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DEEP BRAIN STIMULATION HELPS MANY PEOPLE WITH CHRONIC DEPRESSION REGAIN THEIR LIVES

"What is 'well'?" asks **Professor Helen Mayberg** from the Icahn School of Medicine at Mount Sinai in New York. Deep brain stimulation to treat depression has been proven in some patients, who do not respond to psychotherapy, medication and electroconvulsive therapy, to be highly effective in helping them become well enough to regain their lives.

Deep brain stimulation (DBS) is a surgical procedure whereby electrodes are implanted into a specific area of the brain known as the subcallosal cingulate from where they send electrical impulses within the brain to regulate mood. The electrodes are connected to a battery pack placed in the patient's chest which can be controlled by a hand-held device.

DBS was first used in people with movement disorders, such as essential tremor and Parkinson's disease. In the early 2000s, Professor Mayberg pioneered the use of DBS for depression and other mood disorders that failed all conventional treatments including ECT. The technique has developed considerably in recent years, to a point where the impact of DBS treatment for extreme depression can be analysed more rigorously.

In her lecture today (8 July) at the FENS Forum of Neuroscience in Berlin, Professor Mayberg describes on-going research involving small groups of patients to refine the techniques to target more accurately the electrodes and the impulses they deliver. Key to this line of enquiry is to work out who will benefit from DBS. Over the last nine years, the number of patients who have had a sustained benefit as a result of continuous treatment and improvements in the technique is about 70%.

There is a very rapid change in negative mood during and immediately after DBS surgery, with the pace of change in other depression symptoms requiring chronic stimulation combined with ongoing psychotherapy and rehabilitation. "We are closely watching the natural history of recovery. The absence of depression does not mean the absence of distress caused by daily problems or sad events. But it is how you cope with them that matters so that you can get on with a productive life," she says.

A person with depression commonly experiences intense negativity, lack of interest and inability to experience pleasure as well as anxiety, disturbances in thinking, sleeping and basic drives leading to hopelessness and helplessness. According to the World Health Organization, five percent of the world's population have some form of depression.

Professor Mayberg observes an evolution in people who regain the ability to manage their lives following DBS. "DBS is not a quick fix." Using a broken leg as an analogy she continues, "You do not run a marathon when you have your leg in a cast. The same is true for treating depression with DBS. As with any disease, people have to take care of themselves. They have to recognise the triggers for their depression, learn how to cope with a bad day without going back down into depression. Having supportive family and friends is important too. Then the DBS is most likely to work well."

In the years following DBS Professor Mayberg and her team scan the brains of her patients to trace the nerve pathways involved in the response to the stimulation to find out how to target precisely the location of the electrodes and the direction and intensity of the electrical pulses. A distance less than the width of a strand of vermicelli, about 1-2mm, may determine the right or wrong location.

But technology is not the entire solution. "Everyone is different. As clinicians, we have to read people's facial and vocal expressions and their moods. We have to watch and listen to our patients, try and understand how they are feeling, and what being well means to them as individuals. Then we use the technology in order to look at the brain to make a scientific analysis. That way we can make subtle adjustments to the implant and maximise the effectiveness of DBS," she says.

It is important to understand why some people recover more quickly than others. A slow recovery could indicate a more severe depression at baseline requiring a more protracted repair process. In ongoing studies, the theory that DBS may enhance plasticity relevant to recovery is being tested. If all a person's responses while depressed have been negative by default, recovery requires their brain to recalibrate to experience the full range of good and bad; this is where DBS may be facilitating its most critical effects.

People who undergo DBS will have had chronic depression for many years and may have had medical treatment which could interfere with the action of the electrical impulses. Ideally, patients would be medication free at the time of DBS implantation, but that is not realistic or safe in patients being treated with an experimental intervention. The trial strategy is to taper off over medications if there is evidence that there is clinical improvement on DBS, but discontinuation of medications is a slow process and most patients remain on medication in addition to receiving long-term DBS. In an effort to get back to being 'the real you' after years of living with depression, does the patient and their family or carers even know who 'the real you' is? Recovery, therefore, can be challenging for relationships, hence the need for ongoing psychotherapy in patients doing well.

Research into refining DBS, like recovery from depression or any major illness, is a long-term process. "If it doesn't go the way you expect, you figure it out and adjust your strategy," says Professor Mayberg. Her lecture on the ethics of DBS raises issues on the point she decides that the scientific evidence makes it worth going forward. "Always put the needs of the patient first. Be unbiased. Involving patients leads to better research and better results. If you are not listening, you won't learn – and that's unethical," she advised.

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European Dana Alliance for the Brain - Special Lecture: SL04 – What is well? Reconciling First- and Third- Person Perspectives on Depression Recovery with DBS

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