VENTROMEDIAL PREFRONTAL CORTEX ACTIVITY IS REQUIRED FOR ANXIETY EXPRESSION: DISTINCT NEUROCHEMICAL MECHANISMS EVIDENCE

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PURPOSE OF STUDY

✓ The ventromedial prefrontal cortex (vmPFC) has been implicated in anxiety regulation;

✓ Lesion studies aimed to the vmPFC have shown an anxiolytic-like effect in rats exposed to the elevated plus-maze (EPM), while others have reported an anxiogenic-like or even none effect;

✓ We sought to clarify the vmPFC role in anxiety by blocking the local synaptic activity using cobalt infusion prior to the EPM test. Next, we investigated whether the antagonism of vmPFC adrenergic beta-1, cholinergic muscarinic or glutamatergic NMDA receptors reduces anxiety-related behavior.

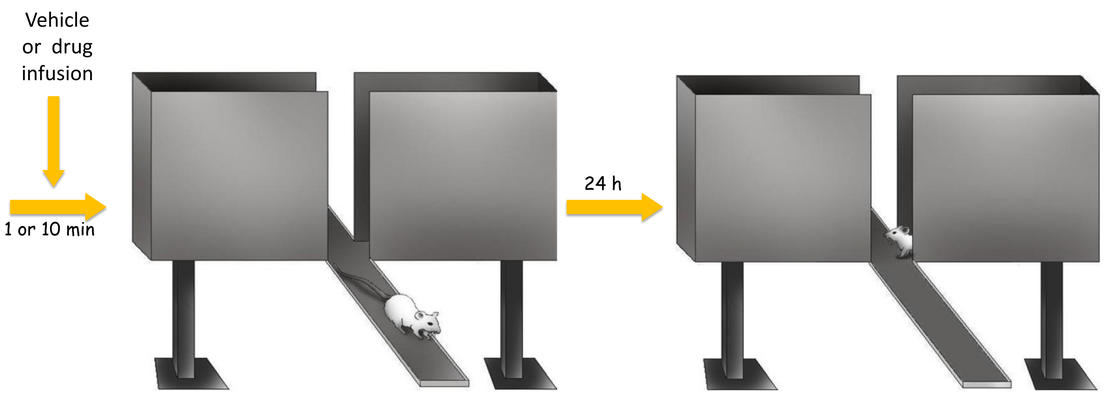
METHODS

General procedures

Male Wistar Rats (300-350 g)

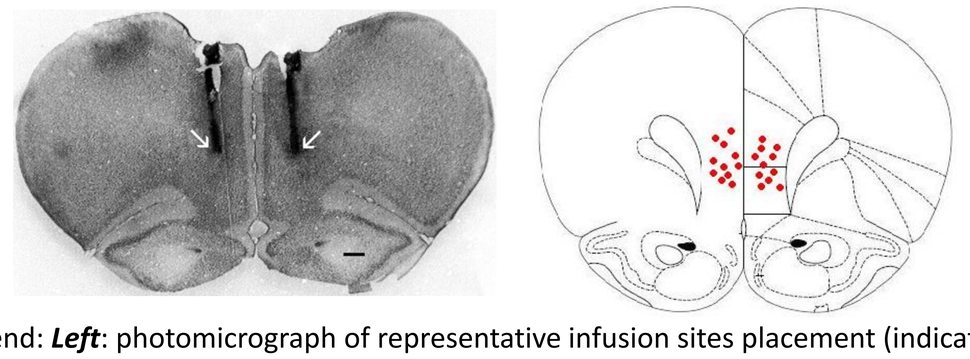
vmPFC stereotaxic surgery → 7 days →

- **Experiment 1**
  - Vehicle
  - Cobalt 1.0 mM
- **Experiment 2**
  - Vehicle
  - Atenolol 10 nmol (**ATE 10**)
  - Scopolamine 20 nmol (**SCO 20**)
  - AP5 6.0 nmol (**AP5 6.0**)



