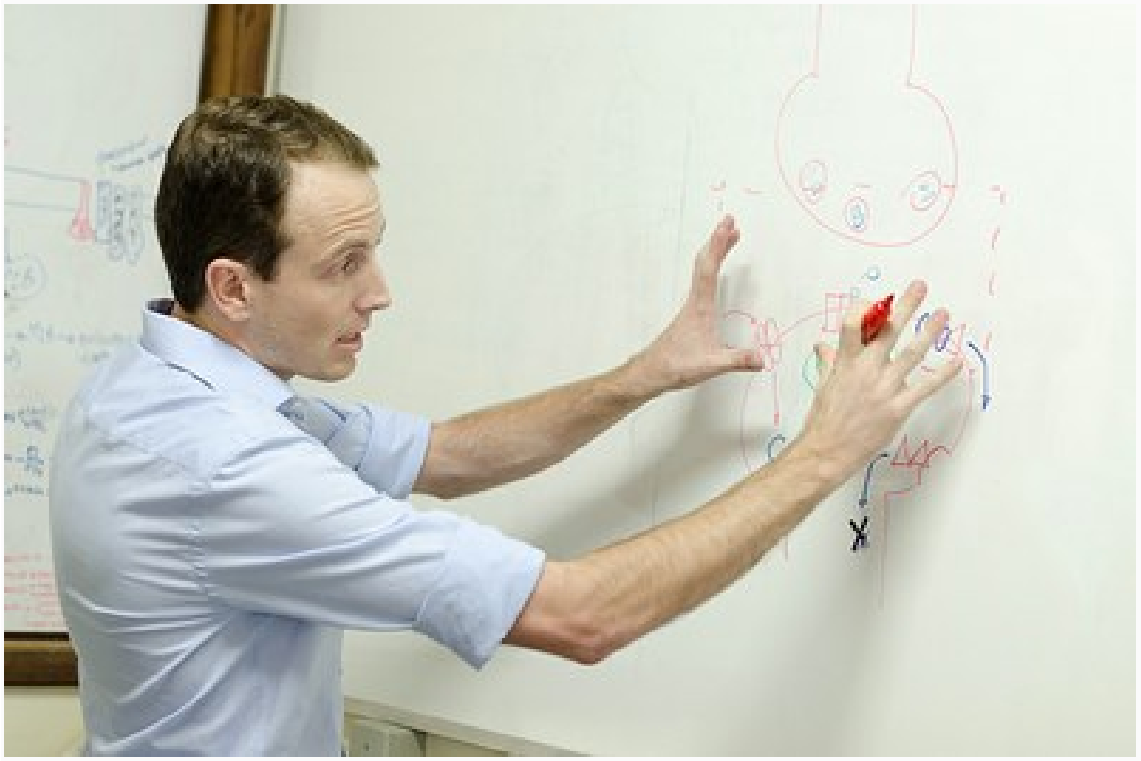
Research Investigates the Neurobiological

A study from the Neurobiology of Memory Lab explains how forgetting occurs in the brain and the importance of calcium in this process

Author: Carolina Golenia

What did we have for lunch two days ago? Which pair of shoes did we wear last week? These are commonplace facts that we experience, but that we forget as days go by. The investigation of the mechanisms that work both in forming and forgetting memories was the object of a study published by a group of researchers from UFRGS' Neurobiology of Memory Lab in *Scientific Reports*, a journal of the Nature Publishing Group. The paper is part of Ricardo Sachser's doctoral research in Neurosciences, under the supervision of Professor Lucas de Oliveira. His goal is to understand how the process of forgetting works.

The tests were performed with laboratory rats in an experiment in which they were encouraged to memorize the position of obstacles within a large box in which they were placed daily. "We used a protocol whereby rats formed a memory that they forgot about the third day. By making an analogy, it would be like you remember what you wore three days ago," explains Lucas.



The paper is part of the doctoral research of Ricardo Sachser – Photo: Gustavo Diehl

The role of calcium in stabilizing the memory and in its forgetting

According to the studies, calcium (Ca^{2+}) is largely responsible both for forming and forgetting memory. "It is a flag that activates before a series of waterfalls. Depending on its location and concentration, it may be involved in forming memories or forgetting them," says Lucas. This whole process of memorization happens in the dendrites of the neurons, in the region of the brain called the hippocampus**.**

According to Ricardo, calcium coordinates, at first, the process of stabilization of the neuron membrane, but also works in the processes of destabilization. "At the moment of recording information, calcium entry is made necessary," he reports. However, the large amount of this ion leads to the process of forgetting, due to the destabilization it causes. The substance enters and leaves the cell by the calcium receptors, which are fixed means in the membrane, or by the active enzymes, that are not fixed, like calcineurin. "It does not matter where calcium comes from. After the stability of the memory, if it enters, it will destabilize," comments Ricardo.

In addition to behavioral analysis, researchers investigated the mechanism directly involved at the cellular level by studying the electrical activities of neurons. "In electrophysiology, rats receive anesthesia, and it is possible to analyze whether or not a population of neurons will be triggered," says Lucas. A drug that blocks calcium entry has been injected into the animals after induction of response in a particular memory trait – in a process called long-term potentiation. "We waited around 30 minutes for the memory trace to stabilize and then injected the drug, and that memory did not fall. That is, the trace remained potent," explains Ricardo. "We use drugs as a pharmacological tool to understand the mechanism of action, and not as a therapeutic proposal. The idea is that the rat should learn something and then it must forget it. We use tasks that we call non-aversive, because they are not remembered for a long time naturally," adds Lucas.

Post-traumatic stress and possible applications

The main findings of the research were the neurobiological mechanisms responsible for forgetting, the characterization of the receptors and the importance of calcium in this process. "Once you understand the mechanism involved in this stabilization/destabilization, you can prevent the decline from its occurrence. And in the case of people who have suffered post-traumatic stress? Have you thought

about speeding up the forgetting of that? This is one of the next issues we will try to solve," stresses Ricardo.

In human patients, trauma treatment is carried out in therapy sessions. "It is only possible to tackle the memory structure by evoking it. In a clinical session, you recall greater details of that memory, and when it is unstable again, it is time to start pharmacological intervention to block this circuit," he explains. "This is an important issue: we want to accelerate the forgetting of that specific memory, not of others," adds Lucas.

The paper also has the collaboration of students from the Psychobiology and Neurocomputation Lab, coordinated by Professor Jorge Quillfeldt, and the Centre for Cognitive and Neural Systems at the University of Edinburgh, Scotland.

Scientific article

Sachser, R. M. *et al.* Forgetting of long-term memory requires activation of NMDA receptors, L-type voltage-dependent Ca^{2+} channels, and calcineurin. *Sci. Rep.* 6, 22771; doi: 10.1038/srep22771 (2016).

Keywords: Brain, Forgetting, Memory, Neurosciences

Translated by Camila Wisnieski Heck, under the supervision and translation revision of Professor Elizamari Becker (IL/UFRGS).