**Supplementary methods**

**Trial Search**

In March 2024, a comprehensive search for past and ongoing lesional and non-lesional devise-based neuromodulation clinical trials related to movement disorders was conducted. Two publicly available trial registries were queried independently: ClinicalTrials.gov (<https://www.clinicaltrials.gov/>) and the International Clinical Trials Registry Platform (ICTRP; <https://www.who.int/ictrp/en/>) of the World Health Organization (WHO). ClinicalTrials.gov was used in accordance with previous clinical trial reviews. (1-4) The ICTRP database, which collates clinical trial information from numerous national and regional registries, was used to decrease US-centric bias. (5-7)

We conducted a search for trials investigating neuromodulation of the central nervous system (CNS) involving the following movement disorders (inspired by International Classification of Diseases (ICD) 11 terminology and in consultation with movement disorder experts [VB]): Parkinson’s disease, tremor, dystonia, dyskinesia, dyskinesis, chorea, tics and Tourette, Meige syndrome, myoclonus, Huntington's disease, ballism, cerebral palsy, Parkinson’s plus syndrome (multiple system atrophy and ​​Corticobasal Degeneration). (8-10) In order to limit the scope of this study, trials focusing on functional movement disorders and less common disorders such as Wilson’s disease and Rett syndrome were excluded. Based on existing literature and previous reviews investigating neuromodulation clinical trials, the following techniques were specifically examined: deep brain stimulation (DBS); cortical stimulation (ECS); transcranial magnetic stimulation (TMS – including repetitive TMS, theta burst TMS, and deep [H-coil] TMS); electrical stimulation (tES - including transcranial direct current stimulation (tDCS), transcranial alternating current stimulation (tACS) and transcranial random noise stimulation (tRNS)); transcranial ultrasound (tUS); electroconvulsive therapy (ECT); magnetic seizure therapy (MST); MR-guided focus ultrasound (MRgFUS); low-field magnetic stimulation (LFMS); gamma knife radiosurgery (GKRS); radiofrequency ablation (RFA); and spinal cord stimulation. (1,2,7,11-15) Instead of conducting a highly specific search, we conducted a broad search for each aforementioned neuromodulation technique for a combined list of movement disorders outlined above in order to avoid missing clinical trials. (5-6) The ClinicalTrials.gov and ICTRP registries were searched independently. In total, 42 discrete searches were performed across the two databases (see Supplementary Table 1 for full search syntaxes).

**Screening process**

Following the dual-database search, screening was performed following PRISMA guidelines. First, duplicate trials were identified and removed. Each unique entry was then independently screened by two reviewers (D.G. and C.C.) for relevance (the sole inclusion criterion), with disagreements being settled by a consensus decision after discussion with a third reviewer (A.L.). Relevant trials were defined as those that involved the assessment of clinical outcomes of neuromodulatory treatment of the CNS in patients with movement disorders.

**Variable extraction**

Relevant trials were categorized according to the primary clinical disorder(s) and specific neuromodulation technique(s) they involved. Information regarding study details and recruitment information – registration date, completion status, reasons for withdrawal or termination, eligibility criteria, study type, phase, design (randomization, number of arms, projected enrollment numbers, blinding), primary and secondary outcomes, follow-up duration brain target (where applicable, and counting each target separately in the case of multi-target trials), stimulation laterality/parameters, funding source (industry or non-industry), and location(s) were extracted from the trial entry. (1,2,4,7) If a trial’s country of origin was not specified, it was determined based on the location of the primary institution (i.e., the lead center in multi-center trials). Data extraction was accomplished through a combination of automated and manual data extraction. Additional steps were taken to categorize trials by their reported outcomes and research focuses. Primary and secondary outcomes were categorized according to their use of other techniques and outcome measures as per the following categories: cognitive/behavioural/psychological tests, MR imaging, molecular imaging (i.e., PET or SPECT), laboratory tests (e.g., bloodwork, urine tests, genomic analysis), intervention safety/feasibility, electrical/magnetic signal recording (e.g., EEG, MEG, ERP), and biological rhythms (e.g., sleep, sexual activity, exercise).

**Retrieval of published results**

A stepwise approach to identifying trials with published results was employed. Trials were first inspected for publication entries that were automatically indexed based on the inclusion of the trial ID. Then, the PubMed databases (<https://pubmed.ncbi.nlm.nih.gov/>) were queried for the trial ID number. The same search was performed using the Google Scholar database (<https://scholar.google.com/>), to identify any publications not registered on PubMed. Identified publications were reviewed by two authors (M.B. and A.T.) and were included if they reported partial or full results about the corresponding trial. Abstracts, letters or full-length publications that omitted results (i.e., trial protocols) were excluded.

