“Neural dynamics underlying object and action naming across languages: Insights from health and disease”

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Declaration of Authorship

I, Shuang Geng, declare that this thesis entitled “Neural dynamics underlying object and action naming across languages: Insights from health and disease” and the work presented in it are my own. I confirm that:

- This work was done wholly or mainly while in candidature for a research degree at the University of the Basque Country.
- No part of this thesis has previously been submitted for a degree or any other qualification at this University or any other institution.
- Where I have consulted the published work of others, this is always clearly attributed.
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- I have acknowledged all main sources of help.

- Where the thesis is based on work done by myself jointly with others, I have made clear exactly what was done by others and what I have contributed myself.

Shuang Geng

Signed:

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Resumen en castellano

De manera casi universal, los idiomas poseen palabras para denotar objetos (sustantivos) y palabras para denotar acciones (verbos). Investigaciones previas sostienen que, al menos en lo que respecta a su organización conceptual, estas categorías se representan de forma diferente en el cerebro. En este contexto, se ha sugerido (Gleichgerrcht et al., 2016; Lubrano, Filleron, Demonet, & Roux, 2014; Shapiro, Moo, & Caramazza, 2006; Shapiro et al., 2005; Vigliocco, Vinson, Druks, Barber, & Cappa, 2011); que la representación del conocimiento de objetos estaría mediada por regiones infero-temporales (sistema ventral), mientras que el conocimiento de acciones estaría mediado por regiones fronto-parietales (sistema dorsal).

A pesar de la amplia investigación sobre el tema, aún no se cuenta con una visión completa de la dinámica neural subyacente a este proceso, que incluye no solo los patrones espaciales involucrados (e.g., localización de los efectos), sino también los ritmos cerebrales y sus modulaciones en el tiempo (e.g., patrones spectro-temporales). Además, la potencial variabilidad de la representación de dicho conocimiento en los distintos idiomas, así como su posible reorganización en presencia de daño cerebral, distan aún de ser comprendidos.

En esta tesis doctoral se abordan dos preguntas principales: (1) ¿Cuáles son los correlatos neurales que subyacen a la denominación de sustantivos y verbos en los diferentes idiomas que habla una persona? (2) ¿Cómo afecta la presencia de un tumor cerebral en las vías ventrales y dorsales al procesamiento léxico-semántico de sustantivos y verbos?

Para dar respuesta a estos interrogantes, se recolectaron datos conductuales y registros magnetoencefalográficos (MEG) mientras los participantes realizaban una tarea de denominación de imágenes (objetos y acciones), la prueba estándar para investigar la producción del habla y los procesos neurocognitivos asociados a la misma. Se evaluaron hablantes sanos monolingües y bilingües, así como pacientes con tumores cerebrales en regiones ventrales y dorsales del hemisferio izquierdo, tanto antes como después de la cirugía para la extracción del tumor.

En primer lugar, nuestros hallazgos en hablantes monolingües sanos muestran que los ritmos cerebrales alfa-beta (8-25 Hz) desempeñan un papel crítico en el acceso a las representaciones léxico-semánticas de sustantivos y verbos durante la producción del habla.

Específicamente, observamos (Amoruso et al., 2021) una disociación de los ritmos alfa-beta en las vías ventrales y dorsales durante la recuperación semántica (~250-500 ms) del conocimiento de objetos (sustantivos) y acciones (verbos), respectivamente. Este hallazgo sugiere que la producción del habla involucra redes parcialmente diferentes dependiendo de la categoría semántica que se procese.

En segundo lugar, nuestros resultados en bilingües sanos altamente competentes (Geng et al., 2022) muestran que dicha disociación en los ritmos alfa-beta es similar en la L1 y la L2. Este resultado es consistente con la hipótesis de convergencia semántica (Abutalebi, 2008; Abutalebi & Green, 2007; Hut & Leminen, 2017), la cual postula que a medida que la competencia lingüística en la L2 mejora, las representaciones conceptuales de ambos idiomas tienden a procesarse de manera similar, al menos en lo que respecta al nivel semántico.

En tercer lugar, nuestros resultados revelan que las oscilaciones beta (13-28 Hz) desempeñan un papel fundamental en la compensación del lenguaje en pacientes con tumores cerebrales (Amoruso et al., 2021, Geng et al., 2023). Estas oscilaciones son particularmente intrigantes, ya que respaldan una amplia gama de funciones cognitivas. Hasta ahora, se han propuesto varias explicaciones para comprender su función mecanística en los seres humanos. Una de estas explicaciones sugiere que las oscilaciones beta facilitan interacciones de alto nivel entre áreas cerebrales que se encuentran espacialmente distantes (Kopell et al., 2001). Esta característica adquiere una importancia crucial al considerar los cambios funcionales que surgen debido a la presencia de un tumor, los cuales pueden afectar la comunicación a nivel de redes y provocar el reclutamiento compensatorio de áreas remotas en el hemisferio contralateral. Por lo tanto, los ritmos beta se convierten en un candidato plausible para respaldar el fenómeno de "migración" de funciones lingüísticas desde áreas dañadas hacia áreas cerebrales sanas.

Esta idea encuentra respaldo en la evidencia neurofisiológica proveniente de pacientes con accidente cerebrovascular, quienes muestran un desplazamiento del procesamiento del lenguaje hacia el hemisferio derecho (contralateral a la lesión) mediado por bandas de baja frecuencia, incluyendo la banda beta (Kielar, Panamsky, Links, & Meltzer, 2015; Piai, Meyer, Dronkers, & Knight, 2017; Spironelli, Manfredi, & Angrilli, 2013; Traut et al., 2019).

Cabe destacar que las modulaciones beta observadas en los pacientes monolingües presentaron variaciones que dependían de la localización del daño y la categoría semántica. En el caso de las lesiones ventrales se observó una compensación longitudinal (post- vs. pre-cirugía) selectiva para el nombrado de objetos. La misma involucró el reclutamiento del giro frontal inferior izquierdo y del giro temporal medio en el hemisferio derecho. Por otra parte, en el caso de las lesiones dorsales, se encontró una compensación selectiva para el nombrado de acciones. La misma involucró el reclutamiento de una red dorsal homóloga incluyendo áreas fronto-parietales derechas.

En ambos casos, estas modulaciones reflejaron un aumento en la potencia de las ondas beta después de la cirugía, en un intervalo de tiempo consistente con el procesamiento léxico-semántico. Además, independientemente de la ubicación del tumor, todos los pacientes mostraron una reorganización estructural longitudinal en el volumen de tractos específicos de la sustancia blanca, incluyendo el fascículo longitudinal superior (SLF) que conecta la corteza parietal y premotora (Kamali, Flanders, Brody, Hunter, & Hasan, 2014; Makris et al., 2005), el fascículo arcuato (AF) que conecta las áreas de Broca y Wernicke, y el fascículo fronto-occipital inferior (IFOF), que conecta regiones occipitales y frontales (Herbet, Moritz-Gasser, & Duffau, 2017). Esto sugiere que el impacto de los gliomas en el cerebro va más allá de su ubicación específica y puede desencadenar reorganizaciones a gran escala.

Por un lado, se ha asociado previamente el IFOF con el procesamiento semántico (Herbet et al., 2017). Por otro, el AF y el SLF se han relacionado con el procesamiento fonológico y la recuperación léxica durante la producción del habla, ya que su interrupción mediante estimulación eléctrica directa (DES) produce parafasias fonológicas y anomia, respectivamente (Sarubbo et al., 2015). Si bien nuestros resultados no nos permiten diferenciar específicamente qué funciones fueron compensadas en los pacientes, el hallazgo de una asociación positiva entre el aumento del volumen postoperatorio en el SLF del hemisferio derecho y una mayor potencia de las ondas beta en el mismo hemisferio, sugiere que los componentes de recuperación léxica fueron los más implicados.

Estos resultados son consistentes con estudios previos (Zhang et al., 2018) mostrando que los cambios en los patrones funcionales se correlacionan con cambios a nivel estructural, específicamente con un aumento en el volumen, lo que sugiere una respuesta acoplada entre estructura y función para hacer frente a la presencia del tumor.

Esta interpretación concuerda con nuestros hallazgos. Sin embargo, estos estudios solo analizaron datos preoperatorios. Aquí, presentamos evidencia preliminar que sugiere que dichos cambios estructurales pueden observarse tanto antes como después de la cirugía.

Finalmente, en el último estudio (Geng et al., 2023), mostramos que los pacientes bilingües con tumores en la ruta dorsal exhiben modulaciones selectivas en los ritmos beta para la denominación de acciones (pero no de objetos) y que dichas modulaciones son similares en ambos idiomas. De este modo, la presente tesis extiende los resultados sobre la "convergencia semántica" a la compensación selectiva en el cerebro bilingüe. No obstante, conviene destacar que dicha convergencia se evidenció solo antes de la cirugía para la extracción del tumor.

Contrariamente, tres meses después de la cirugía, se observaron patrones de compensación diferentes para la L1 y la L2. Específicamente, durante el procesamiento de acciones en la L1, se evidenció el reclutamiento de áreas cerebrales sanas ipsilesionales, destacando un papel predominante de las regiones frontales de control ejecutivo. En el caso de la L2, además de los patrones ipsilesionales, se observó un mayor reclutamiento del hemisferio derecho (es decir, contralesional). Estos resultados sugieren que el trauma causado por la cirugía, el cual puede impactar y destruir los patrones de reorganización logrados en presencia del tumor (Duffau, 2020), puede influir de manera diferencial en la L1 y la L2.

Este efecto puede depender, según estudios previos (Giussani, Roux, Lubrano, Gaini, & Bello, 2007), de la existencia de micro-territorios específicos para cada idioma. En otras palabras, aunque ambos idiomas pueden estar representados conjuntamente en regiones frontales, parietales o temporales más amplias, es posible que dentro de dichas regiones exista especificidad para uno u otro idioma (Paradis, 2004).

En su conjunto, los resultados de esta tesis son de gran relevancia para nuestra comprensión actual de los principios que rigen la representación y recuperación del conocimiento semántico asociado a sustantivos (objetos) y verbos (acciones) en individuos con diversos perfiles lingüísticos. Más crucialmente, esta tesis establece un puente entre la ciencia experimental y la práctica clínica a través de un enfoque translacional: los conocimientos derivados de la presente investigación pueden utilizarse para tomar decisiones neurooncológicas basadas en evidencia científica, con el potencial de mejorar el bienestar y preservar las habilidades lingüísticas de los pacientes.

En consecuencia, nuestros hallazgos poseen implicaciones teóricas y clínicas significativas para la comprensión del fenómeno de (re)organización del lenguaje en la salud y la enfermedad.

Abstract

Words representing objects (nouns) and words representing actions (verbs) are essential components of speech across languages. Previous studies have shown that the lexico-semantic processing of object and action knowledge depends on segregated ventral and dorsal pathways, respectively involving inferotemporal and frontoparietal nodes. Despite extensive research, a comprehensive understanding of the neural dynamics (including spatial, temporal, and spectral patterns) underlying this process and its potential variation across languages is currently missing. Furthermore, evidence supporting its functional reorganization in the presence of brain damage is scarse. This doctoral thesis addresses two critical questions: (1) What are the neural signatures of object and action naming across different languages? (2) How does the presence of brain tumors affecting ventral and dorsal pathways impact on the lexico-semantic processing of object and action knowledge? To answer these questions, we collected behavioral and MEG data while participants performed a picture-naming task, the gold standard for investigating speech production. We evaluated healthy monolingual and bilingual speakers, and brain tumor patients with low-grade gliomas in ventral and dorsal regions, both before and after surgery for tumor resection. Results from healthy participants showed segregated beta (13–28 Hz) power decreases in left ventral and dorsal pathways for object and action naming. These modulations occurred during a time-window associated with lexico-semantic processing (~250-500ms), supporting the notion that speech production involves partially different networks depending on the semantic category being processed. Interestingly, we found that these neural patterns overlapped across different languages (Spanish and Basque) in highly proficient bilingual speakers, suggesting that when individuals master both languages to a similar extent, category-based representations overlap at the semantic level. Finally, when longitudinally comparing patients' responses (post- vs. pre-surgery) we found beta modulations mimicking the category-based segregation showed by healthy individuals, with ventral and dorsal damage leading to selective compensation for object and action naming, respectively. A similar pattern was also observed in bilingual patients. Overall, these findings have important theoretical and clinical implications for language (re)organization in health and disease.

Content

1 Overview

1.1 Introduction

Human communication relies heavily on speech production, a seemingly effortless ability that actually involves a complex set of cognitive processes. While psycholinguistic models may differ on certain aspects, they generally agree that speech production involves three main stages (Piai & Zheng, 2019). The first stage is the retrieval and selection of the concept that the speaker wishes to express. The second stage involves the retrieval of the appropriate syntactic, morphological, and phonological information. Finally, the third stage, involves the post-lexical planning of articulation, as well as self-monitoring of speech output (Dell, 1986; Hickok, 2012; Levelt, Roelofs, & Meyer, 1999).

Most languages use nouns and verbs as the basic building blocks of speech during daily conversations (Robins, 1952). These two types of words serve distinct communicative purposes, with nouns typically referring to objects and verbs describing actions, events, or states of being (Kemmerer, 2014). During the last decade, an intense debate has developed around the neurobiological underpinnings of noun and verb representation in the human brain (Vigliocco et al., 2011). Despite this intense debate, the prevailing viewpoint is that, at least when considering these two grammatical classes at the semantic level (i.e., the representation and access of object and action knowledge, respectively), nouns and verbs involve partially distinct networks. In particular, processing object knowledge has been associated with the engagement of the ventral inferotemporal pathway, and action knowledge with the recruitment of the dorsal fronto-parietal network (Gleichgerrcht et al., 2016; Shapiro et al., 2006; Shapiro et al., 2005).

When considering the timing of these responses, neurophysiological differences between nouns and verbs have been reported in the P200 and N400 components, which are typically associated with lexical access and semantic processing, respectively (Carreiras, Armstrong, Perea, & Frost, 2014). Specifically, verbs seem to elicit more positive P200 and N400 responses than nouns, likely reflecting the retrieval of distinct meaning-related features (e.g., visual vs. motoric) within this time window (Amoruso et al., 2013). Nevertheless, previous research on the neural mechanisms involved in noun and verb naming primarily relies on fMRI studies that account for spatial location, or M/EEG studies that investigate ERP responses that account for timing, largely overlooking the potential contribution of brain oscillations. Furthermore, this evidence exclusively focuses on the organizational principles governing the neural representation of noun and verb categories in monolingual speakers leaving unanswered the question of whether a similar organization also stands for bilingual ones. Therefore, a comprehensive understanding of the complex neural processes underlying noun and verb naming, including the role of brain oscillations and their unfolding in time (i.e., spectro-temporal fingerprints), and how they vary depending on the speaker's linguistic background, is currently missing.

Brain tumors, especially low-grade gliomas (LGGs), are particularly interesting in this context as they offer a unique opportunity to directly test current models of noun-verb dissociation. LGGs invade brain tissue slowly, allowing the brain to put in place plasticity mechanisms to compensate for neural damage (Duffau et al., 2005). This plasticity can be studied longitudinally (i.e., before and after surgery) to examine whether changes in brain activity during noun and verb naming are differentially affected depending on lesion location (e.g., ventral vs. dorsal). Additionally, studying bilingual brain tumor patients can shed light on the extent of cross-linguistic effects in these neural responses. However, no study has yet tested this potential dissociation in a longitudinal fashion using LGGs as a model. The present thesis addresses the aforementioned gaps through three publications. Across these studies, we tested different populations combining MEG recordings with a multilingual picture-naming task (Gisbert-Munoz et al., 2021) which I contributed to develop and validate for Chinese language. Briefly, Publication I (Amoruso and Geng et al., 2021) investigates the oscillatory signatures supporting noun and verb naming in monolingual individuals who were either healthy or had brain tumors in ventral and dorsal regions. Publications II (Geng et al., 2022) and III (Geng et al., 2023), extend this evidence to healthy bilinguals and bilingual patients with tumors in dorsal regions, respectively.

Overall, we found segregated beta (13–28 Hz) power decreases in left ventral and dorsal pathways for noun and verb naming, in a time window associated with lexico-semantic processing (~250-500ms), thus supporting the idea that speech production relies on partially distinct networks depending on the semantic category being processed. Similar patterns were observed in highly proficient bilingual speakers across languages (Spanish and Basque), suggesting that category-based representations overlap at the semantic level when individuals are equally skilled in their L1 and L2. Finally, longitudinal comparisons of patients' responses (post- vs. pre-surgery) showed beta modulations that mirrored the category-based segregation observed in healthy individuals. Specifically, patients with ventral damage compensated selectively for object naming, while those with dorsal damage compensated selectively for action naming, with this effect being true across languages.

Overall, these results contribute to our theoretical understanding of the neural mechanisms underlying language(s) production, both in health and disease, and shed light on the potential for language reshaping in the face of neural damage. By doing so, they open translational avenues with clinical implications, such as informing language rehabilitation strategies tailored to patient's linguistic profile and predicting language outcomes following tumor resection.

1.2 Theoretical framework and methodology

1.2.1 Nouns and verbs in the brain

Evidence from noun and verbs dissociations can be traced back to lesion studies on aphasic patients (Miceli, Silveri, Villa, & Caramazza, 1984; Zingeser & Berndt, 1990), which has revealed selective behavioural impairments in either noun or verb production following damage to left temporal and fronto-parietal regions, respectively. Interestingly, studies using direct electrical stimulation (DES) during intra-operative mapping of linguistic functions have consistently emphasized the existence of a category-based segregation. For instance, when regions in the inferotemporal cortex are stimulated, patients commit more errors in noun naming, whereas disruptions in prefrontal and parietal areas result in greater impairments in verb naming (Corina et al., 2005; Corina et al., 2010; Lubrano et al., 2014; Ojemann, Ojemann, & Lettich, 2002).

In recent years, fMRI studies have shown comparable patterns of dissociation between nouns and verbs in temporal and frontal regions (Gleichgerrcht et al., 2016; Shapiro et al., 2006; Shapiro et al., 2005). M/EEG studies measuring evoked responses via means of ERP/ERF analyses (Barber, Kousta, Otten, & Vigliocco, 2010; Preissl, Pulvermuller, Lutzenberger, & Birbaumer, 1995; Pulvermuller, Lutzenberger, & Preissl, 1999) have shown neurophysiological differences between nouns and verbs. Specifically, verbs have been found to elicit more positive P200 responses in fronto-central motor regions, indicating that motor generators may play a role in the differentiation between nouns and verbs. Similarly, verbs have been shown to elicit overall more positive N400 responses than nouns. As the N400 component reflects semantic processing, this finding may suggest differences in the retrieval of meaning-related features from distinct concepts which result in amplitude and/or topographic differences within this time window (Amoruso et al., 2013). In particular, it has been shown that object and action concepts differed in terms of feature types, with visual features being more represented in the object domain, and motoric features in the action one (Huttenlocher & Lui, 1979; Vinson, Vigliocco, Cappa, & Siri, 2003).

Brain oscillations play a key role in neural communication supporting cognition (Fries, 2015), providing spectral fingerprints of distinct cognitive operations that remain blind to traditional ERP/ERF analyses, in which responses are phase-locked to the experimental stimulus (Mouraux & Iannetti, 2008). Indeed, some studies (Laaksonen, Kujala, Hulten, Liljestrom, & Salmelin, 2012; Piai, Roelofs, & Maris, 2014) have shown a limited spatio-temporal correlation between evoked and oscillatory responses, implying that the neural mechanisms measured by these two approaches may be different.

Previous M/EEG studies focused on oscillatory modulations during speech production have consistently reported power decreases in alpha (8-12 Hz) and beta (13-30 Hz) frequency bands, which are thought to index the retrieval of lexical-semantic information from long-term memory (Cao, Oostenveld, Alday, & Piai, 2022; Piai et al., 2017; Piai, Roelofs, Rommers, & Maris, 2015). However, none of these studies accounted for potential spectro-temporal differences between noun and verb naming. Furthermore, to the best of our knowledge, no study has yet examined the oscillatory underpinnings governing the neural representation of these categories in the bilingual brain.

Bilingualism – the sustained contact with both a first and a second language (L1, L2)– (Fabbro, 2001) is known to shape brain structure and function, with this reshaping being largely dependent on experience-based factors (DeLuca, Rothman, Bialystok, & Pliatsikas, 2019) such as L2 age of acquisition (AoA) (Nichols & Joanisse, 2016), L2 proficiency (Abutalebi et al., 2013) and immersion (Pliatsikas, DeLuca, Moschopoulou, & Saddy, 2017).

Interestingly, evidence from highly proficient bilinguals shows similar lexico-semantic processing across L1 and L2, suggesting that, as language proficiency improves, conceptual representations become processed in a similar way across languages

(Abutalebi, 2008; Abutalebi & Green, 2007; Hut & Leminen, 2017). In this context, a few recent fMRI studies on bilingual speakers have shown analogue responses for both languages during noun and verb naming in temporal, parietal, premotor and middle-frontal areas (Consonni et al., 2013; A. E. Hernandez, Dapretto, Mazziotta, & Bookheimer, 2001; Willms et al., 2011), thus supporting the existence of convergent neural substrates across different languages when the L2 is mastered in a native-like fashion. However, as mentioned before, no study has yet explored whether oscillatory dynamics supporting noun–verb dissociations overlap across languages in highly proficient bilinguals.

1.2.2 Neuroplasticity of language: Brain tumors as a model to test noun-verb dissociations

Neuroplasticity refers to the brain's ability to modify its structure and function in response to internal and external factors (Carreiras et al., 2009; E. A. Maguire et al., 2000). Classically, neuroplasticity has been associated with early developmental stages; however, it is now clear that it plays a fundamental role during adulthood allowing, for instance, acquiring a new language, but also coping with brain damage and disease (Payne & Lomber, 2001). An example of this latter case are tumors invading brain areas. In this context, due to their slow growth (~4 mm/year), low-grade gliomas (LGG) constitute and interesting model to approach the study of brain plasticity and the mechanisms allowing functional preservation (Kong, Gibb, & Tate, 2016). The term "glioma" is derived from the glial cells in the central nervous system. The WHO grading system categorizes glioma tumors into four types, ranging from grade I to IV, with grade I being the least malignant. LGGs include grade I and grade II tumors and are the most common primary brain tumors affecting individuals at a young age (Vargo, 2011).

Unlike other brain lesions such as stroke, which destroy tissue instantaneously hindering successful functional reallocation, LGGs infiltrate cortical and subcortical structures gradually, allowing healthy brain regions to overtake the role previously played by the damaged tissue without severe behavioral deficits (Duffau, 2005, 2017). Among the identified compensatory mechanisms the recruitment of peri-lesional and contra-lesional homologous regions have been highlighted. Thus, LGGs open a new window to investigate neuroplasticity mechanisms.

Surgery is currently the first treatment for LGGs affecting the so-called eloquent areas, that is, brain regions of high functional expressivity, including language. Therefore, localizing brain function and its lateralization prior and during the surgery becomes a must to optimize the neurosurgical strategy and improve tumor resection and patient's prognosis.

A popular approach to map language function prior to the surgery and measure plasticity changes is functional magnetic resonance imaging (fMRI). Indeed, during the last decades, fMRI studies have played a key role in advancing our comprehension of the functional and structural architecture of the language network and its reorganization in the lesioned brain. Yet, the temporal resolution of hemodynamic responses is limited. This aspect becomes critical when considering linguistic processing which occurs on the subsecond time-scale (e.g., speech has a production rate of 2-5 words per second) while fMRI allows acquiring brain volumes every two seconds. Thus, neuroplasticity needs also to be examined with high-temporal resolution techniques capable of capturing the unfolding of rhythmic fluctuations (i.e., oscillations) associated with language function in real time.

Recent M/EEG studies have successfully identified markers of language reorganization consistently highlighting the role of low-frequency oscillations in functional compensation. For example, Traut et al. (2019) found a functional shift in language lateralization towards the right hemisphere in brain tumor patients after left tumor resection, reflected in modulations in the beta band. Similarly, Kielar, Deschamps, Jokel, and Meltzer (2016) used MEG and showed that stroke patients exhibit increased right hemisphere alpha-beta activity during semantic processing. Using EEG, Spironelli et al. (2013) reported post-stroke patterns of beta activity in ipsilesional and contralesional frontal areas during semantic processing. Moreover, (Piai et al., 2017) found that stroke patients with left hemispheric lesions exhibited reduced alpha-beta power during lexico-semantic retrieval in the right hemisphere, whereas controls showed a left-lateralized effect.

Overall, these studies show that lexico-semantic processing can be compensated in patients with brain damage and that oscillatory markers constitute a window into the neural mechanisms underlying this compensation. Specifically, low-frequency oscillations, particularly beta rhythms, appear to play a crucial role in functional reorganization. Yet, none of these studies has investigated noun and verb compensation, let alone in a longitudinal (i.e., post- vs. pre-surgery) fashion.

1.2.3 Using MEG to measure oscillatory dynamics involved in language production

Speech production relies on dynamic and rapid cognitive processes, as evinced by the fact that an average speaker produce two to five words per second (Piai & Zheng, 2019; Roelofs, 1992). Thus, investigating such processes requires techniques that can track brain activity at a high temporal resolution. M/EEG fulfill this requirement by directly measuring neural activity at the millisecond level.

Detecting the activity of individual neurons is typically challenging due to its low magnitude. Consequently, when using EEG/MEG techniques to measure brain activity at the scalp level, the synchronized firing of spatially aligned groups of neurons is a prerequisite. Moreover, these signals must originate primarily from a specific type of neurons. Pyramidal neurons in the cerebral cortex are uniquely structured, featuring a long apical dendrite perpendicular to the cortical surface. When many pyramidal neurons are activated simultaneously in synchronization, they produce a "dipole moment" (i.e., a separation of positive and negative charges). Such activity can be detected at the scalp level using EEG and MEG sensors. While both methods provide direct insights into neural activity, they differ in how they measure it. EEG records voltage changes on the scalp, while MEG captures the magnetic fields generated by this electric activity. However, the signal from radial dipoles (which are present in most neurons in gyri) is not detectable by MEG. In contrast, the current flow of tangential dipoles from neurons in sulci generates magnetic fields that are parallel to the surface of the skull, and these fields primarily contribute to the MEG signal.

By studying the patterns of brain activity under different experimental conditions, researchers can gain insights into the neural mechanisms underlying cognition and behavior in health and disease. The picture-naming task is the gold standard to study language production. In this task, participants are presented with a series of pictures (or visual stimuli) and are required to name the depicted object or action as quickly and accurately as possible. The picture-naming task has been used extensively in research on language production, and has been adapted in various forms (e.g., covert vs. overt naming) to investigate different aspects of language processing. Furthermore, this task has been used in individuals with brain tumors to map language before and during surgery (Quinones, Amoruso, Pomposo Gastelu, Gil-Robles, & Carreiras, 2021).

1.2.3.1 Participants and overall design

Healthy individuals were recruited from the BCBL database. Patients, on the other hand, were recruited from Biocruces Hospital (Bilbao), where they received their diagnosis and underwent the awake craniotomy for tumor resection.

Twenty healthy adults (6 men, age mean = 25.04; SD = 3.94) and six patients (3 men, age range 24–59; mean = 40; SD = 12.89) with LGGs in the left hemisphere involving either temporal (n = 3) or fronto-parietal (n = 3) regions took part in the first study (Publication I). All patients and controls reported Spanish as their native language and considered themselves as monolinguals.

The second study (Publication II) involved twenty healthy Spanish–Basque bilinguals (4 male, M = 25.87; SD = 5.25). All participants but one reported Spanish as the L1 and Basque as the L2. Language proficiency was assessed with the Basque, English, and Spanish Test [BEST] (de Bruin, Carreiras, & Dunabeitia, 2017) using the semi-structured interview part of the test which measures fluency, lexical resources, grammatical constructions and pronunciation (Likert-like scale with scores ranging from 1 to 5). The cut-off criteria for considering an individual as a high-proficient bilingual were scores ≥ 4 in their L2. The nonparametric Wilcoxon signed rank test showed no significant differences ($p > 0.05$) between Spanish (M = 5; SD = 0) and Basque (M = 4.83; SD = 0.33), indicating that participants had comparable proficiency in both languages.

Finally, four highly proficient Spanish-Basque bilinguals (3 men, age range 41–56; mean = 40; SD = 12.89) with LGGs in left fronto-parietal regions took part in the third study (Publication III). Again, no differences were observed in the BEST scores ($p > 0.05$) between Spanish (M = 5; SD = 0) and Basque (M = 4.9; SD = 0.2).

In the case of patients, the protocol for the longitudinal (post- vs. pre-surgery) assessment comprised 3 phases (see Figure 1).

1- Pre-surgery: Patients visit the BCBL twice. During the first visit (day 1), they undergo a neuropsychological screening aimed at evaluating various cognitive functions. These include language proficiency via means of the BEST test (de Bruin et al., 2017), cognitive status through the Mini-Mental State Examination (MMSE) (Cockrell & Folstein, 1988); and IQ using the KBIT (Kaufman & Kaufman, 2004). During day 1 they also perform a structural and functional magnetic resonance for tumor localization and T1 acquisition.

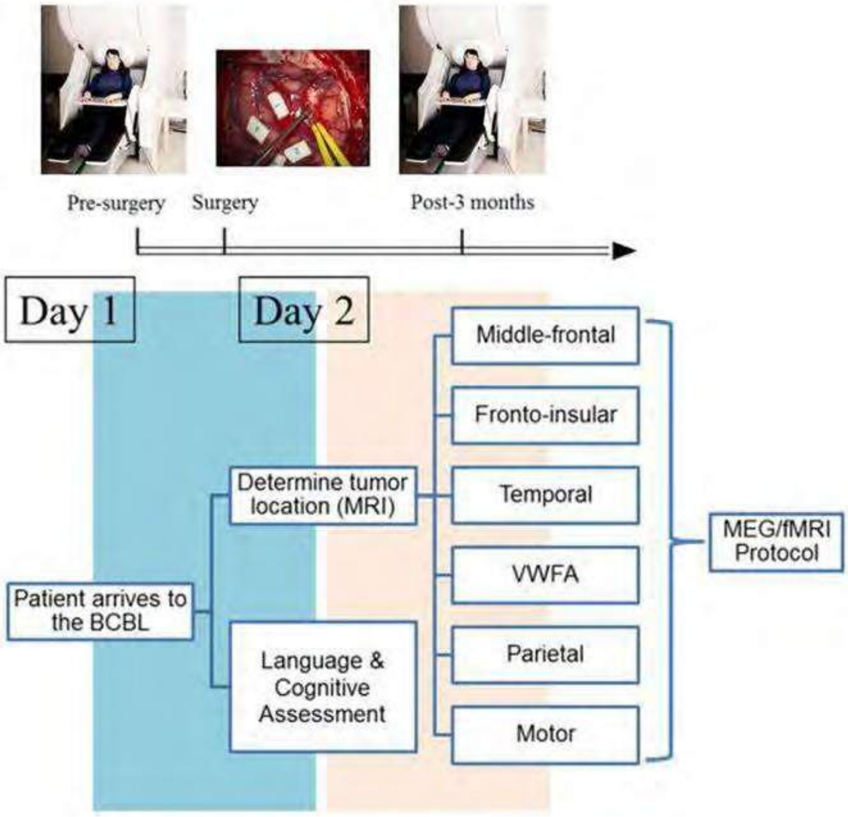

Figure 1. Protocol for patients' evaluation. Patients come to the BCBL before and three months after surgery. Depending on the tumor's location, they undergo different protocols to map cognitive functions. In the case of language, all patients perform the MULTIMAP task while MEG recordings are continuously acquired.

