

Non-invasive prehabilitation before neurosurgery modifies the topography of the language production network without compromising function

Nuria Brault-Boixader^{a,b,c,1,*}, Alba Roca-Ventura^{a,b,d,1}, Selma Delgado-Gallén^{a,b,c}, Edgar Buloz-Osorio^{a,b,c}, Leonardo Boccuni^e, Carlos Laredo^{f,g}, Emma Muñoz-Moreno^{f,g}, Núria Bargalló^{f,g}, David Bartrés-Faz^{a,d,f}, Álvaro Pascual-Leone^{h,i}, José M. Tormos-Muñoz^j, Ruben Perellón-Alfonso^{a,b,d,f,k}, Kilian Abellana-Pérez^{a,l,m,*}, Prehabilita Working Group²

^a Institut Guttmann, Institut Universitari de Neurorehabilitació adscrit a la UAB, Badalona, Barcelona, Spain

^b Fundació Institut d'Investigació en Ciències de la Salut Germans Trias i Pujol, Badalona, Barcelona, Spain

^c Universitat Autònoma de Barcelona, Bellaterra, Spain

^d Departament de Medicina, Facultat de Medicina i Ciències de la Salut, i Institut de Neurociències, Universitat de Barcelona, Barcelona, Spain

^e Scientific Institute, IRCCS E. Medea, Treviso, Italy

^f Institut d'Investigacions Biomèdiques August Pi I Sunyer (IDIBAPS), Barcelona, Spain

^g Magnetic Resonance Image Core Facility (IDIBAPS), Barcelona, Spain

^h Wolk Center for Memory Health & Marcus Center for Aging Research, Hebrew SeniorLife, Boston, MA, USA

ⁱ Department of Neurology, Harvard Medical School, Boston, MA, USA

^j Centro de Investigación Traslacional San Alberto Magno, Universidad Católica de Valencia San Vicente Mártir, Valencia, Spain

^k Cognitive Neuroscience Unit, Institute of Neurosciences, University of Barcelona, Barcelona, Spain

^l Laboratori de Neurociència Cognitiva, Universitat de Lleida, Lleida, Spain

^m Institut de Recerca Biomèdica de Lleida - Fundació Dr. Pifarré (IRBLleida), Lleida, Spain

ARTICLE INFO

Keywords:

Brain tumor
Functional magnetic resonance imaging
Language network
Neuroplasticity
Neurooncology
Non-invasive brain stimulation
Prehabilitation

ABSTRACT

Patients with brain tumors involving language-critical regions face surgical limitations when balancing resection with preservation of function. Non-invasive neuromodulation-induced prehabilitation (NIP) aims to guide pre-operative neuroplastic reorganization, potentially facilitating larger resections while preserving function. We investigated whether NIP selectively modulates the targeted language network, in our case defined as the language production network, compared with control networks, and whether such modulation is behaviorally safe. We enrolled 26 patients (mean age = 55.9 ± 11.8 years) from the Prehabilita project (Clinical Trial: NCT05844605) with operable brain tumors affecting language or motor regions. Eleven received language-targeted NIP, combining transcranial magnetic stimulation and/or transcranial direct current stimulation with intensive language training. Fourteen patients with NIP targeting non-language networks, primarily motor networks, served controls. Assessments included task-based functional magnetic resonance imaging (tb-fMRI) and a neuropsychological battery assessing language and cognitive domains before and after prehabilitation. Results indicated a group-specific NIP effect on the language production network. In the language-targeted group, tb-fMRI revealed reduced overlap between a region of interest centered on the stimulation target and fMRI-derived language activation maps, whereas no comparable changes were observed in controls. No significant modulation effects were detected in the motor network in either group. These findings indicate that NIP can selectively reorganize the language production network, with modulation patterns differing in sensorimotor networks. Importantly, language production network modulation occurred while preserving language and cognitive performance. These results support NIP targeting higher-order functions such as language as a safe

* Correspondence: Kilian Abellana-Pérez, Nuria Brault-Boixader, Institut Guttmann, Institut Universitari de Neurorehabilitació adscrit a la UAB, Badalona, Barcelona, Spain

E-mail addresses: nbrault@guttmann.com (N. Brault-Boixader), kabellana@guttmann.com (K. Abellana-Pérez).

¹ These authors contributed equally to this work

² Prehabilita Working Group: Roger Bragulat; Mònica Buxeda-Rodríguez; María Cabello-Toscano; Gerardo Conesa-Bertrán; Mireia Illueca-Moreno; David Leno Colorado; Ruth Lau; Estela Lladó-Carbó; César Garrido; Jesús Martín-Fernández; Francisco Martínez-Ricarte; Cristóbal Perla Y Perla; José Carlos Pariente; María Redondo-Camós and Gloria Villalba-Martínez

<https://doi.org/10.1016/j.neuroimage.2026.122185>

Received 23 February 2026; Received in revised form 4 June 2026; Accepted 25 August 2026

Available online 26 August 2026

1053-8119/© 2026 The Authors. Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

preoperative strategy that may reduce functional constraints on surgery and enable larger and safer resections in patients with tumors involving language-critical regions.

1. Introduction

Cancers of the central nervous system (CNS) represent a complex group of neoplasms originating from diverse cell types within the brain, spinal cord, and surrounding tissues (Salari et al., 2023; PDQ Adult Treatment Editorial Board, 2024). These tumors are a leading cause of morbidity, severe disability, and mortality, imposing a significant burden on healthcare systems (Deorah et al., 2006; Fan et al., 2022). According to the most recent reports (Bray et al., 2024), in 2022 there were 321,476 newly diagnosed cases of CNS cancers, causing 248,305 deaths worldwide. Despite advances in the fields of neurosurgery, radiotherapy, and chemotherapy, the overall 5-year survival rate for malignant brain tumors is estimated to be 35.7% (Ostrom et al., 2023). In the context of brain tumor surgery, patient survival and quality of life depend not only on the extent of tumor resection, but also on preserving healthy brain tissue and neurological function (Brown et al., 2016; Roh & Kim, 2023). However, the balance between tumor removal and the preservation of functional tissue is often challenging, particularly when tumors are located within or invade brain regions holding critical functions, such as those involved in language (Shah et al., 2025).

Language is a fundamental human cognitive function, subserved by a large-scale neural network characterized by dynamic interactions among distributed brain regions, mainly including the frontal and temporoparietal cortices (Hickok & Poeppel, 2007; Nieberlein et al., 2023). The language system in the brain is highly plastic, as evidenced by its capacity for adaptive reorganization after injuries to mitigate language-related impairments, such as those caused by brain tumors (Fisicaro et al., 2016) or following a stroke (Geranmayeh et al., 2014; Tilton-Bolowsky et al., 2024). Such reorganization includes recruitment of distinct perilesional regions, the activation of homologous areas in the contralateral hemisphere, as well as the engagement of domain-general regions in both hemispheres (i.e., the prefrontal cortex; Cirillo et al., 2019; Fedorenko et al., 2024; Geranmayeh et al., 2014; Martin et al., 2022; Nieberlein et al., 2023).

In this context, non-invasive brain stimulation (NIBS) techniques, which can be used to induce and guide brain plasticity processes (Jannati et al., 2023; Kirton et al., 2021), can be powerful allies. NIBS includes techniques with distinct mechanisms and spatiotemporal profiles (Polanía et al., 2018). Here, we used transcranial magnetic stimulation (TMS) and transcranial direct current stimulation (tDCS). TMS induces electric fields in cortical tissue through brief magnetic pulses and, depending on intensity and protocol, can modulate neural activity or elicit action potentials (Hallett, 2007; Rossini et al., 2015). When applied repetitively, rTMS can produce excitability changes that outlast stimulation, with high- and low-frequency protocols often associated with facilitatory and inhibitory effects, respectively (Fitzgerald et al., 2006; Rossini et al., 2015). In contrast, tDCS applies weak direct currents that modulate ongoing neural activity and plasticity through subthreshold electric fields, rather than directly inducing neuronal firing; its effects depend on polarity, montage, dose, task context, and brain state (Nitsche & Paulus, 2000; Nitsche et al., 2008; Stagg et al., 2018; Polanía et al., 2018). Compared with TMS, tDCS is generally less focal but easier to administer alongside behavioral training, making it suitable for neurorehabilitation protocols. However, NIBS effects show substantial inter- and intra-individual variability, with response magnitude and even response direction varying across participants and sessions (López-Alonso et al., 2014; Chew et al., 2015; Vallence et al., 2015). Previous research has consistently shown that NIBS protocols can modulate functional activity and connectivity across key brain networks in healthy individuals (e.g., Abellana-Pérez et al., 2019; Halko et al., 2014; Wang et al., 2014), including the language network

(e.g., Meinzer et al., 2013). Moreover, NIBS has also been shown to influence network patterns in distinct neurologic and psychiatric conditions (e.g., Liston et al., 2014), including those within the language network (Meinzer et al., 2015). Building on this evidence, NIBS is emerging as a promising interventional approach for pre-surgical conditioning in brain tumor patients, seeking to reconfigure critical brain networks before surgery to enable safer and more extensive resections (e.g., Barcia, Sanz, González-Hidalgo, et al., 2012; Rivera-Rivera et al., 2017; Dadario et al., 2022; Lang et al., 2020; Engelhardt, 2023). These approaches are known as neuromodulation-induced prehabilitation (NIP) and are based on combining NIBS with intensive, function-specific training. A key feature of NIP is the pairing of inhibitory-like neuromodulation applied to peritumoral regions with targeted behavioral training delivered during or immediately after brain stimulation, with the aim of transiently suppressing local activity while exploiting windows of heightened neuroplasticity to facilitate compensatory network recruitment and adaptive functional reorganization (Bolognini, 2009). Ultimately, these approaches aim to enable more extensive tumor resection (potentially reducing recurrence risk) without increasing the likelihood of postoperative functional deficits (Bocconi et al., 2023). Recently, we applied a non-invasive NIP protocol, combining NIBS with intensive training, in a case series of ten patients, initially showing that these protocols are feasible, safe and well tolerated (Bocconi et al., 2024a). Moreover, in an fMRI-based case report, we provided a detailed characterization of the potential neural mechanisms underlying this NIP process within the language network (Bocconi et al., 2024b). Altogether, these findings highlight the potential for language-network plasticity prior neurosurgery, revealing substantial capacity for functional modulation.

Importantly, NIBS effects show substantial inter- and intra-individual variability, with response magnitude and even response direction varying across participants and sessions (Hamada et al., 2013; López-Alonso et al., 2014; Chew et al., 2015; Vallence et al., 2015; Martin-Trias et al., 2018; Goldsworthy et al., 2021). This variability, however, also represents an opportunity to improve outcomes by optimizing protocols through precision and personalization (i.e., Abellana-Pérez et al., 2019; 2023; Cappon & Pascual-Leone, 2024; Perellón-Alfonso et al., 2022). In this context, the present study examined whether an individualized and repeated NIP protocol could induce measurable reorganization of the at-risk functional network without producing detectable worsening in language or broader cognitive performance. Although single-session NIBS effects can be variable, repeated stimulation combined with behavioral training may help reinforce intervention-related neurofunctional changes and increase the likelihood of observing measurable network-level modulation (Wang et al., 2014; Antonenko et al., 2023). Moreover, assessing non-targeted cognitive domains is clinically relevant, to rule out potential crowding effects whereby preservation or reallocation of language functions may occur at the expense of non-verbal abilities (Lidzba et al., 2006; Bisten et al., 2025).

Nonetheless, NIP research remains limited and largely focused on clinical outcomes (Barcia et al., 2012; Bocconi et al., 2024a; Bocconi et al., 2024b; Dadario et al., 2022; Ekert et al., 2024; Lang et al., 2020; Serrano-Castro et al., 2020), leaving the neural mechanisms underlying these changes largely unexplored. In this vein, systematic characterization of NIP-associated network-level topological changes and their relationship to behavioral outcomes remains largely lacking, particularly in cognitive and language-related NIP protocols (e.g., Dadario et al., 2022; Lang et al., 2020; Ekert et al., 2024). This gap is of central importance, as tumors located near language regions are frequently considered inoperable due to the risk of intervention-related

language impairment (Collée et al., 2022; Sanai & Berger, 2008). Indeed, postoperative communication deficits are among the most disabling outcomes of brain surgery, with major consequences for independence and quality of life and they can persist even when function-preserving approaches such as awake mapping are used (Collée et al., 2022; Vogrinic et al., 2025). Furthermore, language preservation is a cross-cutting neurosurgical problem extending beyond neuro-oncology (e.g., epilepsy surgery), reinforcing the broader relevance of understanding language network plasticity and its modulation for distinct translational clinical applications (Zhu et al., 2025). Accordingly, the present study focused on comprehensively characterizing these network-level effects in a larger, more homogeneous cohort and comparing them with a non-language NIP control group.

Specifically, this study aims to: (1) examine whether NIP protocols targeting the language production network (as obtained by task-based fMRI activation maps), elicit brain network changes that are specific to the targeted system (i.e., language production network) and are dissociable from modifications in non-targeted brain networks (i.e. motor network); (2) assess whether these language production network changes are associated with measurable behavioral modifications in language performance during NIP intervention; and (3) determine whether these neural and behavioral NIP-related modulations occur with or without entailing deleterious effects on other cognitive processes (i.e., potential crowding effects). We hypothesize that non-invasive NIP will induce specific topographical reorganization within the targeted language production network, reflected in measurable pre vs. post intervention shifts in task-based functional magnetic resonance imaging (tb-fMRI) activation patterns. Considering the distributed and multimodal architecture of the language network, we hypothesize that induced neural changes will remain behaviorally neutral, with no measurable detrimental effects on language performance or other cognitive domains (e.g., visuospatial constructional and perceptual abilities).

2. Materials and methods

This study is part of the Prehabilita project, conducted at Institut Guttmann (Guttmann Barcelona, Brain Health and Neurorehabilitation, Barcelona, Spain). A detailed description of the prehabilitation protocol employed in this study can be found in Boccuni et al. (2023).

