


Multidimensional inhibitory signatures of sentential negation in behavioral variant frontotemporal dementia

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Background: Processing of linguistic negation has been associated to inhibitory brain mechanisms. However, no study has tapped this link via multimodal measures in patients with core inhibitory alterations, a critical approach to reveal direct neural correlates and potential disease markers. **Methods:** Here we examined oscillatory, neuroanatomical, and functional connectivity signatures of a recently reported Go/No-go negation task in healthy controls and behavioral variant frontotemporal dementia (bvFTD) patients, typified by primary and generalized inhibitory disruptions. To test for specificity, we also recruited persons with Alzheimer's disease (AD), a disease involving frequent but nonprimary inhibitory deficits. **Results:** In controls, negative sentences in the No-go condition distinctly involved frontocentral delta (2–3 Hz) suppression, a canonical inhibitory marker. In bvFTD patients, this modulation was selectively abolished and significantly correlated with the volume and functional connectivity of regions supporting inhibition (e.g. precentral gyrus, caudate nucleus, and cerebellum). Such canonical delta suppression was preserved in the AD group and associated with widespread anatomo-functional patterns across non-inhibitory regions. **Discussion:** These findings suggest that negation hinges on the integrity and interaction of spatiotemporal inhibitory mechanisms. Moreover, our results reveal potential neurocognitive markers of bvFTD, opening a new agenda at the crossing of cognitive neuroscience and behavioral neurology.

Key words: behavioral variant frontotemporal dementia; EEG oscillations; inhibition; multimodal imaging; negation.

Introduction

Negation is a core property of all human languages. In addition to extensive philosophical (Horn 1989) and linguistic (Miestamo 2007) research traditions, accruing neurocognitive evidence highlights its reliance on inhibitory mechanisms (Aravena et al. 2012; Foroni and Semin 2013; Papeo et al. 2016; Beltrán et al. 2018). However, no study has examined this link in brain diseases with differential inhibitory disruptions, let alone integrating neurophysiological, neuroanatomical, and functional connectivity measures. Such an approach would be critical to assess the interplay of inhibitory

systems in negation, leading to multidimensional models and potential disease-specific markers. To these ends, we administered a validated Go/No-go negation task to (i) healthy controls (HCs), (ii) patients with behavioral variant frontotemporal dementia (bvFTD, characterized by primary and generalized disinhibitory symptoms), and (iii) persons with Alzheimer's disease (AD, a disease control group with nonprimary inhibitory deficits), capturing online oscillatory traces alongside structural and functional neuroimaging correlates.

Negating is a species-specific capacity supporting critical communicative functions, such as rejection, denial,

and prohibition (Beltrán et al. 2018, 2019). This process is manifested by multiple linguistic forms, including *no*, *not*, and their counterparts across languages. In particular, since early development, these words are used to signal that particular actions must be interrupted (e.g. *don't touch the knife!*), a tendency that extends into adulthood (e.g. *do not trespass*). Relatedly, their presence in sentences can reduce response speed (Kaup and Zwaan 2003; Kaup et al. 2007) and interfere with manual actions (García-Marco et al. 2019), replicating their effects on daily behavior. Such effects have been attributed to the critical recruitment of inhibitory systems (Feroni and Semin 2013; de Vega et al. 2016; Papeo et al. 2016; Beltrán et al. 2018), responsible for suppressing contextually inappropriate conduct across multiple tasks (Chambers et al. 2009).

This view is supported by neuroscientific research. Electroencephalographic (EEG) studies have targeted frontocentral delta and theta modulations, two critical response inhibition markers (Harmony 2013; Huster et al. 2013), revealing greater power for affirmative than negative sentences in inhibitory contexts—reduced power for negation during inhibition (de Vega et al. 2016; Beltrán et al. 2019). Neuroimaging results consistently link negation with inhibitory regions, including increased activation of inferior frontal and precentral areas (Christensen 2009; Bahlmann et al. 2011), and deactivation of core regions subserving processing of negated action verbs—midfrontal, premotor, primary motor, and posterior cingulate cortices (Tettamanti et al. 2008; Tomasino et al. 2010). This link has been supported by neurostimulation research (Vitale et al. 2022). Thus, insofar as negation suppresses target information (Kaup et al. 2007) while inhibition suppresses motor, cognitive, or affective processes (Phan et al. 2005; Aron and Poldrack 2006), the evidence supports grounded cognition models (Dehaene and Cohen 2007; Pulvermüller 2013; Birba et al. 2017; Pulvermüller 2018) and is fully captured by the “reuse of inhibition for negation” framework, which posits that nonlinguistic inhibitory systems are recycled during negation processing (Beltrán et al. 2021).

However, this research line is undermined by major limitations. First, no study has harnessed strategic neurodegenerative diseases, an approach that has revealed direct correlates of other cognitive domains (Melloni et al. 2015; García-Cordero et al. 2016, 2021; Santamaría-García et al. 2017; Birba et al. 2021). bvFTD represents a relevant condition, as early-stage patients exhibit cardinal (motor and behavioral) inhibitory deficits (Rascovsky et al. 2011), related to critical markers, such as serotonin bioavailability (Hughes et al. 2015). This disease also involves oscillatory abnormalities in the inhibition-sensitive delta band (Chan et al. 2004; Yu et al. 2016; Sami et al. 2018) and other relevant frequencies (Moretti et al. 2016; Ibáñez 2018), as well as anatomofunctional disruptions along inhibitory regions—e.g. precentral, middle and inferior frontal, inferior parietal, and posterior cingulate areas (Lagarde et al. 2013; Hughes et al. 2015;

Scheltens et al. 2018; Matías-Guiu et al. 2019). In particular, designs including Alzheimer's disease (AD) patients can reveal whether the mechanisms disrupted in bvFTD are distinctly implicated in negation. Inhibitory deficits in AD are not primary diagnostic symptoms; they are typically milder than in bvFTD (Kramer et al. 2003; Stopford et al. 2012) and associated to anteroposterior disruptions (Collette et al. 2002). Importantly, this transdiagnostic approach becomes maximally informative when complemented with multidimensional neural measures (Melloni et al. 2015; Santamaría-García et al. 2017). Yet, negation research has favored individual neuroscientific tools, limiting its theoretical import (for informing multidimensional accounts) and translational potential (for capturing multimodal disease-differential markers) (Uludağ and Roebroek 2014; Melloni et al. 2016; Salamone et al. 2021). This study aims to circumvent these limitations with the explicit aim of testing hypotheses couched in the “reuse of inhibition for negation” framework (Beltrán et al. 2021).

Specifically, we examined oscillatory, anatomical, and functional connectivity signatures of sentential negation in bvFTD and AD patients relative to HCs. We employed a validated task that manipulates sentence polarity (negative, affirmative) while eliciting response inhibition (de Vega et al. 2016; Beltrán et al. 2019). We computed two critical EEG indexes: a No-go polarity index and the Go polarity index (subtraction between affirmative and negative sentences during No-go and Go trials, respectively). We tested three hypotheses. First, we predicted that, in HCs, the No-go polarity index would show increased delta and/or theta power (reduced power for negative trials). Second, while we anticipated impaired inhibitory performance across diseases, we hypothesized that oscillatory signatures of the No-go polarity index would be selectively disrupted in bvFTD and associated with anatomofunctional disruptions along precentral, midinferior frontal, and posterior cingulate structures implicated in inhibition. Third, we expected that, for the Go polarity index, oscillatory effects in bvFTD patients would not differ from those of HCs or correlate with anatomofunctional patterns. Finally, we hypothesized that, in AD, oscillatory signatures of the No-go polarity index would be preserved and correlated with disease-specific anteroposterior pattern. With this approach, we seek to inform multidimensional accounts of negation while revealing new disease-differential signatures of neurodegeneration.

