidated fear memory in animals that have experienced a single stressful situation and the influence of D-cycloserine (DCS), a partial NMDA agonist, on the disruptive effect of MDZ on memory reconsolidation.

MATERIALS AND METHODS
Male Wistar rats (280-330g) were used in all the experiments. Animals were subjected to a contextual fear conditioning paradigm (three 0.3 mA footshocks with a 30 s interval among shocks) (7, 10, 13). Stressed animals were subjected to a 30 min restraint period one day prior to the fear conditioning procedure. Memory reactivation was conducted one day after learning by re-exposing the animal in the conditioning environment. Behavioral freezing was scored as an index of fear during the test session one day after memory reactivation. Half of the animals were injected with DCS (15 mg/kg, i.p.) or saline 20 min prior reactivation (13). Rats were systemically administered with MDZ (1 mg/Kg) or vehicle immediately after reactivation.

RESULTS
The results showed that stressed animals were insensitive to the disruptive effect of MDZ. However, the vulnerability to MDZ was evident in stressed rats that were previously administered with DCS.

CONCLUSION
These results show that NMDA receptor activation promotes the onset of the labile phase following reactivation even in resistant memory traces, as those found in rats that have experienced a stressful event prior to fear acquisition. This study highlights the relevance of the combined treatment with DCS and MDZ for attenuating the undesired emotional disturbance associated with the emergence of traumatic memories.

REFERENCES
3. Bucherelli C and Tassoni G. Engram activation reinstates the susceptibility of consolidated memory

V. A. Molina. Tel: +54 0351 4334437, FAX: +54 0351 4334420, E-mail: vmolina@fcq.unc.edu.ar


