BMJ Paediatrics Open

Does Transcranial magnetic stimulation improve motor function in children with acquired brain injury? - A scoping review protocol

Journal:	*BMJ Paediatrics Open*
Manuscript ID	bmjpo-2023-001885
Article Type:	Protocol
Date Submitted by the Author:	05-Feb-2023
Complete List of Authors:	Rathinam, Chandrasekar; Birmingham Children's Hospital NHS Foundation Trust, Therapy Department; University of Birmingham, Mohan, Vikram; Bournemouth University Faculty of Health and Social Sciences Bill, Peter; Birmingham Children's Hospital NHS Foundation Trust, Therapy Department Yates, Derick; Birmingham Children's Hospital NHS Foundation Trust, Therapy Department Gupta, Rajat; Birmingham Children's Hospital NHS Foundation Trust, Therapy Department; University of Birmingham, Peirson, Janet; Private Practitioner
Keywords:	Neurology, Rehabilitation, Technology

I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our licence.

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which Creative Commons licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

Review Protocol

Title

Does Transcranial magnetic stimulation improve motor function in children with acquired brain injury? - A scoping review protocol

Authors

Chandrasekar Rathinam[1,2*]

Vikram Mohan[3]

Peter Bill[1]

Derick Yates[1]

Rajat Gupta[1,2]

Janet Peirson[4]

Affiliations

[1] College of Medical and Dental Sciences, University of Birmingham, UK

[2] Birmingham Women's and Children's NHS Foundation Trust, Birmingham, UK

[3] Department of Rehabilitation and Sports Sciences, Bournemouth University, UK

[4] Independent Practitioner, Cambridge, UK

*Corresponding author

College of Medical and Dental Sciences
University of Birmingham
Edgbaston
Birmingham
B15 2TJ
United Kingdom

Birmingham Women's and Children's NHS Foundation Trust
Steelhouse Lane
Birmingham
B4 6NH
United Kingdom

Contact (Email)

Chandrasekar Rathinam - c.rathnam@bham@ac.uk
chandrasekar.rathinam@nhs.net

Vikram Mohan - vmohan@bournemouth.ac.uk

Derick Yates - derick.yates@nhs.net

Peter Bill - peter.bill@nhs.net

Janet Peirson

Rajat Gupta - rajatgupta@nhs.net

Registration

We registered our review protocol in the Open Science Framework (https://doi.org/10.17605/OSF.IO/5SPHT) to enhance transparency and reproducibility, and to reduce duplication.

Amendments

Any amendments to the protocol will be appended and acknowledged in the final report. An updated version with the changes in the original protocol will be added on the OSF registries.

Does Transcranial magnetic stimulation improve motor function in children with acquired brain injury? - A scoping review protocol

ABSTRACT

Background:

Children with severe acquired brain injury (ABI) require early and effective neurorehabilitation provision to promote a good long-term functional outcome. Transcranial magnetic stimulation (TMS) has been used to improve motor skills for children with cerebral palsy but there is limited material supporting its use in children with ABI who have a motor disorder.

Objective:

In this article, we wrote our scoping review protocol to systematically answer what are the TMS intervention effects on motor function in children with ABI as reported in the literature?

Methods and analysis:

This scoping review will follow Arksey and O'Malley's scoping review methodological framework. A comprehensive computerised bibliographic databases search will be performed in MEDLINE, EMBASE, CINAHL, Allied and Complementary Medicine, British Nursing Index, Ovid Emcare, PsychINFO, Physiotherapy Evidence Database, Cochrane Central Register using keywords related to TMS and children with ABI.

Studies that examine the effect of TMS intervention on motor function as either a primary or secondary objective will be included for this review. Study design and publication detail, participant demographic details, type and severity of ABI and other clinical information, TMS procedure, associated therapy intervention, comparator/control parameters, and the outcome measure used data will be gathered.

The International Classification of Functioning, Disability and Health for Children and Youth (ICF-CY) framework will be used to report the TMS effect in children with ABI. A narrative synthesis of the findings describing the therapeutic effects of TMS intervention, limitations, and adverse effects will be synthesized and reported. This review will help to summarise the existing knowledge base and to guide further research areas.

Ethics and dissemination:

No ethical approval is required for this review as we will be collecting data from the previously published studies. We will present the findings at scientific conferences and publish in a peer review journal.

What is already known on this topic?

Transcranial magnetic stimulation (TMS) has been used to improve motor skills through neural plasticity in adults who have suffered from a stroke; and for children with cerebral palsy. There is limited evidence however of its use in improving motor function in children with acquired brain injury (ABI).

What this study hopes to add?

This scoping review will inform the TMS dose that will elicit motor function recovery and what the underlying mechanism is.

How this study might affect research, practice or policy?

The outcome of the review will inform the existing evidence related to the therapeutic effect of TMS in children with ABI. This will help to identify any knowledge gaps, future research questions and to develop future clinical trials that will be able to assess the effectiveness of TMS in children with ABI rehabilitation.

BACKGROUND

Acquired brain injury (ABI) is the term used to describe traumatic and non-traumatic brain injuries that occur after birth and a period of typical development(1). In the United Kingdom, ABI accounts for 35,000 childhood presentations to emergency departments annually. Of these, 5% have moderate to severe brain injury(2). Children with severe ABI will often have movement difficulties caused by weakness, abnormal muscle tone, poor motor control, poor concentration, fatigue and other comorbidities(3). They may also have difficulties with speech, swallowing, and cognitive impairment. A subgroup of children with ABI present with a stroke like presentation limiting their activity, balance, gait and fine motor skills. They are likely to develop tightness and contracture in both the upper and lower limbs(4). This impairment leads to functional difficulties including self-care, playing and manipulating toys, socialising and academic activities(4). During the acute phase, children with moderate to severe ABI frequently require a period of demanding medical and rehabilitative care to optimise their long-term capabilities and quality of life through neuroplasticity (5). This acute care can last up to twelve months following the initial brain injury which often requires a wide range of neurorehabilitation measures from a multidisciplinary team (6).

Early and effective neurorehabilitation provision promotes a good long-term functional outcome for children with ABI(7). Active rehabilitation begins as soon as they are medically stable. The typical rehabilitation includes facilitation of movements, postural control, postural care management, constraint-induced movement therapy (CIMT), virtual reality (VR), strength training, dysphagia and communication

management; and tone medications to improve motor and functional skills through neuroplasticity (6). Recent advances in technology enable clinicians to use functional electrical stimulation, VR(4), and Transcranial magnetic stimulation (TMS) to improve motor skills for children with central nervous system related movement disorders (8,9).