Materials and methods

Participants

Sixty-two Spanish-speaking individuals, with normal or corrected-to-normal vision, were recruited from two international clinics, in line with recommendations for similar multicentric protocols (Sedeno et al. 2017; Moguilner et al. 2018; Bachli et al. 2020; Salamone et al. 2021). The sample was comprised of 14 bvFTD

Table 1. Demographic and neuropsychological information.

	Healthy controls N = 30	bvFTD patients N = 14	AD patients N = 18	Statistics (all groups)	Pairwise comparisons		
					Groups	Estimate	P-value
Demographic data							
Sex (F:M)	18:12	5:9	9:9	—	bvFTD-HCs	1.38	0.23 ^a
					AD-HCs	0.14	0.70 ^a
Years of age	72.05 (6.65)	68.20 (9.43)	73.30 (4.72)	F = 1.28	bvFTD-HCs	-2.77	0.47 ^c
				P = 0.28 ^b	AD-HCs	1.08	0.92 ^c
Years of education	13.37 (3.08)	14.95 (5.04)	11.87 (4.39)	F = 3.89	bvFTD-HCs	1.59	0.53 ^c
				P = 0.03 ^b	AD-HCs	-2.27	0.18 ^c
Neuropsychological data							
MoCA	25.88 (2.26)	21.78 (4.50)	15.11 (6.19)	F = 36.20	bvFTD-HCs	-4.09	0.02 ^c
				P < 0.001 ^b	AD-HCs	-10.77	<0.001 ^c
Hayling test	7.5 (5.56)	16.28 (12.57)	23.47 (10.62)	F = 16.22	bvFTD-HCs	8.78	0.01 ^c
				P < 0.001 ^b	AD-HCs	15.9	<0.001 ^c

Data presented as mean (SD), except for sex. HCs: healthy controls; bvFTD: behavioral variant frontotemporal dementia; AD: Alzheimer's disease; MoCA: Montreal Cognitive Assessment. ^aP-values calculated via chi-squared test (χ^2). ^bP-values calculated via independent measures ANOVA. ^cP-values calculated via Dunnett's test.

patients, 18 AD patients, and 30 HCs. All but four participants were right-handed (Oldfield 1971). Each patient group was matched with HCs in terms of sex, age, and education (Table 1). Patients were diagnosed by expert neurologists following current clinical criteria for probable bvFTD (Rascovsky et al. 2011) and NINCDS-ADRDA criteria for AD (McKhann et al. 1984, 2011). Diagnoses were supported by an extensive neurological, neuropsychiatric, and neuropsychological examination, as previously reported (Piguet et al. 2011; Baez et al. 2014; Seden et al. 2017; García-Cordero et al. 2019).

Each center implemented the Multi-Partner Consortium to Expand Dementia Research in Latin America (ReDLat) standardized diagnostic assessment (Ibanez, Parra, et al. 2021a; Ibanez, Yokoyama, et al. 2021b) to align local sites' procedures. This protocol comprises a brief questionnaire for every participant, including impressions from the neurologist and neuropsychological assessments. Also, all centers used a common training manual for clinical and cognitive evaluation and a quality assurance checklist. These procedures prevent potential biases in participants' assessment and diagnosis across centers.

BvFTD patients were in early/mild stages and exhibited sociobehavioral impairments as defined by caregivers (Neary et al. 1998; Piguet et al. 2011; Ibanez and Manes 2012). Moreover, they presented with predominantly temporo-hippocampal atrophy in both hemispheres (Supplementary Material 1). AD patients showed atrophy across extended bilateral temporomedial areas, including the left hippocampus, the right amygdala, and, to a lesser extent, bilateral frontal and left cerebellar areas (Supplementary Material 1). Cognitive status and semantic inhibition were assessed through the Montreal Cognitive Assessment (MoCA) (Nasreddine et al. 2005) and the Hayling test (Burgess and Shallice 1997), respectively (Table 1). No patient reported a history of other neurological disorders, psychiatric conditions, or substance abuse. HCs were cognitively preserved, were

functionally autonomous, and had no background of neuropsychiatric disease or alcohol/drug abuse. Each volunteer signed a written informed consent. The study was performed pursuant to the Declaration of Helsinki and approved by the institutional ethics' committees.

Experimental task

Materials

The experiment involved 166 Spanish sentences from a published version of the same task (de Vega et al. 2016; Beltrán et al. 2019; Liu et al. 2020). These stimuli comprised 83 affirmative sentences and a negative version of each of them ($n = 166$). Each participant responded to half the sentences in the affirmative and the other half in the negative, the polarity of each sentence being counterbalanced across participants (accordingly, all relevant psycholinguistic variables were perfectly matched across conditions). All sentences had an identical structure, beginning with the adverb *Ahora* (now), followed by a polarity marker (*sí* for affirmative sentences, *no* for negative sentences), an action verb in the second person singular of the imperfect future tense (e.g. *cortarás*—will cut), and a direct object (made up of a definite article and a noun) that was coherent with the preceding verb (e.g. *el pan*—the bread)—this example sentence translates roughly into *Now you will/won't cut the bread*. Crucially, the verb was accompanied by a cue that, depending on its color, indicated that the participants should either press a key (Go items) or refrain from doing so (No-go items). To generate a prepotent tendency to respond and thus ensure the taxing of inhibitory mechanisms in the No-go trials, 116 of the trials per subject (70%) featured a Go cue, and the remaining 50 (30%) featured a No-go cue. Half of the Go cues appeared in affirmative sentences and the other half appeared in negative sentences. The same was true for the No-go cues. Therefore, the experiment comprised 58 affirmative Go trials, 58 negative Go trials, 25 affirmative No-go trials, and 25 negative No-go trials. Also, to ensure sustained attention during sentence

reading, a forced-choice yes/no verification question was subsequently presented after 40% of the sentences.

Procedure

Each participant responded to 166 experimental trials, evenly divided across conditions into two blocks. Trials were presented randomly within each block. Each of them began with a fixation point in the center of the screen (500 ms), followed by the whole sentence presented word by word. All words, except the sentence's verb segment, were followed by a 150-ms blank. The first word (*Ahora*) was presented for 200 ms, followed by the sentence polarity marker (*sí/no*) for 300 ms. The verb segment, where the Go/No-go cue was displayed, lasted 600 ms overall, with the following sequence of events: first, the verb appeared for 300 ms; then, the Go/No-go cue (yellow circle for Go, blue circle for No-go) appeared above the verb for 150 ms; finally, upon disappearance of the cue, the verb remained visible for another 150 ms. After the final sequence of the verb, another blank screen was presented for 150 ms, followed by a definite article (e.g. *el*) for 200 ms and then a noun (e.g. *pan*) for 300 ms. A blank screen was then shown for another 300 ms.

