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Behavioral and Neurophysiological Measures of Speech Auditory Feedback Processing Impairment in Left Hemisphere Stroke

Stacey Sangtian

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by

Stacey Sangtian

Bachelor of Science
College of Charleston, 2011

Master of Speech Pathology
University of South Carolina, 2016

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Accepted by:

Roozbeh Behroozmand, Major Professor

Dirk-Bart den Ouden, Committee Member

Julius Fridriksson, Committee Member

Yuan Wang, Committee Member

Cheryl L. Addy, Interim Vice Provost and Dean of the Graduate School

ABSTRACT

The purpose of this study was to identify behavioral and neural correlates of impaired speech auditory feedback processing in people with a history of left-hemisphere stroke (LHS). To do this, we used the altered auditory feedback (AAF) paradigm to externally induce speech errors by randomly shifting the pitch frequency of the online auditory feedback up or down at ±100 cents in 38 LHS and 27 neurologically intact control participants under two experimental conditions: 1) active vocalizations of a steady speech vowel sound “ah,” and 2) passive listening to the playback of the same self-produced vocalizations. Randomized control trials were included between AAF trials where no pitch-shift stimuli were delivered to the auditory feedback during vocalization or listening tasks. Following each vocalization or listening trial, participants pressed a button to indicate whether they heard a change (i.e., error) in their speech auditory feedback (“Yes” or “No”). Behavioral (i.e., button press responses and vocal motor compensation to AAF) and electroencephalography (EEG) data were collected. Our results revealed decreased perceptual ability for AAF error detection, slowed speech motor compensation responses, and overall decreased magnitude of ERP activity in the LHS group compared with controls, and expression of the speech perturbation response enhancement effect in the N1 ERP component LHS and control groups without between-group differences. There were no significant correlations between the specific behavioral and neurophysiological measures selected in this study.

Findings from this research will inform our understanding of sensorimotor processing involved in speech perception, error detection, and motor correction, as well as our knowledge of how impacted brain networks following left-hemisphere injury affect expressive and receptive speech processing which is vital for the spoken communication system. Understanding the impacts and underlying sources of sensory, motor, and/or sensorimotor deficit on speech error detection and correction is important for the development of targeted, efficacious diagnostic and treatment tools to improve communication and quality of life of people with speech disorders.

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INTRODUCTION

1.1 BACKGROUND

Speech motor control refers to the motor planning, programming, and execution of movements of structures within the articulatory, laryngeal, and respiratory systems. This neuro-muscular speech motor system is responsible for producing verbal speech and includes neural commands to over 100 muscles that help maintain the subglottal pressure for speech, move the vocal folds, and configure other structures that determine the vocal tract shape including the soft palate, pharynx, tongue, mandible, and facial muscles. Speech is perhaps the most complex motor movement humans make given its intricate combinations of gross and fine motor movements for accurate output for the purpose of communication. For speech to occur, the brain first creates a motor plan and program to instruct and coordinate movements of the articulators. This motor program is then executed with the signals traveling from the central nervous system to the peripheral system. This complex system is capable of speech production at rapid speeds. For example, Guinness World Records lists Canadian Sean Shannon as the world's fastest English talker with a rate of 655 words per minute (Guinness World Records). Yet how is the motor system able to produce speech at such speed while also maintaining accuracy for clear, intelligible verbal communication? How does the system monitor and correct for errors when

necessary? And to what extent can impairment to this system account for speech output problems in speakers with brain damage? This current study aims to address these questions by investigating the speech error processing system in people with brain lesions to the left hemisphere, known to house key areas for speech sensorimotor processing, and to identify behavioral and neural correlates of impairment in speech error detection and correction.

Based on contemporary models of motor control, recent models of speech motor control include a feedback and feedforward control mechanism. *Feedback control*, in the motor speech context, refers to the system that monitors the sensory output of the vocal tract and articulators (i.e., the resulting sounds, movements, and sensations) and uses the information (i.e., the resulting auditory, somatosensory, and proprioceptive feedback) to guide the next set of commands to the articulators for production. This feedback can be used to cancel the signals from the desired sensory output to result in an error signal that can be transformed into a corrective command (Guenther, 2016). *Feedforward control* refers to a generative system that creates the motor commands based on a set of previously learned and stored representations for a syllable or phoneme production without monitoring the incoming acoustic and/or somatosensory feedback from these commands (Guenther, 2016). The understanding of the feedforward system and its components was developed when scientists pondered how both speed and accuracy are achieved with motor movements. If motor movement correction was purely feedback-dependent, it would result in slower movements due to the inherent synaptic delays in the sensory system resulting in increased time required

for the feedback to be received, processed, and motor movements to be corrected. This shortcoming of feedback control was addressed by the conceptualization of the feedforward system and the development of what is now known as the *efference copy* and *corollary discharge* mechanisms.

To understand the concepts of efference copy and corollary discharge, it is first necessary to understand the efference and afference mechanisms. These two systems describe the input and output of neuronal signals to and from the central nervous system when body movement occurs. *Efference* specifies that motor signals are traveling, or descending, from the central nervous system to the peripheral structures to initiate the target movement. Conversely, *afference* is when sensory signals ascend from peripheral structures to the central nervous system. Like a two-lane highway, these pathways for signals help the subject navigate within and engage with their environment.

As mentioned previously, the brain uses feedforward mechanisms that help to regulate the input and output of motor signals. Efference copy is one facet of the feedforward mechanism. Specifically, the *efference copy* is hypothesized to involve projections from the motor to sensory system to provide an internal prediction about anticipated feedback that is used by the brain to process differences between expected body movement and the body movement that actually occurs. The term efference copy was initially coined by von Holst and Mittelstaedt (1950) in their studies of the visual system which will be examined further in the upcoming paragraph. Also in 1950, Roger Sperry first used the term

corollary discharge to refer to a representation of the predicted sensory consequences of a motor act. Roger Sperry's experiment is also detailed below.

von Holst and Mittelstaedt (1950) first broadened our understanding of efference copy in their experiments on the visual system inspired by the problem of space constancy (Vallortigara, 2021). That is, how are we able to perceive stable visual surroundings despite shifts of the visual input from eye movements? Eyes move, heads move, and bodies move; however, visually, our immediate environment is perceived as stable – how can this be? Holst and Mittelstaedt hypothesized a mechanism in which a copy of the signal emitted from the brain's motor areas generates an expected self-induced sensory input that is sent to the visual system (i.e., the retina). This expected signal arising from the efference copy provides negative feedback that is compared to, and subtracted from, the actual retinal image shift. A match between expectation and reality would cancel the effects of self-generated movement resulting in space constancy (Bridgeman 2010, Figure 1.1).

To test this theory, Holst and Mittelstaedt inverted the head of the *Eristalis* fly by anchoring its inverted head to its body with a piece of wax. Under normal conditions, it would be expected that the input from the visual system would allow the fly to move in its desired target direction. However, the fly with the inverted head continuously rotated in circles. Moreover, when the fly was pushed to one direction, it further deviated in the same direction rather than compensated in the opposite direction to stabilize itself. This was because the externally-generated inversion of the head converted the negative feedback to positive feedback

resulting in an additive, rather than cancellation, effect of the feedback resulting in further deviation of movement in the same direction (Bridgeman, 2010; von Holst and Mittelstaedt, 1950; Villortigara, 2021). Interestingly, they observed that in darkness, when there was reduced sensory input from the visual system, the fly's movement appeared normal. These findings supported the presence of an efference copy within the visual system that adjusts for self-generated movements resulting in space constancy. Contemporaneously, Sperry (1950) was also doing animal studies on the visual system. For his studies, Sperry surgically rotated the eyes of southern swellfish by 180 degrees.

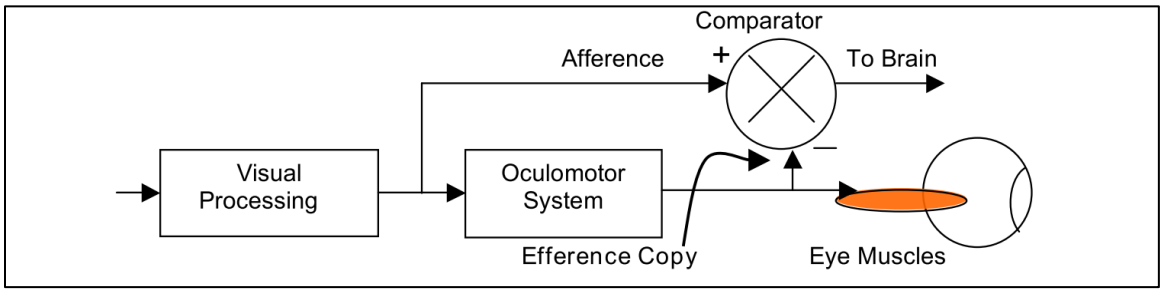


Figure 1.1 Schematic of use of efference copy to achieve space constancy. "Information flows into the system from the left and out to the right. Efference copy is subtracted (-) from the visual input, afference (+), at a comparator to present a stable representation to the brain" (Bridgeman, 2010).

He observed similar findings and came to similar conclusions contributing the term "corollary discharge" to refer to the sensory predictions. Together, these studies provided the foundation for the efference copy and corollary discharge mechanisms within the feedforward system that was later applied to speech motor control.

The phenomena described by Holst, Mittelstaedt, and Sperry were not exclusive to the fly or the frog, nor were they exclusive to the visual system. The concepts of, and evidence for, efference copy and corollary discharge have been

examined in other organisms and other sensorimotor modalities. For example, Crapse and Sommer (2008) reviewed the presence of corollary discharge across the animal kingdom covering a variety of animals such as crayfish, crickets, bats, finches, and monkeys. Blakemore, Wolpert, and Frith (1998) elaborated on the role of an efference copy and corollary discharge in humans to provide a causal relationship between actions that allow for us to distinguish between the sensory consequences from self-produced versus externally-produced stimuli as applied to limb movements and touch. For example, how is it that a self-produced tickle is perceptually less ticklish than when the tickling originates from someone else? This is an illustration of the effects of efference copy and corollary discharge. Theoretically, during the act of self-tickling, the efference copy of the intended hand and finger movements generates a corollary discharge of the predicted sensory consequences of that self-touch. When there is a match between the sensory prediction and the actual sensory consequences of the motor action, there is at least a partial cancellation of the neural activity in response to sensation within the central nervous system. Therefore, the sensory input from self-produced stimuli decreases sensitivity to the stimulus (i.e., the tickle) (Blakemore, Wolpert & Frith, 2006). This is because self-generated movements result in calculable expected sensory consequences that can be predicted, and hence, cancelled within the central nervous system. In contrast, an externally generated tickle lacks the central cancellation of expected sensory consequences because external stimuli do not elicit activation of the efference copy and resulting corollary discharge.

Evidence for the efference copy and corollary discharge has also been studied in the auditory system as it relates to communication. For example, Poulet and Hedwig (2006) provided evidence from the singing cricket on the identification of a single interneuron representative of a corollary discharge that controls the pre-synaptic and post-synaptic inhibition of auditory neurons. Notably, Eliades and Wang (2003, 2008) did extensive work to examine the neural substrates of the auditory-vocal system during vocalizations in non-human primates. Specifically, Eliades and Wang (2003, 2008) were the first to identify neurons in the auditory cortex that were subject to vocalization-induced modulation in non-human primates, marmoset monkeys, under normal auditory feedback (NAF) and altered auditory feedback (AAF) conditions. The use of an animal model here allowed for more invasive and precise exploration of auditory cortex activity through the use of implanted microelectrode arrays and single-unit neural recordings. In 2003, Eliades and Wang reported that single-unit recordings in the auditory cortex expressed two different neural responses during self-initiated vocal production: a vocalization-induced suppression and vocalization-related excitation. *Vocalization-induced suppression* was the term used to describe the reduction in neural activation to below the level of spontaneous activation. This suppression was observed at an average of about 200 ms prior to the onset of self-vocalization and continued after voice onset. The pre-vocal timing of this suppression is suggestive of cortical inhibition, possibly as a result of the corollary discharge (Eliades and Wang, 2003, 2019). The majority (65% to 90%) of neurons in the auditory cortex of the marmosets expressed this suppression. A smaller

percentage of neurons exhibited a vocalization-related excitation response that only began after voice onset. These neurons demonstrated increased neural activation in response to self-vocalization and are suggested to reflect the sensory response to the auditory feedback from vocalization (Eliades and Wang, 2003, 2019).

In 2008, Eliades and Wang reported on an AAF experiment in marmoset monkeys that were implanted with two multi-electrode arrays in bilateral auditory cortices. In this study, the signal from voluntary, self-initiated vocalizations was altered by shifting the voice frequency by ±2 semitones (i.e., ±200 cents where each ±100 cents or semitone is the frequency difference between two adjacent notes on the Western musical scale) and fed back to the marmosets via customized headphones. Interestingly, the neurons that were suppressed during vocalization in the NAF condition tended to exhibit increased activity during vocalization in the AAF condition when compared with the activity measured in the NAF condition. Further, while the firing rate of those neurons increased during AAF, their overall activity was still suppressed as compared with the pre-vocal activity (Figure 1.2). This suppression during vocalization, yet modulation of neuronal activity in response to external alterations in auditory feedback, provided further support for the top-down influence of a feedforward mechanism to modulate tuning properties and increase sensitivity of auditory neurons for feedback error detection during vocal production. It was further demonstrated that the patterns in modulation of neural activity in the auditory cortex could not have been in response to auditory feedback alone (Eliades and Wang, 2008). These studies by Eliades

and Wang informed subsequent studies on feedforward mechanisms within the human auditory-vocal communication system.

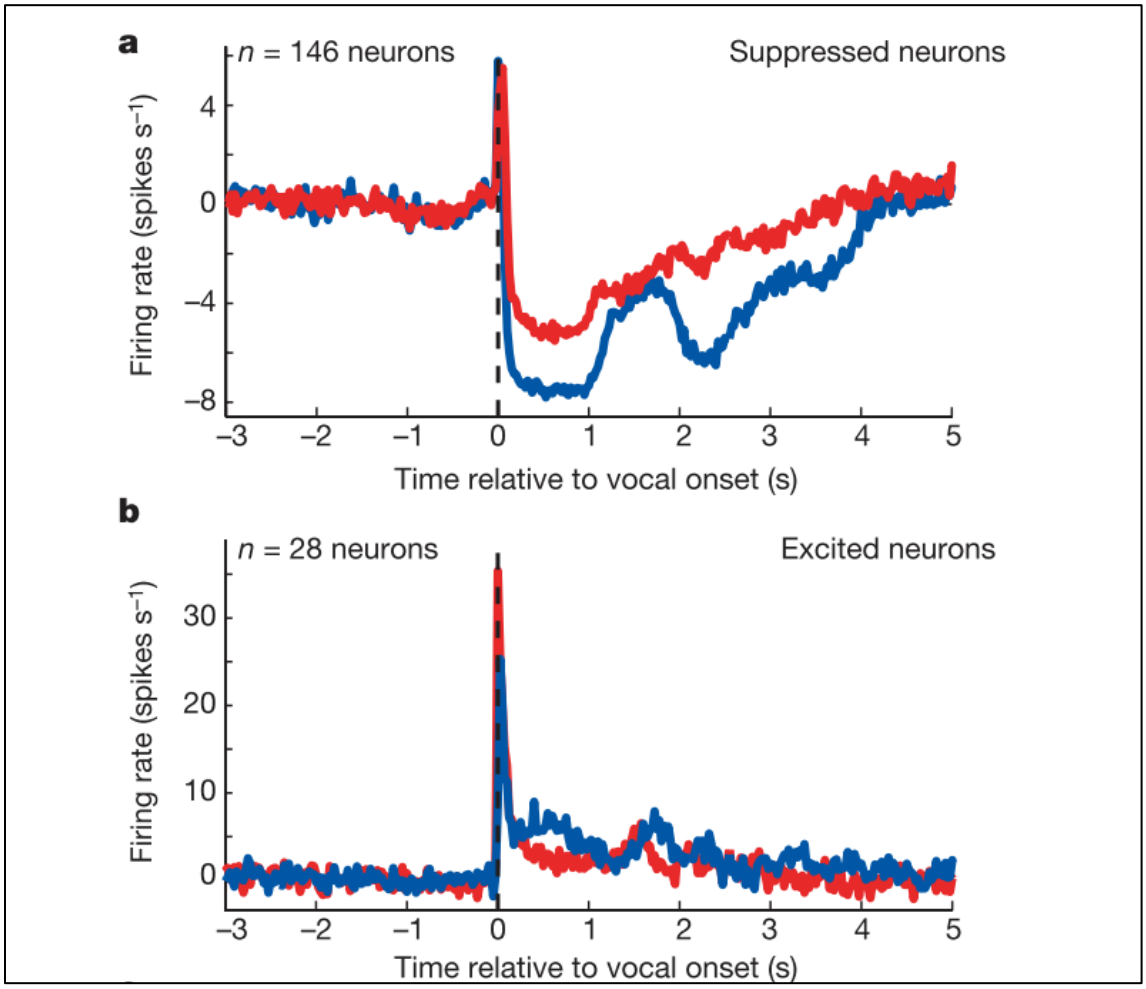


Figure 1.2 Modulation of activity in suppressed and excited neural populations. Average neural population responses to vocalizations in the baseline/NAF condition (blue) and AAF condition (red). Firing rates during AAF were increased in suppressed neurons but slightly decreased in excited neurons (from Eliades and Wang, 2008).