2.1. Participants

A total of 30 patients were enrolled in the prehabilitation program. This cohort included participants recruited within the ongoing clinical trial (ClinicalTrials.gov identifier: NCT05844605) as well as individuals enrolled during a preceding pilot phase of the project. These patients were awaiting neurosurgery for a brain tumor affecting language or other non-language functions. Patients were referred from various Neurosurgery Units at different Hospitals across Catalonia, Spain. Exclusion criteria included contraindications for NIBS protocols, unstable medical conditions, a history of substance abuse, and severe musculoskeletal or cognitive disorders that could impact the intervention. Of the initial 30 participants, 4 were excluded from the current study: one due to fMRI acquisition issues; two because their tumors had non-language or non-motor functional involvement; and one because stimulation was delivered altogether to two functionally distinct targets (i.e., motor and language areas). The final sample comprised 26 patients (10 women; mean age = 55.88 ± 11.81 years), 12 of whom had high-grade gliomas (Table 1). All participants were right-handed, except for two left-handed individuals, both of whom belonged to the group in which the language production network was not targeted for stimulation. Moreover, one participant who received only multifocal tDCS was excluded from one specific fMRI analysis ("2.6.1 Local effects of NIP at the stimulation target") because an individualized ROI could not be defined. Additionally, one participant in the control group was excluded

from the same analysis and another ("2.6.2 Effects of NIP on targeted network size") due to missing post-intervention neuroimaging data on hand function.

Patients underwent comprehensive clinical, cognitive, and motor assessments, as well as all the prehabilitation intervention sessions, at Institut Guttmann in Barcelona, Spain. Neuroimaging assessments were performed at the IDIBAPS Magnetic Resonance Imaging Core Facility at Hospital Clinic de Barcelona, Barcelona, Spain. Recruitment spanned from July 2021 to December 2024, with evaluations conducted at two different time-points: before and after NIP. See Fig. 1 for an overview of the study design and timeline. Informed consent was obtained from all participants. All procedures from the present investigation were performed in accordance with the declaration of Helsinki. The study was approved by the Research Ethical Committee of Fundació Unió Catalana d'Hospitals (approval number: CEI 21/65, version 1, 13/07/2021).

2.2. Clinical, neuropsychological and motor assessments

Comprehensive clinical and neuropsychological assessments were conducted at each time point (pre-NIP and post-NIP) for all patients (see Fig. 1). Evaluations of language and cognitive functions were performed by licensed clinical neuropsychologists, while motor function examinations were performed by physiotherapists specialized in neuro-rehabilitation. For further details on the study assessments, the reader is referred to Boccuni et al. (2023). For this investigation, we focused specifically on data related to the NIP intervention to evaluate the immediate neural and behavioral effects of the prehabilitation process. Postoperative outcomes were beyond the scope of this analysis, which was designed to isolate the direct effects of prehabilitation.

2.2.1. Language and neuropsychological functioning

The neuropsychological assessment used was the Barcelona-Revised Test (TB-R; Peña-Casanova, 2005). This battery of tests includes spontaneous language (conversation and narration, thematic narration, and picture description); fluency and informative content (qualitatively assessed based on the information obtained in the spontaneous language subtest); verbal word repetition; verbal naming (i.e., response by naming); verbal comprehension; reading comprehension (using sentences and texts); automatic language (using both forward and reverse sequential series); verbal repetition (using syllables, logatomes, and sentences); naming (using visuo-verbal naming and naming completion); and verbal comprehension (complex verbal material).

Moreover, to examine whether the functional impact of the prehabilitation-induced brain reorganizations extended beyond the targeted language domain to other cognitive functions (i.e., non-language-related processes), this investigation included neuropsychological assessments of visuospatial constructional and perceptual abilities. These were evaluated using the Block Design subtest of the WAIS-III (Wechsler, 2008) and the visuospatial attention subtest of the TB-R test.

2.3. Neuroimaging acquisition and analysis

2.3.1. MRI acquisition

MRI data was acquired as part of the general NIP protocol (Fig. 1) using a 3-T Siemens scanner (MAGNETOM Prisma) equipped with a 64-channel head coil, except when the patient didn't fit comfortably; in those cases, we use the more spacious 20-channel coil. As detailed in the protocol description (see Section 2.3; Boccuni et al., 2023), comprehensive MRI acquisitions, including structural, diffusion, task-based, and resting-state sequences, were performed before and after NIP. For the purposes of the present study, we focused exclusively on structural and task-based fMRI data.

For structural imaging data, a high-resolution T1-weighted structural image was obtained using a magnetization-prepared rapid acquisition gradient echo (MPRAGE) three-dimensional protocol (repetition time [TR] = 2400 ms, echo time [TE] = 2.22 ms, inversion time = 1000 ms,

Table 1

Characteristics of study participants in each group, including age, sex, patient symptoms, tumor diagnosis, tumor location/side, NIBS protocol, TMS target in MNI coordinates (*x*, *y*, *z*), and the corresponding anatomical region based on the AAL atlas. *Abbreviations*: L/R = left/right; NIBS = non-invasive brain stimulation; TMS = transcranial magnetic stimulation; MNI = Montreal Neurological Institute; AAL = Automated Anatomical Labeling; RLL = right lower limb; LRL = left lower limb.

Language group (n = 11)										
ID	AGE	SEX	PATIENT SYMPTOMS	TUMOR DIAGNOSIS	MAIN TUMOR LOCATION (LOBE, SIDE)	NIBS PROTOCOL	NIBS TARGET MNI COORDINATES (X, Y, Z)			NIBS TARGET ANATOMICAL REGION (AAL atlas)
1	49	M	Comitial crisis	Astrocytoma (WHO grade IV)	Frontal, L	1hz rTMS + multifocal tDCS	-57	12	7	Left inferior frontal gyrus, opercular part
2	37	F	Mild speech disturbance	Cavernoma	Parietal, L	1hz rTMS	-45	-48	48	Left inferior parietal lobe / intraparietal sulcus
3	72	F	Mild speech disturbance (naming , repetition) / mild memory impairment (short term, working memory)	Cavernoma	Temporal, L	1hz rTMS	-63	-46	5	Left middle temporal gyrus
4	47	M	Mild speech disturbance / mild memory impairment / partial comitial crisis (olfactory crisis)	Astrocytoma (WHO grade III)	Frontal & Temporal, R	1hz rTMS + multifocal tDCS	49	20	2	Right inferior frontal gyrus, orbital part
5	53	M	Mild speech disturbance	Glioblastoma (WHO grade IV)	Frontal, L	1hz rTMS	-52	23	26	Left inferior frontal gyrus, triangular part
6	69	F	Mild speech disturbance	Glioma	Frontal, L	1hz rTMS + multifocal tDCS	-56	15	21	Left inferior frontal gyrus, opercular part
7	65	M	Partial comitial crisis (olfactory crisis)	Ganglioglioma (WHO grade I)	Frontal, R	1hz rTMS + multifocal tDCS	52	16	-6	Left inferior frontal gyrus, orbital part
8	56	M	Partial focal crisis in face and neck / paraphasic speech	Glioblastoma (WHO grade IV)	Frontal, L	1hz rTMS + multifocal tDCS	-45	20	25	Left inferior frontal gyrus, opercular and triangular parts
9	59	F	Tonic-clonic seizures, paraphasic speech	Glioblastoma (WHO grade IV)	Frontal, L	1hz rTMS + multifocal tDCS	-43	29	28	Left inferior frontal gyrus, triangular part
10	54	M	Aphasia, paraphasic speech, mild cognitive impairment	Glioblastoma (WHO grade IV)	Temporal, L	1hz rTMS	-68	-46	10	Left middle temporal gyrus
11	47	M	Paraphasic speech, mild cognitive impairment	Oligodendroglioma (WHO grade II)	Frontal, L	1hz rTMS + multifocal tDCS	-51	7	42	Left precentral gyrus
Non-language group (n = 15)										
ID	AGE	SEX	PATIENT SYMPTOMS	TUMOR DIAGNOSIS	TUMOR LOCATION (LOBE, SIDE)	NIBS PROTOCOL	NIBS TARGET MNI COORDINATES (X, Y, Z)			NIBS TARGET ANATOMICAL REGION (AAL atlas)
12	60	F	Moderate-severe right-hand motor and sensory impairment	Meningioma (WHO grade I)	Parietal, L	1hz rTMS	-53	-35	50	Left inferior parietal lobule
13	65	M	Transitory left facial supranuclear paralysis / Involuntary movements / dysarthria	Glioblastoma (WHO grade IV)	Frontal, R	1hz rTMS	47	0.7	59	Right precentral gyrus
14	59	M	Dizziness / presyncope	Astrocytoma (WHO grade II)	Frontal, R	multifocal tDCS	NA			NA
15	30	M	Comitial crisis	Astrocytoma (WHO grade II)	Frontal, R	1hz rTMS	38	-16	64	Right precentral gyrus
16	64	M	Left hand sensory impairment (paraesthesia)	Meningioma (WHO grade II)	Parietal, R	1hz rTMS	23	-35	72	Right postcentral gyrus
17	45	F	Comitial crisis	Oligodendroglioma (WHO grade II)	Frontal, R	1hz rTMS	38	-18	62	Right precentral gyrus
18	45	M	Left hand sensory and motor impairment	Glioblastoma (WHO grade IV)	Frontal, R	1hz rTMS	23	15	62	Right superior frontal gyrus
19	59	F	Left hand sensory and motor impairment (paraesthesia, clumsiness and reduced grip)	Glioblastoma (WHO grade IV)	Frontal, R	1hz rTMS + multifocal tDCS	41	-13	59	Right precentral gyrus
20	69	M	Moderate left lower limb motor impairment (apraxia)	MT: Non-Small Cell Carcinoma	Frontal, L	1hz rTMS + multifocal tDCS	-45	-5	20	Left precentral gyrus and left rolandic operculum
21	35	F	Mild right hemiparesis / RLL Hypoesthesia and dysesthesia / mild motor impairment in RLL / attention deficits	Astrocytoma (WHO grade II)	Frontal & Parietal, L	1hz rTMS	-4	-28	74	Left paracentral lobule
22	60	M	Tonic-clonic seizures	Glioblastoma (WHO grade IV)	Frontal, L	1hz rTMS + multifocal tDCS	-39	-13	63	Left precentral gyrus

(continued on next page)

Table 1 (continued)

Non-language group (n = 15)										
ID	AGE	SEX	PATIENT SYMPTOMS	TUMOR DIAGNOSIS	TUMOR LOCATION (LOBE, SIDE)	NIBS PROTOCOL	NIBS TARGET MNI COORDINATES (X, Y, Z)			NIBS TARGET ANATOMICAL REGION (AAL atlas)
23	49	M	Left frontoparietal haemorrhagic stroke, mild right hemiparesis, mild cognitive impairment	Oligodendroglioma (WHO grade III)	Frontal & Parietal, L	1hz rTMS	-31	-22	65	Left paracentral lobule
24	59	M	LRL paresthesia / focal crisis	Glioblastoma (WHO grade IV)	Frontal, L	1hz rTMS	-36	-18	68	Left precentral gyrus
25	77	F	RLL motor impairment	Meningioma (WHO grade I)	Frontal, L	1hz rTMS	-45	-17	65	Left precentral gyrus
26	69	F	Left arm paresthesia, hand fine motor impairment	Gliosarcoma (WHO grade IV)	Frontal, R	1hz rTMS	52	-12	45	Right precentral gyrus

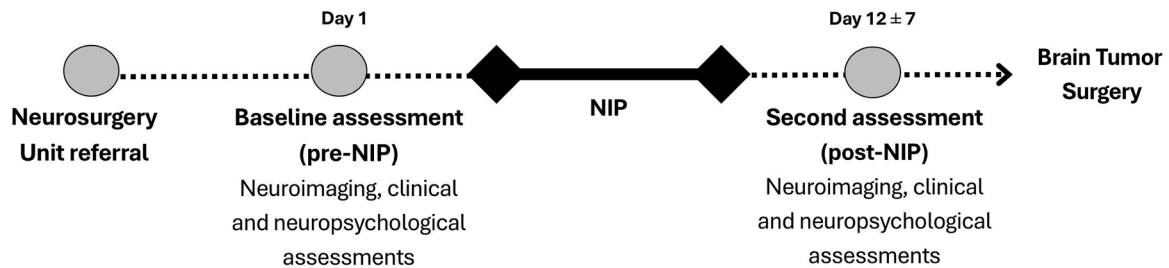


Fig. 1. Study design and timeline, outlining the neuroimaging, clinical and neuropsychological assessments conducted pre- and post-NIP. The prehabilitation program lasted 12 ± 7 days, and surgery was performed 3 ± 2 days after completion.

field of view [FOV] = $256 \times 240 \text{ mm}^2$, flip angle = 8° , and 0.8-mm isotropic voxel). For functional imaging data, the participants underwent task-based fMRI (tb-fMRI) with multiband (anterior-posterior phase-encoding; acceleration factor = 8) interleaved acquisitions (T2-weighted EPI scans, TR = 800 ms, TE = 37 ms, 72 slices, slice thickness = 2 mm, FOV = $208 \times 208 \text{ mm}^2$). Tb-fMRI were acquired during three language and three motor paradigms. Production language (phonemic and semantic) tasks entailed 373 volumes, while the remaining tb-fMRI acquisitions entailed 223 volumes. Task procedures are described in the following section.