Participants were instructed to attentively read each word in the sentence and press a yellow button on the keyboard whenever a yellow cue appeared above the verb (Go trials) and to refrain from pressing the button whenever a blue cue appeared (No-go trials). As previously stated, 40% of the trials were followed by a verification task, which consisted of an initial question mark in the center of the screen (300 ms), followed by the verification sentence (which could match the preceding sentence or not). For these verification items, participants were instructed to press the left arrow if the new sentence matched the preceding one and to press a right arrow if it did not. Prior to the task, for familiarization purposes, participants completed 16 practice trials, the first five corresponding to the Go condition and the remaining seven varying randomly between Go and No-go trials. The practice trials were repeated if so requested. Overall, the experiment lasted roughly 15 minutes. The temporal structure of the task is diagrammed in Fig. 1.

Behavioral data analysis

Overall motor inhibitory performance was inspected by collapsing both affirmative and negative trials for both the No-go and the Go condition. Go trials were analyzed after removing those with RTs below 100 ms (~1.41%). Out of the remaining trials, those below or above 2.5 SDs from the participant's mean (1.7%) were also excluded. Likewise, for commission errors, trials were excluded from analysis if their RT was below 100 ms (~16%) or exceeded 2.5 SDs from the participant's mean (~6.14%). The remaining trials amount did not differ across groups for the Go condition [$F(2, 4617) = 1.94, P = 0.14$] or commission errors [$F(2, 166) = 1.16, P = 0.31$].

First, to inspect the overall manifestation of inhibitory performance per se, we collapsed all Go trials (affirmative and negative), on the one hand, and all No-go trials (affirmative and negative), on the other, and ran a 3×2 linear mixed effects model, with one between-subject factor (group: HC, bvFTD, AD) and one within-subject factor (condition: Go, No-go). Also, following previous reports of the same paradigm (de Vega et al. 2016; Beltrán et al. 2019; Liu et al. 2019), we performed separate analyses for commission errors (on No-go trials) and omission errors (on Go trials), as well as for reaction times (RTs) in correct Go trials and in commission errors on No-go trials. For each of those analyses, we implemented a 3×2 linear mixed effects model, with one between-subject factor (group: HC, bvFTD, AD) and one within-subject factor (polarity: affirmative, negative). Significant effects were further inspected via Tukey's HSD post-hoc tests. Effect sizes were calculated through partial eta-squared (η^2) for main and interaction effects, and via Cohen's d for pairwise comparisons. Alpha levels were set at $P < 0.05$. All behavioral analyses were performed on R (version 3.5.2).

Hd-EEG methods

Data acquisition and preprocessing

Hd-EEG activity was recorded online throughout the task for each participant. Signals were acquired via a BioSemi Active Two 128 Channel System with preamplified sensors and a DC coupling amplifier, at a sampling rate of 1024 Hz. Analog filters were set at 0.03 and 100 Hz. A digital bandpass filter between 0.5 and 50 Hz was applied offline to remove unwanted frequency components. The reference was set to link mastoids for recordings and re-referenced offline to the average of all electrodes. In line with reported procedures (Vilas et al. 2019; Birba et al. 2020; Dottori et al. 2020; García et al. 2020; Cervetto et al. 2021), eye movements or blink artifacts were corrected with independent component analysis (Kim et al. 2012) and with a visual inspection protocol (García-Cordero et al. 2016, 2017; Cervetto et al. 2021). Bad channels were replaced via statistically weighted spherical interpolation (based on all sensors) (Courellis et al. 2016). Epochs were selected from continuous data in a window of -2.5 to 2.5 around the Go/No-go cue. All EEG signal processing steps were implemented on MATLAB software (vR2016a) through the EEGLAB (v14.1.2) toolbox.

Time-frequency analyses

All analyses were run on the Fieldtrip Toolbox (Oostenveld et al. 2011). First, we computed the time-frequency representation (TFR) by convolving four-cycle complex Morlet wavelets with 2 Hz steps for each single-trial epoch to obtain the targeted spectral power (1–40 Hz). As in previous reports of this task (de Vega et al. 2016; Beltrán et al. 2019), the mean of event-related power synchronization across trials was calculated for each condition and subject, with a baseline of 500 ms before the polarity marker (*sí/no*) appeared ($-1150, -650$ ms).

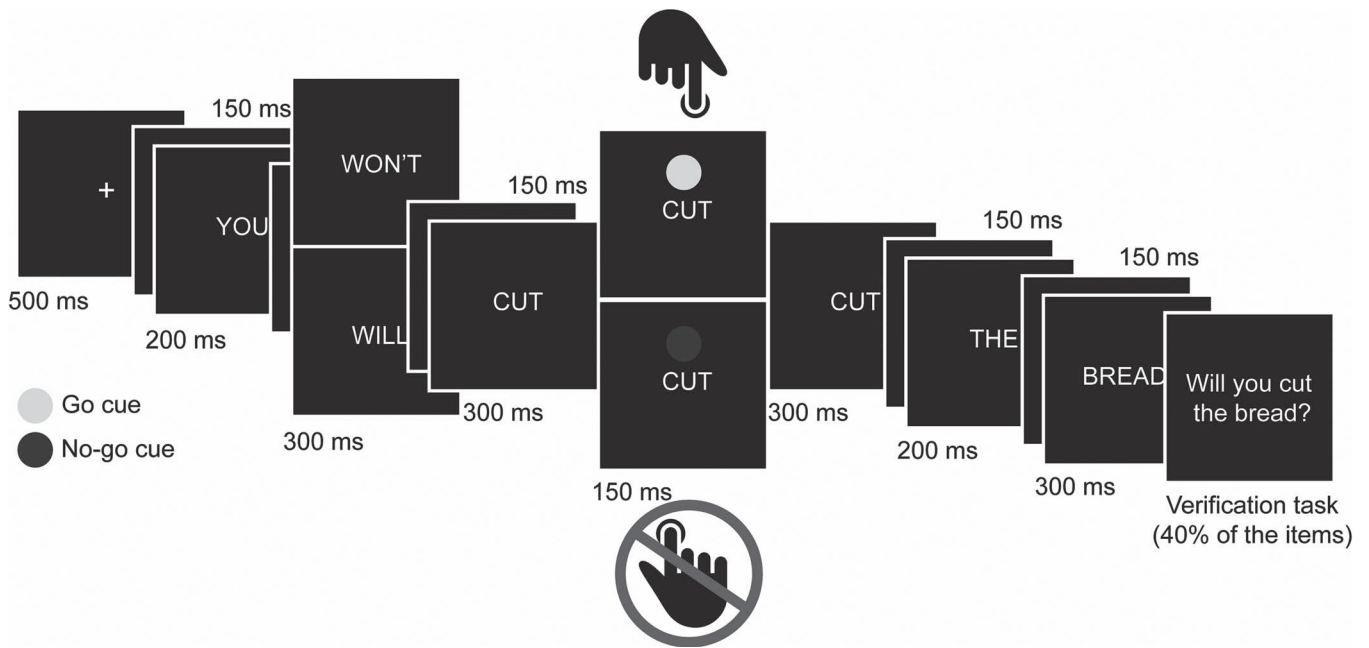


Fig. 1. Temporal structure of the experimental task. Participants first viewed a fixation cross, followed by a word-by-word sentence with the following structure: *Ahora + si/no + verb + definite article + noun* (e.g. *Ahora si/no cortarás el pan* [Now you will/won't cut the bread]). A cue circle appeared above verb, prompting participants to either press a key (lighter color circle) or refrain from doing so (darker color circle). To ensure sustained attention during sentence reading, a forced-choice yes/no verification question was subsequently presented after 40% of the sentences.