During the second visit (day 2), they run a set of functional tasks in the MEG including the MULTIMAP task. Importantly, if patients are bilingual they run the MULTIMAP in Spanish and Basque. Overall, this information has a clinical scope beyond the research questions, as it is utilized to create a report for the neurosurgeons which aids in planning the surgical strategy.

2- Surgery and intra-operative mapping: During the surgery, the patient is woken up from anesthesia to carry out the online functional mapping with direct electrical stimulation (DES). Using a bipolar electrode, neurosurgeons stimulate different cortical and subcortical regions while the patient performs a set of tasks on a tablet (i.e., including object and action naming in different languages) to tailor tissue resection according to individual functional boundaries. A cortical site is classified as "functional", and thus prevented from resection, if the patient elicits the same error (i.e., semantic paraphasia, anomia, speech arrest) in at least 2 out of 3 non-consecutive stimulation trials. This approach is used to maximize the quality of tumor resection while minimizing the risk of severe post-operative deficits like loss of speech or movement.

3- Post-surgery: patients return to BCBL 3 months after the surgery and repeat, on each occasion, the same protocol previously performed in the Pre-surgery phase.

1.2.3.2 Stimuli and task

Language production was assessed using MULTIMAP, a multilingual picture-naming task for mapping eloquent areas during awake surgeries (Gisbert-Munoz et al., 2021). Briefly, MULTIMAP consists of an open access database of standardized color pictures representing both objects and actions. These images have been tested for relevant linguistic features in cross-language combinations including Spanish and Basque. Target words were matched on frequency, familiarity, number of orthographic neighbors, length and name agreement (i.e., > 80 %). Importantly, this task has been previously used to investigate the brain mechanisms underlying bilingual language production in neurotypical (Geng et al., 2022) and brain tumor populations (Quinones et al., 2021).

In separate blocks, participants were instructed to observe the pictures and name them overtly in Spanish or Basque as quickly and accurately as possible. Trials started with a fixation cross in the center of the screen lasting for 1 sec, followed by the picture displayed for 2 secs. ISI randomly varied between 3 and 4 secs. A total of 88 picture items (i.e., 44 for objects and 44 for actions) were used. Each picture was presented twice for a total of 176 trials per condition. Each block lasted ~ 15 min, and participants were allowed to take a short break between them.

Above each object, we added the text “Esto es…” or “Hori da…” (“This is…” in Spanish and Basque, respectively) to force participants to produce a short sentence that agreed in number and gender with the target noun. In the case of the action pictures, we included a pronominal phrase to be used as the subject of the sentence, namely “El/Ella…” or “Hark…” (“He/She…” in Spanish and Basque, respectively). This introductory text cue was used to trigger the production of a sentence that began with the given subject and had a finite verb form in the third person singular. This allowed us tapping into lexico-semantic processing during action naming while controlling for key language features such as syntax (i.e., subject + verb agreement) and morphology (i.e., verbal inflection) (De Martino, Talacchi, Capasso, Mazzotta, & Miceli, 2021). See Figure 2.

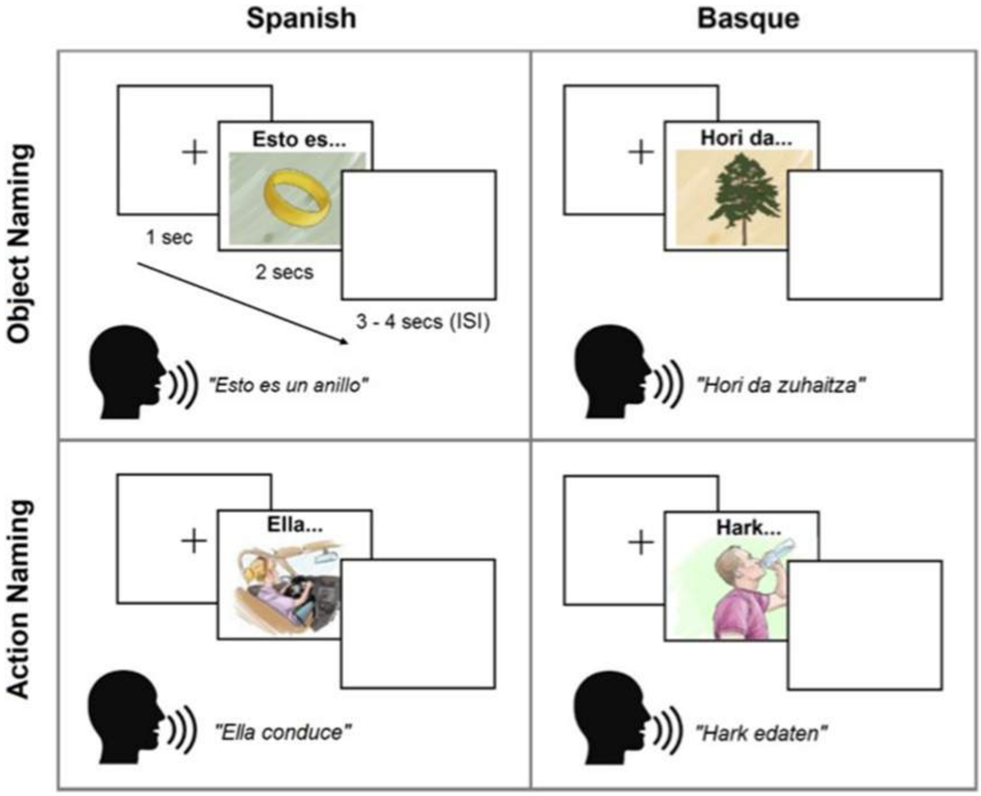

Figure 2. Examples of object and action stimuli and experimental task. In separate blocks, participants were requested to observe the pictures and overtly name them in either Spanish or Basque as quickly and accurately as possible. Production of nouns and verbs was requested in the context of short sentences, which is a more ecological form of speech than isolated naming. Each trial began with a fixation cross on the screen for 1 second followed by the picture presented for 2 seconds. ISI randomly varied between 3-4 secs.

1.2.3.3 Analysis pipeline

Behavioural assessment. Vocal responses were recorded online while participants performed the task and stored for offline preprocessing. Naming latencies were calculated using the Chronset toolbox (Roux, Armstrong, & Carreiras, 2017), which enables the automatic detection of speech onset. Responses containing disfluencies or errors were coded invalid and excluded from MEG analysis. In addition, response latencies shorter than 200ms and deviating from the participant's mean latency by > 2.5 SD in each condition (Miozzo, Pulvermuller, & Hauk, 2015) were also removed. Reaction times (RTs) and naming accuracy (ACC) were compared between groups using parametric and nonparametric t-tests depending on the data. Furthermore, we ran Crawford t-tests (Crawford & Garthwaite, 2012) for single-case analysis using the Psycho Package (Makowski, 2018) (Makowski, 2018)on RStudio (Version 1.2.5019) to compare each patient to the control group.

MEG data acquisition and processing. MEG data were acquired in a magnetically shielded room using a 360-channel Elekta-Neuromag system (Helsinki, Finland). Eye-movements were monitored with two pairs of electrodes in a bipolar montage placed on the external chanti of each eye (horizontal EOG) and above and below right eye (vertical EOG). Electrocardiographic (ECG) activity was also recorded with two electrodes, one positioned just below the right clavicle and the other below the left rib bone. MEG signals were continuously recorded at a 1 kHz sampling rate and on-line filtered to 0.1–330 Hz. The head position inside the helmet was continuously monitored using five head position indicator (HPI) coils. The location of each coil relative to the anatomical fiducials (i.e., the nasion, and left and right preauricular points) was defined with a 3D digitizer (FastrakPolhemus, Colchester, VA). Digitalization of the fiducials plus 200 additional points distributed over the participant's scalp were used during subsequent data analysis to spatially align the MEG sensor coordinates to the native T1 high-resolution 3D structural MRI.

Continuous MEG data were pre-processed off-line utilizing the spatiotemporal signal space separation (tSSS) method (Taulu & Simola, 2006) implemented in Maxfilter 2.2 (Elekta-Neuromag) to subtract the external magnetic noise and correct for participants’ head movements. Subsequent analyses were performed using the Matlab R2014B (The MathWorks, Inc., Natick, Massachusetts, United States) and FieldTrip Toolbox (Oostenveld, Fries, Maris, & Schoffelen, 2011; Popov, Oostenveld, & Schoffelen, 2018). Recordings were down-sampled to 500 Hz and segmented into trials time-locked to picture onset, ranging from 500 ms before to 1000 ms after image onset. A semi-automatic procedure was used to remove trials containing electromyographic artifacts, SQUID jumps, and flat signals. Then, heartbeat and EOG artifacts were detected via means of a fast, independent component analysis (ICA) (Jung et al., 2000).

Time-frequency (TF) analysis. TF analysis can capture oscillatory dynamics (i.e., power modulations in frequencies of interest across time), providing both high temporal and high spectral resolution, making it useful for studying the spectro-temporal dynamics of specific cognitive processes, including language production. TFRs were calculated from the artifact-free MEG segments for frequencies ranging from 1 to 30 Hz. TRFs were obtained using Hanning tapers and a fixed window length of 500 ms advancing in 10 ms steps, giving rise to a 2 Hz frequency resolution. Power estimates were calculated separately for each orthogonal direction of a gradiometer pair and then combined, resulting in 102 measurement channels. Power was expressed as relative change with respect to a ~500 ms pre-stimulus baseline.

Statistical comparisons at the sensor level. Differences in spectral power between conditions were assessed using cluster-based permutation tests (Maris & Oostenveld, 2007). This test controls for multiple comparisons using a cluster-based correction while maintaining sensitivity based on temporal, spatial and frequency dependency of neighboring samples. The permutation *p*-value was calculated using the Monte Carlo method with 1,000 random permutations. The threshold for significance testing was a *p*-value below 5% (two-tailed).

Source reconstruction of sensor-level activity. Participants' high-resolution 3D structural MRIs were segmented using the Freesurfer software (Dale & Sereno, 1993). Co-registration between the MEG sensor coordinates and the participant's MRI coordinates was done by manually aligning the digitized head-surface and fiducial points to the outer scalp surface. The forward model was computed using the Boundary Element Method (BEM) implemented in the MNE software suite (Gramfort et al., 2014) for three orthogonal tangential current dipoles (one for each spatial dimension) placed on a homogeneous 5-mm grid source space covering the whole brain. For each source, the forward model was then reduced to its two principal components of highest singular value, which closely correspond to sources tangential to the skull. All sensors (i.e., gradiometers and magnetometers) were used for source estimation, normalizingthe signal of each sensor by its noise variance, and considering a baseline period before picture onset. Brain source activity was calculated for each participant using Linearly Constrained Minimum Variance (LCMV) beamformer approach (Van Veen, van Drongelen, Yuchtman, & Suzuki, 1997). A common filter was computed by combining the cross-spectral density (CSD) matrices from the time-frequency window of the significant sensor-level effects and an equally-sized baseline period prior to picture onset. To perform group-level analysis, brain maps were transformed from the individual MRIs to the standard Montreal Neurological Institute

(MNI) by applying a nonlinear space transformation algorithm implemented in Statistical Parametric Mapping (SPM8, Wellcome Department of Cognitive Neurology).

Statistical comparisons at the source level. Comparisons between conditions were performed with the location- comparison method (Bourguignon, Molinaro, & Wens, 2018), which has been shown to be robust in dealing with spectral leakage problems. This method generates bootstrap group-averaged maps to build a permutation distribution of location differences between local maxima in the two conditions being compared and test the null hypothesis that the distance between them is zero. Local maxima are defined as sets of contiguous voxels displaying higher power than all other neighboring voxels. The threshold at $p<0.05$ was estimated as the 95 percentile of the sample distribution. All supra-threshold local MEG peaks were interpreted as indicative of brain regions likely contributing to the sensor-level effect.

1.3 Hypotheses and aims

1.3.1 Aims

The present thesis has two general objectives:

1- Determine the spectro-temporal and spatial dynamics underlying noun and verb naming in healthy individuals with different linguistic backgrounds (i.e., monolingual and bilingual speakers).

2- Track the oscillatory dynamics supporting longitudinal plasticity subserving noun and verb naming in patients with ventral and dorsal tumors (LGGs).

The first aim is broached in Publications I and II, the second aim in Publications I and III and the third aim in Publications I and III.

1.3.2 Hypotheses

Overall, based on previous evidence suggesting that (1) the semantic representation and retrieval of object (noun) and action (verb) knowledge are partially underpinned by distinct ventral and dorsal systems (Gleichgerrcht et al., 2016; Lubrano et al., 2014; Shapiro et al., 2006; Shapiro et al., 2005; Vigliocco et al., 2011); and that (2) low frequency oscillations such as alpha and beta rhythms□ play a key role in lexico-semantic retrieval during speech production (Cao et al., 2022; Piai et al., 2017; Piai et al., 2015), we expected that, at the sensor level, noun and verb naming would trigger differential oscillatory patterns within these frequency bands (i.e., between 8-28 Hz) in a time-window associated with lexico-semantic processing (~200 – 500 ms after picture onset). For the source level effects, we predicted a stronger contribution of inferotemporal and fronto-parietal nodes for object and action naming, respectively.

Next, given the lack of M/EEG studies investigating the spectro-dynamics that support object and action naming in highly proficient bilinguals, we based our tentative hypotheses on a few recent fMRI studies on the topic. Briefly, evidence from these studies (Consonni et al., 2013; A. E. Hernandez et al., 2001; Willms et al., 2011) suggests the existence of language-invariant cortical mechanisms in bilingual speakers during the processing of lexico-semantic representations in speech production. Indeed, as bilinguals become more proficient in their L1 and L2, their languages gradually become more similar or "converge", at least, at the semantic level. Therefore, based on these neuroimaging findings, we anticipated the presence of similar category-based oscillatory responses across languages (Spanish and Basque) for object and action naming.

When considering the results from monolingual patients with tumors affecting either ventral or dorsal regions, we expected to see selective compensatory patterns depending on the tumor location and semantic category. Specifically, we predicted that patients with LGGs affecting ventral regions would show longitudinal compensation (i.e., changes in oscillatory activity pre- vs. post-surgery) associated with object naming, while patients with dorsal LGGs would show this effect but for action naming. Furthermore, previous M/EEG studies (Kielar et al., 2016; Piai et al., 2017; Spironelli et al., 2013; Traut et al., 2019) on stroke and glioma patients have shown that beta rhythms (15-28 Hz) play a key role in compensating for language function. Therefore, we anticipated that compensatory effects would likely be reflected in this frequency band. In addition, we anticipated that these brain patterns would be accompanied by preserved behavioral responses, (e.g., similar naming accuracy in patients and controls), thus supporting the idea of preserved linguistic functions.

When considering bilingual patients we predicted similar patterns of adaptive compensation across the L1 and the L2 (A. E. Hernandez et al., 2001), indicating language-invariant semantic processing in the bilingual brain. It is worth noting that, in this latter case, we only tested bilingual patients with LGGs affecting dorsal regions, thus we anticipated selective oscillatory compensation in beta rhythms (13-28Hz) for the retrieval of action knowledge (but not of object knowledge), with this compensation being true for both Spanish and Basque.

Finally, at the source level, we expected that patients would potentially exhibit compensatory patterns in healthy contralesional areas (i.e., within the right hemisphere, given that in all cases LGGs were localized in the left hemisphere).

1.4 Summary of results

1.4.1 Behavioural results

Differences in object and action naming emerged when considering reaction times (RT) across studies, with participants being significantly faster in naming objects as compared to actions. This pattern was consistent irrespectively of the population (i.e., healthy individuals and patients with LGGs) or the language (Spanish and Basque) being tested. Interestingly, when considering highly proficient bilinguals this effect was independent of the language used to name (i.e., no main effect of language or interaction between semantic category and language was observed), suggesting a similar processing across the L1 and the L2, when both languages are mastered at a similar level. In the case of patients, individual longitudinal testing with Crawford-Howell *t*-tests showed that all of them preserved linguistic function in both languages, either before or after the surgery.

1.4.2 Oscillatory dynamics subserving object and action naming in healthy monolingual participants

Both object and action naming showed early (0-200 ms) alpha (8-12 Hz) and beta (15-28 Hz) power increases compared to baseline. Source localization of these effects engaged regions in visual and parietal cortices, being consistent with the initial stages of picture-naming tasks involving image processing and attentional orientation to the stimulus (Indefrey & Levelt, 2004). See Figure 3 (right panel).

During the late time window (200–500 ms) □ our period of interest given it accounts for the lexico-semantic processing of the stimulus□ significant beta effects were found for both objects and actions. Interestingly, this activity was differently distributed depending on the condition, with objects mostly engaging ventro-temporal areas and actions recruiting parietal and pre-motor regions. In addition, we observed significant bilateral alpha activity only for object naming, localized in occipito-temporal areas. See Figure 3 (left panel).

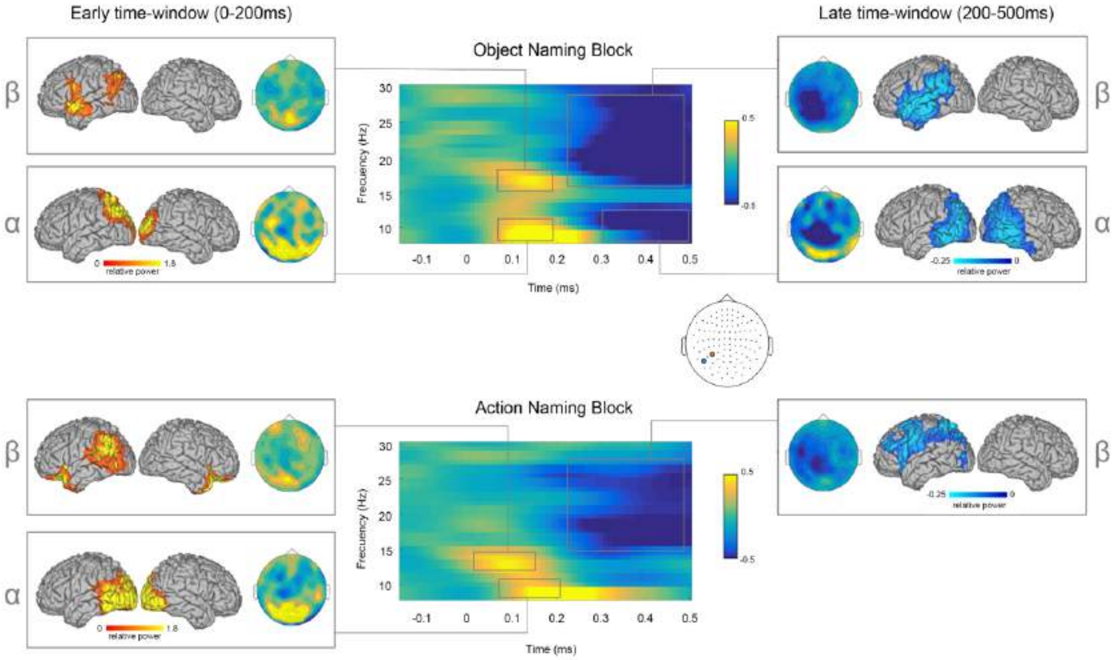

Figure 3. Oscillatory signatures of speech production in healthy monolingual participants. TFR of alpha and beta power in the object (top panel) and action (bottom panel) conditions over time. TFRs are plotted as relative power change compared to the baseline period over representative significant sensors (objects = M1632 + M1633; highlighted in orange; actions = M1722 + M1723; highlighted in blue). Topographic distribution plots show posterior alpha and beta power increases at early stages (0–200 ms), and left-lateralized anterior and posterior beta power decreases at later stages (200–500 ms).

1.4.3 Functional plasticity in monolingual patients with ventral and dorsal LGGs

When comparing oscillatory activity across sessions (i.e., post- vs. pre-surgery for tumor resection) within each group of patients (i.e., ventral and dorsal), we found significant differences between sessions in the beta band (13–28 Hz), with overall power increases after tumor resection. Interestingly, beta power modulations varied depending on damage location and semantic category, with ventral and dorsal lesions specifically modulating object and action naming, respectively. These findings align well with the dissociation observed in the group of healthy controls and with previous evidence (Gleichgerrcht et al., 2016; Kemmerer et al., 2012; Pisoni et al., 2018; Tranel, Adolphs, Damasio, & Damasio, 2001; Vigliocco et al., 2011) suggesting a differential engagement of temporal and fronto-parietal regions in object and action naming.

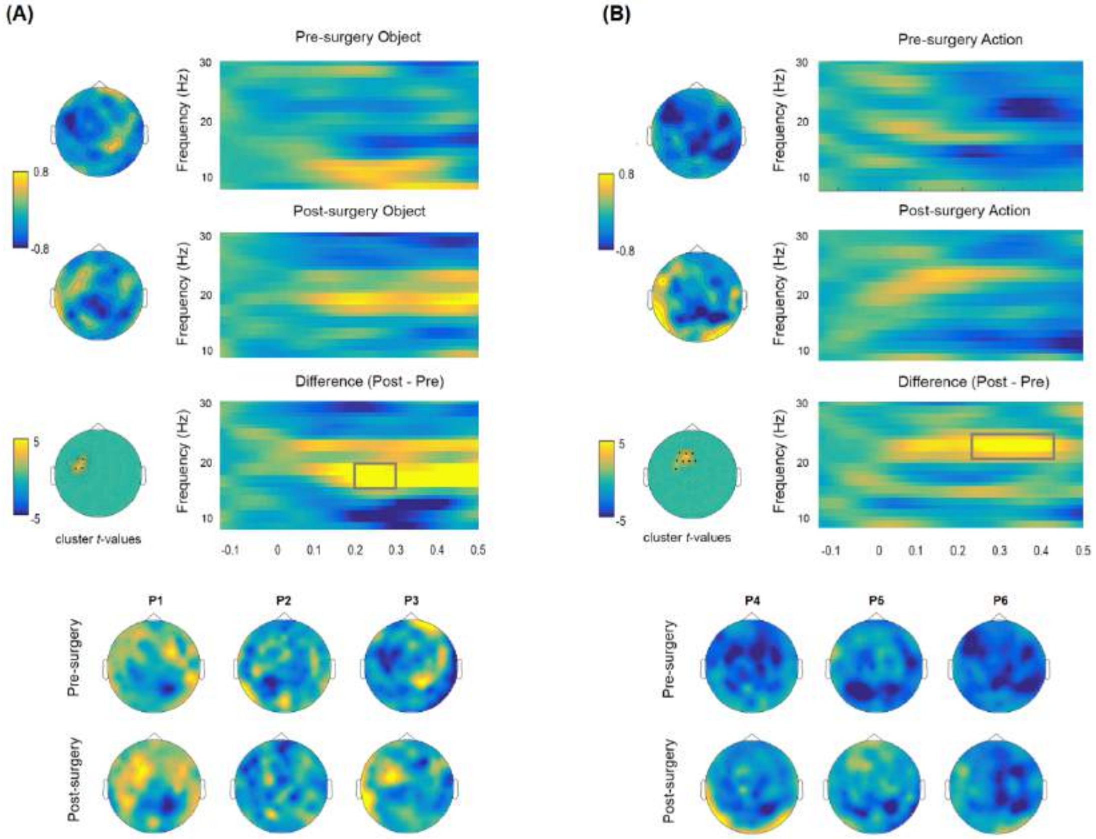

Figure 4. Longitudinal functional plasticity in monolingual patients with LGGs. (A) TFRs of patients with ventral lesions showing beta power increases after surgery only for objects; (B) TFRs of patients with dorsal lesions showing a similar effect but only for actions.

1.4.4 Object and action naming in healthy highly proficient bilinguals

As shown in Figure 5, noun and verb naming in either Spanish or Basque showed theta power increases (4–8 Hz) and alpha–beta (8–25 Hz) power decreases during speech production. When comparing noun and verb naming conditions in Spanish, a significant negative cluster was observed in the theta band, with nouns exhibiting less power than verbs. A significant negative cluster was also observed in the alpha–beta bands, with overall power decreases for nouns as compared to verbs (See Fig.5A).

Similarly, when contrasting both categories in Basque, a significant negative cluster was found in the theta band, with nouns exhibiting less power than verbs in bilateral posterior sensors.

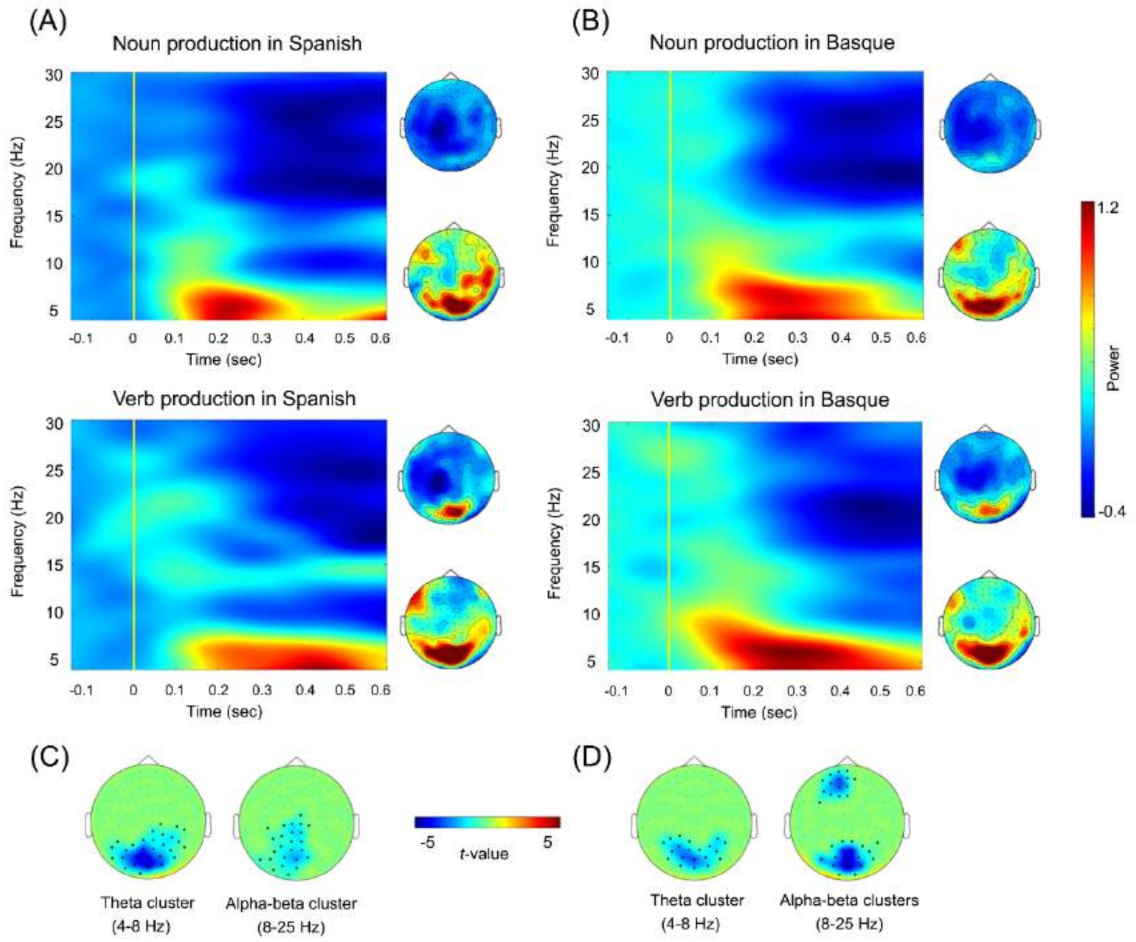

Figure 5. Oscillatory correlates of noun and verb production in healthy highly proficient bilingual speakers. Time–frequency representations (TFRs) for nouns and verbs in Spanish (A) and Basque (B). TFRs and topographic distributions plots showing theta and alpha–beta effects are plotted as relative power change compared to the baseline period (500 ms pre-stimulus) in the combined gradiometers highlighted by the significant clusters (C, D).

Finally, two negative clusters were found in the alpha–beta range, showing decreased power for noun as compared to verb naming. Of note, no significant clusters were observed (all *p*s > 0.2) when comparing noun and verb naming across languages (i.e., Spanish noun vs. Basque noun, and Spanish verb vs. Basque verb), in the theta (4–8 Hz) or the alpha–beta (8–25 Hz) frequency bands.

Significant oscillatory effects at the sensor level were source reconstructed considering the frequency-bands and time-windows highlighted by the significant clusters. In the case of Spanish (see Fig. 6A), theta peaks were found bilaterally in visual cortices and in the left SMA. For Basque (see Fig. 6B), these peaks were localized in bilateral visual cortices as well and in the right middle temporal gyrus. In all cases, regions showed increased power for verbs as compared to nouns.

Brain regions likely contributing to the alpha–beta effects in Spanish, on the other hand, were found in bilateral visual cortices, the left anterior temporal lobe and the right premotor area. While the former regions showed more desynchronization for nouns as compared to verbs, the latter one, namely premotor, showed a reversed pattern, with more desynchronization for verbs as compared to nouns. In the case of Basque, the involved regions were the bilateral visual cortices, the left superior anterior temporal lobe and the right premotor area, with occipito-temporal regions showing stronger alpha–beta power decreases for nouns as compared to verbs, and the right premotor area showing power decreases for verbs as compared to nouns.