RESULTS

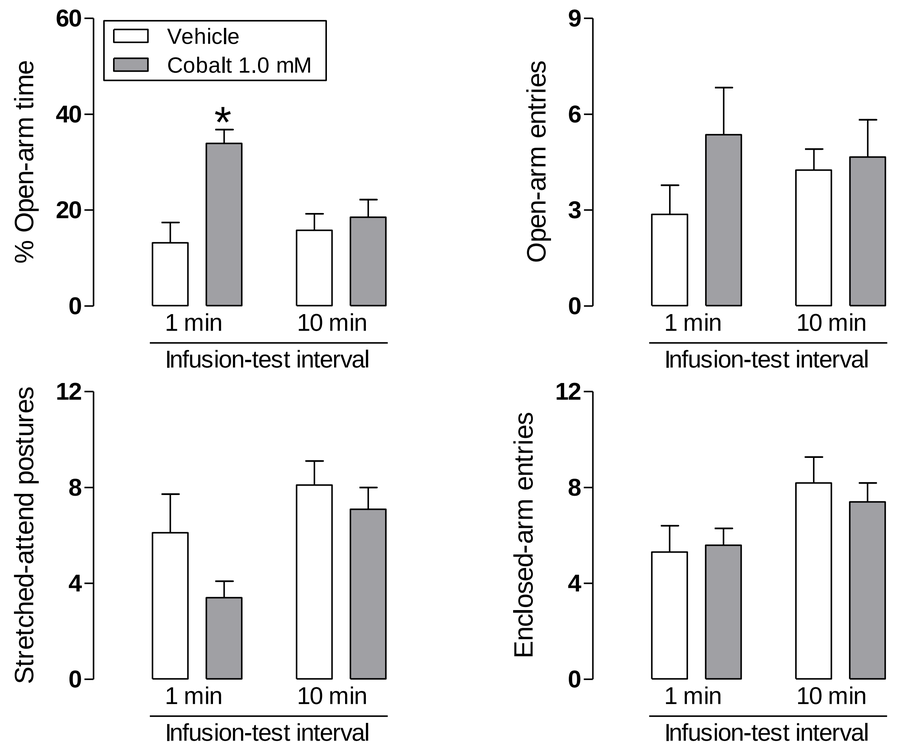
Histological analysis



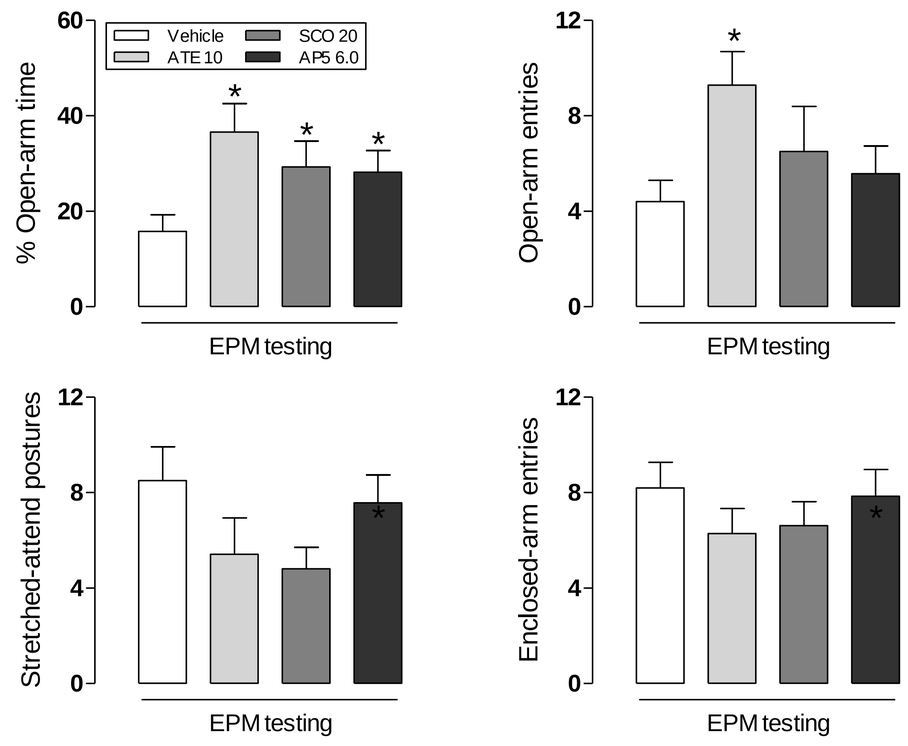
Legend: ***Left***: photomicrograph of representative infusion sites placement (indicated by arrows) in the rat vmPFC (scale bar = 500 µm) ; ***Right***: Schematic diagrams showing the drug injection sites inside (red circles) the vmPFC.

RESULTS

Experiment 1: Cobalt-induced vmPFC inactivation reduces the avoidance to open-arms during the EPM testing



Experiment 2: Bilateral infusion of atenolol, scopolamine or AP5 into the vmPFC produced an anxiolytic-like effect



*p<0.05 relative to controls (one-way ANOVA followed by Neumann Keuls test; values are expressed as mean + S.E.M).

DISCUSSION

✓vmPFC inactivation induced by cobalt attenuates anxiety-related behavior;

✓ The cobalt effect is temporary because it was no longer observed when the interval between drug infusion and EPM testing was 10 min;

✓ vmPFC recruits adrenergic beta-1, cholinergic muscarinic and glutamatergic NMDA receptors to modulate anxiety-related behavior.

We have no conflict of interest

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