Defining Treatment Resistance in DBS for Depression

A Systematic Review and Meta-Analysis

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Background

Major depressive disorder (MDD) is a common psychiatric condition with a prevalence of 8.9 million medication-treated adults in the United States, approximately 31% being treatment-resistant depression (TRD).[1] There is a wide selection of treatment options for treatment resistant depression (TRD) including antidepressant combinations, atypical antipsychotics, inflammatory-immune based, psychotherapy, and neuromodulatory.[2] Of the neuromodulatory options, deep brain stimulation (DBS) is one of the most invasive, costly, and low-volume treatments being trialed for TRD.[3]

Prior literature has found only 19% of investigational studies for antidepressant therapies utilized commonly described criteria for treatment resistant depression including two prior treatment failures with adequate dose confirmation and 4 weeks duration or longer.[4] We sought to characterize the role of DBS in TRD through identification of treatment resistance and efficacy analysis in published randomized controlled trials.

Methods

- Searched Pubmed, Embase, and Cochrane Library through December 2023 via PRISMA guidelines with MeSH terms "deep brain stimulation", "DBS", "depression", "treatment resistant depression" and "TRD"[5]
- Included randomized controlled trials with reporting of either Hamilton depression rating scale (HDRS) or Montgomery–Asberg depression rating scale (MADRS)
- Reported patient clinical characteristics were collected and graded through the Thase and Rush Model[6]
- Meta-analysis of DBS efficacy was completed via Revman using random effects and standardized mean differences

Study	n	Lifetime DE (SD)	Thase Rush[a]	Prior ECT[b]	Medication Hx[c] (SD)	Therapy Hx
Accolla 2016	5	5.4 (2.7)	II-V	80%	NA	NA
Bergfeld 2016	25	NA	V	100%	10.8 (3.3)	NA
Coenen 2019	16	9	IV-V	100%	20.3 (6.3)	NA
Crowell 2019	28	5.7 (7.3)	II-V	96%	13 (5.4)	NA
Dougherty 2015	30	2.8 (1.8)	II-V	97%	10.8 (3.2)	100%
Eitan 2018	9	NA	II-V	NA	NA	NA
Fenoy 2018	6	51.2 (76.1)	V	100%	14.8 (5.9)	100%
Holtzeimer 2017	90	4.8 (5.6)	II-V	82%	7.9 (3.6)	100%
Mayberg 2005	6	4.7 (5)	II-V	83%	NA	NA
Merkl 2018	8	5.0 (2.3)	III-V	88%	NA	100%
Puigdemont 2015	8	5.5 (3.7)	IV-V	100%	15.4 (4.1)	75%
Ramasubbu 2020	22	NA	II-V	86%	22.8 (2.6)	NA
Raymaeker 2017	7	NA	II-V	100%	19.6 (5.2)	NA

Table 1: Clinical characteristics of patient cohort meeting inclusion criteria by study.

[a]Range of patient treatment resistance from reported patient inclusion criteria and characteristics
[b]At least one trial of ECT, not specified by unilateral versus bilateral
[c]Mean medication trials of unspecified dosage or duration
Abbreviations: DE, Depressive Episodes; Hx, History; SD, Standard Deviation

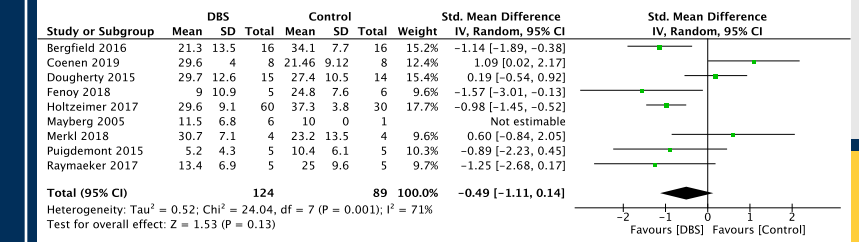

Figure 1: Meta-analysis of DBS versus sham in reduction of depression scores for nine studies that reported adequate treatment and control depression scores.

Results

- Thirteen articles met inclusion criteria with 260 patients total
- Lifetime depressive episodes ranged from an average of 4.7 (5) to 51.2 (76.1)
- Mean lifetime trials of antidepressant medications ranged from 7.9 (3.6) to 22.8 (2.6)
- Four studies required an adequate trial of psychotherapy
  - One reported therapy hours
- 90% of the total patients (227/251) had a history of ECT
- Prior ECT procedures per patient ranged from 13.3 (8.8) to 68.9 (103.6) (five studies reported)
- Treatment resistance ranged from Thase Rush Stage II-V
- DBS showed efficacy in reducing HDRS/MADRS scores over sham stimulation (SMD -0.49; -1.11 to 0.14, 95% CI ***p* = 0.13**)

Conclusion

Interstudy variability in inclusion criteria, definitions of adequate trials and reporting of clinical treatment history made uniform assessment of treatment resistance difficult between studies. Most patients had various trials of antidepressant medication and some form of ECT (unilateral/bilateral) prior to DBS.

Stimulation resulted in reduction of depression scores, however, was not statistically significant. Future randomized controlled trials for treatment resistant disease should rigidly define inclusion criteria.

References

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