Language function was assessed using three task-based fMRI paradigms mapping production and comprehension language-related processes, all performed with covert verbal responses to minimize speech-related head motion during MRI scanning (Gracco et al., 2005; Li et al., 2017): (1) Phonemic fluency: participants were instructed to generate as many words as possible starting with a specific letter (namely, “F”, “A”, “S”, “M”, and “E”, in this same order). (2) Semantic fluency: participants listed objects associated with specific environments (namely, school, kitchen, car, house, and hospital). (3) Auditory comprehension task: participants listened to a story narrated in a made-up language, and right after they listened to a story narrated in Spanish. Each of these tasks was repeated three times. To assess motor function a series of specific tasks targeting different movement patterns were implemented. Given the nature of motor fMRI paradigms, movement could not be fully avoided at the design level; however, tasks were designed to involve controlled movements while minimizing unnecessary head motion. The motor tasks were: (1) Finger tapping task: participants tapped each finger against their thumb, one hand at a time, performing the task separately with the left and right hand. (2) Ankle flexion task: participants moved each foot up and down slowly, performing the task separately with the left and right foot. (3) Tongue movement task: participants moved their tongue in circular motions while keeping their mouth closed.

2.3.2. fMRI preprocessing

Task-based fMRI was processed and analyzed using statistical

parametric mapping (SPM12; Wellcome Trust Centre for Imaging Neuroscience, <http://www.fil.ion.ucl.ac.uk/spm/>) and MAGIC fMRI toolbox18, an in-house application developed with MATLAB 2017b.

Prior to statistical analysis, functional scans from each subject underwent the standard fMRI preprocessing pipeline, including specific procedures to control for motion-related artifacts. Preprocessing involved the following steps: I) realignment of fMRI data using the mean image as a reference to remove any minor motion-related signal change and discarding any subject with a displacement greater than 3mm, II) slice-time correction, III) coregistration of the mean functional image to his corresponding structural image, IV) normalization into standard space ($2 \times 2 \times 2 \text{ mm}$; Montreal Neurology Institute, MNI coordinates) by using deformation fields obtained from the segmentation of the structural image, V) spatial smoothing with a Gaussian kernel of 8mm full width at half maximum (FWHM).

A first-level analysis was performed by fitting a general linear model on a voxelwise basis to model the brain activation of each task. Condition-specific effects were modeled by creating a boxcar function convolved with a canonical hemodynamic response function (HRF). Additionally, motion parameters were entered as regressors of no interest. Contrast images were calculated by subtracting the rest condition from the task condition. A criterion for statistically significant activation was set at a threshold of p-value < 0.001 and a family-wise error cluster threshold of p-value < 0.01 was applied to correct for multiple comparisons. All images were visually inspected for potential artifacts or technical problems. The size of significant clusters of activation reported by SPM were further used to evaluate NIP effect.

2.4. Subject classification and targeting procedures

Participants first underwent task-based fMRI to map functional activation (e.g., language function) allowing identification of critical functional regions at risk due to their proximity to the lesion. For each patient, we primarily used these fMRI activation maps to select NIBS targets. The primary approach was to place the stimulation site over peak fMRI activation clusters within the peritumoral region. In the

present study, the peritumoral region was defined on an individual basis, not according to a predefined anatomical radius or fixed distance from the tumor margin, but rather according to the functionally relevant task-based fMRI activation cluster located closest to the lesion and the surrounding affected tissue, including edema when present. In this context, the stimulation target was selected by integrating the spatial location of the fMRI activation cluster, its intraoperative significance, and its accessibility as a cortical target for NIBS. When this approach was not possible (e.g., the activation peak of the main fMRI cluster was not cortically accessible to NIBS), an alternative target was selected within the same task-related fMRI activation map by identifying the next significant activation peak location that was accessible to stimulation. With this trade-off, alternative targets remained within the functionally relevant network, while being as close to the lesion as feasibility of stimulation allowed.

Following this assessment, participants were divided into two groups according to the targeted stimulation point (see Table 1). The language group (n=11) included individuals in whom language production network was considered at risk (phonemic and semantic fluency); in these cases, language-related fMRI clusters were targeted with NIBS. The non-language group (n=15) comprised participants with motor areas considered at risk; here, stimulation was delivered to motor targets.

For the language group, language production-related activation was assessed using two covert verbal fluency paradigms: phonemic fluency and semantic fluency. These tasks were used to generate individual task-based fMRI activation maps. At the single-participant level, target selection was based on the individual clinical and fMRI profiles, taking into account the spatial relationship between activation peaks and the lesion, the predominant functional profile, and technical accessibility to stimulation. Specifically, the selected target corresponded to a phonemic fluency activation node in cases 5, 7, and 10, to a semantic fluency activation node in cases 4 and 6, and to a spatially overlapping phonemic and semantic fluency activation node in cases 1, 2, 3, 8, 9, and 11. After target selection, the phonemic and semantic fluency maps were jointly used to characterize the broader individualized language production network. This was justified by the observation that in all participants for whom both task maps were available, the phonemic and semantic fluency maps showed spatial overlap at the network level (see Supplementary Material, Fig. S4). In case 10, only one production-task fMRI map was available.

For the non-language group, the “motor network” was operationally defined at the single-participant level as the set of task-evoked fMRI activation maps corresponding to distinct somatotopic motor representations. These included finger tapping for the hand representation, ankle flexion for the lower-limb representation, and tongue movement for the orofacial/tongue representation. The motor network therefore did not correspond to a combined activation map generated by merging all motor tasks, but rather to the relevant task-specific motor representations identified in each participant. For target selection, the clinically relevant motor representation closest to the lesion was identified for each participant, while also considering clinical relevance and technical accessibility for NIBS. The hand motor representation was targeted in all 15 non-language participants and was therefore used for the primary motor analyses to maintain consistency across participants. The lower-limb representation was additionally targeted in two cases because of its clinical relevance. No stimulation target was selected from the tongue-movement map in the present cohort.

In cases 12, 13, 15, and 17, fMRI-based targeting was not conducted prospectively because these participants were enrolled during the preparatory phase of the study, before systematic implementation of the fMRI-guided targeting workflow. In cases 12, 15, and 17, stimulation sites were defined using TMS motor mapping coordinates over the primary motor cortex. In Case 13, target selection for stimulation was guided by clinical and anatomical considerations based on the patient's T1-weighted anatomical MRI, including the spatial relationship of the tumor to the premotor and primary motor cortices. The entire procedure

was supervised by a neurologist with expertise in neuromodulation. These patients were retained in the present analyses because they fulfilled the study inclusion criteria and because the stimulation coordinates were subsequently verified to fall within the corresponding task-based motor fMRI activation maps of interest. The corresponding verification is provided in Fig. S3 of the Supplementary Material.

The choice of neuromodulation technique (i.e., TMS or tDCS) was individualized and guided by each participant's anatomical and functional profile. Specifically, we principally considered tumor location and the amount and extent of peritumoral tb-fMRI activation clusters in the pre-NIP mapping. When the target corresponded to a spatially circumscribed cortical node, TMS was preferred because of its higher focality. When the relevant activation pattern was more spatially extended, tDCS was selected because of its broader electric field distribution. In cases in which both a focal target and broader network modulation were considered relevant, a combined TMS–tDCS approach was applied.

2.5. Non-invasive NIP intervention

The non-invasive NIP intervention program combined inhibitory-like neuromodulation targeting critical peritumoral brain activity with intensive task training, aiming to promote topographical reorganization of functional networks and facilitate the displacement of activity away from the lesion site. When rTMS was used, task training started immediately after the stimulation block. Targets were defined on each participant's native structural MRI and stimulation was delivered using MRI-guided neuronavigation (Brainsight; Rogue Research, Montreal, Canada); details are provided in Boccuni et al. (2023). When tDCS was used, task training was performed concurrently during stimulation. Participants were scheduled to undergo between 10 and 20 treatment sessions, depending on the available preoperative therapeutic window. The NIP intervention was individualized according to each participant's clinical and neural profile, as well as their preoperative schedule. The number and frequency of sessions were determined by the time available before surgery, the participant's scheduled clinical pathway, and logistical factors, including medical appointments, diagnostic procedures, coordination with clinical services, and, when relevant, travel or accommodation constraints related to place of residence. Sessions were therefore delivered once or twice per day depending on the available therapeutic window and logistical viability, while preserving the overall structure and therapeutic goals of the intervention. Each session, lasting approximately one hour, was carefully personalized to suit the individual participant's needs and abilities. Participants 12 and 13 completed a reduced number of treatment sessions, as their data were acquired during the initial pilot phase of the trial and are classified as part of a preliminary cohort comprising the first 10 participants enrolled in our prehabilitation program (Boccuni et al., 2024b; see Table 1).

The primary tasks employed to train language functions comprised phonemic fluency, semantic fluency, categorization exercises, word games, completion of incomplete words, generation of novel words by altering letters in a given word, word list recall, and the narration of a film or story while alternating between languages (typically Catalan, Spanish, and English). Classic games, such as hangman and word search, were also incorporated. Furthermore, the method of loci was employed to enhance memory and language associations (Sousa et al., 2021; de Lange et al., 2017). The tasks were conducted using both conventional pen-and-paper techniques and the Guttman NeuroPersonalTrainer® (GNPT; Solana et al., 2014), a validated online neurotraining platform. To promote progressive learning, the level of difficulty for each task was systematically increased both within each session and across the entire training program. It is important to note that the training tasks described above were administered exclusively to the language group; participants in the non-language group received motor-oriented training instead, with no language training component.

2.6. fMRI analysis

The FMRIB Software Library (FSL, version 5.0.10; <https://fsl.fmrib.ox.ac.uk/fsl/fslwiki/>) and Statistical Parametric Mapping (SPM, version 12; <https://www.fil.ion.ucl.ac.uk/spm/>) were used for analyzing MRI data.

The primary objective of this study was to assess NIBS-induced modulation of the language production network, as reflected in language-related fMRI activation maps. To determine whether any observed effects were specific to stimulation of this network, we implemented complementary control analyses. In the language group, NIBS targeted the language production network, and the motor network was included as a within-subject control to evaluate the anatomical and functional specificity of the effects. For the purposes of this within-subject control analysis, the non-targeted motor control region was defined as the hand motor cluster derived specifically from the finger-tapping condition of the task-based motor fMRI map. For each participant, the cluster showing the main activation peak located in the hemisphere ipsilateral to the lesion was selected and used as a functionally distinct motor reference region against which language production related fMRI changes could be compared. In the non-language group, NIBS targeted the motor network, providing a between-group control condition; in this group, language production network activity served as a reference to assess whether changes in the language group were attributable to direct stimulation rather than nonspecific or global effects. Across analyses, all motor network measures were treated as control comparisons to strengthen inferences about the specificity of modulation within the language production network. Analyses on these regards were conducted at two levels. First, a local effects analysis employed a region of interest (ROI)-based approach to evaluate neural changes at the stimulation target site pre- and post-NIP. Second, a network-level analysis compared the overall extent of task-related fMRI activation maps across individuals before and after NIP.

2.6.1. Local effects of NIP at the stimulation target

To investigate local fMRI effects of the NIP intervention, we defined a spherical ROI (10-mm radius) centered on each individual stimulation target. A 10-mm sphere was chosen to balance anatomical specificity with robust sampling in normalized fMRI data: it provides sufficient voxel coverage for typical whole-brain resolutions ($\approx 2\text{--}3\text{ mm}$) while accommodating residual spatial uncertainty introduced by inter-individual anatomical variability, spatial normalization error and physiological/spatial dispersion of BOLD responses. Therefore, a 10-mm ROI was used to capture a reliable sample of activity in tissue immediately surrounding the stimulation site. In the language group, the ROI was centered on each participant's stimulation target within their language production network. The stimulation target was defined individually from pre-NIP task-based fMRI acquired during phonemic and semantic verbal fluency paradigms. Based on the obtained fMRI activation maps, a functionally relevant cortical node was selected as the stimulation target. For TMS, stimulation target was centered on the selected node, capitalizing on the focal spatial profile of the technique. For tDCS, the montage was optimized to preferentially engage the same functionally defined node while additionally encompassing additional regions of the targeted network. The target was selected following the procedure detailed in Section 2.4. In the non-language group, the ROI was positioned over the individual stimulation target within the motor network, defined using pre-NIP task-based fMRI localizing motor activation. For within-subject specificity control analyses, an additional ROI was placed over the principal activation peak of the non-targeted network (i.e., the hand motor network in the language group and the language production network in the non-language group) following the same functional localization and target-selection procedure.

2.6.2. Effects of NIP on targeted network size

Changes in the spatial extent of functional network activity were

assessed by comparing the number of activated voxels in the fMRI maps between pre- and post-NIP time-points. These analyses were conducted separately for both the language production and motor networks in both the language and the non-language group.

To quantify these changes, we calculated the total volume of each network fMRI activation clusters (V_{net}) by summing the number of suprathreshold voxels (S_k) within the relevant fMRI activation clusters and multiplying by the voxel size, $2 \times 2 \times 2\text{ mm}^3 (V_{vox})$:

$$V_{net} = V_{vox} \sum_{i \in S_k} 1$$

This volume served as an estimate of each participant's individual language production and motor networks overall size and provided a basis for comparing network extent across NIP time points.

See Fig. 2 for the representation of the fMRI analyses performed to assess the effects of NIP.

2.7. Statistical analyses

Statistical analyses were conducted using R version 4.2.2 (R Core Team, 2022) via RStudio version 2022.07.1+554 (RStudio Team, 2022). For normally distributed data, parametric tests were used: t-tests (paired or independent, as appropriate) and mixed-design ANOVA for comparisons involving more than two groups or conditions. When the normality assumption was violated, nonparametric alternatives were applied: Wilcoxon signed-rank tests for paired comparisons and Wilcoxon rank-sum (Mann–Whitney U) tests for independent samples. Statistical significance was set at $p \leq 0.05$.

2.7.1. Neuroimaging-derived statistical analysis

2.7.1.1. Local effects at the stimulation target. To investigate changes in brain activity at the stimulation site, we measured neuroimaging-derived data from the spatial overlap between the 10 mm-radius ROI (centered on the stimulation target) and the selected fMRI activation cluster in the targeted region at two time points (pre- and post-NIP). A mixed design ANOVA was conducted with group (language vs. non-language) as a between-subject factor, and time (pre-NIP vs. post-NIP) as within-subject factor, including both groups in the same model. Significant effects were further examined using post-hoc paired-samples t-tests (to assess within-group changes over time) and independent-samples t-tests (to compare groups at each time point).