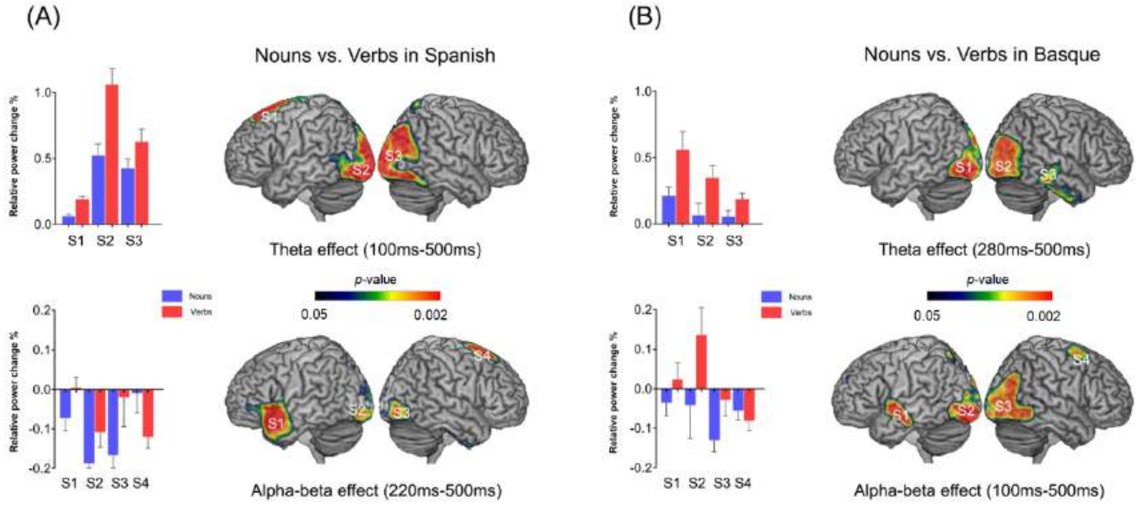

Figure 6. Neural correlates of the TFR sensor-level effects. We localized regions of local maxima with respect to baseline in Spanish (A) and Basque (B), and restricted between-condition comparisons (nouns vs. verbs) to those sites. Localization of activation peaks was circumscribed to the theta (4–8 Hz) and alpha–beta (8–25 Hz) frequency bands in the time intervals highlighted by the significant clusters in each language. For visualization purposes, we use bar plots showing relative power change for each category (nouns in blue and verbs in red) at each peak maxima to clarify the direction of the effect. All plotted regions reached a p value < 0.05.

1.4.5 Functional plasticity of action naming in bilingual patients with dorsal tumors

In this last experiment, we used a similar approach as in the first one (i.e., longitudinal contrast in monolingual patients with LGGs). However, in this latter case, we only evaluated highly proficient Spanish-Basque bilingual patients with LGGs affecting the dorsal pathway. Briefly, based on previous findings in monolingual patients, we wanted to move one-step further and test the hypothesis that the semantic representation/retrieval of action-based knowledge is mainly supported via the dorsal stream and overlaps across the two languages a highly proficient bilingual speaks.

Given previous oscillatory findings, we focused on the beta frequency band (13-28 Hz).

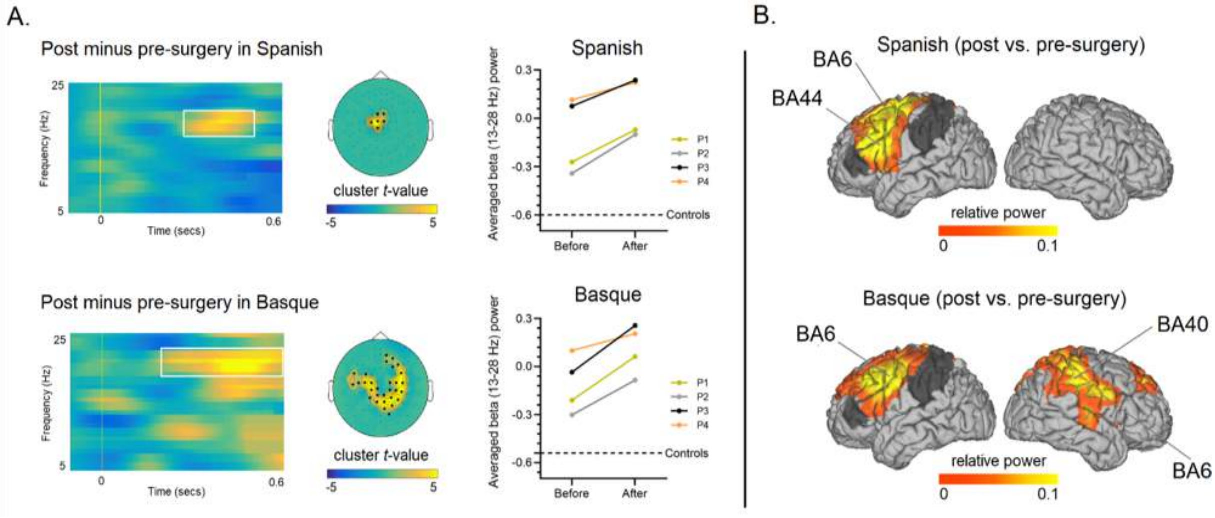

Figure 7. Longitudinal effect in highly proficient bilingual patients for action naming. Panel A shows TFR of the longitudinal action naming effect in Spanish (top left) and Basque (bottom left), together with the positive clusters in the beta band (13–28 Hz), indicating power increases after surgery. Line charts show individual patients' mean beta power at each session, averaged over significant sensors. Mean beta values are also shown for healthy bilingual controls as indicated by black dotted lines. Panel B shows source localization of the longitudinal action naming effect in each language. All plotted regions reached a *p*-value <0.01.

Overall, the longitudinal contrast (post- vs. pre-surgery) showed specific significant effects for actions in both languages (all Monte Carlo *p*s = 0.002, two tailed) in the beta band. No significant differences were observed for the object naming condition (all Monte Carlo*p*s > 0.45, two tailed). Figure 7A shows time-resolved spectra of the action naming longitudinal contrast for each language. In the case of Spanish, beta power modulations across sessions were highlighted by a positive cluster in left middle-frontal sensors.

In the case of Basque, the positive cluster was evident in left frontal sensors and right fronto-parietal ones.

Source localization results (Fig. 7B) indicated that the longitudinal action effect for Spanish mainly originated in premotor and inferior frontal regions in the left hemisphere. The same effect in Basque showed a similar involvement of left premotor cortex but with the additional recruitment of parietal and premotor regions in the right hemisphere.

Overall, we observed beta power increases after the surgery along with preserved cognitive and linguistic abilities, thus suggesting successful adaptive compensation. Importantly, the direction of the action post vs. pre-surgery effect was consistent at the individual patient's level. Namely, all patients showed stronger beta power increases after tumor removal.

Furthermore, when contrasting languages (Spanish vs. Basque) within each session (i.e., before and after surgery), a significant language effect (Monte Carlo *p*-value = 0.002, two- tailed) was observed for action naming after the surgery. This effect was highlighted by a negative cluster in the right parietal-temporal sensors, showing less beta power (13-28 Hz) for Spanish as compared to Basque (see Fig. 8A). Source localization results indicated that the post-surgery language effect originated in parietal, superior temporal and prefrontal regions of the right hemisphere (see Fig. 8B). No significant language differences were observed for action naming during the pre-surgery stage. In addition, no significant differences were observed for either pre- or post-surgery sessions in the case of objects (all Monte Carlo *p*s > 0.12, two tailed).

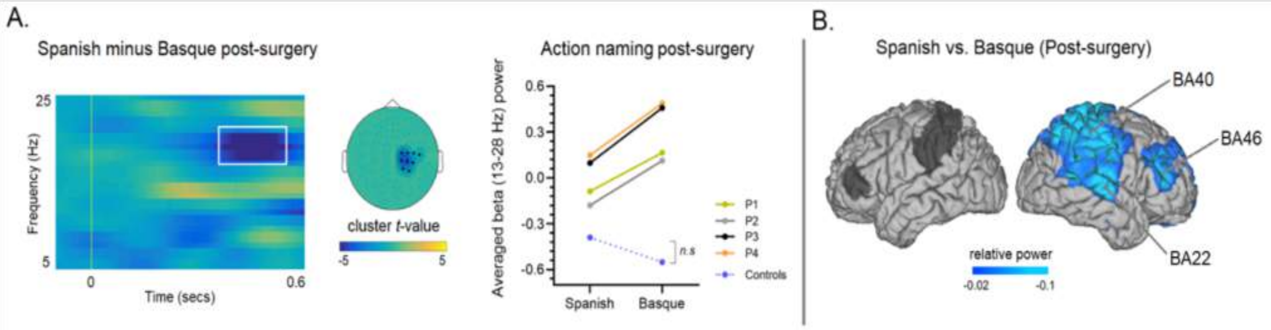

Figure 8. Language effect in highly proficient bilingual patients after surgery. Panel A shows TFRs of the language contrast (Spanish vs. Basque) after tumor resection, together with the negative cluster in the beta frequency band (13–28 Hz), indicating lower beta power for Spanish. Line charts show individual patients' mean beta power for each language, averaged over significant sensors. Mean beta values are also shown for healthy bilingual controls as indicated by the blue dotted line. Panel B shows source localization of the language effect, circumscribed to the time interval highlighted by the significant cluster. All plotted regions reached a *p*-value <0.01.

1.5 Discussion

The current thesis aimed to address two critical gaps in the literature. Firstly, it sought to provide a comprehensive characterization of the spectro-temporal and spatial dynamics involved in naming nouns and verbs among healthy individuals with different linguistic backgrounds, including both monolingual and bilingual speakers. Secondly, it aimed to track the oscillatory dynamics that underpin the longitudinal plasticity involved in noun and verb naming among patients with brain tumors (LGGs) affecting critical linguistic hubs. To achieve these aims, we collected both behavioral and MEG data while participants performed a picture-naming task, the gold standard for investigating speech production. Our experiments included a diverse range of populations, such as healthy monolingual and bilingual speakers, as well as brain tumor patients with LGGs, both prior to and after surgery for tumor resection.

Overall, the results from these experiment are broached in three scientific articles (Amoruso and Geng et al., 2021; Geng et al., 2022; Geng et al., 2023) published in Q1 peer-reviewed journals (see Appendix). In this section, I will discuss these results, focusing first on the oscillatory patterns of neural responses in healthy monolingual and highly proficient bilinguals. Afterward, I will proceed to discuss the results obtained in patients with LGGs.

1.5.1 Oscillatory correlates of noun and verb naming in the healthy brain

Earlier studies investigating speech production in healthy individuals via means of M/EEG, classically associated beta activity to motor aspects involved in articulation (Saarinen, Laaksonen, Parviainen, & Salmelin, 2006; Salmelin & Sams, 2002). However, as precisely pointed out by Piai et al. (2015) these studies compared the production of words vs. pseudo-words, which do not exist in memory and hence do not allow tapping into memory and semantic components involved in speech production. Here, by using a picture-naming task—which does capture the aforementioned aspects—we first tested monolingual speakers and found a left involvement of beta (13-28 Hz) activity. In keeping with previous findings (Laaksonen et al., 2012; Liljestrom, Kujala, Stevenson, & Salmelin, 2015; Liljestrom, Stevenson, Kujala, & Salmelin, 2015; Piai et al., 2015), this beta modulation likely reflects lexico-semantic processing of object and action knowledge. Indeed, the timing of the beta effects (~200-500 ms) also speaks in favor of our task tapping into conceptual preparation and/or lexical access related processes, as suggested by classical models of word production (Indefrey & Levelt, 2004; Levelt et al., 1999).

Importantly, there was a distinct distribution of beta power during object and action naming, with ventro-temporal areas predominantly involved in the former condition and dorsal parietal and pre-motor regions engaged in the latter. This evidence aligns well with current views suggesting that the representation and retrieval of object (noun) and action (verb) knowledge are partially underpinned by distinct ventral and dorsal systems (Gleichgerrcht et al., 2016; Lubrano et al., 2014; Shapiro et al., 2006; Shapiro et al., 2005; Vigliocco et al., 2011) at least when underscoring the semantic and pragmatic nature of these categories.

These findings can be also interpreted from an “weak” embodied perspective (Meteyard, Cuadrado, Bahrami, & Vigliocco, 2012) in which concepts are partly grounded in perceptual and motor experiences with the world. From this perspective, object and action concepts may engage different brain regions more strongly involved in representing visual (e.g., color and shape features) and motor aspects (e.g., motion features), respectively. Accordingly, at the neural level, the lexical retrieval of object (nouns) would primarily recruit occipito-temporal regions responsible for storing visual features, whereas the retrieval of action (verbs) will primarily engage motor/pre-motor structures associated with the representation of motoric features (Gainotti, Silveri, Daniele, & Giustolisi, 1995; Moseley, Pulvermuller, & Shtyrov, 2013; Pulvermuller et al., 1999). Consistent with this prediction, object naming elicited alpha-beta cortical activations in occipito-temporal areas, while action naming recruited the classical dorsal fronto-parietal network involved in processing action concepts, with this effect primarily confined to beta activity (Kemmerer, Rudrauf, Manzel, & Tranel, 2012; Watson, Cardillo, Ianni, & Chatterjee, 2013).

When examining oscillatory patterns in healthy highly proficient bilinguals, we found similar alpha-beta power decreases for nouns as compared to verbs across Spanish and Basque. Furthermore, when directly comparing noun and verb conditions across languages no differences were observed in any of the frequency-bands of interest, suggesting the existence of common oscillatory dynamics in Spanish and Basque. Of note, these results were mirrored at the behavioural level, with RTs showing no differences in noun and verb naming across languages. This is in agreement with prior neuroimaging (Consonni et al., 2013; Willms et al., 2011) and lesion (de Diego Balaguer, Costa, Sebastian-Galles, Juncadella, & Caramazza, 2004; M. Hernandez et al., 2008) evidence, showing similar neural substrates for noun-verb dissociations across languages.

Here, we add converging evidence from a neurophysiological standpoint by showing that the oscillatory fingerprints supporting the lexico-semantic processing of nouns-verbs are shared across languages, at least in highly proficient bilinguals.

When considering source level findings, we observed stronger alpha-beta power decreases in premotor areas during verb processing and in visuo-occipital areas in noun naming across languages. These findings are further in keeping with a "weak" embodied view of conceptual knowledge, in which semantic representations for objects and actions are at least partly rooted in sensory and motor related areas.

Interestingly, another region that showed a stronger involvement for noun naming across languages was the anterior temporal cortex, a hub region for semantic processing (Lau, Gramfort, Hamalainen, & Kuperberg, 2013; McCarthy, Nobre, Bentin, & Spencer, 1995). Previous evidence suggests its critical involvement during object naming (Clarke, Taylor, & Tyler, 2011; Price, Devlin, Moore, Morton, & Laird, 2005; Price, Moore, Humphreys, Frackowiak, & Friston, 1996) and, particularly, in mapping concepts to words during speech production. Importantly, the ATL is thought to house language-invariant semantic representations in bilinguals (Correia et al., 2014; Phillips & Pylkkanen, 2021; Zheng et al., 2020), showing a stronger involvement for object-related ones (Baldo, Arevalo, Patterson, & Dronkers, 2013; Buchweitz, Shinkareva, Mason, Mitchell, & Just, 2012; Lambon Ralph, Pobric, & Jefferies, 2009).

During speech production, lexico-semantic processing is closely intertwined with cognitive control. The finding that verbs exhibited higher theta (4-8 Hz) power as compared to nouns may reflect the increased semantic processing demands associated with this category (M. J. Maguire, Abelb, A. D., Schneider, J. M., Fitzhugh, A., McCord, J., Jeevakumar, V., 2015). Our cortical MEG analysis revealed that theta effects were found in the right MTG for Basque, and in the left SMA for Spanish. Notably, these regions have been identified as important nodes in the inhibitory control network and have been also implicated in bilingual language control (Luk, Green, Abutalebi, & Grady, 2011). Furthermore, neurophysiological evidence suggests that theta increases in the SMA, starting around ~ 150 ms (as in our study) and continuing throughout the task, may reflect the initiation of item search in memory and the retrieval of semantic features with different levels of complexity (Hart et al., 2013).

Overall, our findings from healthy monolingual and highly proficient bilingual speakers indicate that alpha-beta rhythms are crucial for the lexico-semantic processing of noun and verb categories. Specifically, our findings provide evidence for the existence of partially distinct ventral and dorsal pathways that are involved in retrieving conceptual knowledge for objects and actions during speech production, respectively. Furthermore, our results suggest that this category-based dissociation is similar in the L1 and the L2 in bilinguals, supporting the view that, as proficiency improves, conceptual representations become semantically processed in similar fashion across languages (Abutalebi, 2008; Abutalebi & Green, 2007).

1.5.2 Oscillatory correlates of noun and verb naming in the damaged brain

Previous research indicates that patients with LGGs can show normal outcomes on standard neuropsychological assessments (Duffau & Capelle, 2001; Walker & Kaye, 2003). Our findings support this view, by showing that all patients evaluated across studies were able to accurately retrieve object and action knowledge both before and after surgical intervention. These results suggest that patients underwent successful reorganization of language function and preserved their language abilities.

All patients being either monolingual or bilingual, showed significant longitudinal changes in the beta rhythms (13-28 Hz). Beta synchronization is thought to facilitate high-level interactions between distant brain areas and support long-range communication (Kopell, Ermentrout, Whittington, & Traub, 2000; Varela, Lachaux, Rodriguez, & Martinerie, 2001). This property becomes even more critical when considering that functional reshaping triggered by LGGs can affect network-level communication (Cargnelutti, Ius, Skrap, & Tomasino, 2020) and potentially involve the compensatory recruitment of remote areas in the contralateral hemisphere (Duffau, 2005). This aspect makes beta a plausible candidate to support reallocation of linguistic functions. Indeed, previous M/EEG studies from stroke and brain tumor patients have shown a shift of language processing toward the right hemisphere mediated by beta oscillations (Kielar et al., 2015; Piai et al., 2017; Spironelli et al., 2013; Traut et al., 2019). Interestingly, it has been reported that increased beta connectivity between distant regions of the brain is associated with improved quality of life in patients with brain injuries (Castellanos et al., 2010).

A critical aspect of our findings is that beta power modulations varied depending on tumor location and semantic category, with ventral and dorsal lesions specifically affecting object and action naming, respectively. These findings are consistent with the dissociation observed in the healthy individuals and with previous research (Gleichgerrcht et al., 2016; Kemmerer et al., 2012; Lubrano et al., 2014; Pisoni et al., 2018; Tranel, Adolphs, Damasio, & Damasio, 2001; Vigliocco et al., 2011) that suggests differential involvement of temporal and fronto-parietal regions in object and action naming.

When considering source level results, patients with ventral damage displayed beta modulations in the left IFG and the right posterior MTG. These regions are part of the semantic control network (Noonan, Jefferies, Visser, & Lambon Ralph, 2013; Wright, Stamatakis, & Tyler, 2012) and were also engaged by healthy individuals during object naming. Such an oscillatory pattern likely reflects the re-weighting of semantic representations in preserved healthy regions, implying that some of these areas become more active to support adaptive compensation (York & Steinberg, 2011).

On the other hand, patients with dorsal damage showed beta power modulations in the left IFG and healthy contra-lateral homologues in the right hemisphere, such as the right superior parietal, premotor, and middle-frontal areas. Interestingly, these right hemisphere areas were not activated in healthy individuals during action naming, which suggests that language reorganization is supported by unmasking a homologue network in the healthy hemisphere (Vassal et al., 2017). This finding is also consistent with previous research showing compensatory recruitment of the right hemisphere during language processing in patients with brain tumors and strokes (Kielar et al., 2016; Piai et al., 2017).

When considering bilingual patients with LGGS affecting areas in the dorsal pathway, oscillatory effects in the beta band (13-28 Hz) were specifically observed for the action naming condition (and were absent for the object one). In keeping with previous findings in monolinguals, longitudinal compensation was indexed by post-surgery beta power increases. This effect was true for both Spanish and Basque and consistent at the individual patient's level. Nevertheless, it is worth noting that beta patterns for Spanish and Basque differed in terms of timing, scalp an source location. Indeed, while Spanish showed a left lateralized effect in premotor and inferior frontal regions, Basque additionally engaged right-hemisphere sources.

To better understand this differential pattern, we contrasted action naming between Spanish and Basque separately before and after surgery. Prior to the surgery, action naming in did not differ, indicating comparable adaptive compensation for accessing action-based knowledge across languages.

However, after the surgery, differences between languages became evident. On the one hand, Basque showed higher activity in right parietal, superior temporal and prefrontal regions contralateral to the tumor's cavity. Importantly, this rightward activation was not present in healthy controls during action naming, suggesting that this set of regions was secondary engaged to achieve accurate lexico-semantic processing of action knowledge in the L2 once the tumor was resected.

This is in keeping with previous findings from our lab (Quinones et al., 2021) combining fMRI and MEG techniques to map language lateralization in bilingual brain tumor patients and showing a stronger shift of activity toward the right hemisphere for Basque as compared to Spanish after surgery. On the other hand, no recruitment of the right hemisphere was observed for Spanish, which instead showed more local changes in ipsilateral areas similarly recruited by controls during action naming.

Previous evidence (Gatignol, Duffau, Capelle, & Plaza, 2009) indicates that L1 and L2 can follow different postoperative trajectories in glioma patients, probably due to factors such as AoA, language proficiency, frequency of use, and tumor location. Nonetheless, it is true that while Spanish and Basque differed in terms of their oscillatory patterns after tumor removal, naming performance was well preserved in both languages, indicating successful post-operative reorganization - albeit supported by different compensatory strategies – rather than differential L1 vs. L2 deficits.

Based on evidence from intraoperative cortical mapping in bilingual individuals (Giussani, Roux, Lubrano, Gaini, & Bello, 2007), it is possible to speculate that although there is a general L1-L2 organizational pattern in gross anatomical regions, more refined and distinctive microanatomical systems can be localized within these regions for each language (Paradis, 2004). Therefore, it is plausible that the functional connections among the microanatomical systems of Spanish and Basque and their plasticity may have been differently affected by the surgical trauma, leading to distinct postoperative compensatory patterns. In fact, research has suggested that there is higher variability in network(s) reconfiguration after tumor resection than before (Duffau, 2020).

Another interpretation, which is not mutually exclusive, is that language proficiency may have played a role in the results. Despite all patients being highly proficient bilinguals who acquired Basque before the age of four, they reported Spanish as their L1. The activation of control regions in the right prefrontal cortex supports this perspective, suggesting that action naming in Basque may have required more cognitive resources for language control (A. E. Hernandez et al., 2001) and semantic monitoring (Shen et al., 2016) than Spanish.

This implies that preserving semantic processing after surgery may have involved additional engagement and/or modifications in the interactions between the language network and other systems, such as the executive control network.

1.5.3 Limitations and avenues for future research

There are some limitations to the current thesis that should be considered. Firstly, one element that requires consideration relates to the overt nature of the task used across the three experiments reported here. Speech production tasks have been long avoided in neurophysiological studies due to the potential existence of muscle artifacts, which may lead to a lousy signal-to-noise ratio in the recordings (Ganushchak, Christoffels, & Schiller, 2011). While we cannot completely rule out the existence of myogenic contamination in our recordings, we find this possibility unlikely for several reasons. First, we focused on the first ~500 ms period after picture onset, which is classically considered a "safe" window of artifact-free brain responses; and ran robust state-of-the-art pipelines for semiautomatic detection of muscle artifacts (Oostenveld et al., 2011). Second, previous MEG studies using a similar methodological approach as the one implemented here, have being successful in estimating brain non-contaminated activity (Monsalve, Bourguignon, & Molinaro, 2018; Piai et al., 2015; Quinones et al., 2021). Third, the beamformer technique used to reconstruct underlying brain sources is known to attenuate myogenic artifacts by suppressing signals whose single dipolar source cannot be explained by spatial scalp distribution (Piai et al., 2015). Finally, the specificity of the observed effect (i.e., present in the action but not in the object naming condition and *vice versa*) speaks in favor of a category-related modulation and fits well with evidence showing that beta oscillations sourced in premotor regions play a key role in action semantics (Weiss & Mueller, 2012). Secondly, while longitudinal data collection in patients with LGGs is quite challenging, the most prominent limitation is the relatively small sample size used in our two experiments with brain tumor patients (n = 6, and n = 4), which requires careful interpretation and generalization of the results. Nevertheless, it has been shown (Zeger & Liang, 1992) that longitudinal studies effectively minimize the confounding influence of inter-individual variability and enhance the statistical power when compared to cross-sectional ones. Therefore, one advantage of our design is that each patient serves as his/her own control across sessions. Additionally, appropriate Crawford t-tests were implemented to handle patient’s data at the individual level.

Notably, the longitudinal oscillatory effects observed across experiments were consistent across all individual patients, indicating the robustness of the findings. This strengthens the validity and reliability of our results and suggests that the observed patterns of brain activity are not simply idiosyncratic to individual patients. Yet, future studies with larger patient samples are necessary to replicate these findings anddetermine if observed compensatory patterns can be indeed generalized to a larger population.

Thirdly, it should be noted that while source reconstruction methods have been widely used in M/EEG studies, they suffer from well-known limitations due to the ill-posed inverse problem. Therefore, the current approach used in these experiments cannot provide fine-grained information about underlying cortical sources, particularly subcortical ones. Further research using techniques with better spatial resolution, such as fMRI, is required to disentangle this issue. Some recent efforts from our lab (Quinones et al., 2021), in combining MEG and fMRI data recorded from the same task within the same patients have yielded promising results in this direction.

2. Conclusions

Overall, the present dissertation sheds lights on the spectro-temporal and spatial underpinnings supporting noun and verb naming in individuals with different linguistic backgrounds and on how neuroplasticity processes can preserve this ability even in the presence of a brain tumor. Firstly, our findings from healthy monolingual and bilingual speakers indicate that alpha-beta (8-25 Hz) rhythms play a critical role in supporting the lexico-semantic processing of noun and verb categories during speech production. Specifically, our findings provide evidence for the existence of segregated alpha-beta rhythms differently engaging ventral and dorsal pathways while retrieving conceptual knowledge for objects (nouns) and actions (verbs), respectively. Secondly, our results suggest that this category-based segregation is similar in the L1 and the L2 in bilinguals, supporting the view that, as proficiency improves, conceptual representations become semantically processed in a similar fashion across languages. Thirdly, this thesis shows that beta rhythms (13-28 Hz) constitute a key signature of language compensation in patients with brain tumors, by enabling the reallocation of linguist functions to healthy regions.

Interestingly, we show that beta modulations vary depending on damage location and semantic category, with ventral and dorsal lesions compensating object and action naming, respectively. Finally, the thesis partly extends previous evidence to the bilingual brain by demonstrating that bilingual patients with dorsal damage show similar beta compensatory changes across languages for actions only.

Taken together, these results have significant theoretical implications for our current understanding of the core principles governing the representation and retrieval of nouns and verbs in individuals with diverse linguistic backgrounds. More crucially, this thesis bridges a gap between experimental science and clinical practice through a translational approach: by applying the insights gained from this research, evidence-based neuro-oncological decisions can be made with the potential to enhance patients' well-being and preserve their language abilities.

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3. Appendix: Published works

Article I:

“Oscillatory and structural signatures of language plasticity in brain tumor patients: A longitudinal study”

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RESEARCH ARTICLE

WILEY

Oscillatory and structural signatures of language plasticity in brain tumor patients: A longitudinal study

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Abstract

Recent evidence suggests that damage to the language network triggers its functional reorganization. Yet, the spectro-temporal fingerprints of this plastic rearrangement and its relation to anatomical changes is less well understood. Here, we combined magnetoencephalographic recordings with a proxy measure of white matter to investigate oscillatory activity supporting language plasticity and its relation to structural reshaping. First, cortical dynamics were acquired in a group of healthy controls during object and action naming. Results showed segregated beta (13–28 Hz) power decreases in left ventral and dorsal pathways, in a time-window associated to lexico-semantic processing (~250–500 ms). Six patients with left tumors invading either ventral or dorsal regions performed the same naming task before and 3 months after surgery for tumor resection. When longitudinally comparing patients' responses we found beta compensation mimicking the category-based segregation showed by controls, with ventral and dorsal damage leading to selective compensation for object and action naming, respectively. At the structural level, all patients showed preoperative changes in white matter tracts possibly linked to plasticity triggered by tumor growth. Furthermore, in some patients, structural changes were also evident after surgery and showed associations with longitudinal changes in beta power lateralization toward the contralesional hemisphere. Overall, our findings support the existence of anatomo-functional dependencies in language reorganization and highlight the potential role of oscillatory markers in tracking longitudinal plasticity in brain tumor patients. By doing so, they provide valuable information for mapping preoperative and postoperative neural reshaping and plan surgical strategies to preserve language function and patient's quality of life.

KEYWORDS
brain rhythms, brain tumors, language, magnetoencephalography, neuroplasticity

1 | INTRODUCTION

Neuroplasticity refers to the brain's ability to modify its structure and function throughout the lifespan, allowing the acquisition of new skills (Carreiras et al., 2009; Maguire et al., 2000) but also coping with brain damage and disease (Payne & Lomber, 2001). When considering this latter aspect, evidence from human studies in stroke (Butefisch et al., 2005; Shimizu et al., 2002) and brain tumor patients (Duffau, 2005; Robles, Gatignol, Lehericy, & Duffau, 2008) underscores the existence of different plasticity patterns, including function persistence within the tumor, function redistribution in perilesional areas, ipsilesional activation of more distant areas and recruitment of contralesional homologs. In line with a hodotopical understanding of brain organization (Catani, 2007; De Benedictis & Duffau, 2011; Duffau, Moritz-Gasser, & Mandonnet, 2014), functional reallocation would be possible thanks to the existence of redundant cortico–subcortical parallel networks potentially unmasked by the lesion. It has been suggested (Ius, Angelini, Thiebaut de Schotten, Mandonnet, & Duffau, 2011) that this high potential for reorganization would be almost confined to the cortical level, with subcortical white matter showing limited to null plasticity. Nonetheless, evidence from stroke (Schlaug, Marchina, & Norton, 2009) and epileptic patients following temporal lobectomy (Jeong, Asano, Juhasz, Behen, & Chugani, 2016; Li et al., 2019), suggests that white matter plasticity in the contralesional hemisphere is somehow possible.

Brain function and its reshaping in the damaged brain has been classically studied by means of functional magnetic resonance imaging (fMRI). However, hemodynamic responses are slow (one volume every ~2 s) and functions as language, which occur on the subsecond timescale, need also to be examined with high-temporal resolution techniques capable of tracking linguistic processing in real-time. Electro- and magneto-encephalography (M/EEG) meet this requirement as they can capture neuronal activity and its oscillatory dynamics with millisecond time resolution, offering a new perspective to study brain plasticity (Reid et al., 2016).

