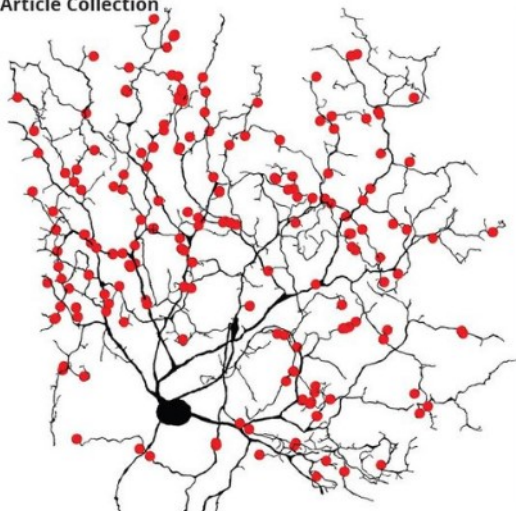




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Corollary discharge function in healthy controls: Evidence about self-speech and external speech processing

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Abstract

As we speak, corollary discharge mechanisms suppress the auditory conscious perception of the self-generated voice in healthy subjects. This suppression has been associated with the attenuation of the auditory N1 component. To analyse this corollary discharge phenomenon (agency and ownership), we registered the event-related potentials of 42 healthy subjects. The N1 and P2 components were elicited by spoken vowels (*talk* condition; agency), by played-back vowels recorded with their own voice (*listen-self* condition; ownership) and by played-back vowels recorded with an external voice (*listen-other* condition). The N1 amplitude elicited by the *talk* condition was smaller compared with the *listen-self* and *listen-other* conditions. There were no amplitude differences in N1 between *listen-self* and *listen-other* conditions. The P2 component did not show differences between conditions. Additionally, a peak latency analysis of N1 and P2 components between the three conditions showed no differences. These findings corroborate previous results showing that the corollary discharge mechanisms dampen sensory responses to self-generated speech (agency experience) and provide new neurophysiological evidence about the similarities in the processing of played-back vowels with our own voice (ownership experience) and with an external voice.

KEYWORDS

agency, auditory N1, efference copy, event-related potentials, ownership

Abbreviations: ANOVA, analysis of variance; EEG, electroencephalography; ERP, event-related potential; ICA, independent component analysis; IQ, intelligence quotient; ROI, region of interest; SD, standard deviation; SPL, sound pressure level; WAIS, Wechsler Adult Intelligence Scale.

Rosa M. Beño-Ruiz-de-la-Sierra and Antonio Arjona-Valladares share co-first authors.

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1 | INTRODUCTION

The accurate identification of actions and thoughts arising from ourselves constitutes a basic element to develop adequate and adaptive cognitive and motor functioning. Sensations caused by our actions are distinguishable from those of external origin, playing a key role in developing an intact sense of self.

At least two different processes known as agency and ownership, with two different underlying neurobiological mechanisms (Bühler et al., 2016; Hubl et al., 2014), determine the experience of performing an action. Agency refers to causality and how the action of the subject is followed by an effect at a specific moment (Hubl et al., 2014). Thus, agency corresponds to the awareness that 'I' am generating the consequences of the action. On the other hand, ownership focuses on the features of the effect regardless of the action being performed by the subject, comparing the stimulus features with the memory content. Corollary discharge allows pre-consciously attributing this agency to sensations arising from self-generated but not externally generated perceptions, prioritizing the processing of the latter (Crapse & Sommer, 2008; Frith, 2019). It is underpinned by an efference copy sent from the motor command to sensory regions, which conveys the comparison between the predicted sensory consequences of the motor act and its actual sensory consequences (Ford & Mathalon, 2019; Frith, 2019). This sensory-motor integration has been described in all sensory modalities. During vocalization, the corollary discharge mechanisms would be activated through a feed-forward inhibitory process in which interneurons located in the auditory cortex inhibit pyramidal neurons (Eliades & Wang, 2008; A. Nelson et al., 2013; Reznik & Mukamel, 2019; Schneider et al., 2014). Consequently, cortical responses generated by self-generated speech are suppressed.