TMS is a non-invasive treatment technique(10). It is safe to use for children and adolescents with neurological conditions(11). It delivers repetitive magnetic pulses directly to specifically targeted brain area through electromagnetic induction. TMS is applied over the scalp either on the same or opposite side to modulate cortical excitability through electromagnetic induction. In TMS, an electric charge is applied to a small coil and this produces a magnetic field perpendicular to the coil. This magnetic field creates an electrical current in the brain tissue parallel to the coil. This activates the localised neurons through cortical excitation(12). Low frequency TMS reduces cortical excitability but the high frequency increases it, thereby producing the desired therapeutic effect (13). Navigated repetitive TMS is delivered to a targeted brain area to change polarization and it influences cortical excitability many minutes after initial stimulation(14). This will help to facilitate, inhibit or interrupt the cortical network depending upon the frequency and intensity of the stimulus, thus promoting a cortical function change through neuroplasticity(15).

TMS has been widely used in adult stroke rehabilitation to facilitate cortical excitability and to promote neuroplasticity(16). Early application of TMS (from 2 weeks to 2 months, 5 – 15 sessions; 1 Hz to 10 Hz) coupled with other rehabilitation therapy intervention has been shown to result in decreased motor impairment, improved activity and participation level in stoke population(14). TMS has been used to treat

children with neuropsychiatric disorders including children on the autistic spectrum; those with attention deficit hyperactivity disorder, obsessive compulsive disorder, and also tics (8). A systematic review investigated the effectiveness of non-invasive brain stimulation for rehabilitation of children with cerebral palsy (CP)(17). This review identified 4 studies that used repetitive TMS (5 – 10 sessions, with each session lasting between 10 – 20 minutes). Three studies used inhibitory low frequency repetitive TMS over the contralateral motor cortex and one study used both high and low frequency repetitive TMS over the primary motor area. A meta-analysis of the outcome measure indicated improved upper limb function following repetitive TMS(17).

It is worth noting that some literature includes children with CP as ABI. An injury to the brain occurs in very early life in CP, whereas in ABI an injury sustained after a period of normal development (18). It could be argued that the description and presentation of CP is markedly different from those who sustained moderate to severe ABI at a later time in their childhood. Enhanced neuroplasticity in the developing brain may prove to be advantageous in rehabilitation following ABI. Structural and functional neural plasticity is attributed to change in regional volumes in brain cells or formation of neural pathways through synaptogenesis, axonal or dentritic sprouting, and creating of new neurons (19). Synaptic and intrinsic mechanism regulates neural excitability which influences neural plasticity (20). TMS coupled with regular rehabilitation could provide improved outcomes through neural plasticity(21). If this is the case, TMS combined with intensive rehabilitation appears to be a promising new intervention approach with wider future applications for the children with ABI. There is, however, limited material supporting its use in children with ABI who have a motor disorder.

The intervention effect in rehabilitation research has been widely reported using the International Classification of Functioning, Disability and Health for Children and Youth (ICF-CY) framework (22). The ICF-CY domain consists of body structures and function, activity, participation, and contextual factors (environment and personal) which can be used to classify the level of functioning in childhood (6). This model can be applied to report the functional outcome of children and young people (CYP) with ABI who has impaired physical, cognitive and emotional difficulties and their impact on activity limitation and participation restriction following an intervention (6).

To our knowledge, there is no review that has examined the therapeutic effect of TMS for children with ABI. The overall objective of this scoping review will be to examine the literature relating to the therapeutic effect of TMS in children with ABI. The outcome of this review will be categorised according to the ICF-CY dimensions. This review will help to summarise the existing knowledge base and to identify areas requiring further research.

METHODS

This review protocol will follow both the Preferred Reporting Items for Systematic Reviews and Meta-Analysis extension for Scoping Reviews (PRISMA-ScR) checklist(23) and Arksey and O'Malley's scoping review approach(25). In addition, the PRISMA Protocol guidelines will be followed to ensure scientific rigor (24) (see supplementary file). We registered our review protocol in the Open Science Framework (https://doi.org/10.17605/OSF.IO/5SPHT).

Identifying the research question

The primary aim of this scoping review will be to characterise TMS intervention. We will specifically answer the question 'what are the TMS interventions effect on motor functions in children with ABI as reported in the literature?'.

Identifying relevant studies

Search Strategy

A copy of the full search strategy as run in Ovid Medline is provided in the appendix. This search will be modified as necessary to be completed in the following databases.

- Electronic database search: A comprehensive computerised bibliographic databases search will be performed in the following databases:
  - MEDLINE (1946–current)
  - EMBASE (1974 to current)
  - Cumulative Index to Nursing and Allied Health Literature
  - Allied and Complementary Medicine (1985 to present)

- British Nursing Index (1992–present)
- Ovid Emcare (1994 to current)
- PsychINFO (1806–current)
- Physiotherapy Evidence Database
- Cochrane Central Register

- Trial registers: The unpublished and on-going clinical trial information will be gathered by searching www.clinicaltrial.gov, www.who.int/trialsearch and www.controlled-trials.com.

- Contacting the corresponding authors of the included articles and asking them to provide the details of any other TMS related research studies in ABI either by their team or by their associates and research group.

- Citation Searching from the included individual studies.

- Other sources
  - The references included in the list of papers selected from the electronic database
  - A hand search will be carried out in specific key journals that have published the maximum number of relevant articles selected for this review. This option will only be carried out if there are more than 3 articles selected from a particular journal.

- Searching Dissertation Abstracts (using ProQuest), conference proceedings and abstracts related to TMS and contacting the researchers to provide any additional information.

- The following TMS equipment manufacturers/distributors will be contacted via email and asked for the details of any trials related to TMS in paediatric ABI population (Axilum Robotics, Brainbox, Brainsway, DEYMED Diagnostic' EB Neuro, eNeura, Jiangsu Aegean Technology, MAG & more, Magstim, MagVenture, Neuronetics, Neurosoft, Nexstim, NIBBOT International, Remed, Sebers Medical, Shenzhen Yingchi Technology, Soterix Medical, Syneika, Xuzhou Kejian)

Eligibility criteria

Inclusion and Exclusion

The searches will be confined to children with ABI only (age group 2-18 years; different variations denoting the age limit which include child, pre-school and adolescent) wherever possible. Some studies include the adolescent population (15–25 years) and the review team will contact the authors to seek data for 2 – 18 years old only. If no response is received, the article will be excluded and this will be documented. All the subgroups of ABI including traumatic, non-traumatic and brain tumour will be included but children with CP will be excluded. If a study has children with CP along with the ABI population, the review team will exclude data related to the CP population. If such information is not clearly available, the review team will contact the authors to seek clarification. If no response is received, the article will be excluded and this will be documented.

Studies that examine the effect of TMS intervention on motor function as either a primary or secondary objective will be included. Research studies that include TMS for diagnostic purposes will be excluded.

No exclusion criteria will be set for language or publication years, and these studies will be considered if the title and abstracts have been written in English. The review team will contact the corresponding authors and request the information in English within two weeks. If no response is received, those studies will be excluded and this will be documented.