Oscillations at different frequency-bands and their synchronization are thought to reflect communication within and between regions (Fries, 2005), relevant for behavior and disease (Uhlhaas et al., 2017). Recently, M/EEG studies have been successful in identifying oscillatory markers of brain damage and language recovery, underscoring the involvement of low-frequency activity in functional compensation. For instance, using MEG, Kielar, Deschamps, Jokel, and Meltzer (2016) reported the involvement of contralesional right alpha-beta activity during semantic processing in stroke patients. Similarly, Traut et al. (2019) found that brain tumor patients exhibited a functional shift in beta language lateralization toward the right hemisphere after left tumor resection. Using EEG, Spironelli, Manfredi, and Angrilli (2013) evaluated post-stroke language reorganization and found bilateral patterns of beta activity in ipsilesional frontal areas and contralesional homologs during semantic processing. Piai, Meyer, Dronkers, and Knight (2017) reported alpha–beta power decreases associated to lexico-semantic retrieval in stroke patients with left hemispheric lesions. Interestingly, while controls showed a left lateralized effect, patients exhibited a right lateralized one, which was ultimately predicted by the probability of splenium damage.

Here, we tracked oscillatory dynamics subserving language plasticity in brain tumor patients before and 3 months after surgery for tumor resection. We recorded MEG activity while healthy controls and patients overtly named object and action pictures in Spanish. Of note, brain tumors could affect either ventral or dorsal areas within the left hemisphere which are known to play different roles in representing object and action categories. Briefly, previous evidence (Gleichgerrcht et al., 2016; Lubrano, Filleron, Demonet, & Roux, 2014; Vigliocco, Vinson, Druks, Barber, & Cappa, 2011) suggests that the semantic processing of object and action knowledge is underpinned by partially distinct networks preferentially involving inferior-temporal and fronto-parietal nodes, respectively. Thus, we capitalized on this dissociation to evaluate language function in the healthy and the lesioned brain. Specifically, we expected different alpha-beta compensation patterns depending on tumor location and semantic category, with ventral and dorsal lesions mainly compromising object and action processing, respectively. We also expected that functional changes would be related to structural ones. Thus, we calculated a proxy measure of white matter involvement in language-related tracts and assessed if potential preoperative and/or postoperative structural reshaping was associated with functional longitudinal changes.

2 | MATERIALS AND METHODS

2.1 | Participants

A total of 26 participants took part in this study. Twenty healthy adults (6 men, age mean = 25.04; SD = 3.94) were recruited through the BCBL database and received economical compensation for their participation. Six patients (3 men, age range 24–59; mean = 40; *SD* = 12.89) with brain tumors in the left hemisphere mainly involving temporal (*n* = 3), fronto-parietal (*n* = 2) or parietal regions (*n* = 1) were recruited at the Cruces Hospital where they received their diagnosis and performed the awake craniotomy for tumor resection (see Figure 1 for lesion profile). One out of 6 patients had cavernous angiomas, while the other 5 exhibited astrocytomas Grade I and II. Individual patient demographics, lesion and clinical characteristics are summarized in Table 1. All participants were right handed as measured by Edinburgh Handedness Inventory (Oldfield, 1971). They all had normal hearing and normal or corrected to normal vision. All patients and controls reported Spanish as their first language and the average naming BEST score (de Bruin, Carreiras, & Duñabeitia, 2017) in Spanish was 63.17/65 for patients and 64.81/65 for controls. It should be noted, however, that patients and controls also reported knowing some Basque (40/65 for patients and 49/65 for controls), as is common in the population of Donostia-San Sebastian. The study protocol was approved by the Ethics Board of the Euskadi Committee and the Ethics and Scientific Committee of the BCBL, following the declaration of Helsinki. All participants gave their written consent prior to the study.

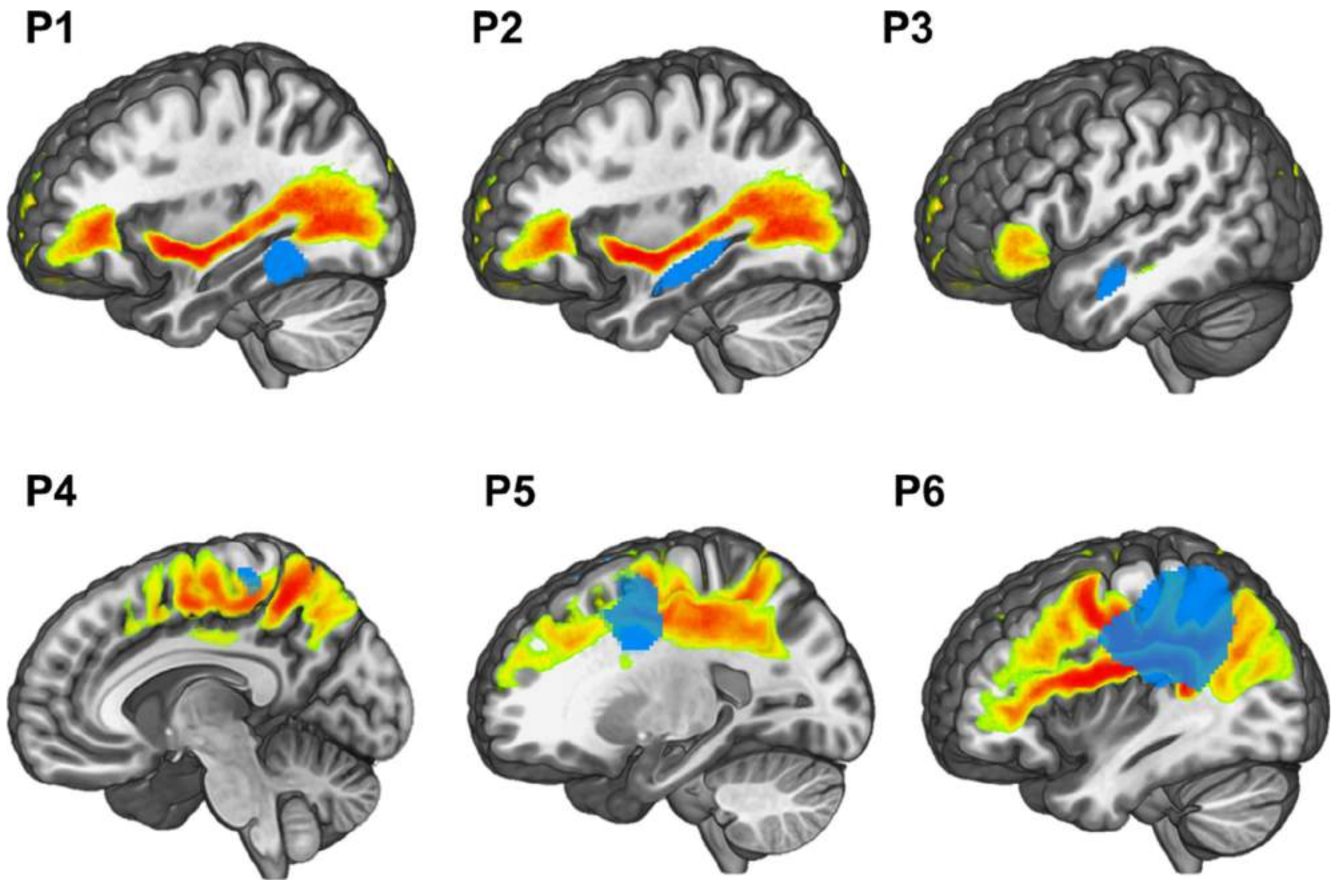


FIGURE 1 Lesion profile with respect to major dorsal and ventral white matter tracts. Tumors are shown in blue. Probabilistic location of superior longitudinal fasciculus (SLF, I, II), arcuate fasciculus (AF) and inferior fronto-occipital fasciculus (IFOF) are shown in orange. Patients 1, 2 and 3 (on top) exhibit tumors invading the left temporal lobe, however, none of them compromises the IFOF. Patients 4, 5, and 6 (on bottom) exhibit tumors invading fronto-parietal regions affecting, in all cases, the SLF and in cases 5 and 6 also the AF

TABLE 1 Demographics and clinical characteristics of patients

Patient ID	Age (years)	Gender	Education (years)	Handedness	Type of tumor	Tumor volume (cm^3)	Extent of resection (%)
P1	33	F	21	R	Cavernous Angioma	2.53	84.48
P2	59	M	12	R	Astrocytoma Grade II	5.8	100
P3	24	M	16	R	Astrocytoma Grade I	1.85	100
P4	46	F	14	R	Astrocytoma Grade II	0.55	75.83
P5	31	F	21	R	Astrocytoma Grade II	16.44	100
P6	47	M	19	R	Astrocytoma Grade II	74.25	100

2.2 | Stimuli and task

Semantic processing was assessed with a picture naming task. Pictures were selected from a standardized battery developed by NEURE clinic® (https://www.neure.eu/). The task included two separate sets of 30 colored images with line drawings either depicting objects or a person performing an action, respectively. Object and action stimuli were matched as close as possible for different linguistic variables and differences between stimuli were calculated using Student tests for normally distributed variables and Mann–Whitney for non-normally distributed ones. More specifically, stimuli were matched for frequency (Objects: mean = 25.94, *SD* = 29.19; Actions: mean = 14.79, *SD* = 17.06, *W* = 562, *p* = .055), word length in terms of number of letters (Objects: mean = 5, *SD* = 1; Actions: mean = 6, *SD* = 1, *t* = −1.519, *p* = .13), and familiarity (Objects: mean = 6.26, *SD* = 0.5; Actions: mean = 6.17, *SD* = 0.56, *t* = 0.68, *p* = .49). Name agreement was ≥85% in both conditions.

In separate blocks, participants were requested to observe the pictures and name them overtly in Spanish. Production of nouns and verbs was requested in the context of short sentences, which is a more ecological form of speech than isolated naming. More specifically, on top of the object-related images we added the text "Esto es…" ["This is…" in Spanish] to force the production of a short sentence that had to agree in number with the target noun (e.g., "This is a bird", "This is an apple"). Similarly, on top of the action-related pictures, we included the pronouns "El…" or "Ella…" ["He…" or "She…", in Spanish]. This introductory text was used as a cue for the production of a sentence that started with the given subject and had a finite verb form in third person singular (e.g., "She sings," "He writes"). Importantly, the use of these pictures led to participants eliciting sentences comprising concrete nouns (i.e., as opposed to abstract concepts like "love") and dynamic motor actions (i.e., as opposed to verbs referring to static states like "thinking"). We used MatlabR2012B and Cogent Toolbox for picture presentation. Trials started with a fixation cross lasting for 500 ms, followed by the stimulus displayed for 1 s. ISI randomly varied between 2 and 4 s. Each picture was presented 3 times for a total of 90 trials per block. Each block lasted ∼10 min, and participants were allowed to take a short break between them.

2.3 | Behavioral assessment

Vocal responses were recorded and monitored online by the experimenter while participants performed the task. Naming latencies were calculated using the Chronset tool (Roux, Armstrong, & Carreiras, 2017) which enables the automatic detection of speech onset. Responses containing disfluencies or errors were coded as invalid and excluded from MEG analysis. In addition, response latencies shorter than 200 ms and deviating from participant's mean latency by >2.5 *SD* in each condition (Miozzo, Pulvermuller, & Hauk, 2015) were also removed (in total, ∼5.9% of the trials were eliminated). Reaction times (RTs) and correct naming responses were compared between groups using nonparametric Welch's *t*-tests and Wilcoxon signed-rank for pre- versus post-surgery stages within the patient's group (see Table 2). Furthermore, we also ran Crawford-Howell (1998) frequentist *t*-tests for single-case analysis using the psycho Package (Makowski, 2018) on RStudio (Version 1.2.5019) to compare each patient to the control group (see Table 3).

2.4 | MEG and MRI acquisition

MEG data were acquired in a magnetically shielded room using a 360-channel Elekta-Neuromag system (Helsinki, Finland). Eye-movements were monitored with two pairs of electrodes in a bipolar montage placed on the external chanti of each eye (horizontal EOG) and above and below right eye (vertical EOG). Electrocardiographic (ECG) activity was also recorded with two electrodes, one positioned just below the right clavicle and the other below the left rib bone. MEG signals were continuously recorded at a 1 kHz sampling rate and on-line filtered to 0.1–330 Hz. The head position inside the helmet was continuously monitored using five head position indicator (HPI) coils. The location of each coil relative to the anatomical fiducials (i.e., the nasion, and left and right preauricular points) was defined with a 3D digitizer (FastrakPolhemus, Colchester, VA). Digitalization of the fiducials plus 200 additional points distributed over the participant's scalp were used during subsequent data analysis to spatially align the MEG sensor coordinates to the native T1 high-resolution 3D structural MRI. Structural images were acquired before and 3 months after surgery for each participant with a Siemens 3T MAGNETOM PRISMAfit MR scanner (Siemens, Munich, Germany) in a separate session (i.e., 1 day before the MEG session). T1-weighted MPRAGE anatomical volumes were acquired with the following parameters: echo time = 2.97 ms, repetition time = 2,530 ms, flip angle = 7° and field of view = 256 × 256 × 176 mm^3, number of axial slices = 176, slice thickness = 1 mm, in-plane resolution = 1 mm × 1 mm. The T2-weighted fluid-attenuated inversion recovery (FLAIR) sequence used the following parameters: echo time = 394 ms, repetition time = 5,000 ms, flip angle = 7° and field

TABLE 2 Behavioral results. Mean (M) and *SD* of accuracy and reaction time (RT) in each condition for each group, with *p*-values from Welch's *t*-tests comparing performance between patients and controls and Wilcoxon signed-rank for pre- versus post-surgery stages within the patient's group

				Controls versus patients (PRE)	Controls versus patients (POST)	Patients PRE versus POST
	Controls M (*SD*)	**Patients (PRE) M (*SD*)**	**Patients (POST) M (*SD*)**	***p*-value**	***p*-value**	***p*-value**
Accuracy (%)						
Object naming	98.75 (2.06)	98.27 (2.83)	98.27 (2.83)	.71	.71	1.0
Action naming	97.5 (3.33)	97.6 (3.63)	95.43 (3.54)	.93	.24	.34
Reaction time (ms)						
Object naming	946.6 (275.5)	963.8 (144.5)	958.8 (219.2)	.36	.74	.68
Action naming	1,059.2 (263.7)	1,105.4 (191.3)	1,096.2 (196)	.36	.44	.68

TABLE 3 Comparison of individual patient scores to control group performance during naming. Mean (M), *t*-values, and *p*-values from Crawford-Howell *t*-tests comparing accuracy and reaction time (RT) during object and action naming before and after surgery for tumor resection

	Pre-surgery			**Post-surgery**		
	Mean	***t*-value**	***p*-value**	**Mean**	***t*-value**	***p*-value**
Object naming						
Reaction times (ms)						
P1	958.76	0.04	.96	1,014.09	0.23	.81
P2	1,198.29	0.88	.38	1,357.76	1.45	.16
P3	868.91	−0.27	.78	789.25	−0.55	.58
P4	818.81	−0.45	.65	762.78	−0.64	.52
P5	1,067.23	0.42	.67	973.62	0.09	.92
P6	870.76	−0.26	.79	855.33	−0.32	.75
Accuracy (%)						
P1	96.29	−1.16	.26	96.29	−1.16	.26
P2	93.33	−1.21	.24	93.33	−1.21	.24
P3	100	0.58	.56	100	0.58	.56
P4	100	0.58	.56	100	0.58	.56
P5	100	0.58	.56	100	0.58	.56
P6	100	0.58	.56	100	0.58	.56
Action naming						
Reaction times (ms)						
P1	1,004.07	−0.20	.84	1,087.4	0.10	.91
P2	1,444.15	1.42	.17	1,467.46	1.5	.15
P3	890.12	−0.62	.54	882.57	−0.65	.52
P4	1,027.25	−0.11	.9	1,022.13	−0.13	.89
P5	1,177.37	0.43	.67	1,071.77	0.04	.96
P6	1,089.62	0.11	.91	1,046.11	−0.04	.96
Accuracy (%)						
P1	100	0.72	.47	100	0.72	.47
P2	92.6	−1.43	.17	92.6	−1.43	.17
P3	100	0.72	.47	100	0.72	.47
P4	93.33	−1.21	.24	93.33	−1.21	.24
P5	100	0.72	.47	93.33	−1.21	.24
P6	100	0.72	.47	93.33	−1.21	.24

of view = $256 \times 256 \times 176\ \text{mm}^3$, number of axial slices = 192, 1 mm isotropic resolution.

2.5 | MEG data pre-processing

Continuous data were initially pre-processed off-line using the temporal extension of the signal space separation method (Taulu and Simola, 2006) implemented in Maxfilter 2.2 (Elekta-Neuromag), which subtracts external magnetic noise from the MEG recordings, corrects for head movements and interpolates bad channels with algorithms implemented in the software. Subsequent analyses were performed using the FieldTrip toolbox version 20170911(Oostenveld, Fries, Maris, & Schoffelen, 2011) in MatlabR2014B. Recordings were downsampled to 500 Hz and segmented into epochs time-locked to stimulus presentation (i.e., picture to be named) from 500 ms before image onset to 1,000 ms after image onset.

Data were filtered with a DFT filter to remove line noise. A semi-automatic procedure was then employed to remove epochs with electromyographic artifacts, SQUID jumps and flat signal. A fast independent component analysis (ICA) was used to identify eye movements, blinks and electrocardiographic artifacts (Jung et al., 2000). The datasets of four healthy participants were excluded from the analysis due to excessive blinking and/or muscular artifacts resulting in the loss of a large number of trials (~70%). Thus, subsequent analyses were performed on a total of 16 healthy participants.

2.6 | Sensor level analysis

Time-frequency representations (TFR) were calculated from the artifact-free MEG segments for frequencies ranging from 1 to 30 Hz. TRFs were obtained using Hanning tapers and a fixed window length of 500 ms advancing in 10 ms steps, giving rise to a 2 Hz frequency resolution. Power estimates were calculated separately for each orthogonal direction of a gradiometer pair and then combined, resulting in 102 measurement channels. Power was expressed as relative change with respect to a ~500 ms pre-stimulus baseline. On average, conditions comprised 42.33 (*SD* = 2.02) artifact- and error-free trials for patients (no differences in trial number between object and action naming conditions or pre- and post-surgery sessions, Wilcoxon signed rank, all *ps* > .11) and 46.22 (*SD* = 7.22) for healthy controls (no difference between object and action conditions, *p* = .22). Importantly, no differences in the number of trials between patients and healthy adults were observed for object and action naming either before or after surgery (Welch's *t*-tests, all *ps* > .18).

2.7 | Selection of frequency-band and time-windows

Previous M/EEG studies indicate that power changes in the alpha and beta frequency-bands (Piai, Roelofs, Rommers, & Maris, 2015) reflect the retrieval of lexical-semantic information. Furthermore, evidence from studies on stroke (Kielar et al., 2016; Piai et al., 2017; Spironelli et al., 2013) and brain tumor patients (Lizarazu et al., 2020; Traut et al., 2019) points to an involvement of alpha and beta activity in functional compensation. Thus, we focused our analysis on low-frequency activity including alpha (8–12 Hz) and beta (13–28 Hz) oscillations. The time window was primarily chosen based on methodological constraints imposed by our task. Indeed, previous studies show that in overt production tasks artifact-free brain recordings can be measured up to approximately ~400 ms post-stimulus presentation (Ganushchak, Christoffels, & Schiller, 2011). Based on this evidence and visual inspection of the onset of speech production in our data, we focused our TFR analysis to the 0–500 ms time window after picture onset. More specifically, we selected two time-windows capturing early (0–200 ms) and late (200–500 ms) picture-naming related processes, including visual recognition, and conceptualization and lexical selection, respectively (Indefrey, 2011; Indefrey & Levelt, 2004; Liljestrom, Kujala, Stevenson, & Salmelin, 2015).

2.8 | Statistical analysis

In order to evaluate functional compensation within patients' language network we first explored the spectro-temporal pattern of responses triggered by our picture naming task in a group of healthy controls. More specifically, we calculated TFRs for object and action naming in early and late time-windows relative to picture onset and compared each of them relative to pre-stimulus baseline activity. Then, once main oscillatory patterns triggered by the task were identified in controls, we assessed longitudinal changes in the group of patients. Specifically, we calculated TFRs for object and action naming before tumor resection and contrasted them with those obtained 3 months after the surgery.

In all cases, differences in spectral power between conditions at the sensor level were assessed using cluster-based permutation tests (Maris & Oostenveld, 2007). This test controls for multiple comparisons using a cluster-based correction while maintaining sensitivity based on temporal, spatial and frequency dependency of neighboring samples. The permutation *p*-value was calculated using the Monte Carlo method with 1,000 random permutations. The threshold for significance testing was a *p*-value below 5% (two-tailed). Please note that the finding of a significant cluster implies that there is a significant difference between conditions. However, the cluster does not provide exact information about the timing and the spatial location of the effect. In other words, no statements about the onset/offset of the effect at the millisecond level or about its spatial extent can be made (Sassenhagen & Draschkow, 2019). While we had clear hypotheses about the frequency-bands potentially involved in the language effects (i.e., alpha-beta), no specific a priori hypotheses about timing and/or location were held. Thus, we averaged over frequency bins (alpha central frequency = 10.13 Hz and beta central frequency = 20.66 Hz;) but considered all sensors (i.e., combined gradiometers) and time-points within early and late time-windows in the analysis.

2.9 | Source localization

Participants' high-resolution 3D structural MRIs were segmented using Freesurfer software (Dale & Sereno, 1993). Co-registration between the MEG sensor coordinates and the participant's MRI coordinates was done by manually aligning the digitized head-surface and fiducial points to the outer scalp surface. The forward model was computed using the Boundary Element Method (BEM) implemented in the MNE software suite (Gramfort et al., 2014); RRID:SCR_005972) for three orthogonal tangential current dipoles (one for each spatial dimension) placed on a homogeneous 5-mm grid source space covering the whole brain. For each source, the forward model was then reduced to its two principal components of highest singular value, which closely correspond to sources tangential to the skull. We used both gradiometers and magnetometers in the source estimation, normalizing each sensor signal by its noise variance (500-ms baseline period prior to picture onset). Brain source activity was calculated for each participant using Linearly Constrained Minimum Variance (LCMV) beamformer approach (Van Veen, van Drongelen, Yuchtman, & Suzuki, 1997). A common filter was computed by combining the cross-spectral density (CSD) matrices from the time-frequency window of the significant sensor-level effects and an equally-sized baseline period prior to picture onset. The common filter was then applied separately to each condition to estimate source power. Since we focused our analysis on the local source power, we only used real-valued filter coefficients (Grutzner et al., 2010). To normalize source activity, the neural activity index (NAI) was calculated as a certain ratio between the power in the experimental conditions and the pre-stimulus baseline (Pcond-Pbase./Pbase). For each session (pre- and post-surgery), the MEG maps were first co-registered with their corresponding individual MRIs and then normalized to the standard MNI to run group level analyses. This was done by applying a non-linear transformation using the spatial-normalization algorithm implemented in SPM8 and it was checked by one of the authors (LA).

Group analyses were performed with the location-comparison method described in (Bourguignon, Molinaro, & Wens, 2018). Briefly, this method generates bootstrap group-averaged maps to build a permutation distribution of location difference between local maxima in the two conditions being compared, and test the null hypothesis that this distance is zero. Local maxima is defined as sets of contiguous voxels displaying higher power than all other neighboring voxels. The threshold for statistical testing at $p < .05$ was computed as the 95-percentile of the permutation distribution. All supra-threshold local MEG peaks were interpreted as indicative of brain regions likely triggering the sensor-level effects. This robust method has shown to deal well with the spectral leakage of the source-projected MEG data which can result from directly contrasting brain maps for different conditions.

2.10 | 3D lesion reconstruction

Lesions were manually drawn on the native space of participants' T1-weighted MPRAGE image by a trained technician using the MRIcron software (Rorden, Karnath, & Bonilha, 2007) and further supervised by the neurosurgeons in charge of the patients' awake craniotomy (SGR and IPG). The reconstruction was performed also using information from T2 images when lesion boundaries were not clear in the T1 MRI. The lesion was then normalized to the MNI template and alignment between the reconstructed lesion and the lesion in the native space was checked by one of the authors (IQ). A volume of interest (VOI) was created for each patient each time point. From each pre- and post-surgery 3D reconstruction, the tumor volume (cm^3) was calculated. Extent of resection (cm^3) was measured on postoperative imaging as: (Volume of (preoperative 3D Tumor Reconstruction ∩ postoperative Resection)*100/preoperative tumor volume).

2.11 | Structural measure of white mater changes

For the structural analysis, preoperative and postoperative T1 and T2 images were pre-processed and analyzed using the Voxel-Based Morphometry (VBM) toolbox and the SPM12 software package. Images were corrected for bias-field inhomogeneity; classified into gray, white matter and cerebrospinal fluid; registered to a standard MNI space using high-dimensional DARTEL normalization (Ashburner, 2007) and further smoothed with a 6 mm full width half maximum (FWHM) Gaussian kernel. We used a segmentation approach based on an adaptive maximum, a posterior technique which does not need a priori information about tissue probabilities (Rajapakse, Giedd, & Rapoport, 1997). We further refined this procedure, by accounting for partial volume effects and by applying a hidden Markov random field model which incorporates spatial prior information of the adjacent voxels into the segmentation estimation (Tohka, Zijdenbos, & Evans, 2004).

To assess potential differences in white matter involvement we used a region of interest (ROI) approach. ROIs were defined using a probabilistic tractography atlas (Rojkova et al., 2016). The selected tracts were the superior longitudinal fasciculus (SLF I), the arcuate fasciculus (AF, long branch) and the inferior-fronto-occipital fasciculus (IFOF), which constitute key bundles within dorsal and ventral language pathways and their damage is known to affect language processing (Agosta et al., 2013; Almairac, Herbet, Moritz-Gasser, de Champfleur, & Duffau, 2015; Catani & Mesulam, 2008; Mandelli et al., 2014). For each of these ROIs, we extracted preoperative and postoperative mean volumes in left and right hemispheres and corrected it for brain size using the total intracranial volume (TIV). By doing so, we obtained a proxy marker of white matter involvement based on lesion distribution in relation to white-matter probabilistic distribution derived from the tractography atlas (Rojkova et al., 2016). Comparisons between patient's morphometric values and controls were performed using Crawford-Howell *t*-tests.

2.12 | Correlational analysis between structure and function

First, we calculated a Language laterality index (LI) using the following formula:

$$\mathrm{LI} = (R - L)/(R + L).$$

where "*R*" and "*L*" represent power averaged across sensors for naming conditions (object and action pooled together) in right and left hemispheres, respectively; thus yielding positive values for right-lateralized and negative values for left-lateralized language-related activity. Given the left-lateralized pattern of oscillatory beta responses observed in the healthy control group as well as previous studies using beta power for calculating LI in speech production tasks (Traut et al., 2019), we reasoned that beta activity (13–28 Hz) was better suited than alpha to capture a potential shift toward the right hemisphere triggered by tumor presence and/or resection. Thus, the index was calculated for each patient and session (i.e., before and after surgery) only in the beta band. Furthermore, given the common left-lateralized pattern observed in both object and action naming, we combined them into a unique naming condition to reduce dimensionality and obtain a higher signal-to-noise ratio in the data. Please note, that this methodological choice (i.e., focus on beta responses) was further supported by the longitudinal contrast in patients, showing oscillatory effects circumscribed to the beta frequency-band (see below). LI was tested separately in controls and patients with Wilcoxon signed rank tests against zero and between groups using Welch's *t*-tests.

In addition, the same index was used to calculate lateralization of white matter tracts in controls and patients. More specifically, in the case of patients, this index was calculated separately in preoperative and postoperative stages and, in each case, individually compared against the control group using Crawford-Howell *t*-tests.

Finally, Pearson correlations between preoperative and postoperative white matter ROIs LI and beta longitudinal changes (post – presurgery beta LI) were run to establish whether potential reshaping at the structural level was associated with functional one.

3 | RESULTS

3.1 | Behavioral results

Table 2 shows mean accuracy and reaction time values (RT) for healthy controls and patients, as well as contrasts between groups and surgery stages. Overall, no differences in performance (i.e., accuracy and RTs) were observed between groups. These results were further confirmed at the individual patient level with Crawford-Howell *t*-tests, which supported the absence of significant behavioral effects (see Table 3). In addition, no differences were observed within patients when comparing performance before and after surgery. This finding was well expected, given that patients with slow-growing brain tumors typically exhibit a normal neurological and behavioral exploration, at least when considering relatively easy low-level tasks (DeAngelis, 2001). Furthermore, the maintenance of this behavioral pattern after surgery speaks in favor of successful language compensation.

3.2 | Oscillatory signatures of picture naming in healthy controls

Figure 2 shows the time-frequency representations (TFRs), topographical distributions and source localization plots of the naming conditions as compared to baseline in the alpha (8–12 Hz) and beta (13–28 Hz) frequency-bands.

Early time-window effects (0–200 ms): Object and action naming showed early alpha power increases as compared to baseline. This effect was highlighted by significant positive clusters (both Monte Carlo *ps* = .004, two-tailed), over bilateral posterior and left middle sensors, in the case of objects; and bilateral posterior sensors in the case of actions. Source localization of early alpha effects identified the related local maxima in occipito-parietal regions. In addition, similar beta power increases were observed for object and action naming conditions as indicated by significant positive clusters over left posterior and middle sensors (both Monte Carlo *ps* = .01, two-tailed).