2.7.1.2. Changes in network size. To evaluate changes in the size of task-related networks following NIP, suprathreshold activation maps were generated from the SPM first-level contrasts using a voxel-wise family-wise error-corrected threshold of $T > 4.69$ ($p < 0.01$ FWE) and a minimum cluster extent of $k \geq 30$ voxels. Thresholded, binarized maps were combined (summed) in FSL (v1.11.0) and then imported into MRICroGL (v1.2.20220720) for volumetric quantification. For each participant, the volume (mm^3) of the language production and motor networks was computed as the number of suprathreshold voxels multiplied by voxel volume. A mixed design ANOVA was then performed from this neuroimaging-derived data with group (language vs. non-language) as a between-subject factor, and network (targeted vs. control) and time (pre-NIP vs. post-NIP) as within-subject factors.

2.7.1.3. Descriptive analysis of the language production network. To further characterize NIP-related changes in the language production network, which was the focus of this investigation, we conducted an additional qualitative, case-by-case inspection of fMRI activation patterns in the 11 participants assigned to the language group. This descriptive assessment allowed us to explore patterns beyond the overall amount of activation within the language production network. Given the modest sample size and clinical heterogeneity, this qualitative approach

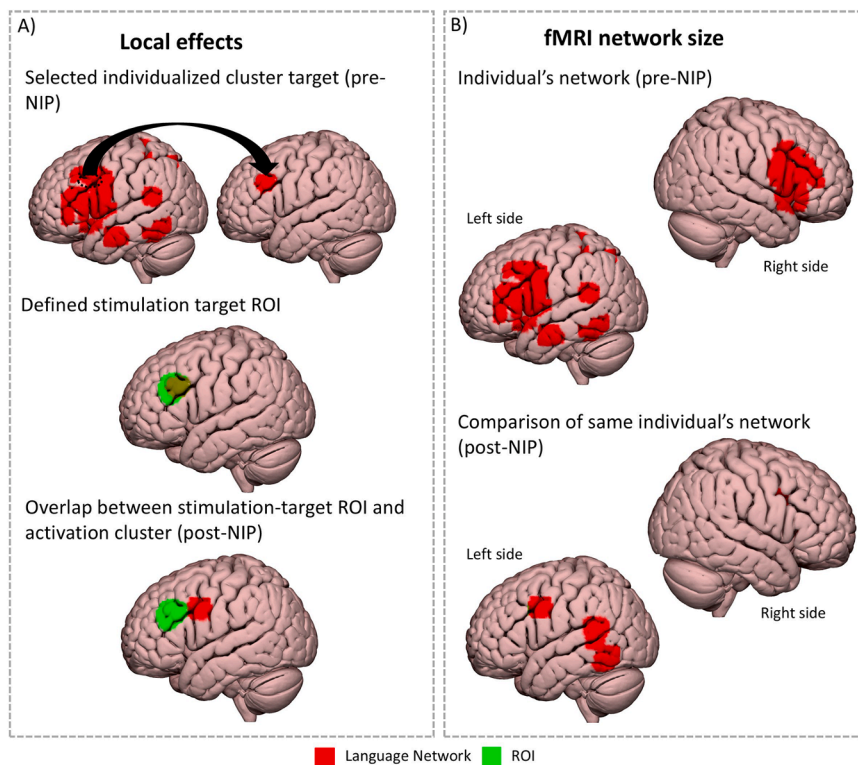


Fig. 2. Schematic representation (illustrative example) of the main fMRI-based analyses performed to assess the effects of NIP. **A.** Local effects analysis: Individualized stimulation targets were identified within pre-NIP task-based fMRI activation clusters for language production (shown in red). A 10mm-radius spherical ROI (shown in green) was defined around this peak and later used to evaluate pre/post overlap of functional activation in the same region. **B.** Comparison of fMRI network size: Language-related activation maps from task-based fMRI (phonemic and semantic fluency tasks) were compared before and after the NIP intervention. The total number of suprathreshold voxels was computed for each individualized language network (shown in red), providing a quantitative measure of network extent.

was well suited to capturing patient-specific reorganization patterns. This analysis complements the quantitative results by describing spatial reorganization patterns that cannot be captured by volume-based statistics alone. All qualitative ratings were performed independently by two authors (N.B.-B.; A.R.-V.).

2.7.2. Cognitive performance statistical analysis

To examine potential effects of NIP on cognitive performance, statistical analyses were conducted on both language and non-language tasks, as previously described in Section 2.2.1. Specifically, paired-sample t-tests were used to compare pre- and post-intervention scores for each cognitive measure. Language tasks were analyzed to monitor changes in the targeted domain, while non-language tasks (i.e. visuo-spatial constructional and perceptual abilities) were included to assess possible transfer effects beyond language. Measures of central tendency and dispersion were reported using the median and interquartile range (IQR). Wilcoxon signed-rank tests were used for paired comparisons, and Kendall's tau was used to assess associations between variables.

3. Results

3.1. Topographical changes in functional brain networks

3.1.1. Local effects to the stimulation target

There was a significant interaction between group (language vs. non-language) and time (pre- vs. post-NIP) in ROI-activation cluster overlap within the language production network, $F(1,23) = 4.61$, $p = .04$ (see Fig. 3A for an illustrative example), indicating that the change over time differed between groups. Post-hoc analyses showed a significant reduction in overlap from pre- to post-NIP in the language group, $t(10) = 5.68$, $p < .001$, $d = 1.71$, whereas the non-language group

showed no change, $t(13) = 0.50$, $p = .62$, $d = 0.14$ (Fig. 3.B1). Between-group comparisons indicated no baseline difference, $t(23) = 0.57$, $p = .57$, but a significant group difference emerged post-NIP, $t(23) = 2.43$, $p = .02$. Analyses focused on the motor network revealed no effects of NIP on ROI-activation cluster overlap. In the non-language group, stimulation of the motor network did not induce changes in ROI-cluster overlap (no main effect of time: $F(1,21) = 0.13$, $p = .72$; no group $\times$ time interaction: $F(1,21) = 0.62$, $p = .44$). Similarly, the language group showed no significant change in overlap within the hand motor cluster between pre- and post-NIP, $t(9) = -0.60$, $p = .56$, $d = -0.19$ (Fig. 3.B2).

3.1.2. Comparison of overall fMRI network size

For the language production network, there was no significant interaction between group (language vs. non-language) and time (pre- vs. post-NIP) on task-related language production network size, $F(1, 24) = 1.02$, $p = .32$, indicating that volume changes over time did not differ between groups. However, there was a main effect of time, with network size decreasing from pre- to post-NIP across participants, $F(1, 24) = 5.34$, $p = .03$, consistent with a general reduction in the extent of task-related activation over time. Additional illustrations of the activation of language production clusters before and after prehabilitation in the language group (language production network) and the non-language group (language production network) are provided in the Supplementary Material (Figures S1–S2). Analyses of the motor network revealed no significant effects on motor network size (main effect of time: $F(1, 23) = 0.74$, $p = .40$; group $\times$ time interaction: $F(1, 23) = 0.03$, $p = .87$; main effect of group: $F(1, 23) = 0.54$, $p = .47$), indicating stable motor-network size across time and groups.

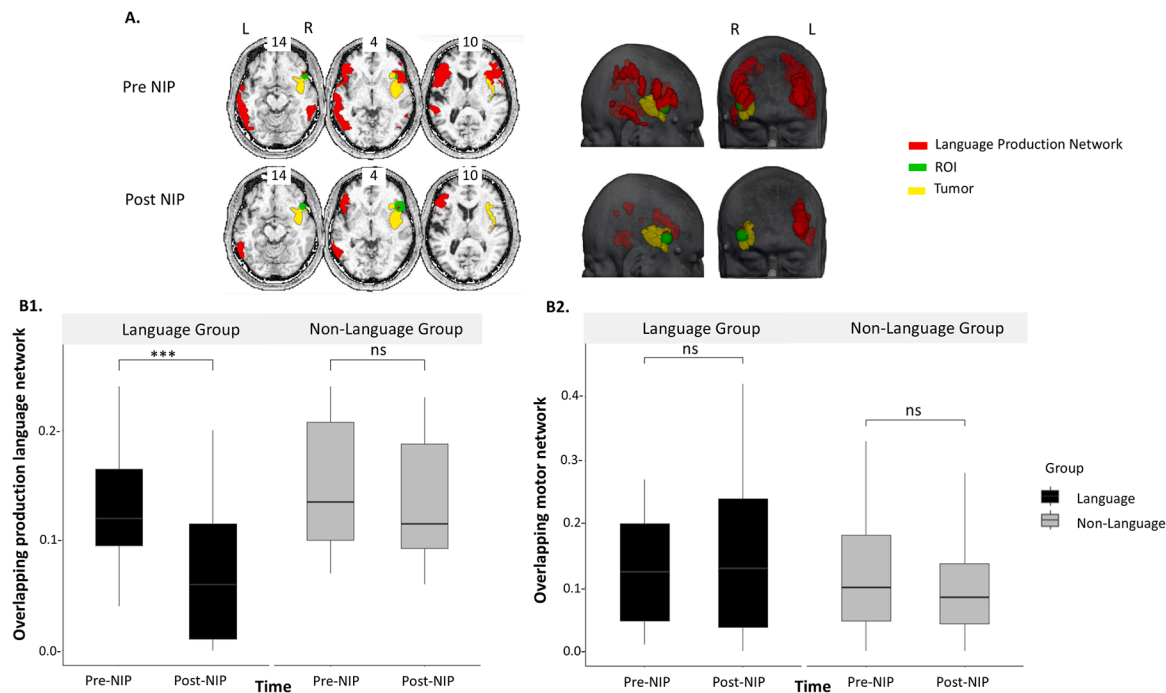


Fig. 3. A. Example of the activation in fMRI language tasks: Pre vs Post intervention. In yellow the tumor, in red the task-related language network and in green the 10mm-radius ROI on the stimulation target. Shown here is Case 7 with a right-hemisphere tumor. **B1.** Comparison of the overlapping of language network within the ROI, for the language and non-language group. In both groups the ROI's localization was within language network. Overall, a significant reduction of the overlapping and extent network size is shown in the language group, but not in the non-language group. **B2.** Comparison of the overlapping of motor network within the ROI, for the language and non-language group. In both groups the ROI's localization was within motor network. The asterisk indicates a significant main effect of Time (pre- vs post-NIP) on network size across groups. Asterisks indicate statistical significance levels: * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$; ns = not significant.

3.1.3. Descriptive analysis of overall fMRI language production network size

Reorganization patterns were heterogeneous (Table 2). Some participants showed intra- and/or interhemispheric recruitment, whereas others showed localized intrahemispheric shifts or no clear cross-hemispheric reorganization. Activation clusters shifted anteriorly, posteriorly, or in mixed directions, generally moving away from the tumor. Intrahemispheric network volume decreased in most participants (9/11), while interhemispheric volume changes were more variable (see Supplementary Material, fMRI language production network results).

3.2. Language and other cognitive domain performance results

Clinical outcomes are presented in Table 3. Language performance remained stable in both the language and non-language groups, with no significant changes observed (all p 's > 0.05). Furthermore, non-language domains, including visuospatial constructional and perceptual abilities, also showed no significant differences in all groups before and after the NIP intervention (all p 's > 0.05).

4. Discussion

This study shows that preoperative NIP combining non-invasive neuromodulation (rTMS and/or tDCS) with intensive language

Table 2
Quantitative description of the language production network in the 11 cases of the language group. For each participant, the table reports intrahemispheric and interhemispheric reorganization, direction of displacement, changes in intra- and interhemispheric network volume, and the post-NIP proximity of language-related clusters to the tumor. Coding scheme: intrahemispheric/interhemispheric reorganization – Y = present, N = absent; direction of displacement – A = predominantly anterior, P = predominantly posterior, M = mixed anterior–posterior; volume change (intra-/interhemispheric) – ↓ = decreased post-NIP, ↑ = increased post-NIP, = = no relevant change, 0 = no suprathreshold activation; proximity to tumor (post-NIP) – Near = clusters remain close to the peritumoral region, Away = clusters clearly displaced from the peritumoral region.

ID	Intrahemispheric reorganization	Interhemispheric reorganization	Direction of displacement (post vs. pre)	Intrahemispheric volume change post-NIP	Interhemispheric volume change post-NIP	Post-NIP proximity of language production clusters to tumor
1	Y	Y	A	↓	↓	Away
2	N	N	A	↓	↓	Away
3	Y	N	P	↓	0	Away
4	Y	Y	P	↓	↑	Away
5	Y	Y	A	=	↓	Away
6	Y	Y	M	↓	↑	Away
7	Y	Y	M	↓	↓	Away
8	N	Y	M	=	↑	Near
9	N	N	A	↓	↓	Away
10	N	Y	P	0	↑	Away
11	N	N	A	↓	↓	Near

Table 3

Overall cognitive outcomes before and after NIP. Values are presented as mean (standard deviation), p-value, and bootstrap 95% confidence interval for the within-group pre-post change. Change scores were computed as post-NIP minus pre-NIP values; therefore, positive values indicate higher scores after NIP. Bootstrap confidence intervals refer to the mean change and were estimated using paired, subject-level resampling with 5,000 bootstrap resamples and the percentile method. Note: p-values were obtained using two-sided Wilcoxon signed-rank tests for paired comparisons of pre- and post-NIP scores within each group and were not adjusted for multiple comparisons. NA = p-value could not be computed due to absence of variability, as pre- and post-NIP scores were identical. Abbreviation: TB-R = Barcelona Test-Revised.