We calculated the power for each trial relative to its respective baseline and then averaged the ensuing values across trials per subject. The single-trial time–frequency representations in each band were averaged separately for each of the four experimental conditions (affirmative No-go; negative No-go; affirmative Go; negative Go).

Within-group analyses

To detect canonical oscillatory signatures of response inhibition, we first collapsed all affirmative and negative trials corresponding to the No-go and Go conditions. Then, we conducted a within-group analysis in HCs comparing power modulations between No-go and Go trials (henceforth, “inhibitory index”). We further performed a one-tailed cluster-based permutation analysis on time–frequency data based on previous research (de Vega et al. 2016; Beltrán et al. 2019). Analyses were performed targeting two canonic inhibitory frequency bands (delta: 2–3 Hz; theta: 4–7 Hz) and an additional band to test for specificity (alpha: 8–12 Hz).

To detect inhibitory oscillatory signatures of negation, we followed the same approach described above. First, we compared power modulations in HCs between affirmative and negative sentences in No-go trials (henceforth, “No-go polarity index”), as in previous reports of the same task (de Vega et al. 2016; Beltrán et al. 2019). To test for specificity, we applied the same procedure on Go trials (henceforth, “Go polarity index”). Analyses were performed in two target frequency bands (delta: 2–3 Hz; theta: 4–7 Hz) assessed in previous reports of this task (de Vega et al. 2016; Beltrán et al. 2019), together with an additional control band (alpha: 8–12 Hz).

Between-group analyses

To examine possible inhibitory disruptions, we compared power modulations of the inhibitory index between HCs and each patient group. To this end, the specific spatiotemporal cluster obtained in HCs was used as a mask for every patient to calculate his or her own inhibitory indexes. Each participant’s mean was compared among all three groups via an omnibus permutation test analogous to a one-way analysis of variance using the function “aovperm” from the R package “permuco” (Frossard et al. 2021). Post-hoc comparisons were performed via two-sample pairwise permutation tests with Bonferroni correction. The alpha level was set to 0.05.

In a similar fashion, to examine potential oscillatory inhibitory alterations during negation processing, we compared power modulations between HCs and all patient groups. The specific spatiotemporal cluster underlying the No-go polarity index in HCs was used as a mask in each patient group to calculate his or her own No-go polarity indices. The ensuing results were compared among all three groups via an omnibus permutation test. Post-hoc comparisons were performed via two-sample pairwise permutation tests with Bonferroni correction. The alpha level was set to 0.05. These nonparametric methods are preferred to minimize the impact of possible extreme values, guaranteeing robustness without compromising statistical power (Hayes 1996). The exact same procedure was repeated for Go trials, to reveal whether predicted alterations in the patient groups were specific to the No-go polarity index (i.e. negation-specific modulations during response inhibition).

Neuroimaging methods

Data acquisition

MRI acquisition and preprocessing steps are reported in line with the practical guide from the Organization for Human Brain Mapping (Nichols et al. 2017; Poldrack et al. 2017). We obtained whole-brain T1-weighted anatomical 3D scans from 26 HCs, 12 bvFTD patients, and 12 AD patients—these groups were also matched for sex, age, and education (Supplementary Material 2, Table S2). Additionally, resting-state functional MRI (fMRI) recordings were obtained for all of them, except one bvFTD patient, who did not take part in that session. For this protocol, participants were asked to keep their eyes closed, not to think about anything in particular, and to avoid moving or falling asleep. Structural and resting-state acquisition parameters for each center are reported in Supplementary Material 3.

MRI data preprocessing

For VBM analysis, data were processed using the DARTEL Toolbox following validated procedures (Ashburner and Friston 2000; García-Cordero et al. 2016; Seden et al. 2017) via the Statistical Parametric Mapping software (SPM12) (<http://www.fil.ion.ucl.ac.uk/spm/software/spm12/>). T1-weighted images in native space were first segmented using the default parameters of the SPM12 (bias regularization was set to 0.001 and bias FWHM was set to 60-mm cutoff) into white matter (WM), gray matter (GM), and cerebrospinal fluid (CFS) (these three tissues were used to estimate the total intracranial volume, TIV). DARTEL (create template) module was run later using the GM and WM segmented images—following SPM12 default parameters—to create a template that is generated from the complete dataset (increasing the accuracy of intersubject alignment) (Ashburner and Friston 2000). Next, we used the “Normalise to MNI Space” module from DARTEL Tools to affine register the last template from the previous step into the MNI Space. This transformation was applied to all the individual GM-segmented scans to also be brought into standard space. Subsequently, all images were modulated to correct volume changes by Jacobian determinants and to avoid bias in the intensity of an area due to its expansion during warping. Finally, data were smoothed using a 10-mm full-width-at-half-maximum isotropic Gaussian kernel to accommodate for intersubject differences in anatomy. The size of the kernel was selected based on previous recommendations (Ashburner and Friston 2000; Good et al. 2001; Burton et al. 2004).

Based on previous literature (Jack et al. 1997; La Joie et al. 2012; Ossenkoppele et al. 2015; van Loenhoud et al. 2017), in order to analyze the images of each center together and avoid a resonator effect in our results, the normalized and smoothed DARTEL outputs were transformed to *w*-score images. *W*-scores, similar to *Z*-scores (mean = 0, SD = 1), represent the degree to which the observed GM volume in each voxel is higher or lower (positive or negative *W*-score) than expected, based

on an individuals' global composite score adjusted for specific covariates (age, disease, TIV, and scanner type). *W*-scores were calculated for the healthy control sample of each acquisition center, dividing subjects' observed and predicted GM volumes (residuals) by their standard deviation, resulting in *W*-score maps for each subject.

Resting-state fMRI data preprocessing

The first five volumes of each subject's resting-state sequence were discarded to ensure that magnetization achieved a steady state. Then, images were then preprocessed using the Data Processing Assistant for Resting-State fMRI (DPARSF V2.3) (Chao-Gan and Yu-Feng 2010) (<http://rfmri.org/DPARSF>), an open-access toolbox that generates automatic pipeline for fMRI analysis by calling the SPM 12 and the Resting-State fMRI Data Analysis Toolkit (REST V1.7). Following previous studies (Salamone et al. 2018; Yoris et al. 2018; Fittipaldi et al. 2020), preprocessing steps included slice-timing correction (using middle slice of each volume as the reference scan), realignment to the first scan of the session to correct head movement (SPM functions), normalization to the MNI space using the echo-planar imaging (EPI) template from SPM (Ashburner and Friston 1999), smoothing using a 8-mm full-width-at-half-maximum isotropic Gaussian kernel (SPM functions), and bandpass filtering (0.01–0.08 Hz). Six motion parameters, CFS, and WM signals were regressed to reduce the effect of motion and physiological artifacts such as cardiac and respiration effects (REST V1.7 toolbox). Motion parameters were estimated during realignment, and CFS and WM masks were derived from the tissue segmentation of each subject's T1 scan in native space with SPM12 (after coregistration of each subject's structural image with the functional image). Participants did not show translation movements greater than 3 mm and/or rotations higher than 3°. Finally, there were no statistically significant differences between groups in the different estimated motion parameters (Supplementary Material 4, Table S3).