Study screening and selection

Electronic database search will be completed by the professional librarian and uploaded in the Ryaan software after removing duplicated studies. The collected titles and structured abstracts from the electronic database will be scrutinised independently by two reviewers by following the set inclusion and exclusion criteria. The excluded studies will be classified as irrelevant and the reasons will be documented. Grey literature and the trial database will be searched by two reviewers independently.

Full articles that meet the selection criteria from the above source will be collected from the NHS library services and the University of Birmingham library services. Two reviewers will decide which articles will be suitable for the final review and any disagreement will be managed after discussing with the third reviewer.

The selection process will be piloting 20% of the collected electronic and grey literature at the beginning to ensure reliable interpretation and agreement between the reviewers. Disagreement will be resolved with a consensus meeting. If no consensus reached, a third reviewer will be consulted. A PRISMA flowchart will be used to inform the selection process.

Charting the data / data extraction

After the screening, two reviewers will independently extract the data (CR & VM) in an excel spreadsheet data extraction tool. Data extraction protocol will be piloted on the first 5 articles. This will help to maintain consistency in data extraction and to make the required changes in the data extraction tool. The above process will be documented. One of the reviewers will extract the data (CR) in an excel spreadsheet from the remaining included studies and the second reviewer (VM) will independently check the collected data.

The review team will gather data about

- Study design and publication detail (reviews, RCT, comparative study, case reports, technical reports, authors detail, year of publication, study location)
- Participants demographical, type of ABI and other clinical information
- TMS procedure (Technique, equipment specification, stimulation parameters such as coil placement, intensity, duration, frequency, adverse effects)
- Any associated therapy intervention (physiotherapy, occupational therapy, VR and other therapy techniques such as CIMT, bimanual therapy, gait training etc) with or without TMS intervention

But are these separate interventions to the TMS intervention? Or is TMS combined with these interventions

- Comparator/control parameters
- Outcome measures used in the individual studies and the relevant observation relating to ICF-CY domains.

This review will be aimed at identifying the changes in motor function of children with ABI. All of the motor function related outcomes reported in the selected articles will be classified under ICF-CY domains. Additional details explaining how these outcomes were measures and at what time points these were collected will be reported. This review will not assess the risk of bias on the included studies but will report their level of evidence.

Collating, summarizing and reporting the results

This review is expected to find heterogeneity across the studies, therefore a narrative synthesis of the findings describing the therapeutic effects of TMS intervention, limitations, adverse effects and the gaps will be synthesized and reported. A table summarizing ICF-CY domain for each study will be presented along with the narrative results.

Patient and Public Involvement (PPI)

The review team consulted two parents of children with ABI in the design of this protocol. The review team will contact the Child Brain Injury Trust (CBIT), a national charity organization for children with ABI (United Kingdom), when conducting the

review and seek their help interpreting the findings and dissemination. Any recommendations made by the CBIT will be implemented.

DISCUSSION

Our protocol explains the methodology to guide our review. The outcome of the review is carefully planned and documented to ensure transparency and research integrity to allow replication(24).

From this scoping review, the review team will provide a descriptive analysis of TMS for children with ABI and how this has been delivered. This review will help to understand the range of TMS dose which includes frequency, intensity, duration, stimulation site, motor function outcome and the corresponding actual or proposed mechanism. This information will guide future trial development with the TMS treatment components that are being commonly used and how they are being delivered. Such treatment information can be organised in the Template for Intervention Description and Replication (TIDieR) checklist to assist future research work to plan and report(26) TMS intervention. This review will help to conduc high-quality patient and public involvement for future studies, designing feasibility studies, and may guide to identify eligible CYP with ABI for TMS intervention.

This review outcome may help to develop therapists' role from conventional hands-on therapy provision to next-generation technology-based neurorehabilitation programmes. This will also likely to have an impact on CYP is access to advanced technology during their acute phase to aid enhanced recovery and helps improve their patient experience.

Funding

This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

Competing Interests Statement

None to declare

Authors contribution

CR, VM and JP - involved in study conceptualization

CR, VM, JP, PB and RG – responsible for study design and protocol development

CR and VM - responsible for screening, selecting articles, and data entry

CR, VM, JP, PB and RG – responsible for data interpreting and reporting

DY – responsible for constructing search strategy and conducting searches

CR, VM, PB, RG, and JP – responsible for preparing final manuscript

CR - guarantor of the review

All authors will read, provide feedback and approve the final manuscript

References:

1. Wales L, Davis K, Kelly G, Lynott H. Long Term Participation Outcomes for Severe Acquired Brain Injury in Childhood - An Expanded Scoping Review. Dev Neurorehabil. 2021 Aug;24(6):379–87.
2. Trefan L, Houston R, Pearson G, Edwards R, Hyde P, Maconochie I, et al. Epidemiology of children with head injury: a national overview. Arch Dis Child. 2016 Jun;101(6):527–32.
3. Hypher RE, Brandt AE, Risnes K, Rø TB, Skovlund E, Andersson S, et al. Paediatric goal management training in patients with acquired brain injury: study protocol for a randomised controlled trial. BMJ Open [Internet]. 2019 Aug 1;9(8):e029273. Available from: http://bmjopen.bmj.com/content/9/8/e029273.abstract
4. Rathinam C, Mohan V, Peirson J, Skinner J, Nethaji KS, Kuhn I. Effectiveness of virtual reality in the treatment of hand function in children with cerebral palsy: A systematic review. J Hand Ther. 2018;
5. McKinlay A, Linden M, DePompei R, Aaro Jonsson C, Anderson V, Braga L, et al. Service provision for children and young people with acquired brain injury: Practice recommendations. Brain Inj. 2016;30(13–14):1656–64.
6. Gmelig Meyling C, Verschuren O, Rentinck IR, Engelbert RHH, Gorter JW. Physical rehabilitation interventions in children with acquired brain injury: a scoping review. Dev Med Child Neurol. 2022 Jan;64(1):40–8.
7. Shen J, Johnson S, Chen C, Xiang H. Virtual Reality for Pediatric Traumatic Brain Injury Rehabilitation: A Systematic Review. Am J Lifestyle Med [Internet]. 2018 Feb 6;14(1):6–15. Available from:

https://pubmed.ncbi.nlm.nih.gov/31903073

8. Bejenaru AM, Malhi NK. Use of Repetitive Transcranial Magnetic Stimulation in Child Psychiatry. Innov Clin Neurosci. 2022;19(4–6):11–22.
9. Dobney DM, Miller MB, Tufts E. Non-pharmacological rehabilitation interventions for concussion in children: a scoping review. Disabil Rehabil [Internet]. 2019;41(6):727–39. Available from: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=med16&NEWS=N&AN=29157025
10. Dayan E, Censor N, Buch ER, Sandrini M, Cohen LG. Noninvasive brain stimulation: from physiology to network dynamics and back. Nat Neurosci. 2013 Jul;16(7):838–44.
11. Krishnan C, Santos L, Peterson MD, Ehinger M. Safety of noninvasive brain stimulation in children and adolescents. Brain Stimul. 2015;8(1):76–87.
12. Iglesias AH. Transcranial Magnetic Stimulation as Treatment in Multiple Neurologic Conditions. Curr Neurol Neurosci Rep. 2020 Feb;20(1):1.
13. Kubis N. Non-Invasive Brain Stimulation to Enhance Post-Stroke Recovery. Front Neural Circuits. 2016;10:56.
14. Schambra HM. Repetitive Transcranial Magnetic Stimulation for Upper Extremity Motor Recovery: Does It Help? Curr Neurol Neurosci Rep. 2018 Oct;18(12):97.
15. Lefaucheur J-P. Transcranial magnetic stimulation. In: Levin KH, Chauvel PBT-H of CN, editors. Clinical Neurophysiology: Basis and Technical Aspects [Internet]. Elsevier; 2019. p. 559–80. Available from: https://www.sciencedirect.com/science/article/pii/B9780444640321000370
16. Chervyakov A V, Poydasheva AG, Lyukmanov RH, Suponeva NA, Chernikova