During vocalization, the auditory N1 component has been studied as an index of corollary discharge-mediated auditory cortical suppression. This event-related potential (ERP) shows the maximum negative peak at about 100 ms after the auditory stimulus onset and is followed by the positive P2 component, at about 200 ms. Both are produced in the primary and secondary auditory cortex (Ford et al., 2016) and are associated with attentional processing, reflecting different perceptual stages in auditory perception. Healthy subjects show suppression of N1 during self-generated speech (Whitford, 2019), perhaps in order to allocate cognitive resources for processing externally generated stimuli. Therefore, self-generated spoken sounds are not consciously processed compared with passive listening of external stimuli. The correct functioning of this inhibitory mechanism contributes to

differentiating our own thoughts and memories from externally generated stimuli.

Our current study analyses the corollary discharge mechanisms in healthy male and female controls by measuring the possible suppression of N1 and P2 components with electroencephalography (EEG). We aim to distinguish the process of agency and ownership and to prove whether it is not the perceptual recognition of our own voice but the motor act of speaking that makes us differentiate between external and internal stimuli. To this end, based on Ford et al. (2010), we propose an experiment that introduces (i) a *talk* condition, which refers to the agency experience reflected in the processing of the own speech; (ii) a *listen-self* condition, assessing the ownership experience by playing (from an external source) the own recorded voice; and (iii) a *listen-other* condition (Heinks-Maldonado et al., 2005), to understand whether the identification of the self-generated speech is due to motor or sensory processes associated with the recognition of physical characteristics.

2 | MATERIALS AND METHODS

2.1 | Sample

Forty-two healthy adults participated in the study (21 males and 21 females). The mean age was 28.34 years (range = 18–54, standard deviation [SD] = 10.68). Subjects' recruitment and data acquisition were conducted at the Medical Faculty of the University of Valladolid and the UCM-ISCIH Center for Human Evolution and Behaviour of Madrid. Demographic and cognitive data were screened through a personal interview, and the intelligence quotient (IQ) was scored using the Spanish version of *Wechsler Adult Intelligence Scale* (WAIS) (Wechsler, 1997) (Table 1). The exclusion criteria were a total IQ below 70 and a history of psychiatric/neurological disorders or substance abuse (except for nicotine or caffeine). All participants provided written informed consent, and the research board endorsed the study according to The Code of Ethics of the World Medical Association (Declaration of Helsinki).

2.2 | Experimental procedure

Participants seated 60 cm from a computer screen with a white cross in the centre of a black background. A microphone was placed 15 cm from the subject's mouth. Each participant accomplished a task with three

TABLE 1 Demographic, cognitive and neurophysiological values of the participants.

	N = 42
Sex (M/F)	21/21
Age (years)	28.34 (10.68)
Education (years)	14.77 (2.24)
WAIS-Total IQ	110.87 (9.39)
Amplitude N1 LO (μ V)	-3.66 (1.65)
Amplitude N1 LS (μ V)	-3.09 (1.96)
Amplitude N1 TK (μ V)	-.58 (2.56)
Latency N1 LO (ms)	81.69 (18.4)
Latency N1 LS (ms)	85.53 (21.33)
Latency N1 TK (ms)	86.47 (22.8)
Amplitude P2 LO (μ V)	1.55 (2.22)
Amplitude P2 LS (μ V)	.97 (2.22)
Amplitude P2 TK (μ V)	.84 (3.43)
Latency P2 LO (ms)	160.34 (17.65)
Latency P2 LS (ms)	166.11 (11.29)
Latency P2 TK (ms)	169.91 (17.34)

Note: Data are given as mean (standard deviation).

Abbreviations: IQ, intelligence quotient; LO, listen-other condition; LS, listen-self condition; M/F, male/female; TK, talk condition.