Whole cohort (n = 26)								
Clinical assessment, cognitive function	Language group (n = 11)				Non-language group (n = 15)			
	Mean (SD) Pre	Mean (SD) Post	p-value*	Bootstrap 95% CI	Mean (SD) Pre	Mean (SD) Post	p-value*	Bootstrap 95% CI
TB-R (conversation and narration)	7.64 (1.21)	7.64 (1.21)	NA	[0, 0]	8.00 (0)	8.00 (0)	NA	[0, 0]
TB-R (thematic narration)	5.73 (0.9)	5.55 (1.04)	1.00	[-0.55, 0]	5.87 (0.35)	6.00 (0)	0.35	[0, 0.36]
TB-R (picture description)	5.64 (0.92)	5.91 (0.3)	0.37	[0, 0.64]	5.73 (0.59)	5.93 (0.27)	0.37	[0, 0.54]
TB-R (verbal word repetition)	9.36 (2.11)	9.55 (1.21)	1.00	[-0.27, 0.82]	9.87 (0.52)	10.00 (0)	1.00	[0, 0.46]
TB-R (verbal naming)	5.73 (0.9)	5.91 (0.3)	1.00	[0, 0.55]	6.00 (0)	6.00 (0)	NA	[0, 0]
TB-R (verbal comprehension)	15.27 (1.85)	16 (0)	0.37	[0, 1.82]	15.6 (1.3)	16.00 (0)	1.00	[0, 1.15]
TB-R (reading comprehension)	7.82 (0.6)	7.82 (0.41)	1.00	[-0.27, 0.27]	8.00 (0)	8.00 (0)	NA	[0, 0]
TB-R (automatic language)	2.73 (0.90)	2.73 (0.90)	1.00	[0, 0.82]	2.78 (0.8)	2.79 (0.8)	NA	[0, 0]
Forward	2.6 (0.97)	2.82 (0.41)	1.00	[0, 0.6]	2.79 (0.8)	2.71 (0.83)	NA	[0, 0]
Reverse								
TB-R (verbal repetition) Syllables	8.00 (0) 7.36 (2.11)	8.00 (0)			8.00 (0) 8.00 (0)	8.00 (0)	NA NA	[0, 0]
Logatomes	55 (16.58)	7.46 (1.81) 54.82 (17.19)	NA 1.00	[0, 0]	8.00 (0)	8.00 (0)	1.00	[0, 0]
Sentences			1.00	[0, 0.27]	60.00 (0)	56.3 (13.39)		[0, 12]
TB-R (naming)								
Visuoverbal naming Naming completion	13.81 (0.41) 5.72 (0.9)	13.55 (1.21) 5.82 (0.6)	0.59 1.00	[-0.91, 0.18] [0, 0.27]	13.47 (2.7) 6.00 (0)	14.00 (0) 6.00 (0)	NA NA	[0, 0] [0, 0]
TB-R (visuospatial attention)	28.00 (0)	28.00 (0)	1.00	[-0.75, 0]	27.93 (0.27)	27.92 (0.29)	1.00	[-0.25, 0]
WAIS-IV blocks (visuoconstruction)	31.82 (11.52)	33.9 (9.24)	0.32	[-1.27, 5.64]	37.27 (17.2)	40.27 (20.17)	0.09	[0.13, 5.29]

training can modulate the language production network in patients with brain tumors. Specifically, we observed a reduction in peritumoral language-related activation without comparable effects in the motor network, indicating networkspecific reorganization. Importantly, this neuromodulation occurred without deterioration in language or broader cognitive performance, supporting the capacity of targeted NIP to guide selective neuroplasticity prior to surgery.

4.1. Specific reorganization of the language production network through NIP

Our neuroimaging results revealed selective modulation of the language production network in the language-targeted cohort, supporting the hypothesis that network-targeted NIP procedures can drive topographically specific reorganization within multimodal functional networks, with significant translational relevance in brain tumor surgery. In this study, we observed a consistent reduction in the spatial extent of fMRI activation clusters within the NIBS target region, which was defined based on individual critical fMRI language maps, supporting successful topographical reorganization of the language production network. Indeed, the combination of local fMRI signal reduction and preserved performance is consistent with adaptive neuroplasticity mechanisms described in prior work, where stimulation of critical areas is associated with compensatory recruitment of alternative, structurally preserved regions (Hartwigsen, 2021; Nieberlein et al., 2023).

Notably, the imaging changes following NIP were specific to the targeted language production network, as confirmed by control analyses (Momi et al., 2021a; 2021b). Because stimulation was combined with language training that engages the same network, the relative contribution of each component cannot be disentangled. Nevertheless, the observed reduction in peritumoral language production activation and the broader topographical reorganization within the network are consistent with the goals of prehabilitation: decreasing reliance on vulnerable cortex adjacent to the tumor while preserving function

(Bocconi et al., 2023).

4.2. Reorganization patterns in fMRI activation maps

The ROI analysis identified a significant reduction in peritumoral language production activation following NIP, representing the primary effect of the intervention. Descriptive analyses further suggested redistribution of activation away from peritumoral regions, with heterogeneous intra- and interhemispheric patterns across participants. Although exploratory, these changes are consistent with mechanisms of remapping, functional unmasking (Pascual-Leone et al., 2005), and compensatory recruitment reported in brain tumor populations (Duffau, 2005). Together, these findings extend prior evidence of tumor-related network reorganization (Aerts et al., 2016; Morell et al., 2022; Manso-Ortega et al., 2023) by indicating that neuromodulation combined with training may further modulate language production network topography.

4.3. Multimodal vs. unimodal network responsiveness to NIP

In the present study, we observed that multimodal or higher-order networks, such as the language production network, are differentially modulated compared with unimodal or low-order sensorimotor systems. A key theoretical implication is that multimodal association networks may be particularly amenable to targeted neuromodulation and topographical reorganization, likely due to their distributed cortical architecture. The language network integrates information across multiple cortical regions, whereas primary motor networks are more spatially constrained and somatotopically organized (Yeo et al., 2011; Mesulam, 1998; Duffau, 2014). Recent evidence supports this distinction: hierarchical neurodevelopment prolongs plasticity windows in association cortices, enabling sustained flexibility in multimodal regions (Sydnor et al., 2021), and neocortical gradients reveal tighter structure-function coupling in unimodal areas versus more flexible alignment in

transmodal regions, facilitating reconfiguration after perturbation (Vázquez-Rodríguez et al., 2019). Stimulation mapping further demonstrates greater excitability and inter-network integration in higher-order systems (e.g., language, default mode) compared to sensorimotor networks (Momi et al., 2025), with rapid short-term reorganization observed following neuromodulation (Hartwigsen et al., 2017). Consistent with these frameworks, language-targeted NIP in our study produced measurable network-specific reorganization, whereas motor-targeted NIP (which can also entail potential neural and clinical effects) did not produce similar modulations measurable with a 10 mm ROI and whole-network size. This pattern observed in our data aligns with models of high-order plasticity mechanisms and is consistent with the notion that multimodal systems exhibit higher network plasticity and greater flexibility for reconfiguration following perturbation, while unimodal systems show greater functional stability and constraint (Gatica et al., 2025; Cramer et al., 2011).

4.4. Targeted neuromodulation and language production network plasticity

Selective reorganization of the language production network following NIP is consistent with models of experience-dependent plasticity, in which repeated modulation combined with task engagement promotes redistribution within large-scale networks. The multi-session, individually targeted stimulation approach used here aligns with prior evidence showing that repeated neuromodulation can reinforce plastic changes and enhance network reorganization over time (Klooster et al., 2023; Maeda et al., 2000; Wang et al., 2014; Liu et al., 2018; Lefaucheur et al., 2020). Given the known variability in neuromodulation outcomes (López-Alonso et al., 2014; Hamada & Rothwell, 2015; Perellón-Alfonso et al., 2018), personalized targeting and repeated sessions appear particularly important for achieving reliable network-level effects. These approaches may help stabilize network reorganization and ensure meaningful clinical benefits (Maeda et al., 2000; Klooster et al., 2023). Notably, in our study modulation was observed despite tumor–brain crosstalk and anatomical constraints (Ghinda, Wu & Duffau, 2023), suggesting that TMS and tDCS can influence functional organization even in structurally compromised systems (Bocconi et al., 2024a; 2024b). Our findings suggest that NIP may facilitate reorganization process and presumably support a more favorable network configuration ahead of surgery.

4.5. Language production network modulation and functional preservation across NIP intervention

Neuroimaging effects were confined to the targeted language production network, with no evidence of modulation in non-targeted systems. Both between-subject comparisons and within-subject controls confirmed this network specificity. These observations align with prior NIBS studies demonstrating that modulation of specific neural nodes on concrete brain networks can induce specific effects within these brain networks, which can be captured with functional neuroimaging techniques (i.e., Abellaneda-Pérez et al., 2019; Momi et al., 2021b; Wang et al., 2014). The use of targeted, functionally unrelated regions (i.e. motor) as control conditions aligns with strategies previously described in the literature, as those outlined by Hartwigsen (2016) on the possibility of stimulating neighboring or contralateral regions that are not expected to contribute to the task under investigation, to control for unspecific effects while preserving anatomical and procedural comparability across groups.

Interestingly, our observations indicated a general reduction in the overall size of task-related activation across both groups, without measurable decline in language or broader neuropsychological performance. Because participants completed identical fMRI tasks at two time points, this pattern may partly reflect task repetition or familiarity effects, consistent with the phenomenon of repetition suppression (Gobel

et al., 2011; Ewbank et al., 2011). The phenomenon of repetition suppression refers to reduced neuronal activation upon repeated exposure to the same stimulus, indicating a refined engagement of neural resources, rather than a loss of function (Stam et al., 2021; Lee, Henson, & Lin, 2020; Barron et al., 2016; Vannini et al., 2012). However, this potential interpretation should be considered cautiously. The verbal fluency tasks were performed covertly to minimize speech-related head motion during fMRI acquisition, constraining the collection of in-scanner behavioral performance. Therefore, although a repetition suppression-like phenomenon may likely account for the observed effects, other phenomena, namely habituation and automatization, may also have contributed to the reduced activation (Mohr et al., 2016; Kirwan et al., 2020).

4.6. Network plasticity in a preoperative context

These findings indicate that network plasticity remains accessible in brain tumor patients and can be modulated through targeted neuromodulation combined with training. The integration of NIBS and neuroimaging may therefore provide a framework for guiding adaptive reorganization prior to surgery (Zhang et al., 2021; Pi et al., 2019; Voss et al., 2010). Preservation of language and non-language performance suggests that such modulation can occur without behavioral compromise, a critical consideration in brain tumor patients vulnerable to crowding effects or maladaptive reorganization (François et al., 2019; Martínez-Lozada et al., 2025).

5. Limitations

The first limitation of this study was that the data comes from a phase 1 clinical trial and from a previous pilot phase (Bocconi et al., 2023), conducted as a case series without a control group. To mitigate this limitation, we implemented internal control strategies: non-targeted networks served as controls to verify that the observed effects were specific to the targeted system. Additionally, the sample size was small, particularly after stratification into language and non-language groups. Recruitment for preoperative neuromodulation protocols in brain tumor patients is inherently challenging due to clinical and logistical constraints. Moreover, the cohort was clinically heterogeneous, reflecting variability in tumor location, tumor characteristics, and baseline patient clinical status. These factors limit the generalizability of the findings and reinforce the need to interpret the present results as a proof-of-concept. Another important limitation concerns the inability to disentangle the relative contributions of neuromodulation and intensive language training. Because stimulation was systematically paired with training, their independent effects cannot be isolated. It is plausible that the local reduction of activation near the stimulation target was primarily driven by neuromodulation, whereas the broader topographical redistribution observed in descriptive analyses may reflect training-related influences. A further limitation is that behavioral performance during the covert verbal fluency fMRI tasks was not recorded in the scanner. Although this design minimized speech-related head motion, it limits the interpretation of pre–post changes in task-related BOLD activation. In addition, although an auditory comprehension task was acquired, scanner-related hearing difficulties reduced task engagement during the language comprehension blocks, thereby compromising the reliability of the resulting fMRI activation maps. These maps were therefore not included in the present analysis. This represents a limitation given the clinical relevance of language comprehension, which should be addressed in future studies through technical optimization of MRI research settings. The observed ceiling effects in the language and cognitive assessments are plausibly attributable to the limited sensitivity of the neuropsychological tests employed. These ceiling effects may have reduced the sensitivity to detect subtle post-intervention changes. As a statistical approach to improve the interpretation of these potentially constrained behavioral changes, we complemented the paired pre–post comparisons

with non-parametric bootstrap confidence intervals for the estimated within-group change scores. Nevertheless, future studies should incorporate more refined and sensitive language evaluation tools to better capture subtle behavioral changes. Finally, the present study was designed as a mechanistic investigation focused specifically on short-term fMRI and behavioral changes induced by NIP, based on pre- and post-NIP assessments. Therefore, postoperative outcomes were beyond the scope of the current manuscript. Future investigations should examine postoperative language outcomes and their longitudinal relationship with post-NIP fMRI and behavioral changes to determine whether NIP-related reorganization translates into sustained post-surgical language preservation in the long term.

6. Conclusions

In conclusion, our findings suggest that preoperative NIP may contribute to selectively reorganize the language production network in brain tumor patients while preserving language and cognitive performance. The absence of modulation in non-targeted networks supports the specificity of this effect. This targeted modulation highlights the potential to guide adaptive neuroplasticity prior to surgery, potentially reducing functional constraints and supporting safer, more extensive resections in language-critical regions. However, given the exploratory nature of the study, its small sample size, and the notable heterogeneity in tumor location and patient characteristics, these results should be interpreted with caution as preliminary, proof-of-concept data.

