

# Scientists unveil the mechanisms underlying the immediate effect of deep brain stimulation in depression

February 18 2014

---

A team of UCA researchers led by Professor Esther Berrocoso and in joint collaboration with the mental health research groups of the Centro de Investigación Biomédica en Red de Salud Mental (CIBERSAM) have carried out a pioneering project in Spain.

A research team at the University of Cadiz, headed by Professor Esther Berrocoso, in joint collaboration with mental health research groups of the Centro de Investigación Biomédica en Red de Salud Mental (CIBERSAM) and the Instituto de Salud Carlos III, have conducted a pioneering translational study on the immediate antidepressant effect of [deep brain stimulation](#) (DBS) which, so far, has yielded outcomes that are scientifically and clinically significant for patients who suffer from major depression and do not respond to currently available treatments.

In fact, last 28 May, the most prestigious scientific journal of mental health, with the highest impact factor, *Molecular Psychiatry*, published a paper on DBS by UCA's PhD student and Laura Perez-Caballero and Professor Esther Berrocoso, as main researchers. The paper was also written by Juan Antonio Micó, also from UCA, as well as scientists at Salus Infirmorum (Cádiz), Hospital de la Santa Creu i Sant Pau (Barcelona) and Universidad Complutense (Madrid): Carmen Romero-Grimaldi, Rosario Pérez-Egea, Dolors Puigdemont, Victor Pérez, Joan Molet, Javier R. Caso and Juan Carlos, all of them members of the CIBERSAM network.

In order to fully understand the finding, it is worth pointing out that, in Spain, one out of five women and one out of ten men will suffer from depression sometime in their lifetime. Nowadays, half of the patients with major depression (the most severe type of depression) do not respond to treatment: symptoms persist despite complying with treatment for enough time. In such cases, the patient often ends up with chronic functional disorder. However, resistance to treatment can have more severe consequences. It is estimated that major depression is present in 70% of completed suicides and this is why research into new therapeutic approaches is needed.

The studies, conducted at basic and clinical levels, have unveiled that the immediate or early effect of the DBS technique to treat patients with [major depression](#) is conditioned by delivery of analgesic and anti-inflammatory drugs after surgery.

That being said, it must be explained that DBS is a neurosurgical procedure that has been successfully used to treat patients with Parkinson's disease for a long time now. Since 2005, the technique has been used as a neurosurgical treatment to treat diverse psychiatric disorders and mainly treatment-resistant depression due to its special severity. The procedure is a surgical treatment in which an electrode is placed into the patient's brain in order to stimulate the subgenual cingulate, an area in the cerebral cortex which shows altered activity in patients suffering from such a disorder. Clinical trials conducted to date across different countries have shown that the response rate, one year after start of treatment, is higher than 60% (nearly two out of three patients). Notwithstanding, the studies had also unveiled that a transitory improvement, whose underlying mechanisms were unknown, took place immediately after the surgical procedure.

"It must be noted that patients with treatment-resistant depression is a difficult case since they are patients who have not responded to

conventional treatment. When the technique was introduced, the first results yielded were very promising – to the extent that the initial antidepressant effect after electrode implant was attributed to the patients' own great recovery expectations. However, in our study we posit the existence of an additional neurobiological mechanism," as UCA researcher Esther Berrocoso explains.

Thus, a series of pre-clinical studies were conducted at UCA in order to research into the neurobiological mechanisms responsible for the immediate and early response caused by the technique. Unsurprisingly, as it sometimes happens in science, the data provided by our studies suggested that a clear antidepressant effect resulting from an inflammatory phenomenon taking place in the area of the injury appeared during the early stages of treatment. To put it another way, it was found out that the neurosurgical procedure involving implantation of the electrodes over the cerebral cortex caused the production of molecular mediators for a short period of time, causing a clear and immediate antidepressant effect," as the head of the study, Dr Berrocoso, explains.

The research work done in the study has unveiled some of such mechanisms. In particular, the technique's immediate or early response involves a complex local inflammatory phenomenon accompanied by protein molecule synthesis over the cerebral cortex, highly important for producing the antidepressant effect. In other words, the immediate antidepressant effect is associated with the protein expression (p11) and a local inflammatory phenomenon taking place in a very specific area of the brain which "is not precisely bad but useful in improving of depressive state."

In fact, thanks to the work done by the UCA researchers and the various CIBERSAM research teams, "we can suggest that shortly after electrode implantation a series of other beneficial molecular phenomena takes

place, apart from the ones caused by brain stimulation itself," as Professor Esther Berrocoso explains.

As a result of the findings on inflammation, the team of scientists believes that "the analgesic/anti-inflammatory drugs that are delivered to control pain in patients after surgery could be, at first, counterproductive to the antidepressant effect". In fact, "we have retrospectively examined resistant-treatment depression patients that had been treated with the technique at Hospital de la Santa Creu i Sant Pau in Barcelona and taken analgesic drugs, and then compared them with those who had not needed them. The result was that the patients who had not taken anti-inflammatories recovered better from depression during the initial stage".

Therefore, to continue the investigations being carried out, "we are studying the use of analgesic drugs that have no anti-inflammatory effects. That is to say, we are working on the development of other protocols for pain control that do not interrupt the aforementioned beneficial and antidepressant effect, since this is the way patients with a severe type of depression can be treated effectively the soonest possible." Moreover, the UCA researcher also highlighted that "even though the results are promising, it is necessary to speak cautiously as our hypothesis needs to be tested in a larger sample [patients](#)."

Consequently, researchers at UCA have already decided to take a step further, and "although the outcomes relating to the technique's antidepressant effect are promising, we must not forget that we are talking about a technique that requires precise intracranial surgery. Therefore, the aim of our team is to examine what particular neurochemical changes are caused by the neurosurgical technique in detail in order to turn such changes into a possible therapeutic target by adopting a less intrusive approach," as Esther Berrocoso says.

Provided by Universidad de Cádiz

Citation: Scientists unveil the mechanisms underlying the immediate effect of deep brain stimulation in depression (2014, February 18) retrieved 23 April 2024 from <https://medicalxpress.com/news/2014-02-scientists-unveil-mechanisms-underlying-effect.html>

This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.