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**Supplemental Table 1:** Search terms for ClinicalTrials.gov and the WHO ICTRP database (Search date August 19, 2021)

Clinicaltrials.gov

|  |  |
| --- | --- |
| Intervention | Condition/Disease |
| deep brain stimulation OR DBS | Dyskinesis OR meige OR ballism OR myoclonus OR tourette OR tics OR chorea OR palsy OR tardive dyskinesia OR parkinson OR dystonia OR tremor OR huntington OR multiple system atrophy OR corticobasal degeneration |
| electroconvulsive therapy OR ECT | Dyskinesis OR meige OR ballism OR myoclonus OR tourette OR tics OR chorea OR palsy OR tardive dyskinesia OR parkinson OR dystonia OR tremor OR huntington OR multiple system atrophy OR corticobasal degeneration |
| vagus nerve stimulation OR VNS | Dyskinesis OR meige OR ballism OR myoclonus OR tourette OR tics OR chorea OR palsy OR tardive dyskinesia OR parkinson OR dystonia OR tremor OR huntington OR multiple system atrophy OR corticobasal degeneration |
| transcranial magnetic stimulation OR TMS | Dyskinesis OR meige OR ballism OR myoclonus OR tourette OR tics OR chorea OR palsy OR tardive dyskinesia OR parkinson OR dystonia OR tremor OR huntington OR multiple system atrophy OR corticobasal degeneration |
| transcranial electrical stimulation OR tES | Dyskinesis OR meige OR ballism OR myoclonus OR tourette OR tics OR chorea OR palsy OR tardive dyskinesia OR parkinson OR dystonia OR tremor OR huntington OR multiple system atrophy OR corticobasal degeneration |
| transcranial alternating current stimulation OR tACS | Dyskinesis OR meige OR ballism OR myoclonus OR tourette OR tics OR chorea OR palsy OR tardive dyskinesia OR parkinson OR dystonia OR tremor OR huntington OR multiple system atrophy OR corticobasal degeneration |
| transcranial direct current stimulation OR tDCS | Dyskinesis OR meige OR ballism OR myoclonus OR tourette OR tics OR chorea OR palsy OR tardive dyskinesia OR parkinson OR dystonia OR tremor OR huntington OR multiple system atrophy OR corticobasal degeneration |
| transcranial random noise stimulation OR tRNS | Dyskinesis OR meige OR ballism OR myoclonus OR tourette OR tics OR chorea OR palsy OR tardive dyskinesia OR parkinson OR dystonia OR tremor OR huntington OR multiple system atrophy OR corticobasal degeneration |
| low-field magnetic stimulation OR LFMS | Dyskinesis OR meige OR ballism OR myoclonus OR tourette OR tics OR chorea OR palsy OR tardive dyskinesia OR parkinson OR dystonia OR tremor OR huntington OR multiple system atrophy OR corticobasal degeneration |
| transcranial focused ultrasound OR tFUS OR fUS OR MRgFUS | Dyskinesis OR meige OR ballism OR myoclonus OR tourette OR tics OR chorea OR palsy OR tardive dyskinesia OR parkinson OR dystonia OR tremor OR huntington OR multiple system atrophy OR corticobasal degeneration |
| transcranial ultrasound OR  tUS | Dyskinesis OR meige OR ballism OR myoclonus OR tourette OR tics OR chorea OR palsy OR tardive dyskinesia OR parkinson OR dystonia OR tremor OR huntington OR multiple system atrophy OR corticobasal degeneration |
| cortical stimulation OR ECS | Dyskinesis OR meige OR ballism OR myoclonus OR tourette OR tics OR chorea OR palsy OR tardive dyskinesia OR parkinson OR dystonia OR tremor OR huntington OR multiple system atrophy OR corticobasal degeneration |
| magnetic seizure therapy OR MST | Dyskinesis OR meige OR ballism OR myoclonus OR tourette OR tics OR chorea OR palsy OR tardive dyskinesia OR parkinson OR dystonia OR tremor OR huntington OR multiple system atrophy OR corticobasal degeneration |
| gamma knife OR GKRS OR radiosurgery | Dyskinesis OR meige OR ballism OR myoclonus OR tourette OR tics OR chorea OR palsy OR tardive dyskinesia OR parkinson OR dystonia OR tremor OR huntington OR multiple system atrophy OR corticobasal degeneration |
| radiofrequency ablation OR RF ablation OR ablation | Dyskinesis OR meige OR ballism OR myoclonus OR tourette OR tics OR chorea OR palsy OR tardive dyskinesia OR parkinson OR dystonia OR tremor OR huntington OR multiple system atrophy OR corticobasal degeneration |

