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Intracranial stimulation proved efficient in the recovery of learning and memory in rats

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Stimulation of the hypothalamus completely reverses learning and memory deficits caused by brain lesions in rats, according to a first time discovery by a group of researchers led by the UAB. The research has also served to study the mechanisms through which this recovery occurs, suggesting that the stimulation of the hypothalamus activates several regions of the brain, especially the memory systems, which offer compensatory effects.

The research, published in *Behavioural Brain Research*, was conducted by Pilar Segura and Ignacio Morgado (coordinators), Laura Aldavert and Marc Ramoneda, psychobiologists of the Institute of Neurosciences and the Department of Psychobiology and Health Sciences Methodology of the UAB and by Elisabet Kadar and Gemma Huguet, molecular biologists of the University of Girona, to explore the power of Deep Brain Stimulation treatments in the hypothalamus to recover the ability to learn and remember after a severe lesion of the amygdala.

The amygdala is a critical region for basic emotions, especially the ones that alert us of an imminent danger, and the region is involved in the learning and fear conditioning. Dysfunctions in this part of the brain block the ability to learn stimulus association, such as seeing a fire and relating it to the danger of being burnt, and can be caused by things such as biochemical alterations of the neurotransmitters, extremely tense situations, strokes or tumours.

The research verified how animals whose amygdala was damaged in

more than 70% totally recovered the ability to learn and remember after being submitted to several sessions, first in learning and then in the intracranial self-stimulation of the hypothalamus, which consists of sending electric impulses to that region of the brain. The effects last up to three months after ten 60-minute treatment sessions, contributing to the consolidation of implicit and explicit memory. Moreover, the learning and retention levels of the injured animals were even better than that of healthy animals.

Researchers affirm that this is the first study to show what a strong effect this treatment has in animals with brain injuries.

Changes in the Brain

How can stimulation to the hypothalamus compensate damages in the amygdala, an area which is essential to learning and remembering? Researchers already highlighted in previous studies that this activation produced structural changes in the brain, increasing neural connections, the expression of genes with functions related to neural plasticity and neuroprotection. In this study, researchers also were able to verify that in a small part of the amygdala which was not damaged there was more acetylcholinesterase activity, a key enzyme in the metabolism of acetylcholine, a neurotransmitter which is essential for learning and remembering.

"This regulation of the cholinergic activity must form part of the recovery and improvement produced by the stimulation, it may even regulate this activity in other parts of the brain, especially in the memory systems, which here would work as compensatory mechanisms", explains Pilar Segura. "This makes us think that the stimulation of the hypothalamus does not affect only one part, rather it has several action paths and depending on where the lesion is located, it can stimulate different mechanisms with the aim of repairing different dysfunctions."

The study, researchers say, demonstrates the exceptional therapeutic power of DBS and points to the fact that, in addition to learning and remembering, the treatment could be effective in "unlearning", i.e. in disconnecting the stimulus of disabling emotions such as those caused by post-traumatic stress.

More Predisposed to Learning

The hypothalamus is a region of the brain in which the most basic impulses are found, helping us to survive and providing us with pleasure. It is part of the brain's reward system, which makes us feel good after carrying out an activity and helps us change our behaviour through positive reinforcement.

"We've discovered that when we stimulate the hypothalamus, there is a greater predisposition to learn," Ignacio Morgado explains. "We believe that DBS causes these changes in the memory system in a way similar to when we are learning. The release of neurotransmitters, changes in synaptic connections, more expression in the genes involved in learning and memory demonstrate just that," he adds.

Previously, DBS had proved efficient in the partial reversal of memory deficits and in spatial learning affected by stress, also in rats. According to researchers, it is an invasive technique in which the benefits must be weighed closely against the risks.

"In the future, similar and not as invasive treatments such as transcranial magnetic stimulation could provide similar effects. This technique is being tested on animals and, although it is not as precise, it seems to be yielding good results. That is why it is essential to conduct more studies and analyse the complex neural circuits and the role of techniques such as these in modifying brain functions and specifically in improving the memory", Pilar Segura concludes.

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More information: Kádár E, Ramoneda M, Aldavert-Vera L, Huguet G, Morgado-Bernal I, Segura-Torres P. "Rewarding brain stimulation reverses the disruptive effect of amygdala damage on emotional learning." *Behav Brain Res*. 2014 Nov 1;274:43-52. DOI: 10.1016/j.bbr.2014.07.050.

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