

Appendix 2 (as supplied by authors): DBS Studies

Study	Study Type	Number/Type of Patients	Control group	Outcome
Subcallosal Cingulate Gyrus				
Holtzheimer et al. 2012 (1)	Prospective open label trial with sham lead-in phase	17 (10 MDD, 7 with bipolar II)	Single-blind, sham lead-in phase in all patients for 4 weeks after initial implantation. Second sham phase following 24 weeks of active stimulation; abandoned after 3 subjects due to significant deterioration in depressive symptoms after stimulation was discontinued	At one year follow-up, remission and response rate of 36%. At 2 years, remission rate of 58% and response rate of 92%. Remission and response rates based on Hamilton Depression Rating Scale (HDRS). Efficacy similar for MDD and bipolar patients
Lozano et al. 2012 (2)	Prospective open label trial	21 (MDD)	No control group	At 6 months follow-up, response rate of 48%; at one year follow-up, response rate of 29%. Response measured by HDRS
Mayberg et al. 2005 (3)	Case series	5 (MDD, one patient with bipolar II)	No control group	Follow-up 6 months. 4/6 responders, 2/6 remission as measured by HDRS
Kennedy et al. 2011 (4)	Case series	20 (MDD, one patients with bipolar II)	No control group	At last follow-up (3-6 years following implantation, mean=3.5), response rate=64.3% and remission rate=42.9% (by HDRS). Considerable improvement in social functioning: 65% of patients engaged in work-related activity at last follow-up compared to 10% prior to DBS
Ventral caudate/Ventral Striatum				
Malone et al. 2009 (5)	Case series	15 (MDD)	No control group	Follow-up from 6-51 months. 8/15 responders and 6/15 in remission at

				last follow-up measured by Montgomery-Asberg Depression Scale (MADRS)
Nucleus Accumbens				
Schlaepfer et al. 2008 (6)	Case series	3 (MDD)	No control group	Double-blind changes to stimulation parameters and assessment. HDRS scores decreased with stimulation and increased with stimulation off.
Bewernick et al. 2010 (7)	Case series	10 (MDD)	No control group	At 12 months, 5/10 had achieved >50% reduction in HDRS scores (i.e., responders). Antidepressant, antianhedonic, and antianxiety effects observed
Inferior Thalamic Peduncle				
Jimenez et al. 2005 (8)	Case report	1 (MDD with comorbid bulimia nervosa and borderline personality disorder)	No control group	Double-blind assessment protocol following initial period of 8 months with "on" stimulation. No relapse of depressive symptoms with DBS turned off for 12 months. Sustained remission at 24 months with DBS on.

References

1. Holtzheimer PE, Kelley ME, Gross RE, et al. Subcallosal cingulate deep brain stimulation for treatment-resistant unipolar and bipolar depression. *Arch Gen Psychiatry* 2012;69:150-8.
2. Lozano AM, Giacobbe P, Hamani C, et al. A multicenter pilot study of subcallosal cingulate area deep brain stimulation for treatment-resistant depression. *J Neurosurg* 2012;116:315-22.
3. Mayberg HS, Lozano AM, Voon V, et al. Deep brain stimulation for treatment-resistant depression. *Neuron* 2005;45:651-60.

4. Kennedy SH, Giacobbe P, Rizvi SJ, et al. Deep brain stimulation for treatment-resistant depression: follow-up after 3 to 6 years. *Am J Psychiatry* 2011;168:502-10.
5. Malone DA Jr, Dougherty DD, Rezai AR, et al. Deep brain stimulation of the ventral capsule/ventral striatum for treatment-resistant depression. *Biol Psychiatry* 2009;65:267-75.
6. Schlaepfer TE, Cohen MX, Frick C, et al. Deep brain stimulation to reward circuitry alleviates anhedonia in refractory major depression. *Neuropsychopharmacology* 2008;33:368-77.
7. Bewernick BH, Hurlemann R, Matusch A, et al. Nucleus accumbens deep brain stimulation decreases ratings of depression and anxiety in treatment-resistant depression. *Biol Psychiatry* 2010;67:110-6.
8. Jiménez F, Velasco F, Salin-Pascual R, et al. A patient with a resistant major depression disorder treated with deep brain stimulation in the inferior thalamic peduncle. *Neurosurgery* 2005;57:585-93.