ICTRP (https://trialsearch.who.int/Default.aspx)

|  |  |
| --- | --- |
| Intervention | Condition/Disease |
| deep brain stimulation OR DBS | Dyskinesis OR meige OR ballism OR myoclonus OR tourette OR tics OR chorea OR palsy OR tardive dyskinesia OR parkinson |
| deep brain stimulation OR DBS | dystonia OR tremor OR huntington OR multiple system atrophy OR corticobasal degeneration |
| electroconvulsive therapy OR ECT | Dyskinesis OR meige OR ballism OR myoclonus OR tourette OR tics OR chorea OR palsy OR tardive dyskinesia OR parkinson |
| electroconvulsive therapy OR ECT | dystonia OR tremor OR huntington OR multiple system atrophy OR corticobasal degeneration |
| vagus nerve stimulation OR VNS | Dyskinesis OR meige OR ballism OR myoclonus OR tourette OR tics OR chorea OR palsy OR tardive dyskinesia OR parkinson |
| vagus nerve stimulation OR VNS | dystonia OR tremor OR huntington OR multiple system atrophy OR corticobasal degeneration |
| transcranial magnetic stimulation OR TMS | Dyskinesis OR meige OR ballism OR myoclonus OR tourette OR tics OR chorea OR palsy OR tardive dyskinesia OR parkinson |
| transcranial magnetic stimulation OR TMS | dystonia OR tremor OR huntington OR multiple system atrophy OR corticobasal degeneration |
| transcranial electrical stimulation OR tES | Dyskinesis OR meige OR ballism OR myoclonus OR tourette OR tics OR chorea OR palsy OR tardive dyskinesia OR parkinson |
| transcranial electrical stimulation OR tES | dystonia OR tremor OR huntington OR multiple system atrophy OR corticobasal degeneration |
| transcranial alternating current stimulation OR tACS | Dyskinesis OR meige OR ballism OR myoclonus OR tourette OR tics OR chorea OR palsy OR tardive dyskinesia OR parkinson |
| transcranial alternating current stimulation OR tACS | dystonia OR tremor OR huntington OR multiple system atrophy OR corticobasal degeneration |
| transcranial direct current stimulation OR tDCS | Dyskinesis OR meige OR ballism OR myoclonus OR tourette OR tics OR chorea OR palsy OR tardive dyskinesia OR parkinson |
| transcranial direct current stimulation OR tDCS | dystonia OR tremor OR huntington OR multiple system atrophy OR corticobasal degeneration |
| transcranial random noise stimulation OR tRNS | Dyskinesis OR meige OR ballism OR myoclonus OR tourette OR tics OR chorea OR palsy OR tardive dyskinesia OR parkinson |
| transcranial random noise stimulation OR tRNS | dystonia OR tremor OR huntington OR multiple system atrophy OR corticobasal degeneration |
| low-field magnetic stimulation OR LFMS | Dyskinesis OR meige OR ballism OR myoclonus OR tourette OR tics OR chorea OR palsy OR tardive dyskinesia OR parkinson |
| low-field magnetic stimulation OR LFMS | dystonia OR tremor OR huntington OR multiple system atrophy OR corticobasal degeneration |
| transcranial focused ultrasound OR tFUS OR fUS OR MRgFUS | Dyskinesis OR meige OR ballism OR myoclonus OR tourette OR tics OR chorea OR palsy OR tardive dyskinesia OR parkinson |
| transcranial focused ultrasound OR tFUS OR fUS OR MRgFUS | dystonia OR tremor OR huntington OR multiple system atrophy OR corticobasal degeneration |
| transcranial ultrasound OR  tUS | Dyskinesis OR meige OR ballism OR myoclonus OR tourette OR tics OR chorea OR palsy OR tardive dyskinesia OR parkinson |
| transcranial ultrasound OR  tUS | dystonia OR tremor OR huntington OR multiple system atrophy OR corticobasal degeneration |
| cortical stimulation OR ECS | Dyskinesis OR meige OR ballism OR myoclonus OR tourette OR tics OR chorea OR palsy OR tardive dyskinesia OR parkinson |
| cortical stimulation OR ECS | dystonia OR tremor OR huntington OR multiple system atrophy OR corticobasal degeneration |
| magnetic seizure therapy OR MST | Dyskinesis OR meige OR ballism OR myoclonus OR tourette OR tics OR chorea OR palsy OR tardive dyskinesia OR parkinson |
| magnetic seizure therapy OR MST | dystonia OR tremor OR huntington OR multiple system atrophy OR corticobasal degeneration |
| gamma knife OR GKRS OR radiosurgery | Dyskinesis OR meige OR ballism OR myoclonus OR tourette OR tics OR chorea OR palsy OR tardive dyskinesia OR parkinson |
| gamma knife OR GKRS OR radiosurgery | dystonia OR tremor OR huntington OR multiple system atrophy OR corticobasal degeneration |
| radiofrequency ablation OR RF ablation OR ablation | Dyskinesis OR meige OR ballism OR myoclonus OR tourette OR tics OR chorea OR palsy OR tardive dyskinesia OR parkinson |
| radiofrequency ablation OR RF ablation OR ablation | dystonia OR tremor OR huntington OR multiple system atrophy OR corticobasal degeneration |