TABLE 2 Counterbalancing condition order across subjects.

	Condition		
Order 1	Listen-other	Talk	Listen-self
Order 2	Talk	Listen-other	Listen-self
Order 3	Talk	Listen-self	Listen-other

different conditions and the order was alternated across subjects so that the *listen-other* condition appeared in the three order possibilities (Table 2):

- *Talk* condition: Subjects were instructed to vocalize [a:] about every 1–2 s for 4 min with 30 s of resting after the two first minutes. On each vocalization, the sound was picked up by a microphone (model *NT1*), amplified and heard in real time through headphones (model *SE215*). This condition assessed the agency process.
- *Listen-self* condition: The recorded vocalizations from the *talk* condition were played back through the headphones (each subject listened to his own voice). Subjects were instructed to stay quiet and listen to the whole record. This condition assessed the ownership process.

- *Listen-other* condition: The only difference from the *listen-self* condition was the recorded voice played back through the headphones, belonging now to one of the authors. This condition assessed the processing of an alien voice.

Prior to the *talk* condition, subjects were trained to maintain the 15-cm gap between their mouth and the microphone and vocalize the phoneme ‘ah’ for a short duration (<300 ms) while the authors gave them feedback on performance. Subjects were also instructed to remain still and open their mouths before uttering the sound, to fix their eyes on the white cross during the whole recording and to maintain their voice volume between 65 and 75 dB of sound pressure level (*SPL*). The volume intensity was measured with a sound level metre (model *PCE-353N-ICA*), held 6 cm in front of the mouth. Loudness was the same across conditions based on the equilibration of the headphone audio output as measured by a decibel metre. During all three conditions, the sound signal was sent, through a preamplifier (*actiCHamp*), to a sound-processing software so it could generate a trigger pulse. The trigger pulse was produced on the rising edge of the rectified signal and included in the EEG recording. There were no significant differences in median speech volume intensity between the authors’ and the participants’ recordings (volumes out of the 65–75 dB range were not recorded). To mask the effect of bone conduction during vocalization, the mean speech *SPL* reproduced through headphones was increased by 15 dB over each subject’s mean speech *SPL* in all three conditions (Ford et al., 2007; Heinks-Maldonado et al., 2007).

2.3 | EEG data acquisition and analysis

A 64-channel EEG system recorded the EEG data (BrainVision, 2006, Brain Products GmbH). Active electrodes were placed in an elastic cap using the international 10–10 system (FP1, FP2, F7, F8, F3, F4, Fz, FC5, FC6, FC1, FC2, T7, T8, C3, Cz, C4, CP5, CP6, CP1, CP2, TP9, TP10, P7, P8, P3, P4, Pz, O1, O2, Oz, AF7, AF3, AFz, F1, F5, FT7, FC3, FCz, C1, C5, TP7, CP3, P1, P5, PO7, PO3, POz, PO4, PO8, P6, P2, CPz, CP4, TP8, C6, C2, FC4, FT8, F6, F2, AF4, AF8). The impedance did not exceed 5 k Ω , and the sampling frequency was 500 Hz. The online reference was the average mastoid ((TP9 + TP10)/2) to minimize talking artefacts from the nose. Data pre-processing was performed using EEGLAB v13.6.5b (Delorme & Makeig, 2004) and Matlab R2020b (MathWorks Inc., MA, USA). A low-pass filter of 30 Hz and a high-pass filter of .05 Hz were applied. Each

continuous EEG recording during the talk condition was visually monitored trial by trial for excessive speech onset muscle artefacts. Any trial onset whose noise signal was indistinguishable from the background EEG activity was excluded from further analysis. Ambiguous speech onsets implying some peaks of abnormal activities were also excluded (Ford et al., 2010). Subsequently, eye movements, blinking and any artefact related to facial muscle activity (especially during the *talk* condition) were identified and rejected with an independent component analysis (ICA) (Delorme et al., 2007). EEG data epochs were established from -100 ms prior to the auditory stimulus onset (used for baseline correction) to 350 ms after. Trials containing artefacts (voltages exceeding ± 90 μ V) were rejected and eight subjects with fewer than 30% trials on average were excluded from the analysis.

