CONVENIO DE COLABORACIÓN ENTRE LA ASOCIACIÓN INSTITUTO BIODONOSTIA Y EL BASQUE CENTER ON COGNITION BRAIN AND LANGUAGE (BCBL)

En Donostia, a 13 de marzo de 2023

REUNIDOS

De una parte,

De una parte, **ASOCIACION INSTITUTO BIODONOSTIA** con C.I.F G-75020313 y sede en Pº Dr. Beguiristain s/n, 20014 Donostia (Gipuzkoa), inscrita en el Registro General de Asociaciones con número AS/G/15251/2010, y en su nombre y representación Doña María Icíar Vergara Micheltorena con D.N.I. número 15.250.908-E , actuando en calidad de Directora Científica en virtud de la escritura de poder otorgada en fecha 24 de noviembre de 2022, ante el Notario de Bilbao, Don Juan Ignacio Bustamante Esparza, bajo el número 4.299 de su protocolo (en adelante "BIODONOSTIA")

Y de la otra, **BASQUE CENTER ON COGNITION BRAN AND LANGUAGE,** (en adelante BCBL) con CIF: G-20988929, representado en este acto por D. Miguel Angel Arocena Expósito, mayor de edad, con domicilio a efectos de notificaciones en Paseo Mikeletegi 69 de San Sebastián (Gipuzkoa) y DNI 15378329T que actúa en su condición de Gerente del mismo,

Las partes intervienen en la representación y con las facultades que sus respectivos cargos les confieren, reconociéndose mutuamente capacidad y legitimación para obligarse y convenir, y al efecto:

EXPONEN

PRIMERO.- Que BIODONOSTIA es un Instituto de Investigación Sanitaria adscrito a la OSI Donostialdea cuyos fines son: promover la investigación biomédica, epidemiológica, de salud pública y en servicios sanitarios, fundamentar científicamente los programas y políticas del sistema sanitario y potenciar de forma preferente la investigación traslacional, orientada a acelerar el traslado de los conocimientos científicos a la práctica clínica, según recomendaciones internacionales, en el ámbito territorial de Gipuzkoa y formación en Investigación e Innovación en virtud de convenios de colaboración con Osakidetza/SVS, en los que se le encomienda la gestión de la I+D+i que se desarrolle en su seno.

SEGUNDO.- Que BCBL es un centro internacional de investigación interdisciplinar para el estudio de la cognición, el cerebro y el lenguaje fundado conjuntamente por Ikerbasque, Innobasque, la UPV-EHU y la Diputación de Guipúzcoa, siendo algunos de sus objetivos fundamentales los siguientes:

- Desarrollar la investigación y la innovación en el campo de la Neurociencia Cognitiva con especial énfasis en el procesamiento del lenguaje y el bilingüismo.
- Promover la investigación científica y las relaciones científicas nacionales e internacionales en el ámbito de la Neurociencia Cognitiva y transferir los resultados de esta investigación a la comunidad socioeconómica en general.
- Establecer vínculos de colaboración y áreas de interés común con instituciones públicas y privadas, centros y empresas, con el objetivo de proporcionar la investigación, formación, servicios tecnológicos y de consultoría para utilizar el trabajo desarrollado en BCBL de una manera provechosa en el marco económico y social.

TERCERO.- Que es voluntad de las entidades comparecientes colaborar conjuntamente en el desarrollo y gestión, de actividades de investigación científica y desarrollo tecnológico, en el campo de neurología con el fin de avanzar en el desarrollo del Proyecto de Investigación "COMPRENSIÓN DE LA ENTONACIÓN TRAS UN ICTUS" (en adelante el Proyecto).

CUARTO.- Que, como consecuencia de lo anterior y con el fin de regular los términos y condiciones por los que se regirán las relaciones entre las Partes en el marco del desarrollo del Proyecto, así como la explotación de los resultados que puedan derivarse del mismo, se establecen las siguientes:

CLÁUSULAS

Primera.- **OBJETO**

El presente Acuerdo tiene por objeto establecer los términos y condiciones básicas de la colaboración entre las Partes en relación con la ejecución del Proyecto así como la regulación de la participación, las responsabilidades y los derechos de las Partes y la propiedad y explotación de los Resultados a que éste diese lugar.

Segunda.- **DESARROLLO DEL PROYECTO**

2.1. Definición del Proyecto

"El Proyecto" tiene como objeto principal investigar el papel de las señales acústicas y funcionales en la determinación de la lateralización de la prosodia y el impacto de las lesiones corticales en la sincronización neuronal con el fin no sólo de detectar el déficit en la comprensión de la entonación de manera fina, sino también caracterizarlo en términos de fuentes y funciones neuronales, lo que podría ayudar a orientar las intervenciones terapéuticas personalizadas.

Como Anexo I, se adjunta memoria científica del proyecto.
Como Anexo II, se adjunta Informe del Comité de Ética.

2.2. EQUIPO INVESTIGADOR

Por parte del Instituto de Investigación Sanitaria (IIS BIODONOSTIA) colaboran:

- Patricia de la Riva como Investigadora Responsable perteneciente al servicio de neurología del Hospital Universitario Donostia y clínico asociado al IIS BIODONOSTIA.
- Jon Equiza Bazan perteneciente al servicio de neurología del Hospital Universitario Donostia y clínico asociado al IIS BIODONOSTIA.
- Raquel Sofia Laspiur Gandara perteneciente al IIS BIODONOSTIA.

Por la otra parte colabora:

- Simona Mancini, como Investigador Responsable
- Nicola Molinaro
- Giada Antonicelli

2.3. COMPROMISO DE LAS PARTES O TAREAS A DESARROLLAR

Cada participante se compromete a realizar las tareas asignadas y a colaborar para el exitoso desarrollo del proyecto de conformidad con la Memoria Científica, asumiendo las tareas y responsabilidades detalladas en los apartados de la memoria, siendo las labores que realizará cada una de ellas las siguientes:

BIODONOSTIA:

- El reclutamiento de aquellos participantes que, a su juicio, sean buenos candidatos para participar en el proyecto. Esto significa dar a los participantes una breve explicación del proyecto, informarles de que se realiza en colaboración con BCBL y preguntarles si acceden a participar.

- La documentación y material bibliográfico del que dispone BIODONOSTIA que resulte necesario para la realización de las actividades programadas.

- La coordinación entre paciente e investigadores del BCBL para organizar las sesiones de estudio de la manera más efectiva.

- Las instalaciones pertenecientes o de las que el IIS BIODONOSTIA dispone de un derecho de uso necesarias para la realización de los estudios.

BCBL:

- La participación en el diseño y desarrollo de las actividades que se ejecuten dentro del ámbito de actuación del presente Convenio.
- La gestión, planificación, ejecución y análisis de estudios sobre la comprensión de la entonación lingüística y emocional tras un ictus.
- Los investigadores del BCBL explicarán de forma detallada el proyecto a los pacientes participante, facilitándoles el consentimiento informado y contestando a cualquier duda o pregunta.
- Administrar a los pacientes las distintas pruebas o tests.
- Las instalaciones pertenecientes a BCBL necesarias para la realización de los estudios.