Association between oscillatory indices and brain volume

SPM12 was used to perform multiple regression analyses to assess associations between gray matter volume and (i) No-go polarity index and (ii) the Go polarity index. To increase power and data variance, each patient group (bvFTD, AD) was included alongside the HC group, as in previous works (Sollberger et al. 2009; O'Callaghan et al. 2016; Salamone et al. 2021). TIV was added as a covariate of no interest. As this is an exploratory study with a modest sample size, statistical significance was set to $P < 0.001$, uncorrected, with an extent threshold of 30 voxels. These parameters match recommended lower limits for the power levels reached by our study (Woo et al. 2014), circumventing biases of liberal primary thresholds on false positives and achieving good balance between Type-I and Type-II errors (Lieberman and Cunningham 2009), as in previous imaging studies

Table 2. Accuracy and response time measures on overall inhibitory performance.

	Healthy controls N = 30	bvFTD patients n = 14	AD patients n = 18	Statistics (all groups)	Pairwise comparisons		
					Groups	Estimate	P-value
Overall error rate	0.07 (0.09)	0.22 (0.31)	0.42 (0.48)	F = 25.70 P = 0.001 ^a	bvFTD-HCs AD-HCs	-1.15 0.35	0.02 ^b <0.001 ^b
Commission errors	0.05 (0.07)	0.05 (0.1)	0.06 (0.09)	F = 24.47 P < 0.01 ^a	bvFTD-HCs AD-HCs	0.003 0.009	1.00 ^b 0.99 ^b
Omission errors	0.09 (0.10)	0.39 (0.35)	0.78 (0.41)	F = 24.47 P < 0.01 ^a	bvFTD-HCs AD-HCs	-0.30 0.68	<0.01 ^b <0.001 ^b
Overall response time	0.54 (0.16)	0.62 (0.20)	0.62 (0.20)	F = 5.91 P = 0.004 ^a	bvFTD-HCs AD-HCs	-0.10 0.09	0.008 ^b 0.03 ^b

Data presented as mean (SD). HCs: healthy controls; bvFTD: behavioral variant frontotemporal dementia; AD: Alzheimer's disease. ^aP-values calculated via independent measures ANOVA. ^bP-values calculated via Tukey HSD post-hoc test.

(Donix et al. 2013; Irish et al. 2014; Melloni et al. 2016; Sedenó et al. 2017; de la Fuente et al. 2019; Santamaría-García et al. 2019) and FC (Yu-Feng et al. 2007; Jabbi et al. 2008; Kanske et al. 2016).

Association between oscillatory indices and resting-state fMRI connectivity

We explored associations between resting-state functional connectivity (rs-FC) data and (i) No-go polarity index and (ii) the Go polarity index. First, for each subject, we extracted the mean time course of the BOLD signal in each of the 116 regions of the Automated Anatomical Labelling Atlas (Tzourio-Mazoyer et al. 2002), by averaging the signal in all voxels comprising each region. Second, we constructed a connectivity matrix for each subject indicating the strength of association between all pairs of regions (Pearson's correlation coefficient; DPARSF toolbox). Third, we performed a Fisher z-transformation. Finally, to prevent scanner type effects in our results, we performed a site normalization following published procedures for multicenter-imaging data (Donnelly-Kehoe et al. 2019). The rs-FC data of each subject (patients and HCs) was z-scored based on the mean and SD of the corresponding centers' HC group (Donnelly-Kehoe et al. 2019). The resulting rs-FC z-scores between all pairs of regions were used to perform Spearman's correlations with (i) No-go polarity index and (ii) Go polarity index for each tandem of patients and HCs. To consider results as significant, the alpha level was set at $P < 0.001$ (uncorrected). Only positive associations are reported (Fittipaldi et al. 2020; Salamone et al. 2021).

Results

Behavioral results

Behavioral results revealed a higher error rate for bvFTD and AD patients compared to HCs. Commission errors did not differ significantly across groups. Commission errors on No-go trials revealed nonsignificant main and interaction effects. Omission errors on Go trials were significantly greater for bvFTD and AD patients than for HCs. RTs for correct Go trials were slower for bvFTD

and AD than HCs. For statistical details, see Table 2 and Supplementary Material 5.

Time-frequency results

Results from healthy controls

In HCs, the inhibitory index yielded a higher theta power increase for No-go trials than Go trials over an occipito-fronto-central cluster ranging from 0 to 620 ms [$T_{(\maxsum)} = 4193.56$, $P = 0.02$]. No other band yielded significant effects (all P -values > 0.05)—Supplementary Material 6, Fig. S1.

Also, in HCs, the No-go polarity index involved higher delta power (for affirmative than negative sentences) over a frontocentral cluster from cue onset to 469 ms [$T_{(\maxsum)} = 2906.24$, $P = 0.01$]—Fig. 2A1. No other band yielded significant effects (all P -values > 0.54). The Go polarity index yielded no significant effects in any band (all P -values > 0.05).

Comparisons between healthy controls and patient groups

The comparison between HCs and patient groups for the inhibitory index relating to theta modulations yielded a significant main effect of group [$F(2, 59) = 3.02$, $P < 0.05$]. A post-hoc two-sample pairwise permutation test showed that the bvFTD group significantly differed from HCs [$t = 2.51$, $P = 0.03$, $d = 0.87$], there being no significant differences between HCs and AD patients ($t = -.72$, $P > 0.05$, $d = 0.21$).

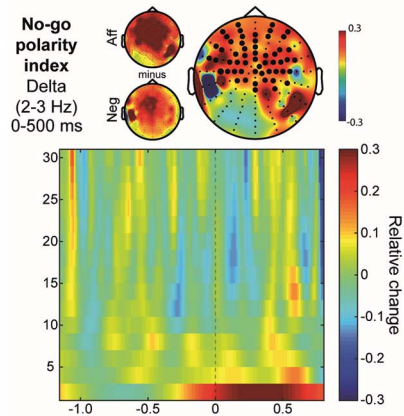
The comparison between HCs and patient groups yielded a significant main effect of group for the No-go polarity index [$F(2, 59) = 2.83$, $P = 0.004$]. A post-hoc two-sample pairwise permutation test showed that the bvFTD group significantly differed from HCs [$t = 3.069$, $P = 0.006$, $d = 1.11$], there being no significant differences between HCs and AD patients ($t = -2.35$, $P = 0.06$, $d = 0.74$)—Fig. 2A2, left inset. In contrast, the Go polarity index revealed a nonsignificant effect of group [$F(2, 59) = 1.42$, $P = 0.27$]—Fig. 2A2, right inset.