After exploration of the temporal and spatial regions of interest (ROIs) (depicted in Figure S1) and based on previous literature (Ford et al., 2010, 2014; Mathias et al., 2020), N1 was identified as a negative fronto-central activity between 50 and 100 ms after the [a:] phoneme onset, and P2 was the subsequent fronto-central positivity between 150 and 200 ms. Twelve electrodes around the fronto-central area (F1, Fz, F2, FC1, FCz, FC2, C1, Cz, C2, CP1, CPz and CP2) were selected for statistical analyses.

2.4 | Statistical analysis

N1 and P2 amplitude and peak latency were analysed with a single-factor repeated-measures analysis of variance (ANOVA) on averages of trials. The within-subject factor was task condition (*talk*, *listen-self* and *listen-other*). p values were corrected with the Greenhouse–Geisser when necessary, and effect sizes were assessed using partial eta-squared values. Student's t -tests for repeated measures with Bonferroni correction were computed for post hoc analyses. To assess the relative support of the effect on the amplitude of the N1 and P2 components between task conditions, we performed a Bayesian t -test for related samples (SPSS Statistics for Windows, Version 23.0, Chicago: SPSS Inc.).

3 | RESULTS

Table 1 shows demographic data, cognitive characteristics and amplitude/latency values of N1 and P2 components. Figure 1 depicts the waves and topographies of the two ERPs analysed. The statistical analyses did not show gender differences in N1 nor P2 amplitude/peak latency in any of the three conditions.

3.1 | ERP amplitude and peak latency analyses

The ANOVA results on the N1 component showed significant differences in amplitude related to the task condition ($F[1.47, 59.17] = 27.7$, $p < .001$, $\eta_p^2 = .40$). The significant results were due to a lower amplitude in *talk* compared with *listen-other* ($F[1, 41] = 39.19$, $p < .001$, $\eta_p^2 = .49$) and *listen-self* ($F[1, 41] = 23.83$, $p < .001$, $\eta_p^2 = .37$) conditions. There were no significant differences between *listen-other* and *listen-self* conditions. P2 amplitude did not show significant differences related to the task condition.

The Bayesian t -test for related samples showed an N1 Bayesian Factor₀₁ (BF_{01}) = .00 for *listen-other* versus *talk*, a $BF_{01} = .00$ for *listen-self* versus *talk*, favouring the alternative hypothesis, and a $BF_{01} = .89$ for *listen-self* versus *listen-other*. The results on P2 yielded a $BF_{01} = 4.64$ for *listen-other* versus *talk*, a $BF_{01} = 7.95$ for *listen-self* versus *talk* and a $BF_{01} = 4.07$ for *listen-self* versus *listen-other*, favouring the null hypothesis. After Bonferroni correction for multiple comparisons, only the differences in N1 between *talk* and *listen-self*/*listen-other* remain statistically significant.

There were neither significant differences on N1 or P2 peak latencies related to the task condition.