LA, Piradov MA, et al. Effects of Navigated Repetitive Transcranial Magnetic Stimulation After Stroke. J Clin Neurophysiol [Internet]. 2018;35(2):166–72. Available from: http://europepmc.org/abstract/MED/29394175

17. Elbanna ST, Elshennawy S, Ayad MN. Noninvasive Brain Stimulation for Rehabilitation of Pediatric Motor Disorders Following Brain Injury: Systematic Review of Randomized Controlled Trials. Arch Phys Med Rehabil. 2019 Oct;100(10):1945–63.
18. Forsyth R, Kirkham F. Predicting outcome after childhood brain injury. C Can Med Assoc J = J l'Association medicale Can. 2012 Aug;184(11):1257–64.
19. Dan B. Neuroscience underlying rehabilitation: what is neuroplasticity? Vol. 61, Developmental medicine and child neurology. England; 2019. p. 1240.
20. King ES, Tang AD. Intrinsic Plasticity Mechanisms of Repetitive Transcranial Magnetic Stimulation. Neurosci a Rev J bringing Neurobiol Neurol psychiatry. 2022 Sep;10738584221118262.
21. Johnston M V. PLASTICITY IN THE DEVELOPING BRAIN: IMPLICATIONS FOR REHABILITATION. Dev Disabil Res Rev. 2009;15:94–101.
22. Martinuzzi A, De Polo G, Bortolot S, Pradal M. Pediatric neurorehabilitation and the ICF. NeuroRehabilitation. 2015;36(1):31–6.
23. Tricco AC, Lillie E, Zarin W, O'Brien KK, Colquhoun H, Levac D, et al. PRISMA Extension for Scoping Reviews (PRISMA-ScR): Checklist and Explanation. Ann Intern Med. 2018 Oct;169(7):467–73.
24. Moher D, Shamseer L, Clarke M, Ghersi D, Liberati A, Petticrew M, et al. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. Syst Rev. 2015 Jan;4(1):1.
25. Arksey H, O'Malley L. Scoping studies: towards a methodological framework.

Int J Soc Res Methodol [Internet]. 2005 Feb 1;8(1):19–32. Available from: https://doi.org/10.1080/1364557032000119616

26. Hoffmann TC, Glasziou PP, Boutron I, Milne R, Perera R, Moher D, et al. Better reporting of interventions: template for intervention description and replication (TIDieR) checklist and guide. BMJ. 2014 Mar;348:g1687.

Appendix: Search Strategy: Ovid MEDLINE(R) ALL <1946 to Present>

1 exp Child/

2 exp Adolescent/

3 (p?ediatric* or child* or youth* or adolescen* or juvenile* or teenage* or boy* or girl*).ab,jn,ti.

4 1 or 2 or 3

5 exp Brain Injuries/ or exp Craniocerebral Trauma/ or exp Skull Fractures/

6 ((brain or head or skull or cranio* or cranial or occipital) adj3 (injur* or trauma* or fracture*)).ab,ti.

7 exp Meningitis/

8 Meningitis.ab,ti.

9 exp Encephalitis/

10 Encephalitis.ab,ti.

11 exp Stroke/

12 (Stroke or cerebrovascular accident*).ab,ti.

13 exp Arteriovenous Malformations/

14 Arteriovenous Malformation*.ab,ti.

15 exp Intracranial Aneurysm/

16 ((intracranial or brain or cerebral) adj3 Aneurysm*).ab,ti.

17 exp Cerebral Hemorrhage/ or exp Intracranial Hemorrhages/

18 ((intracranial or brain or cerebral) adj3 H?emorrhage*).ab,ti.

19 exp Hypoxia, Brain/ 14043

20 ((brain or cerebral or encephalopath*) adj3 (hypox* or anox*)).ab,ti.

21 exp Asphyxia/

22 "asphyxia*".ab,ti.

23 exp Brain Neoplasms/ or exp Central Nervous System Neoplasms/

24 (((brain or cerebral or CNS or central nervous system) and (tumo?r* or glioma* or blastoma* or sarcoma* or cancer* or neoplasm* or astrocytoma* or ependymoma* or glioblastoma* or oligoastrocytoma* or oligodendroglioma* or Meningioma* or medulloblastoma*)) or "posterior fossa syndrome").ab,ti.

25 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24

26 exp Transcranial Magnetic Stimulation/

27 (Transcranial adj2 magnetic adj2 stimulation*).ab,ti.

28 exp Transcranial Direct Current Stimulation/

29 (noninvasive adj2 brain adj2 stimulation).ab,ti.

30 (noninvasive adj2 cerebral adj2 stimulation).ab,ti.

31 (Transcranial adj2 direct adj2 Current adj2 Stimulation).ab,ti.

32 (electromagnetic induction and brain).ab,ti.

33 (TMS or rTMS or NIBS or NrTMS).ab,ti.

34 (transcranial adj2 electric* adj2 stimulation).ab,ti.

35 ((Anodal or Cathodal) and stimulation TDCS).ab,ti.

36 transcranial random noise stimulation.ab,ti.

37 transcranial alternating current stimulation.ab,ti.

38 Theta Burst Stimulation.ab,ti.

39 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 32106

40 4 and 25 and 39

****

BMJ Paediatrics Open

Impact of Transcranial magnetic stimulation on motor function in children with acquired brain injury - A scoping review protocol

Journal:	*BMJ Paediatrics Open*
Manuscript ID	bmjpo-2023-001885.R1
Article Type:	Protocol
Date Submitted by the Author:	26-Mar-2023
Complete List of Authors:	Rathinam, Chandrasekar; University of Birmingham, ; Birmingham Children's Hospital NHS Foundation Trust, Therapy Department Mohan, Vikram; Bournemouth University Faculty of Health and Social Sciences Bill, Peter; Birmingham Children's Hospital NHS Foundation Trust, Therapy Department Yates, Derick; Birmingham Children's Hospital NHS Foundation Trust, Therapy Department Gupta, Rajat; Birmingham Children's Hospital NHS Foundation Trust, Therapy Department; University of Birmingham, Peirson, Janet; Private Practitioner
Keywords:	Neurology, Rehabilitation, Technology

I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our licence.