Associations between oscillatory indices and gray matter volume

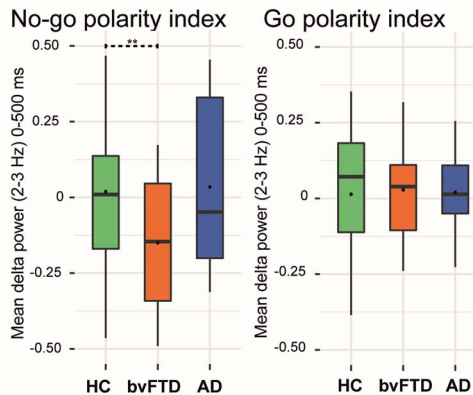
Associations between oscillatory indices and gray matter volume revealed differential patterns in each patient

A. Time-frequency analyses: Affirmative minus Negative

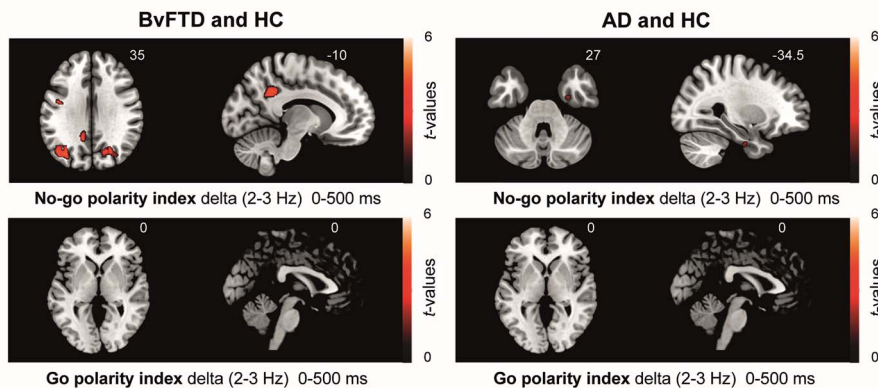
A1. Within-group analysis in HCs



A2. HCs vs patient groups



B. Associations between No-go and go polarity indexes and grey matter volume



C. Associations between No-go and go polarity indexes and whole-brain rs-FC

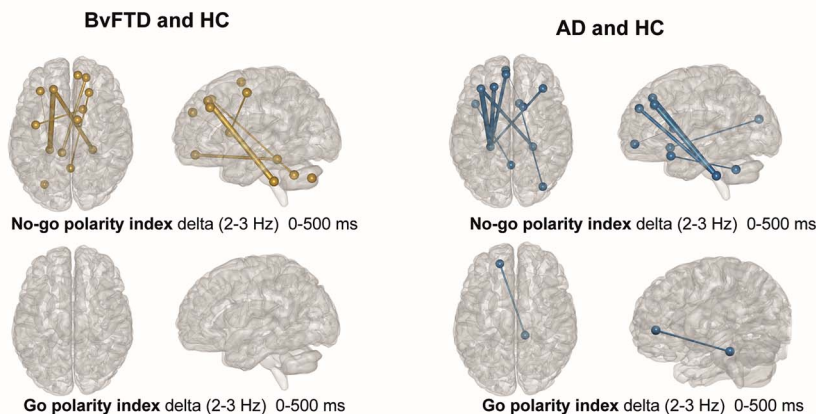


Fig. 2. (A) Time–frequency analyses for polarity (affirmative vs negative trials). (A1). Significant spatiotemporal cluster from the comparison between affirmative and negative No-go trials (No-go polarity index) for the delta band (2–3 Hz) in HCs. (A2) Between groups comparisons for the mean No-go polarity and the Go polarity indexes, respectively. The dashed line represents the significant difference between HCs and the bvFTD group ($P < 0.01$). (B) Associations between No-go and Go polarity indexes and gray matter volume. For the bvFTD and HC tandem, the No-go polarity index was positively associated with gray matter volume of the left medial–posterior cingulum, precentral gyrus, and angular gyrus, as well as the left midinferior and right superior occipital cortices (top left inset); instead, the Go polarity index presented no significant associations (bottom left inset). For the AD and HC tandem, the No-go polarity index was significantly associated with the volume of the right fusiform gyrus (top right inset); instead, the Go polarity index presented no significant associations (bottom right inset). (C) Associations between No-go and Go polarity indexes and rs-FC. For the bvFTD and the HC tandem, the No-go polarity index was associated with connectivity between frontocerebellar regions (top left inset); instead, the Go polarity index presented no significant associations (bottom left inset). For the AD and HC tandem, the No-go polarity index was associated with connectivity of frontocerebellar regions as well as occipital and temporal areas (top right inset); contrariwise, the Go-polarity index also correlated with connectivity between frontocerebellar regions (bottom right inset). Results were obtained from whole-brain analyses over 90 regions of interest, considering an uncorrected $P < 0.001$. Link thickness indicates connectivity strength.

group. First, in the bvFTD-HC tandem, the No-go polarity index was positively associated with gray matter volume of the left medial–posterior cingulum, precentral gyrus, and angular gyrus, as well as the left midinferior and right superior occipital cortices (Fig. 2B, top left inset). No significant associations were found between the Go polarity index and gray matter volume (Fig. 2B, bottom left inset). Second, in the AD-HC index, the No-go polarity index was significantly associated with the volume of the right fusiform gyrus (Fig. 2B, top right inset). No association was found between the Go polarity index and the volume of any brain area (Fig. 2B, bottom right, inset). For details, see [Supplementary Material 7, Table S7](#).

Associations between oscillatory indices and fMRI resting-state connectivity

Each patient group showed different associations between oscillatory indices and fMRI connectivity patterns. First, in the bvFTD-HC tandem, the No-go polarity index was associated with connectivity between (i) the bilateral superior frontal gyrus and bilateral cerebellar regions, (ii) frontal/prefrontal (midfrontal and superior orbital) regions and the left cerebellum, (iii) the superior motor area and the left cerebellum, (iv) the right precentral gyrus and the caudate nucleus, and (v) the supplementary motor area and cerebellum (Fig. 2C, top left inset). In contrast, the Go polarity index was not significantly associated with any connectivity pattern (Fig. 2C, bottom left inset). Second, in the AD-HC tandem, the No-go polarity index was associated with connectivity between (i) the left superior frontal gyrus and the left cerebellum, (ii) the midsuperior frontal cortex and the left cerebellum, (iii) the bilateral medial frontal cortex and the bilateral cerebellum, (iv) the midorbital frontal cortex and the right caudate nucleus, (v) the right olfactory area and the right medial occipital cortex, and (vi) the left superior temporal cortex and the vermis (Fig. 2C, top right inset). Also, the Go polarity index was associated with connectivity between the left superior orbital cortex and the right cerebellum, suggesting nonspecific relations with inhibitory processes (Fig. 2C, bottom right inset). Briefly, the bvFTD group showed frontocerebellar associations restricted to the No-go polarity index only. On the other hand, AD presented widespread anteroposterior associations with the No-go polarity index, comprising frontocerebellar, occipital, and temporal areas; moreover, it presented frontocerebellar associations with the Go polarity index. For details, see [Supplementary Material 8](#).

Discussion

This multilevel study examined the interplay of negation and inhibition in strategic neurodegenerative models. In HCs, negation distinctly suppressed frontocentral delta power, a canonical inhibitory marker. This modulation, along with canonical oscillatory signatures of motor inhibition, was abolished in bvFTD but not in AD patients.