2.4. RELACIONES ECONÓMICAS:

La suscripción del presente convenio no implica la aportación de recursos económicos.
Las partes se comprometen, en la medida en la que les sea posible, a buscar financiación para la consecución del objeto del presente Acuerdo por alguno de los siguientes canales: autofinanciación, convocatorias públicas o privadas u otras.
A tal efecto, cuando las solicitudes de ayuda se realicen entre las Partes de manera que ambas sean beneficiarias de dicha ayuda, la distribución de los fondos concedidos deberá corresponder al porcentaje indicado en la solicitud de ayuda de inicio siempre que ello no perjudique la consecución de los objetivos del Proyecto.
En el caso de que las solicitudes de ayuda se realicen por una Parte, las Partes se comprometen, siempre que las posibilidades de concesión de la ayuda y la calidad del Proyecto no se vean afectados, a:
- Incluir a la otra Parte como miembro participante (la figura podrá ser la de colaborador o subcontratado).
- Compartir la ayuda con la otra Parte siempre que ello no dificulte la justificación de la misma a la Parte solicitante de la ayuda.

En caso de que posteriormente a la firma de este acuerdo las partes obtuvieran una financiación externa, habrán de suscribir un anexo especificando dicho punto.

Tercera.- PROPIEDAD INDUSTRIAL E INTELECTUAL

Por "Resultados" se entiende toda información o resultado generado por cualquier Parte, o por un tercero que trabaje para él, en la ejecución del Proyecto, así como el producto o productos finales resultantes del mismo.

Cada parte continuará siendo propietaria y titular de los conocimientos, equipos, sistemas, ensayos, programas, normativas, especificaciones, pruebas de investigación, procesos de ejecución y cualquier otro know-how siempre y cuando sean anteriores en propiedad y titularidad a la realización del presente proyecto.

Los participantes se proveerán unos a otros de derechos de acceso al conocimiento necesario para el desarrollo de los trabajos en el marco del proyecto. Este acceso será libre y gratuito.

La titularidad industrial y/o intelectual de los resultados que pueden producirse en la realización del proyecto, corresponderá a BCBL y al IIS BIODONOSTIA (Administración General de la Comunidad Autónoma de Euskadi), en la proporción basada en la aportación intelectual y material realizada por las partes al Proyecto del presente Convenio.

Cabe mencionar que la titularidad de los derechos de propiedad industrial e intelectual que puedan derivarse por la colaboración del IIS BIODONOSTIA en este acuerdo, corresponden a la Administración General de la Comunidad Autónoma de Euskadi (AGCAE) y serán gestionados por la Fundación Vasca de Investigación e Innovación Sanitarias (BIOEF) según el convenio de colaboración de fecha 2 de octubre de 2020 suscrito entre la AGCAE y BIOEF sobre gestión de derechos de propiedad intelectual e industrial derivados de la actividad investigadora e innovadora en el sistema sanitario de Euskadi. En virtud de este convenio los derechos de propiedad intelectual e industrial de los resultados derivados de la actividad investigadora e innovadora desarrollada en el sistema sanitario de Euskadi, en sus entidades de I+D+i, y cuya titularidad corresponde a la AGCAE serán gestionadas por BIOEF.

En el caso en el que una o varias de las partes participantes en el Proyecto desee llevar a cabo la protección, comercialización o explotación de los resultados del proyecto, deberá formalizarse un acuerdo específico en el que se regulen los derechos y obligaciones de cada uno, la representatividad, la cesión de derechos y licencias así como las oportunas regalías que deban ser satisfechas al resto de los participantes.

La Administración General de la Comunidad Autónoma de Euskadi, mantendrá la titularidad, y Osakidetza/SVS un derecho de uso del resultado derivado del

Proyecto a los efectos de cualquier actividad docente o de investigación (no comercialización).
En todo caso, se deberá reflejar la condición de inventores y/o autores de todos aquellos investigadores que hayan contribuido a los resultados objeto de patente y/o registro.

Cuarta. - DIFUSIÓN Y PUBLICACIONES

Como principio general, las Partes acuerdan que no podrá ser difundida información que pudiera menoscabar la protección del conocimiento generado en la Colaboración a través de los derechos de propiedad industrial e intelectual que se pudieran derivar de dicho conocimiento.
La Parte que pretenda difundir información relativa a la Colaboración deberá remitir el documento cuya publicación se pretenda a la otra Parte. Se dispondrá de un plazo de treinta (30) días, a contar desde la recepción del documento, para formular cuantas objeciones o comentarios se estimen al respecto.
Cualquier objeción a la difusión o publicación deberá contener:
- Una solicitud de modificación del documento, especialmente si la publicación o difusión de la información contenida en el mismo pudiera menoscabar las opciones de explotación del conocimiento generado en la Colaboración a través de derechos de propiedad industrial o perjudicar intereses legítimos de terceros; o,
- Un requerimiento para posponer la difusión o publicación de la información que pueda ser objeto de protección mediante derechos de propiedad industrial.

El silencio será entendido como la tácita autorización para la difusión.
En las publicaciones se respetará siempre la mención a los autores del trabajo.
En cualquiera de los casos de difusión de resultados se hará siempre referencia especial a la Colaboración.

Quinta.- SEGUIMIENTO

Con el fin de facilitar la coordinación y el seguimiento del presente Convenio se constituirá una Comisión Mixta, que estará formada por un representante de cada una de las partes.

Asimismo, la Comisión Mixta se encargará de planificar, fomentar, supervisar y evaluar los programas y acciones que se vayan a emprender al amparo del presente Convenio.

La Comisión se reunirá tantas veces como sea necesario para la buena marcha de las actuaciones a desarrollar en el marco del Convenio.

La comisión mixta de seguimiento estará formada por:

- Dra. Simona Mancini por parte del BCBL.
- Dra. Patricia de la Riva Juez parte del IIS BIODONOSTIA

Sexta.- CONFIDENCIALIDAD

Salvo que de otra forma se disponga en el presente Acuerdo, toda la información comunicada por una de las Partes a la otra, ya sea con anterioridad o con posterioridad a la fecha de la firma del presente Acuerdo, en relación con su preparación o su cumplimiento, se entenderá confidencial, utilizándose exclusivamente para los fines del Acuerdo (en adelante, la "Información Confidencial").
El uso de la Información Confidencial estará sujeto a los términos y condiciones recogidos en este Acuerdo y se mantendrá en vigor con independencia de la vigencia del presente Acuerdo, mientras dicha información mantenga su carácter confidencial y no devenga de dominio público por medios distintos del incumplimiento de este Acuerdo.

Las Partes se obligan a guardar secreto sobre la Información Confidencial y no transmitirla a terceros, salvo con el previo consentimiento por escrito de la otra Parte.

Los subcontratistas de las tareas del Proyecto que las Partes pudieran contratar podrán acceder a la Información Confidencial siempre y cuando sea estrictamente necesario para desempeñar la tarea subcontratada y previa firma de un compromiso de confidencialidad de iguales características al establecido en esta Cláusula sexta.

Las Partes velarán para que la Información Confidencial no se ponga en conocimiento de más personas que los empleados, agentes, representantes, o asesores que precisen conocerla para garantizar el adecuado desarrollo del presente Acuerdo o para el cumplimiento de las tareas que les son propias. Todas estas personas deberán haber asumido con carácter previo a la comunicación de la Información Confidencial compromisos expresos de confidencialidad y secreto sobre la misma.