List of abbreviations

NIP: Neuromodulation-induced prehabilitation
 TMS: Transcranial magnetic stimulation
 tDCS: Transcranial direct current stimulation
 tb-fMRI: task-based functional MRI
 ROI: Region of Interest
 CNS: Central nervous system
 FWHM: Full width at half maximum
 HRF: Hemodynamic response function
 IFG: Inferior frontal gyri
 pSTG: Posterior superior temporal gyri
 NIBS: Non-invasive brain stimulation
 SPM: Statistical parametric mapping
 iTBS: Intermittent theta-burst stimulation
 TB-R: Barcelona-Revised Test

Funding

This research was funded by the Joan Ribas Araquistain Foundation (reference project 2020.330). D.B.-F. was supported by an Institut Català de Recerca i Estudis Avançats, ICREA Academia 2019 award from the Catalan government. A.P.-L. is partly supported by the Healthy Aging Initiative, the Eleanor and Herbert Bearak Memory Wellness for Life Program and grants from the National Institutes of Health (R01AG076708; R01AG059089), Jack Satter Foundation, and Bright-Focus Foundation. This work was performed thanks to the 3T MRI equipment at IDIBAPS (grant IBPS15-EE-3688 confunded by MINECO and by ERDF).

Ethics approval and consent to participate

All procedures from the present study were performed in accordance with the Helsinki declaration. The study was approved by the Research Ethical Committee of Fundació Unió Catalana d'Hospitals (approval number: CEI 21/65, version 1, 13/07/2021). Clinician participants provided informed consent by reviewing and agreeing to a consent statement presented by the research team, prior to responding to any questions or proceeding with any treatment.

Consent for publication

Participants in the study provided consent for the use of anonymized quotations in research publications. All identifying details have been excluded to ensure participant confidentiality.

Declaration of generative AI and AI-assisted technologies in the writing process

During the preparation of this work the authors used [OpenAI. GPT-5.2 model] to support language editing and improve the clarity, readability, and structure of the manuscript text.

After using this tool/service, the authors reviewed and edited the content as needed and take full responsibility for the content of the publication.

Data and code availability statement

To protect participant confidentiality and in accordance with ethical approval and informed consent, the datasets from this study are not publicly accessible. Access is restricted and may be granted upon reasonable request and subject to data use agreement. The analysis code is available from the corresponding author(s) upon reasonable request.

CRediT authorship contribution statement

Nuria Brault-Boixader: Writing – review & editing, Writing – original draft, Visualization, Investigation, Formal analysis, Data curation. **Alba Roca-Ventura:** Writing – review & editing, Writing – original draft, Visualization, Investigation, Formal analysis, Data curation. **Selma Delgado-Gallén:** Writing – review & editing, Investigation, Data curation. **Edgar Buloz-Osorio:** Writing – review & editing, Investigation. **Leonardo Boccuni:** Investigation. **Carlos Laredo:** Software, Methodology, Investigation. **Emma Muñoz-Moreno:** Software, Methodology, Investigation. **Núria Bargalló:** Software, Methodology, Investigation. **David Bartres-Faz:** Writing – review & editing, Investigation. **Álvaro Pascual-Leone:** Writing – review & editing, Resources, Methodology, Investigation, Conceptualization. **José M. Tormos-Muñoz:** Writing – review & editing, Resources, Methodology, Investigation, Conceptualization. **Ruben Perellón-Alfonso:** Writing – review & editing, Investigation. **Kilian Abellaneda-Pérez:** Writing – review & editing, Supervision, Resources, Project administration, Methodology, Investigation, Conceptualization.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

Kilian Abellaneda-Perez reports financial support was provided by Joan Ribas Araquistain Foundation (reference project 2020.330). David Bartres-Faz reports was provided by Institut Català de Recerca i Estudis Avançats, ICREA Academia 2019. Alvaro Pascual-Leone reports a relationship with Linus Health, TI Solutions Neuroelectrics, Magstim Inc., TetraNeuron, Skin2Neuron, MedRhythms, Bitbrain, and AscenZion. That includes: board membership and consulting or advisory. None of these companies have any interest in or have contributed to the present work. Alvaro Pascual-Leone is partly supported by the Healthy Aging Initiative, the Eleanor and Herbert Bearak Memory Wellness for Life Program and grants from the National Institutes of Health (R01AG076708; R01AG059089), Jack Satter Foundation, and Bright-Focus Foundation. Alvaro Pascual-Leone is listed as an inventor on several issued pending patents on the real-time integration of transcranial magnetic stimulation with electroencephalography and magnetic resonance imaging and applications of noninvasive brain stimulation in various neurological disorders; as well as digital biomarkers of cognition and digital assessments for early diagnosis of

dementia. This work was performed thanks to the 3T MRI equipment at IDIBAPS (grant IBPS15-EE-3688 confunded by MINECO and by ERDF). If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgments

The authors express their gratitude to all participants of the Prehabilita program, as well as to the dedicated research staff and neurosurgical units involved in this study. We are also indebted to the Magnetic Resonance Imaging Core Facility of the Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS) for the scientific and technical support in MRI acquisition and analysis.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at [doi:10.1016/j.neuroimage.2026.122185](https://doi.org/10.1016/j.neuroimage.2026.122185).

References

- Abellaneda-Pérez, K., Vaqué-Alcázar, L., Vidal-Piñero, D., Jannati, A., Solana, E., Bargalló, N., Santarnecchi, E., Pascual-Leone, A., Bartres-Faz, D., 2019. Age-related differences in default-mode network connectivity in response to intermittent theta-burst stimulation and its relationships with maintained cognition and brain integrity in healthy aging. *NeuroImage* 188, 794–806. <https://doi.org/10.1016/j.neuroimage.2018.11.036>.
- Abellaneda-Pérez, K., Miquel, L., Lusilla-Palacios, P., Gual, A., 2023. Non-invasive brain stimulation combined with neuroimaging: Towards precision medicine in the treatment of addictions. *Estimulación cerebral no invasiva combinada con neuroimagen: Hacia una medicina de precisión en el tratamiento de las adicciones*. *Adicciones* 35 (1), 3–8. <https://doi.org/10.20882/adicciones.1923>.
- Aerts, H., Fias, W., Caeyenberghs, K., Marinazzo, D., 2016. Brain networks under attack: Robustness properties and the impact of lesions. *Brain* 139 (12), 3063–3083. <https://doi.org/10.1093/brain/aww194>.
- Antonenko, D., Fromm, A.E., Thams, F., Grittner, U., Meinzer, M., Flöel, A., 2023. Microstructural and functional plasticity following repeated brain stimulation during cognitive training in older adults. *Nature Communications* 14, 3184. <https://doi.org/10.1038/s41467-023-38910-x>.
- Barcia, J.A., Sanz, A., González-Hidalgo, M., de Las Heras, C., Alonso-Lera, P., Díaz, P., Pascual-Leone, A., Oliviero, A., Ortiz, T., 2012. rTMS stimulation to induce plastic changes at the language motor area in a patient with a left recidivant brain tumor affecting Broca's area. *Neurocase* 18 (2), 132–138. <https://doi.org/10.1080/13554794.2011.568500>.
- Barron, H.C., Garvert, M.M., Behrens, T.E., 2016. Repetition suppression: a means to index neural representations using bold?. *Philosophical Transactions of the Royal Society. B: Biological Sciences* 371 (1705), 20150355. <https://doi.org/10.1098/rstb.2015.0355>.
- Bisten, J., Grün, J., Hoppe, C., Bauer, T., Held, N.R., Rose, R., Althausen, A., Witt, J.A., Borger, V., Schneider, M., Vatter, H., Helmstaedter, C., Radbruch, A., Surges, R., Schultz, T., Rüber, T., 2025. Structural White Matter Correlates of the Crowding Effect: Insights From a Tractography Study of the Arcuate Fasciculus Post-Hemispherotomy. *Human brain mapping* 46 (9), e70258. <https://doi.org/10.1002/hbm.70258>.
- Boccuni, L., Abellaneda-Pérez, K., Martín-Fernández, J., Leno-Colorado, D., Roca-Ventura, A., Prats Bisbe, A., Buloz-Osorio, E.A., Bartres-Faz, D., Bargalló, N., Cabello-Toscano, M., Pariente, J.C., Muñoz-Moreno, E., Trompetto, C., Marinelli, L., Villalba-Martínez, G., Duffau, H., Pascual-Leone, A., Tormos Muñoz, J.M., 2023. Neuromodulation-induced prehabilitation to leverage neuroplasticity before brain tumor surgery: A single-cohort feasibility trial protocol. *Frontiers in Neurology* 14. <https://www.frontiersin.org/articles/10.3389/fneur.2023.1243857>.
- Boccuni, L., Roca-Ventura, A., Buloz-Osorio, E., Leno-Colorado, D., Martín-Fernández, J., Cabello-Toscano, M., Perellón-Alfonso, R., Pariente Zorrilla, J.C., Laredo, C., Garrido, C., Muñoz-Moreno, E., Bargalló, N., Villalba, G., Martínez-Ricarte, F., Trompetto, C., Marinelli, L., Sacchet, M.D., Bartres-Faz, D., Abellaneda-Pérez, K., Tormos Muñoz, J.M., 2024a. Exploring the neural basis of non-invasive prehabilitation in brain tumour patients: An fMRI-based case report of language network plasticity. *Frontiers in Oncology* 14, 1390542. <https://doi.org/10.3389/fonc.2024.1390542>.
- Boccuni, L., Roca-Ventura, A., Buloz-Osorio, E., Leno-Colorado, D., Delgado-Gallén, S., Cabello-Toscano, M., Perellón-Alfonso, R., Villalba-Martínez, G., Martínez-Ricarte, F., Martín-Fernández, J., Buxeda-Rodríguez, M., Conesa-Bertrán, G., Illueca-Moreno, M., Lladó-Carbó, E., Perla Y Perla, C., Garrido, C., Pariente, J.C., Laredo, C., Muñoz-Moreno, E., ... Tormos-Muñoz, J.M., 2024b. Non-invasive prehabilitation to foster widespread fMRI cortical reorganization before brain tumor surgery: Lessons from a case series. *Journal of Neuro-Oncology*. <https://doi.org/10.1007/s11060-024-04774-4>.
- Bolognini, N., Pascual-Leone, A., Fregni, F., 2009. Using non-invasive brain stimulation to augment motor training-induced plasticity. *Journal of neuroengineering and rehabilitation* 6, 8. <https://doi.org/10.1186/1743-0003-6-8>.
- Bray, F., Laversanne, M., Sung, H., Ferlay, J., Siegel, R.L., Soerjomataram, I., Jemal, A., 2024. Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA: A Cancer Journal for Clinicians* 74 (3), 229–263. <https://doi.org/10.3322/caac.21834>.
- Brown, T.J., Brennan, M.C., Li, M., Church, E.W., Brandmeir, N.J., Rakszawski, K.L., Patel, A.S., Rizk, E.B., Suki, D., Sawaya, R., Glantz, M., 2016. Association of the Extent of Resection With Survival in Glioblastoma: A Systematic Review and Meta-analysis. *JAMA Oncology* 2 (11), 1460. <https://doi.org/10.1001/jamaoncol.2016.1373>.
- Cappon, D.B., Pascual-Leone, A., 2024. Toward Precision Noninvasive Brain Stimulation. *The American journal of psychiatry* 181 (9), 795–805. <https://doi.org/10.1176/appi.ajp.20240643>.
- Chew, T., Ho, K.-A., Loo, C.K., 2015. Inter- and intra-individual variability in response to transcranial direct current stimulation (tDCS) at varying current intensities. *Brain Stimulation* 8, 1130–1137. <https://doi.org/10.1016/j.brs.2015.07.031>.
- Cirillo, S., Caulo, M., Pieri, V., Falini, A., Castellano, A., 2019. Role of Functional Imaging Techniques to Assess Motor and Language Cortical Plasticity in Glioma Patients: A Systematic Review. *Neural Plasticity* 2019, 4056436. <https://doi.org/10.1155/2019/4056436>.
- Collée, E., Vincent, A., Dirven, C., Satoer, D., 2022. Speech and Language Errors during Awake Brain Surgery and Postoperative Language Outcome in Glioma Patients: A Systematic Review. *Cancers* 14 (21), 5466. <https://doi.org/10.3390/cancers14215466>.
- Cramer, S.C., Sur, M., Dobkin, B.H., O'Brien, C., Sanger, T.D., Trojanowski, J.Q., Rumsey, J.M., Hicks, R., Cameron, J., Chen, D., Chen, W.G., Cohen, L.G., deCharms, C., Duffy, C.J., Eden, G.F., Fetz, E.E., Filart, R., Freund, M., Grant, S.J., Vinogradov, S., 2011. Harnessing neuroplasticity for clinical applications. *Brain* 134 (6), 1591–1609. <https://doi.org/10.1093/brain/awr039>.
- Dadario, N., Young, I., Zhang, X., Teo, C., Doyen, S., Sughrue, M., 2022. Prehabilitation and rehabilitation using data-driven, parcel-guided transcranial magnetic stimulation treatment for brain tumor surgery: Proof of concept case report. *Brain Network and Modulation* 1 (1), 48. <https://doi.org/10.4103/2773-2398.340144>.
- de Lange, A.G., Bråthen, A.C.S., Rohani, D.A., Grydeland, H., Fjell, A.M., Walhovd, K.B., 2017. The effects of memory training on behavioral and microstructural plasticity in young and older adults. *Human brain mapping* 38 (11), 5666–5680. <https://doi.org/10.1002/hbm.23756>.
- Deorah, S., Lynch, C.F., Sibenaller, Z.A., Ryken, T.C., 2006. Trends in brain cancer incidence and survival in the United States: Surveillance, Epidemiology, and End Results Program, 1973 to 2001. *Neurosurgical Focus* 20 (4), E1. <https://doi.org/10.3171/foc.2006.20.4.E1>.
- Duffau, H., 2005. Lessons from brain mapping in surgery for low-grade glioma: insights into associations between tumour and brain plasticity. *The Lancet. Neurology* 4 (8), 476–486. [https://doi.org/10.1016/S1474-4422\(05\)70140-X](https://doi.org/10.1016/S1474-4422(05)70140-X).
- Duffau, H., 2014. The huge plastic potential of adult brain and the role of connectomics: New insights provided by serial mappings in glioma surgery. *Cortex* 58, 325–337. <https://doi.org/10.1016/j.cortex.2013.08.005>.
- Ekert, J.O., Goyal, A., Young, J.S., Hervey-Jumper, S.L., Berger, M.S., 2024. Interventional neurorehabilitation for glioma patients: A systematic review. *Neuro-Oncology Practice* 11 (6), 679–690. <https://doi.org/10.1093/nop/npae066>.
- Engelhardt, M., Grittner, U., Krieg, S., Picht, T., 2023. Preconditioning of the motor network with repetitive navigated transcranial magnetic stimulation (rTMS) to improve oncological and functional outcome in brain tumor surgery: A study protocol for a randomized, sham-controlled, triple-blind clinical trial. *Trials* 24 (1), 638. <https://doi.org/10.1186/s13063-023-07640-2>.
- Ewbank, M., Lawson, R., Henson, R.N., Rowe, J.B., Passamonti, L., Calder, A.J., 2011. Changes in “top-down” connectivity underlie repetition suppression in the ventral visual pathway. *The Journal of Neuroscience* 31 (15), 5635–5642. <https://doi.org/10.1523/jneurosci.5013-10.2011>.
- Fan, Y., Zhang, X., Gao, C., Jiang, S., Wu, H., Liu, Z., Dou, T., 2022. Burden and trends of brain and central nervous system cancer from 1990 to 2019 at the global, regional, and country levels. *Archives of Public Health* 80, 209. <https://doi.org/10.1186/s13690-022-00965-5>.
- Fedorenko, E., Ivanova, A.A., Regev, T.I., 2024. The language network as a natural kind within the broader landscape of the human brain. *Nature Reviews Neuroscience* 25 (5), 289–312. <https://doi.org/10.1038/s41583-024-00802-4>.
- Fisicaro, R.A., Jost, E., Shaw, K., Brennan, N.P., Peck, K.K., Holodny, A.I., 2016. Cortical Plasticity in the Setting of Brain Tumors. *Topics in Magnetic Resonance Imaging: TMRI* 25 (1), 25–30. <https://doi.org/10.1097/RMR.0000000000000077>.
- Fitzgerald, P.B., Fountain, S., Daskalakis, Z.J., 2006. A comprehensive review of the effects of rTMS on motor cortical excitability and inhibition. *Clinical Neurophysiology* 117 (12), 2584–2596. <https://doi.org/10.1016/j.clinph.2006.06.712>.
- François, C., Ripollés, P., Ferreri, L., Muchart, J., Sierpowska, J., Fons, C., Solé, J., Rebollo, M., Zatorre, R.J., Garcia-Alix, A., Bosch, L., Rodríguez-Fornells, A., 2019. Right structural and functional reorganization in four-year-old children with perinatal arterial ischemic stroke predict language production. *eNeuro* 6 (4). <https://doi.org/10.1523/ENEURO.0447-18.2019>. Article ENEURO.0447-18.2019.
- Gatica, M., Atkinson-Clement, C., Coronel-Oliveros, C., Alkhawashki, M., Mediano, P.A.M., Tagliazucchi, E., Rosas, F.E., Kaiser, M., Petri, G., 2025. Understanding the high-order network plasticity mechanisms of ultrasound neuromodulation. *PLoS Computational Biology* 21, e1013514. <https://doi.org/10.1371/journal.pcbi.1013514>.

