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EFFECTS OF MYOSIN IIB INHIBITION ON AVERSIVE MEMORIES

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Introduction. Synaptic plasticity events are intrinsically linked to dendritic spines and both are substrates for the formation, storage and expression of a fear memory. Myosin IIB is a main component for the morphophysiology of the dendritic spines and for the regulation of synaptic plasticity through the binding to the actin filament, hydrolyzing the ATP to generate force and movement contracting the actin filament. Thus, we aim to evaluate the role of Myosin IIB in different memory phases. **Methodology.** We used *wistar* rats (*Rattus novergicus*) and implanted metal cannuli into three different brain structures, the hippocampus, the amygdala and the anterior cingulate cortex, and pharmacologically blocked myosin IIB's activity on those regions by using blebbistatin (Blebb). To assess animal's memory retention and observe their freezing behavior we used two different tasks, the contextual fear conditioning (CFC) and the auditory fear conditioning (AFC). **Results.** Firstly we wanted to determine the most effective dose of blebbistatin, for that we used both the 45 and 90μM concentrations infusing it immediately after the training session in the CFC, the 90μM being the most efficient one impairing long-term memory consolidation ($p = 0.0162$). As expected, short-term memory was not affected by that dose ($p = 0,8540$). Next, we evaluated memory storage (hippocampus-dependent), for that we infused blebb only 24 hours after the training session in the CFC and tested them one day later after the infusion. The drug group's performance was severely impaired ($p < 0,0001$) showing that myosin IIB is indeed involved with memory persistence. Moreover, blebbistatin was sufficient to disrupt the memory of two different contexts (drug factor; $p < 0,0001$), but animals were still able to learn a new task in a novel context ($p = 0,0222$), showing that the drug did not lesion the hippocampus. The amygdala is another structure important for fear memories so in order to analyze the effects of blocking the myosin IIB in that structure we infused blebbistatin 24 hours after the training session in the AFC. Memory was severely impaired in the drug group when animals were tested in a different context ($p < 0,0001$) or in the same context ($p = 0,0069$), suggesting that myosin IIB has an important role for the maintenance of aversive associative memories in the amygdala. We also wanted to evaluate the consequences of infusing blebb into the anterior cingulate cortex (a region involved with storage of remote memories) right after the training session in the CFC and testing the animals 48h later and after 40 days. We found that the drug damaged the animal's performance both on test 1 ($p = 0,0007$) and test 2 ($p = 0,0236$) showing that at the same time the memory trace is being formed in the hippocampus it might be encoded in the ACC and that the same impairments you'd observe on the first test happens 40 days later. We also trained another group of rats and tested them 40 days later, infusing blebb into the hippocampus 24h before the test session to see the structure's involvement with remote memories. Our results suggest that once a memory is fully consolidated and stored in the cortex, inhibiting MIIB in the hippocampus does not disrupt that aversive memory anymore ($p = 0,6823$). Thus, our results suggest that the myosin IIB has an essential role in the persistence and expression of aversive memories. **Conclusions.** We conclude that Myosin IIB is an important protein of the cytoskeleton and it is involved with memory consolidation, storage, persistence and expression, but it is not related to the short-term memory. Finally, further studies of this protein's properties may shed light on its therapeutics' use for people who suffers from Post-traumatic Stress Disorder (PTSD).