Las obligaciones de confidencialidad establecidas en la presente Cláusula cederán (i) ante cualquier requerimiento administrativo o judicial u otro imperativo legal en contrario, (ii) en el caso de que la Información Confidencial sea del dominio público, (iii) en el caso de que sea conocida con anterioridad a la negociación del Acuerdo, (iv) en el caso de que haya sido recibida de terceros sin que recaiga sobre ella deber de confidencialidad, o (v) en el caso de que su transmisión haya sido consentida previamente y por escrito por la Parte de la que procede la información.

Séptima. - PROTECCIÓN DE DATOS

Para la correcta aplicación del presente acuerdo, las partes podrían eventualmente acceder a datos de carácter personal protegidos por la Ley Orgánica 3/2018, de 5 de diciembre, de Protección de Datos Personales y garantía de los derechos digitales, como por el Reglamento (UE) 2016/679 del Parlamento Europeo y del Consejo de 27 de abril de 2016 relativo a la protección de las personas físicas en lo que respecta al tratamiento de datos personales y a la libre circulación de estos datos y por el que se deroga la Directiva 95/46/CE.

Por lo que, las partes, se comprometen a que el uso y tratamiento de los mismos será acorde con las actuaciones necesarias para el desarrollo del presente acuerdo según las instrucciones que sean facilitadas en cada momento.
Asimismo, las partes asumen la obligación de guardar secreto profesional sobre cuanta información pudieran recibir, gestionar y articular con relación a los datos personales y a no comunicarlos a terceros, así como a destruirlos, cancelarlos o devolverlos en el momento de la finalización de la colaboración entre las partes, así como a aplicar las medidas de seguridad necesarias, de conformidad con la legislación vigente.

Octava.- VIGENCIA Y PRÓRROGA

El presente Acuerdo entrará en vigor en la fecha indicada en el encabezamiento y tendrá una duración inicial de 3 años, pudiendo ser prorrogado posteriormente si las Partes lo acordaran por escrito.

No obstante, cualquiera de las Partes podrá, previa comunicación por escrito a la otra Parte y con treinta (30) días naturales de antelación, cesar en su colaboración en el marco del presente Acuerdo, sin perjuicio de su obligación de cumplir con cualquier compromiso que hubiera adquirido con carácter previo a la citada comunicación. La otra Parte podrá exigir dicho cumplimiento, sin perjuicio de las indemnizaciones que pudieran reclamar al respecto.

Serán causas de resolución del presente Acuerdo, además de las generales de la Ley, las siguientes:
a) El mutuo consentimiento de las Partes.
b) La finalización del Proyecto.
c) En general, en caso de incumplimiento por cualquiera de las Partes de sus respectivas obligaciones contractuales.
d) Por cualquier circunstancia justificada ajena a las Partes que imposibilite el cumplimiento de las obligaciones adoptadas.

Ninguna de las Partes será responsable del incumplimiento o retraso en la ejecución de las obligaciones aquí contempladas siempre y cuando sea causado por circunstancias que van más allá de un control razonable o que hacen su ejecución impracticable.
En caso de terminación del Acuerdo, cualquiera que fuere la causa, cada una de las Partes deberá entregar a la otra un informe escrito que incluya la evaluación y los resultados obtenidos hasta la fecha por parte de su equipo investigador.
En caso de resolución del convenio se mantendrán en vigor las cláusulas correspondientes a confidencialidad y propiedad de los resultados.

Novena.- NOTIFICACIONES

Toda notificación o petición relacionada con el presente acuerdo se enviará por las partes a las personas y a las direcciones que a continuación se indican:

BIODONOSTIA:

Catalina Arrieta Villalante
Paseo Dr. Begiristain, s/n, 20014 San Sebastián, Gipuzkoa
Teléfono: 943 00 62 54
Correo electrónico: CATALINA.ARRIETA@biodonostia.org

ASOCIACIÓN BCBL- BASQUE CENTER ON COGNITION, BRAIN AND LANGUAGE
D. Miguel Ángel Arocena
Paseo Mikeletegi 69, 20009 Donostia-SanSebastián
Teléfono: 943 309300
Correo electrónico: m.arocena@bcbl.eu

Decima. MODIFICACIONES

Ninguna modificación, alteración o adición a este Acuerdo será válida a menos que esté firmada por las Partes. Las aprobaciones o consentimientos aquí establecidos deberán también constar por escrito.
Con independencia de lo anterior, las Partes se obligan recíprocamente a promover y completar la adaptación de este Acuerdo cuando ello fuere necesario como consecuencia de una modificación legislativa (legal o reglamentaria) o una alteración relevante de la interpretación y aplicación que de la misma llevan a cabo los tribunales de justicia o las autoridades administrativas competentes.

Decimoprimera. INTEGRIDAD

Este Acuerdo anula cualquier otro acuerdo, verbal o escrito, existente entre las Partes relativo al objeto y estipulaciones del presente Acuerdo.

Decimosegunda. NULIDAD PARCIAL

La nulidad de cualquiera de las estipulaciones no esenciales de este Acuerdo no acarreará la nulidad del Acuerdo en su totalidad.

Decimotercera. CESIÓN DEL ACUERDO

Las Partes no podrán ceder el Acuerdo o parte del mismo a terceros, o los derechos y obligaciones que surgen del mismo, salvo que, con carácter previo y por escrito, la otra Parte otorgue su consentimiento. En todo caso, la cesión supondrá que el cedente y cesionario responderán solidariamente frente a la otra Parte por cualquier concepto relativo al presente Acuerdo.

Decimocuarta. JURISDICCIÓN Y LEY APLICABLE

Las partes se comprometen a resolver de manera amistosa cualquier desacuerdo que pueda surgir en el desarrollo del presente Acuerdo.

Para la resolución de todas las cuestiones derivadas de la interpretación, ejecución o terminación del presente Acuerdo, las partes se someten expresamente y con renuncia expresa a cualquier otro fuero que pudiera corresponderles, a los Juzgados y Tribunales de Donostia-San Sebastián

Como expresión de su consentimiento, las Partes firman electrónicamente, en un solo efecto, el presente Acuerdo, en el lugar y la fecha indicada en el encabezamiento.

Por BIODONOSTIA	Por el BCBL
15250908E MARIA ICIAR VERGARA (R: G75020313) Firmado digitalmente por 15250908E MARIA ICIAR VERGARA (R: G75020313) Fecha: 2023.03.20 12:37:10 +01'00'	15378329T MIGUEL ANGEL AROCENA (R: G20988929) Digitally signed by 15378329T MIGUEL ANGEL AROCENA (R: G20988929) Date: 2023.03.13 08:24:49 +01'00'
María Iciar Vergara Micheltorena	Miguel Angel Arocena

Asumiendo los compromisos del Convenio,

Patricia de la Riva Juez
Investigadora Principal

PATRICIA DE LA RIVA JUEZ - 72460889X Firmado digitalmente por PATRICIA DE LA RIVA JUEZ - 72460889X Fecha: 2023.03.20 12:26:12 +01'00'

ANEXO I

MEMORIA CIENTIFICA

Antecedentes y estado actual del tema

Prosody and categories of prosody

Prosody refers to the suprasegmental acoustic phenomena of spoken language, the most prominent being the energy (envelope) and the fundamental frequency (pitch) of the signal. Since modulations of such parameters can convey distinct kinds of information, prosody has been subcategorized accordingly. Emotional prosody (EP) communicates the speaker's state of mind (e.g., anger, sadness, happiness, irony), while linguistic prosody (LP) can distinguish between syntactic categories (e.g., REcord vs reCORD), segment sentences into phrases (add example), and perform different speech acts (e.g., question, command, assertion).