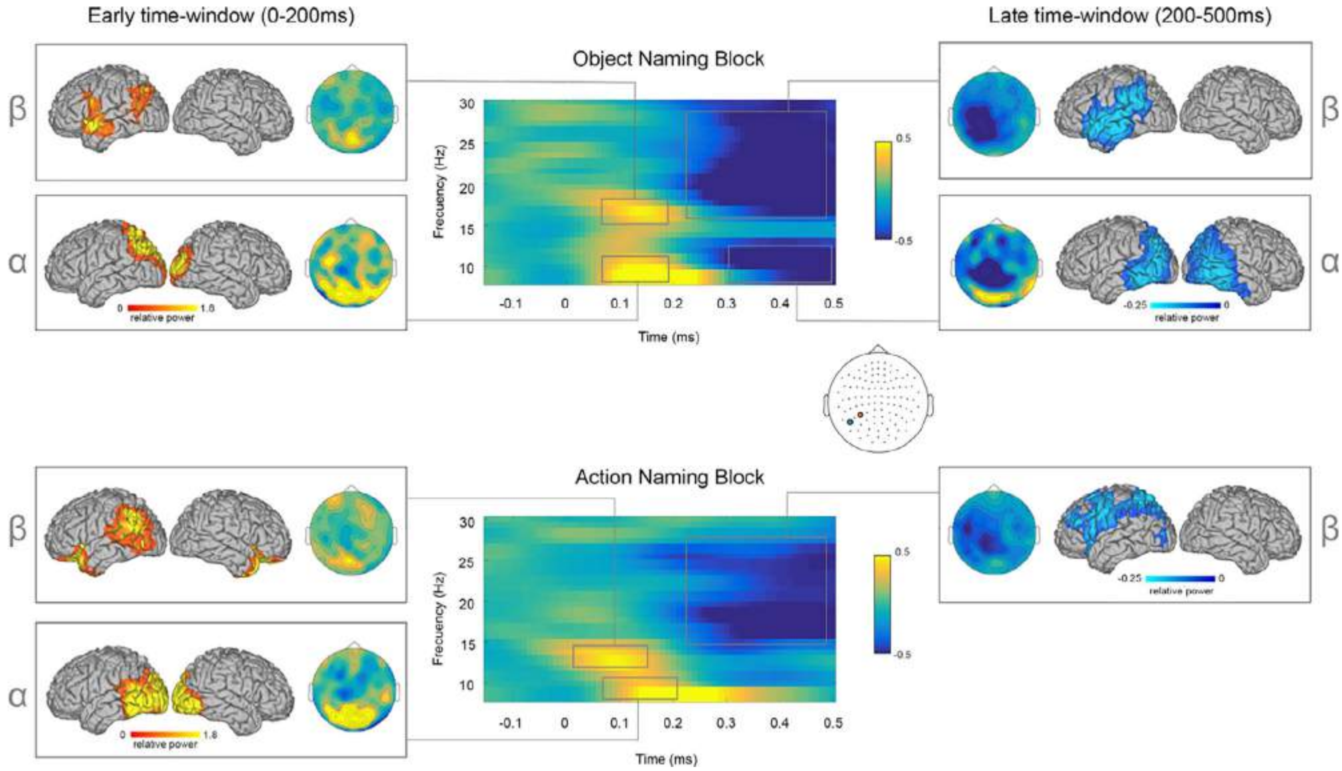


FIGURE 2 Oscillatory signatures of speech production in healthy controls. TFR of alpha and beta power in the object (top panel) and action (bottom panel) conditions over time. TFRs are plotted as relative power change compared to the baseline period over representative significant sensors (objects = M1632 + M1633; highlighted in orange; actions = M1722 + M1723; highlighted in blue). Topographic distribution plots show posterior alpha and beta power increases at early stages (0–200 ms), and left-lateralized anterior and posterior beta power decreases at later stages (200–500 ms)

Source localization showed local maxima peaking in left angular gyrus and inferior frontal gyrus (IFG) for objects; and in left supramarginal and orbitofrontal areas for actions (Figure 2, right panel).

Late time-window effects (200–500 ms): During this period, a significant negative cluster (Monte Carlo *p* = .01, two-tailed) encompassing bilateral posterior and middle sensors revealed alpha power decreases only for the object naming condition. At the source level, this effect showed local minima in bilateral occipito-temporal regions.

Finally, both conditions showed beta power decreases that were underscored by significant negative clusters over bilateral posterior and anterior sensors in the case of objects (Monte Carlo *p* = .004, two-tailed); and bilateral posterior and left anterior sensors in the case of actions (Monte Carlo *p* = .01, two-tailed). Source localization of beta effects showed local minima in the left IFG, irrespectively of the naming condition, while object naming additionally recruited the left anterior temporal pole and action naming the left superior parietal and dorsal premotor cortex (Figure 2, left panel).

Overall, these findings provide a baseline to interpret potential language reshaping in patients. In brief, they support previous M/EEG studies (Piai et al., 2015, 2017) showing the involvement of alpha-beta oscillations in speech production and align well with evidence indicating the existence of partially non-overlapping networks for the processing of object and action knowledge, showing a diverse contribution of ventral and dorsal nodes of the language network, respectively (Vigliocco et al., 2011).

3.3 | Functional plasticity in brain tumor patients

Figure 3 shows TFRs, topographic distributions of the object effect found in patients with ventral temporal lesions (Figure 3a) and of the action effect, found in patients with dorsal fronto-parietal lesions (Figure 3b). Overall, when comparing oscillatory activity across sessions (post- vs. pre-surgery for tumor resection) within each group of patients, we found significant differences between sessions in the beta band (13–28 Hz), with power increases after tumor resection.

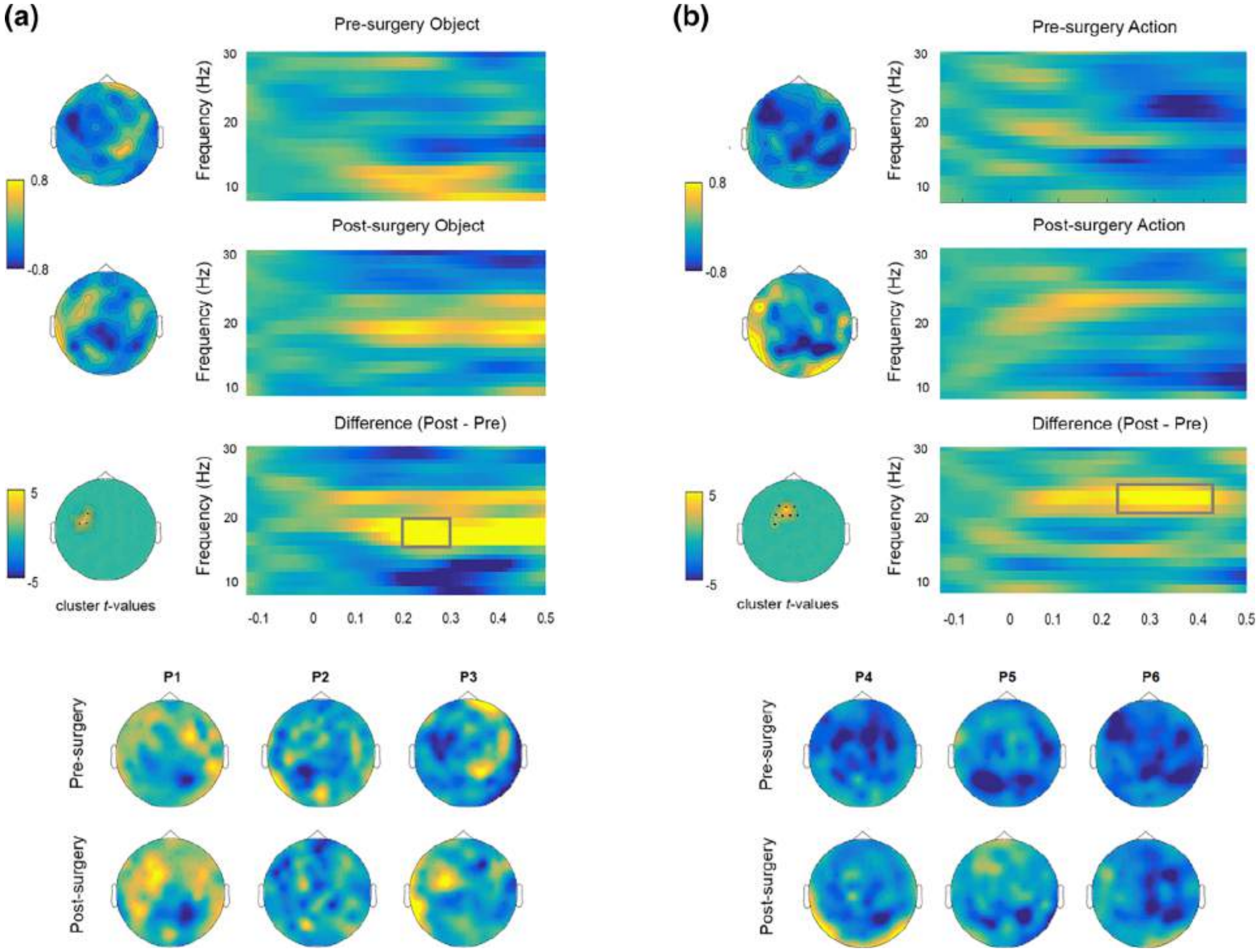


FIGURE 3 Longitudinal functional plasticity in brain tumor patients. (a) TFRs of patients with ventral lesions showing beta power increases after surgery only for objects; (b) TFRs of patients with dorsal lesions showing a similar effect but only for actions. TFRs are plotted as relative power changes compared to the baseline period in averaged significant sensors (shown in black over the topographical distribution of the significant clusters)

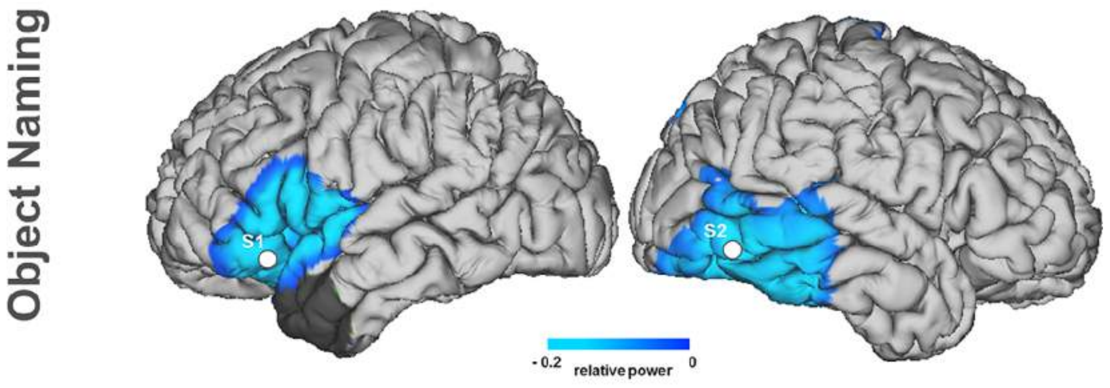
Longitudinal effect for objects in patients with ventral lesions. A positive cluster (Monte Carlo $p < .001$, two-tailed) over left frontal sensors highlighted the presence of significant differences between pre and post conditions in the beta range. No effects were observed in the alpha range (all p-clusters > .24). Importantly, no significant differences were observed for the action naming condition in any of the low-frequency bands (all p-clusters > .46). Source localization of the object-related beta effect involved the left IFG and the right posterior middle temporal cortex (see Figure 4).

Longitudinal effect for actions in patients with dorsal lesions. A positive cluster was found over left frontal sensors (Monte Carlo $p = .001$, two-tailed), underscoring post vs. pre significant differences in the beta range. No effects were found in alpha activity (all p-clusters > .49). Importantly, no differences were observed for the object condition in any of the low-frequency bands (all p-clusters > .25). Source localization of the action-related beta effect involved the left IFG, the right middle-frontal gyrus, the right superior parietal and the right dorsal premotor cortex (see Figure 4).

3.4 | Structural reshaping in patients

To detect possible alterations in right white matter structures as a consequence of left-hemispheric tumor growth (i.e., preoperative) and /or neurosurgical intervention (i.e., postoperative), we estimated a proxy measure of white matter volume in language-related tracts of interest in patients and healthy controls. First, we measured ROI volumes in patients and controls within each hemisphere and compared them separately using Crawford-Howell t-tests. This was done to rule out that potential differences in LI were trivially quantifying the damage in the left hemisphere rather than compensatory volume increases. Table 4 shows patients mean TIV-normalized preoperative and postoperative volume values for each white matter ROI in each hemisphere as well as comparison statistics at the individual level. When comparing TIV-normalized values in left and right ROI before surgery, differences between patients and controls were observed in all the tracts irrespectively of the hemisphere (all ps < .001). After

(a) Patients with ventral lesions



(b) Patients with dorsal lesions

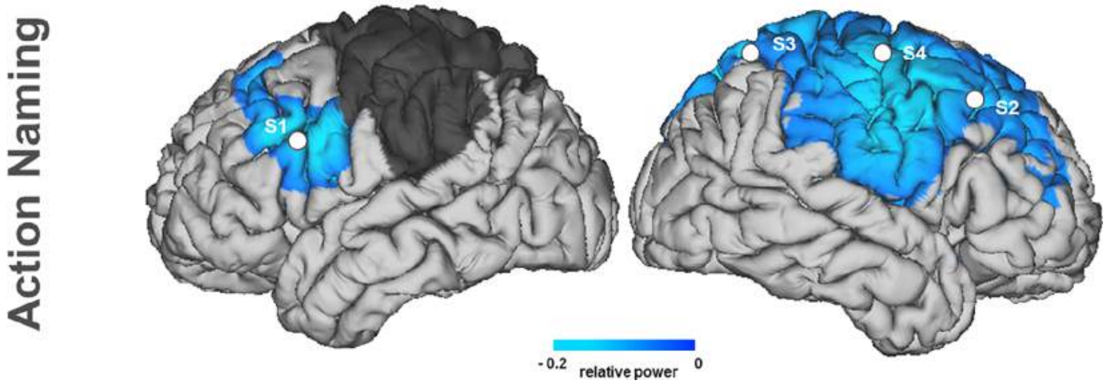


FIGURE 4 Source reconstruction of oscillatory longitudinal effects (post vs. pre). Regions showing beta power changes for patients with ventral (a) and dorsal (b) lesions. Significant peak activity locations (MNI coordinates [x, y, z]) within these areas are marked with white dots. Post-surgery lesion mask overlap is displayed in gray. For the object naming condition: S1 = left IFG [BA45: −52, 19, 4] and S2 = right posterior middle-temporal gyrus [BA21: 64, −36, −1]. For the action naming condition: S1 = left IFG [BA44: −50, 16, 27], S2 = right medial-frontal gyrus [BA9: 34, 39, 34], S3 = right superior parietal cortex [BA7: 19, −67, 62], and S4 = right dorsal premotor cortex [BA6: 43, −7, 50]

surgery, most of the patients showed no differences with controls in any of the ROI. However, patient 6 showed differences in the left AF and left SFL, and patient 4 in the left SLF.

Afterwards, we calculated ROI laterality indexes in patients (before and after surgery) and controls and used Crawford-Howell *t*-tests to compare each patient against the control group (see Table 5). Before surgery, all patients showed significant alterations in ROI lateralization as compared to controls in the AF and the IFOF. Also, most of them showed differences in the SLF with the exception of patients 2 and 5. After the surgery, no differences between controls and patients were observed for IFOF lateralization. Similarly, in the case of the AF, most of the patients showed no differences when compared to controls, with the exception of patient 6 and 3. Finally, in the case of the SLF, the patients with ventral damage showed no differences with controls. However, those patients with dorsal lesions, showed a significant shift in ROI lateralization toward the right, contralesional hemisphere.

3.5 | Correlational analysis between functional and structural laterality indexes

In healthy controls, a Wilcoxon signed rank test against zero showed that beta power was lateralized toward the left hemisphere ($W = 102$, $p = .04$, $M = –0.22$, $SE = 0.13$). The same test performed in patients showed a leftward lateralization of language-related beta activity before surgery ($W = 21$, $p = .03$, $M = –0.13$, $SE = 0.04$) and a rightward shift after tumor resection ($p = .03$, $M = 0.61$, $SE = 0.24$; see Figure 5a). When comparing patients to controls, no significant differences were observed before tumor resection (Welch $t[17] = –0.65$, $p = .51$; Cohen's $d = –0.24$). However, after surgery, patients significantly differed from controls ($t[8] = 3.05$, $p = .01$; Cohen's $d = 1.5$), with this effect likely reflecting the shift of beta power toward the right hemisphere. See Figure 5a.

Finally, we correlated structural ROI LIs with the beta longitudinal LI and found a significant positive correlation between beta and post-surgery SLF laterality index (Pearson $r = 0.92$; $p = .009$), overall indicating that postoperative lateralization of beta power and SLF toward the right hemisphere were associated (see Figure 5b).

4 | DISCUSSION

In the present study, we considered brain tumor patients as an experimental model to test oscillatory patterns supporting language plasticity and reorganization. Specifically, we combined functional and structural measures by means of MEG and MRI and: (a) tracked the oscillatory dynamics subserving object and action naming in the intact and the damaged brain; (b) measured structural reshaping in contralesional white matter tracts involved in language processing. Overall, two main findings can be underscored. First, longitudinal functional changes in object and action naming within patients were observed in the beta band. Interestingly, plasticity patterns were specifically

TABLE 4 Volume values of white matter ROIs in patients and comparison statistics. Individual patients TIV-normalized volumes for white matter regions of interest (ROI) before (PRE) and after (POST) surgery within each hemisphere, including the superior longitudinal fasciculus (SLF), arcuate fasciculus (AF) and inferior fronto-occipital fasciculus (IFOF). Crawford-Howell *t*-values and *p*-values comparing each patient to the control group are provided

	PRE	*t*-value	*p*-value	POST	*t*-value	*p*-value
SLF left						
P1	0.0926	13.6	<.001	0.0411	1.13	.27
P2	0.102	15.8	<.001	0.0424	1.34	.19
P3	0.0862	12	<.001	0.0377	0.3	.76
P4	0.0938	13.8	<.001	0.024	–3	.008
P5	0.0903	13	<.001	0.024	–3	.008
P6	0.101	15.6	<.001	0.0302	–1.5	.15
SLF right						
P1	0.085	12.3	<.001	0.039	1.06	.3
P2	0.095	14.8	<.001	0.039	1.06	.3
P3	0.077	10.4	<.001	0.036	0.33	.74
P4	0.0844	12.2	<.001	0.036	0.33	.74
P5	0.0839	12	<.001	0.0344	–0.06	.95
P6	0.0897	13.5	<.001	0.0356	0.23	.81
AF left						
P1	0.0534	12.5	<.001	0.0219	–1.09	.29
P2	0.0582	14.5	<.001	0.0229	–1.04	.31
P3	0.0498	10.9	<.001	0.0237	–0.31	.76
P4	0.0542	12.8	<.001	0.0225	–0.82	.42
P5	0.0517	11.7	<.001	0.021	–1.47	.16
P6	0.0585	14.7	<.001	0.0148	–4.14	<.001
AF right						
P1	0.0356	4.79	<.001	0.022	–0.53	.6
P2	0.0391	6.43	<.001	0.022	–0.53	.6
P3	0.0335	3.98	<.001	0.02	–1.35	.19
P4	0.0349	4.79	<.001	0.02	–1.35	.19
P5	0.035	4.79	<.001	0.021	–0.93	.36
P6	0.0389	6.02	<.001	0.021	–0.93	.36
IFOF left						
P1	0.092	11.5	<.001	0.036	0.17	.86
P2	0.101	–5.08	<.001	0.035	0.049	.96
P3	0.0838	9.86	<.001	0.036	0.17	.86
P4	0.0913	11.4	<.001	0.0355	–0.03	.97
P5	0.0891	10.9	<.001	0.0357	0.11	.91
P6	0.0982	12.8	<.001	0.0345	–0.13	.89
IFOF right						
P1	0.088	10.2	<.001	0.0387	0.44	.66
P2	0.096	11.8	<.001	0.0394	0.58	.56
P3	0.08	8.65	<.001	0.0385	0.41	.68
P4	0.087	10	<.001	0.0377	0.25	.8
P5	0.086	9.84	<.001	0.0383	0.37	.7
P6	0.092	11	<.001	0.0374	0.19	.85

TABLE 5 Comparison of individual patient white matter ROI lateralization index to control group profiles. Laterality indexes (LI), *t*-values and *p*-values from Crawford-Howell *t*-tests comparing preoperative and postoperative lateralization profiles of white matter ROIs in each individual patient against the control group. Percentage (%) of damage to the tract in the left hemisphere is provided

	LI pre	*t*-value	*p*-value	LI post	*t*-value	*p*-value	% LD
SLF I							
Controls	−0.0254						
P1	−0.043	−2.22	.04	−0.023	0.28	.78	0
P2	−0.039	−1.72	.1	−0.039	−1.72	.1	0
P3	−0.054	−3.6	.002	−0.015	1.28	.21	0
P4	−0.052	−3.35	.004	0.191	26.9	<.001	0.338
P5	−0.036	−1.34	.19	0.178	25.4	<.001	15.358
P6	−0.06	−4.35	<.001	0.082	13.4	<.001	3.676
AF							
Controls	−0.0243						
P1	−0.199	−13.6	<.001	0.002	2.03	.06	0
P2	−0.195	−13.3	<.001	−0.012	0.93	.36	0
P3	−0.195	−13.3	<.001	−0.072	−3.74	.001	0.016
P4	−0.215	−14.9	<.001	−0.042	−1.4	.18	0
P5	−0.192	−13.1	<.001	−0.0002	1.85	.08	0.767
P6	−0.201	−13.8	<.001	0.174	15.4	<.001	3.941
IFOF							
Controls	0.0186						
P1	−0.022	−3.12	.007	0.028	0.73	.47	0.03
P2	−0.026	−3.43	.003	0.053	2.66	.01	0
P3	−0.018	−2.81	.01	0.032	1.04	.31	0
P4	−0.023	−3.19	.006	0.029	0.81	.43	0
P5	−0.012	−2.35	.03	0.034	1.2	.25	0
P6	−0.028	−3.58	.002	0.039	1.58	.13	0.554

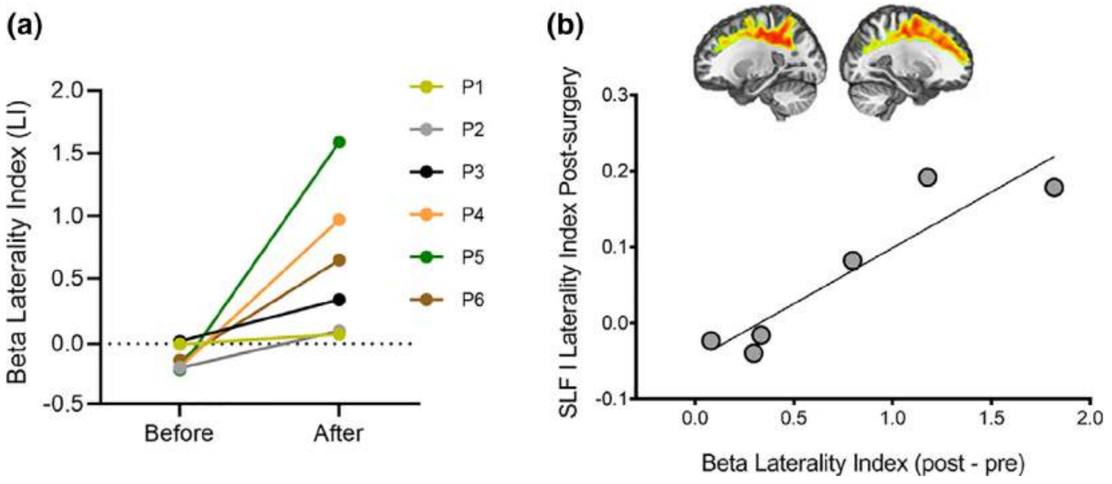


FIGURE 5 Structural reshaping and association with beta power lateralization. (a) Beta laterality index (LI) before and after tumor resection is shown for each individual patient. Positive values indicate rightward lateralization, negative values indicate leftward laterlization. (b) Scatterplot shows significant positive correlation between SLF lateralization after surgery and beta longitudinal LI (post − pre-surgery LI)

related to tumor location, with ventral damage leading to compensation in object naming and dorsal damage to compensation in action naming. Of note, this category-related dissociation was present in healthy controls, with beta power decreases showing a different engagement of ventral and dorsal nodes in the language network during object and action naming, respectively (Gleichgerrcht et al., 2016; Lubrano et al., 2014; Vigliocco et al., 2011). Second, at the structural level, patients showed preoperative reshaping in white matter regions underscored by significant lateralization differences in the IFOF, the AF and the SLF as compared to controls. Postoperative differences were also evident mostly in patients with dorsal damage, showing a rightward shift in SLF lateralization. Interestingly, this structural change positively correlated with the longitudinal shift of beta power toward the right hemisphere, suggesting that functional and structural components of brain plasticity go hand to hand in language reorganization.

Oscillatory signatures of speech production in the intact brain. We first ran a picture-naming task in a group of healthy participants in order collect normative data to better understand the potential uniqueness of patients' responses due to language reshaping. When considering previous studies measuring speech production in healthy adults, beta activity has been classically associated to motor aspects involved in articulation (Saarinen, Laaksonen, Parviainen, & Salmelin, 2006; Salmelin & Sams, 2002). However, as precisely pointed out by Piai et al. (2015) these studies compared the production of words vs. pseudo-words, which do not exist in memory and hence do not allow tapping into memory and semantic components involved in speech production. Here, by using a picture-naming task—which does capture the aforementioned aspects—we found a left involvement of beta activity which, in keeping with previous findings (Laaksonen, Kujala, Hulten, Liljestrom, & Salmelin, 2012; Liljestrom et al., 2015; Piai et al., 2015), likely reflects lexico-semantic processing of object and action knowledge. Furthermore, beta activity was differently distributed for object and action naming, with the former condition mostly engaging ventro-temporal areas and the latter one parietal and pre-motor regions. In addition, bilateral alpha activity was only observed for object naming. A potential interpretation of these findings is that object and action concepts differed in terms of feature types, with visual features more represented in the object domain and motoric features in the action one (Huttenlocher & Lui, 1979; Vinson, Vigliocco, Cappa, & Siri, 2003). Indeed, this view predicts that, at a neural level, the lexical retrieval of object nouns will mainly recruit occipito-temporal regions storing visual features, while the retrieval of action verbs will mainly recruit motor/pre-motor structures associated to motoric features (Gainotti, Silveri, Daniele, & Giustolisi, 1995; Moseley, Pulvermuller, & Shtyrov, 2013; Pulvermuller, Lutzenberger, & Preissl, 1999). In support of this prediction, object naming showed alpha-beta cortical activations in occipito-temporal areas, while action naming engaged the classical dorsal fronto-parietal network involved in processing action concepts with this effect being mainly circumscribed to beta activity (Kemmerer, Rudrauf, Manzel, & Tranel, 2012; Watson, Cardillo, Ianni, & Chatterjee, 2013).

Nevertheless, due to the overt nature of the task implemented here, it can be argued that beta modulations sourced in the premotor cortex, could actually reflect myogenic activity rather than semantic processing. While we cannot completely rule out this possibility, we find it quite unlikely due to several reasons. First, beta activity preceded vocal responses for more than 400 ms. Second, the beamformer technique used in the present study is known to attenuate myogenic artifacts by suppressing signals whose spatial scalp distribution cannot be explained by a dipolar source in the brain (Piai et al., 2015). Finally, the specificity of the observed effect (i.e., present in the action but not in the object naming condition) speaks in favor of a category related modulation and fits well with evidence showing that motor beta oscillations sourced in premotor regions play a key role in action semantics (Grisoni, Dreyer, & Pulvermuller, 2016; Hauk, Johnsrude, & Pulvermuller, 2004; Weiss & Mueller, 2012).

4.1 | Neuroplasticity of language in brain tumor patients

Previous studies indicate that patients with slow-growing brain tumors exhibit normal clinical exams -at least when considering standard neuropsychological assessment (Duffau & Capelle, 2001; Walker & Kaye, 2003). In agreement with this evidence, we found that patients were able to correctly retrieve object and action knowledge either before or after surgery, overall suggesting successful reorganization and language preservation.

At the neurophysiological level, when comparing functional patterns longitudinally (post- vs. pre-surgery activity), beta rhythms (13–28 Hz) were called into play. Beta synchronization is assumed to facilitate long-range communication between distant brain areas supporting high-level interactions (Kopell, Ermentrout, Whittington, & Traub, 2000; Varela, Lachaux, Rodriguez, & Martinerie, 2001). Furthermore, it has been shown that increased beta connectivity between distant brain regions correlates with greater quality of life in brain injured patients (Castellanos et al., 2010). Thus, this brain rhythm may play a key role in the successful recruitment of remote ipsilesional and contralesional regions necessary to preserve high-level cognitive functions at the network level. Interestingly, beta power modulations varied depending on damage location and semantic category, with ventral and dorsal lesions specifically modulating object and action naming, respectively. These findings align well with the dissociation observed in the group of healthy controls and with previous evidence (Gleichgerrcht et al., 2016; Kemmerer et al., 2012; Pisoni et al., 2018; Tranel, Adolphs, Damasio, & Damasio, 2001; Vigliocco et al., 2011) suggesting a differential engagement of temporal and fronto-parietal regions in object and action naming. Nevertheless, our results contrast with the dominant view suggesting that frontal areas are exclusively associated to action processing. Indeed, we found evidence for increased beta activity in the left IFG irrespectively of the naming condition, possibly reflecting controlled semantic retrieval (Noonan, Jefferies, Visser, & Lambon Ralph, 2013) or lexical selection processes (Thompson-Schill, D'Esposito, & Kan, 1999).

When considering the net output of the longitudinal analysis, patients with ventral and dorsal lesions showed overall increases in beta power after tumor resection. However, while in the dorsal group power decreases were present both before and after surgery, being larger before tumor resection; in the ventral group, power increases were present after but not before surgery. Thus, even though the net output is similar (i.e., beta power increases), these effects might involve distinct physiological mechanisms. In the first case, less power decreases after tumor resection seem to reflect, as shown by their topographical distribution, a downregulation of left frontal activity, which was instead playing a stronger role before tumor resection, possibly through the compensatory recruitment of ipsilesional frontal areas as it has been previously shown in the literature (see Spironelli et al., 2013). In the second case, left frontal beta power decreases present in the preoperative but absent in the postoperative stage, likely indicate the disengagement of left frontal nodes following tumor resection. Nevertheless, these assumptions are rather speculative and further studies need to zoom into the different compensatory mechanisms and their relation to tumor resection.

From an anatomical standpoint, longitudinal beta modulations in patients with ventral damage were localized in the left IFG and the right posterior MTG. These regions have been implicated in the semantic control network (Noonan et al., 2013; Wright, Stamatakis, & Tyler, 2012) and were recruited by controls during object naming, thus likely reflecting compensatory activity in preserved healthy regions. When considering patients with dorsal damage, longitudinal beta power modulations were observed in the left IFG and contralesional healthy homologs, including right superior parietal, premotor and middle-frontal areas. Of note, this latter collection of right areas was not found to be activated in healthy controls during action naming, which instead showed a completely left-lateralized network. Thus, this pattern possibly reflects language reorganization supported by the unmasking of a homolog network in the healthy hemisphere. Indeed, recent studies (Duffau, 2008; Vassal et al., 2010) using direct electrical stimulation have revealed a right mirror organization of language networks, pointing to the existence of functional redundancies that can undertake functions previously supported by damaged areas. Furthermore, this finding also aligns well with neurophysiological evidence from brain tumor (Piai et al., 2020; Traut et al., 2019) and stroke patients (Kielar et al., 2016; Piai et al., 2017) showing compensatory recruitment of the right hemisphere during language processing. Of note, one of these studies (Piai et al., 2017) showed that contralesional recruitment in the alpha-beta band was associated with the integrity of the posterior bundles of the corpus callosum. Indeed, it has been shown that the integrity of these withe matter bundles are critical for recruiting healthy areas contralateral to the lesion (Celeghin et al., 2017).

