

Efficacy of deep brain stimulation for the treatment of monogenic dystonia symptoms: a systematic review



DG/WG
Dystonia, NBIA,
Parox. Syndr.



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Introduction

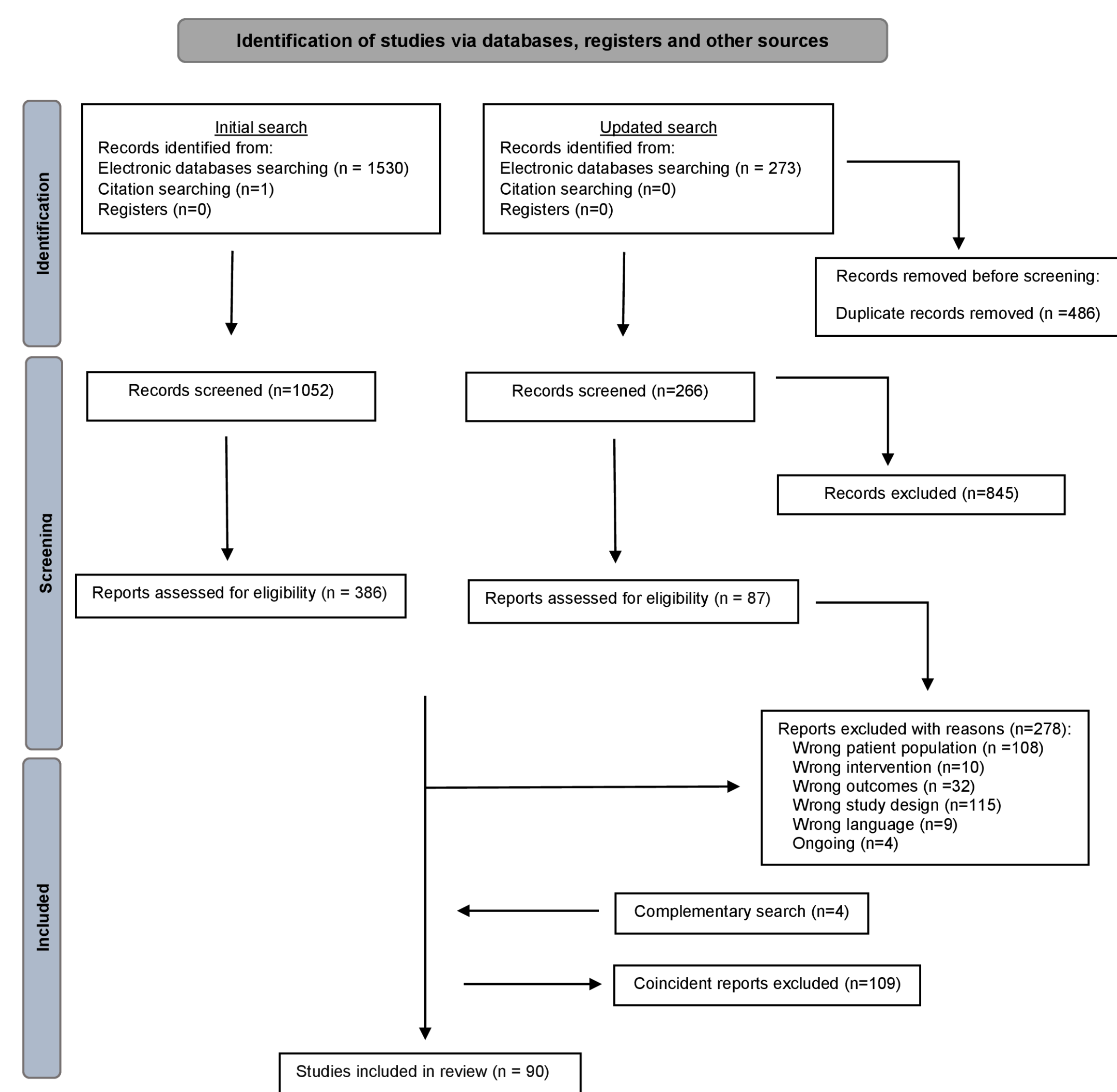
Deep brain stimulation (DBS) is an essential treatment option for disabling segmental or generalized dystonia. An underlying monogenic etiology is increasingly recognized as an important predictor of DBS outcomes. Moreover, the genetic background of dystonia is continuously expanding, posing new challenges in the tailored counseling of patients regarding advanced therapies.