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which Creative Commons licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

Review Protocol

Title

Impact of Transcranial magnetic stimulation on motor function in children with acquired brain injury - A scoping review protocol

Authors

Chandrasekar Rathinam[1,2*]

Vikram Mohan[3]

Peter Bill[1]

Derick Yates[1]

Rajat Gupta[1,2]

Janet Peirson[4]

Affiliations

[1] College of Medical and Dental Sciences, University of Birmingham, UK

[2] Birmingham Women's and Children's NHS Foundation Trust, Birmingham, UK

[3] Department of Rehabilitation and Sports Sciences, Bournemouth University, UK

[4] Independent Practitioner, Cambridge, UK

*Corresponding author

College of Medical and Dental Sciences
University of Birmingham
Edgbaston
Birmingham
B15 2TJ
United Kingdom

Birmingham Women's and Children's NHS Foundation Trust
Steelhouse Lane
Birmingham
B4 6NH
United Kingdom

Contact (Email)

Chandrasekar Rathinam - c.rathnam@bham@ac.uk
chandrasekar.rathinam@nhs.net

Vikram Mohan - vmohan@bournemouth.ac.uk

Derick Yates - derick.yates@nhs.net

Peter Bill - peter.bill@nhs.net

Janet Peirson - janetpeirson@me.com

Rajat Gupta - rajatgupta@nhs.net

Registration

We registered our review protocol in the Open Science Framework (https://doi.org/10.17605/OSF.IO/5SPHT) to enhance transparency and reproducibility, and to reduce duplication.

Amendments

Any amendments to the protocol will be appended and acknowledged in the final report. An updated version with the changes in the original protocol will be added on the OSF registries.

Impact of Transcranial magnetic stimulation on motor function in children with acquired brain injury - A scoping review protocol

ABSTRACT

Background:

Children with severe acquired brain injury (ABI) require early and effective neurorehabilitation provision to promote a good long-term functional outcome. Transcranial magnetic stimulation (TMS) has been used to improve motor skills for children with cerebral palsy but there is limited material supporting its use in children with ABI who have a motor disorder.

Objective:

To systematically answer what are the TMS intervention effects on motor function in children with ABI as reported in the literature.

Methods and analysis:

This scoping review will follow Arksey and O'Malley's scoping review methodological framework. A comprehensive computerised bibliographic databases search will be performed in MEDLINE, EMBASE, CINAHL, Allied and Complementary Medicine, BNI, Ovid Emcare, PsychINFO, Physiotherapy Evidence Database, Cochrane Central Register using keywords related to TMS and children with ABI.

Studies that examine the effect of TMS intervention on motor function as either a primary or secondary objective will be included for this review. Study design and publication detail, participant demographic details, type and severity of ABI and other clinical information, TMS procedure, associated therapy intervention, comparator/control parameters, and the outcome measure used data will be gathered.

The International Classification of Functioning, Disability and Health for Children and Youth (ICF-CY) framework will be used to report the TMS effect in children with ABI. A narrative synthesis of the findings describing the therapeutic effects of TMS intervention, limitations, and adverse effects will be synthesized and reported. This review will help to summarise the existing knowledge base and to guide further research areas. This review outcome may help to evolve therapists' role to next-generation technology-based neurorehabilitation programmes.

Ethics and dissemination:

No ethical approval is required for this review as we will be collecting data from the previously published studies. We will present the findings at scientific conferences and publish in a peer review journal.

What is already known on this topic?

Transcranial magnetic stimulation (TMS) has been used to improve motor skills through neural plasticity in adults who have suffered from a stroke; and for children with cerebral palsy. There is limited evidence however of its use in improving motor function in children with acquired brain injury (ABI).

What this study hopes to add?

Evidence of the impact of TMS on motor function in children with ABI.

How this study might affect research, practice or policy?

The outcome of the review will inform the existing evidence related to the therapeutic effect of TMS in children with ABI. This will help to identify any knowledge gaps, future research questions and to develop future clinical trials that will be able to assess the effectiveness of TMS in children with ABI rehabilitation.

BACKGROUND

Acquired brain injury (ABI) is the term used to describe traumatic and non-traumatic brain injuries that occur after birth and a period of typical development(1). In the United Kingdom, ABI accounts for 35,000 childhood presentations to emergency departments annually. Of these, 5% have moderate to severe brain injury(2). Children with severe ABI will often have movement difficulties caused by weakness, abnormal muscle tone, poor motor control, poor concentration, fatigue and other comorbidities(3). They may also have difficulties with speech, swallowing, and cognitive impairment. A subgroup of children with ABI present with a stroke like presentation limiting their activity, balance, gait and fine motor skills. They are likely to develop tightness and contractures in both the upper and lower limbs(4). This impairment leads to functional difficulties including self-care, playing and manipulating toys, socialising and academic activities(4). During the acute phase, children with moderate to severe ABI frequently require a period of demanding medical and rehabilitative care to optimise their long-term capabilities and quality of life through neuroplasticity(5). This acute care can last up to twelve months following the initial brain injury which often requires a wide range of neurorehabilitation measures from a multidisciplinary team(6).

Early and effective neurorehabilitation provision promotes a good long-term functional outcome for children with ABI(7). Active rehabilitation begins as soon as they are medically stable. The typical rehabilitation includes facilitation of movements, postural control, postural care management, constraint-induced movement therapy (CIMT), virtual reality (VR), strength training, dysphagia and communication

management; and tone medications to improve motor and functional skills through neuroplasticity(6). Recent advances in technology enable clinicians to use functional electrical stimulation, VR(4), and Transcranial magnetic stimulation (TMS) to improve motor skills for children with central nervous system related movement disorders(8,9).

TMS is a non-invasive treatment technique(10). It is safe to use for children and adolescents with neurological conditions(11). It delivers repetitive magnetic pulses directly to specifically targeted brain areas through electromagnetic induction. TMS is applied over the scalp either on the same or opposite side to modulate cortical excitability through electromagnetic induction. In TMS, an electric charge is applied to a small coil and this produces a magnetic field perpendicular to the coil. This magnetic field creates an electrical current in the brain tissue parallel to the coil. This activates the localised neurons through cortical excitation(12). Low frequency TMS reduces cortical excitability but the high frequency increases it, thereby producing the desired therapeutic effect(13). Navigated repetitive TMS is delivered to a targeted brain area to change polarization and it influences cortical excitability many minutes after initial stimulation(14). This will help to facilitate, inhibit or interrupt the cortical network depending upon the frequency and intensity of the stimulus, thus promoting a cortical function change through neuroplasticity(15).