Efference copy and corollary discharge in human speech motor control are integrated into contemporary models of human speech motor control to explain self-monitoring of output and self-correction of speech errors and the contribution of the auditory system for the purpose of communication. In typically developed, neurologically intact speakers, contemporary models of speech motor control

propose that speech is controlled by a feedforward motor system that incorporates sensory feedback from auditory and somatosensory modalities for online detection and correction of speech production errors (Golfinopoulos, Tourville, & Guenther, 2010; Guenther, Ghosh, & Tourville, 2006; Hickok, 2012; Houde & Chang, 2015; Houde & Nagarajan, 2011; Tourville & Guenther, 2011). The principles of these integrative mechanisms are based on the notion of an internal forward model that translates the efference copies of speech motor commands into corollary discharges that provide predictions about the sensory consequences of intended verbal outputs (Wolpert, Ghahramani, & Jordan, 1995). During speech production, the difference between the predicted sensory feedback from the forward system and the actual sensory feedback results in an error signal that is translated into corrective motor commands in the auditory-motor system for speech control (Figure 1.3). In the following sections, the principles of some of the contemporary models of speech production are reviewed in the context of current theories about the role of efference copy mechanisms in sensorimotor integration and motor control.

1.2 CONTEMPORARY MODELS OF SPEECH MOTOR CONTROL

Three prominent models of speech motor control reviewed here include the following: the State Feedback Control (Houde and Nagarajan, 2011), Hierarchical State Feedback Control (Hickok, 2012), and Directions Into Velocities of Articulators (Guenther, 1995; Guenther, Ghosh, & Tourville, 2006; Guenther, Hampson, & Johnson, 1998; Guenther & Vladusich, 2012; Tourville & Guenther, 2011). Commonly, these models consist of a feedback and feedforward

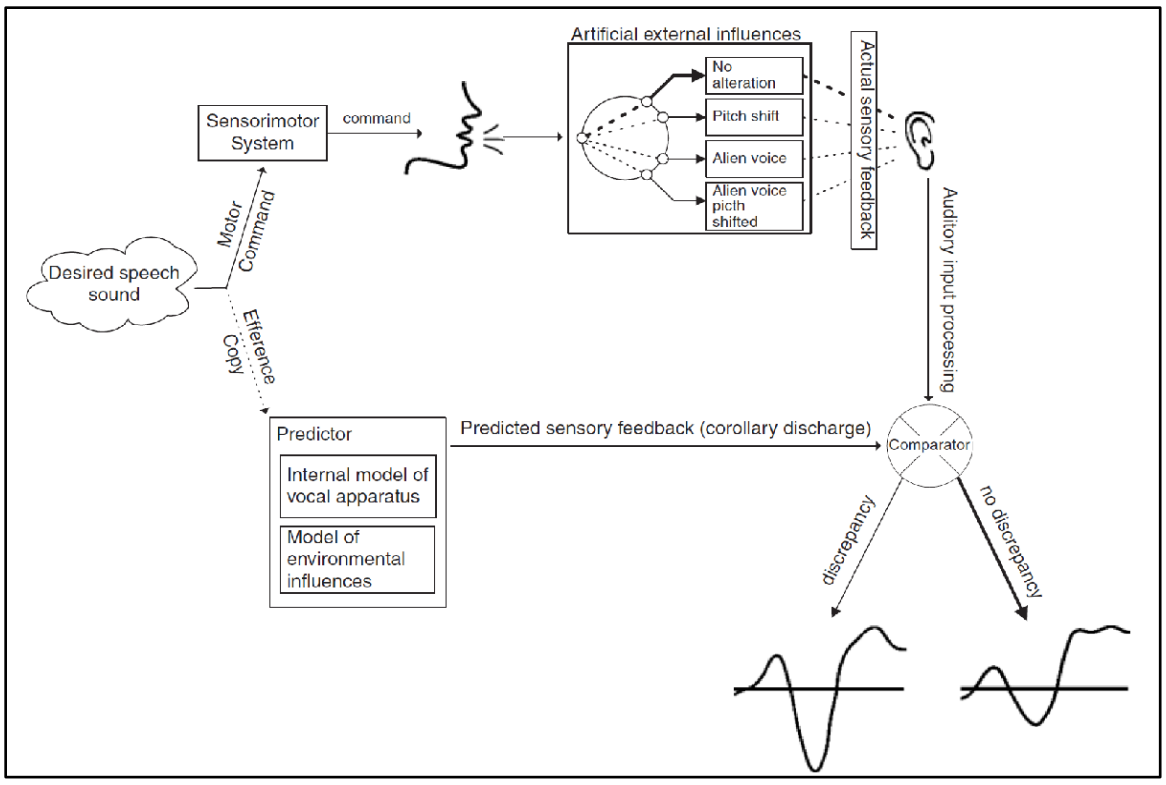


Figure 1.3: Model of the auditory neural consequences of speech (Heinks-Maldonado et al., 2005).

component, with feedback being the incorporation of the sensory (i.e., auditory) information. The feedforward component varies in name and origin, depending on the model. Feedforward control may be referred to as the efference copy, predictive control, or predictive feedforward mechanism.

State Feedback Control

The State Feedback Control model (SFC; Figure 1.4) as applied to speech motor control was posited by Houde and Nagarajan (2011) and was derived from state feedback control theory in limb and hand motor control studies (Shadmehr & Krakauer, 2008; Todorov, 2004; Todorov & Jordan, 2002). SFC features the use of an efference copy that is utilized to generate a prediction (the term corollary discharge is not explicitly used in this model) of the expected sensory feedback

from the vocal tract. During speech, the articulatory motor plan is sent from the primary motor cortex to the vocal tract. Control of the vocal tract is driven by an estimate of the current state (i.e., the current position of the structures) of the vocal tract which consists of an interaction between feedback predictions generated in the motor cortex compared with the actual feedback from the somatosensory and auditory cortices. From this, corrections to the system are generated if errors are detected (Houde & Chang, 2015).

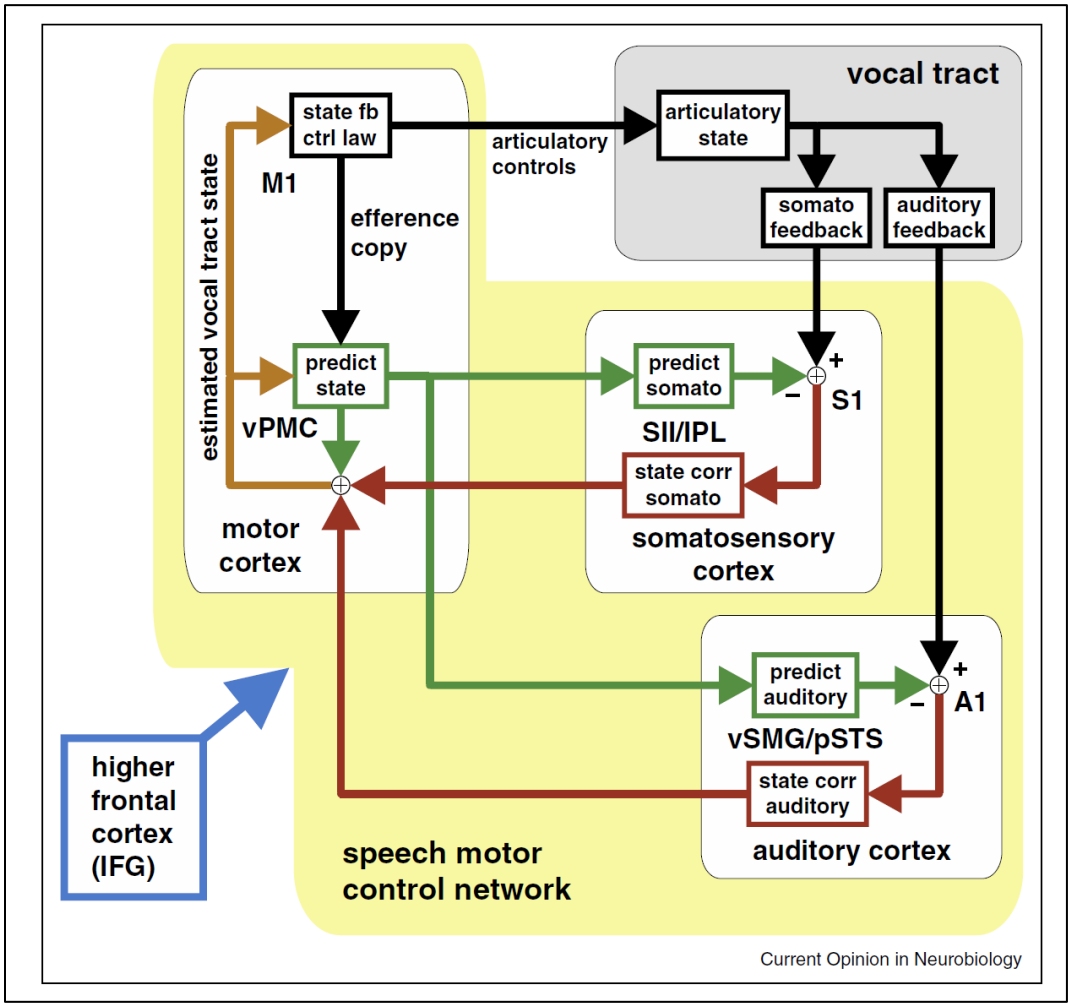


Figure 1.4 State Feedback Control Model by Houde and Chang (2015)

Hierarchical State Feedback Control

Created as a descendant of SFC, the Hierarchical State Feedback Control (HSFC) model (Figure 1.5) was proposed by Hickok (2012) and was named for its hierarchical organization with a higher- and lower-level. The higher-level codes speech information at the syllable level whereas the lower-level codes speech information at the level of articulatory features (i.e., voice, place, and manner). Each hierarchical level has its own forward prediction and feedback control loops and consists of motor programs (syllable or phoneme), sensory targets, and a coordinate transform where the computation between sensory and motor representations of speech units (i.e., sensorimotor integration) occurs. Speech production occurs with activation of the motor and auditory units for the intended utterance. When the motor system is activated, a forward prediction of the expected corresponding auditory units is compared within the coordinate transform. When the motor and sensory units match, the sensory targets are inhibited. When there is a mismatch, or error, between motor and sensory units, an excitatory inverse correction signal is generated to allow the sensory targets to excite the correct motor units while nontarget units are inhibited (Guenther and Hickok, 2016).

Directions Into Velocities of Articulators

The Directions Into Velocities of Articulators (DIVA) model (Figure 1.6) was derived from non-speech motor control models and was developed by Frank Guenther as a computational model of speech acquisition and production (Guenther 1995, 2016; Guenther et al., 2006; Tourville & Guenther, 2011) based

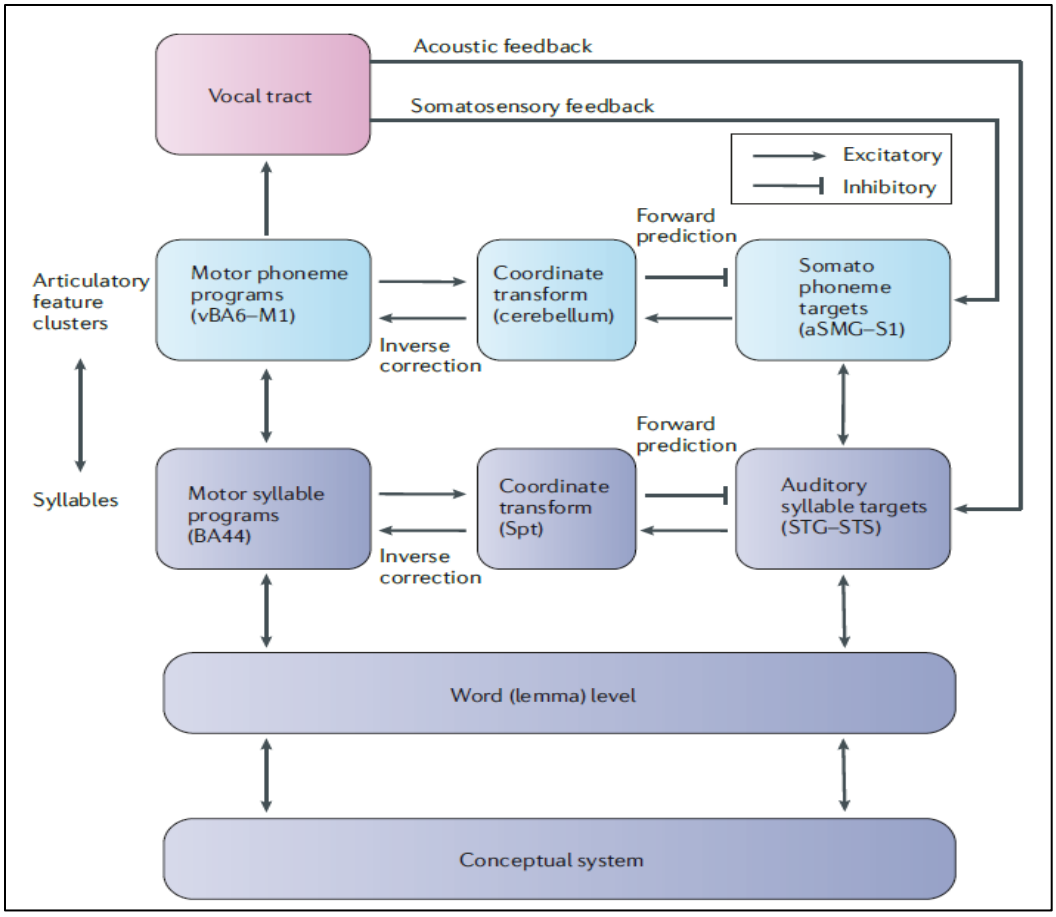


Figure 1.5 Hierarchical State Feedback Control model by Hickok (2012)

on the feedback error learning model of control (Kawato & Gomi, 1992). The DIVA model is comprised of a feedforward and feedback control system. The feedforward control system uses learned motor programs to produce speech sounds and is comprised of an initiation map, a speech sound map, and an articulator map. The feedback control system is where mismatches between sensory expectations and actual sensory feedback are monitored. The feedback control system consists of separate auditory and somatosensory feedback components that are invoked when errors from their respective sensory modalities are detected. The desired positions and velocities of the speech articulators are

guided by a final motor command that is the sum of the output from the feedforward and feedback controllers (Guenther, 2006, 2016).

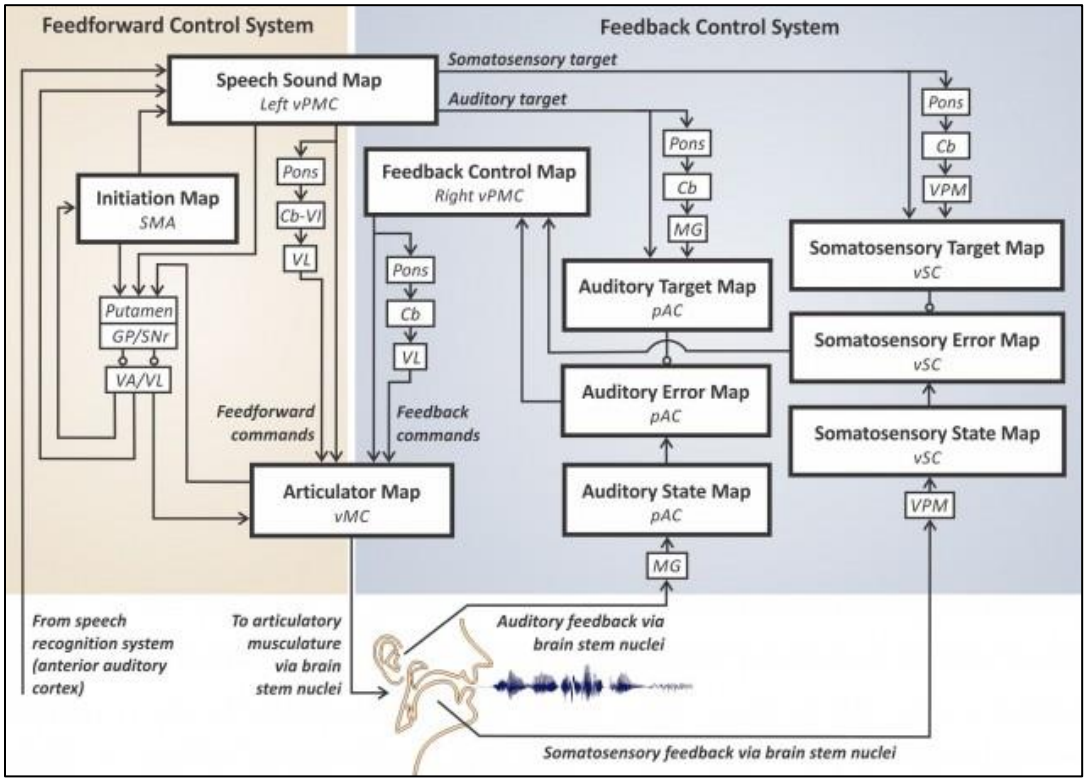


Figure 1.6 Directions Into Velocities of Articulators model (Guenther, 2016)

As exemplified by the three speech motor control models above, components corresponding to the motor actions of the articulators and the predicted sensory correlates of the intended utterance are involved in self-monitoring, error detection, and correction of speech errors. There are notable differences between the models such as external error monitoring mechanism in DIVA versus the internal and external error monitoring mechanisms in HSFC, or the hierarchical arrangement of the lower-level somatosensory feedback loop and higher-level auditory loop (Guenther and Hickok, 2016). However, the common concept of the forward system is most relevant to this current study: it is still not

well understood to what extent impairment to the forward system mechanisms (e.g., efference copy, corollary discharge) accounts for deficits in speech error processing for motor control.