Here, irrespectively of tumor location, all patients showed preoperative structural reshaping in the SLF connecting parietal and premotor cortex (Kamali, Flanders, Brody, Hunter, & Hasan, 2014; Makris et al., 2005) the AF (long branch) connecting Broca and Wernicke areas and the IFOF, connecting occipital and frontal regions (Herbet, Moritz-Gasser, & Duffau, 2017). It is well documented that glioma invasions trigger reorganizations at the whole-brain network level which are not circumscribed to the area invaded by the tumor (Cargnelutti, Ius, Skrap, & Tomasino, 2020).

On the one hand, the IFOF has been previously associated with semantic processing (Herbet et al., 2017). The AF and the SLF, on the other hand, have been related to phonological processing and lexical retrieval during language production, since their disruption with DES produces phonological paraphasias and pure anomia, respectively (Sarubbo et al., 2015). While current data do not allow dissociating which of these functions were specifically compensated in the patients, the finding of a positive association between postoperative right volumetric increases in the SLF and greater beta power in the right hemisphere may suggest that lexical retrieval components were those mostly implicated.

In line with recent studies (Almairac, Duffau, & Herbet, 2018; Zhang et al., 2018) using a VBM approach and showing volumetric increases in contralesional gray matter homologs, here we observed a similar pattern but for white matter ones. Interestingly, Zhang and collaborators (2018) also reported that structural changes correlated with functional ones, such that increased functional activity was related to structural alterations reflected in greater volume, whereas decreased neural activity was independent of structural change. Overall, the authors related macrostructural variations to functional compensation (i.e., suggesting a structure–function coupled response to deal with the tumor), an interpretation that aligns well with our results. However, these studies only analyzed preoperative data. Here, we provide preliminary evidence suggesting not only that similar compensatory mechanisms might be also involved in white matter macrostructural reshaping but that these changes can be observed before but also after surgery.

Nevertheless, it is worth mentioning that the present study is not without limitations. Even though collecting longitudinal data in this type of populations is quite challenging, the most evident limitation is the use of a relatively small sample size, thus requiring caution when generalizing and interpreting current results. Second, we cannot completely rule out the potential effect that differences in corticospinal fluid (CSF) may have in the observed effects. Indeed, one can expect an asymmetrical amount of CSF given that, between the two sessions, resections occurred in only one hemisphere. However, magnetic fields are quite insensitive to CSF conductivity as it has been shown by previous studies (Vorwerk et al., 2014), thus turning unlikely a significant contribution of CSF to the source reconstruction. Nevertheless, future studies are necessary to replicate current findings in larger patient samples and disentangle if observed compensatory patterns can be generalized to a larger population and further specify under which circumstances white matter changes are prone to take place.

5 | CONCLUSIONS

In line with previous neurophysiological findings, our results point to a fundamental role of beta oscillations in language reorganization. Furthermore, by showing white matter changes and their link to the rightward shift in beta laterality following tumor resection, they suggest that structure and function work concertedly in supporting plastic changes involved in this process. Together, these results provide new insights into the potential for language plasticity in preoperative and postoperative stages, which ultimately help to delineate personalized surgical strategies to preserve linguistic functions in brain tumor patients.

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CONFLICT OF INTEREST

The authors declare no potential conflict of interest.

DATA AVAILABILITY STATEMENT

Data availability statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

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Oscillatory dynamics underlying noun and verb production in highly proficient bilinguals

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Words representing objects (nouns) and words representing actions (verbs) are essential components of speech across languages. While there is evidence regarding the organizational principles governing neural representation of nouns and verbs in monolingual speakers, little is known about how this knowledge is represented in the bilingual brain. To address this gap, we recorded neuromagnetic signals while highly proficient Spanish–Basque bilinguals performed a picture-naming task and tracked the brain oscillatory dynamics underlying this process. We found theta (4–8 Hz) power increases and alpha–beta (8–25 Hz) power decreases irrespectively of the category and language at use in a time window classically associated to the controlled retrieval of lexico-semantic information. When comparing nouns and verbs within each language, we found theta power increases for verbs as compared to nouns in bilateral visual cortices and cognitive control areas including the left SMA and right middle temporal gyrus. In addition, stronger alpha–beta power decreases were observed for nouns as compared to verbs in visual cortices and semantic-related regions such as the left anterior temporal lobe and right premotor cortex. No differences were observed between categories across languages. Overall, our results suggest that noun and verb processing recruit partially different networks during speech production but that these category-based representations are similarly processed in the bilingual brain.

Speech production constitutes the bedrock of human communication. This seemingly effortless ability actually depends on a set of complex neural processes, including the retrieval of lexical-semantic information from long-term memory, its translation to articulatory motor programs and the monitoring of what is being verbally expressed[1].

In daily life conversational settings, nouns and verbs constitute basic components of speech across almost all languages[2]. Nouns and verbs have distinct communicative roles, with the former ones prototypically involving reference to objects, and the latter ones the predication of actions, events and states of being[3]. A growing body of evidence suggests that noun and verb processing are represented in partially non-overlapping networks supporting grammatical and/or lexical/semantic language dimensions, for a review see[4,5].

Much of what is known about noun and verb representation can be traced back to neuropsychological studies in aphasic patients showing selective difficulties in producing either nouns or verbs after damage to left temporal areas and to fronto-parietal regions, respectively[6–8]. More recently, neuroimaging studies have shown similar patterns of noun–verb dissociation in temporal and frontal regions[9–11]. Moreover, studies using cortical stimulation during awake brain surgery also converge in underscoring a category-based segregation, with greater number of errors in noun naming when stimulating regions in the inferotemporal cortex and greater impairment in verb naming when disrupting activity in prefrontal and parietal areas[12–15].

At the neurophysiological level, M/EEG studies[16–18], have reported event-related (i.e., ERP/ERF) differences between nouns and verbs in the P200 and the N400 components which are typically related to lexical access and semantic processing, respectively[19]. For instance, more positive P200 responses in fronto-central motor regions have been found for verbs[16,17], potentially suggesting that neural generators outside classical language areas may contribute to differences between nouns and verbs. In the case of the N400, a similar effect has been shown, with verbs being overall more positive than nouns[18]. Since this latter component reflects semantic processing, this finding has been interpreted in terms of how meaning-related information from different concepts is retrieved

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(e.g., visual vs. motoric semantic features), resulting in amplitude and/or topographic differences within this time window.

Nonetheless, these studies have examined the organizational principles governing the neural representation of noun and verb categories in monolingual speakers, leaving unanswered the question of whether a similar organization also stands for bilingual ones. A few recent neuroimaging studies on bilingual speakers have shown similar responses for both languages during noun and verb generation in temporal, parietal, premotor and middle-frontal areas[20,21], thus supporting the existence of convergent neural substrates across different languages. Yet, there is also evidence[22] showing that high proficient bilinguals exhibit differential neural patterns of activation for nouns and verbs in their two languages, suggesting that the early bilingual brain can be also sensitive to language-specific properties or, alternatively, that it can be modulated by experiential factors (e.g., proficiency, age of acquisition), even when the L2 is mastered in a native-like fashion.

In this context, inconsistencies yielded by fMRI studies can be potentially overcome with more fine-grained techniques. It could be, for instance, that differences and/or similarities across languages during noun and verb production may rely on temporal and spectral properties of brain activity, which are not captured by fMRI signals. Indeed, hemodynamic responses are slow (i.e., starting approximately ~ 2 s after stimulus presentation) and linguistic functions, occurring on the subsecond time-scale, need to be examined with high-temporal resolution techniques capable of tracking language processing in real-time. Furthermore, fMRI does not allow decomposing brain signals into their different oscillatory rhythms. Interestingly, neurophysiological techniques such as magnetoencephalography (MEG), offer the unique opportunity of capturing this information and, thus to test whether oscillatory dynamics (i.e., the unfolding in time of rhythmic fluctuations) are similar (or not) across languages in the bilingual brain.

It has been suggested that oscillations play a key role in neural communication supporting cognition[23], providing spectral fingerprints of distinct cognitive operations that would remain blind to traditional evoked analysis (e.g., ERP/ERF), in which responses are phase-locked to the experimental stimulus[24,25]. Indeed, some studies have reported weak spatio-temporal overlap between evoked and rhythmic responses during picture naming, potentially suggesting that the neural processes captured by these two approaches actually differ[26].

When considering previous M/EEG studies measuring oscillatory dynamics during speech production in monolinguals, theta (4–8 Hz) power increases[27] and alpha–beta (8–25 Hz) power decreases[28–30] have been reported in association to the retrieval of lexical-semantic information from long-term memory. In addition, frontal theta power increases during speech production have been related to executive control in the face of increased cognitive demands[31].

In a recent study[32] conducted in L1 Spanish speakers, we have shown a different engagement of ventral and dorsal streams during the production of nouns and verbs, respectively; involving decreases in alpha and beta frequency bands between 200 and 500 ms after picture presentation. Yet, whether these oscillatory brain responses remain similar when accessing different categories (i.e., nouns vs. verbs) in bilingual speakers remains largely unexplored.

Here, we sought to move further by shedding light on the neurophysiological signatures of nouns and verbs in two languages within a study population of highly proficient Spanish–Basque bilinguals by means of MEG. Participants were asked to overtly name pictures depicting objects or actions in the context of minimal sentences, thus forcing them to produce utterances involving nouns or action verbs, respectively. Importantly, items from both languages and categories were carefully matched for several variables, including word frequency, familiarity and length[33].

Overall, under the hypothesis that nouns and verbs are underpinned by different oscillatory brain responses[32], we predicted distinct alpha–beta patterns for the use of these categories in a time-window typically associated to lexico-semantic processing (~ 200–500 ms). In addition, we expected increased theta power for verbs than nouns likely related to greater processing demands during semantic integration[34]. Indeed, verbs exhibit more shallow relations to other words in the lexicon as compared to nouns, which stay relatively consistent in their meaning[5,35]. Furthermore, based on previous neuroimaging evidence[20,21] showing that the same neural structures are involved in the differential processing of nouns and verbs in two languages (language invariance) during speech production, we likely expected similar activation patterns in Spanish and Basque potentially reflecting the engagement of similar brain networks across languages.

Results

Performance in picture naming.

Overall, information from both categories and languages was retrieved equally well (Spanish: ~ 99% for nouns and ~ 98.7% for verbs; Basque: ~ 98.9% for nouns and ~ 98.5% for verbs). Differences in terms of categories emerged when considering reaction time values (RT). More specifically, the RM-ANOVA conducted on them yielded a main effect of category ($F_{1,15} = 74.61$, $p < 0.0001$; partial eta = 0.83) with faster RTs for nouns (Spanish: mean = 1001.47; SD = 454.94; Basque: mean = 961.11; SD = 431.68) as compared to verbs (Spanish: mean = 1115.79; SD = 446.1; Basque: mean = 1133.83; SD = 433.7) independently of the language used to name. No main effect of language ($p = 0.68$) or interaction between category and language ($p = 0.22$) were observed.

Oscillatory dynamics underlying noun and verb naming in Spanish and Basque.

As shown by the TFRs depicted in Fig. 1, noun and verb naming in either Spanish or Basque showed theta power increases (4–8 Hz) and alpha–beta (8–25 Hz) power decreases during speech production within the first 500 ms after picture onset.

When comparing noun and verb naming conditions in Spanish, a significant negative cluster was observed in the theta band (4–8 Hz; Monte Carlo $p = 0.002$, two-tailed), with nouns exhibiting less power than verbs. The

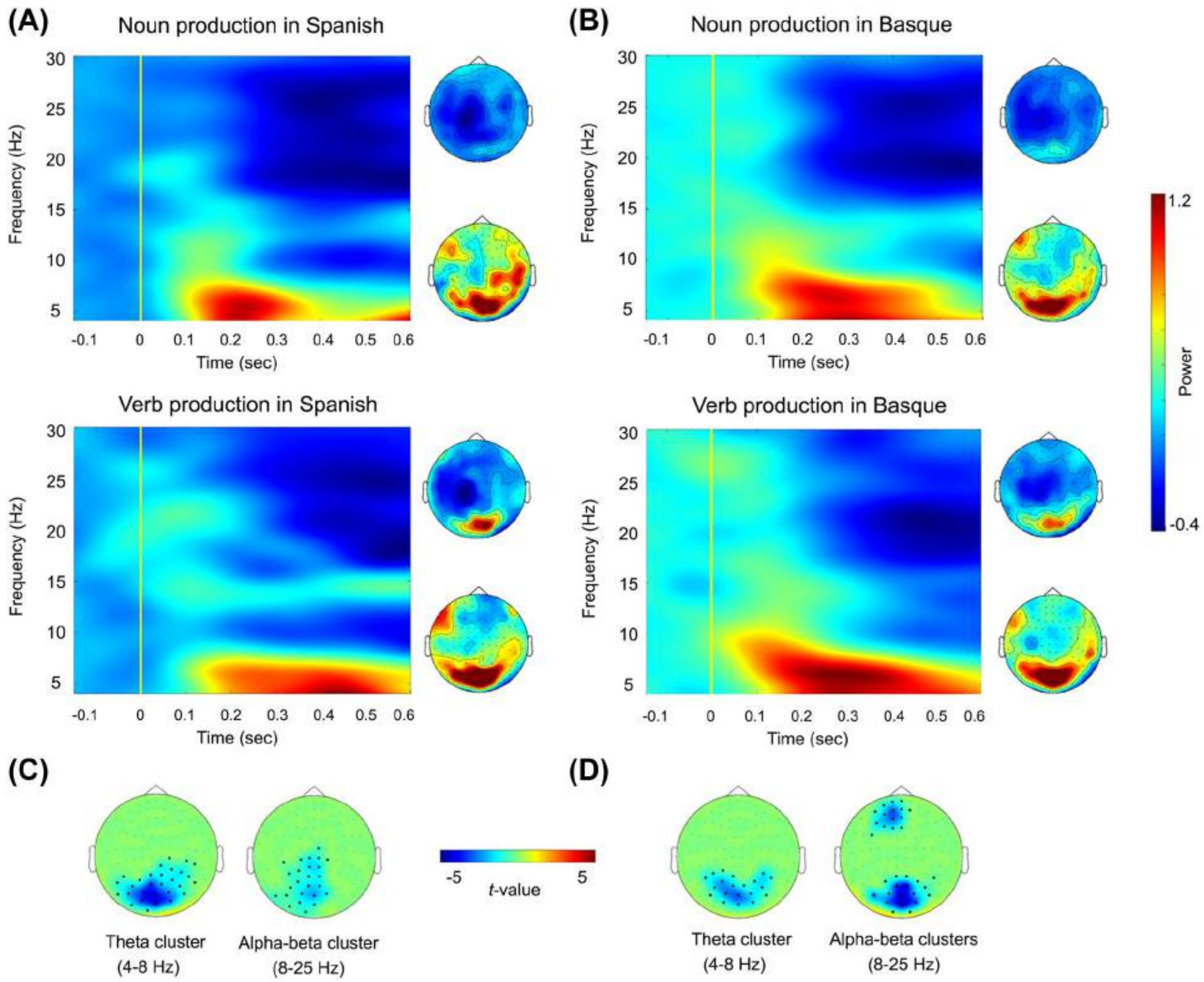

Figure 1. Oscillatory correlates of noun and verb production in bilingual speakers. Time–frequency representations (TFRs) for nouns and verbs in Spanish (**A**) and Basque (**B**). TFRs and topographic distributions plots showing theta and alpha–beta effects are plotted as relative power change compared to the baseline period (500 ms pre-stimulus) in the combined gradiometers highlighted by the significant clusters (**C**, **D**).

cluster extended from 100 to 500 ms and comprised bilateral posterior sensors. A significant negative cluster was also observed in the alpha–beta bands (8–25 Hz; Monte Carlo $p = 0.02$, two-tailed), with overall power decreases for nouns as compared to verbs. This cluster was evident from 220 to 500 ms in posterior bilateral sensors as well (See Fig. 1A).

Similarly, when contrasting both categories in Basque, a significant negative cluster (4–8 Hz; Monte Carlo $p = 0.01$, two-tailed), was found in the theta band. Paralleling Spanish findings, nouns exhibited overall less power than verbs in bilateral posterior sensors, as highlighted by a significant cluster extending from 280 to 500 ms. Finally, two negative clusters were found in the alpha–beta range (8–25 Hz; Monte Carlo $p = 0.01$ and $p = 0.03$, two-tailed, respectively; see Fig. 1B), showing decreased power for noun as compared to verb naming. The clusters were evident from 100 to 460 ms and from 180 to 500 ms, with the former comprising posterior sensors and the latter, left frontal ones.

Finally, no significant clusters were observed (all ps > 0.2) when comparing noun and verb naming conditions across languages (i.e., Spanish noun vs. Basque noun and Spanish verb vs. Basque verb), in the theta (4–8 Hz) or the alpha–beta (8–25 Hz) frequency bands.

Source level analysis of category-related effects. Significant oscillatory effects at the sensor level were source reconstructed considering the frequency-bands and time-windows highlighted by the significant clusters. In the case of Spanish (see Fig. 2A), theta peaks were found bilaterally in visual cortices and in the left SMA. For Basque (see Fig. 2B), these peaks were localized in bilateral visual cortices as well and in the right middle temporal gyrus. In all cases, regions showed increased power for verbs as compared to nouns.

Brain regions likely contributing to the alpha–beta effects in Spanish, on the other hand, were found in bilateral visual cortices, the left anterior temporal lobe and the right premotor area. While the former regions showed

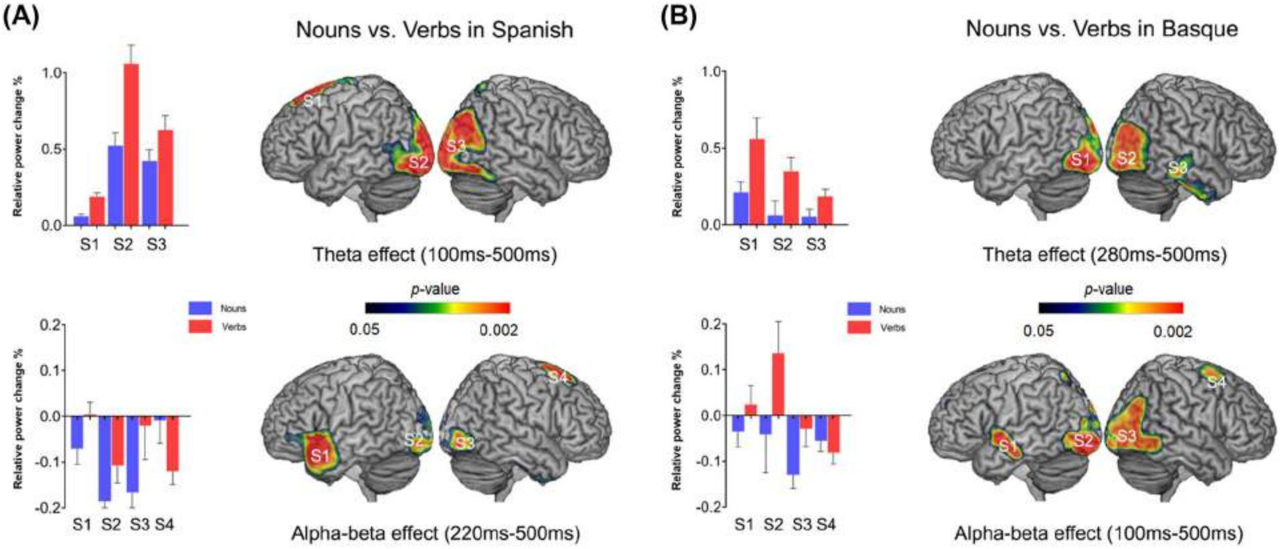

Figure 2. Neural correlates of the TFR sensor-level effects. We localized regions of local maxima with respect to baseline in Spanish (**A**) and Basque (**B**), and restricted between-condition comparisons (nouns vs. verbs) to those sites. Localization of activation peaks was circumscribed to the theta (4–8 Hz) and alpha–beta (8–25 Hz) frequency bands in the time intervals highlighted by the significant clusters in each language. For visualization purposes, we use bar plots showing relative power change for each category (nouns in blue and verbs in red) at each peak maxima to clarify the direction of the effect. All plotted regions reached a p value <0.05.

more desynchronization for nouns as compared to verbs, the latter one, namely premotor, showed a reversed pattern, with more desynchronization for verbs as compared to nouns. In the case of Basque, the involved regions were the bilateral visual cortices, the left superior anterior temporal lobe and the right premotor area, with occipito and temporal regions showing stronger alpha–beta power decreases for nouns as compared to verbs, and the right premotor area showing power decreases for verbs as compared to nouns.

Discussion

In the present study, we sought to investigate the spectro-temporal and neural underpinnings of noun and verb production in highly proficient Spanish–Basque bilinguals. To this end, MEG signals were recorded while participants performed a picture naming task, the gold standard for studying the cognitive architecture of speech production[36]. Overall, bilingual speakers showed similar oscillatory patterns within the first 500 ms after picture onset, exhibiting theta power increases and alpha–beta power decreases regardless of the condition and the language used to name. When comparing noun and verb conditions separately in Spanish and Basque, stronger theta power increases in the case of verbs and stronger alpha–beta power decreases in the case of nouns, were observed irrespectively of the language at use. Regions involved in the theta modulations were localized in occipital cortices, MTG and SMA, showing in all cases increased power for verbs than nouns. Candidate regions mostly contributing to the alpha–beta scalp effects were localized in occipital and temporal regions in the case of nouns and in premotor cortices in the case of verbs. When comparing noun and verb conditions across languages no differences were observed in any of the frequency-bands of interest. Of note, these results were mirrored at the behavioural level, with RTs showing no differences in noun and verb processing across languages. All in all, our findings underscore the existence of common oscillatory dynamics in Spanish and Basque, suggesting that the core principles governing the organization of lexico-semantic representations and their retrieval in the bilingual brain are similar in both languages, at least when considering highly proficient bilinguals.

A large body of neuroimaging evidence suggests that multiple languages share a common neuroanatomical system, with differences in L1 and L2 reflecting varying computational demands mediated by factors such as proficiency, age of acquisition, and level of language exposure[37,38]. In this context, the presence of noun–verb dissociations sustained in two languages in highly proficient bilinguals has been previously reported in fMRI[20,21,39] and brain lesion studies[40,41]. These findings have been taken as evidence for the existence of language-invariant cortical mechanisms in bilingual speakers while processing lexico-semantic representations during speech production.

Here, we add converging evidence from a neurophysiological standpoint by showing that the oscillatory fingerprints supporting noun–verb dissociations are similar across languages in highly proficient Spanish–Basque bilinguals.

In line with the view that the retrieval of lexico-semantic information is enabled via power decreases of alpha–beta (8–25 Hz) oscillations[31], we observed reduced alpha–beta power for nouns as compared to verbs in both Spanish and Basque, suggesting that similar mechanisms as those used by monolinguals might be called to play in bilingual speakers when both languages are mastered in a native-like fashion. This is also in keeping with previous evidence from our lab[32], showing that L1 Spanish speakers recruit different networks in the alpha and beta bands while processing nouns and verbs, with a stronger involvement of occipital and temporal nodes within the ventral stream in the case of nouns; and of premotor and superior parietal nodes within the dorsal stream in the case of verbs, at least when underscoring semantic aspects dissociating these categories (i.e., objects vs. actions). More specifically, noun and verb representations are known to differ in terms of feature types, with visual features more represented in the object domain and sensory-motor features in the action one[42,43]. This view predicts that, at a neural level, the lexical retrieval of object nouns will mainly recruit occipito-temporal regions storing visual features, while the retrieval of action verbs will mainly recruit motor/premotor regions storing sensory-motor features[44–46]. In line with this view, we observed that premotor areas, were more strongly involved in verb processing as shown by stronger alpha–beta power decreases in either Spanish or Basque. Furthermore, visual areas in bilateral occipital cortices and the anterior temporal lobe (ATL) were highlighted by our source analysis in both languages as being more involved in noun naming. The engagement of bilateral visual areas was well expected given the nature of the task, which implies the recognition of the item to be named as a necessary stage occurring within ~ 200 ms of picture presentation[47–49]. The ATL, on the other hand, has been proposed as a hub region in semantic processing[50,51] and there is evidence supporting its involvement during object recognition and overt naming[52–55]. Furthermore, it has been shown that this region houses language-invariant semantic representations in bilinguals[56,57].

Lexico-semantic processing, however, does not occur in isolation but rather is closely intertwined with cognitive control during speech production. In this regard, the finding of higher theta power for verbs as compared to nouns seems to reflect the increased semantic processing demands imposed by the different categories. This finding is in keeping with previous evidence[34] showing similar theta power increases for verbs as compared to nouns in monolinguals. In that study, the authors interpreted theta power modulations in terms of differences in the semantic organization of noun and verb categories. Indeed, while concrete nouns are known to share many semantic features among different levels; verbs are more abstract and typically exhibit a shallower semantic organization[5]. Cortical MEG peaks contributing to the theta effects were found in bilateral visual cortices for both languages, in the right middle temporal gyrus (MTG) for Basque and in the left SMA for Spanish, in all cases showing increased power for verbs as compared to nouns. Of note, the right MTG and left SMA have been highlighted as important nodes in the inhibition network and also reported to be involved in bilingual management of two languages in functional neuroimaging studies[58]. Furthermore, neurophysiological evidence[59] suggests that theta increases in the SMA and posterior visual cortices—starting around ~ 150 ms and continuing throughout the task—may index initiation of the item search in memory, reflecting the retrieval of semantic features with different levels of complexity. Nevertheless, it is also true that even though pictures denoting nouns and verbs were carefully matched for many linguistic variables, the visual complexity of pictures depicting actions might have been higher than the one exhibited by single objects. Since we did not measure this aspect (e.g., by asking participants to rate the pictures), we cannot completely rule out that theta power increases for verbs as compared to nouns, sourced in visual cortices, could actually reflect task-related visual attention differences rather than top-down control mechanisms. Indeed, visual theta rhythms have been previously linked to sustained attention[60–62]. This aspect needs to be addressed by future studies experimentally dissociating visual and linguistic stages during speech production or, alternatively, by using the same pictorial stimuli for the different categories.

Another aspect that needs to be considered is that, at the source level, MEG peaks contributing to maximal differences between noun and verb naming did not completely overlap for Spanish and Basque. Specifically, while both languages showed comparable activations in bilateral visual cortices, left anterior temporal areas and right premotor cortex; regions involved in the theta effect (i.e., SMA and MTG) differed. This might be explained by timing and/or methodological aspects, potentially reflecting that within the first 500 ms after stimulus onset, brain regions in the language network may have differently contributed, in terms of power engagement, to the category-related effects in the different languages. Furthermore, the timing of the significant clusters involved in the theta and alpha–beta effects varied across languages. Specifically, the one found in Spanish within the theta frequency-band started earlier in time as compared to the one observed in Basque (i.e., 100 ms and 280 ms after stimulus onset, respectively). While the timing of the cluster is not indicative of the onset of the effect[63], the source localization was performed on the significant time-windows highlighted by them. Thus, it is likely that this methodological aspect may have also played a role. Alternatively, observed differences may stem from the fact that, despite the balanced mastery of both languages, Basque was acquired in most cases as the L2. Although L2 was acquired early, neurophysiological specialization may nevertheless differ between the languages and this might explain that areas supporting noun–verb segregation do not entirely converge, even though they are recruited via similar oscillatory mechanisms.

Nevertheless, MEG source localization has its own limitations given the ill-posed inverse problem, and fine-grained statements about underlying cortical sources cannot be formulated with the approach used in the present study. Further research zooming into these aspects are required to disentangle this issue.

Another aspect that requires further consideration relates to the overt nature of the task. Indeed, as highlighted by[64], speech production tasks have been long avoided in neurophysiological studies due to the potential existence of muscle artifacts, which may lead to a bad signal-to-noise ratio in the recordings. Here, we focused on the first 500 ms after picture onset—which can be considered as a "safe" window of artifact-free brain responses[65]—and ran state-of-the-art pipelines for semiautomatic detection of muscle artifacts[66]. Yet, even if we only considered the initial 500 ms time-window for the final analysis, it is true that these methods reflect the deviation of the whole epoch (i.e., 1000 ms in our case) and look for abnormality given the evolution of the recording. Thus, we cannot completely rule out that the segments of analysis may have still contained some noise. Nevertheless, we find this unlikely for several reasons. First, previous studies have used a similar methodological approach leading in all cases to adequate estimates of brain non-contaminated activity[30,32,67,68]. Second, the beamformer technique used here to reconstruct underlying brain sources is known to attenuate myogenic artifacts by suppressing signals whose spatial scalp distribution cannot be explained by a dipolar source in the brain (please see[30] for a further discussion of this aspect). Third, the specificity of the observed effect (i.e., increased power for verbs in premotor structures as compared to nouns) speaks in favor of a category related modulation rather than the presence of myogenic activity and fits well with evidence showing that motor alpha–beta oscillations play a key role in action semantics[69–71].

Finally, it is worth mentioning that our sample size was rather small, although not smaller than those reported in similar MEG studies approaching the study of speech production in bilinguals[72–76]. Thus, future studies with larger sample sizes are needed to strengthen our conclusions.

Conclusions

Overall, in the present study, we show that the oscillatory networks involved in noun and verb production in highly proficient bilinguals exhibit similar theta (4–8 Hz) and alpha–beta (8–25 Hz) dynamics across languages. Specifically, the finding of theta power increases for verbs and alpha–beta power decreases for nouns irrespectively of the language at use underscores the existence of common principles supporting the organization and retrieval of lexico-semantic information in bilingual speakers, at least during early stages of speech production. While similar modulations in low-frequency brain rhythms have been previously reported in monolingual speakers, to the best of our knowledge, this is the first study in showing that comparable oscillatory patterns also stand for highly proficient bilinguals.