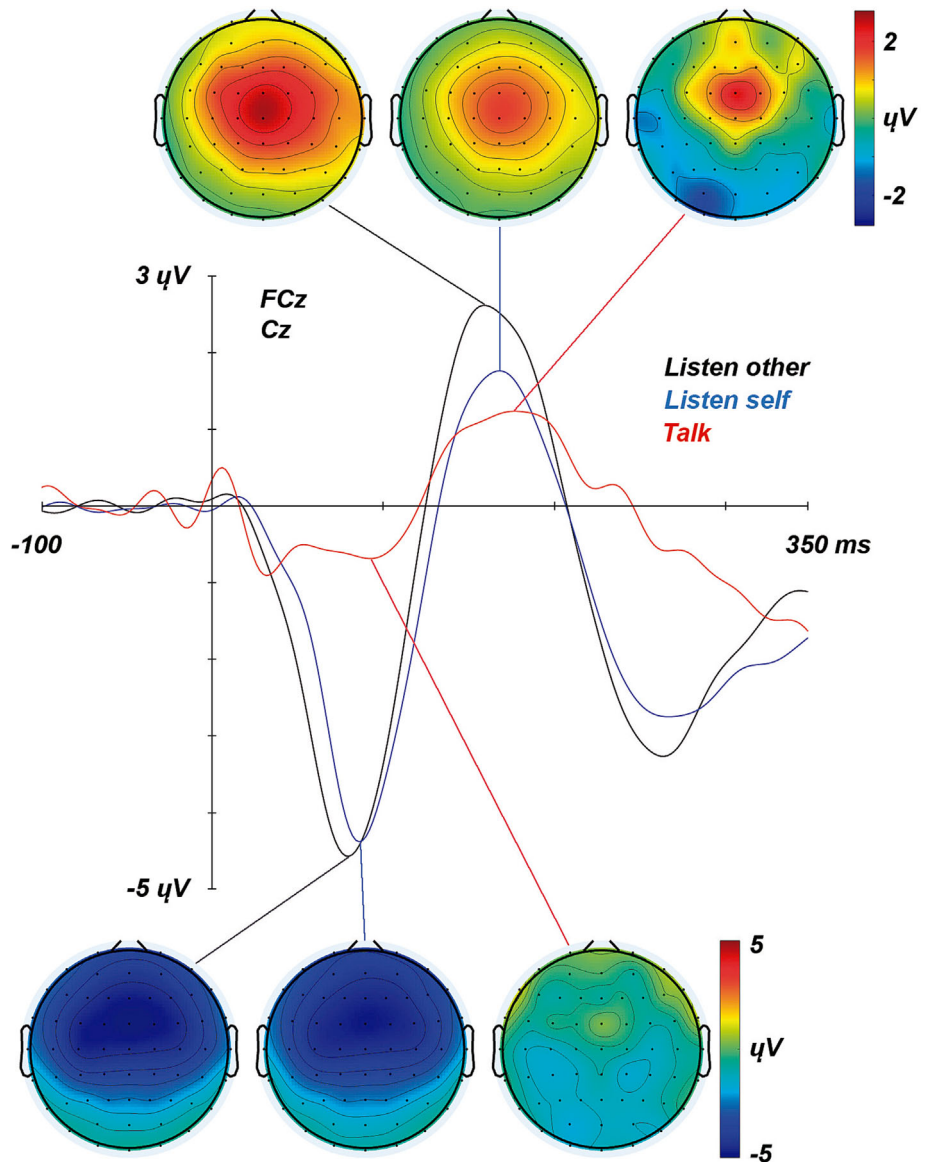
4 | DISCUSSION

The primary aim of this study was to assess speech-related suppression of N1 and P2 ERPs in healthy subjects differentiating between agency and ownership processes as well as the motor and sensory mechanisms involved in the perception and recognition of the stimuli.

Several neurocognitive correlates may be involved in the basic self-experience (B. Nelson et al., 2014), such as the corollary discharge mechanism (Poulet & Hedwig, 2007). Our results are consistent with an involvement of the corollary discharge in the auditory N1 suppression during self-generated speech, whose purpose would be to inform other brain regions that these actions are self-generated and facilitate the processing of the external ones. During the *talk* condition, participants also hear their own voice through headphones, which elicits a P2 wave, confirming the sensory detection of the sound.