- Geranmayeh, F., Brownsett, S.L.E., Wise, R.J.S., 2014. Task-induced brain activity in aphasic stroke patients: What is driving recovery? *Brain* 137 (10), 2632–2648. <https://doi.org/10.1093/brain/awu163>.
- Ghinda, D.C., Wu, J.S., Duffau, H., 2023. Neuroplasticity in diffuse low-grade gliomas: From fundamental concepts to clinical translation. *Cancers* 15 (14), 3698.
- Gobel, E.W., Parrish, T.B., Reber, P.J., 2011. Neural correlates of skill acquisition: decreased cortical activity during a serial interception sequence learning task. *NeuroImage* 58 (4), 1150–1157. <https://doi.org/10.1016/j.neuroimage.2011.06.090>.
- Goldsworthy, M.R., Hordacre, B., Ridding, M.C., 2021. Effects of rTMS on the brain: Is there value in variability? *Cortex* 139, 43–59. <https://doi.org/10.1016/j.cortex.2021.02.024>.
- Gracco, V.L., Tremblay, P., Pike, B., 2005. Imaging speech production using fMRI. *NeuroImage* 26 (1), 294–301. <https://doi.org/10.1016/j.neuroimage.2005.11.002>.
- Halko, M.A., Farzan, F., Eldaief, M.C., Schmahmann, J.D., Pascual-Leone, A., 2014. Intermittent theta-burst stimulation of the lateral cerebellum increases functional connectivity of the default network. *Journal of Neuroscience* 34 (36), 12049–12056. <https://doi.org/10.1523/JNEUROSCI.1776-14.2014>.
- Hallett, M., 2007. Transcranial magnetic stimulation: A primer. *Neuron* 55 (2), 187–199. <https://doi.org/10.1016/j.neuron.2007.06.026>.
- Hamada, M., Rothwell, J.C., 2015. Introduction to non-convulsive brain stimulation: Focus on transcranial magnetic stimulation. In: Reti, I.M. (Ed.), *Brain Stimulation: Methodologies and Interventions*. John Wiley & Sons, pp. 149–164. <https://doi.org/10.1002/9781118568323.ch9>.
- Hamada, M., Murase, N., Hasan, A., Balaratnam, M., Rothwell, J.C., 2013. The role of interneuron networks in driving human motor cortical plasticity. *Cerebral cortex* (New York, N.Y. : 1991) 23 (7), 1593–1605. <https://doi.org/10.1093/cercor/bhs147>.
- Hartwigsen, G., Volz, L.J., 2021. Probing rapid network reorganization of motor and language functions via neuromodulation and neuroimaging. *NeuroImage* 224, 117449. <https://doi.org/10.1016/j.neuroimage.2020.117449>.
- Hartwigsen, G., Bzdok, D., Klein, M., Wawrzyniak, M., Stockert, A., Wrede, K., Classen, J., Saur, D., 2017. Rapid short-term reorganization in the language network. *eLife* 6, e25964. <https://doi.org/10.7554/eLife.25964>.
- Hartwigsen, G., 2016. Adaptive Plasticity in the Healthy Language Network: Implications for Language Recovery after Stroke. *Neural plasticity* 2016, 9674790. <https://doi.org/10.1155/2016/9674790>.
- Hickok, G., Poeppel, D., 2007. The cortical organization of speech processing. *Nature Reviews Neuroscience* 8 (5), 393–402. <https://doi.org/10.1038/nrn2113>.
- Jannati, A., Oberman, L.M., Rotenberg, A., Pascual-Leone, A., 2023. Assessing the mechanisms of brain plasticity by transcranial magnetic stimulation. *Neuropsychopharmacology: Official Publication of the American College of Neuropsychopharmacology* 48 (1), 191–208. <https://doi.org/10.1038/s41386-022-01453-8>.
- Kirton, A., Metzler, M.J., Craig, B.T., Hilderley, A., Dunbar, M., Giuffrè, A., Wrightson, J., Zewdie, E., Carlson, H.L., 2021. Perinatal stroke: Mapping and modulating developmental plasticity. *Nature Reviews Neurology* 17 (7), 415–432. <https://doi.org/10.1038/s41582-021-00503-x>.
- Kirwan, C.B., Bjorn, D.K., Anderson, B.B., Vance, A., Eargle, D., Jenkins, J.L., 2020. Repetition of Computer Security Warnings Results in Differential Repetition Suppression Effects as Revealed With Functional MRI. *Frontiers in psychology* 11, 528079. <https://doi.org/10.3389/fpsyg.2020.528079>.
- Klooster, D.C.W., Ferguson, M.A., Boon, P.A.J.M., Baeken, C., 2023. Personalizing rTMS parameters for depression treatment using multimodal neuroimaging. *Biological Psychiatry: Cognitive Neuroscience & Neuroimaging*. <https://doi.org/10.1016/j.bpsc.2021.11.004>.
- López-Alonso, V., Cheeran, B., Río-Rodríguez, D., Fernández-Del-Olmo, M., 2014. Inter-individual variability in response to non-invasive brain stimulation paradigms. *Brain Stimulation* 7 (3), 372–380. <https://doi.org/10.1016/j.brs.2014.02.004>.
- Lang, S., Gan, L.S., McLennan, C., Kirton, A., Monchi, O., Kelly, J.J.P., 2020. Preoperative transcranial direct current stimulation in glioma patients: A proof of concept pilot study. *Frontiers in Neurology* 11, 593950. <https://doi.org/10.3389/fneur.2020.593950>.
- Lee, S.-M., Henson, R.N.A., Lin, C.-Y., 2020. Neural correlates of repetition priming: A coordinate-based meta-analysis of fMRI studies. *Frontiers in Human Neuroscience* 14, 565114. <https://doi.org/10.3389/fnhum.2020.565114>.
- Lefaucheur, J.-P., Aleman, A., Baeken, C., Benninger, D.H., Brunelin, J., Di Lazzaro, V., Filipović, S.R., Grefkes, C., Hasan, A., Hummel, F.C., Jääskeläinen, S.K., Langguth, B., Leocani, L., Londero, A., Nardone, R., Nguyen, J.-P., Nyffeler, T., Oliveira-Maia, A.J., Oliviero, A., Padberg, F., Ziemann, U., 2020. Evidence-based guidelines on the therapeutic use of repetitive transcranial magnetic stimulation (rTMS): An update (2014–2018). *Clinical Neurophysiology* 131 (2), 474–528. <https://doi.org/10.1016/j.clinph.2019.11.002>.
- Li, Y., Li, P., Yang, Q.X., Eslinger, P.J., Sica, C.T., Karunanayaka, P., 2017. Lexical-semantic search under different covert verbal fluency tasks: An fMRI study. *Frontiers in Behavioral Neuroscience* 11, 131. <https://doi.org/10.3389/fnbeh.2017.00131>.
- Lidzba, K., Staudt, M., Wilke, M., Grodd, W., Krägeloh-Mann, I., 2006. Lesion-induced right-hemispheric language and organization of nonverbal functions. *Neuroreport* 17 (9), 929–933. <https://doi.org/10.1097/01.wnr.0000221841.12632.d6>.
- Liston, C., Chen, A.C., Zebly, B.D., Drysdale, A.T., Gordon, R., Leuchter, B., Voss, H.U., Casey, B.J., Etkin, A., Dubin, M.J., 2014. Default Mode Network Mechanisms of Transcranial Magnetic Stimulation in Depression. *Biological Psychiatry* 76 (7), 517–526. <https://doi.org/10.1016/j.biopsych.2014.01.023>.
- Liu, Z., Ma, H., Poole, V., Wang, X., Wang, Z., Yang, Y., Meng, L., Manor, B., Zhou, J., Feng, T., 2018. Effects of multi-session repetitive transcranial magnetic stimulation on motor control and spontaneous brain activity in multiple system atrophy: A pilot study. *Frontiers in Behavioral Neuroscience* 12, 90. <https://doi.org/10.3389/fnbeh.2018.00090>.
- Maeda, F., Keenan, J.P., Tormos, J.M., Topka, H., Pascual-Leone, A., 2000. Interindividual variability of the modulatory effects of repetitive transcranial magnetic stimulation on cortical excitability. *Experimental Brain Research* 133 (4), 425–430. <https://doi.org/10.1007/s002210000432>.
- Manso-Ortega, L., De Frutos-Sagastuy, L., Gisbert-Muñoz, S., Salamon, N., Qiao, J., Walshaw, P., Quiñones, I., Polczyńska, M.M., 2023. Grey Matter Reshaping of Language-Related Regions Depends on Tumor Lateralization. *Cancers* 15 (15), 3852. <https://doi.org/10.3390/cancers15153852>.
- Martínez-Lozada, P.S., Poz-Neira, J., Leon-Rojas, J.E., 2025. From tumor to network: Functional connectome heterogeneity and alterations in brain tumors—A multimodal neuroimaging narrative review. *Cancers* 17 (13), 2174. <https://doi.org/10.3390/cancers17132174>.
- Martin, K.C., Ketchabaw, W.T., Turkeltaub, P.E., 2022. Plasticity of the language system in children and adults. *Handbook of Clinical Neurology* 184, 397. <https://doi.org/10.1016/B978-0-12-819410-2.00021-7>.
- Martin-Trias, P., Lanteaume, L., Solana, E., Cassé-Perrot, C., Fernández-Cabello, S., Babiloni, C., Marzano, N., Junqué, C., Rossini, P.M., Micallef, J., Truillet, R., Charles, E., Jouve, E., Bordet, R., Santamaria, J., Jovicich, J., Rossi, S., Pascual-Leone, A., Blin, O., Bartres-Faz, D., 2018. Adaptability and reproducibility of a memory disruption rTMS protocol in the PharmaCog IMI European project. *Scientific Reports* 8, 9371. <https://doi.org/10.1038/s41598-018-27502-1>.
- Meinzer, M., Lindenberg, R., Antonenko, D., Flaisch, T., Floel, A., 2013. Anodal Transcranial Direct Current Stimulation Temporarily Reverses Age-Associated Cognitive Decline and Functional Brain Activity Changes. *Journal of Neuroscience* 33 (30), 12470–12478. <https://doi.org/10.1523/JNEUROSCI.5743-12.2013>.
- Meinzer, M., Lindenberg, R., Phan, M.T., Ulm, L., Volk, C., Flöel, A., 2015. Transcranial direct current stimulation in mild cognitive impairment: Behavioral effects and neural mechanisms. *Alzheimer's & dementia: the journal of the Alzheimer's Association* 11 (9), 1032–1040. <https://doi.org/10.1016/j.jalz.2014.07.159>.
- Mesulam, M.M., 1998. From sensation to cognition. *Brain* 121 (6), 1013–1052. <https://doi.org/10.1093/brain/121.6.1013>.
- Mohr, H., Wolfensteller, U., Betzel, R.F., Misić, B., Sporns, O., Richiardi, J., Ruge, H., 2016. Integration and segregation of large-scale brain networks during short-term task automatization. *Nature Communications* 7, 13217. <https://doi.org/10.1038/ncomms13217>.
- Momi, D., Wang, Z., Parmigiani, S., Mikulan, E., Bastiaens, S.P., Oveisi, M.P., Griffiths, J. D., 2025. Stimulation mapping and whole-brain modeling reveal gradients of excitability and recurrence in cortical networks. *Nature Communications* 16, 3222. <https://doi.org/10.1038/s41467-025-58187-6>.
- Morell, A.A., Eichberg, D.G., Shah, A.H., Luther, E., Lu, V.M., Kader, M., Higgins, D.M.O., Merenzon, M., Patel, N.V., Komotar, R.J., Ivan, M.E., 2022. Using machine learning to evaluate large-scale brain networks in patients with brain tumors: Traditional and non-traditional eloquent areas. *Neuro-oncology advances* 4 (1), vdacl42. <https://doi.org/10.1093/naonj/vdacl42>.
- Nieberlein, L., Ramm, S., Gussew, A., Prell, J., Hartwigsen, G., 2023. Reorganization and Plasticity of the Language Network in Patients with Cerebral Gliomas. *NeuroImage: Clinical* 37, 103326. <https://doi.org/10.1016/j.nicl.2023.103326>.
- Nitsche, M.A., Paulus, W., 2000. Excitability changes induced in the human motor cortex by weak transcranial direct current stimulation. *The Journal of Physiology* 527 (3), 633–639. <https://doi.org/10.1111/j.1469-7793.2000.t01-1-00633.x>.
- Nitsche, M.A., Cohen, L.G., Wassermann, E.M., Priori, A., Lang, N., Antal, A., Paulus, W., Hummel, F., Boggio, P.S., Fregni, F., Pascual-Leone, A., 2008. Transcranial direct current stimulation: State of the art 2008. *Brain Stimulation* 1 (3), 206–223. <https://doi.org/10.1016/j.brs.2008.06.004>.
- Ostrom, Q.T., Price, M., Neff, C., Cioffi, G., Waite, K.A., Kruchko, C., Barnholtz-Sloan, J. S., 2023. CBTRUS Statistical Report: Primary Brain and Other Central Nervous System Tumors Diagnosed in the United States in 2016–2020. *Neuro-oncology* 25 (12 Suppl 2), iv1–iv99. <https://doi.org/10.1093/neuonc/noad149>.
- Pascual-Leone, A., Amedi, A., Fregni, F., Merabet, L.B., 2005. The plastic human brain cortex. *Annual review of neuroscience* 28, 377–401. <https://doi.org/10.1146/annurev.neuro.27.070203.144216>.
- PDQ Adult Treatment Editorial Board, 2024. Adult central nervous system tumors treatment (PDQ®): Patient version. PDQ cancer information summaries [Internet]. National Cancer Institute (US). <https://www.ncbi.nlm.nih.gov/books/NBK66023/>.
- Peña-Casanova, J., 2005. Programa integrado de exploración neuropsicológica: Test Barcelona-Revisado (TBR). Masson, Barcelona.
- Perellón-Alfonso, R., Kralik, M., Pileckyte, I., Prinic, M., Bon, J., Matzhold, C., Fischer, B., Šlahorová, P., Pirtošek, Z., Rothwell, J., Kojovic, M., 2018. Similar effect of intermittent theta burst and sham stimulation on corticospinal excitability: A 5-day repeated sessions study. *The European journal of neuroscience* 48 (4), 1990–2000. <https://doi.org/10.1111/ejn.14077>.
- Perellón-Alfonso, R., Redondo-Camós, M., Abellana-Pérez, K., Cattaneo, G., Delgado-Gallén, S., España-Irla, G., Solana Sánchez, J., Tormos, J.M., Pascual-Leone, A., Bartres-Faz, D., 2022. Prefrontal reactivity to TMS perturbation as a toy model of mental health outcomes during the COVID-19 pandemic. *iScience* 25 (8), 104508. <https://doi.org/10.1016/j.isci.2022.104508>.
- Pi, Y.-L., Wu, X.-H., Wang, F.-J., Liu, K., Wu, Y., Zhu, H., Zhang, J., 2019. Motor skill learning induces brain network plasticity: A diffusion-tensor imaging study. *PLOS ONE* 14 (2), e0210015. <https://doi.org/10.1371/journal.pone.0210015>.
- Polanía, R., Nitsche, M.A., Ruff, C.C., 2018. Studying and modifying brain function with non-invasive brain stimulation. *Nature neuroscience* 21 (2), 174–187. <https://doi.org/10.1038/s41593-017-0054-4>.