The limited availability of evidence and clinical trials is a major hurdle in counseling patients with rare diseases. This problem is also faced by clinicians involved in the selection and counseling of dystonia patients for DBS.

Previous reviews on the efficacy of DBS in the treatment of monogenic dystonia focused on single outcome measures to assess efficacy, reported findings in single dystonia genes, or in defined age groups.

Within a project initiated by the ERN-RND, we conducted a systematic review of the literature with the support of methodological experts with the aim of maximizing the available evidence for the use of DBS in monogenic dystonia.

Results

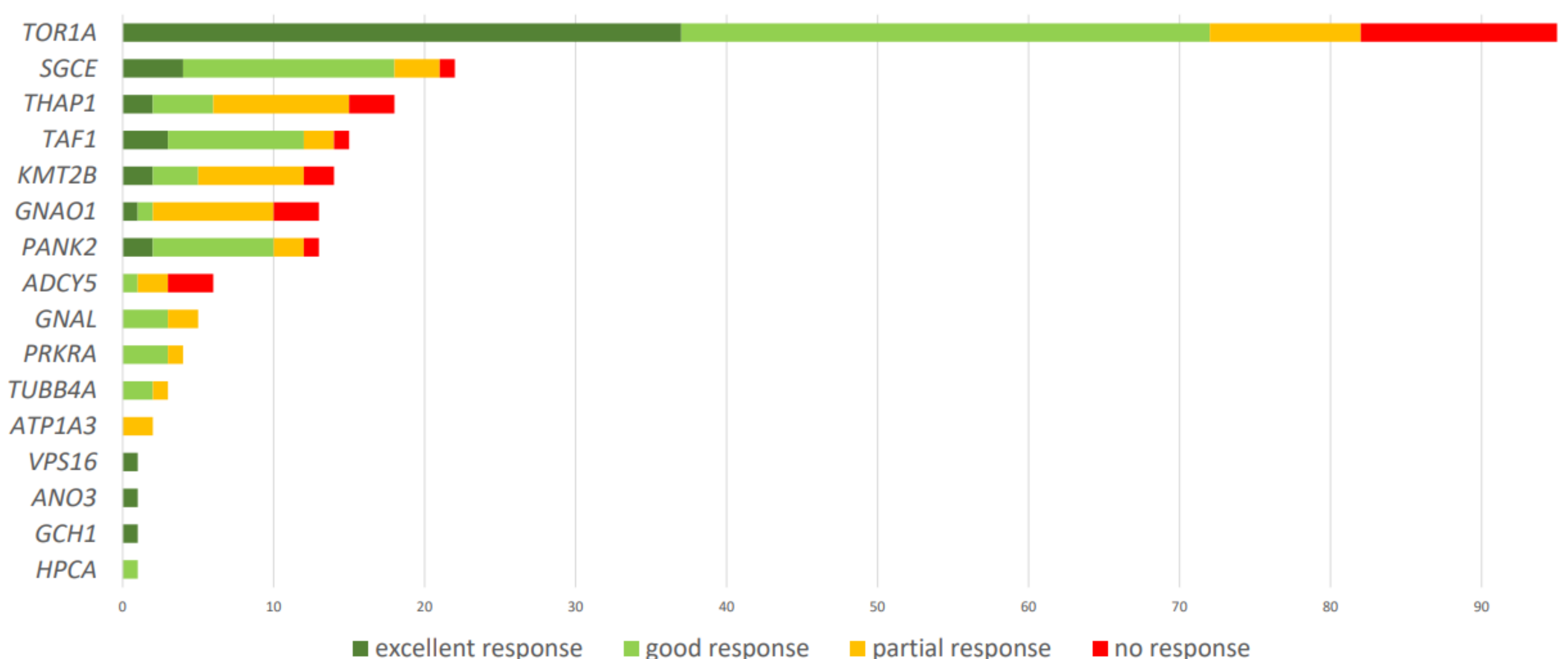


Work Plan

We performed a systematic review of the efficacy of DBS for the treatment of monogenic dystonia symptoms. Our research question was formulated following the Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA) statement. We addressed dystonia genes as reported in the MDSgene database at the time of the study initiation

PICO question	What is the efficacy of deep brain stimulation for the treatment of monogenic dystonia symptoms?
Population	<ul style="list-style-type: none"> Patients of all ages with monogenic dystonia who have genetic confirmation of the disease. Monogenic dystonia due to variants in: ADCY5, ANO3, AOPEP, ATP1A3, EIF2AK2, GCH1, GLB1, GNAO1, GNAL, HPCA, KMT2B, PANK2, PRKRA, SGCE, TAF1, TH, THAP1, TOR1A, TUBB4A, VPS16.
Intervention	<ul style="list-style-type: none"> Deep brain stimulation (DBS)*. *Follow-up (at least 3 months after surgery) Targets: <ul style="list-style-type: none"> Globus pallidus internus (GPI). Subthalamic nucleus (STN). Ventral intermediate nucleus (VIM) Pedunculopontine Nucleus (PPN) Other targets
Comparator	None
Outcomes	<ul style="list-style-type: none"> Clinical response as reported by rating scales assessing: <ul style="list-style-type: none"> Motor symptoms: BFMDRS, UMRS, TWSTRS, UDRS, BADS, TSUI, GDSRS. Non-motor symptoms: CCHQ, GQL, AIMS, SF-36, UPDRS, VAS, CGI-S, BPRS, BDI, PRI, WMI, PSI, SBRS, CMS, SEDS, EDCS, MHC, PHC, PSQ, TMCA, VCI Efficacy of DBS Safety of DBS Adverse events of DBS Quality of life, activities of daily living (ADL) or PROMS Medication regimen changes

