ANXIOLYTIC EFFECT OF BLOCKING ANGIOTENSIN II AT1 RECEPTORS ON THE CENTRAL AMYGDALA IN A FEAR POTENTIATED ANIMAL MODEL

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INTRODUCTION
The central amygdala (CAN) is one of the most important brain nuclei for emotional processes regulation (1). Recent evidence suggests a key role for the angiotensinergic system in the regulation of stress responses. Activation of brain angiotensin II AT1 receptors is required for stress-induced hormone secretion, and stimulation of the central sympathetic activity (2). The aim of this work was to assess the role of losartan (Ang II AT1 receptors antagonist) on the anxiety state in a fear potentiated animal model.

MATERIALS AND METHODS
Male adult wistar rats weighing 250-300g kept in a 12 h light-dark period under controlled temperature conditions, with food and water “ad libitum”. The animals were stereotaxically implanted under anesthesia with bilateral stainless-steel cannuli in CAN.

Fear potentiated model: the animals received three electric foot shocks, 24 hs later were reexposed to the conditioning box without electric foot shock stimulation. The control animals did not receive electric shocks (3).

Both groups (stressed and non-stressed animals) were injected with 0.5 µl Losartan (4 µg / µl ), or 0.5 µl AngII (1ng/ µl ). Controls were injected with 0.5 µl of saline solution.

The animals were tested on the elevated plus-maze 15 min after intraamigdalar injection of drugs (3). Percentage of open arm entries, time spent in the open arms, number of extreme arrivals of the open arm, and grooming, were determined as indexes of anxiety. Total number of arm entries, and total traveled distance, were recorded as a locomotor activity index.

RESULTS
The injection of AngII, decreased time spent on open arms in non-stressed and stressed groups compared to their respective controls (66,14 ± 13.0 sec vs 29,14 ± 6.2 sec) and (38,75 ± 6.2 sec vs 14,00 ± 4.6 sec). The stress-induced anxiogenic effect was equivalent to that of Ang II non-stress group. Losartan completely reversed the stress-induced anxiogenic effect.

The microinjection of Ang II decreased the preference for open arms under stress and non-stress conditions (0.62 ± 0.11 vs 0, 31± 0.06) and (0.62 ± 0.16 vs 0.36 ± 0.17) respectively. Losartan completely reversed the anxiogenic effect of Ang II under stress conditions.

The total distance average was 6, 7 m and no differences were found between groups. The stress-induced grooming increase was equivalent to Ang II non-stress conditions. Losartan decreased grooming to control levels.

DISCUSSION
Since treatment with Losartan completely reversed the stress-induced anxiogenic effect, we conclude that Ang II AT1 receptors of CAN are mainly involved in the generation of the anxiety state induced by the fear potentiated.

REFERENCES


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