TMS has been widely used in adult stroke rehabilitation to facilitate cortical excitability and to promote neuroplasticity(16). Early application of TMS (from 2 weeks to 2 months, 5 – 15 sessions; 1 Hz to 10 Hz) coupled with other rehabilitation therapy intervention has been shown to result in decreased motor impairment, improved activity and participation level in the stroke population(14). TMS has been used to treat

children with neuropsychiatric disorders including children on the autistic spectrum, those with attention deficit hyperactivity disorder, obsessive compulsive disorder, and also tics(8). A systematic review investigated the effectiveness of non-invasive brain stimulation for rehabilitation of children with cerebral palsy (CP)(17). This review identified 4 studies that used repetitive TMS (5 – 10 sessions, with each session lasting between 10 – 20 minutes). Three studies used inhibitory low frequency repetitive TMS over the contralateral motor cortex and one study used both high and low frequency repetitive TMS over the primary motor area. A meta-analysis of the outcome measure indicated improved upper limb function following repetitive TMS(17).

It is worth noting that some literature includes children with CP as ABI. An injury to the brain occurs in very early life in CP, whereas in ABI the injury is sustained after a period of normal development(18). It could be argued that the description and presentation of CP is markedly different from those who sustained moderate to severe ABI at a later time in their childhood. Enhanced neuroplasticity in the developing brain may prove to be advantageous in rehabilitation following ABI. Structural and functional neural plasticity is attributed to change in regional volumes in brain cells or formation of neural pathways through synaptogenesis, axonal or dendritic sprouting, and the creation of new neurons(19). Synaptic and intrinsic mechanism regulates neural excitability which influences neural plasticity(20). Metaplasticity, an activity-dependent modulation of synaptic plasticity was induced by TMS in adult neurological disorders such as stroke, and Parkinson's disease. TMS can be an effective tool to treat brain disorders through inducing metaplasticity(21). TMS coupled with regular rehabilitation could provide improved outcomes through neural plasticity(22) and metaplasticity. If

this is the case, TMS combined with intensive rehabilitation appears to be a promising new intervention approach with wider future applications for children with ABI. There is, however, limited material supporting its use in children with ABI who have a motor disorder.

The intervention effect in rehabilitation research has been widely reported using the International Classification of Functioning, Disability and Health for Children and Youth (ICF-CY) framework(23). The ICF-CY domain consists of body structures and function, activity, participation, and contextual factors (environment and personal) which can be used to classify the level of functioning in childhood(6). This model can be applied to report the functional outcome of children and young people (CYP) with ABI who have impaired physical, cognitive and emotional difficulties and the impact on activity limitation and participation restriction following an intervention(6).

The overall objective of this scoping review will be to examine the literature relating to the therapeutic effect of TMS in children with ABI. The outcome of this review will be categorised according to the ICF-CY dimensions. This review will help to summarise the existing knowledge base and to identify areas requiring further research.

METHODS

This review protocol will follow both the Preferred Reporting Items for Systematic Reviews and Meta-Analysis extension for Scoping Reviews (PRISMA-ScR) checklist(24) and Arksey and O'Malley's scoping review approach(25). In addition, the PRISMA Protocol guidelines will be followed to ensure scientific rigor(26) (see supplementary file). We registered our review protocol in the Open Science Framework (https://doi.org/10.17605/OSF.IO/5SPHT).

Identifying the research question

The primary aim of this scoping review will be to characterise TMS intervention. We will specifically answer the question 'what are the TMS interventions effect on motor functions in children with ABI as reported in the literature?'.

Identifying relevant studies

Search Strategy

A copy of the full search strategy as run in Ovid Medline is provided in the appendix. This search will be modified as necessary to be completed in the following databases.

- Electronic database search: A comprehensive computerised bibliographic databases search will be performed in the following databases:
  - MEDLINE (1946–current)
  - EMBASE (1974 to current)
  - Cumulative Index to Nursing and Allied Health Literature
  - Allied and Complementary Medicine (1985 to present)

- British Nursing Index (1992–present)
- Ovid Emcare (1994 to current)
- PsychINFO (1806–current)
- Physiotherapy Evidence Database
- Cochrane Central Register

- Trial registers: The unpublished and on-going clinical trial information will be gathered by searching www.clinicaltrial.gov, www.who.int/trialsearch and www.controlled-trials.com.

- Contacting the corresponding authors of the included articles and asking them to provide the details of any other TMS related research studies in ABI either by their team or by their associates and research group.

- Citation Searching from the included individual studies.

- Other sources
  - The references included in the list of papers selected from the electronic database
  - A hand search will be carried out in specific key journals that have published the maximum number of relevant articles selected for this review. This option will only be carried out if there are more than 3 articles selected from a particular journal.

- Searching Dissertation Abstracts (using ProQuest), conference proceedings and abstracts related to TMS and contacting the researchers to provide any additional information.

- The following TMS equipment manufacturers/distributors will be contacted via email and asked for the details of any trials related to TMS in paediatric ABI population (Axilum Robotics, Brainbox, Brainsway, DEYMED Diagnostic' EB Neuro, eNeura, Jiangsu Aegean Technology, MAG & more, Magstim, MagVenture, Neuronetics, Neurosoft, Nexstim, NIBBOT International, Remed, Sebers Medical, Shenzhen Yingchi Technology, Soterix Medical, Syneika, Xuzhou Kejian)

Eligibility criteria

The searches will be confined to children under 18 years old with ABI only. Some studies include the adolescent population (15–25 years) and the review team will contact the authors to seek data for the children under 18 years old only. If no response is received, the article will be excluded and this will be documented. All the subgroups of ABI including traumatic, non-traumatic and brain tumour will be included but children with CP will be excluded. If a study has children with CP along with the ABI population, the review team will exclude data related to the CP population. If such information is not clearly available, the review team will contact the authors to seek clarification. If no response is received, the article will be excluded and this will be documented.

Studies that examine the effect of TMS intervention on motor function as either a primary or secondary objective will be included. Research studies that include TMS for diagnostic purposes will be excluded.

All type of studies such as reviews, clinical trials, cohort studies, case series, case reports, and technical reports will be included. No exclusion criteria will be set for language or publication years, and these studies will be considered if the title and abstracts have been written in English. The review team will contact the corresponding authors and request the information in English within two weeks. If no response is received, those studies will be excluded and this will be documented.

Study screening and selection

Electronic database search will be completed by the professional librarian and uploaded in the Ryaan software after removing duplicated studies. The collected titles and structured abstracts from the electronic database will be scrutinised independently by two reviewers by following the set inclusion and exclusion criteria. The excluded studies will be classified as irrelevant and the reasons will be documented. Grey literature and the trial database will be searched by two reviewers independently.

Full articles that meet the selection criteria from the above source will be collected from the NHS library services and the University of Birmingham library services. Two reviewers will decide which articles will be suitable for the final review and any disagreement will be managed after discussing with the third reviewer.