Moreover, disruptions of the No-go polarity index over the delta band in bvFTD correlated with anatomofunctional patterns mainly implicating inhibitory regions (precentral gyrus and frontocerebellar networks). Though preliminary due to the study's sample size, our results suggest that multidimensional inhibitory mechanisms are involved in negation processing and point to potential disease-differential markers of bvFTD.

The No-go polarity index showed greater delta power for affirmative than negative sentences, indicating delta suppression for the latter. No such effect was observed in other bands or in the Go polarity index. This supports the involvement of inhibitory mechanisms during negation processing. In fact, delta activity is a canonical signature of inhibitory processing, being typically reduced during response suppression (Harmony 2013; Huster et al. 2013) and significantly modulated during cognitive (Cooper et al. 2016) and affective (Benvenuti et al. 2017) inhibition. Intriguingly, prior studies with the same task in healthy participants found similar effects only in the theta and beta bands (de Vega et al. 2016; Beltrán et al. 2019). However, these studies focused on young populations, while the present work targeted elderly subjects. As argued below, this might reflect differences in the sensitivity of theta and delta modulations during inhibition across the lifespan (Kolev et al. 2009; Schmiedt-Fehr and Basar-Eroglu 2011). Compatibly, our study suggests that this inhibitory marker may be a crucial correlate of negation processing in late adulthood.

Such specific delta marker was altered only in bvFTD. As confirmed by motor inhibition EEG results, this disease presents early inhibitory disruptions (Rascovsky et al. 2011) affecting not only bodily action (Hughes et al. 2015) but also cognitive (Hornberger et al. 2008) and socioemotional (Ibáñez 2018; Godefroy et al. 2021) domains. To our knowledge, delta oscillations have not been previously studied during inhibition in bvFTD. However, their sensitivity to inhibitory disruptions has been validated in other populations exhibiting high impulsivity and socially inadequate behavior, including bipolar (Atagün et al. 2014) and schizophrenic (Ergen et al. 2008; Ford et al. 2008) patients, and alcoholic individuals with suspected frontal damage (Kamarajan et al. 2004; Pandey et al. 2016). Similar disinhibited behavior has been reported in bvFTD (Young et al. 2010; Rascovsky et al. 2011; Baez et al. 2014). Thus, the No-go polarity index in bvFTD patients suggests that their abnormal negation reflects disrupted inhibitory mechanisms. In this sense, the multidomain behavior-suppression disruptions characterizing bvFTD seem to affect linguistic processes, potentially revealing new forms of altered cognitive inhibition.

Compatibly, in the bvFTD-HC tandem, this No-go polarity index was associated with the volume of the precentral and angular gyri, alongside the medial posterior cingulum and the middle occipital cortex, linked to motor (Chambers et al. 2009; Huster et al. 2013), cognitive (Langenecker et al. 2004;

Bernal and Altman 2009), and socioemotional (Hung et al. 2018; Ibáñez 2018) inhibition, as well as negation processing (Tettamanti et al. 2008; Christensen 2009; Bahlmann et al. 2011). Congruently, the No-go polarity index correlated with rs-FC between key areas implicated in inhibition, such as superior and prefrontal regions (Karch et al. 2008; Beltrán et al. 2018), the caudate nucleus (Chambers et al. 2009), and the cerebellum (Zheng et al. 2008; Mannarelli et al. 2020). Importantly, some such structures are also implicated in negation—e.g. midsuperior motor and left precentral areas (Tettamanti et al. 2008; Christensen 2009; Tomasino et al. 2010; Bahlmann et al. 2011). These patterns were absent in the Go polarity index, which might suggest that multilevel alterations of negation processing emerged only when response suppression mechanisms were engaged. Briefly, the integration of both domains seems to be distinctly and cross-dimensionally disrupted in patients with primary inhibitory deficits.

Indeed, selective oscillatory disruptions were absent in AD patients, who also exhibited preserved EEG signatures during motor inhibition. While AD often involves disinhibitory manifestations, these are neither systematic nor diagnostic (Kramer et al. 2003; Stopford et al. 2012), which might account for such partly preserved marker. Indeed, in this group, the No-go polarity index correlated with the volume of the right fusiform gyrus, a region typically implicated in lexicosemantic deficits across AD cohorts (Kuperberg et al. 2000; Forseth et al. 2018). The potential role of such domain in the disruptions of AD patients is reinforced by the magnitude of their deficits in the Hayling test (Table 1), which hinges heavily on lexicosemantic systems (Belleville et al. 2006) that are commonly impaired in this population (Bondi et al. 2002; Nestor et al. 2006). Moreover, the No-go polarity index in AD patients was mainly associated with frontocerebellar networks as well as temporal and occipital hubs. Given that the No-go polarity index was preserved, such associations might be driven by overall cognitive demands, which, in AD, involve reduced delta activity (Yener et al. 2008; Başar and Güntekin 2013) and modulations along frontocerebellar regions (Zheng et al. 2017; Jacobs et al. 2018). In fact, frontocerebellar networks in AD also correlated with the Go polarity index, highlighting the lack of distinct associations with inhibition. Briefly, the neural integration of negation and inhibition might be differentially disrupted in persons typified by primary inhibitory deficits (namely, bvFTD patients).

From a theoretical stance, this study supports the “reuse of inhibition for negation” framework (Beltrán et al. 2021), but its results might enable alternative interpretations. Indeed, delta and/or theta suppression has also been related to attentional (Harmony 2013) and working memory (Polich 2007; Harper et al. 2014) functions, both of which may be more markedly taxed during No-go than during Go trials (O’Connell et al. 2009; Redick et al. 2011; Chen and Cave 2016; Harper et al. 2016). Moreover, these domains have been linked to some of the brain

regions and networks captured in our correlations results (Criaud and Boulinguez 2013; Yaple et al. 2019). Accordingly, the inhibitory mechanisms we postulate may be accompanied by other associated effects. That being said, the study’s design and multidimensional results strongly converge to support the proposed interpretation. Indeed, our main findings (i) pertain to the No-go polarity (as opposed to the Go polarity) condition; (ii) replicate previous EEG findings motivating our hypotheses (de Vega et al. 2016; Beltrán et al. 2019); (iii) reveal selective alterations in that condition only for patients with primary inhibitory disorders (bvFTD), as opposed to those with nondiagnostic inhibitory difficulties (AD); and (iv) correlate with regions and networks that are systematically linked to inhibition in the literature. Notwithstanding, future research could incorporate specific manipulations to ascertain the role of other functions that might mediate the observed results, disentangling possible competing explanations.

At the same time, this study challenges recent localizationist views linking negation to a single putative area (in the anterior insula) specialized for nonverbal logical processes (Grodzinsky et al. 2020). In particular, Grodzinsky et al. (2020, 29) interpret their findings on negation as evidence “that the border between the insula and Broca’s region is where language stops and logic begins.” Conversely, we found that key negation markers are associated with fronto-striato-cerebellar circuits, supporting network-based accounts of neurocognition (Mišić and Sporns 2016). Moreover, by demonstrating that core mechanisms subserving (nonverbal) inhibition are involved in processing (verbal) negation, our findings suggest that the latter function operates at the crossing of linguistic and nonlinguistic systems, further clashing against modularist accounts.

