Brain pacemakers: A long-lasting solution in the fight against depression

January 31 2011

Physicians from the University of Bonn, Germany, together with colleagues from the US, have suggested a new target structure for a very promising depression therapy, the so-called deep brain stimulation. They hope to achieve an even better success rate with fewer side effects.

Nearly ten percent of all cases of depression are so severe that the patients do not respond to any established treatment method. Targeted stimulation of areas in the brain using a type of "brain pacemaker" has recently raised hopes: According to initial studies, half of patients with the most severe depression treated in this manner see a significant improvement in mood. Physicians from the University of Bonn, together with colleagues from the US, have suggested a new target structure for deep brain stimulation (as it is technically called). They hope to achieve an even better success rate with fewer side effects. The work has been published in the renowned Neuroscience *and Biobehavioral Reviews*.

In deep brain stimulation, physicians implant electrodes in the brain. Using an electrical pacemaker implanted under the patient's clavicle, physicians can influence the function of certain areas of the brain in a lasting manner. The method was originally developed for treating patients with Parkinson's disease, in order to alleviate the typical movement problems.

For several years, the method has also been investigated in the treatment of the most severe cases of depression, with striking and completely unexpected success: In patients who had undergone many years of

unsuccessful treatment, the symptoms sometimes significantly resolved. The most striking aspect: "Depression does not return in patients who responded to the stimulation," emphasizes Professor Dr. Thomas Schläpfer from the Bonn Hospital for Psychiatry and Psychotherapy. "The method appears to have lasting effects - and this is in the case of the most treatment-resistant patient group described in the literature. This has never before happened."

Deep brain stimulation has been tested to date in three different areas of the brain: the nucleus accumbens, the internal capsule, and a structure known as cg25. Surprisingly, the effects are nearly identical - regardless of which of these centers the physicians stimulate. Together with colleagues from Baltimore and Washington, the Bonn researchers have since been able to explain why this is the case: Using a novel tomography method, they were able to make the "cable system" of the three brain centers visible. "In doing this, we determined that at least two of these three areas - probably even all three - are attached to one and the same cable harness," explains the Bonn brain surgeon, Professor Dr. Volker Coenen.

This is the so-called medial forebrain bundle, a structure which has been known in animals for a long time. The forebrain bundle forms a kind of feedback loop which allows us to anticipate positive experiences. "This circuit motivates us to take action," says Coenen. "In patients with depression, it is apparently disrupted. This results in, among other things, an extreme lack of drive - a characteristic symptom of the disease."

The nucleus accumbens, internal capsule, und cg25 all appear to be connected to the medial forebrain bundle - rather like leaves are connected to the branch from which they arise. Whoever stimulates one of these regions of the brain simultaneously influences the other components of the motivation circuit to a certain extent. Coenen, who was the first to anatomically describe the forebrain bundle in humans,

now proposes implanting the electrode for deep brain stimulation directly into this structure. "We would use the electrode to send the current pulses to the base of the network and not to the periphery, as before," explains Schläpfer. "We could thus potentially work with lower currents and yet achieve greater success."

Observations of patients with Parkinson's disease appear to support this idea: in this case, a network of brain structures responsible for movements is stimulated. The more basally (figuratively speaking: near the branch) the electrical stimulation is applied, the greater its effect. At the same time, the risk of adverse side effects is reduced.

By now, more than 80,000 patients with Parkinson's disease worldwide have a brain pacemaker in their body. "Experiences to date demonstrate that the brain intervention necessary for this is relatively low-risk," stresses Professor Coenen. "Thus from a medical point of view, there is nothing that argues against also using this method to help people with very severe depression."

More information: doi: 10.1016/j.neurobiorev.2010.12.009

Provided by University of Bonn