1.3 SPEECH-INDUCED SUPPRESSION AND SPEECH PERTURBATION RESPONSE ENHANCEMENT EFFECTS

Electrophysiological and neuroimaging studies in humans have provided evidence for the presence of an efference copy and corollary discharge in speech motor control through two neurophysiological response patterns: *speech-induced suppression (SIS)*, also referred to as vocalization-induced suppression, and *speech-perturbation response enhancement (SPRE)*, or vocalization-induced enhancement. SIS occurs when the neural response to one's self-produced speech is significantly suppressed relative to the neural response produced when the person passively listens to a playback of their speech. The notion behind SIS is that the suppression occurs when the predicted sensory consequence from the corollary discharge at least partially cancels out the actual sensory consequences from the auditory feedback. That is, in a normal system, when there is a match between the sensory prediction and reality, there is at least a partial cancellation, or suppression, of the neural activity. In the context of forward models, when the corollary discharge generated by the efference copy during active vocalization is a close match to the actual auditory feedback, a small auditory response is elicited due to the central cancellation of sensory signals. The SIS effect provides evidence for the implication of efference copy and corollary discharge mechanisms in the speech system. When there is no active motor system producing a corollary

discharge for sensory prediction and cancellation of effects, such as in a passive listening condition, a larger auditory response is elicited (Behroozmand and Larson, 2011; Chang, Niziolek, Knight, Nagarajan, & Houde, 2013; Houde et al., 2002; Niziolek, Nagarajan, & Houde, 2013).

The ability to differentiate between self-produced and externally-produced speech aids in self-regulation. This response pattern has been observed in marmoset monkeys (Eliades & Wang, 2003) as well as in crickets (Poulet & Hedwig, 2006). In humans, SIS has been observed using a variety of brain measures, including magnetoencephalography (MEG; Curio et al., 2000; Houde et al., 2002; Niziolek et al. 2013; Numminen & Curio, 1999), electroencephalography (EEG; Behroozmand 2009; Heinks-Maldonado, 2005, 2006), positron emission tomography (PET; Hirano et al., 1996, 1997; Wise et al., 1999), and electrocorticography (EcoG; Chang et al., 2013; Greenlee et al., 2011; Houde & Chang, 2015), with paradigms in which neural responses are compared during active vocalization vs. passive listening to the playback of the same self-produced vocalizations.

The SIS effect tends to be observed in early auditory neural response components, elicited in areas within the primary cortical auditory networks. Such neural responses can be detected with various noninvasive brain imaging methods. For example, MEG and EEG directly measure brain activity with high temporal resolution in a matter of milliseconds, with the tradeoff of poorer spatial resolution compared with neuroimaging techniques such as magnetic resonance imaging (MRI). MEG records magnetic fields whereas EEG records electrical

potentials resulting from firing of a large number of neurons in the brain. MEG studies have observed SIS at the M100 component, and EEG studies have observed this in the N1 (or N100) event-related potential (ERP) component, though the SIS effect does not necessarily occur exclusively at these specific neural components and can vary in latency depending on the dynamic nature of the performed speech tasks (Houde et al., 2002; Houde & Chang, 2015; Heinks-Maldonado et al., 2005; Rollnik, 2019). ERPs are changes in the recorded brain activity that are time-locked to the onset of an event including, but not limited to, the processing of sensory stimuli and performing a wide range of sensorimotor and cognitive tasks. For example, several studies on speech auditory feedback processing have shown the N1 ERP component to be suppressed in response to NAF during production vs. listening tasks. This suppression is dampened when the person's auditory feedback is altered to mismatch their expected feedback (Houde et al., 2002; Houde & Chang, 2015; Heinks-Maldonado et al., 2005). In another study, Houde et al. (2002) found that bilateral magnetic field recordings of human participants revealed that evoked responses to self-produced speech were weaker than responses to a taped playback of their speech (Houde et al., 2002).

In addition, the underlying neural mechanisms of speech auditory feedback have been examined using other non-invasive methods such as PET that indirectly measures brain activity through changes in hemodynamic responses. Hirano et al. (1997) conducted the first PET study that reported a SIS effect where there was significant auditory cortical activation in the supplementary motor area (SMA) but no activity in the superior temporal gyrus (STG) during vocalization. The opposite

activation pattern was observed when participants' voices were externally manipulated during playback: there was significant activation of the STG but no activity in the SMA (Hirano et al., 1997).

In more recent years, researchers have leveraged the advantages of invasive ECoG recordings to better understand the neural mechanisms of speech feedback processing via directly measuring brain activity from subdural electrodes implanted I neurosurgical patients. This allows for both high temporal and spatial resolution, though ECoG data are difficult to obtain given the invasiveness of the procedure. ECoG studies have also shown the SIS effect localized to clusters within the superior temporal gyrus (STG) - anterior and posterior to the lateral termination of the transverse temporal sulcus (TTS) – and a portion of the posterior STG (Chang, Niziolek, Knight, Nagarajan, & Houde, 2013; Greenlee et al., 2011; Houde & Chang, 2015).

Another neurophysiological response pattern reflective of efference copy in speech sensorimotor control mechanism is SPRE. Compared to the neural response to passive listening, SPRE is an enhanced auditory cortical response, observed when an unexpected perturbation (e.g., pitch shift) is applied to the online auditory feedback during vocalization (Chang et al., 2013; Greenlee et al., 2013). The underlying neural responses associated with the SPRE effect may receive contributions from multiple networks in the primary and higher-level cortical auditory areas as well as sensorimotor networks implicated in speech error processing. For example, Behroozmand et al. (2009) showed a significant enhancement of the P2 ERP component during vocalization in humans with an

online pitch perturbation, ranging from +100 to +500 cents applied to the auditory feedback when compared to the ERP activity during passive listening. They also found a significant main effect of pitch-shift magnitude with a greater SPRE effect for the smaller pitch-shift magnitudes shedding light on the sensitivity of the auditory system. It was suggested that the sensorimotor system is more sensitive to smaller deviations in auditory feedback from the expected target as these are perceived as self-produced versus externally-induced errors. Larger deviations from the target, however, may be perceived as non-self which would not be deemed necessary to correct and therefore would require relatively less allocation of neural resources to process (Behroozmand et al., 2009). Similar to SIS, SPRE was expressed only in select electrode sites in an ECoG study by Chang et al. (2013) (Figure 1.7). The cortical areas in the Chang et al., (2013) ECog study that expressed SPRE included sites within the ventral premotor cortex, posterior superior temporal cortex including the temporal-parietal junction, and the anterior extent of the STG. (Chang et al., 2013). Notably, the Chang et al., (2013) ECog study showed that many electrode sites expressed SIS but not SPRE, and vice versa (Chang et al., 2013; Houde & Chang, 2015). Additionally, their study also showed that electrode sites with greater SPRE activity were more likely to be predictive of the correlation between electrode site and vocal compensatory behavior. This prediction was not observed for SIS activity (Chang et al., 2013).

In summary, select auditory neurons that are activated during self-vocalization have heightened sensitivity to external stimuli as there is a specific speech and communication target to be achieved. Additionally, select auditory

neurons fired during passive listening have dampened response comparatively because there is a lack of internal comparator and passive listening is not as specifically goal directed as active self-vocalizations.

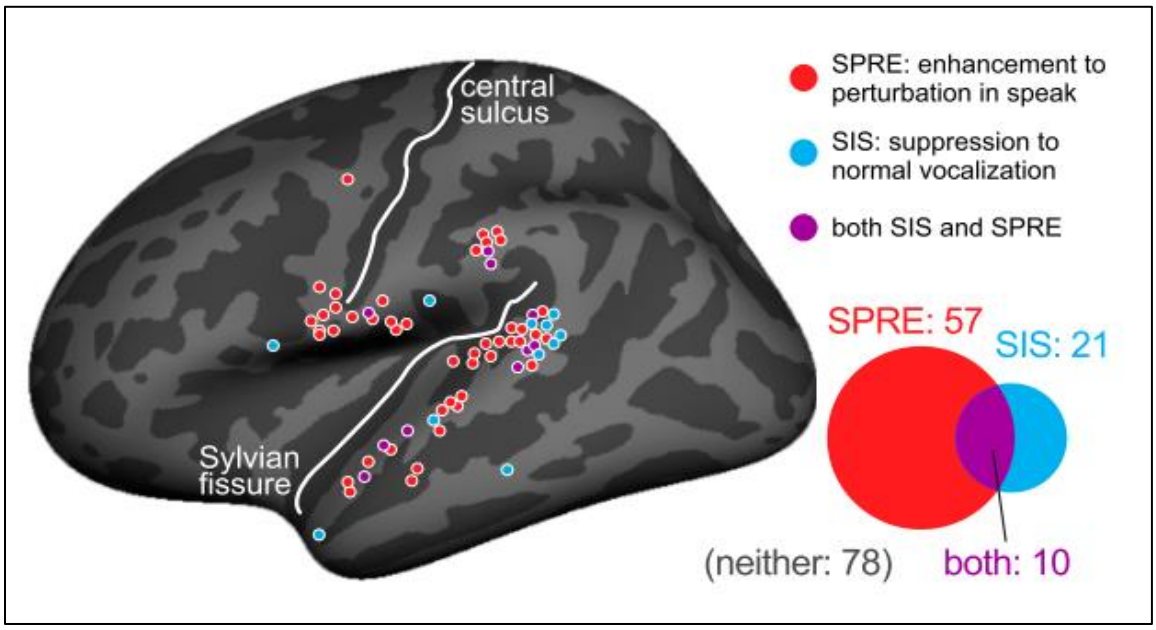


Figure 1.7 Spatial distribution of SPRE and SIS electrodes from Chang et al.'s (2013) ECoG study. "Points were mapped from individual subject's brains to an average surface; any electrodes that appear to be positioned in the sulci are the result of surface coregistration inaccuracies. Gyri are light gray; sulci are dark gray." (Chang et al., 2013)

1.4 SPEECH ERROR DETECTION AND THE AAF PARADIGM

The altered auditory feedback (AAF) paradigm is utilized in many speech production studies to investigate the speech sensorimotor system (e.g., Behroozmand et al., 2009; Burnett et al., 1998; Chen et al., 2012; Elman, 1981; Houde et al., 2002; Korzyukov et al., 2012; Larson, 1998; Scheerer and Jones, 2014). In AAF studies, the speech signal is electronically manipulated (i.e., altered) and fed back to the person's auditory system. Common forms of AAF include delayed auditory feedback (DAF), formant-shifted AAF, loudness-shifted AF, and pitch-shifted AAF. The AAF paradigm may be used to probe the integrity of the

speech system and give an indication of error detection and sensorimotor control processes. Specific auditory neurophysiological ERP responses are elicited from the AAF paradigm, highlighting important aspects of sensory-motor mechanisms involved in voice motor control that has been the focus of a number of studies (e.g., Behroozmand et al., 2009; Behroozmand & Larson, 2011; Chen, Chen, Liu, Huang, & Liu, 2012; Heinks-Maldonado et al., 2005; Heinks-Maldonado, Nagarajan, & Houde, 2006; Houde, Nagarajan, Sekihara, & Merzenich, 2002; Korzyukov, Karvelis, Behroozmand, & Larson, 2012; Scheerer & Jones, 2014). In particular, amplitude and latency differences of the P1-N1-P2 ERP components in response to pitch-shifts in voice auditory feedback are often examined (e.g., Behroozmand et al., 2009; Korzyukov et al., 2012; Scheerer & Jones, 2018). For example, in neurologically intact adults, AAF studies using unexpected pitch-shift stimuli (PSS) in auditory feedback have shown that a compensatory motor response is produced to correct for the perceived error (e.g., Liu, Wang, Metman, & Larson, 2012) accompanied by the activation of P1, N1, and P2 ERP components at different latencies relative to the onset of stimuli (e.g., Behroozmand et al., 2009; Scheerer, Behich, Liu, & Jones, 2013).

Contemporary speech motor control models provide an account for speech error detection and correction as it relates to activation of the sensorimotor system, though there are other perspectives to speech error monitoring, detection and correction to consider such as comprehension-based monitoring (Levelt, 1983; Roelofs, 1997) and conflict-based monitoring (Nozari et al., 2011). For example, Levelt's Perceptual Loop Theory consists of a central comprehension system that

monitors errors in both the accuracy of the phonetic plan of the inner speech and the accuracy of the overtly produced utterance via comparison with the intended message (Levelt 1983, 1989; Wheeldon and Levelt, 1995). Nozari et al. (2011) proposed the application of conflict-based error-detection can be applied to speech production which involves a domain-general error monitoring system, though they recognized the possibility that complementary speech monitoring mechanisms, including language-specific accounts, may simultaneously be involved. Their study on persons with aphasia revealed no significant correlation between speech error detection and comprehension measures but a strong correlation between error-detection ability and their model's characterization of the participants' production skills (Nozari et al., 2011).

As for cortical areas involved in error awareness and error detection in speech production, studies implicate the frontal, temporal, and parietal lobes of the brain to be involved in this process (Gauvin, De Baene, Brass, & Hartsuiker, 2016; Klein et al., 2007; Zarate & Zatorre, 2005, 2008). For example, an fMRI study by Zarate and Zatorre (2005) involving pitch-shifted auditory feedback in singers and non-singers revealed that both groups commonly showed increased activation in the inferior parietal lobule (IPL) and anterior cingulate cortex (ACC) in the presence of a pitch-shift condition. Another study by the same group also found that non-singers showed increased activity in the left supramarginal gyrus and primary motor cortex when instructed to ignore the pitch-shift in auditory feedback (Zarate & Zatorre, 2008). Furthermore, a study on error awareness revealed error-related activity bilaterally in the rostral cingulate zone, pre-supplementary motor area, and

insular cortex (Klein et al., 2007). Additionally, increased activation in the left anterior inferior insular cortex was noted for aware compared to unaware errors (Klein et al., 2007). Other studies have also supported the role of ACC in conflict monitoring (see Botvinick, Cohen, & Carter, 2004 for review). Studies on people with left-hemisphere lesions have also implicated left-hemisphere regions such as the inferior frontal, precentral, inferior parietal, and superior temporal cortices in auditory feedback error processing (Behroozmand et al., 2018, 2022; Hickok, 2012).

1.5 EVIDENCE FOR IMPAIRED EFFERENCE COPY AND COROLLARY DISCHARGE IN CLINICAL POPULATIONS

Dysfunction of the efference copy and corollary discharge has been described as a possible contributor to speech impairment and clinical symptoms such as stuttering (Brown et al., 2005), voice disorder in Parkinson's disease (Liu et al., 2012), and auditory hallucinations in psychosis and schizophrenia (Heinks-Maldonado; Ford and Mathalon, 2019). In stuttering, it is suggested that the repetition of the initial speech sound could be due to an over-active motor system resulting in impairment of the efference copy where the corollary discharge is delivered repeatedly as an inhibitory response to cancel out the effects of the actual input. This repeated delivery of the inhibitory response attenuates the effects of successful utterances (Brown et al., 2015). Alternatively with stuttering, it is proposed that stutterers can generate the efference copy signal but have difficulty with using the predictive information about the sensory consequences of

speech production which leads to repeated attempts to of correction resulting in fluency breakdown (Kim & Max, 2014; Daliri & Max, 2015).

AAF studies on people with Parkinson's disease (PD) found that participants with PD had significantly larger magnitudes of vocal response to pitch-shift stimulus applied to the auditory feedback compared with age- and sex-matched neurotypical control participants (Liu et al., 2012). The role of the efference copy in this has a couple of different potential explanations: First, individuals with PD may have a reduced efference copy leading to incorrect comparisons of predicted and actual sensory feedback resulting in larger compensatory responses. Second, if individuals with PD have laryngeal somatosensory deficits, as shown by Hammer and Barlow (2010), then the feedback from the intact sensory modality (i.e., auditory) will be given increased weight. This could result in the enhanced magnitude of vocal responses in PD (Hammer and Barlow, 2010).

Efference copy and corollary discharge dysfunction may contribute to clinical symptoms in schizophrenia where individuals have symptoms involving difficulty to differentiate self from non-self (Feinberg, 1978). Auditory hallucinations are one example. Ford et al. (2001; 2007) provided neurophysiological evidence of impaired corollary discharge during speech in persons with schizophrenia. The SIS effect was observed in neurotypical control participants with respect to the N1 ERP component. However, a reduction in N1 magnitude during speech was not observed in patients with schizophrenia suggesting dysfunction of the mechanism for auditory cortex suppression in this clinical population. Deficient efference copy

and corollary discharge may result in overreliance on predictions contributing to auditory verbal hallucinations. In this context, individuals with overreliance on predictions believe auditory events have occurred when in reality there was no external auditory event (Ford et al., 2007; Heinks-Maldonado et al.; Ford and Mathalon 2019).