Prosody is one of the ways in which the quasi-periodicity of language manifests. In general, speech frequency ranges between 0.1-4 Hz (delta) and 4-8 Hz (theta) bands, corresponding to sentence/phrase and syllable time scales, respectively. As discussed below, brain oscillatory activity can entrain to this periodicity and the extent to which it does so can give insights into the way language processing unfolds.

Traditional hypotheses on prosody processing lateralization and criticism

Early models of prosody processing hypothesized that prosody as a whole is mainly supported by right hemisphere (RH) activity (Klouda et al., 1988). Clinical and experimental evidence, though, soon revealed that a distinction was necessary between emotional and linguistic prosody. This paved the way to hemispheric models, which attempted at localizing each prosodic function in either hemisphere of the brain. A traditional idea is that EP processing is right-lateralized, while LP is left-lateralized (*functional lateralization hypotheses*, Paulmann, 2016; Witteman et al., 2011, 2012; Diehl & Paul, 2009; Peppé, 2009; Van Lancker, 1980). Other accounts focus on the physical properties of the input (*cue-dependent lateralization hypotheses*, Witteman et al., 2011, 2012). For example, the *acoustic-lateralization hypothesis* maintains that slow acoustic changes, like those involved in prosody, are processed in the RH, while faster ones, associated with syllable-level modulations, are more left-lateralized (Paulmann, 2016; Price, 2012; see also Moen, 2009 for similar conclusions). Another claim within this account is that the right hemisphere would be specialized in pitch and intonation perception, while temporal aspects would be mainly processed in the left hemisphere (LH).

Neuroimaging and electrophysiological data, however, have led many researchers to argue for a bilateral distribution of prosody processing as well as a less clear-cut distinction between kinds of prosody (Paulmann 2016). Contra a right-left hemisphere functional dichotomy, extant research suggests that in brain-damaged individuals, responses to prosody vary depending on lesion localization, tasks, and the linguistic feature involved. In a behavioral experiment, Geigenberger & Ziegler (2001) reported that subjects with right-hemisphere damage (RHD) had most difficulties in emotion identification and turn-taking, while those with left-hemisphere damage (LHD) especially struggled with focus recognition, and both groups performed worse than controls. A recent meta-analysis by Ukaegbe and colleagues (2022) only found some evidence that the RH is more implicated in EP comprehension than the LH, but none in support of hemispheric specialization for linguistic prosody comprehension and production and for emotional prosody production (see also Stockbridge et al., 2021). The authors underlined that while compatible with functional accounts, their results should be taken with caution given the heterogeneity and the small effect sizes present in the sample under study. Remarkably, a bihemispheric distribution of prosody processing would fit in with the widely accepted dual route model, in which speech perception and production take place via a ventral and a dorsal stream, respectively (Hickok & Poeppel, 2016, 2007). In particular, the ventral stream, which maps acoustic input to meaning, would encompass the bilateral posterior superior temporal sulcus (STS) for sub-lexical sounds and the left temporal lobe for basic combinatorial operations and lexical access. Unfortunately, this overarching model still does not include emotional prosody.

Linguistic prosody

Two commonly investigated LP phenomena are prosodic boundaries and accents. Evidence from functional magnetic resonance imaging (fMRI), Electroencephalography (EEG) and Magnetoencephalography

(MEG) suggests that the lateralization of these phenomena depends more on contingent task and function than on purely acoustic properties.

Healthy subjects

FMRI studies showed that the right posterior superior temporal sulcus/gyrus (STS/STG) is particularly sensitive to pitch variations (Meyer et al., 2002), and together with its left homologue, it is implied in prosodic boundary perception (Ischebeck, 2008). Frontal regions activation has been linked with integration processes (Meyer et al., 2002) and it has been reported to be more left lateralized when intonation is essential to disambiguate syntactic structure Van der Burght et al. (2019).

A considerable bulk of EEG research on LP focused on prosodic boundaries. The component associated with sentence segmentation is a positive deflection, called closure positive shift (CPS) (Sheppard et al., 2019, Nickels & Steinhauer, 2018; Glushko et al., 2016; Steinhauer et al., 1999), which seems to be specific to prosody regardless of the presence of semantics and syntax (Pannekamp et al., 2005). Phrasal boundaries are a slow phenomenon, while accents related to focus structure involve a sudden change in speech intensity. Key components in this case are the P3a, interpreted as stress perception (Chevallier et al., 2010), the N400, linked to misplaced focus detection (Dimitrova et al., 2010, but see Bögels, 2011, who only found this effect for missing accents), and the P600, which has been associated with reanalysis (Dimitrova et al., 2010) and integration processes (Chevallier et al.,2010), depending on the task.

MEG studies localized the homologous of the CPS to auditory cortices, which is more leftward for stronger boundaries, that is, when structure and prosody converge (Anurova et al.,2022). Word and syllable level acoustic variations have been mainly reported to elicit a mismatch negativity (MMNm), whose lateralization has been argued to be function- and language-driven (Fournier et al., 2010; Gandour et al., 2004). Some studies have also investigated the brain correlates of speech acts processing. For instance, Tomasello et al. (2022) compared assertive and question (rising) intonation in sentences, hummed speech and music. They found that assertions and questions differentiated as soon as 100ms after critical noun onset in sentence but not in hummed speech and music stimuli. Questions relative to assertions led to a positive deflection which was localized to the left motor area that controls tongue movements. They interpreted such a pattern as a sort of simulation of the verbal reply expected after a question.

Studies monitoring the cortical tracking of speech unravelled entrainment between brain oscillations - especially in the delta, 0.1-4 Hz, and theta, 4-8 Hz, bands- and external linguistic stimuli (Glushko et al., 2022; Keitel et al., 2018; Meyer et al., 2017; Ding et al., 2016) which is more evident in healthy than impaired (e.g., dyslexic) subjects (Goswami & Leong, 2013). Evidence to date points to the fact that this effect can appear in both hemispheres depending on the experimental design. Bourguignon et al. (2013) localized it to the right posterior STS/STG for speech as opposed to humming. On the other hand, in Keitel et al. (2018), where stimuli were all linguistic and participants performed a previous-word recognition task, better synchronization was detected in the left hemisphere (premotor and inferior temporal areas) in correct relative to incorrect trials. However, experiments involving passive listening with no task reported bilateral activity (Teoh et al., 2019). Further, entrainment appears to be modulated by internal representations in a top-down fashion. Ding et al. (2016) and Meyer et al. (2017) linked tracking to abstract syntactic structure building. The latter additionally demonstrated that structural preferences influence the coherence between acoustic and brain signals. Glushko et al. (2022) expanded on this idea shining a light on prosodic preferences in sentence comprehension. In their experiment, participants listened to sentences with either a symmetrical (2+2) or asymmetrical (1+3) syntactic structure, pronounced with flattened or 2+2-compatible prosody. In one additional condition they were instructed to silently apply the 2+2-compatible prosody contour to flattened stimuli. Results showed an increase in delta entrainment in sentence mid position when the 2+2 structure was involved, but a reduction in the 1+3 conditions. Moreover, prosody-related activity was more frontally distributed while syntactic-related activity localized to posterior sites. They concluded that covert prosody interacts online with structure building during sentence comprehension.

