

H. Schroeder¹, N. Violle¹, M. Messaoudi², C. Lefranc-Millot³, A. Nejdj²,
B. Demagny³ & D. Desor¹

¹ Laboratoire de Neurosciences Comportementales, Université Henri Poincaré, 54000 Nancy, France

² ETAP-Applied Ethology, 54500 Vandoeuvre-les-Nancy, France

³ INGREDIA, 62000 Arras, France

INTRODUCTION

ING-911 is a tryptic hydrolysate of bovine milk α_{s1} -casein that contains as a major component a peptide named α -casozepine. This peptide corresponds to the 91-100 fragment of the α_{s1} -casein and was demonstrated to express a high affinity for the benzodiazepine site of the GABA_A receptor. *In vivo*, ING-911 exhibited an anticonvulsant activity in the pentylenetetrazole-induced seizures test, suggesting a possible anxiolytic activity. Then, the purpose of the present study was to assess the effects of ING-911 on anxiety of Wistar male rats in two animal models: the conditioned defensive burying paradigm and the elevated plus maze test.

DRUG TREATMENT

ING-911 was suspended in 0.3% methyl cellulose and administered p.o. at a dose of 15 mg/kg 60 min before testing. Control animals received the same volume of methyl cellulose. A third group of rats was treated with diazepam (3 mg/kg, p.o., 60 min before testing) which was used as a reference anxiolytic substance.

BEHAVIOURAL PROCEDURE

Conditioned defensive burying

APPARATUS: The experiment was done in a Plexiglas chamber (40x25x30cm) where the rats were able to receive a slight electric shock (120 V, 1 mA) from a probe (7x2x0.5cm) inserted into the chamber. Then, the rat responds by heaping litter on the probe. Immediately after shock administration, the behaviour of each rat was observed for 5 min.

BEHAVIOURAL SCORING: anxiety global score that was calculated from the probe burying duration, the number of head stretchings directed towards the probe and the percentage of approaches towards the probe followed by retreats.

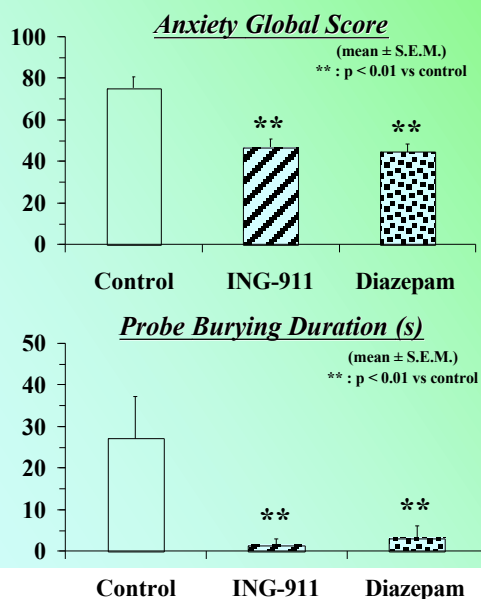
Elevated plus maze

APPARATUS: The maze consists of two open arms (50x10cm) and two enclosed arms (50x10x50cm) that extended from a central platform (10x10cm). The whole apparatus is elevated to a height of 70 cm above floor level. The behaviour of each animal was observed for 5 min.

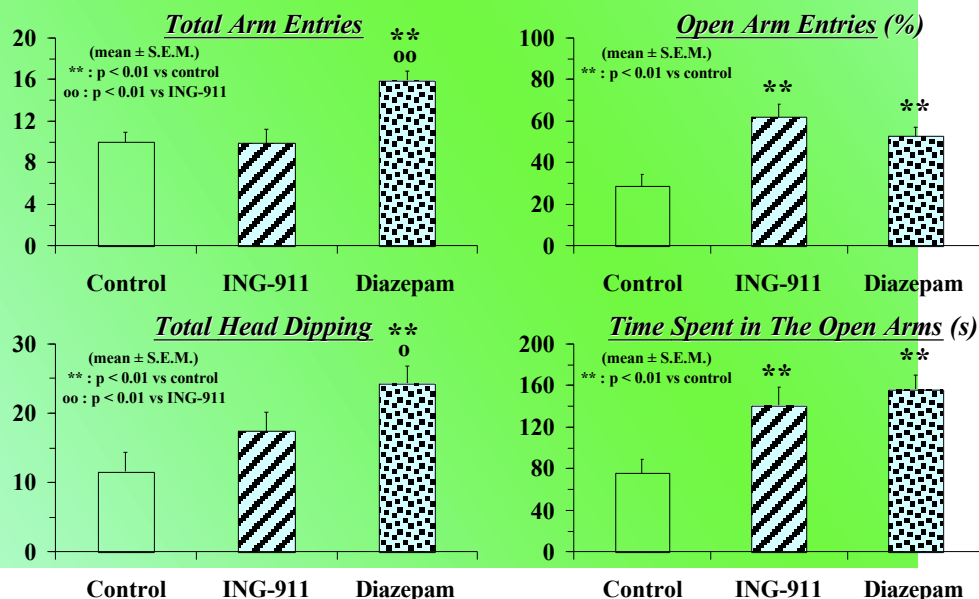
BEHAVIOURAL SCORING: total number of arm entries, open and closed arm entries, time spent in the different parts of the maze, total number of head dippings.

RESULTS

Conditioned defensive burying



Elevated plus maze



CONCLUSION

The present results provide some evidence of the potent anxiolytic-like activity of the bovine milk α_{s1} -casein hydrolysate ING-911 with a behavioural profile which is different from that observed with diazepam. The