Another clinical population of interest is people with left-hemisphere stroke (LHS) as it has been established that brain areas in the left hemisphere are of significance for speech sensorimotor integration and processing (Hickok, 2012; Hickok et al., 2011; Hickok and Poeppel, 2004 ; Rauschecker, 2011). Thus, investigating the impact of lesions to the left hemisphere on speech production and error processing is of importance. Research attention has been directed toward investigating the speech processing system in persons with aphasia (PWA) as a consequence of left-hemisphere stroke. While aphasia is identified as a language disorder, there is evidence that some PWA may demonstrate deficits in lower-level audio-vocal processing (Robson et al., 2013), speech monitoring (Mandal et al., 2020; Oomen, Postma, & Kolk, 2005; Marshall et al., 1998, 2006; Sampson & Faroqi-Shah, 2011), and feedforward mechanisms in speech planning (Niziolek and Kiran, 2018), as well.

For some PWA, deficits can include impaired auditory speech processing following damage to areas in the left hemisphere causing a disruption in speech error processing (Basilakos et al., 2014; Feenaughty et al., 2017; Fridriksson, Guo, Fillmore, Holland, & Rorden, 2013). Previous studies from Behroozmand on participants with LHS, many with acquired aphasia, have utilized the pitch-shifted

AAF paradigm to investigate the speech sensorimotor system in this clinical population (e.g., Behroozmand et al., 2018; Johnson et al., 2020; Behroozmand et al., 2022). Behroozmand et al. (2018) studied 16 PWAs and 16 neurologically intact control subjects and combined lesion-symptom mapping analysis and vocal behavioral testing and showed that magnitude of vocal motor responses to AAF were significantly diminished in PWA compared with controls. Specifically, in PWA, the diminished AAF vocal motor response early on at 50 – 150 ms after pitch-shift onset was predicted by damage to auditory cortical regions within the superior and middle temporal gyrus. Further, the diminished AAF vocal motor responses in PWA at 150 – 250 ms was predicted by damage to the IFG, and, lastly, the magnitude of vocal responses at 250 – 350 ms were predicted by damage to the SMG. Additionally, PWAs with lower speech repetition task scores had greater degree of diminished vocal responses. Taken together, the findings suggested an association between damage to sensorimotor, more specifically auditory-motor, integration networks and impaired speech error processing that may relate to speech impairment such as deficits in repetition in PWAs (Behroozmand et al., 2018).

Johnson et al. (2020) reported on vocal compensation responses to AAF on a total of 24 PWA, including 15 PWA from the Behroozmand et al. (2018) study. They found that PWA generate slower vocal compensation response to AAF compared with controls, though there was not significant difference in magnitude of vocal response between PWA and neurologically intact controls when controlling for timing of responses. They also found no relationship between self-

correction of naming errors and the timing and magnitude of vocal responses, which may be suggestive of a dissociation between lower-level voicing and higher-level linguistic processing.

Following the Behroozmand et al., (2018) study, Sangtian et al. (2021) reported on vocal motor responses and conscious error detection using the pitch-shifted AAF paradigm during vocalization and listening. While the Sangtian et al. (2021) study did include the control and PWA participants from the earlier studies (e.g., Behroozmand et al., 2018; Johnon et al., 2021), additional participants were added to both groups, resulting in an increased sample size of 34 individuals with left-hemisphere stroke and 25 neurologically intact control participants. Yes/No button press responses were collected immediately after each trial for participants to indicate whether they detected a pitch-shift in their auditory feedback. They showed the LHS group had a statistically significant lower error detection accuracy rate compared with control participants, irrespective of task (vocalization vs listening) and trial conditions (pitch-shift vs. no-pitch-shift). In the LHS group, speech error detection accuracy rate during the listening task was correlated with the magnitude of vocal response in the time window of 150 – 250 ms following pitch-shift onset. Further, the speech error detection accuracy rate during the vocalization task was correlated with repetition scores according to the Western Aphasia Battery-Revised (Kertesz, 2007) in the LHS group as an index of language impairment.

Most recently, Behroozmand et al. (2022) reported on vocal behavioral, ERP, and lesion-mapping results from the pitch-shifted AAF paradigm during

vocalization and listening to examine how damage to left-hemisphere sensorimotor brain networks impairs speech auditory feedback processing and motor control, combining techniques to provide both good temporal and spatial resolution. They found group differences in modulation of ERP responses during normal (no-pitch-shift) auditory feedback with neurologically intact control participants exhibiting stronger ERP activity compared with LHS at the P0, N1, and P1 components with largest contributions from the left fronto-centro and temporo-parietal electrodes. A main effect of task was found, with the P0 ERP component significantly stronger for vocalization vs. listening before voice onset and significant suppression of N1 and P1 components during vocalization vs. listening. Post-hoc analyses of the group-by-task interaction revealed significant suppression of N1 and P1 components in control participants but only significant N1 vocalization-induced suppression in the aphasia group. In general, the LHS group demonstrated reduced SIS response as reflected by activity in the N1 and P1 ERP components compared with controls. Group differences in modulation of ERP responses during AAF were also found, again with stronger ERP activity in control compared with LHS participants, but with respect to the P1, N1, and P2 components. A main effect of task showed stronger ERP responses for vocalization vs listening for the P1 and N1 components during AAF. Post-hoc analyses revealed stronger SPRE effects at P1 and N1 for controls and at N1 for LHS. There was an overall reduced SPRE effect in LHS versus control for P1 and N1, providing evidence for impaired efference copy mechanism. Vocal response analyses showed the LHS group had a significantly diminished magnitude of

response compared with controls from 150 – 350 ms post-stimulus onset. Lesion-symptom mapping analysis showed a negative correlation between SIS responses to NAF at the P1 component and larger vocal responses for controls but not LHS. In response to AAF, there was a positive correlation between SPRE of the N1 component and larger magnitude of vocal response in controls but not LHS indicating impairment or disconnect in sensorimotor processing and responses due to damage in LHS. ERP activity was correlated with reduced magnitude of vocal response to AAF compared with neurologically intact control participants (Behroozmand et al., 2022). As a whole, the Behroozmand et al. (2022) study identified specific cortical networks implicated in the processing of speech auditory feedback, error detection, and vocal motor control.

1.6 RESEARCH AIMS

The purpose of this study is to further our understanding of the speech error processing system and to identify behavioral and neural correlates of impaired vocal efference copy mechanisms in the speech of people with history of left-hemisphere stroke. The neural mechanisms underlying speech deficits in this clinical population are still poorly understood. Deficits in sensory, motor, and/or sensorimotor integration mechanisms may account for the impaired vocal response behavior observed in previous studies of this clinical population. However, to what extent do these separate and integrated sensory and motor systems contribute to the deficit?

The current study uses a novel AAF paradigm by incorporating button press responses to determine whether deficits in vocal compensation are associated with

decreased ability in detecting pitch-shift error changes in the auditory feedback and/or aberrant modulation of ERP activities. The combination of behavioral and neural data in the current study can provide a more inclusive explanation for the source(s) of speech impairment. Yes/No button press responses provide indicators of the status of the sensory system for speech auditory feedback error detection while measures of speech AAF compensation and ERPs may provide behavioral and neurophysiological indicators of the status of the feedforward system (including the efference copy and corollary discharge), their influence on auditory feedback processing, and the status of the sensorimotor systems for speech motor control.

The first goal of this study is to examine behavioral correlates of speech error detection and vocal motor response in participants with LHS. Notably, previous pitch-shifted AAF studies on neurotypical adults have shown mixed findings with respect to the presence of an association between auditory perception and vocal motor response. For example, Hafke (2008) showed that participants could consciously perceive 50 and 99 cent pitch-shift magnitude changes in auditory feedback with a group average of greater than 80% accuracy of conscious pitch-shift detection. On the other hand, there is evidence of dissociation between perception and motor action with participants able to compensate vocally for AAF without perceptual detection of the pitch shift (Franken et al., 2018; Hain et al., 2000). Franken et al. (2018) conducted an experiment that intentionally set the PSS at a subliminal threshold of 25 cents and showed that behavioral vocal compensatory responses still occurred with activation of bilateral

auditory cortical areas via source reconstruction of early latency onset and offset related-responses. Event-related field analysis showed right-lateralized responses in auditory cortical areas and left-lateralized response to motor-related areas. These findings supported the concepts of an integrated auditory-motor system with presence of an efference copy.

In this current study examining speech error detection and vocal motor response in participants with LHS and neurologically intact controls, I hypothesized that participants with LHS would have poorer accuracy on the perceptual error detection task than controls. This impaired perception would be a result of damage to left-hemisphere networks that contribute to accurate auditory-feedback error processing (Hickok, 2012; Klein et al., 2007; Zarate and Zatorre, 2008). Additionally, previous studies on a subset of this current study's LHS sample revealed the LHS group had decreased accuracy, differences in magnitude and/or latency of vocal compensation, and aberrant ERP modulation (Behroozmand et al., 2018, 2022; Johnson et al., 2020; Sangtian et al., 2021). Further, I did not expect a difference in error detection accuracy between the vocalization versus listening tasks in controls, due to intact auditory processing mechanisms in this group. However, it is possible that deficits in auditory processing for speech error detection in LHS would be at least partially compensated for via access to efference copies (even residual), which in turn may lead to higher accuracy rates for error detection during vocalization compared with listening in this group.

With regard to the magnitude of vocal response to pitch shift during AAF, I hypothesized that the LHS group will demonstrate a significantly decreased

magnitude of vocal response compared with controls as a result of damage to sensorimotor networks implicated in speech error detection and motor correction (Behroozmand et al., 2018, 2022; Chang et al., 2013; Hickok 2012 Johnson et al., 2020). Decreased magnitude and slowed compensation in LHS compared with control participants has previously been demonstrated in a subgroup of this current study's participant pool (Behroozmand et al., 2018, 2022; Johnson et al., 2020; Sangtian et al., 2021).

Finally, in examining the association between magnitude of vocal response and average correct rate during vocalization among groups, I hypothesized that greater average correct rates during vocalization would be associated with increased magnitude of vocal response within the control group due to their intact auditory processing and vocal motor response mechanisms. I expect a weaker association between average correct rates and magnitude of vocal response in the LHS group compared with controls as a result of their cortical damage to sensorimotor networks affecting the speech error detection and processing system.

Aim1: To examine behavioral correlates of speech error detection and vocal motor response in participants with left-hemisphere stroke using the AAF paradigm.

Question 1: Are there differences in error detection ability between a) groups (left-hemisphere stroke versus control), and b) tasks (vocalization versus listen) as indicated by average correct scores from button press responses to AAF stimuli?

Hypothesis: There would be a significant difference between groups with lower average correct rates in the left-hemisphere stroke group compared with controls but no significant difference in average correct rates between tasks for either group. Alternatively, there would be no significant difference in rates between tasks in the control group; however, within the LHS group, there would be a higher average correct rate during vocalization compared with listening.

Question 2: Are there differences in magnitude of vocal response to AAF stimuli during vocalization between LHS and control groups?

Hypothesis: The LHS group would demonstrate significantly decreased magnitude of vocal response to AAF compared with controls.

Question 3: Are there associations between the magnitude of vocal compensation and average correct rate responses to AAF stimuli across tasks and groups?

Hypothesis: Greater average correct rates during vocalization would be associated with increased magnitude of vocal response for the control group. The association between average correct rates and magnitude of vocal response will be weaker for the LHS group compared with controls.

The second goal of this study is to examine neurophysiological correlates of speech error detection and vocal motor response in participants with left-hemisphere stroke compared with neurologically intact control participants. To do this, EEG data was collected concurrently with the behavioral data during the pitch-shifted AAF paradigm during vocalization and listening. ERP responses were analyzed with particular focus ERP components that reflect speech error

processing in the cortical auditory as well as potential higher-level sensorimotor networks. In this context, we aimed to focus on ERP components that express SIS and SPRE effects during vocalization and listening tasks consistent with previous literature (Behroozmand and Larson, 2011; Chang et al., 2013; Chen et al., 2012; Heinks-Maldonado et al., 2005; Heinks-Maldonado et al., 2006; Houde et al., 2002; Korzyukov et al., 2012). Within-group comparisons of ERP amplitude between tasks and difference waves of the mean amplitudes of ERP components during vocalization (a sensory-motor task) minus listening (a sensory task) were calculated. The resulting difference wave would reflect the motor-related, or vocalization-induced, neural activity that highlights the influence of efference copy mechanisms in speech sensorimotor processing. The hypothesis is that sensorimotor impairment due to left-hemisphere damage would be expressed as a deficit of efference copies and their forward sensory representations, which in turn is predicted to result in diminished suppression of ERP responses to NAF during vocalization vs. listening (i.e., a diminished SIS effect) in the LHS group compared with controls. Likewise, damage to sensorimotor mechanisms in the LHS group would result in diminished enhancement of ERP responses to AAF during vocalization vs. listening (i.e., a diminished SPRE effect) compared with the control group (Behroozmand et al., 2022; Chang et al., 2013; Houde and Chang, 2015).

Additionally, associations between neurophysiological responses and behavioral responses (i.e., average correct rates and vocal motor compensation magnitudes) were examined. I hypothesized there would be significant

associations between vocalization-induced ERP activity and average correct responses within the control group among both vocalization and listening tasks given this group's intact sensorimotor system. However, for the LHS group, I would only expect to find a significant association between vocalization-induced ERP activity and average correct rates during vocalization in case of relatively intact activation of efference copies. Otherwise, I would not expect significant associations between vocalization-induced ERP activity and average correct rates in the LHS group. Additionally, I hypothesized there would be a significant association between difference wave activity and magnitude of vocal motor response in the control group, but not in the LHS group, given the impact of damage to left-hemisphere sensorimotor networks.

Aim 2: To examine neurophysiological correlates of speech error detection and vocal motor response in participants with left-hemisphere stroke.

Question 1: What are the differences in neural processing of pitch-shifted altered auditory feedback (AAF) and normal auditory feedback (NAF) in participants with left-hemisphere stroke compared with neurologically intact controls?

Hypothesis 1a: There would be diminished suppression of ERP response to NAF (i.e., the SIS effect) during vocalization versus listening in the LHS compared with the control group.

Hypothesis 1b: There would be diminished enhancement of ERP response to AAF (i.e., the SPRE effect) during vocalization versus listening in the left-hemisphere stroke compared with the control group.

Question 2: Are there associations between vocalization-induced ERP activity under NAF and AAF and A) the magnitude of vocal motor responses across groups, and B) average correct rates across tasks and groups?

Hypothesis: There would be significant associations between vocalization-induced ERP activity and average correct responses within the control group among both vocalization and listening tasks. However, for the LHS group, there would be a significant association between vocalization-induced ERP activity and average correct rates during vocalization only. Additionally, there would be a significant association between difference wave activity and magnitude of vocal motor response in the control group, but not in the LHS group.

CHAPTER 2

METHODOLOGY

2.1 PARTICIPANTS

Forty-one participants with left-hemisphere stroke and 29 neurologically intact participants were recruited for this study. However, three participants with left-hemisphere stroke and two neurologically intact participants were unable to complete the full experiment due to fatigue or severity of speech and/or language impairment and were excluded. Therefore, a total of 38 participants with left-hemisphere stroke (LHS; 16 females; age range 38.43 – 80.02; mean age 61.28 years) and 27 neurologically intact control participants (19 female; age range 47.49 – 86.72; mean age 63.10 years) participated in this study. Stroke survivors were recruited from the Aphasia Lab and the Center for the Study of Aphasia Recovery at the University of South Carolina. Stroke survivor inclusion criteria were as follows: 1) history of left-hemisphere stroke, confirmed by MRI or CT scan, at least 6 months prior to testing in this study; 2) have undergone language assessments using the Western Aphasia Battery-Revised (WAB-R; Kertesz, 2007); 3) ages 30 years or above; 4) able to provide verbal and/or written informed consent.

This project was part of a study approved by the University of South Carolina Institutional Review Board (study title “Sensorimotor processing of auditory feedback in aphasia,” IRB Number Pro00066288 / Continuing Review Number CR00026696). LHS participants participated in the experiment at an

average of 5.76 years post-stroke and have a mean WAB-R Aphasia Quotient of 63.75 (range 17.8 – 99.6). The breakdown of participant demographic information and language assessment scores are found in Tables 2.1, 2.2, and 2.3. A map of the LHS participants' lesions is found in Figure 2.1. Neurologically intact control participants recruited from the greater Columbia, SC area were age-matched with LHS participants and had self-reported normal speech and hearing. Exclusionary criteria for both groups include self-reported history of dementia, traumatic brain injury, psychiatric disorder, other neurologic disorder, or alcohol abuse. Participants gave informed consent and were monetarily compensated for their time.

