

Deep Brain Stimulation for Depression

- Concurrent examination of gamma-stimulated variability in heart rate and auditory steady-state response in patients with major depressive, bipolar, and schizophrenia spectrum disorders
- Interventional psychiatric procedures and novel substances for the treatment of affective disorders: An overview and outlook
- The Targets of Deep Brain Stimulation in the Treatment of Treatment-Resistant Depression: A Review
- Is the Treatment Worse than the Disease?: Key Stakeholders' Views about the Use of Psychiatric Electroceutical Interventions for Treatment-Resistant Depression
- Safety profile of intracranial neuromodulation for drug-resistant epilepsy in children
- Best practices for clinical trials of deep brain stimulation for neuropsychiatric indications
- A Habenula Neural Biomarker Simultaneously Tracks Weekly and Daily Symptom Variations during Deep Brain Stimulation Therapy for Depression
- Deep transcranial ultrasound stimulation using personalized acoustic metamaterials improves treatment-resistant depression in humans

Deep Brain Stimulation (DBS) is an emerging [neuromodulation therapy](#) for **treatment-resistant depression (TRD)**. It involves implanting [electrodes](#) in specific brain [regions](#) to regulate dysfunctional [neural circuits](#).

Mechanism of Action

DBS works by delivering electrical impulses to targeted brain areas, modulating abnormal activity associated with depression.

Target Brain Regions

- **Subcallosal Cingulate (SCG/BA25)** - Overactive in TRD, modulating this region can improve mood regulation.
- **Nucleus Accumbens (NAc)** - Involved in reward processing and anhedonia.
- **Ventral Capsule/Ventral Striatum (VC/VS)** - Modulates motivation and emotional regulation.
- **Medial Forebrain Bundle (MFB)** - Affects the reward circuitry and can provide rapid antidepressant effects.
- **Lateral Habenula (LHb)** - Plays a role in processing negative emotions and stress.

Clinical Trials and Efficacy

Several studies have explored the effectiveness of DBS in depression:

- Early open-label studies showed significant symptom reduction.

- The **BROADEN trial** targeting VC/VS did not meet primary efficacy endpoints.
- Newer trials suggest that **individualized target selection** and **adaptive stimulation** might improve outcomes.

Patient Selection

DBS is considered only for **severe, treatment-resistant depression**, typically defined as:

- Failure to respond to multiple antidepressants.
- Ineffectiveness of psychotherapy.
- Lack of improvement with electroconvulsive therapy (ECT).

Risks and Challenges

- **Surgical risks** - Infection, hemorrhage, lead migration.
- **Side effects** - Mood instability, hypomania, anxiety.
- **Cost** - High cost and limited availability.
- **Ethical concerns** - Long-term safety and effectiveness require further research.

Future Directions

- **Personalized Stimulation** - AI-driven adjustments based on patient-specific needs.
- **Closed-loop DBS** - Real-time adaptive stimulation based on neural activity.
- **Biomarkers** - Identifying objective indicators to predict response.

External Links

- [PubMed Research on DBS](#)
- [National Institute of Neurological Disorders and Stroke](#)
- [Ongoing Clinical Trials on DBS for Depression](#)

Studies of [DBS](#) in the treatment of treatment resistant depression (TRD) have suggested safety and efficacy for several targets. The most experience to date is with the [subcallosal cingulate](#) (SCC) white matter target. Unique among these studies are data on the MFB target which suggest more rapid antidepressant efficacy than with the other targets. However, in interpreting these data, caution is warranted. The majority of the studies are small and open-label. The one sham-controlled study of a DBS target (VC/VS) showed no separation between active and sham stimulation for antidepressant efficacy. This highlights the importance of sham-controlled trials before embracing treatment modalities with encouraging preliminary data ¹⁾

Deep brain stimulation (DBS) of the **subcallosal cingulate gyrus** (SCG) is an experimental approach in treatment-resistant **depression** (TRD). Short-term results of efficacy in DBS are incongruent and studies investigating long-term effects are warranted.

Merkl et al. assessed efficacy of SCG-DBS in eight patients randomized into a delayed-onset group (sham-DBS four weeks) and a non-delayed-onset group. The primary outcome measure was improvement on the Hamilton Depression Rating-Scale (HAMD-24-item-version). Response was defined as HAMD-24 reduction of at least 50% compared to baseline. Assessment was double-blind for a period of eight weeks and after 6,- 12,- 24,- and 28,- months open-label.

The average improvement in HAMD-24 scores after 6,- 12,- and 24-months were 34%, 25%, and 37%. After 6 months, HAMD-24 revealed a significant difference ($P = .022$) and 37.5% of the patients were responders. After 12 months, HAMD-24 scores dropped, but no significant difference was observed. After 24 months, a significant improvement was found ($P = .041$). After the four weeks lasting sham vs. DBS-ON period, there was no group difference ($P = .376$) in HAMD-24 and patients did not improve during sham stimulation. Patients were followed until 28 months and two up to 4 years under SCG-DBS and average response rate was 51%, whereas two patients were remitters (33,3%).

The small sample size limited the statistical power and external validity.

Long-term improvement after SCG-DBS revealed a stable effect. There was no significant difference in response rates between the delayed and non-delayed-onset group. DBS for TRD remains experimental and longitudinal investigations of large samples are needed ²⁾.

Editorials

Nadeem U, Fatima T, Khan A. Role of Deep Brain Stimulation in Treatment-Resistant Depression: A Way Forward. J Coll Physicians Surg Pak. 2025 Feb;35(2):262. doi: 10.29271/jcpsp.2025.02.262. PMID: 39936213.

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<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3984894/>

²⁾

Merkl A, Aust S, Schneider GH, Visser-Vandewalle V, Horn A, Kühn AA, Kuhn J, Bajbouj M. Deep brain stimulation of the subcallosal cingulate gyrus in patients with treatment-resistant depression: A double-blinded randomized controlled study and long-term follow-up in eight patients. J Affect Disord. 2017 Nov 8;227:521-529. doi: 10.1016/j.jad.2017.11.024. [Epub ahead of print] PubMed PMID: 29161674.

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