Brain-damaged individuals

As mentioned in the previous section, both RHD and LHD can present with prosody processing deficits and there is little evidence that linguistic prosody is significantly more affected by left than right lesions. A recent meta-analysis (Stockbridge et al., 2021) characterized linguistic prosody processing in RHD. It seems that in this population syntactic category recognition and chunking are quite preserved relative to sentence-level prosody, in which speech acts seem to be more compromised than clause boundaries and emphasis identification. In line with this, individuals with left-brain damage often exhibit a delayed CPS to prosodic boundaries with a different scalp distribution compared to healthy controls, which may be due to the reorganization of impaired functions (Sheppard et al., 2019, 2017).

So far, very few studies investigated cortical tracking in people with aphasia. In Dial et al. (2021), people with logopenic variant primary progressive aphasia -in which the thinning of the left temporoparietal cortex leads to major phonological deficits- listened to connected speech while their EEG signal was recorded. Relative to matched healthy controls, the patients demonstrated abnormal brain-input coherence in the theta -but not in the delta- band and lower scores in comprehension. The authors explained this as the consequence of a compensatory mechanism. Given that leftward fast-rate (gamma band) oscillations -linked to phonetic decoding- are disrupted, the system would rely more on the rightward theta band activity -responsible for syllable-level analysis- to reconstruct the envelope. Indeed, results from experiments manipulating speech rate conducted with healthy subjects indicated that at lower intelligibility acoustic tracking increases but linguistic tracking drops (Verschueren et al., 2022).

Emotional prosody

Extant electrophysiological and neuroimaging evidence has driven the development of a model of emotional prosody processing that encompasses three stages. Emotional prosody comprehension would involve (1) acoustic analysis in the bilateral auditory cortices, (2) extraction of perceptual features relevant to emotional encoding in the right posterior (STS/STG), and (3) access to the semantic representation of emotions for evaluation in the bilateral inferior frontal areas (Sheppard et al., 2021b; Witteman et al., 2012; Kotz & Paulmann, 2011; Wildgruber et al., 2009). Stages 2 and 3 would be influenced by attentional focus driven by task demands, while stage 1 would mainly involve bottom-up processes. EEG correlates of such steps would be (1) early negativities, followed by (2) a positivity, and (3) a later positivity or negativity (Paulmann et al., 2013; Witteman et al., 2012; Kotz & Paulmann, 2011; Thönnessen et al., 2010; Wittfoth et al., 2010; Yagura et al., 2005).

Healthy subjects

To study emotional prosody processing, many experiments employed an oddball paradigm and found a pattern in line with the model above, that is, an early component located in temporal regions followed by a later frontal component. Once more, lateralization appears to depend much on experimental design. Yagura et al. (2005) observed that emotion recognition was right-lateralized relative to an N-back task. However, when emotional prosody is contrasted with other linguistic functions, right-lateralization appears to be weaker. For instance, Wittfoth et al. (2010) compared emotional (angry, happy) to neutral sentences with either interfering or non-interfering semantic content. The emotion effect was bilateral, while incongruency detection was associated with increased activation of the dorsal anterior cingulate cortex as well as of the right mid and superior temporal cortex. Bilateral emotion effects were also observed in the fMRI study by Seydell-Greenwald et al. (2020). They disentangled sentence comprehension and emotional prosody, by contrasting -respectively- regular and reversed sentences, on the one hand, and neutral and emotional sentences, on the other. They also computed the degree of lateralization of the two effects and found that sentence processing was more left-lateralized than prosody processing was right-lateralized. Further, the areas activated in the two hemispheres were only partially the mirror image of one another, with several non-overlapping regions which were specific to emotional prosody (bilateral pars orbitalis (BA 47), amygdala) or sentence comprehension (the right cerebellum, left fusiform gyrus, and left inferior parietal cortex). In addition, it was apparent that right-lateralization was not driven by acoustic features only, but also task demands (emotion vs situation recognition via sentence-picture matching), the integrity of the sound-emotion link, and semantic content.

Brain-damaged individuals

Recent meta-analyses found that aprosodia does not concern only people with RHD, although it is especially frequent in this population. Sheppard et al. (2021) estimated that, among those 50% RHD who experience communication deficits, 70% show receptive emotional aprosodia at the acute stage, and 12-44% do at the subacute/chronic stage (cfr. Stockbridge et al., 2021). Sheppard et al. (2021b), correlating lesions and behavior in RHD, evidenced that people with damages to the frontotemporal areas had most difficulties in matching acoustic features to emotions (stage 2 of their model described above) and those with posterior and thalamic lesions were mainly impaired in acoustic analysis (stage 1), while those with subcortical damages (caudate nucleus) displayed a deficit in all the operations involved in emotional prosody processing. Witteman et al. (2011)'s meta-analysis found that both people with RHD and LHD display impairment in emotional prosody processing, but right hemisphere lesions seem to be more detrimental than left hemisphere lesions.

In line with the above, Kotchoubey et al. (2009) reported that people with neurological disorders were much less sensitive than controls to stimuli in an oddball paradigm, and that RHD were significantly less likely

to show any effect whatsoever. Further support to a RH specialization in EP might also come from adults that had a perinatal stroke in the LH. Despite having been developed in the same hemisphere (the RH), sentence and emotional prosody processing proved to be anatomically segregated from one another (Martin, 2022, unpublished doctoral thesis). It is imaginable, then, that regions exclusive to emotional processing can be regarded as core hubs for this function.

Summary

In summary, research to date has provided converging evidence that prosody processing is a multi-stage process that involves both hemispheres and that lateralization is dynamic and depends upon both functional and perceptual factors. Cortical tracking methods gave some hints that coherence between the acoustic input and brain responses may correlate with successful comprehension. However, major issues still need to be taken into consideration. First, it is not clear how functional and acoustic features interact, nor how this interaction modulates the lateralization of prosody processing. Second, prosody processing is understudied in people with aphasia, which may prevent the development of targeted treatment and research-informed therapies.

In our research we will be guided by the following research questions (RQ):

1. What are the factors influencing prosody lateralization? Which among the cue-dependent, the function-dependent and the dynamic accounts better explain the results?
2. How do lesions to the RH or the LH impact prosody processing as indexed by cortical tracking in the delta and theta band and behavioral responses?

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Hipótesis

From a theoretical point of view, the extant literature failed to provide strong evidence in favor of any of the accounts of prosody lateralization. In addition, prosody processing is still peripheral in language assessment for clinical populations. By testing people with post-stroke brain damage, we can address both these issues, as the correlation (or the lack of it) between behavior and neural profile can give us insights on the functional role of the lesioned brain structures. In particular, we advance the following hypotheses:

1. Prosody comprehension is a multi-stage process that is supported by auditory cortex, superior temporal and frontal regions and premotor areas. Lesions to these areas or to the connections between them should impinge on prosody processing and cortical tracking.
2. If function-dependent accounts are correct, RH lesions should lead to poorer EP processing, while LH lesions to deficits in LP processing.
3. If cue-dependent accounts are correct, patients with right hemisphere lesions should be more impaired overall as both LP and EP involve slow acoustic changes. Or, at least, acoustic features should explain data significantly better than functional features.
4. If distributed processing accounts are correct, both patient groups should show some kind of impairment due to either diminished acoustic or higher order processing. In particular:
   4a. Lesions to bilateral auditory cortex should hinder acoustic perception, possibly depending on the physical properties of the input (e.g., pitch, intensity). In this case, increased acoustic tracking related to effort might be anticipated (Verschueren et al., 2022).
   4b. Lesions to the right and left STS/STG should be more detrimental to emotional and linguistic prosody, respectively, possibly modulated by the physical properties of the input (pitch, intensity).
5. We expect behavioral responses to correlate with both screening measures and brain signal: normal cortical tracking should lead to better accuracy than anomalous cortical tracking.

