

Peer Review

Review of: "Deep Brain Stimulation Is Beneficial for Treatment-Resistant Depression: A Systematic Review and Meta-Analysis of Clinical Trials and Long-Term Follow-Ups"

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We carefully reviewed the present article, and we appreciated the authors' effort to evaluate DBS targets and efficacy in drug-resistant depression treatment. Although the matter is interesting, there are some structural and conceptual issues that prevent its publication.

Please accept the following criticisms:

- Authors define this manuscript as "the first assessment of the efficacy of DBS for TRD." This definition sounds inappropriate as previous studies have already addressed the matter;
- There are some methodological inconsistencies: the trim-and-fill method cannot be systematically used in the presence of substantial heterogeneity between studies in a meta-analysis; authors underline $I^2 > 60\%$;
- The statistical approach is not adequately described. The criteria for selecting fixed versus random effects are unclear, and the handling of confounding factors or variability across studies (diagnostic criteria, outcome definitions, follow-up duration) is not explained. Greater transparency on the model construction is required.
- Graphical elements, especially forest plots and funnel plots, are difficult to interpret due to poor labeling and scale definition. Figures should be revised for clarity, with consistent axis labels, legends, and readable resolution;
- The conclusions appear overstated given the small number of included studies ($n=11$), which is below the generally accepted threshold for reliable meta-regression. The high heterogeneity and limited

number of covariates considered further weaken the robustness of the findings.

- The discussion on DBS targets is superficial. The authors should elaborate on the neurobiological and clinical rationale for each target (e.g., sgACC, VC/VS, NAc, MFB, ITP) and how target selection may influence efficacy and outcomes. This is essential, as it represents one of the paper's key stated objectives.
- The manuscript merges short-term and long-term outcomes without acknowledging differences in methodology, follow-up duration, or confounders such as medication changes. These should be analyzed separately or at least discussed explicitly.

References

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Declarations

Potential competing interests: No potential competing interests to declare.