The selection process will be piloting 20% of the collected electronic and grey literature at the beginning to ensure reliable interpretation and agreement between the reviewers. Disagreement will be resolved with a consensus meeting. If no consensus reached, a third reviewer will be consulted. A PRISMA flowchart will be used to inform the selection process.

Charting the data / data extraction

After the screening, two reviewers will independently extract the data (CR & VM) in an excel spreadsheet data extraction tool. Data extraction protocol will be piloted on the first 5 articles. This will help to maintain consistency in data extraction and to make the required changes in the data extraction tool. The above process will be documented. One of the reviewers will extract the data (CR) in an excel spreadsheet from the remaining included studies and the second reviewer (VM) will independently check the collected data.

The review team will gather data about

- Study design and publication detail (reviews, RCT, comparative study, case reports, technical reports, authors detail, year of publication, study location)
- Participants demographical, type of ABI and other clinical information
- TMS procedure (Technique, equipment specification, stimulation parameters such as coil placement, intensity, duration, frequency, adverse effects)
- Any associated therapy intervention (physiotherapy, occupational therapy, VR and other therapy techniques such as CIMT, bimanual therapy, gait training etc) with or without TMS intervention
- Comparator/control parameters

- Outcome measures used in the individual studies and the relevant observation relating to ICF-CY domains

This review will be aimed at identifying the changes in motor function of children with ABI. All of the motor function related outcomes reported in the selected articles will be classified under ICF-CY domains. Additional details explaining how these outcomes were measures and at what time points these were collected will be reported. This review will not assess the risk of bias on the included studies but will report their level of evidence.

Collating, summariszing and reporting the results

This review is expected to find heterogeneity across the studies, therefore a narrative synthesis of the findings describing the therapeutic effects of TMS intervention, limitations, adverse effects and the gaps will be synthesized and reported. A table summarizing ICF-CY domain for each study will be presented along with the narrative results.

Patient and Public Involvement (PPI)

The review team consulted two parents of children with ABI in the design of this protocol. The review team will contact the Child Brain Injury Trust (CBIT), a national charity organization for children with ABI (United Kingdom), when conducting the review and seek their help interpreting the findings and dissemination. Any recommendations made by the CBIT will be implemented.

DISCUSSION

Our protocol explains the methodology to guide our review. The outcome of the review is carefully planned and documented to ensure transparency and research integrity to allow replication(26).

From this scoping review, the review team will provide a descriptive analysis of TMS for children with ABI and how this has been delivered. This review will help to understand the range of TMS dose which includes frequency, intensity, duration, stimulation site, motor function outcome and the corresponding actual or proposed mechanism. Due to the known variation in neuroplastic ability in the developing brain, it will be important to understand the TMS influence on functional motor recovery across different age groups within our overall age range.

This scoping review will also provide some insight related to the factors influencing TMS outcome. Age, gender, duration of illness, concordance with the treatment plan, associated comorbidities such as increased tone, tightness/contracture in joints and concurrence with the treatment may be some of the patient related factors that influence the TMS outcome. Anatomical variations such as skull size, previous neurosurgeries, and structural changes in brain will be a challenge to apply TMS(27). These procedure related factors associated with the Illness related factors such as children with a high level of motor disability, medications to manage tone, seizure activity, and other conditions may have an impact of the therapeutic outcome. Stimulation factors such as site of stimulation, intensity, frequency, duration, and the

number of stimulation episode will be other factors determining the outcome strength. The above factors will be observed and reported in our review.

This information will guide future trial development with TMS treatment components that are being commonly used and how they are being delivered. Such treatment information can be organised in the Template for Intervention Description and Replication (TIDieR) checklist to assist future research work to plan and report(28) TMS intervention. This review will help to conduct high-quality patient and public involvement for future studies, designing feasibility studies, and may guide to identify eligible CYP with ABI for TMS intervention.

Our scoping review has certain limitations. The majority of the studies on ABI included children with CP and the review team is not intending to include this population. Any related studies will be excluded and the associated knowledge will be missed. It may be possible that there are a very limited number of studies related to TMS in ABI and this may lead to inconclusiveness about the predicted motor response. This could be because of small sample size, duration and techniques of TMS, and also the associated comorbidities such as mental health issues, fatigue, cognitive and memory problems. Observed limitations will be reported and mitigated in our future systematic review.

This review outcome may help to develop therapists' role from conventional hands-on therapy provision to next-generation technology-based neurorehabilitation programmes. It is also likely to have an impact on CYP access to advanced technology during their acute phase to aid enhanced recovery and helps improve their patient experience.

Funding

This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

Competing Interests Statement

None to declare

Authors contribution

CR, VM and JP - involved in study conceptualisation

CR, VM, JP, PB and RG – responsible for study design and protocol development

CR and VM - responsible for screening, selecting articles, and data entry

CR, VM, JP, PB and RG – responsible for data interpreting and reporting

DY – responsible for constructing search strategy and conducting searches

CR, VM, PB, RG, and JP – responsible for preparing final manuscript

CR - guarantor of the review

All authors will read, provide feedback and approve the final manuscript

References:

1. Wales L, Davis K, Kelly G, Lynott H. Long Term Participation Outcomes for Severe Acquired Brain Injury in Childhood - An Expanded Scoping Review. Dev Neurorehabil. 2021 Aug;24(6):379–87.
2. Trefan L, Houston R, Pearson G, Edwards R, Hyde P, Maconochie I, et al. Epidemiology of children with head injury: a national overview. Arch Dis Child. 2016 Jun;101(6):527–32.
3. Hypher RE, Brandt AE, Risnes K, Rø TB, Skovlund E, Andersson S, et al. Paediatric goal management training in patients with acquired brain injury: study protocol for a randomised controlled trial. BMJ Open. 2019 Aug 1;9(8):e029273.
4. Rathinam C, Mohan V, Peirson J, Skinner J, Nethaji KS, Kuhn I. Effectiveness of virtual reality in the treatment of hand function in children with cerebral palsy: A systematic review. J Hand Ther. 2019 Oct-Dec;32(4):426-434.e1
5. McKinlay A, Linden M, DePompei R, Aaro Jonsson C, Anderson V, Braga L, et al. Service provision for children and young people with acquired brain injury: Practice recommendations. Brain Inj. 2016;30(13–14):1656–64.
6. Gmelig Meyling C, Verschuren O, Rentinck IR, Engelbert RHH, Gorter JW. Physical rehabilitation interventions in children with acquired brain injury: a scoping review. Dev Med Child Neurol. 2022 Jan;64(1):40–8.
7. Shen J, Johnson S, Chen C, Xiang H. Virtual Reality for Pediatric Traumatic Brain Injury Rehabilitation: A Systematic Review. Am J Lifestyle Med. 2018 Feb 6;14(1):6–15.
8. Bejenaru AM, Malhi NK. Use of Repetitive Transcranial Magnetic Stimulation in Child Psychiatry. Innov Clin Neurosci. 2022;19(4–6):11–22.