**Supplemental Table 2:** Clinical trials by brain target.

|  |  |
| --- | --- |
| **Brain target** | **Number of DBS trials** |
| STN | 200 |
| GP | 3 |
| Gpi | 70 |
| VIM | 37 |
| PPN | 9 |
| Thalamus | 9 |
| cZI | 4 |
| VO | 4 |
| NBM | 4 |
| SNr | 4 |
| DRT | 2 |
| GPE | 2 |
| SCP | 2 |
| ANT | 1 |
| Basal Ganglia-Cortex Loops | 1 |
| Caudate Putamen | 1 |
| Centromedian thalamus-parafascicular complex | 1 |
| Cuneiform Nucleus | 1 |
| Hypothalamus | 1 |
| Nacc | 1 |
| PAG/PVG | 1 |
| rZI | 1 |
| SNpc | 1 |
| ventrolateral thalamus | 1 |
| VIM/DRT | 1 |
| VLP | 1 |
| **Brain target** | **Number of TMS trials** |
| Motor cortex | 51 |
| SMA | 19 |
| PFC | 15 |
| Cerebellum | 11 |
| Spinal cord | 9 |
| DLPFC | 7 |
| Unspecified cortical area cortex | 5 |
| Somatosensory cortex | 3 |
| Dentate nucleus | 1 |
| Parietal cortex | 1 |
| Superior temporal gyrus | 1 |
| **Brain target** | **tES** |
| SMA | 1 |
|  | tACS |
| Motor cortex | 1 |
| Cerebellum | 1 |
| **Brain target** | **Number of tDCS trials** |
| Motor cortex | 42 |
| Cerebellum | 16 |
| PFC | 13 |
| DLPFC | 12 |
| Supraorbital area | 5 |
| Unspecified cortical area cortex | 1 |
| SMA | 3 |
| Frontal ocular field | 2 |
| Frontal cortex | 2 |
| Parietal cortex | 2 |
| Spinal cord | 1 |
| **Brain target** | **Number of MRgFUS trials** |
| Thalamus | 19 |
| VIM | 8 |
| STN | 5 |
| GPi | 3 |
| PTT | 2 |
| DRT | 1 |
| SCP | 1 |
| **Brain target** | **Number of GKRS trials** |
| Thalamus | 3 |
| VIM | 2 |
| **Brain target** | **Number of RFA trials** |
| VIM | 1 |
| PTT | 1 |
| **Brain target** | **Number of SCS trials** |
| Spinal cord | 12 |
| **Brain target** | **Number of CS trials** |
| Motor cortex | 4 |

Abbreviations: ANT=anterior thalamic nucleus, cZI=caudal zona incerta, DLPFC=dorsolateral prefrontal cortex, DRT=dentatorubrothalamic tract, GP=globus pallidus, Gpe=globus pallidus externa, Gpi=globus pallidus interna, Nacc=nucleus accumbens, NBM=nucleus basalis of Meynert, PAG/PVG=periaqueductal gray/periventricular gray, PFC=prefrontal cortex, PPN=pedunculopontine nucleus, PTT=pallidothalamic tractotomy, rZI=rostal zona incerta, SCP=superior cerebellar peduncles, SMA=supplementary motor area, SNc=substantia nigra pars compacta, SNr=substantia nigra pars reticulata, STN=subthalamic nucleus, VIM=ventralis intermedius of the thalamus, VLP=ventral lateral posterior thalamus, VO=ventral-oralis complex nucleus of the thalamus.

**Supplemental Table 3:** Clinical trials by country

|  |  |
| --- | --- |
| **Country** | **Number of trials** |
| United States | 256 |
| France | 83 |
| China | 67 |
| Germany | 63 |
| Japan | 38 |
| Brazil | 37 |
| Canada | 35 |
| Italy | 25 |
| United Kingdom | 25 |
| Netherlands | 18 |
| Spain | 18 |
| Australia | 16 |
| Israel | 16 |
| South Korea | 16 |
| Taiwan | 15 |
| Switzerland | 10 |
| Belgium | 9 |
| Austria | 7 |
| India | 6 |
| Poland | 6 |
| Denmark | 5 |
| Iran | 5 |
| Turkey | 5 |
| Egypt | 4 |
| Finland | 4 |
| Hungary | 3 |
| Norway | 3 |
| Argentina | 2 |
| Hong Kong | 2 |
| Sweden | 2 |
| Czechia | 1 |
| Lebanon | 1 |
| Mexico | 1 |
| Russia | 1 |
| Saudi Arabia | 1 |
| Thailand | 1 |