Table 2.1 Demographic Data for Control Participants

Participant	**Sex**	**Age**	**Education (Years)**
C1	Male	67.89	14
C2	Male	58.06	10
C3	Male	56.53	23
C4	Male	71.38	18
C5	Female	67.88	13
C6	Female	86.72	17
C7	Female	59.44	22
C8	Female	67.73	14
C9	Female	60.76	20
C10	Male	65.35	18
C11	Female	56.51	18
C12	Female	63.40	18
C13	Female	60.22	16
C14	Female	59.26	17

C15	Male	75.32	23
C16	Female	68.59	23
C17	Female	50.60	16
C18	Female	71.20	13
C19	Female	53.05	16
C20	Female	64.78	18
C21	Female	47.49	12
C22	Female	60.42	15
C23	Male	53.00	16
C24	Male	69.28	NR
C25	Female	68.00	12
C26	Female	63.80	16
C27	Female	57.00	16
Mean		63.10	16.69
Standard Deviation		8.35	3.48

Table 2.2 Demographic Data for Left Hemisphere Stroke Participants

Participant	Sex	Age	Edu-cation (Years)	Aphasia Type	Number of Strokes	Time Post-Stroke (Years)	Apraxia of Speech	Dys-arthria
LHS1	M	61.53	14	Anomic	1	15.54	No	Yes
LHS2	M	64.47	18	Conduction	1	7.66	No	No
LHS3	M	80.02	16	Anomic	1	5.17	NR	NR
LHS4	M	72.76	16	Broca's	1	20.45	No	No
LHS5	F	44.73	16	Broca's	1	13.16	Yes	No
LHS6	F	42.57	12	Above cutoff	1	10.79	NR	NR
LHS7	M	59.64	12	Anomic	1	6.47	NR	NR
LHS8	M	69.33	16	Broca's	1	4.91	No	Yes
LHS9	M	69.73	12	Conduction	1	2.92	Yes	Yes
LHS10	M	61.83	12	Broca's	1	2.80	Yes	No
LHS11	F	71.85	12	Broca's	1	2.08	Yes	No
LHS12	F	38.43	18	Broca's	1	1.63	Yes	No
LHS13	M	60.08	18	Broca's	1	9.30	No	No
LHS14	M	72.48	16	Anomic	1	1.90	No	Yes
LHS15	M	44.61	16	Broca's	1	2.15	Yes	Yes

LHS16	M	51.22	12	Broca's	1	1.75	Yes	No
LHS17	M	49.78	14	Global	1	3.17	Yes	No
LHS18	M	60.38	12	Broca's	1	2.31	Yes	Yes
LHS19	F	64.43	18	Broca's	2	17.51	Yes	No
LHS20	F	76.19	14	Broca's	1	4.99	Yes	Yes
LHS21	M	72.44	16	Broca's	1	4.09	Yes	Yes
LHS22	F	39.11	12	Anomic	1	1.85	Yes	No
LHS23	F	61.66	16	Conduction	2	2.14	Yes	No
LHS24	M	59.60	12	Broca's	1	4.11	Yes	No
LHS25	F	70.39	18	Above cutoff	1	7.90	NR	NR
LHS26	M	53.00	12	Conduction	1	5.59	No	No
LHS27	M	58.02	16	Wernicke's	1	1.16	Yes	No
LHS28	M	78.73	18	Conduction	2	7.59	No	No
LHS29	F	65.84	16	Anomic	1	1.52	No	No
LHS30	M	63.24	16	Broca's	2	1.33	Yes	Yes
LHS31	F	53.52	16	Conduction	2	2.51	No	Yes
LHS32	F	66.41	16	Anomic	1	3.72	No	No
LHS33	M	44.78	12	Broca's	1	4.58	No	No
LHS34	M	70.33	14	Broca's	2	0.92	Yes	Yes
LHS35	F	74.58	12	Broca's	1	5.66	No	No
LHS36	F	58.67	22	Above cutoff	1	8.31	No	No
LHS37	F	56.33	14	Above cutoff	1	15.61	No	Yes
LHS38	F	65.92	14	Conduction	1	3.81	NR	NR
MEAN		**61.28**	**14.89**			**5.76**		
Standard Deviation		**11.08**	**2.49**			**4.95**		

Table 2.3 Lesion Volume and Language Scores for Left Hemisphere Stroke Participants

Participant	Lesion volume (1000 voxels)	Fluency (10)	Spon-taneous Speech (20)	Auditory-Verbal Comp-rehension (10)	Rep-etition (10)	Naming (10)	WAB-AQ
LHS1	96.7	9	17	10	9.2	8.9	90.2
LHS2	148.8	6	9	7.1	0.9	0.2	34.4
LHS3	84.6	5	13	7.55	8.2	7.3	72.1
LHS4	234.6	3	10	7.05	4.4	6.2	55.3
LHS5	59	4	10	7.8	4	5.8	55.2
LHS6	53.4	9	19	9.55	10	9.8	96.7
LHS7	7.9	9	18	9.35	9.2	9	91.1
LHS8	210.9	2	5	6.95	4.2	2	36.3

LHS9	114.4	5	14	8.55	5.6	8.2	72.7
LHS10	220.1	7	11	4.15	7.4	3.5	52.1
LHS11	113.3	3	4	8.2	0.7	1.4	28.6
LHS12	185.1	4	11	7.15	6.7	7.9	65.5
LHS13	147.8	9	13	7.9	6.8	8.4	72.2
LHS14	5	6	15	9.8	8.8	8.5	84.2
LHS15	52.3	4	12	9.85	5.1	6	65.9
LHS16	177.1	2	8	6.7	6.6	5.2	53
LHS17	225.2	3	6	3.45	4.4	1.8	31.4
LHS18	114.4	1	3	8.3	1.6	2.8	31.4
LHS19	142.5	4	11	8.9	5.6	6.5	64
LHS20	225.9	1	3	7.5	0.9	1.3	25.4
LHS21	160.6	0	0	8	0.3	0.6	17.8
LHS22	139	9	19	8.6	8.9	9.6	92.2
LHS23	119	9	17	9	6.7	9	83.4
LHS24	116.7	4	11	7.55	6.2	8.3	33.05
LHS25	170	10	20	10	9.8	9.5	98.6
LHS26	63.5	6	13	9	6.2	8.7	73.8
LHS27	168.2	6	14	6.6	4.9	8.4	67.8
LHS28	118.3	5	13	8.45	3.7	5.1	60.5
LHS29	67.8	9	17	10	9.4	8.8	90.4
LHS30	120.9	4	13	9.5	7.7	8.5	77.4
LHS31	13.5	7	11	7.55	3.9	3.1	51.1
LHS32	43.9	8	17	7.75	8.5	6.7	79.9
LHS33	379.7	2	9	6.55	2	4.7	44.5
LHS34	57.123	4	11	9.95	7.1	7.8	71.7
LHS35	156.597	3	7	5.8	4.6	1.4	37.6
LHS36	1.088	10	20	10	9.8	10	99.6
LHS37	98.841	9	19	10	10	9.3	96.6
LHS38	92.269	5	14	8.3	5.4	6.8	69
MEAN	**123.84**	**5.42**	**12.03**	**8.12**	**5.93**	**6.24**	**63.75**
Standard Deviation	**77.31**	**2.84**	**5.11**	**1.57**	**2.86**	**3.03**	**23.49**

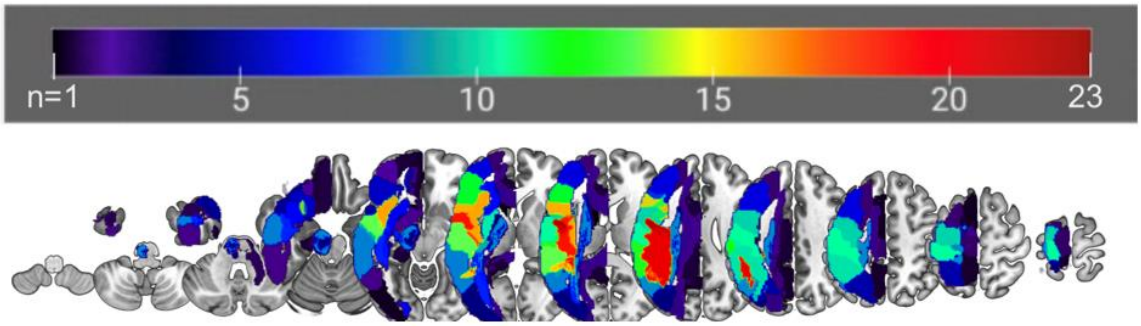


Figure 2.1 Lesion overlap map in left-hemisphere stroke participants (*n* = 38). The maps show lesion distribution on coronal (top) slices in MNI space with warmer colors representing more lesion overlap across LHS participants (dark red areas represent lesion overlap across at least *N* = 23 LHS participants). Maximum overlap areas include precentral and postcentral gyrus, inferior frontal gyrus (opercular and triangular), Rolandic operculum, insula, superior and inferior parietal gyrus, supramarginal gyrus, angular gyrus, middle frontal gyrus, caudate nucleus, putamen, Heschl's gyrus, superior temporal gyrus, superior temporal pole, and middle temporal gyrus where about 60% (23 out of 38) participants had lesions.

2.2 HEARING SCREEN

Participants underwent a pure-tone hearing screen prior to testing. 27 of 38 LHS participants and 20 of 27 control participants had thresholds of 25 dB HL (normal hearing) or less at 250, 500, 1000 and 2000 Hz in each ear. These hearing screening frequencies were selected based on the range of the natural human speech fundamental frequency (F0; perceived as pitch) for speech vowel sound production. Of the remaining LHS participants, six participants had hearing thresholds in the mild hearing loss range (26 to 40 dB HL); two in the moderate hearing loss range (41 to 55 dB HL) or below; one in the moderately severe hearing loss range (56 to 70 dB HL) or below; and two did not have a hearing screen on file. Of the remaining control participants, five had thresholds in the mild hearing loss range or below; one had thresholds in the moderate range or below; and one did not have a hearing screen on file. All participants were able to detect pitch-shift

stimuli as evidenced during the training session, and therefore, were included in this study.

2.3 EXPERIMENTAL DESIGN

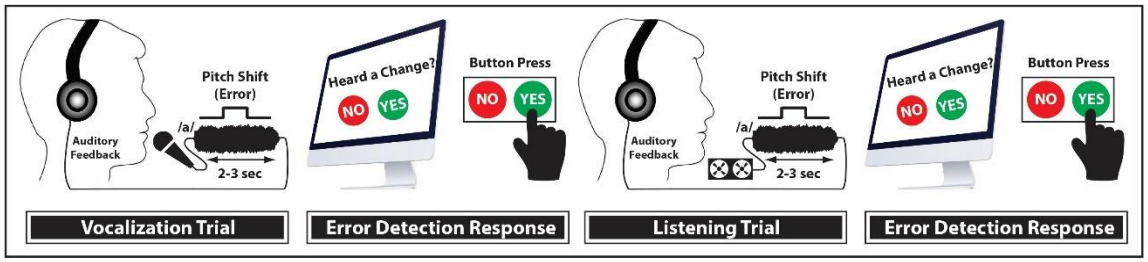


Figure 2.2 Experimental setup: Participants were cued to vocalize a speech vowel sound or listen to the playback of their self-vocalizations while a pitch-shift stimulus (i.e., error) altered the online auditory feedback or playback signal. In randomized control trials, no pitch-shift was delivered to vowel sound vocalization or its playback. Following each trial, participants were prompted to indicate whether or not they heard a pitch-shift change by pressing a green (Yes) or red (No) button (error detection response).

This study was conducted in a sound-attenuated booth at the University of South Carolina. Speech, EEG signals, and button responses were recorded during an altered auditory feedback task presented under two conditions: vocalization of the speech vowel sound “ah” listening to the playback of self-produced vocalizations. Participants viewed a computer screen that cycled through three visual cues: picture of a head (vocalization trial), picture of an ear (listen trial), and a red and green button with the words “Heard a Change? Yes or No” presented after each vocalization or listen trial (Figure 2.2). The experiment alternated between a vocalization trial, button press response, listening trial, and a button press response continuously over the span of two 45-minute blocks, with a ~10-minute break between blocks to reduce participant fatigue. Each vocalization and button press trial was followed by a listening trial to the playback of previous

vocalization and button press responses to indicate the presence or absence of AAF stimuli while the order and direction of pitch shifts were randomized across vocalization and listening trials. During the vocalization trial, participants viewed a picture of a head and were instructed to produce a steady vocalization of the vowel sound “ah” at their conversational pitch and loudness for approximately 2-3 seconds while listening to their voice feedback. A brief (200 ms) pitch shift stimulus of +/- 100 cents (100 cents = 1 semitone) randomly perturbed auditory feedback during vocalization trials with a time delay between voice and pitch shift stimulus onset randomized between 750-1250 ms. Next, participants engaged in a perceptual decision-making task where they were presented with the prompt “Heard a change? No or Yes” and were instructed to press a corresponding No or Yes button to indicate if they perceptually detected a pitch shift applied to their auditory feedback during active vocalization. Afterward, participants underwent a listening trial where they were presented with a picture of an ear with the instructions to sit quietly and listen to one of their previously recorded vocalization trials. During the listen trial, the pitch shift stimulus was randomly applied to the auditory feedback as described in the vocalization trial. Participants then pressed a button to indicate if they perceptually detected a pitch shift during the listen trial. The visual cues cycled repeatedly for an average of 360 trials in total per participant, i.e., an average of 180 trials per task (vocalization and listening) with a breakdown of approximately 60 trials with an upward pitch shift, 60 trials with a downward pitch shift, and 60 trials with no pitch shift. For this study, the upward

and downward pitch shift trials were combined for the pitch shift condition in analyses.

Training was provided prior to recording to ensure participants understood the instructions. Participants demonstrated understanding by appropriately responding to the visual cues and correctly detecting the pitch-shift during practice. Further instructions were provided in the form of additional verbal, written, and/or picture cues as necessary. Participants were monitored during the task and were allowed additional rest breaks as needed.

2.4 SPEECH AND EEG DATA ACQUISITION

Participants' speech signals were picked up using a head-mounted AKG condenser microphone (model C520), amplified by a Motu Ultralite-MK3 and recorded at 44.1 kHz on a laboratory computer. A custom-designed program in Max/Msp v5.0 (Cycling '74, Inc.) controlled an Eventide Eclipse Harmonizer that was used to pitch-shift the vowel sound vocalizations online and feed them back to the ears through insert Etymotic earphones (model ER1-14A). The Max/Msp program controlled all aspects of the visual cues and pitch-shift stimuli (e.g., direction, magnitude, onset time etc.) and also generated transistor-transistor logic (TTL) pulses to accurately mark the onset of each event during vocalization, listening, and button press tasks as well as synchronizing them with the simultaneously recorded EEG signals. A 10 dB gain between voice and its feedback was maintained to partially mask air-born and bone-conducted voice feedback during vocalizations. The EEG signals were recorded from 64 BrainVision actiCAP active electrodes (Brain Products GmbH, Germany) following

the standard 10-10 montage and a common average reference. A BrainVision actiCHamp amplifier (Brain Products GmbH, Germany) on a computer integrated with Pycorder software recorded the EEG signals at a 1 kHz sampling rate after applying a low-pass anti-aliasing filter with a 200 Hz cut-off frequency.

2.5 ANALYSIS OF BUTTON PRESS RESPONSES

True positive and true negative error detection rates, i.e., correct error detection accuracy rates for pitch-shifted trials (regardless of stimulus direction) and correct error rejection accuracy rates for control trials (no-pitch-shift), respectively, were computed for each LHS and control participant. Correct error detection (i.e., true positive) accuracy rates in percentage (i.e., correct detection of errors during pitch-shifted trials) were calculated for vocalization and listening tasks separately using the following formula:

$$Accuracy\ Rate_{\ Error\ Detection} = \frac{T_{Correct\ Error\ Detection}}{T_{Error}} \times 100$$

Here, $T_{Correct\ Error\ Detection}$ is the number of trials of correct error detection during pitch-shifted trials and T_{Error} is the total number of pitch-shifted (i.e., error) trials. Correct error rejection accuracy (i.e., true negative) rates in percentage (i.e., correct rejection of error during control/no-pitch-shift trials) were calculated for vocalization and listening tasks separately using the following formula:

$$Accuracy\ Rate_{\ Error\ Rejection} = \frac{T_{Correct\ Error\ Rejection}}{T_{NoError}} \times 100$$

Here, $T_{Correct\ Error\ Rejection}$ is the number of trials of correct error rejection during control/no-pitch-shift trials and $T_{NoError}$ is the total number of no-pitch-shift (i.e., no error) trials.

Button press (error detection) responses were analyzed by averaging the true positive and true negative rates for each individual to result in one average correct percent rate per task (i.e., each individual had one average correct percent rate for the vocalization task and another average correct rate for the listening task). This approach handled inflated or deflated rates due to response bias, where participants may have either responded “Yes” for all trials, resulting in 100% true positive and false positive rates and 0% false negative and true negative rates, or “No” for all trials, resulting in 0% true positive and false positive rates and 100% false negative and true negative rates.