There is evidence of motor system involvement in sensory prediction as the efference copy signals (Von Holst & Mittelstaedt, 1950) and the corollary discharge mechanisms have also been related to visual perception (Sperry, 1950). The auditory N1 suppression in our healthy participants during talking compared with listening to external stimuli (both self and alien voices)

FIGURE 1 Averaged evoked waves of FCz and Cz in *listen-other*, *listen-self* and *talk* conditions. The topographical maps are obtained from the peak latency of N1 and P2 components.



supports the anticipation of the sensory effects elicited by an action, which has been called the agency process (Hubl et al., 2014). This N1 attenuation allows identifying the source of the stimuli (Pinheiro et al., 2020; Whitford, 2019). Throughout our paradigm, we have equalized the decibel level of the three experimental conditions so that the N1 differences are unlikely due to the volume of the sounds, as some studies have reported (Whitford, 2019). The absence of a clearer N1 topography during the *talk* condition (while P2 seems more consistent) may be due to the low amplitude of this auditory component (between 0 and 1 μV) on the cleanest recordings. Choosing a vowel rather than a more complex sound has the advantages of introducing less muscle noise into the EEG recordings and it does not require a complex cognitive processing.

Consistent with previous studies (Heinks-Maldonado et al., 2005), we found no differences for the amplitude and latency of the ERPs during *listen-other* versus *listen-self* conditions. Thus, the auditory N1 and P2 are similar when the sound comes from an external source, regardless of whether we recognize it as our voice (ownership process) or not. However, N1 amplitude in the *talk* condition is significantly decreased (Figures 1, S1 and S2). The P2 preservation and N1 attenuation during the *talk* condition mean that sensory stimulation originated in self-generated actions is perceived in a different fashion than stimulation from an external source. Sensory regions receive inputs from external stimuli and from motor neurons that originate sensory inputs due to our own actions. In other words, this process is reflected in a closed-loop system in which the outside world and the internal

computation can be compared (Buzsáki, 2018). The brain does not passively register the stimuli we perceive; instead, perception is an action-based process. In this context, previous studies show that utterances in a series that vary from the prior utterance result in a larger N1 ERP during speech, but not during playback condition, reflecting the involvement of an active feedback mechanism related to speech, and not basic auditory perception processes unrelated to the speech motor plan (Sitek et al., 2013). To function more effectively, the brain explores the environment while recording the consequences of its own actions, so that pre-established neuronal patterns become meaningful, and experience takes place (Buzsáki, 2018). There is evidence that this effect is caused by central rather than peripheral mechanisms (Horváth & Burgyán, 2013), and that highlights the influence of motor-related signals to auditory processing at cortical levels, through direct excitation of auditory pyramidal cells and indirect inhibition mediated by parvalbumin interneurons (Eliades & Wang, 2008; A. Nelson et al., 2013; Reznik & Mukamel, 2019; Schneider et al., 2014).

Two types of auditory response suppression have been described, one related to efference copies and prediction, and one that is non-predictive and general during movement, suggesting the latter that intention is not a necessary component of such modulations (Reznik & Mukamel, 2019). Due to the characteristics of our paradigm and the previous literature, our results are consistent with the implication of corollary discharge mechanism. Our participants were trained to remain as still as possible. The movement of the vocal folds is unlikely to be the reason of the suppression, or at least of much smaller magnitude than what is found in other paradigms in which there are clear motor movements, such as the freely movement of the mice (Rummell et al., 2016). Even in this case, the responses of auditory cortical neurons to self-generated sounds were consistently attenuated, compared with the same sounds generated independently of the animals' behaviour (Rummell et al., 2016). Furthermore, paradigms in which the auditory feedback has been manipulated (Heinks-Maldonado et al., 2005), even in the presence of the motor acts involved in speech, the N1 suppression is reduced if the predicted sensory feedback elicited by an efference copy of the motor act does not match the actual sensory feedback.