9. Dobney DM, Miller MB, Tufts E. Non-pharmacological rehabilitation interventions for concussion in children: a scoping review. Disabil Rehabil. 2019;41(6):727–39.

10. Dayan E, Censor N, Buch ER, Sandrini M, Cohen LG. Noninvasive brain stimulation: from physiology to network dynamics and back. Nat Neurosci. 2013 Jul;16(7):838–44.

11. Krishnan C, Santos L, Peterson MD, Ehinger M. Safety of noninvasive brain stimulation in children and adolescents. Brain Stimul. 2015;8(1):76–87.

12. Iglesias AH. Transcranial Magnetic Stimulation as Treatment in Multiple Neurologic Conditions. Curr Neurol Neurosci Rep. 2020 Feb;20(1):1.

13. Kubis N. Non-Invasive Brain Stimulation to Enhance Post-Stroke Recovery. Front Neural Circuits. 2016 July 27;10:56.

14. Schambra HM. Repetitive Transcranial Magnetic Stimulation for Upper Extremity Motor Recovery: Does It Help? Curr Neurol Neurosci Rep. 2018 Oct;18(12):97.

15. Lefaucheur J-P. Transcranial magnetic stimulation. In: Levin KH, Chauvel PBT-H of CN, editors. Clinical Neurophysiology: Basis and Technical Aspects. Elsevier; 2019. p. 559–80.

16. Chervyakov A V, Poydasheva AG, Lyukmanov RH, Suponeva NA, Chernikova LA, Piradov MA, et al. Effects of Navigated Repetitive Transcranial Magnetic Stimulation After Stroke. J Clin Neurophysiol. 2018;35(2):166–72.

17. Elbanna ST, Elshennawy S, Ayad MN. Noninvasive Brain Stimulation for Rehabilitation of Pediatric Motor Disorders Following Brain Injury: Systematic Review of Randomized Controlled Trials. Arch Phys Med Rehabil. 2019 Oct;100(10):1945–63.

18. Forsyth R, Kirkham F. Predicting outcome after childhood brain injury. C Can Med Assoc J = J l'Association medicale Can. 2012 Aug;184(11):1257–64.
19. Dan B. Neuroscience underlying rehabilitation: what is neuroplasticity? Vol. 61, Developmental medicine and child neurology. England; 2019. p. 1240.
20. King ES, Tang AD. Intrinsic Plasticity Mechanisms of Repetitive Transcranial Magnetic Stimulation. Neurosci a Rev J bringing Neurobiol Neurol psychiatry. 2022 Sep;10738584221118262.
21. Cantone M, Lanza G, Ranieri F, Opie GM, Terranova C. Non-invasive brain stimulation in the study and modulation of metaplasticity in neurological disorders. Vol. 12, Frontiers in Neurology. Frontiers Media SA; 2021. p. 721906.
22. Johnston M V. Plasticity in the developing brain: implications for rehabilitation. Dev Disabil Res Rev. 2009;15:94–101.
23. Martinuzzi A, De Polo G, Bortolot S, Pradal M. Pediatric neurorehabilitation and the ICF. NeuroRehabilitation. 2015;36(1):31–6.
24. Tricco AC, Lillie E, Zarin W, O'Brien KK, Colquhoun H, Levac D, et al. PRISMA Extension for Scoping Reviews (PRISMA-ScR): Checklist and Explanation. Ann Intern Med. 2018 Oct;169(7):467–73.
25. Arksey H, O'Malley L. Scoping studies: towards a methodological framework. Int J Soc Res Methodol. 2005 Feb 1;8(1):19–32.
26. Moher D, Shamseer L, Clarke M, Ghersi D, Liberati A, Petticrew M, et al. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. Syst Rev. 2015 Jan;4(1):1.
27. Kar SK. Predictors of response to repetitive transcranial magnetic stimulation in depression: a review of recent updates. Clin Psychopharmacol Neurosci.

2019;17(1):25.

28. Hoffmann TC, Glasziou PP, Boutron I, Milne R, Perera R, Moher D, et al. Better reporting of interventions: template for intervention description and replication (TIDieR) checklist and guide. BMJ. 2014 Mar;348:g1687.

Appendix: Search Strategy: Ovid MEDLINE(R) ALL <1946 to Present>

1 exp Child/

2 exp Adolescent/

3 (p?ediatric* or child* or youth* or adolescen* or juvenile* or teenage* or boy* or girl*).ab,jn,ti.

4 1 or 2 or 3

5 exp Brain Injuries/ or exp Craniocerebral Trauma/ or exp Skull Fractures/

6 ((brain or head or skull or cranio* or cranial or occipital) adj3 (injur* or trauma* or fracture*)).ab,ti.

7 exp Meningitis/

8 Meningitis.ab,ti.

9 exp Encephalitis/

10 Encephalitis.ab,ti.

11 exp Stroke/

12 (Stroke or cerebrovascular accident*).ab,ti.

13 exp Arteriovenous Malformations/

14 Arteriovenous Malformation*.ab,ti.

15 exp Intracranial Aneurysm/

16 ((intracranial or brain or cerebral) adj3 Aneurysm*).ab,ti.

17 exp Cerebral Hemorrhage/ or exp Intracranial Hemorrhages/

18 ((intracranial or brain or cerebral) adj3 H?emorrhage*).ab,ti.

19 exp Hypoxia, Brain/ 14043

20 ((brain or cerebral or encephalopath*) adj3 (hypox* or anox*)).ab,ti.

21 exp Asphyxia/

22 "asphyxia*".ab,ti.

23 exp Brain Neoplasms/ or exp Central Nervous System Neoplasms/

24 (((brain or cerebral or CNS or central nervous system) and (tumo?r* or glioma* or blastoma* or sarcoma* or cancer* or neoplasm* or astrocytoma* or ependymoma* or glioblastoma* or oligoastrocytoma* or oligodendroglioma* or Meningioma* or medulloblastoma*)) or "posterior fossa syndrome").ab,ti.

25 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24

26 exp Transcranial Magnetic Stimulation/

27 (Transcranial adj2 magnetic adj2 stimulation*).ab,ti.

28 exp Transcranial Direct Current Stimulation/

29 (noninvasive adj2 brain adj2 stimulation).ab,ti.

30 (noninvasive adj2 cerebral adj2 stimulation).ab,ti.

31 (Transcranial adj2 direct adj2 Current adj2 Stimulation).ab,ti.

32 (electromagnetic induction and brain).ab,ti.

33 (TMS or rTMS or NIBS or NrTMS).ab,ti.

34 (transcranial adj2 electric* adj2 stimulation).ab,ti.

35 ((Anodal or Cathodal) and stimulation TDCS).ab,ti.

36 transcranial random noise stimulation.ab,ti.

37 transcranial alternating current stimulation.ab,ti.

38 Theta Burst Stimulation.ab,ti.

39 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 32106

40 4 and 25 and 39

****