2.6 ANALYSIS OF VOCAL MOTOR RESPONSES

Participants’ speech data were analyzed to extract the behavioral measure of AAF compensation responses relative to the onset of upward and downward pitch-shift stimuli during vocalization trials. First, the pitch frequency of the recorded speech signals was extracted in Praat (Boersma & Weenik, 1996), using an autocorrelation method, and then exported to a custom-made MATLAB code for further processing. The extracted pitch frequencies were segmented into epochs ranging from −100 ms before to 500 ms after the onset of pitch-shift stimuli. Pitch frequencies were then converted from Hertz to the Cents scale to calculate speech compensation magnitude in response to the pitch-shift stimulus using the following formula:

$$Speech\ Compensation\ Magnitude = 1200 \times \log_2(F/F_{Baseline})$$

Here, F is the post-stimulus pitch frequency and $F_{Baseline}$ is the baseline pitch frequency from −100 to 0 ms pre-stimulus. Artefactual responses to pitch shifts in

the auditory feedback due to large-magnitude voluntary vocal pitch modulations were rejected by removing trials in which speech responses exceeded +/-200 cents in magnitude. The extracted pitch contours were then averaged for each individual participant across all trials for upward and downward pitch shifts, separately. The upward pitch shift response values were multiplied by -1 to match the orientation of the downward pitch shift responses. The individual pitch contours were averaged across all participants to obtain the grand-average profile of the speech compensation responses for the aphasia and control groups. A minimum number of 115 trials were used to calculate the vocal motor response for each participant. Following this process, a total of 35 LHS and 26 control participants survived the analysis and were included in the final behavioral analyses for vocal motor response. Three LHS and 1 control participant were excluded from the final vocal motor responses as they did not meet the a priori minimum number of trials for inclusion due to artefact from excess noise from equipment and/or quality of vocal data collected. The local peak magnitude of vocal response was extracted from each individual during the time range of 100 to 400 ms post pitch-shift onset, as was the average vocal magnitude from each individual in 100 ms time-bins from 100 to 400 ms post pitch-shift onset. Additionally, exploratory tests were conducted on the time latency of the local peak magnitude of vocal response extracted from each individual during the time range of 100 to 400 ms post pitch-shift onset.

2.7 EEG DATA ANALYSIS

The EEGLAB toolbox (Delorme and Makeig, 2004) was used to analyze recorded EEG signals in order to calculate ERPs time-locked to the onset of voice

(NAF) and pitch-shift stimuli (AAF) during vocalization and listening trials, separately. The recorded EEG were filtered offline using a band-pass filter with cut-off frequencies at 1 and 30 Hz (−24 dB/oct), corrected for muscle artefacts (e.g., eye movements, saccades, etc.) using independent component analysis (ICA), and then segmented into epochs ranging from −200 ms before and 500 ms after the onset of voice (NAF) and pitch-shift stimuli (AAF). Individual epochs for each trial were subjected to baseline correction by removing the mean amplitude of ERP neural activity in a time window from −200 to-100 ms before pitch-shift stimulus onset in the altered auditory feedback condition, and -600 to -400 ms before voice onset in the normal auditory feedback condition based on visual inspection for stable baseline. The extracted epochs were averaged across trials to calculate ERPs for each participant across groups (LHS versus control) and tasks (vocalization versus listening), separately. A total of 10 different regions of interest (ROIs; 6 in AAF condition, 4 in NAF condition) were included in the analysis. The electrodes for each ROI are listed and visualized in Figure 2.3. The electrode sites were chosen based on visual inspection of topographic maps of regions demonstrating robust modulation of early ERP components. P1-N1-P2 ERP components were extracted at time windows of 20 to 80 ms, 100 to 180 ms, and 200 to 300 ms, respectively, during the AAF condition for both groups based on visual inspection of the prominent ERP latency visualized in the ERP profile at Cz, the central medial electrode, for consistency. P1-N1 components in the NAF condition, representing the first prominent positive and first prominent negative ERP components after voice onset, were extracted at time windows of 20 to 80 ms

and 100 to 180 ms, respectively. The speech motor-induced activity of ERP components was calculated by obtaining the differences in amplitudes between tasks (i.e., vocalization minus listening) for the LHS and control groups, separately.

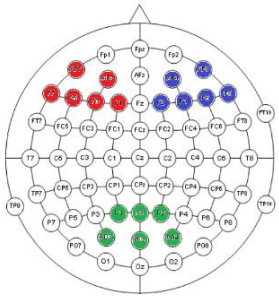
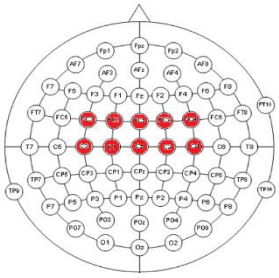
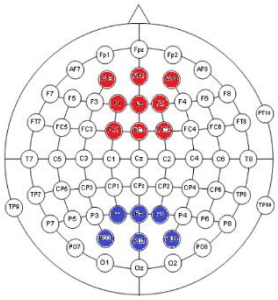
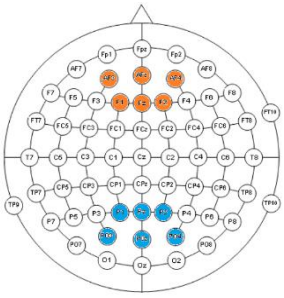
Regions of Interest for ERP Analyses	Electrodes Included in Each ROI
 **AAF P1** (20-80 ms)	**RED = ANTERIOR LEFT** AF7, AF3, F1, F3, F5, F7 **BLUE = ANTERIOR RIGHT** AF4, AF8, F2, F4, F6, F8 **GREEN = POSTERIOR** P1, Pz, P2, PO3, POz, PO4
 **AAF N1** (120-180 ms)	**RED = MEDIAL** FC3, FC1, FCz, FC2, C4, C3, C1, Cz, C2, C4
 **AAF P2** (200-300 ms)	**RED = ANTERIOR** AF3, AFz, AF4, F1, Fz, F2, FC1, FCz, FC2 **BLUE = POSTERIOR** P1, Pz, P2, PO3, POz, PO4
 **NAF N1** (20-80 ms) **and P1** (120-180 ms)	**ORANGE = ANTERIOR** AF3, AFz, AF4, F1, Fz, F2 **BLUE = POSTERIOR** P1, Pz, P2, PO3, POz, PO4

Figure 2.3 Electrode montages of ROIs.

2.8 STATISTICAL METHODS

Model diagnostics for testing the assumptions of normality and equal variance of the residuals were assessed using Q-Q plots for normality, and residual plots or Levene's test for homoscedasticity and homogeneity of variance, respectively. In the event of violation of homogeneity of variance, the adjusted values for equal variances not assumed were reported. Effect sizes were reported as partial eta-squared in the case of ANOVAs, and Cohen's d in the case of t-tests. Of note, button press and ERP responses to AAF were analyzed irrespective of pitch-shift stimulus direction in order to create a more consistent approach for analyzing data compared with the NAF condition in which all trials are averaged together for analysis. The raw p-values were reported for each test.

Aim 1 Statistical Methods

To investigate perceptual error detection performance based on button press responses (Aim 1, Question 1), a two-way analysis of variance (ANOVA) was conducted to examine the effects of group (LHS versus control) and task (vocalization versus listening) on average correct response rates as described in section 2.5. To examine differences in magnitude of vocal motor responses to AAF (Aim 1, Question 2) average vocal motor response magnitudes between groups were subject to independent sample t-tests in separate time bins of 101 – 200 ms, 201 – 300 ms, and 301 – 400 ms post stimulus onset with significance level for multiple comparisons corrected to alpha = 0.0167 using Bonferroni's method. Additionally, an independent t-test was conducted separately for the average local peak magnitude of vocal motor responses in the time range from 100 – 400 ms.

Correlation analyses examined the relationship between average correct rates during vocalization and vocal motor response magnitude among groups (Aim 1, Question 3). A subsequent correlation analysis was also conducted to examine the relationship between average correct rates during vocalization and average peak vocal motor response latency among groups.

Aim 2 Statistical Methods

To assess differences in neural processing of pitch-shifted altered auditory feedback (AAF) and normal auditory feedback (NAF) (Aim 2, Question 1), a few steps were taken. First, a two-way ANOVA was conducted to examine the effects of task (vocalization versus listening) and group (LHS versus control) on activity of ERP responses for each ERP component within each region of interest, separately. Statistical significance was assessed using a corrected Bonferroni threshold of alpha = 0.004 for the AAF condition and alpha = 0.006 for the NAF condition. This analysis focused on examining task and group as factors of interest as higher priority within the context of study hypotheses. Electrode location (e.g., frontality, laterality etc.) was irrelevant to study hypotheses and therefore was not included as a factor. This approach was important to minimize the number of factors in the statistical models for data analysis. Next, independent t-tests were conducted to assess between-group variations in difference amplitude (i.e., vocalization-induced ERP activity). Finally, linear regression models were used to see whether vocalization-induced ERP activity is associated with changes in a) vocal motor response magnitudes among groups, and b) average correct rates among tasks (vocalization versus listening) and groups (Aim 2, Question 2).

CHAPTER 3

RESULTS

3.1 HEARING THRESHOLD FREQUENCIES

Given the engagement of the auditory system, the Welch's t-test was used to examine if there were differences in hearing thresholds at the 250, 500, 1000, and 2000 Hz frequencies between the 35 LHS and 26 control group participants whose threshold data were collected (see Chapter 2). Results indicated no significant differences between these two groups for any frequency. Results are reported in Table 3.1.

3.2 BUTTON PRESS RESPONSES

A two-way ANOVA was conducted to examine the effects of group (LHS versus control) and task (vocalization versus listening) on average correct response rates for 38 LHS and 27 control participants. Results revealed a significant main effect of group ($F(1,63) = 17.763$, $p < .001$; partial $\eta 2 = .220$) with lower rates in the LHS group compared with controls (Figure 3.1). There was no effect of task ($F(1,63) = 1.347$, $p = 0.250$; partial $\eta 2 = .021$) and no interaction between task and group ($F(1,63) = 1.077$, $p = 0.303$; partial $\eta 2 = .017$). Additionally, an ANCOVA was conducted to examine the effect of task on average correct response rates while controlling for total lesion volume in the LHS group only. The covariate of total lesion volume was statistically significant ($F(1,36) = 4.526$, $p = 0.04$; partial $\eta 2 = 0.112$). The main effect of task was not significant

Table 3.1 Pure-Tone Hearing Thresholds and Statistical Output

Frequency Ear	Group	Mean	Standard Deviation	t-value	df	p-value
250 Hz Right	LHS	9.143	13.69	0.590	58.87	0.558
	Control	7.308	10.60			
500 Hz Right	LHS	4.429	14.34	-0.604	58.99	0.548
	Control	6.346	10.45			
1000 Hz Right	LHS	11.000	13.11	0.415	58.92	0.680
	Control	9.808	9.325			
2000 Hz Right	LHS	15.86	17.59	0.280	58.31	0.780
	Control	14.81	11.62			
250 Hz Left	LHS	8.429	13.33	0.267	57.16	0.791
	Control	7.692	8.152			
500 Hz Left	LHS	6.000	14.74	0.265	57.12	0.792
	Control	5.192	8.998			
1000 Hz Left	LHS	8.714	14.67	0.467	56.67	0.643
	Control	7.308	8.744			
2000 Hz Left	LHS	14.29	19.18	0.540	57.67	0.591
	Control	12.12	12.10			

(F(1,36) = 0.088, p =768; partial η2 = 0.002). Total lesion volume significantly affects the behavioral response rates. However, total lesion volume was not regressed from any measure as the impact from lesions is of interest to this study.

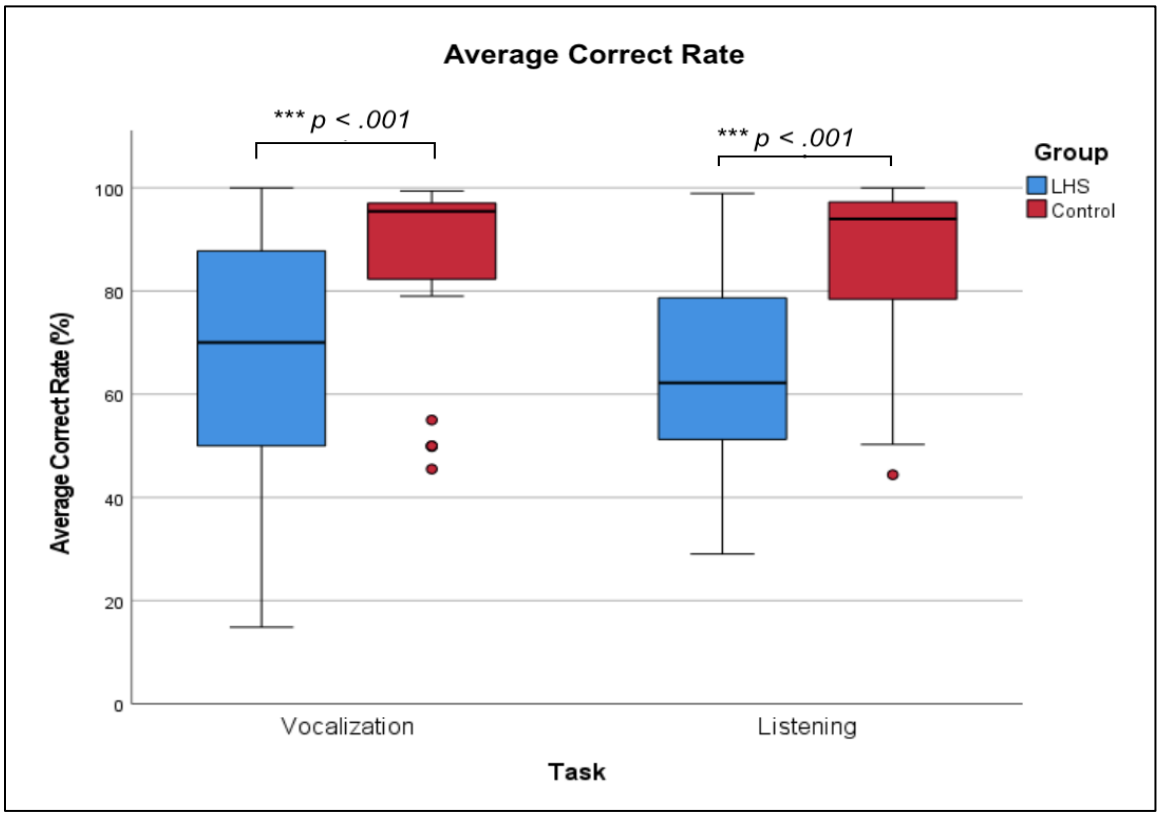


Figure 3.1 Box plots showing the average correct rate of button press responses for vocalization and listening tasks in LHS (blue) and control (red) groups.

3.3 VOCAL MOTOR RESPONSE MAGNITUDE AND LATENCY

In the time window of 100 ms to 400 ms post pitch-shift onset, there was not a significant difference between average local peak magnitude of vocal response to AAF in the LHS group (15.6 +/- 9.5 cents) compared with controls (19.8 +/- 9.6 cents), t(59)= -1.69, p = .096. Scatter plots showing the vocal

response magnitudes over time for individual control and LHS participants are visualized in Figures 3.2 and 3.3, respectively.

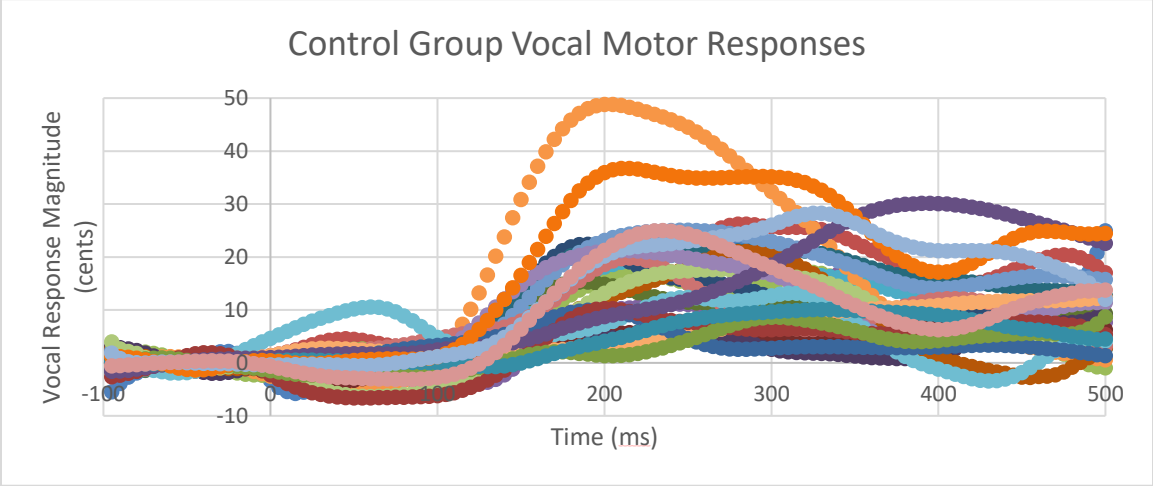


Figure 3.2 Scatter plot showing the vocal response magnitude over time for individual control participants. Time 0 indicates time of pitch-shift stimulus onset.