- R Core Team, 2022. R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. URL: <https://www.R-project.org/>.
- Rivera-Rivera, P.A., Rios-Lago, M., Sanchez-Casarrubios, S., Salazar, O., Yus, M., González-Hidalgo, M., Sanz, A., Avecillas-Chasin, J., Alvarez-Linera, J., Pascual-Leone, A., Oliviero, A., Barcia, J.A., 2017. Cortical plasticity catalyzed by prehabilitation enables extensive resection of brain tumors in eloquent areas. *Journal of Neurosurgery* 126 (4), 1323–1333. <https://doi.org/10.3171/2016.2.JNS152485>.
- Roh, T.H., Kim, S.H., 2023. Supramaximal Resection for Glioblastoma: Redefining the Extent of Resection Criteria and Its Impact on Survival. *Brain tumor research and treatment* 11 (3), 166–172. <https://doi.org/10.14791/btrt.2023.0012>.
- Rossini, P.M., Burke, D., Chen, R., Cohen, L.G., Daskalakis, Z., Di Iorio, R., Di Lazzaro, V., Ferreri, F., Fitzgerald, P.B., George, M.S., Hallett, M., Lefaucheur, J.P., Langguth, B., Matsumoto, H., Miniussi, C., Nitsche, M.A., Pascual-Leone, A., Paulus, W., Rossi, S., Ziemann, U., 2015. Non-invasive electrical and magnetic stimulation of the brain, spinal cord, roots and peripheral nerves: Basic principles and procedures for routine clinical and research application. *Clinical Neurophysiology* 126 (6), 1071–1107. <https://doi.org/10.1016/j.clinph.2015.02.001>.
- RStudio Team, 2022. RStudio: Integrated Development for R. RStudio, PBC, Boston, MA. URL: <https://www.posit.co/>.
- Salari, N., Ghasemi, H., Fatahian, R., Mansouri, K., Dokaneheifard, S., Shiri, M.H., Hemmati, M., Mohammadi, M., 2023. The global prevalence of primary central nervous system tumors: A systematic review and meta-analysis. *European Journal of Medical Research* 28, 39. <https://doi.org/10.1186/s40001-023-01011-y>.
- Sanai, N., Berger, M.S., 2008. Glioma extent of resection and its impact on patient outcome. *Neurosurgery* 62 (4), 753–764. <https://doi.org/10.1227/01.neu.0000318159.21731.cf> discussion 264–266.
- Serrano-Castro, P.J., Ros-López, B., Fernández-Sánchez, V.E., García-Casares, N., Muñoz-Becerra, L., Cabezedo-García, P., Aguilar-Castillo, M.J., Vidal-Denis, M., Cruz-Andreotti, E., Postigo-Pozo, M.J., Estivill-Torrús, G., Ibañez-Botella, G., 2020. Neuroplasticity and Epilepsy Surgery in Brain Eloquent Areas: Case Report. *Frontiers in Neurology* 11, 698. <https://doi.org/10.3389/fneur.2020.00698>.
- Shah, H.A., Duehr, J., Abramyan, A., Mittelman, L., Galvez, R., Winby, T., Silverstein, J. W., D'Amico, R.S., 2025. Enhancing brain tumor surgery precision with multimodal connectome imaging: Structural and functional connectivity in language-dominant areas. *Clinical Neurology and Neurosurgery* 249, 108760. <https://doi.org/10.1016/j.clineuro.2024.108760>.
- Solana, J., Cáceres, C., García-Molina, A., Opisso, E., Roig, T., Tormos, J.M., Gómez, E.J., 2014. Improving brain injury cognitive rehabilitation by personalized telerehabilitation services: Guttman neuropersonal trainer. *IEEE Journal of Biomedical and Health Informatics* 19 (1), 124–131. <https://doi.org/10.1109/JBHI.2014.2354537>.
- Sousa, A.E., Mahdid, Y., Brodeur, M., Lepage, M., 2021. A feasibility study on the use of the method of loci for improving episodic memory performance in schizophrenia and non-clinical subjects. *Frontiers in Psychology* 12, 612681. <https://doi.org/10.3389/fpsyg.2021.612681>.
- Stagg, C.J., Antal, A., Nitsche, M.A., 2018. Physiology of Transcranial Direct Current Stimulation. *The Journal of ECT* 34 (3), 144–152. <https://doi.org/10.1097/YCT.0000000000000510>.
- Stam, D., Huang, Y.-A., Vansteelandt, K., Sunaert, S., Peeters, R., Vrancken, L., VandenStock, J., 2021. Long-term fMRI adaptation depends on adapter response in face-selective cortex. *Communications Biology* 4, 731. <https://doi.org/10.1038/s42003-021-02235-6>.
- Sydnor, V.J., Larsen, B., Bassett, D.S., Alexander-Bloch, A., Fair, D.A., Mackey, A.P., Milham, M.P., Pines, A., Roalf, D.R., Seidlitz, J., Xu, T., Raznahan, A., Satterthwaite, T.D., 2021. Neurodevelopment of the association cortices: Patterns, mechanisms, and implications for psychopathology. *Neuron* 109 (18), 2820–2846. <https://doi.org/10.1016/j.neuron.2021.06.016>.
- Tilton-Bolowsky, V., Stockbridge, M.D., Hillis, A.E., 2024. Remapping and Reconnecting the Language Network after Stroke. *Brain Sciences* 14 (5), 419. <https://doi.org/10.3390/brainsci14050419>.
- Vázquez-Rodríguez, B., et al., 2019. Gradients of structure-function tethering across neocortex. *Proceedings of the National Academy of Sciences* 116 (42), 21248–21256.
- Vallence, A.M., Goldsworthy, M.R., Hodyl, N.A., Semmler, J.G., Pitcher, J.B., Ridding, M. C., 2015. Inter- and intra-subject variability of motor cortex plasticity following continuous theta-burst stimulation. *Neuroscience* 304, 266–278. <https://doi.org/10.1016/j.neuroscience.2015.07.043>.
- Vannini, P., Hedden, T., Sullivan, C., Sperling, R., 2012. Differential functional response in the posteromedial cortices and hippocampus to stimulus repetition during successful memory encoding. *Human Brain Mapping* 34 (7), 1568–1578. <https://doi.org/10.1002/hbm.22011>.
- Vogrinic, B., Mooijman, S., Vincent, A., Bulté, B., De Witte, E., Visch-Brink, E., Satoer, D., 2025. Precision in long-term language evaluation after awake brain tumor surgery. *Neuro-Oncology Practice*. <https://doi.org/10.1093/nop/npaf090>.
- Voss, M.W., Prakash, R.S., Erickson, K.I., Basak, C., Chaddock, L., Kim, J.S., Kramer, A.F., 2010. Plasticity of brain networks in a randomized intervention trial of exercise training in older adults. *Frontiers in Aging Neuroscience* 2, 32. <https://doi.org/10.3389/fnagi.2010.00032>.
- Wang, J.X., Rogers, L.M., Gross, E.Z., Ryals, A.J., Dokucu, M.E., Brandstatt, K.L., Hermiller, M.S., Voss, J.L., 2014. Targeted enhancement of cortical-hippocampal brain networks and associative memory. *Science (New York, N.Y.)* 345 (6200), 1054–1057. <https://doi.org/10.1126/science.1252900>.
- Wang, J.X., Rogers, L.M., Gross, E.Z., Ryals, A.J., Dokucu, M.E., Brandstatt, K.L., Hermiller, M.S., Voss, J.L., 2014. Targeted enhancement of cortical-hippocampal brain networks and associative memory. *Science* 345 (6200), 1054–1057. <https://doi.org/10.1126/science.1252900>.
- Wechsler, D., 2008. *Wechsler Adult Intelligence Scale—Fourth Edition (WAIS-IV)*. Pearson.
- Yeo, B.T.T., Krienen, F.M., Sepulcre, J., Sabuncu, M.R., Lashkari, D., Hollinshead, M., Roffman, J.L., Smoller, J.W., Zöllei, L., Polimeni, J.R., Fischl, B., Liu, H., Buckner, R. L., 2011. The organization of the human cerebral cortex estimated by intrinsic functional connectivity. *Journal of Neurophysiology* 106 (3), 1125–1165. <https://doi.org/10.1152/jn.00338.2011>.
- Zhang, P., Ilagan, R., Bai, Y., Zhang, X., Deng, Y., Ding, Y., 2021. Editorial: Plasticity and reconstruction of neural network in brain injury. *Frontiers in Cellular Neuroscience* 15, 710499. <https://doi.org/10.3389/fncel.2021.710499>.
- Zhu, H., Korona, E., Shirani, S., Samadian, F., Alarcon, G., Valentin, A., Stavropoulos, I., 2025. Electrical cortical stimulation for language mapping in epilepsy surgery—A systematic review. *Brain Sciences* 15 (12), 1267. <https://doi.org/10.3390/brainsci15121267>.