Objetivos

The present project bears both clinical and theoretical relevance. Understanding speaker's intentions is crucial in communication and deficits in this ability can dramatically affect the quality of daily life. By distinguishing speech acts from emotions processing, we aim to assess the impact of right- and left-brain lesions on prosody comprehension in a fine-grained manner. Indeed, our goal is not just to detect the impairment, but also to characterize it in terms of neural sources and functions. This might help orient customized therapeutical interventions. For instance, depending on the neural profile, a treatment focusing on acoustic features perception could be more beneficial than one centred on semantic content, and vice versa.
From a theoretical perspective, our work will test the tenets of two traditional accounts of prosody processing, the cue-dependent and the function-dependent hypotheses.

Metodología

Technique

We plan to address the aforementioned issues in a MEG experiment. This technique measures the variations in the magnetic field generated by coherent electrical activity of cortical neurons. Since the propagation of the electrical signal is instantaneous, like the EEG, it has a millisecond-by-millisecond temporal resolution. Moreover, as the magnetic field is not distorted by the skull and tissues, spatial information can be modelled with good reliability via source reconstruction (Salmelin et al., 2019). Such features make the MEG a suitable method to address our research questions regarding the time-course and dynamic localization of prosody processing. The MEG facility at the BCBL is a 306-sensor (204 planar gradiometers and 102 magnetometers; arranged in a helmet configuration) Elekta Neuromag® device with 16 digital trigger lines and 8 auxiliary analog input channels. This setup allows us to deliver both auditory and visual stimuli. The facility at the BCBL includes passive shielding to reduce external noise, as well as MaxFilter™ software, which filters artifacts as well as internal and external noise sources.

Stimuli

17tudio17 sake of ecology, our stimuli 17tud be free speech recordings from which we 17tud extract the temporal course of relevant linguistic (speech act), emotional (emotion) and acoustic cues (e.g., pitch, duration, intensity). We 17tud prepare 200 matrix Spanish sentences with subject-verb-complement-adjuncts structure and manipulate their intonation in three conditions. The linguistic condition (LC) 17tud encompass question intonation, while the emotional condition (EC) 17tud comprise happy intonation. This 17tud result in a total of 1000 stimuli (200 per condition), which 17tud be pre-recorded by a male or female actor prior to the experiment. Sample stimuli are provided in Table 1. We 17tud also take a set of pictures

of faces expressing each of the attitudes conveyed by the intonation contours for the task of facial 18tudio18s18 recognition. In our design we 18tud have three conditions, namely, linguistic, emotional, and neutral declarative, which 18tud serve as a baseline (BC) for the other two. The kind of emotion and speech act 18tud be counterbalancing factors but 18tud not be factorized as separate conditions. This choice guarantees a certain degree of variability in the stimuli set, which is highly desirable in mTRF 18tudio18s, without leading to a proliferation of experimental conditions.

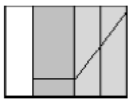
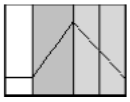
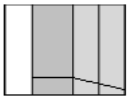
Matrix sentence	**LC: question**	**EC: happy**	**BC: assertion**
Pedro cocina asado con patatas hoy			

Table 1 – Sample stimuli in the three conditions with schematic representations of pitch configurations. Figures are taken from Estebas-Vilaplana & Prieto (2010).

Procedure

Linguistic and cognitive assessment. Prior to their participation in the MEG study, brain-damaged participants 18tud be administered language and cognitive assessment tasks to determine their degree of linguistic and executive function impairment. Linguistic and cognitive assessment 18tud be conducted in three sessions of about 1.5 hr each, with breaks scheduled at regular 18tudio18s18 any time the participant manifests the need to rest. Executive function integrity is assessed with the Corsi Blocks test, Memory Span tests and Trail Making Test. Linguistic assessment is conducted through a series of digital tasks (ACS.esp, Ansorena et al. 2022) administered with a 18tudio that are meant to evaluate the integrity of spontaneous speech, naming, repetition, 18tud/sentence comprehension. Following linguistic assessment, the MEG session 18tud take place (about 1 hr). Therefore, each participant 18tud be invited to take part in a 18tudio18 of 4 sessions (1.5h each). As indicated in the information sheet, the duration and number of sessions can be adapted to the need of the clinical group.

Participants in the control group 18tud be also invited to take part in four sessions, with linguistic assessment being conducted prior to the MEG session.

MRI scanning. Prior to the MEG experiment, all subjects 18tud undergo a structural MRI scanning in a single session, using the same 3.0 Tesla Siemens Magnetom Trio Tim scanner (Siemens AG, Erlangen, Germany), located at the BCBL in Donostia-San Sebastián. A high-resolution T1-weighted scan 18tud be acquired with a 3D ultrafast gradient echo (MPRAGE) pulse sequence using a 32-channel head coil and with the following acquisition parameters: FOV = 256; 160 contiguous axial slices; voxel resolution 1x1x1mm3; TR = 2300 ms, TE = 2.97 ms, flip angle = 9˚. Cortical reconstruction and volumetric segmentation 18tud be performed with the Freesurfer image 18tudio18s suite, (http://surfer.nmr.mgh.harvard.edu/).

MEG experiment. MEG recording 18tud take place in a dimly lit room while subjects listen to a total of 200 sentences of about 3 seconds duration each. After each sentence they 18tud be presented with three pictures, one 18tudi interrogative 18tud, one of a happy 18tud, and one of a neutral 18tud. Their task 18tud be to choose which 18tud best fits the speaker's state of mind via button press. A graphic summary of the procedure is represented in Figure 1. Participants will not spend more than 60 minutes in the MEG booth, including scheduled breaks every 10 minutes (but note that participants can interrupt the experimental session at any time).

MRI and MEG data will be acquired during the same session.

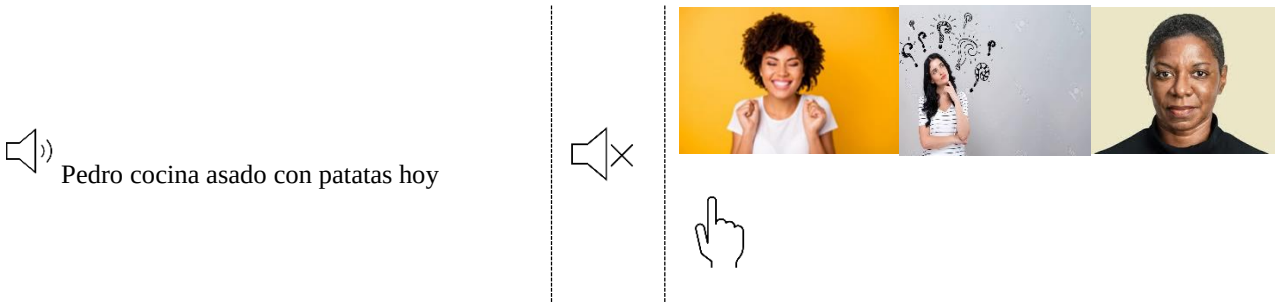


Figure 1 – Trial structure. After auditory sentence stimulus there is a silent gap followed by the active task: "Could this be the speaker's expression?".