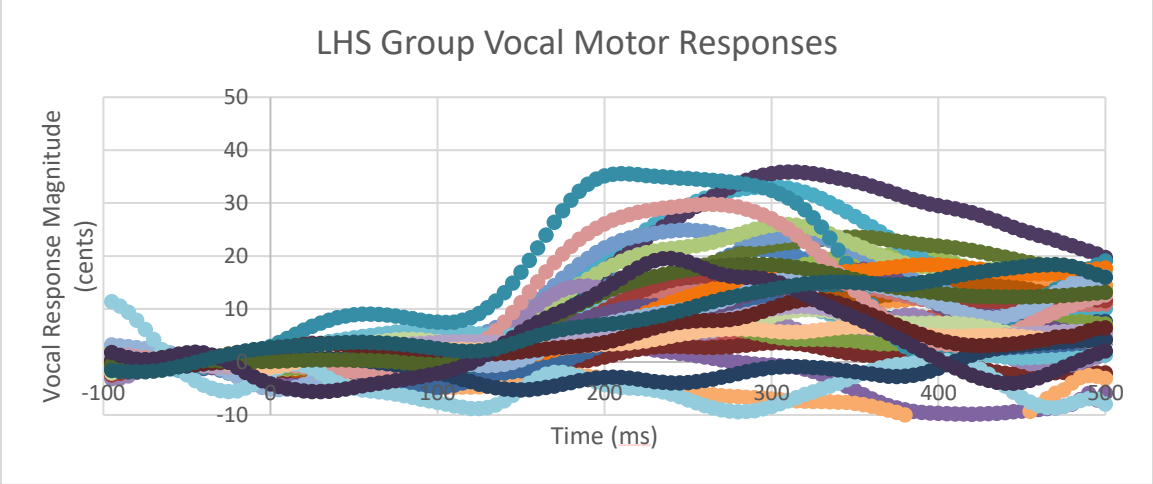


Figure 3.3 Scatter plot showing the vocal response magnitude over time for individual LHS participants. Time 0 indicates time of pitch-shift stimulus onset.

The magnitude of vocal responses was further analyzed by comparing the average magnitude of vocal response in 100 ms time bins from 100 ms to 400 ms post pitch shift onset (Figure 3.4). In the 101 to 200 ms time bin, the LHS group had significantly decreased magnitude of vocal response to the pitch shift in

auditory feedback (4.4 +/- 4.8 cents) compared with controls (8.2 +/- 6.3 cents), t(59)= -2.63, p =.004 (alpha = .016 after adjustment for multiple comparisons).

There were no significant differences between groups in the 201 to 300 (t(59) = -1.7, p = .031) or 301 to 400 ms (t(59) = -0.42, p = 0.225) time bins.

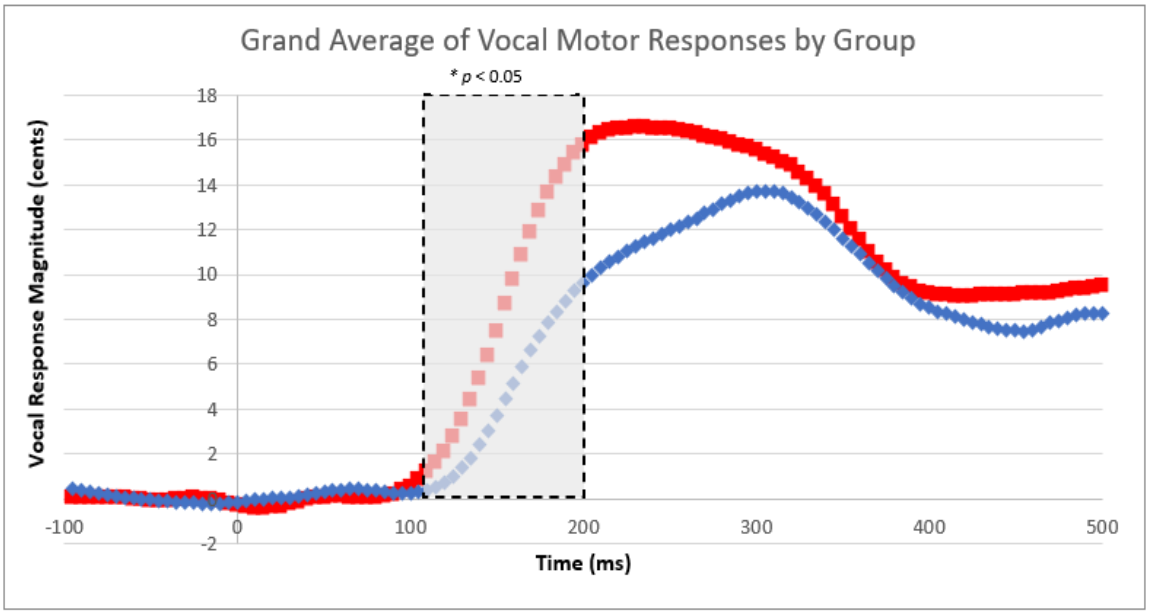


Figure 3.4 Scatter plot showing the grand average vocal response magnitude over time for the LHS (blue) and control (red) groups. Time 0 indicates time of pitch-shift stimulus onset.

An exploratory t-test was conducted comparing the latency of the peak magnitude of vocal responses, which revealed the LHS group had a statistically significantly longer time latency of peak vocal response (307.429 +/- 59.265ms) compared with controls (265.769 +/- 69.709ms), t(59) = 2.518, p = 0.015 (Figure 3.5).

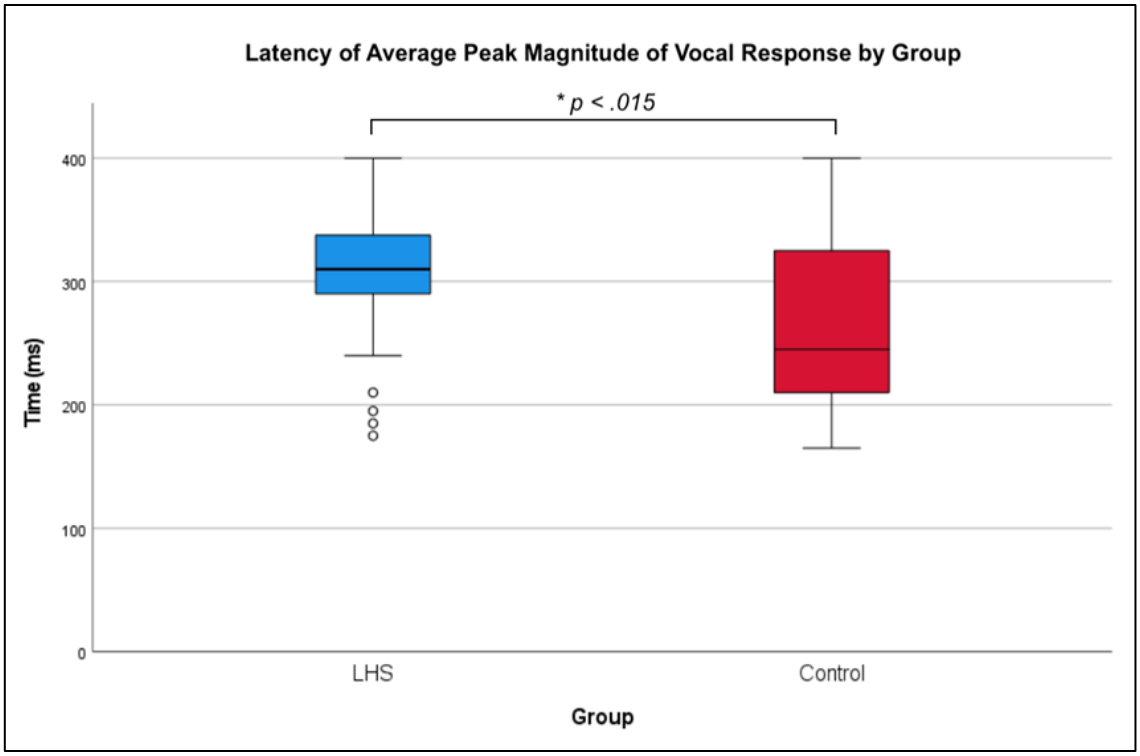


Figure 3.5 Box plots showing the average time latency of the average peak magnitude of vocal response in the 100 to 400 ms time window in LHS (blue) and control (red) groups.

3.4 ASSOCIATION BETWEEN BUTTON PRESS RESPONSES AND VOCAL MOTOR RESPONSE

Correlation analyses were used to examine the relationship between average correct rates during vocalization and vocal motor response magnitude among groups. No significant correlations were revealed. Results are reported in Tables 3.2 and 3.3. A scatterplot showing the average peak magnitude of vocal response in the 100 to 400 ms time window by average correct rate during vocalization among groups is in Figure 3.6A.

An exploratory correlation analysis was run to examine the relationship between average correct rates during vocalization and average peak vocal motor response latency among groups. There was not a significant correlation between

average correct rates during vocalization and average peak vocal motor response latency in the LHS group (r(33) = .002, p = 0.99) or control group (r(24) = .036, p = 0.86).

Table 3.2 Results of correlation analyses between average correct rates during vocalization and vocal motor response magnitude within the LHS group.

LHS Group		**Pearson Correlation (r)**	***df***	***p*-value**
Average Correct Rate during Vocalization	**Average Vocal Motor Response 101 – 200 ms**	.225	33	.194
	Average Vocal Motor Response 201 – 300 ms	.225	33	.194
	Average Vocal Motor Response 301 – 400 ms	.041	33	.813
	Average Peak Vocal Motor Response between 100 – 400 ms	.136	33	.437
Average Correct Rate during Listening	**Average Vocal Motor Response 101 – 200 ms**	.228	33	.187
	Average Vocal Motor Response 201 – 300 ms	.201	33	.246
	Average Vocal Motor Response 301 – 400 ms	.037	33	.835
	Average Peak Vocal Motor Response between 100 – 400 ms	.156	33	.370

Table 3.3 Results of correlation analyses between average correct rates during vocalization and vocal motor response magnitude within the control group.

Control Group		**Pearson Correlation (r)**	***df***	***p*-value**
Average Correct Rate during Vocalization	**Average Vocal Motor Response 101 – 200 ms**	.041	24	.842
	Average Vocal Motor Response 201 – 300 ms	-.074	24	.718
	Average Vocal Motor Response 301 – 400 ms	.02	24	.921
	Average Peak Vocal Motor Response between 100 – 400 ms	.015	24	.940
Average Correct Rate during Listening	**Average Vocal Motor Response 101 – 200 ms**	.266	24	.188
	Average Vocal Motor Response 201 – 300 ms	.064	24	.757
	Average Vocal Motor Response 301 – 400 ms	.195	24	.340
	Average Peak Vocal Motor Response between 100 – 400 ms	.152	24	.458

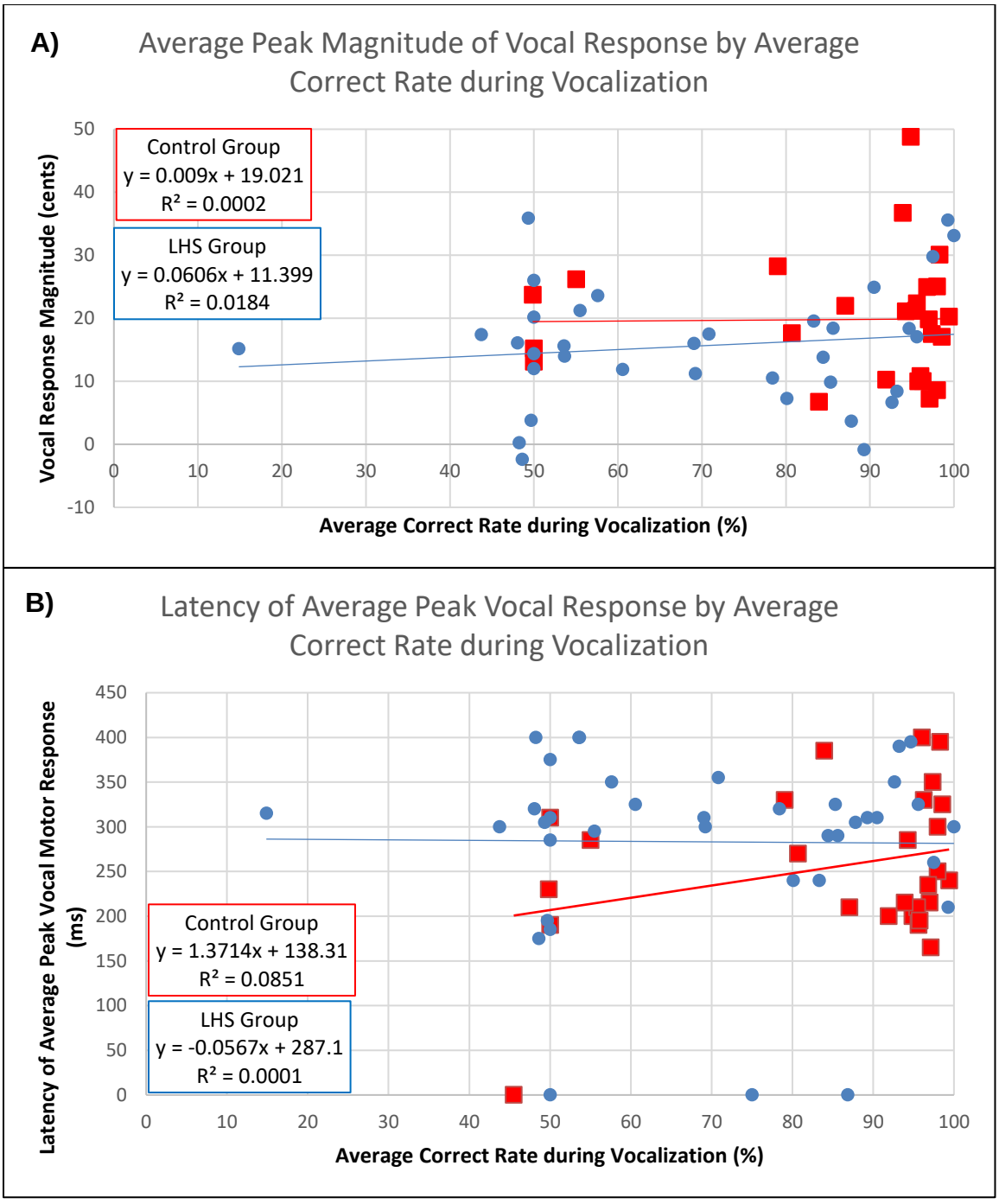


Figure 3.6 Scatter plots showing A) the average peak magnitude of vocal response in the 100 to 400 ms time window by average correct rate during vocalization, and B) the latency of the average peak vocal response in the 100 to 400 ms time window by average correct rate during vocalization for the control (red) and LHS (blue) groups.

3.5 NAF ERP RESPONSES

A two-way ANOVA was conducted to examine the effects of group (LHS versus control) and task (vocalization versus listening) on modulation of ERP responses for each ERP component within each region of interest, separately. The threshold for statistical significance was corrected for multiple comparisons at 0.006 for the NAF condition. Raw p values were reported. Results are found in Table 3.4. Results revealed a statistically significant main effect of group at the P1 anterior ROI ((F(1,63) = 9.649, p = .003; partial η2 = .133) with greater amplitude of ERP activity in the control group compared with the LHS group. By contrast, the t-tests conducted to compare vocalization-induced ERP activity between groups revealed no significant results (see Table 3.5).

Table 3.4 Results of the ANOVAs examining the effects of group and task on modulation of ERP responses within each NAF ROI.

ROI	**Variable**	***df***	***F***	**Raw *p*-value**	***partial η2***
NAF N1 Anterior	**Group**	(1,63)	7.517	**0.008	.107
	Task	(1,63)	0.990	0.323	.015
	Task*Group	(1,63)	2.741	0.103	.042
NAF N1 Posterior	**Group**	(1,63)	7.116	*0.010	.101
	Task	(1,63)	1.971	0.165	.030
	Task*Group	(1,63)	2.434	0.124	.037
NAF	**Group**	(1,63)	9.649	**0.003	.133

P1 Anterior	**Task**	(1,63)	.001	0.980	.000
	Task*Group	(1,63)	0.456	0.502	.007
NAF P1 Posterior	**Group**	(1,63)	5.696	*0.020	.083
	Task	(1,63)	1.234	0.271	.019
	Task*Group	(1,63)	0.758	0.387	.012
Asterisks distinguish the following probabilities based on raw *p*-values: *p<.05; **p <.01; ***p <.001					

Table 3.5 Results of t-tests comparing the amount of vocalization-induced ERP activity between groups in the NAF condition.