Methods

Participants. A total of 20 Spanish–Basque bilinguals were recruited through the BCBL database and received economical compensation for their participation in the study. However, four participants were discarded from the study due to excessive artifacts in MEG recordings. Thus, all subsequent behavioural and MEG statistical comparisons were performed on a total of 16 participants (4 male, $M = 25.87$; $SD = 5.25$). All participants but one reported Spanish as the first language (L1) and Basque as the second one (L2). Language proficiency was assessed with the Basque, English, and Spanish Test [BEST][77], using the semi-structured interview part of the test which measures fluency, lexical resources, grammatical constructions and pronunciation (Likert-like scale with scores ranging from 1 to 5). The cut-off criteria for considering an individual as a high-proficient bilingual were scores ≥ 4 in their L2. The nonparametric Wilcoxon signed rank test showed no significant differences ($p = 0.053$) between Spanish ($M = 5$; $SD = 0$) and Basque ($M = 4.83$; $SD = 0.33$), indicating that participants had comparable proficiency in both languages. In addition, no significant differences ($t = -0.62$, $p = 0.53$) were observed in the age of acquisition (AoA) between Spanish ($M = 0.62$; $SD = 1.2$; range: 0–3 years) and Basque ($M = 0.93$; $SD = 1.12$; range: 0–3 years), with both languages being acquired early in life. All participants were right-handed as measured by the Edinburgh Handedness Inventory[78], possessed normal or corrected-to-normal vision and no history of neurological or psychiatric disease. The Ethics and Scientific Committee of the BCBL, following the declaration of Helsinki, approved the study protocol. All participants gave their written informed consent prior to the study.

Stimuli and task. Language production was assessed using the MULTIMAP, a multilingual picture naming task for mapping the language network developed by our group[33]. MULTIMAP consists of an open-access database of standardized color pictures representing objects and actions. These pictures have been tested for name agreement with speakers of different languages including Spanish and Basque, and have been controlled for relevant linguistic features (e.g., word frequency, word length, number of letters, number of phonemes, number of syllables, number of substitution neighbors, familiarity, imageability, and concreteness) in cross-language combinations.

In separate blocks, participants were instructed to observe the pictures and name them overtly in Spanish or Basque as quickly and accurately as possible. Production of nouns and verbs was requested in the context of short sentences, which is a more ecological form of speech than isolated naming. More specifically, on top of the object-related images we added the text "Esto es…" or "Hori da" ["This is…" in Spanish and Basque, respectively] to force the production of a short sentence that had to agree in number with the target noun (e.g. "Esto es una manzana" in Spanish or "Hori da sagarra" in Basque, English translation: "This is an apple").

Similarly, on top of the action-related pictures, we included "El…"/"Ella…" or "Hark…" ["He…" or "She…" in Spanish and Basque]. This introductory text was used as a cue for the production of a sentence that started with the given subject and had a finite verb form in 3rd person singular (e.g. Spanish: "Él corta", Basque: "Hark ebakitzen", English translation: "He cuts").

We used MATLAB Release 2012b (The MathWorks, Inc., Natick, Massachusetts, United States) and Cogent Toolbox for picture presentation. Trials started with a fixation cross lasting for 1000 ms, followed by the stimulus displayed for 2 s. ISI randomly varied between 3 and 4 s. A total of 80 picture items (i.e., 40 for nouns and 40 for verbs) were used. Each picture was presented twice for a total of 80 trials per condition. Each block lasted ~ 10 min, and participants were allowed to take a short break between them.

MEG and MRI recordings. Neuromagnetic signals were continuously recorded by means of an Elekta Neuromag 306-channels system (Helsinki, Finland) in a shielded room at a sampling rate of 1000 Hz. MEG signals were online filtered with a passband between 0.1 and 330 Hz and sampled at 1 kHz. Participant's head position inside the helmet was monitored with five head position indicator coils (HPI) located on the scalp, throughout the experiment. Six electrode pairs were used to control for ocular (i.e., placed in the external chanti of each eye and above and below the right eye) and cardiac activity (i.e., placed below the right clavicle and under the left rib bone). Three anatomical fiducials (i.e., nasion and left and right prearicular points) plus ~ 300 additional points registered over the scalp and nose area were digitalized and further used to spatially align the

MEG sensor coordinates to the native T1 high-resolution 3D structural MRI of each participant. Structural MRIs were acquired with a Siemens 3 T magnetom prismafit MR scanner (Siemens, Munich, Germany) in a separate session using the following parameters: echo time = 2.97 ms, repetition time = 2530 ms, flip angle = 7° and field of view = 256 × 256 × 176 mm^3, number of axial slices = 176, slice thickness = 1 mm, in-plane resolution = 1 mm × 1 mm.

Behavioural assessment. Participant's vocal responses were recorded and monitored online by a research assistant during the task. Automatic detection of naming latencies was done with the Chronset tool[79]. Erroneous responses or utterances containing disfluencies were excluded from the final analyses. Response latencies were trimmed at 2.5 standard deviations (SD) above participant's mean in each condition and analysed using a 2-way ANOVA with Language (Spanish, Basque) and Category (Noun, Verb) as within-subject factors.

Data preprocessing. Continuous MEG data were initially pre-processed off-line using the temporal extension of the signal space separation method[80] implemented in Maxfilter 2.2 (Elekta-Neuromag), which allows for external magnetic noise suppression, head movement correction and bad channels interpolation. MEG analyses were performed using FieldTrip (version 20170911)[66] in MATLAB Release 2014b. Data were down-sampled to 500 Hz and segmented into epochs from 500 ms before picture onset to 1000 ms after picture onset.

A semi-automatic procedure was then employed to remove epochs with myogenic activity, SQUID jumps and flat signal related artefacts. To this end, we used the Fieldtrip function ft_artifact_zvalue. This algorithm computes a z-score time-course for each sensor by subtracting the mean and dividing by the standard deviation across trials. The obtained z-values are then averaged across sensors providing an index of the global standardized deviation. Afterward, a threshold for the global z-score is chosen in order to reject those epochs deviating from it. Muscle artifacts and SQUID jumps were independently identified with different sets of parameters (e.g., sensors to consider, filtering bands, type of padding). In all cases, the default Fieldtrip parameter values were used. Finally, a fast independent component analysis (ICA) was used to correct for heartbeat and eye movement artefacts. ICA rejection was performed manually based on the topographical patterns of the components. One clear eye-movement component and one heartbeat component were removed for all participants. Importantly, no significant differences were observed (all p values > 0.066) between conditions or languages in terms of the number of trials kept for the final MEG analysis (Spanish: nouns $M = 55.94$, $SD = 8.96$; verbs, $M = 52.88$, $SD = 8.19$; Basque: nouns, $M = 53.75$, $SD = 7.21$; verbs, $M = 53.94$, $SD = 7.87$).

Data analysis. Time–frequency representations (TFR) were obtained for clean MEG data segments in the theta (4–8 Hz) and the alpha–beta (8–25 Hz) frequency-bands using Hanning tapers and a fixed window length of 500 ms advancing in 10 ms steps. These frequency-bands were selected based on previous M/EEG literature suggesting a role for theta in cognitive control during semantic integration[34] and a role for alpha–beta oscillations[28–30] in the retrieval of lexical-semantic information from long-term memory.

Power estimates were calculated separately for each orthogonal direction of a gradiometer pair and then combined, resulting in a total of 102 measurement sensors. Power was expressed as relative change with respect to a ~ 500 ms pre-stimulus baseline period.

Cluster-based permutation tests[81] were used to assess power differences between languages and categories at the sensor-level. For the contrasts, we averaged over frequency bins of interest (i.e., 4–8 Hz and 8–25 Hz) while considering all time-points between 0 and 500 ms after picture onset and all 102 combined gradiometers, since no a-priori hypotheses about timing or locations were held. The 0–500 ms time-window was chosen based on previous neurophysiological evidence[64] suggesting that, in overt speech production tasks, artifact-free recordings (e.g., not contaminated with articulatory activity) can be safely acquired during this period.

The permutation p value was calculated using the Monte-Carlo method with 1000 random permutations. The alpha threshold for significance testing was a p-value below 5% (two-tailed).

MEG source reconstruction. Source reconstruction was performed in order to estimate the brain regions likely contributing to the sensor-level effects. Anatomical MRI data from each participant (T1-weighted) was segmented using the Freesurfer software[82]. Co-registration between MEG sensor and individual's MRI coordinates was manually performed by aligning the digitized head-surface and the three fiducial points to the outer scalp surface. The forward model was calculated using the Boundary Element Method (BEM) implemented in MNE suite (RRID:SCR_005972,[83] for three orthogonal tangential current dipoles, placed on a homogeneous 5-mm grid covering the entire brain. For each source, the forward model was then reduced to its two principal components of highest power, which closely correspond to sources tangential to the skull. All sensors (i.e., planar gradiometers and magnetometers) were used in the source localization analysis. Each sensor signal (and the corresponding forward-model coefficient) was normalized by its noise variance (estimated from the 500 ms baseline period prior to picture onset).

Based on previous studies from our lab[32], we used the Linearly Constrained Minimum Variance (LCMV) method for estimating brain source activity[84]. Cross-spectral density (CSD) matrices were calculated in the time–frequency window of the significant sensor-level effects and in an equally-sized baseline period. The real part of the combined matrices was used to compute a common filter (i.e., LCMVB beamformer).

In order to run group-level analysis, brain maps were transformed from the individual MRIs to the standard MNI using the spatial-normalization algorithm implemented in Statistical Parametric Mapping (SPM8, Wellcome Department of Cognitive Neurology, London, UK).

Then we identified the coordinates of the local maxima in group-level power maps with respect to baseline and restricted statistical comparisons between conditions to those sites. Local maxima were defined as contiguous voxels displaying higher power than all other neighboring voxels[85]. Group-level difference maps were calculated by subtracting *f*-transformed trial and baseline group-level power maps for each frequency of interest. Under the null hypothesis that power maps are the same regardless the experimental condition, genuine and baseline levels are exchangeable at the participants-level prior to difference map computation. In order to reject this hypothesis and compute a statistical significance threshold for the correctly labelled difference map, the sample distribution of the maximum of the difference map's absolute value was computed using a permutation approach. The threshold at $p < 0.05$ was estimated as the 95 percentile of the sample distribution. All supra-threshold MEG peaks were interpreted as indicative of brain regions likely contributing to the sensor-level effects.

The coordinates of significant local power maxima were statistically compared using the location-comparison method[86]. This robust method uses a bootstrap approach[87] to build a permutation distribution of the coordinates of the local maxima in two conditions and tests the probability that the distance between them is zero[88]. To do so, it uses a multivariate location test similar to the Hotelling T^2 test, which is the multivariate extension of the classical Student t-test. Importantly, the location-comparison method has shown to successfully deal with spectral leakage problems resulting from directly contrasting brain maps from different conditions.

Data availability

All the data that support the findings of this study as well as the code for data preprocessing and analysis are available on request from the corresponding author.

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Author contributions

L.A., I.Q., and M.C. designed the study. S.G. and P.T. performed the experiment. L.A. and S.G. analyzed the data. L.A. wrote the original draft of the manuscript. L.A., I.Q., M.C., S.G., and N.M., reviewed and edited the final version of the manuscript.

Competing interests

The authors declare no competing interests.

Additional information

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"Neural dynamics supporting longitudinal plasticity of action naming across languages: MEG evidence from bilingual brain tumor patients"

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ABSTRACT

Previous evidence suggests that distinct ventral and dorsal streams respectively underpin the semantic processing of object and action knowledge. Recently, we found that brain tumor patients with dorsal gliomas in fronto-parietal hubs show a selective longitudinal compensation (post-vs. pre-surgery) during the retrieval of lexico-semantic information about actions (but not objects), indexed by power increases in beta rhythms (13–28 Hz). Here, we move one-step further and ask whether a similar organizational principle also stands across the different languages a bilingual speaks. To test this hypothesis, we combined a picture-naming task with MEG recordings and evaluated highly proficient Spanish-Basque bilinguals undergoing surgery for tumor resection in left frontoparietal regions. We assessed patients before and three months after surgery. At the behavioral level, we observed a similar performance across sessions irrespectively of the language at use, suggesting overall successful function preservation. At the oscillatory level, we found longitudinal selective power increases in beta for action naming in Spanish and Basque. Nevertheless, tumor resection triggered a differential reorganization of the L1 and the L2, with the latter one additionally recruiting the right hemisphere. Overall, our results provide evidence for (i) the specific involvement of frontoparietal regions in the semantic retrieval/representation of action knowledge across languages; (ii) a key role of beta oscillations as a signature of language compensation and (iii) the existence of divergent plasticity trajectories in L1 and L2 after surgery. By doing so, they provide new insights into the spectro-temporal dynamics supporting postoperative recovery in the bilingual brain.

1. Introduction

Semantic processing is central to everyday life as it allows humans to fluently manipulate stored knowledge and build meaning on the fly, thus supporting essential communicative functions such as language production and comprehension.

Mounting evidence from behavioral, neurophysiological and imaging studies in healthy individuals and brain tumor patients (Amoruso et al., 2021; Gleichgerrcht et al., 2016; Shapiro et al., 2006; Vigliocco et al., 2011) suggests that the semantic representation/retrieval of object and action knowledge is underpinned via partially distinct ventral and dorsal systems respectively involving inferotemporal and fronto-parietal nodes. Interestingly, studies using electrical stimulation for intraoperative language mapping during awake brain surgery support this category-based segregation, showing greater number of errors for objects when stimulating temporal regions; and greater number of errors for actions when disrupting activity in prefrontal and parietal cortices (Corina et al., 2005, 2010; Lubrano et al., 2014; Ojemann et al., 2002).

In a recent study (Amoruso et al., 2021), we recorded magnetoencephalographic (MEG) activity in healthy controls and patients with low-grade gliomas (LGGs) compromising either ventral or dorsal brain regions while performing a picture-naming task including object and

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action stimuli. Patients were evaluated in a longitudinal fashion, namely before and after surgery for tumor resection. Results from controls showed segregated beta (13–28 Hz) power decreases in left ventral and dorsal streams for object and action naming, respectively; in a time-window classically associated to lexico-semantic retrieval (~250–500 ms). When longitudinally comparing patients' oscillatory MEG responses we found post-surgery beta (13–28 Hz) modulations mimicking the category-based segregation showed by healthy controls, with ventral and dorsal damage leading to selective compensation for object and action naming. Overall, our previous findings provided evidence for the existence of two separable object vs. action semantics subsystems, and pointed to a key involvement of beta oscillations as a signature of adaptive compensation in brain tumor patients.

Yet, information about language reorganization and oscillatory compensation in bilingual speakers harboring brain tumors is scarce. Specifically, the question of whether and to what extent semantic knowledge is integrated across languages in the bilingual brain is a topic of debate. For instance, it has been suggested that the degree of overlapping across semantic representations varies depending on variables such as age of acquisition (AoA) and language proficiency. In other words, the earlier and more accurately a second language (L2) develops, the more likely it will recruit the same neural devices responsible for the first language (L1) (Abutalebi, 2008; Abutalebi and Green, 2007; Paradis, 2000; Perani and Abutalebi, 2005). Indeed, it has been shown that as proficiency improves, L2 conceptual representations become semantically processed in the same way as in the L1 (Hut and Leminen, 2017). Furthermore, imaging (Consonni et al., 2013; Hernandez et al., 2001; Willms et al., 2011) and neurophysiological (Geng et al., 2022) evidence indicates that object-action distinctions are sustained by common neuroanatomical and oscillatory components across the two languages a proficient bilingual speaks, further supporting the existence of shared semantic sub-systems across L1 and L2, at least when both are mastered in a native-like fashion.

Given this evidence, in the present study we wanted to move one-step further and test the hypothesis that the semantic representation/retrieval of action-based knowledge is mainly supported via the dorsal stream and overlaps across the two languages a highly proficient bilingual speaks. To this end, we focused on brain tumor patients with dorsal lesions in fronto-parietal hubs as an experimental model. More specifically, we combined an object/action picture-naming task (Gisbert-Munoz et al., 2021) with MEG recordings and longitudinally evaluated (i.e., before and three months after surgery) four highly proficient Spanish-Basque bilinguals undergoing surgery for tumor resection.

Overall, given the involvement of the dorsal pathway in action processing, we expected to find a selective post-surgery compensation in beta rhythms (13–28 Hz) for the retrieval of action (but not object) knowledge (Amoruso et al., 2021). More critically to the present study, we expected to extend this evidence to bilingual patients and to find similar patterns of adaptive compensation across L1 and L2, indicating language-invariant semantic processing in the bilingual brain.

2. Materials and methods

2.1. Participants

Four highly proficient Spanish-Basque bilingual patients with low-grade gliomas (LGGs) in left fronto-parietal regions took part in this study (see Fig. 1 for lesion profile). Patient's demographics, clinical information and lesion characteristics are summarized in Table 1. All patients were recruited at the Cruces University Hospital (Bilbao, Spain) where they received their diagnosis and performed the awake brain surgery for tumor resection. The initial neurological exploration at the hospital revealed no severe motor, somatosensory, or linguistic deficits thus qualifying for the awake brain surgery procedure. Admission diagnoses were weakness/sensory loss in the contralesional leg in patients 1, 2 and 4; and seizure in the case of patient 3.

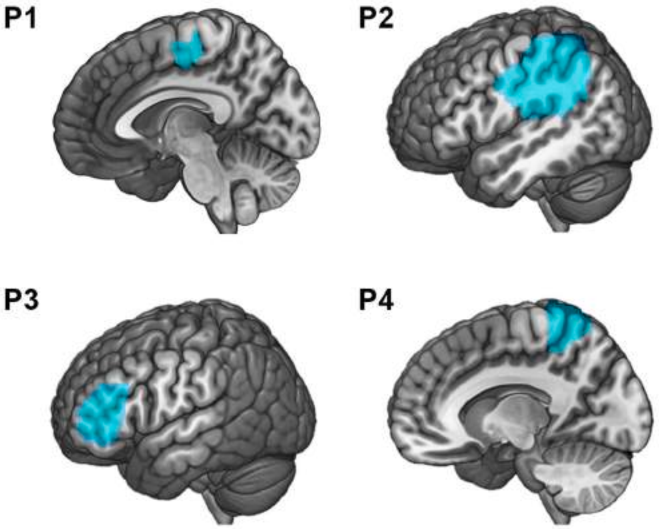

Fig. 1. Lesion delineation for individual patients.

Patients were evaluated in two sessions: a first session one week before the surgery, and a second session approximately three/four months after the surgery. In each session, behavioral, MEG and structural MRI data were collected.

In addition, healthy-control data from sixteen highly proficient Spanish-Basque bilinguals (4 men, Mean age = 25.87; SD = 5.25) performing the same picture-naming task were reutilized from a previous study (Geng et al., 2022). This provided a baseline to compare with patient's data and to assist the interpretation of potential divergent patterns indicating language reshaping/compensation in patients.

All participants were right-handed as assessed via the Edinburgh Handedness Inventory (Oldfield, 1971), had normal hearing and normal or corrected to normal vision. The study protocol was conducted in accordance to the Declaration of Helsinki for experiments involving humans, and approved by the Ethics Board of the Euskadi Committee and the Ethics and Scientific Committee of the BCBL (protocol code PI2020022). Informed consents were obtained from all participants involved in the study before the experiment.

2.2. Cognitive and linguistic assessment

A battery of standardized neuropsychological and linguistic tests was used to longitudinally evaluate participants on relevant linguistic and cognitive abilities. This battery included measures of general cognitive status as assessed via means of the 30-point screening Mini-Mental State Examination (MMSE) (Folstein et al., 1975); verbal and non-verbal intelligence measured using the KBIT (Kaufman and Kaufman, 2014), and language production in Spanish and Basque via means of the BEST test (de Bruin et al., 2017).

2.3. Picture-naming task

Language production was assessed using MULTIMAP, a multilingual picture-naming task for mapping eloquent areas during awake surgeries (Gisbert-Munoz et al., 2021). Briefly, MULTIMAP consists of an open access database of standardized color pictures representing both objects and actions. These images have been tested for relevant linguistic features in cross-language combinations including Spanish and Basque. Target words were matched on frequency, familiarity, number of orthographic neighbors, length and name agreement (i.e., higher than 80%). Importantly, this task has been previously used to investigate the brain mechanisms underlying bilingual language production in neurotypical (Geng et al., 2022) and brain tumor populations (Quinones et al., 2021).

Table 1
Patient's demographics, linguistic and clinical characteristics.

	Age	Sex	Educ. (years)	Occupation	L1	L1 AoA	L2	L2 AoA	L1/L2% of use	Tumor Location	Tumor Volume (cm^3)	EOR (%)
P1	45	F	14	Businesswoman	Spanish	0	Basque	5	50/50	Motor	23.00	76
P2	47	M	20	Aircraft pilot	Spanish	0	Basque	3	95/5	Parietal	87.83	100
P3	56	M	12	Mechanic	Spanish	0	Basque	0	40/60	Frontal	28.68	100
P4	41	M	20	Administrator	Spanish	0	Basque	3	50/50	Parietal	18.29	100

In separate blocks, participants were instructed to observe the pictures and name them overtly in Spanish or Basque as quickly and accurately as possible. Trials started with a fixation cross in the center of the screen lasting for 1 s, followed by the picture displayed for 2 s. ISI randomly varied between 3 and 4 s. A total of 88 picture items (i.e., 44 for objects and 44 for actions) were used. Each picture was presented twice for a total of 176 trials per condition. Each block lasted ~15 min, and participants were allowed to take a short break between them. Above each object, we added the text "Esto es …" or "Hori da …" ("This is …" in Spanish and Basque, respectively) to force participants to produce a short sentence that agreed in number and gender with the target noun. In the case of the action pictures, we included a pronominal phrase to be used as the subject of the sentence, namely "El/Ella …" or "Hark …" ("He/She …" in Spanish and Basque, respectively). This introductory text cue was used to trigger the production of a sentence that began with the given subject and had a finite verb form in the third person singular. See Fig. 2.

Participants' responses were recorded to estimate accuracy and naming latencies. We used MATLAB version 2012b and Cogent Toolbox (http://www.vislab.ucl.ac.uk/cogent.php) to present the images. Stimuli, Matlab script, and its compiled version are available at https://git.bcbl.eu/sgisbert/multimap2.

2.4. MEG and MRI data acquisition

MEG signals were recorded in a magnetically shielded room by means of a 360-channel Elekta -Neuromag system (360-channels, Helsinki, Finland). Signals were acquired continuously at a sampling rate of 1 kHz and online filtered between 0.1 and 330 Hz. Eye movements (EOG) were monitored using in a bipolar montage placed on the external chanti of each eye (horizontal EOG) and above and below the right eye (vertical EOG). Cardiac activity (ECG) was monitored as well by positioning an electrode below the right clavicle and another under the left rib bone.

Participant's head position inside the helmet was tracked during the recording session with five head position indicator (HPI) coils. The location of each coil relative to standard anatomical fiducials (i.e., nasion, left, and right pre-auricular points) was defined with a 3D digitizer (Fastrak Polhemus, Colchester, VA). In addition, ~300 points were digitalized over the scalp and eyes/nose contours to subsequently align the MEG sensor coordinates space to the participant's T1 MRI.

All participants underwent an MRI session separated in time from the MEG session by at least two days in a 3 T Siemens Magnetom Prisma Fit scanner (Siemens AG, Germany). High-resolution T1-and T2-weighted images were acquired with a 3D ultrafast gradient echo (MPRAGE) pulse sequence using a 64-channel head coil with the following acquisition parameters: FOV = 256; 160 contiguous axial slices; voxel resolution 1 × 1x1mm3; TR = 2530 ms, TE = 2.36 ms, flip angle = 7°. For each patient, the origin of the T1/T2 weighted images (pre- and post-surgery) was set to the anterior commissure. Functional event-related scans consisting of 320 echo-planar images were acquired using a T2*-weighted gradient-echo pulse sequence with the following parameters: field of view: 192 mm; matrix = 64 × 64; echo time = 30 ms; repetition time = 2 s; flip angle = 90°. The volume was comprised of 33 axial slices

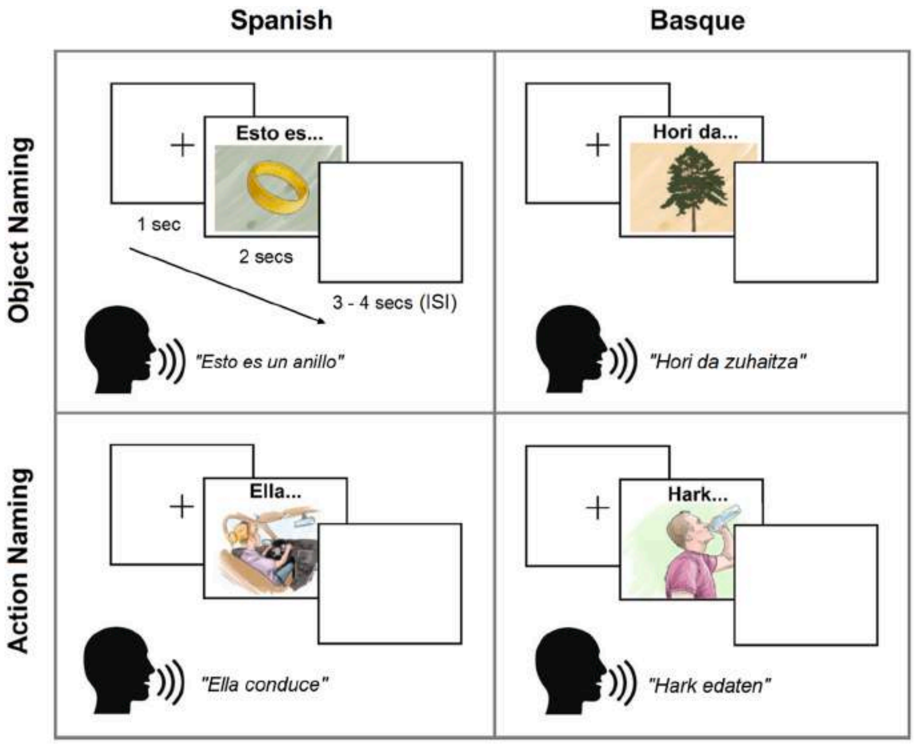

Fig. 2. Examples of object and action stimuli and experimental task. In separate blocks, participants were requested to observe the pictures and overtly name them in either Spanish or Basque as quickly and accurately as possible. Production of nouns and verbs was requested in the context of short sentences, which is a more ecological form of speech than isolated naming. Each trial began with a fixation cross on the screen for 1 s followed by the picture presented for 2 s. ISI randomly varied between 3 and 4 s.

with 3 mm isotropic voxels without slice gap. The first six volumes of each functional run were discarded to ensure steady-state tissue magnetization.

2.5. Lesion mapping

Lesions were manually drawn using the MRIcron software (Rorden et al., 2007) on the native space of participants' T1-weighted MPRAGE image by one of the neurosurgeons in charge of the patients' awake craniotomy (Garazi Bermudez). In addition, information from T2-weighted images was used when lesion boundaries were not clear in the T1. The lesion was then normalized to the MNI template and one of the authors (Ileana Quiñones) checked alignment between the delignated lesion and the lesion in the native space. A volume of interest (VOI) was created for each patient at each time point (i.e., pre- and post-surgery). Extent of resection (EOR; in cm3) was measured on postoperative imaging as: (Volume of (preoperative 3D Tumor Reconstruction ∩ postoperative Resection)*100/preoperative tumor volume).

2.6. Behavioral data analysis

Participant's vocal responses were recorded and monitored online by a research assistant during the task. An open-source in-house software ("SPONGE", available at https://github.com/Polina418/Audio_processing) was used to decode and convert the audio files into. wav format and semi-automatically detect speech onsets. Reaction times were measured as the interval between picture presentation and the onset of participant's verbal response. Erroneous responses or utterances containing disfluencies were excluded from the final analyses. Reaction times (RTs) and naming accuracies from individual patients were analyzed using Crawford and Howell (1998) frequentist *t*-tests for single-case analysis, and compared to the control group. This analysis was implemented on RStudio (Version 1.2.5019) using the psycho Package (Makowski, 2018).

2.7. MEG data preprocessing

Continuous MEG data were pre-processed off-line by means of the spatio-temporal signal space separation (tSSS) method (Taulu and Simola, 2006) implemented in Maxfilter 2.2 (Elekta-Neuromag) to subtract the external magnetic noise and correct for participants' head movements. Subsequent analyses were performed using the MatlabR_2014B (The MathWorks, Inc., Natick, Massachusetts, United States) and FieldTrip Toolbox [version 20170911] (Oostenveld et al., 2011). Recordings were down-sampled to 500 Hz and segmented into trials time-locked to picture onset, ranging from 500 ms before to 1000 ms after image onset. A semi-automatic procedure was used to remove trials containing electromyographic artifacts, SQUID jumps, and flat signals. Then, heartbeat and EOG artifacts were detected via means of a fast independent component analysis (FastICA) (Hyvarinen, 1999; Jung et al., 2000) and were linearly subtracted from the recordings. Across participants, the number of heartbeat and EOG components that were removed varied from 1 to 3 and 1–2 components, respectively.

2.8. MEG sensor-level analysis

Time-frequency representations (TFRs) were calculated on the clean MEG segments. Specifically, we focused on the beta band (13–28 Hz). This choice was methodologically motivated by previous findings from our group (Amoruso et al., 2021), showing that brain tumor patients show longitudinal language plasticity in this frequency band using a similar speech production task. TFRs were obtained using a Hanning tapers approach and a fixed window length of 500 ms, advancing in 10 ms steps, resulting in a 2 Hz frequency resolution. Power was separately estimated for each orthogonal direction of a gradiometer pair and further combined, for a total of 102 measurement sensors. Power was calculated as the relative change with respect to a ~500 ms pre-stimulus baseline. Statistical differences in spectral power between conditions were evaluated using cluster-based permutation tests (Maris and Oostenveld, 2007).

We averaged over frequency bins of interest (13–28 Hz; central frequency = 20.71 Hz) and tested a time-window from 100 ms to 600 ms after picture onset. This time-window was chosen based on methodological constraints imposed by the overt nature of the task, data inspection and neurophysiological evidence from previous studies using this picture naming task (Amoruso et al., 2021; Geng et al., 2022; Quinones et al., 2021), suggesting that recordings not contaminated with articulatory activity can be safely acquired around these time points. The permutation *p*-value was obtained with the Monte-Carlo method, using 1000 random permutations. The alpha threshold for significance testing was a *p*-value below 5% (two-tailed).

