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2008 : December 2008 : Helen S. Mayberg &amp; Andres M. Lozano

## EMERGING RESEARCH FRONTS - 2008

December 2008



Helen S. Mayberg & Andres M. Lozano talk with *ScienceWatch.com* and answer a few questions about this month's Emerging Research Front Paper in the field of Psychiatry/Psychology. The authors have also sent along an image of their work.



### Article: Deep brain stimulation for treatment-resistant depression

Authors: Mayberg, HS;Lozano, AM;Voon, V;McNeely, HE;Seminowicz, D; Hamani, C;Schwalb, JM;Kennedy, SH

Journal: NEURON, 45 (5): 651-660 MAR 3 2005

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(addresses have been truncated.)

### SW: Why do you think your paper is highly cited?

This paper describes a first proof-of-principle experiment testing a potential new treatment for intractable major depression. The work served to unite the fields of brain imaging of neuropsychiatric disorders with neurosurgery and specifically deep brain stimulation (DBS) surgery. Clinical and behavioral effects were robust, the procedure was safe, and correlative imaging results supported the initial hypotheses.

### SW: Does it describe a new discovery, methodology, or synthesis of knowledge?

The new discovery is that modulating a specific area of the brain involved in mood regulation with deep brain stimulation could possibly be effective in patients with treatment-resistant depression.

### SW: Would you summarize the significance of your paper in layman's terms?

The subcallosal cingulate—Brodmann Area 25 (BA25)—has been implicated in the pathophysiology of depression and antidepressant response mechanisms. BA25 is an area in the cerebral cortex of the brain and delineated based on its cytoarchitectonic characteristics. It is also called the subgenual area or area subgenualis. It is the 25th "Brodmann area" defined by Korbinian Brodmann, a German neurologist who became famous for his definition of the cerebral cortex into 52 distinct regions.

Based on converging evidence, we piloted the use of continuous deep brain stimulation (DBS) to modulate subcallosal cingulate activity as a novel treatment strategy for patients resistant to other available treatments. Chronic stimulation of this region using implantable electrodes was associated with a striking and sustained remission of depression in four of six patients. If these encouraging first findings



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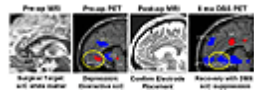
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are replicated in controlled clinical trials, this new treatment strategy may offer a new treatment option for depression when other available treatments are not helpful.

**SW:** How did you become involved in this research and were any particular problems encountered along the way?

Figure 1:



+View larger image & details

Based on a long series of previous studies of antidepressant treatment mechanisms studied using functional neuroimaging, we tested the potential application of deep brain stimulation to modify the activity in these pathological brain circuits. There were no problems that weren't anticipated based on past experience with this surgical procedure or in treating a severely ill and refractory treatment resistant depressed patient population.

**SW:** Where do you see your research leading in the future?

The study has already been expanded from the original six patients reported in *Neuron*. A second paper extending this work was just published reporting on a total of 20 patients followed for one year (Lozano AM, et al., "Subcallosal cingulate gyrus deep brain stimulation for treatment resistant depression" *Biol Psych* 64: 461-67, 2008).

This procedure is now also being tested in an FDA-approved, industry-sponsored, placebo-controlled, multicenter clinical trial. New studies of clinical efficacy, mechanisms, and procedural optimization (patient selection, targeting) are underway at both Emory University and the University of Toronto. These clinical studies further provide foundation for complementary translational studies of both depression pathophysiology and DBS mechanisms in new animal models.

**SW:** Do you foresee any social or political implications for your research?

A new treatment option for treatment resistant depressed patients has considerable social and medical implications, if the safety and efficacy of the treatment is confirmed in randomized, placebo-controlled clinical trials.

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Figure 1:

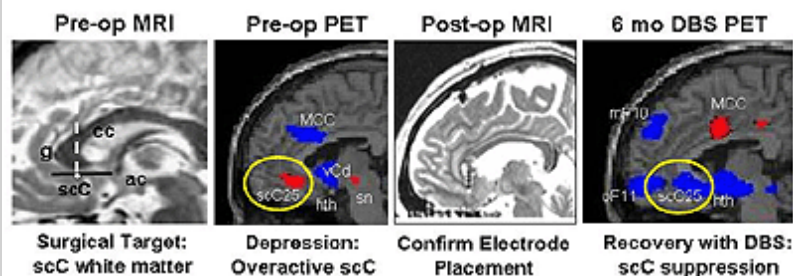



Figure 1:

Adapted from Mayberg, HS, et al., *Neuron*, 45:651-660, 2005. [Click](#) for a larger view of this figure.

Keywords: treatment-resistant depression, brain imaging, neuropsychiatric disorders, neurosurgery, deep brain stimulation, subcallosal cingulate, brodmann area 25, pathophysiology of depression, antidepressant response mechanisms, cerebral cortex, antidepressant treatment mechanisms, functional neuroimaging, pathological brain

circuits.

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