Tipo de 19tudio

Our study is cross-sectional in nature, as it involves the comparison of two clinical and one control groups.

Sujetos a studio

We will recruit two clinical groups, one with damage in the left hemisphere (LH, N=30) and one with damage in the right hemisphere (RH, N=30). Patients will be recruited from the Neurology Department of Donostia University Hospital after having been admitted in the Stroke Unit with the index event at least 3 months prior to this study. They will all be native speakers of Spanish. A control group (N=30) with age-, education- and sex-matched participants will be also recruited through the BCBL database. The size of the sample has been chosen considering statistical criteria and the duration of the project.

Control group: inclusion criteria

- Native speaker of Spanish.
- Same age range as the clinical group.
- Same education level as the clinical group.
- No history of neurological disorder.
- No cognitive impairment.
- Normal or corrected to normal hearing and vision.

Clinical groups: inclusion criteria

- Native speaker of Spanish
- First RH or LH cortical ischemic or haemorrhagic stroke (at least 3 months before testing). Lacunar and vertebrobasilar ischemic strokes will be excluded.
- No neurodegenerative disorder.
- No cognitive impairment prior to testing.
- Absence of severe hearing or visual impairment.
- Absence of unstable psychiatric disorder.

Tamaño muestral

The experiment will involve two clinical groups and one control group of 30 participants each.

Variables

Our dependent variables will be the MEG signal (especially in the frequency domain) and the accuracy in the task, measured as percentage correct over 200 trials. We will consider as predictors the acoustic properties of signal and the kind of information conveyed by prosody (emotion or speech act). For patients, we will additionally consider the size and location of the lesions. Regions of interest will be the bilateral temporal (superior temporal sulcus/gyrus, STS/STG), frontal lobes (especially the inferior frontal gyrus, IFG), and temporo-parietal areas. Frequency bands of interest will be the delta (0.1-4 Hz) and theta (4-8 Hz) ranges.

Análisis estadístico

Preprocessing. For data analysis, the initial pre-processing steps of the MEG signal will be performed using MaxFilter and the Fieldtrip MATLAB toolbox. Special care will be taken in avoiding a conservative

approach in filtering and artifact correction (Crosse et al., 2021, 2016). The presence of significant effects will be investigated by performing a cluster-based permutation test.
Cortical tracking. In order to model the relationship between continuous auditory input and brain signals, we will employ the Multivariate Temporal Response Function (mTRF) MATLAB Toolbox. This method will provide information about the best neural response function that can explain the relation between the stimulus properties and the neural recordings. Its multivariate dimension could dissociate the temporal course of the neural tracking of different input properties. Differently from classical evoked analysis approaches, we will have information from a highly natural speech stimulus, thus avoiding the constraints of standard "conditions comparison" methods.
Factor-response modelling. To model the relationship between independent and dependent variables (task accuracy and neural signal) we will use linear mixed effect models (*lmer* package, R Core Team 2022). We may also employ a Bayesian approach for further analyses. Our independent variables will be screening scores, acoustic features, experimental conditions, lesion location and size (for patients).

Limitaciones del estudio

In our study, we will confront with three main limitations. A general issue might be an uneven distribution of language experience within and across groups. Indeed, some of our participants will be simultaneous Spanish-Basque bilinguals, while others will be Spanish monolinguals, depending on age and region of birth. We will take this into account by keeping track of socio-demographic and linguistic profile information.
The other two concerns are specific to the clinical group. First, it is possible that poor accuracy in the task is due to impaired facial expressions recognition, rather than prosody comprehension deficits per se. We will try to control for this by assessing facial recognition in the screening phase. Second – and even more importantly- functional reorganization might have occurred in some participants but not others. This would be a source of variability within the group and could make it harder to interpret the results. We plan to address this point by crossing behavioral scores and MEG data. For example, if a patient demonstrates good behavioral performance despite having divergent patterns of activation from controls, it is likely that a compensatory mechanism is at play and that functions supported by the damaged areas have been taken over by other structures.

Consideraciones éticas

The proposed study will be conducted with human brain-damaged and healthy volunteers. It includes the acquisition of behavioral (i.e., response times and accuracy) and neuroimaging data (MEG). All the experiments will be conducted in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki, with the local committee approval of both BCBL and Comité Ético de Investigación (CEI) de Gipuzkoa, and on the basis of informed consent from participants. Annexes with copies of consent forms and information sheets are provided in Spanish.
Other ethics issues are illustrated below, together with how we intend to deal with them.

Confidentiality

Participants are informed that their private details remain confidential. Both at BCBL and HUD, identifiable information on each participant is stored in a dedicated, locked filing. Data stored on computers will be protected by password and encryption encoding (SSL-technology). Electronic data for analyses on BCBL computers are anonymized and can only be linked back to the hard copy physical files via an ID code.

Data management

This study involves the collection of several types of data, as illustrated below. After giving their informed consent, all participants will be assigned a code such as:

- P01_RH, where P stands for patient, 01 indicates the progressive number, and RH indicates whether s/he belongs to the right- or left-hemisphere group
- C01, where C stands for control and 01 indicates the progressive number.

Socio-demographic data

Socio-demographic data will be obtained from each participant recruited for the study. These data will be collected through questionnaires that are handed to participants (or their caregivers) prior to the start of each experimental session. These data include:

- Personal information: age, sex, date of birth (see Consent Form and Information sheet)

- Socio-demographic information, such as:
    - educational level and cognitive reserve
    - linguistic profile
    - socio-economic status

Socio-demographic information can be used as covariate during data analysis to assess the impact that it has in the performance of these tasks (see questionnaires attached).

Clinical information

Only the medical staff of the hospital has access to patients' clinical data. Dr. De La Riva or Arantza Lopez Turiso (stroke-specialized nurse) will contact patients (or their caregivers) that comply with the study's inclusion criteria and if they accept to participate, a consent form and information sheet are provided to sign. Only when a participant has agreed to participate, medical information will be shared by Dr. De La Riva with Dr. Mancini, Dr. Molinaro and Giada Antonicelli.
Control participants will be recruited through the BCBL data base, which contains socio-demographic information (age, gender, date of birth, linguistic profile, handedness) of individuals who have already taken part in experimental studies at the center. This information is only visible to the lab staff and to the researchers involved in a study. Candidates who present a matching demographic and linguistic profile with the patients' group will be contacted and invited to participate by the BCBL lab staff.