A variety of paradigms reflects the importance of predictive modelling in perception and in higher cognitive functions (for a review, see Bendixen et al., 2012). The suppression of the auditory N1 when listening to a self-generated sound is consistent with similar results using other motor acts to evoke a sound, such as pressing a

button (Baess et al., 2008, 2011; Hazemann et al., 1975; Horváth & Burgyán, 2013; Jo et al., 2019; Klaffehn et al., 2019; Martikainen et al., 2005; Sowman et al., 2012) or blowing (Mifsud & Whitford, 2017), with motor artefacts being of less concern in these situations. Similar results are reported in paradigms involving imaged movements and inner speech (Brumberg & Pitt, 2019; Jack et al., 2019; Pinheiro et al., 2020; Whitford et al., 2017). The brain interacts with the environment not only through physical movements but also by means of thoughts. The prefrontal cortex sends efferent signals to the limbic system allowing generating action plans before overt movement by comparing potential actions and their expected consequences with stored information. Thanks to the interaction with the external world, the corollary discharge mechanism is able to simulate real actions without sending signals to the muscles, but activating the same target circuits (Buzsáki, 2018).

Ford et al. (2002) found that speaking produces greater coherence between frontal and temporal regions in all frequency bands than listening. In this regard, the theta-band activity would have great importance in long-range communication between motor and sensitive areas during vocalization (Wang et al., 2014), being theta inter-trial phase coherence a sensitive index of cortical suppression due to corollary discharge (Roach et al., 2020). Furthermore, gamma-band phase synchrony is higher during vocalization than while listening to a record of the spoken sounds between electrodes located over the inferior frontal gyrus and auditory cortex (Chen et al., 2011; Ford et al., 2005). This neural synchrony of gamma has been assessed in the 50-ms time window before the speech onset and showed a positive correlation with the N100 suppression in the auditory cortex, suggesting an implication of this activity with the corollary discharge mechanisms (Chen et al., 2011).

These findings support the relevance of a forward model that regulates motor control, sensory processing and cognition, acting as an internal loop between motor commands and sensations (Crapse & Sommer, 2008) and likely underpinning automatic distinction between internally and externally generated precepts (Feinberg, 1978). The accurate discrimination of self-generated stimuli from external stimuli would be associated with the development of an intact sense of self. In this regard, the distinction in healthy subjects between agency/motor acts and ownership/perception, guided by an inside-out model (Buzsáki, 2018), would help to understand the corollary discharge mechanism and opens up the path to investigate disorders with altered self-experience, such as the psychosis spectrum (for a review, see Whitford, 2019).

5 | CONCLUSIONS

Sensory identification of our own voice while talking occurs at a pre-stimulus level. This is coherent with the view of our brain as a self-organized system that may examine and predict the consequences of our actions based on pre-existing connectivity and dynamics. Furthermore, ERPs elicited by listening to external voices (ownership property) show no differences in whether we recognize these voices as ours or not.

5.1 | Limitations

The temporal order effect in the administration of the paradigm cannot be completely rule out. Still, due to the counterbalancing performed and based on previous literature (Ford et al., 2010; Heinks-Maldonado et al., 2005; Wang et al., 2014; Whitford, 2019), we consider that the different changes in the amplitude of N1 are unlikely explainable by the order of presentation of the three task conditions.

AUTHOR CONTRIBUTIONS

Rosa M. Beño-Ruiz-de-la-Sierra: Data curation; formal analysis; investigation; methodology; software; validation; writing—original draft; writing—review and editing. **Antonio Arjona-Valladares:** Conceptualization; formal analysis; methodology; software; validation; writing—original draft; writing—review and editing. **Sabela Fondevila Estevez:** Conceptualization; investigation; methodology; writing—review and editing. **Inés Fernández-Linsenbarth:** Conceptualization; investigation; methodology; writing—review and editing. **Álvaro Díez:** Conceptualization; formal analysis; writing—review and editing. **Vicente Molina:** Conceptualization; data curation; funding acquisition; investigation; project administration; resources; validation; writing—original draft; writing—review and editing.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

PEER REVIEW

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DATA AVAILABILITY STATEMENT

The data underlying this article will be shared on reasonable request to the corresponding author.

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