Moreover, while previous EEG reports linking negation with inhibition observed theta-band modulations in adults (de Vega et al. 2016; Beltrán et al. 2019), our work revealed oscillatory correlates of negation in the delta band for elderly participants. However, theta band activity was, indeed, associated with motor inhibition, replicating previous works (Nigbur et al. 2011; Huster et al. 2013). This indicates that, at least in elderly persons, the inhibitory mechanisms mediating physical action suppression may not be identical to those subserving sentential negation. Thus, as suggested elsewhere (Kolev et al. 2009; Schmiadt-Fehr and Basar-Eroglu 2011), theta and delta oscillations may become differentially (in)sensitive to relevant processes throughout aging. This finding motivates a new ontogenetic hypothesis, suggesting that critical signatures of negation may adapt to age-related neural profiles, as observed for lexeme retrieval (den Hollander et al. 2019), word anticipation (Wlotko et al. 2012; Broderick et al. 2021), and sentence comprehension (Wingfield and Grossman 2006).

Interestingly, neurophysiological disruptions of the No-go polarity index were not mirrored by behavioral results, as in previous reports of the same task

(de Vega et al. 2016; Beltrán et al. 2019). The same was true for the motor inhibition index, replicating the absence of behavioral deficits in Go/No-go tasks and other motor inhibition paradigms for both bvFTD (Dimitrov et al. 2003; Collette et al. 2007; Hughes et al. 2018) and AD (Collette et al. 2007). These patterns align with language grounding research capturing neural effects alongside null behavioral signatures (e.g. Kiefer et al. 2008; Willems et al. 2010; Hauk and Tschentscher 2013; Dalla Volta et al. 2018; García et al. 2019). Similarly, our task seems sensitive to fine-grained neural effects, which may not be mirrored behaviorally, inviting further research with alternative paradigms.

Finally, from a clinical perspective, negation tasks could reveal differential markers across neurodegenerative disorders. Previous works have leveraged other linguistic materials, such as emotion-laden sentences (Santamaría-García et al. 2017) or action-laden texts (Moguilner et al. 2021), to capture discriminatory neural markers of diseases presenting different brain disturbances. Tentatively, our results point to negation as a promising target for bvFTD, reinforcing the value of linguistic assessments for differential characterizations of the disease (Hardy et al. 2016; Geraudie, Díaz Rivera, et al. 2021b). More generally, while previous clinical research on inhibition has focused on motoric (Collette et al. 2007), cognitive (Hornberger et al. 2008), and affective (Godefroy et al. 2021) dimensions, these findings open a new avenue to capture (dis)inhibitory dynamics elicited by negation. As seen in other studies on bvFTD (Santamaría-García et al. 2017; Legaz et al. 2021), broadening the canonical dimensions of a critical domain can reveal nosological distinctions and favor more fine-grained phenotyping.

Limitations and avenues for further research

Our study presents some limitations. First, the sample sizes are modest. Although these *N*s match those of previous reports yielding replicable findings (Hughes et al. 2011; Premi et al. 2014) and mirror the size of multiple bvFTD reports assessing language (Geraudie, Battista, et al. 2021a), inhibition (Dimitrov et al. 2003; Hornberger et al. 2010; Hornberger et al. 2011; O'Callaghan et al. 2013; Santillo et al. 2016), and other domains (Farag et al. 2010; Mendez and Shapira 2011; Agosta et al. 2012; Couto et al. 2013; Filippi et al. 2013; Henry et al. 2014; Nasseroleslami et al. 2019; Pasquini et al. 2020), further studies should test our approach with more participants to ensure better statistical power and more robust effects. Second, since our task did not require fast-paced key presses, the need to suppress prepotent responses on No-go trials was not at its highest. While this promoted task feasibility for patients, further works should employ alternative tasks with more stringent action-suppression demands. Third, the No-go polarity index may be partly influenced by other mechanisms related to response inhibition, such as conflict monitoring or error detection (Harper et al. 2016). Future studies should develop new paradigms to

disentangle inhibition- and control-related processes underlying negation comprehension.

Also, our work leads to novel research questions. We have surmised that delta and theta modulations might be differentially sensitive to inhibitory dynamics in younger and elderly populations. Direct testing of this hypothesis, via comparisons between participants from different age groups, could open a lifespan perspective on the neural mechanisms underpinning negation processing. Additionally, while we focused on negated action verbs, future studies should examine whether bvFTD patients present similar disruptions during negation of abstract verbs (Beltrán et al. 2019). Also, the atrophy pattern of the bvFTD sample corresponded to a temporal subtype. Although inhibitory alterations are prominent in this presentation (Whitwell et al. 2009; Ranasinghe et al. 2016) and are often associated to temporal atrophy (Liu et al. 2004; Zamboni et al. 2008; Chan et al. 2009; Whitwell et al. 2009; Ranasinghe et al. 2016) and hypoperfusion (Ber et al. 2006; McMurtray et al. 2006) across bvFTD cohorts, it would be vital to replicate our work on bvFTD patients typified by more canonical frontal disruptions. Finally, since our imaging protocol did not include active paradigms, task-related EEG modulations could only be correlated with offline MRI/fMRI measures. Future studies could replicate our work with online imaging recordings.

Conclusion

In conclusion, this is the first study examining multi-dimensional neurocognitive links between negation and inhibition across neurodegenerative diseases. Canonical oscillatory signatures of inhibition during negation processing were selectively disrupted in bvFTD (but not AD) patients and related to anatomofunctional properties of inhibitory regions. Our results indicate that negation hinges on the *integrity and interaction* of spatiotemporal inhibitory mechanisms while potentially revealing differential markers of neurodegenerative dementias. Further research along these lines may inspire basic and translational breakthroughs across neuroscientific and clinical fields.

Author contributions

Mariano N. Díaz-Rivera: Methodology, Investigation, Data Curation, Formal Analysis, Writing—original draft preparation, Visualization. Agustina Birba: Methodology, Investigation, Formal Analysis, Writing—original draft preparation, Visualization. Sol Fittipaldi: Software, Data Curation, Formal analysis, Visualization. Débora Mola: Data Curation. Yurena Morera: Software, Data Curation. Manuel de Vega: Conceptualization, Software, Investigation. Sebastian Moguilner: Formal analysis. Patricia Lillo: Resources, Data Curation. Andrea Slachevsky: Resources, Data curation. Cecilia González Campo: Software, Data Curation, Formal analysis, Visualization. Agustín Ibáñez:

Conceptualization, Methodology, Resources, Writing—review & editing, Project administration, Funding acquisition. Adolfo M. García Conceptualization, Methodology, Resources, Writing—original draft preparation, Writing—review & editing, Visualization, Supervision, Project administration, Funding acquisition.

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Supplementary material

Supplementary material is available at *Cerebral Cortex Journal* online.

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Competing interests

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Data availability

All experimental data and the scripts used are fully available online via the Open Science Framework at https://osf.io/n2abf/?view_only=3a56a65940db440f9c5af4ce88fb93f2 (data from "Multidimensional inhibitory signatures of sentential negation in neurodegenerative disorders").

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