Response to DBS in monogenic dystonias



Outlook

The heterogeneity of outcome measures and modalities of efficacy assessment is a major obstacle to the systematic investigation of the efficacy of DBS in monogenic dystonia. Based on the expert consensus that was reached, we formulated the following key recommendations:

- We **recommend** a systematic preoperative and postoperative outcome assessment in patients with monogenic dystonia undergoing DBS.
- Within this assessment, we **recommend** the regular collection of at least the following: i) one dystonia rating scale, i) one rating scale for each other concomitant movement disorder, and iii) one patient-reported outcome scale.

Based on the expert consensus that was reached, we formulated the following key recommendation on genetic testing:

- In all patients with dystonia**, the need for genetic testing should be routinely evaluated according to the criteria defined by Zech et al.
- Regardless of these criteria**, genetic testing should be part of the routine workup for all patients with dystonia for whom DBS is considered.

Our review refines the available evidence on the association between genotype and DBS outcome. Based on the expert consensus that was reached, we formulated the following key recommendations:

- DBS **is recommended** in the treatment of generalized or segmental dystonia due to *TOR1A*, *SGCE*, *TAF1* and *PANK2* variants, after non-invasive therapies have failed to provide adequate improvement.
- DBS **can be effective** for the treatment of generalized or segmental dystonia due to *THAP1* and *KMT2B* variants, after non-invasive therapies have failed to provide adequate improvement.
- DBS **might be considered** for the treatment of *DYT/CHOR-GNAO1*, particularly during dyskinetic crises, when non-invasive therapies have failed to provide adequate improvement.