Informed consent

Verbal informed consent. When the patient/participant is first invited to participate by the hospital, they will be briefly explained the experimental procedure, the technique to be used and the kind of safety measure that will be taken. Details about data protection and confidentiality will also be provided. An appointment will be arranged after participant's or caregiver's verbal consent, in order to read and sign the Informed Consent and start with the experiments.
Written informed consent. Before the first session starts, an information sheet will be provided. Apart from generic information, the document also describes the tasks and characteristics of the technique used for each experiment. This written informed consent will be given during a short interview before the session starts. During this interview, the caregiver/participant will be also informed verbally and any questions will be answered. The information sheets are written in clear Spanish and explain the purpose of the study, the procedures, the risks or discomforts, benefits, incidental findings and data protection issues of the study. It also clearly indicates that any experimental session can be terminated at any time if the participant (or the caregiver) requires so, and that withdrawing one's availability to participate in the study does not have any consequence. A copy of the signed information sheet and consent form will be handed to the participant.
For control participants, the consent form indicates that if they agree, they can be invited to a short MR session at the BCBL, in order to obtain structural data from brain-undamaged patients. An MRI safety questionnaire will be administered to ensure that the participant can safely enter an MRI machine.
Having read and asked questions about the information sheet, volunteers fill the informed consent. They can only participate after responding yes to all questions and signing the informed consent. If patients cannot autonomously give or sign the written informed consent, the caregiver will be administered all the necessary information.

Data storage

At the BCBL, identifiable information on each participant is stored in a dedicated, locked filing room. Data stored on computers will be protected by password and encryption encoding (SSL-technology). Electronic data for analyses on computers are anonymized and can only be linked back to the hard copy physical files via an ID code. Only the BCBL researchers involved in the study and Dr. de La Riva will be granted access to data both during the development of the project and after its completion.
At HUD, information concerning clinical records of participants is stored in Osakidetza servers that can be accessed only by medical personnel (Dr. Patricia de La Riva and the rest of the HUD collaborators).

Cronograma, Equipo investigador y tareas

We anticipate to develop the project according to the following chronogram:

Year	**1**				**2**				**3**			
Trimester	**1**	**2**	**3**	**4**	**1**	**2**	**3**	**4**	**1**	**2**	**3**	**4**
Research activity												

Design preparation	■											
Pilot study		■										
Data acquisition for patients		■	■	■	■	■	■	■				
Data acquisition for controls			■	■	■	■	■	■				
Data analysis					■	■	■	■	■			
Dissemination												
Participation in international conferences						■	■	■	■	■	■	■
Preparation of Manuscripts for peer-review									■	■	■	■

Equipo investigador

Dr. Simona Mancini (PI, BCBL) is a Ramón y Cajal Fellow and leader of the Neurolinguistics and Aphasia Group. She obtained her PhD in Cognitive Science from the University of Siena (Italy). Her scientific activity lies at the intersection between theoretical linguistics and cognitive neuroscience, focusing on core computational mechanisms and their processing correlates in neurotypical and brain-damaged speakers, as well as on the development of computerized tools for the assessment of language impairment in brain-damaged patients. She has participated as a PI and collaborator in several research projects funded by national (MICINN, MINECO, Basque Government, BBVA Foundation) and international (National Science Foundation, European Molecular Biology Organization) agencies. She has been visiting scholar at the University of La Laguna, University of Trento and IUSS (Institute of Advances University Studies, Pavia, Italia). The network of her active collaborations includes European (University of Siena, University of Trento, IUSS Pavia, University College London, and University of Stockholm), North American (University of Kansas, University of South Carolina, Berkeley) and Canadian universities (University of Toronto, McGill University).

Dr. Nicola Molinaro (BCBL) studies the brain sensitivity to the pseudo-rhythmic nature of speech in typical and atypical populations. He reported that speech-brain oscillatory coupling in the prosody time rate is impaired in developmental dyslexics (compared to control peers) independently of age and reading experience. Ikerbasque Research Associate, works on the (M)EEG correlates of language comprehension, specifically, on the oscillatory mechanisms of speech perception. He is the group leader of the *Brain Rhythms and Cognition group* at the BCBL. PI in several research projects involving typical (bilingual adults, children learning to read), atypical (developmental dyslexia, SLI), and special (toddlers, musicians) populations. He is part of the scientific committee of the BCBL, and coordinator of the MEG lab. Associate Editor for *PlosOne* and *Scientific Reports*.

Giada Antonicelli (BCBL) is a pre-doctoral researcher in the Neurolinguistic and Aphasia group. She obtained her Master's degree in Theoretical and applied Linguistics from the University of Pavia (Italy). She worked in LLEGS lab at the University of Pavia under the supervision of Prof. Stefano Rastelli investigating EEG correlates of verbal aspect processing in Italian native speakers. She is also collaborating on a behavioral experiment from the same lab on the processing of control in Italian gerundive constructions. At BCBL the main focus of her research is on clinical neurolinguistics and prosody processing.

Patricia de La Riva (Hospital Donostia) has been working as a neurologist at the Stroke Unit of Donostia University Hospital for the last 10 years. She develops clinical research in the stroke area with several published articles in indexed journals in the last years. She receives financial support from the Health Department of the Basque Government for research projects and protected time for research. She is the group leader of the stroke research group of Donostia Stroke Unit. She also collaborates with international collaborative clinical trials in the stroke field.

Arantza Lopez de Turiso (Hospital Donostia) is a stroke-specialized nurse attending stroke patients in the acute and chronic phase of the disease for the last 8 years. She also has an interest in stroke research and participates with the group and develops her own research projects.
Jon Equiza (Hospital Donostia) is a neurologist that works both at the Departments of Neurology and Neurosurgery of the Donostia University Hospital. His main areas of interest include hospitalist, stroke,

and critical care neurology. He develops clinical research in the stroke and neurohospitalist area with several published articles in indexed journals in the last years. He is a member of the Stroke Research Group of the Department of Neurology.
Raquel Laspiur (Hospital Donostia) is a neuropsychologist working at Stroke Unit of Donostia University Hospital as part of stroke research group. She has collaborated with different research programs in cognitive aspects of acquired brain damage and neurodegenerative processes. She also has experience in neuropsychological assessment and intervention in patients with stroke, traumatic brain injury and neurodegenerative diseases.

Presupuesto (si no se solicita presupuesto, indicarlo)

Not applicable. The study is partially funded by PID2020-113945RB-I00 awarded by MINECO to Simona Mancini.

Anexo II

INFORME FAVORABLE COMITÉ DE ÉTICA

Osakidetza

OSI-Donostialdea

INFORME DEL COMITÉ ÉTICO DE INVESTIGACIÓN

D. Jon Zabaleta Jiménez, Presidente del Comité Ético de Investigación del Área Sanitaria de Gipuzkoa,

CERTIFICA:

Que este Comité, de acuerdo a la Ley 14/2007 de Investigación Biomédica, Principios éticos de la declaración de Helsinki y resto de principios éticos aplicables, ha evaluado el Proyecto de Investigación titulado: ***"Comprensión de la entonación tras un ictus".*** Código de Protocolo: MAN-ENT-2022-01.

Versión Protocolo: 2 de 16 de Enero de 2023
Versión Hoja de Información al Paciente y Consentimiento Informado voluntarios sanos: 2 de 16 de Enero de 2023
Versión Hoja de Información al Paciente y Consentimiento Informado voluntarios pacientes: 2 de 16 de Enero de 2023

Y que este Comité reunido el día 21/02/2023 (recogido en acta 03/2023) ha decidido Aprobar dicho Estudio y que sea realizado por:

Simona Mancini - BCBL

Lo que firmo en San Sebastián, a 21 de Febrero de 2023

Jon Zabaleta Jiménez
Presidente CEI del AS Gipuzkoa