2.9. Source activity estimation

Individual T1-weighted MRI images were segmented into the scalp, skull, and brain components using the Freesurfer software (Reuter et al., 2012). Co-registration between the MEG sensor space and participant's MRI coordinates was done by manually aligning the digitized points from the Polhemus to the outer scalp surface using the Neuromag tool MRIlab (Elekta Neuromag Oy, version 1.7.25). The lead field matrix was computed using the Boundary Element Method (BEM) model implemented in MNE suite (RRID: SCR_005972) (Gramfort et al., 2014), for three orthogonal tangential current dipoles, placed on a homogeneous 5-mm grid. The forward model was then reduced to the two principal components of the highest singular value for each source, corresponding to sources tangential to the skull. All sensors (i.e., gradiometers and magnetometers) were used for source estimation, normalizing the signal of each sensor by its noise variance considering a baseline period before picture onset. Cortical sources of the MEG signal were estimated using a Linearly Constrained Minimum Variance (LCMV) beamformer approach (Van Veen, van Drongelen, Yuchtman and Suzuki, 1997). The covariance matrix used to derive beamformer weights was computed from the time-frequency window of the significant sensor-level effects and an equally sized baseline period prior to picture onset. To perform group-level analysis, brain maps were transformed from the individual MRIs to the standard Montreal Neurological Institute (MNI) by applying a nonlinear space transformation algorithm implemented in Statistical Parametric Mapping (SPM8, Wellcome Department of Cognitive Neurology).

Finally, statistical comparisons between conditions were performed with the location-comparison method (Bourguignon et al., 2018), which has shown to be robust in dealing with spectral leakage problems. This method generates bootstrap group-averaged maps to build a permutation distribution of location difference between local maxima in the two conditions being compared and tests the null hypothesis that distance between them is zero. Local maxima are defined as sets of contiguous voxels displaying higher power than all other neighboring voxels. The threshold at $p < 0.05$ was estimated as the 95 percentile of the sample distribution. All supra-threshold local MEG peaks were interpreted as indicative of brain regions likely contributing to the sensor-level effects.

3. Results

3.1. Cognitive and linguistic results

Individual longitudinal changes in neurocognitive variables are shown in Fig. 3. Results indicated that all patients preserved linguistic function in both languages after surgery as well as their cognitive status. Specifically, in the case of Spanish, all patients exhibited ceiling accuracy before and after surgery. For Basque, P2 and P4 performed better after surgery while patients P1 and P3 showed a marginal post-surgery decrease in accuracy. None of the patient's values significantly

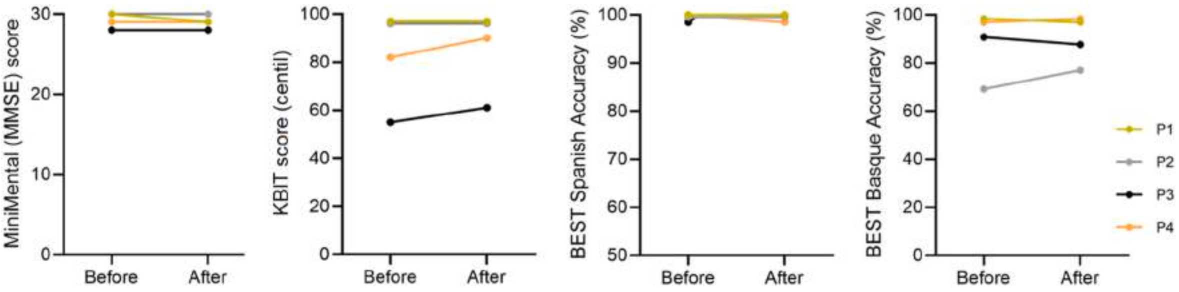

Fig. 3. Patient's cognitive and linguistic performance before and after surgery. Charts showing individual patients' scores for the pre- and post-surgery screening of cognitive status (i.e., Minimental Cognitive State Examination [MMSE], verbal and non-verbal intelligence (KBIT) and language production in Spanish and Basque (BEST).

differed from the control group (Spanish mean value = 98%; Basque mean value = 89%) either before (all *ps* > 0.1) or after the surgery (all *ps* > 0.3), as indicated by Crawford *t*-tests. In the case of the MMSE, some patients obtained similar maximal scores across sessions (e.g., P2, P3 and P4), while P1 showed a marginal lower score after surgery. Nevertheless, across sessions, all patients scored between 30 and 27, which is considered the normal range when evaluating cognitive impairments.

Finally, for the KBIT, P1 and P2 exhibited identical scores across sessions, while patients P3 and P4 showed a considerable improvement after surgery.

3.2. Behavioral results

Table 2 shows mean accuracy and reaction time values (RT) for each patient, as well as *p*-values for the Crawford-Howell *t*-tests comparing individual patients against the control group. Overall, no significant differences were observed in accuracy and RTs, which speaks in favor of successful language compensation. Only P2 showed a significant lower performance in naming accuracy for actions in Basque after surgery. Nevertheless, his performance was still very good (i.e., ~92%).

3.3. MEG results

The longitudinal contrasts (post vs. pre-surgery) performed for each naming condition (objects and actions) and language (Spanish and Basque) in the beta frequency band (13–28 Hz) showed specific significant effects for actions in both languages (all Monte Carlo *ps* = 0.002, two tailed). No significant differences were observed for the object naming condition (all Monte Carlo *ps* > 0.45, two tailed). Fig. 4A shows time-resolved spectra of the action naming longitudinal contrast for each language. In the case of Spanish, beta power modulations across sessions were highlighted by a positive cluster between ~310 and 500 ms in left middle-frontal sensors. In the case of Basque, the positive cluster was evident between ~180 and 600 ms and comprised left frontal sensors and right fronto-parietal ones. Source localization results (Fig. 4B) indicated that the longitudinal action effect for Spanish mainly originated in premotor and inferior frontal regions of the left hemisphere. The same effect in Basque, showed a similar involvement of left premotor cortex but with the additional recruitment of parietal and premotor regions in the right hemisphere.

Overall, in line with previous evidence for a similar longitudinal contrast in patients with dorsal gliomas (Amoruso et al., 2021), we observed beta power increases after the surgery along with preserved cognitive and linguistic abilities. Importantly, the direction of the action post-vs. pre-surgery effect was consistent at the individual patient's

Table 2

Comparison of individual patient scores to control group performance during naming in Spanish and Basque. Mean (M) and *p*-values from Crawford-Howell *t*-tests comparing accuracy and reaction times (RT) during object and action naming in both languages before and after surgery for tumor resection.

Pre-surgery Post-surgery								
	Object		Action		Object		Action	
	Mean	***p*-value**	**Mean**	***p*-value**	**Mean**	***p*-value**	**Mean**	***p*-value**
Accuracy								
Spanish								
P1	100	0.72	99.43	0.77	99.4	0.9	99.43	0.77
P2	100	0.72	100	0.58	100	0.72	100	0.58
P3	97.4	0.5	98.7	0.97	100	0.72	100	0.58
P4	98	0.66	100	0.58	100	0.72	100	0.58
Basque								
P1	99.43	0.82	97.74	0.73	99.4	0.83	99.43	0.68
P2	100	0.62	100	0.5	98.7	0.9	**92.59**	**0.01***
P3	95.65	0.13	100	0.5	100	0.62	98.14	0.87
P4	96.15	0.2	100	0.5	95.34	0.10	100	0.5
RT								
Spanish								
P1	759.9	0.61	897.49	0.64	718.93	0.55	940.6	0.7
P2	868.91	0.78	890.12	0.63	789.25	0.65	882.57	0.61
P3	1009.54	0.98	1209.73	0.84	776.40	0.63	1159.44	0.92
P4	851.7	0.75	1054.56	0.89	981.98	0.96	1113.32	0.99
Basque								
P1	816.41	0.75	1018.07	0.79	881.95	0.86	1075.67	0.89
P2	954.48	0.98	1056.9	0.86	671.65	0.52	789.11	0.45
P3	965.91	0.99	1044.98	0.84	771.97	0.67	1045.46	0.84
P4	856.81	0.81	890.97	0.59	914.55	0.91	1133.53	0.99

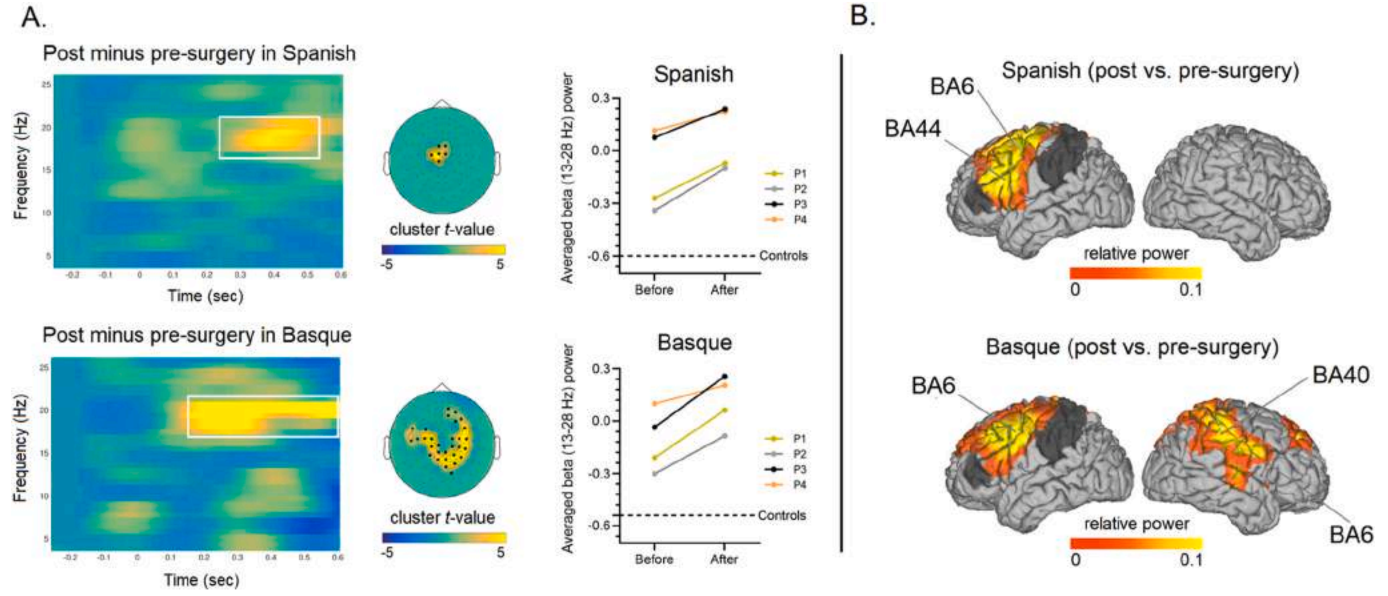

Fig. 4. Longitudinal effect in patients for action naming. Panel A shows time-resolved spectra of the longitudinal action naming effect (post vs. pre) in Spanish (top left) and Basque (bottom left), together with the positive clusters in the beta frequency band (13–28 Hz), indicating power increases after surgery. Line charts show individual patients' mean beta power at each session (before and after tumor resection), averaged over sensors associated with the clusters. Mean beta values are also shown for healthy bilingual controls as indicated by black dotted lines ($n = 16$; Spanish $= -0.538$, Basque $= -0.456$). Panel B shows source localization of the longitudinal action naming effect in each language, circumscribed to the time interval highlighted by the clusters. All plotted regions reached a p-value <0.01.

level, namely all patients showed stronger beta power increases after tumor removal.

Then, we reused MEG data from a previous study (Geng et al., 2022) in which a group of healthy highly proficient bilinguals ($n = 16$) performed the same picture-naming task and estimated beta networks involved in action naming for Spanish and Basque, to better understand patterns of potential reshaping in patients. Healthy controls showed similar negative clusters in the beta band (13–28 Hz) for action naming vs. baseline in Spanish (between ~180 and 500 ms) and Basque (between ~300 and 500 ms) over bilateral posterior, left parieto-temporal and frontal sensors (all Monte Carlo $ps = 0.004$, two-tailed). See Fig. 5. This effect mainly originated in a left-lateralized network comprising superior parietal, premotor and inferior frontal regions, as well as bilateral visual associative areas. Importantly, the contrast between languages did not yield significance, suggesting that action knowledge is similarly processed in the healthy bilingual brain.

Contrariwise, a significant language effect (Spanish vs. Basque; Monte Carlo p-value $= 0.002$, two tailed) was observed for action naming in the group of patients after the surgery. This effect was highlighted by a negative cluster in right parieto-temporal sensors, showing less beta power (13–28 Hz) for Spanish as compared to Basque between ~390 and 600 ms (see Fig. 6A). Source localization results indicated that

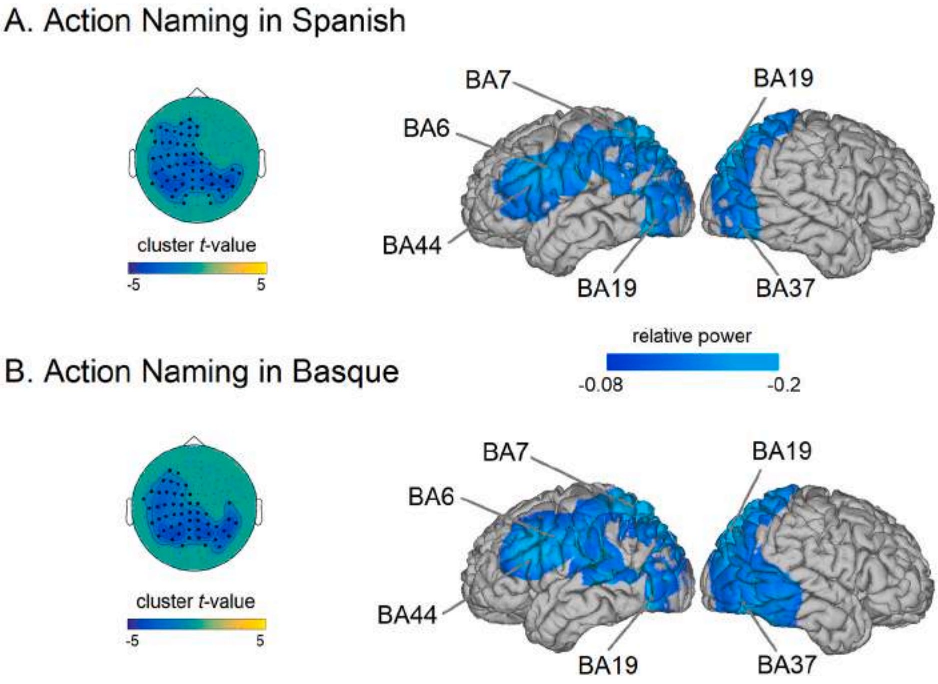

Fig. 5. Action naming in healthy bilingual controls. Panel A shows the negative cluster in the beta frequency band (13–28 Hz), indicating lower beta power for naming as compared to baseline, together with the action naming network resulting from the source level analysis. Panel B shows the negative beta cluster corresponding to the same action naming effect is Basque and the resulting network of areas underscored by the source level analysis. In both cases, source localization of the effect is circumscribed to the time intervals highlighted by the clusters. All plotted regions reached a p-value <0.01.

Fig. 6. Language effect in patients after surgery. Panel A shows time-resolved spectra of the language contrast (Spanish vs. Basque) after tumor resection, together with the negative cluster in the beta frequency band (13–28 Hz), indicating lower beta power for Spanish. Line charts show individual patients' mean beta power for each language, averaged over sensors associated with the cluster. Mean beta values are also shown for healthy bilingual controls as indicated by the blue dotted line ($n = 16$; Spanish $= -0.39$, Basque $= -0.551$). Panel B shows source localization of the language effect, circumscribed to the time interval highlighted by the significant cluster. All plotted regions reached a p-value <0.01.

the post-surgery language effect originated in parietal, superior temporal and prefrontal regions of the right hemisphere (see Fig. 6B). No significant language differences were observed for action naming prior to the surgery. In addition, no significant differences were observed for either pre- or post-surgery sessions in the case of objects (all Monte Carlo $ps > 0.12$, two tailed).

Overall, the finding of a significant language effect over right sensors after surgery is in contrast with the results of the control group, for whom no significant differences across languages were observed. This may suggest that while comparable adaptive compensation for processing action knowledge is present across languages before surgery (i.e., indicating language-invariant semantic processing similar to controls); tumor removal can prompt out different patterns of functional reorganization in the L1 and L2.

4. Discussion

In the present study, we focused on highly proficient Spanish-Basque bilinguals harboring brain tumors in dorsal frontoparietal nodes to investigate (i) whether compensatory longitudinal changes in beta rhythms (13–28 Hz) specifically target action naming and, more critical to our hypothesis, (ii) whether this compensation similarly stands across the two languages a bilingual patient speaks. In keeping with previous findings, we replicated the existence of longitudinal compensation in the beta band, reflected in power increases along with preserved behavioral performance in picture naming. As expected, this oscillatory effect was specifically observed for the action naming condition and was present in both Spanish and Basque, thus supporting the engagement of the dorsal stream in the semantic retrieval/representation of action knowledge across languages. Another critical finding emerged when contrasting action naming between a group of healthy bilinguals and the group of patients (separately within pre- and post-surgery sessions). Prior to the surgery, healthy controls and patients showed no differences across languages, likely indicating language-invariant semantic processing across L1-L2. However, after the surgery, patients exhibited beta power differences between Spanish and Basque in the right hemisphere, suggesting that tumor removal triggered a differential reorganization of the L1 and the L2.

4.1. Lexico-semantic compensation of action naming in bilingual patients with dorsal gliomas

Previous evidence indicates that the semantic processing of object and action knowledge can be partially dissociated in ventral and dorsal functional networks, respectively (Gleichgerrcht et al., 2016; Kemmerer, 2014; Shapiro et al., 2005, 2006). Furthermore, this category-based segregation has been also reported in bilingual speakers (Consonni et al., 2013; Geng et al., 2022; Willms et al., 2011), suggesting the existence of semantic language-invariant systems across L1-L2 supporting object/action dissociations. In line with this evidence, we show that frontoparietal regions in the dorsal stream are critical for processing action-related meaning across the two languages a bilingual speaks and that the resection of tumors affecting dorsal areas lead to a selective compensation for the lexico-semantic processing of action material. Furthermore, we show that this compensation is successful in preserving action naming in L1 and L2, giving the absence of severe production impairments across languages either before or after the surgery.

These findings raise the question of which neuroplasticity mechanisms may have favored language preservation. It has been shown that gliomas can alter functional connectomics profiles and affect global network communication (Cargnelutti et al., 2020; Duffau, 2020). In this context, different compensatory strategies can be called into play, including the recruitment of peritumoral tissue, the engagement of secondary ipsilateral regions functionally connected to areas close to the tumor (or its cavity) as well as contralateral homologues, typically in the right hemisphere (Duffau, 2005, 2020; Duffau et al., 2003). Furthermore, plasticity can be seen as a multistage process, firstly occurring preoperatively due to tumor growth and secondly, postoperatively, with reorganization triggered by the surgical trauma itself. Indeed, preoperative plasticity can be damaged during the surgery, and thus a subsequent development and/or reinforcement of reshaping mechanisms is necessary to explain patient's recovery after the intervention (Duffau et al., 2003; Robles et al., 2008).

In the present study, we focused on this latter aspect, namely the functional compensation resulting from tumor removal as compared to its presence before surgery. In keeping with previous findings (Amoruso et al., 2021), longitudinal compensation was indexed by post-surgery power increases in the beta band (13–28 Hz). This effect was true for both Spanish and Basque and consistent at the individual patient's level.

Beta rhythms are one of the most intriguing oscillations in the brain, supporting a wide range of cognitive functions. So far, several accounts have been advanced to explain their mechanistic role in humans. From a general standpoint, beta synchronization has been associated to network dynamics involved in the (re)activation of cortical representations (Spitzer and Haegens, 2017). Similarly, in the language domain, Weiss and Mueller (2012) have proposed that beta enhancement serves to bind distributed sets of neurons into a meaningful representation of memorized contents. Briefly, according to the authors, this will explain how the brain integrates information processed at different timescales and in separate neural regions in order to produce/understand a coherent speech unit. Interestingly, a critical aspect that both views underscore is the role of beta rhythms in facilitating functional networking in the brain. This aligns well with computational frameworks (Kopell et al., 2000; Sherman et al., 2016), suggesting that beta oscillations can synchronize at long conduction delays, enabling high-level interactions between spatially distant brain areas. This property becomes even more critical when considering that functional reshaping triggered by gliomas can affect network-level communication and potentially involve the compensatory recruitment of remote areas in the contralateral hemisphere. This aspect makes beta a plausible candidate to support reallocation of linguistic functions and is consistent with neurophysiological evidence from stroke and brain tumor patients (Kielar et al., 2016; Piai et al., 2017; Traut et al., 2019) showing a shift of language processing to the right hemisphere mediated by low frequency bands, including beta.

While our study mainly focused on beta rhythms, we acknowledge that other oscillatory changes may have occurred in response to the surgery. For instance, recent evidence indicates that bilingual patients with left LGGs can exhibit a rightward shift of parietal alpha (8–12 Hz) oscillations specifically related to L2 processing (Quinones et al., 2021). This effect could indicate the presence of different cognitive demands when processing L2 representations. Indeed, previous studies have linked right parietal alpha activity to increased load during cognitive control (Obleser et al., 2012) and, in particular, to language control in bilinguals (Bice et al., 2020; Tao et al., 2021).

4.2. *Postoperative differences in L1 and L2 reshaping in bilingual patients*

Nevertheless, it is worth noting that even though beta effects were present in both languages, longitudinal patterns for Spanish and Basque differed in terms of timing, scalp and source location. Indeed, while Spanish showed a left lateralized effect in premotor and inferior frontal regions, Basque additionally engaged right-hemisphere sources. To better understand this differential pattern, we contrasted action naming between Spanish and Basque separately before and after surgery. The same analysis was paralleled in a group of healthy Spanish-Basque bilinguals to assist the interpretation of potential divergent patterns in patients.

Prior to the surgery, action naming in Spanish and Basque did not differ, indicating comparable adaptive compensation for accessing action-based knowledge across languages. This finding was further supported by data from controls showing overlapping oscillatory beta networks in Spanish and Basque during action naming, likely indicating converging lexico-semantic processing in L1 and L2. However, after the surgery, differences between languages became evident. On the one hand, Basque showed higher activity in right parietal, superior temporal and prefrontal regions contralateral to the tumor's cavity. Importantly, this rightward activation was not present in healthy controls during action naming, suggesting that this set of regions was secondary engaged to achieve accurate lexico-semantic processing of action knowledge in the L2 once the tumor was resected. This is in keeping with previous findings from our lab (Quinones et al., 2021) combining fMRI and MEG techniques to map language lateralization in bilingual brain tumor patients and showing a stronger shift of activity toward the right hemisphere for Basque as compared to Spanish after surgery.

On the other hand, no recruitment of the right hemisphere was observed for Spanish, which instead showed more local changes in ipsilateral areas similarly recruited by controls during action naming. Such an oscillatory pattern likely reflects the re-weighting of functional connections between preserved healthy regions, implying that during postoperative recovery, some of these areas become more active to support adaptive compensation (York and Steinberg, 2011).

It has been proposed that plasticity mechanisms follow a hierarchical organization in which the recruitment of the contralesional hemisphere occurs at later stages, when other neural resources (e.g., recruitment of perilesional tissue and/or ipsilesional areas) have been depleted. Yet, the postoperative involvement of the right hemisphere occurred quite early in the case of Basque (i.e., within the ~3 months following surgery; see also Quinones et al., 2021 for a similar finding). While there is evidence showing that contralateral plasticity can be very quickly engaged (Duffau et al., 2003), this still leaves open the question of why this compensatory pattern was specifically observed for the L2.

Previous evidence (Gatignol et al., 2009) indicates that L1 and L2 can follow different postoperative trajectories in glioma patients, probably due to experiential factors such as AoA, language's proficiency and frequency of use. For example, it has been hypothesized that the order of postoperative language recovery mirrors the order of language acquisition (Emmorey and McCullough, 2009; Galloway, 1978). In our study, all bilinguals but one (patient 3) acquired Basque later than Spanish. It could be that the language acquired earlier is more robustly represented in the brain and thus more easily compensated; while the one acquired later may necessitates from the additional recruitment of contralateral homologues ——which can promote language recovery during the acute phase (Saur et al., 2006).

An alternative, although not mutually exclusive interpretation, is that language proficiency might have also played a role. Even though all patients were balanced highly proficient bilinguals, they all reported Spanish as being their L1. The engagement of control regions in the right prefrontal cortex supports this view, suggesting that action naming in Basque may have deployed more cognitive resources, in terms of language control (Hernandez et al., 2001) and semantic monitoring (Shen et al., 2016), than Spanish. This further indicates that reconfigurations preserving semantic processing after surgery may involve the additional engagement and/or changes in the interactions with other networks (i.e., executive control network).

Additionally, the "frequency hypothesis" posits that, in cases of brain damage, the language that is used more frequently before the illness and is more stimulated afterwards is better preserved and will recover better (Gatignol et al., 2009). However, in this study, most of the patients used both languages to an equal degree before and after surgery, which makes it unlikely for this hypothesis to account for the observed results.

An important aspect to stress is that even Spanish and Basque differed in terms of their oscillatory patterns after tumor removal, naming performance was well preserved in both languages, indicating successful postoperative reorganization - albeit supported by different compensatory strategies - rather than differential L1 vs. L2 deficits (Quinones et al., 2021).

We can further speculate, based on evidence from intraoperative cortical mapping in bilinguals (Giussani et al., 2007), that while there is a common pattern of L1-L2 organization in gross anatomical regions; more subtle, distinct microanatomical systems can be localized within these regions for each language (Paradis, 2004). Therefore, the functional connections among the Spanish and Basque microanatomical systems could have been differently impacted by the surgical trauma, resulting in unique postoperative compensation patterns for each language. Indeed, it has been suggested that variability in network(s) reconfiguration is higher after than before tumor resection (Duffau, 2020).

As a final note, it is worth mentioning that gliomas typically show recurrence patterns in the long-term follow-up after initial resection (Ferracci et al., 2019). Additionally, in many cases, tumor resection cannot be total due to the existence of residual functionality in the area infiltrated by the tumor, as it was the case for one of the patients participating in the present study. Thus, a multistage approach in which successive reoperations take place is counseled (Robles et al., 2008), given it favors plasticity and further functional reallocation away from the tumoral region. In this context, our findings of distinct L1 and L2 plasticity patterns following an initial brain surgery (e.g., the differential recruitment of the contralateral unaffected hemisphere) can be informative to plan follow-up strategies, as it has been shown that when decreased ipsi-lesional engagement is compensated with increased contra-lesional one, subsequent reoperations can be facilitated (Duffau, 2020).

4.3. *Limitations and avenues for further research*

Our study is not without limitations. First, while we acknowledge that an obvious limitation of our study is the small sample size ($n = 4$), it is important to note that: (i) it is quite challenging to access this type of population (i.e., highly proficient bilinguals with left dorsal gliomas) and obtain pre- and post-surgery measures within the same individuals; (ii) longitudinal designs, like the one employed here allow each patient to be his/her own control across sessions, thus reducing the confounding effect of inter-individual variability and increasing statistical power (Zeger and Liang, 1992); (iii) appropriate Crawford *t*-tests were used to analyze data while preserving the unique patterns of each individual patient; lastly (iv) the longitudinal oscillatory effects found in the present study are remarkably robust at the individual patient's level (e.g., all patients show the same direction of the effect). While these aspects contribute to the scientific rigor of our findings, future studies are needed to investigate whether they can be replicated in larger samples.

Another potential drawback of this study is that participants were highly proficient bilinguals, so it is uncertain whether the longitudinal patterns observed here would be similar (or not) in individuals with other types of bilingual experience (e.g., less proficient or immersed bilinguals). This is an important consideration for future research as it can provide a more comprehensive understanding of whether changes in beta power can be generalized to other type of bilingual populations.

Finally, our search of neural plasticity indices was circumscribed to functional compensation, overlooking changes in subcortical structures which are critical in supporting reshaping at the cortical level. For instance, dorsal fronto-parietal hubs are known to be subcortically connected by the superior longitudinal fasciculus (SLF) (Kamali et al., 2014; Makris et al., 2005). In a previous study (Amoruso et al., 2021) testing Spanish monolingual patients harboring LGGs in the left dorsal pathway, we found that post-surgery beta power increases in the right hemisphere correlated with volume increases in the right SLF, suggesting that functional and structural plasticity are closely intertwined. Therefore, a potential area of research that could provide a deeper understanding into the mechanisms of brain plasticity in bilinguals would be investigating the microstructural (e.g. FA) and macrostructural properties (e.g. volume changes) of relevant white matter bundles, and how they may be linked to functional changes.*4.4. Conclusions*.

Overall, we replicate previous findings supporting a key role of beta oscillations as a signature of language compensation in brain tumor patients and, more importantly, we extend it to the bilingual population. Furthermore, we show that bilingual patients with dorsal gliomas exhibit a selective compensation for action naming in their L1 and L2, providing evidence for the specific involvement of frontoparietal regions in the semantic retrieval/representation of action knowledge across languages. Finally, we show that while prior to the surgery, L1 and L2 can follow a similar reorganization profile; postoperative reshaping triggered by tumor removal leads to divergent reconfiguration patterns within each language. Taken together, these findings provide new insights into the spectro-temporal dynamics supporting postoperative recovery in the bilingual brain, and the potential roles that disruption of preoperative plasticity triggered by surgical trauma and/or language proficiency may have on this process. Beyond theoretical implications, our results provide valuable clinical information to plan multistage surgical strategies tailored to patients' differential neuroplasticity for each language. Such a strategy can improve EOR in follow-up surgeries while fully preserving all the languages a patient speaks.

Credit author statement

Shuang Geng: Investigation, Formal analysis, Visualization, Writing- Reviewing and Editing; **Ileana Quiñones:** Conceptualization, Investigation, Supervision, Writing- Reviewing and Editing; **Polina Timofeeva:** Software, Investigation; **Santiago Gil Robles:** Investigation, Resources, Writing- Reviewing and Editing; **Iñigo Pomposo:** Investigation, Resources, Writing- Reviewing and Editing; **Garazi Bermudez:** Investigation, Resources; **Nicola Molinaro:** Resources, Writing-Reviewing and Editing; **Manuel Carreiras:** Conceptualization, Supervision, Writing- Reviewing and Editing; **Lucia Amoruso**: Conceptualization, Methodology, Investigation, Formal analysis, Supervision, Writing- Original draft preparation, Writing- Reviewing and Editing.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Data will be made available on request.

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