Difference Wave ROI	**Group**	**Mean**	**Standard Deviation**	**t-value**	**df**	**Raw p-value**	**Cohen's d**
NAF N1 Anterior	LHS	-0.29	2.21	-1.48^	34.04^	0.15^	-0.42
	Control	1.17	4.76				
NAF N1 Posterior	LHS	0.05	2.14	1.56	63	0.12	0.39
	Control	-0.97	3.12				
NAF P1 Anterior	LHS	-0.27	2.19	-0.61^	36.86^	0.54^	-0.17
	Control	0.25	4.03				
NAF P1 Posterior	LHS	-0.06	1.91	0.87	63	0.39	0.22
	Control	-0.57	2.73				
^ Indicates value with equal variances not assumed							

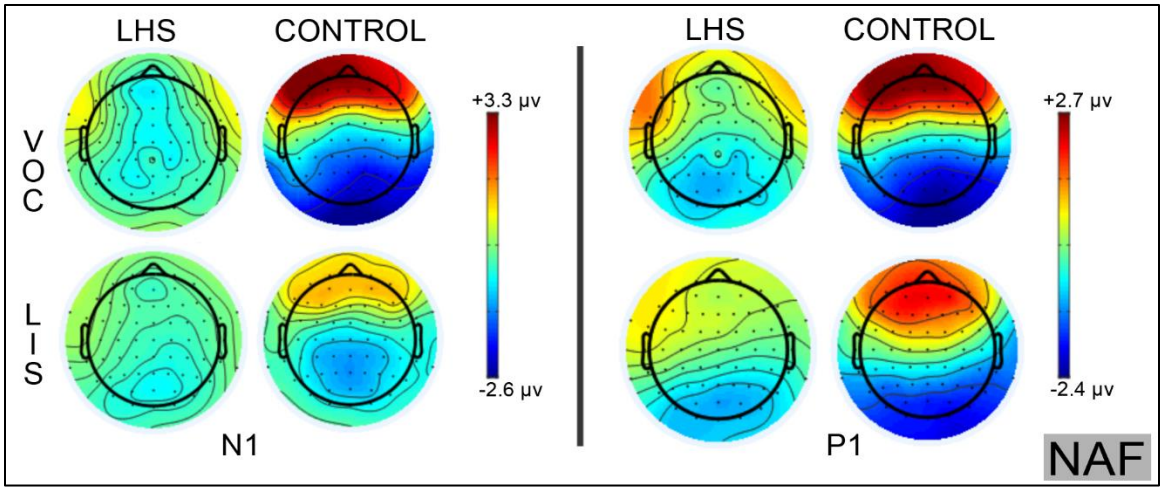


Figure 3.7 Topographical distribution maps of ERP activity in 64 electrodes for the N1 and P1 ERP responses for vocalizations and listening tasks across LHS and control groups in the NAF condition.

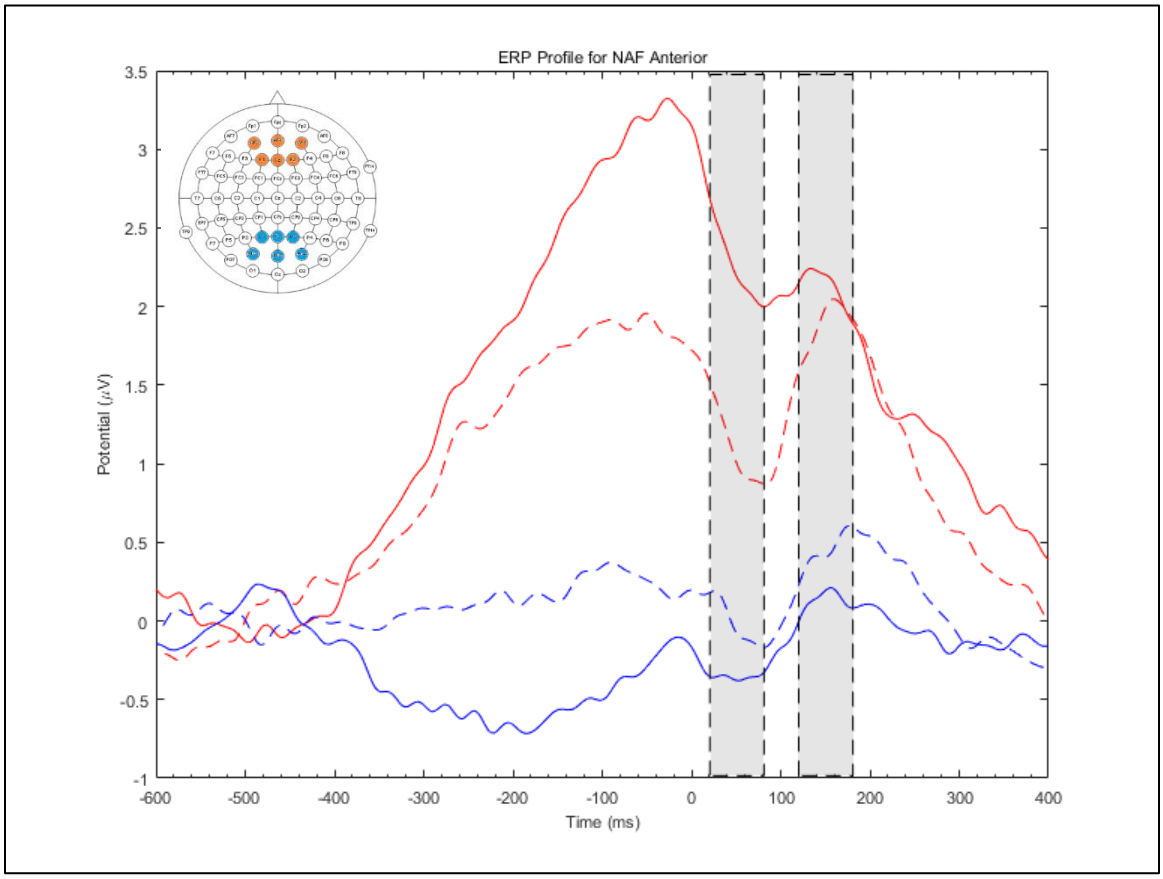


Figure 3.8 Overlaid profiles of ERP responses to NAF during vocalization (solid lines) and listening (dashed lines) for the control (red) and LHS (blue) groups at the NAF Anterior ROI. The gray shaded rectangle indicates the ERP activity at

the time windows submitted for statistical analysis for the P1 (left) and N1 (right) ERP components.

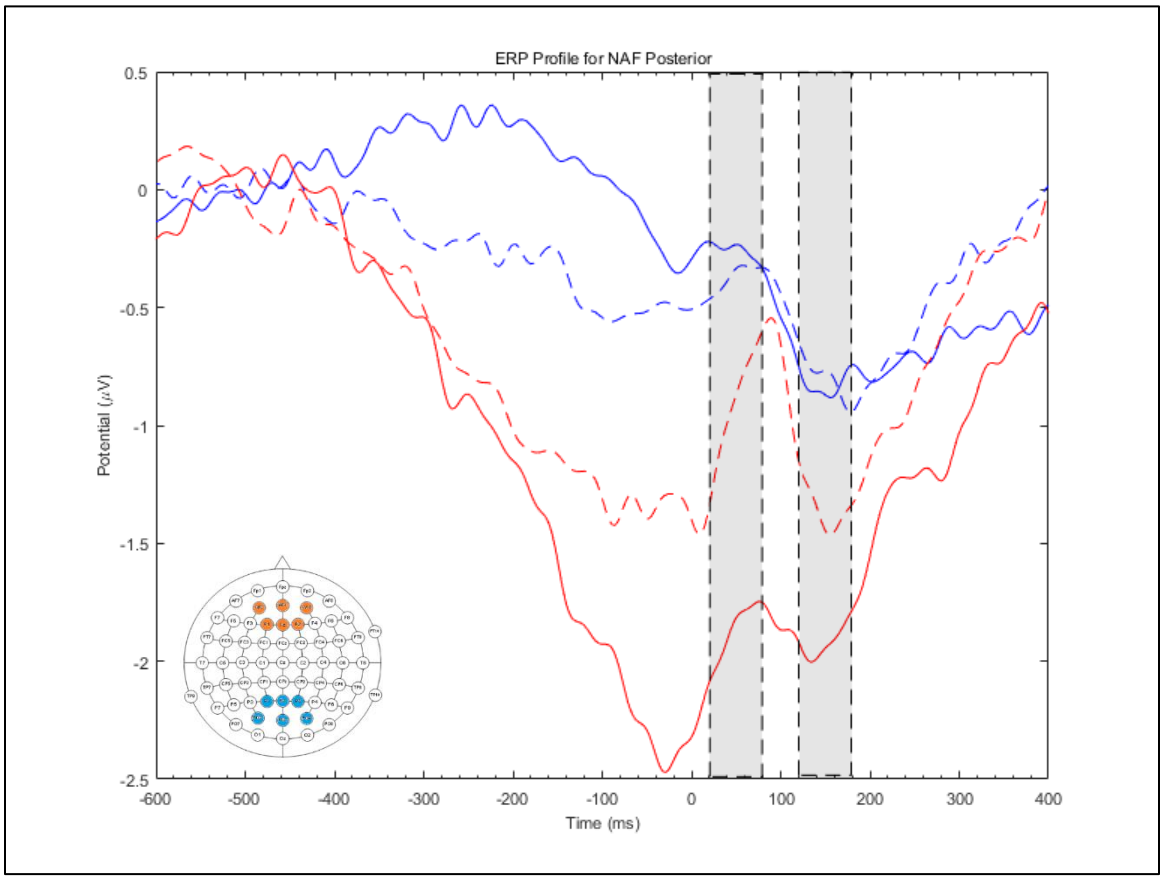


Figure 3.9 Overlaid profiles of ERP responses to NAF during vocalization (solid lines) and listening (dashed lines) for the control (red) and LHS (blue) groups at the NAF Posterior ROI. The gray shaded rectangle indicates the ERP activity at the time windows submitted for statistical analysis for the P1 (left) and N1 (right) ERP components.

3.6 AAF ERP RESPONSES

Similar to the previous condition, a two-way ANOVA was conducted to examine the effects of group (LHS versus control) and task (vocalization versus listening) on modulation of ERP responses for each ERP component within each region of interest, separately. The threshold for statistical significance was corrected for multiple comparisons at 0.004 for the AAF condition. Raw p values were reported. Results are found in Table 3.6. There was a statistically significant

main effect of group at the P2 anterior ROI ($F(1,63) = 21.302$, $p < .001$; partial $\eta 2 = 0.253$) with greater amplitude of ERP response within the control group compared with the LHS group. Additionally, there was a significant main effect of task at the N1 medial ROI ($F(1,63) = 40.90$, $p < 0.001$; partial $\eta 2 = 0.394$) with greater amplitude of ERP response during vocalization than listening in both groups (i.e., SPRE effect). By contrast, the t-tests conducted to compare difference wave activity between groups revealed no significant results (see Table 3.7).

Table 3.6 Results of the ANOVAs examining the effects of group and task on modulation of ERP responses within each AAF ROI.

ROI	Variable	*df*	*F*	Raw *p*-value	*partial η2*
AAF P1 Anterior L	**Group**	(1,63)	3.30	0.074	0.050
	Task	(1,63)	3.39	0.070	0.051
	Task*Group	(1,63)	0.44	0.507	0.007
AAF P1 Anterior R	**Group**	(1,63)	0.99	0.322	0.016
	Task	(1,63)	3.66	0.060	0.055
	Task*Group	(1,63)	0.27	0.602	0.004
AAF P1 Posterior	**Group**	(1,63)	4.39	*0.040	0.065
	Task	(1,63)	3.51	0.066	0.053
	Task*Group	(1,63)	0.02	0.902	0.000
AAF N1 Medial	**Group**	(1,63)	3.57	0.064	0.054
	Task	(1,63)	40.90	***<.001	0.394

	Task*Group	(1,63)	2.15	0.147	0.033
AAF P2 Anterior	**Group**	(1,63)	21.30	***< .001	0.253
	Task	(1,63)	1.38	0.244	0.021
	Task*Group	(1,63)	0.22	0.641	0.003
AAF P2 Posterior	**Group**	(1,63)	7.55	**0.008	0.107
	Task	(1,63)	1.32	0.255	0.021
	Task*Group	(1,63)	1.58	0.214	0.024
Asterisks distinguish the following probabilities based on raw *p*-values: *p<.05; **p <.01; ***p <.001					

Table 3.7 Results of t-tests comparing the amount of vocalization-induced ERP activity between groups in the AAF condition.

Difference Wave ROI	Group	Mean	Standard Deviation	t-value	df	p-value	Cohen's d
AAF P1 Anterior Left	LHS	-0.10	0.62	0.67	63	0.51	0.17
	Control	-0.22	0.77				
AAF P1 Anterior Right	LHS	-0.16	0.59	0.52	63	0.60	0.13
	Control	-0.28	1.23				
AAF P1 Posterior	LHS	0.14	0.58	0.12	63	0.90	0.03
	Control	0.12	0.24				
AAF N1 Medial	LHS	-0.34	0.54	1.47	63	0.15	0.37
	Control	-0.55	0.57				

AAF P2 Anterior	LHS	-0.24	0.84	-0.43^	37.99^	0.67^	-0.12
	Control	-0.10	1.47				
AAF P2 Posterior	LHS	0.01	0.71	1.26	63	0.21	0.32
	Control	-0.29	1.22				
^ Indicates value with equal variances not assumed							

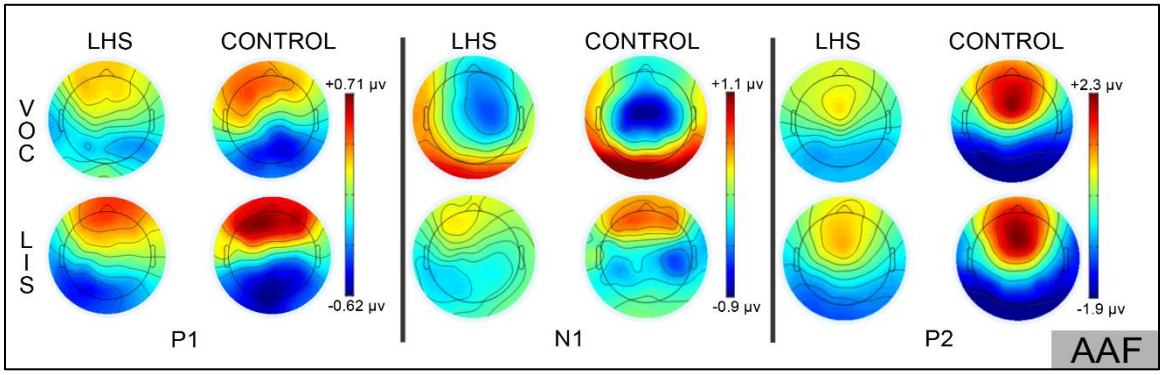


Figure 3.10 Topographical distribution maps of ERP activity in 64 electrodes for the P1, N1, and P2 ERP responses for vocalizations and listening tasks across LHS and control groups in the AAF condition.

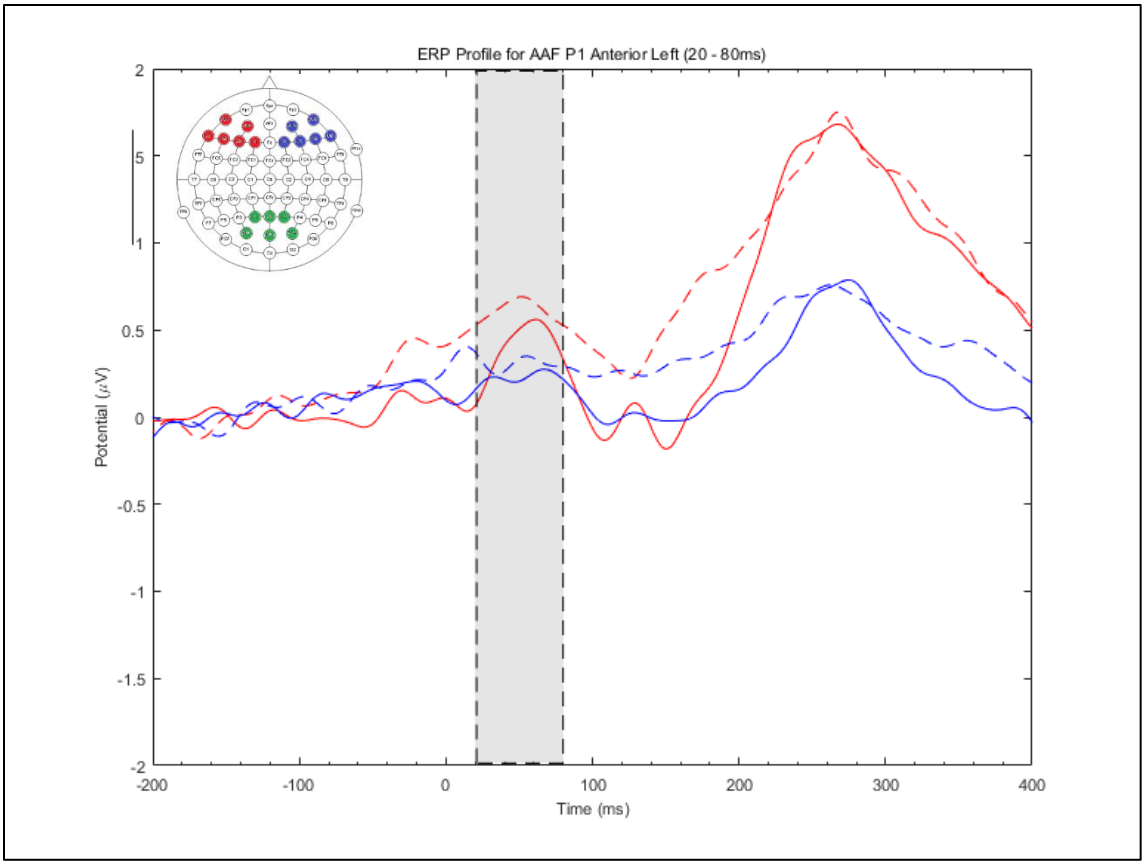


Figure 3.11 Overlaid profiles of ERP responses to AAF during vocalization (solid lines) and listening (dashed lines) for the control (red) and LHS (blue) groups at the AAF P1 Anterior Left ROI. The gray shaded rectangle indicates the ERP activity at the time window submitted for statistical analysis.

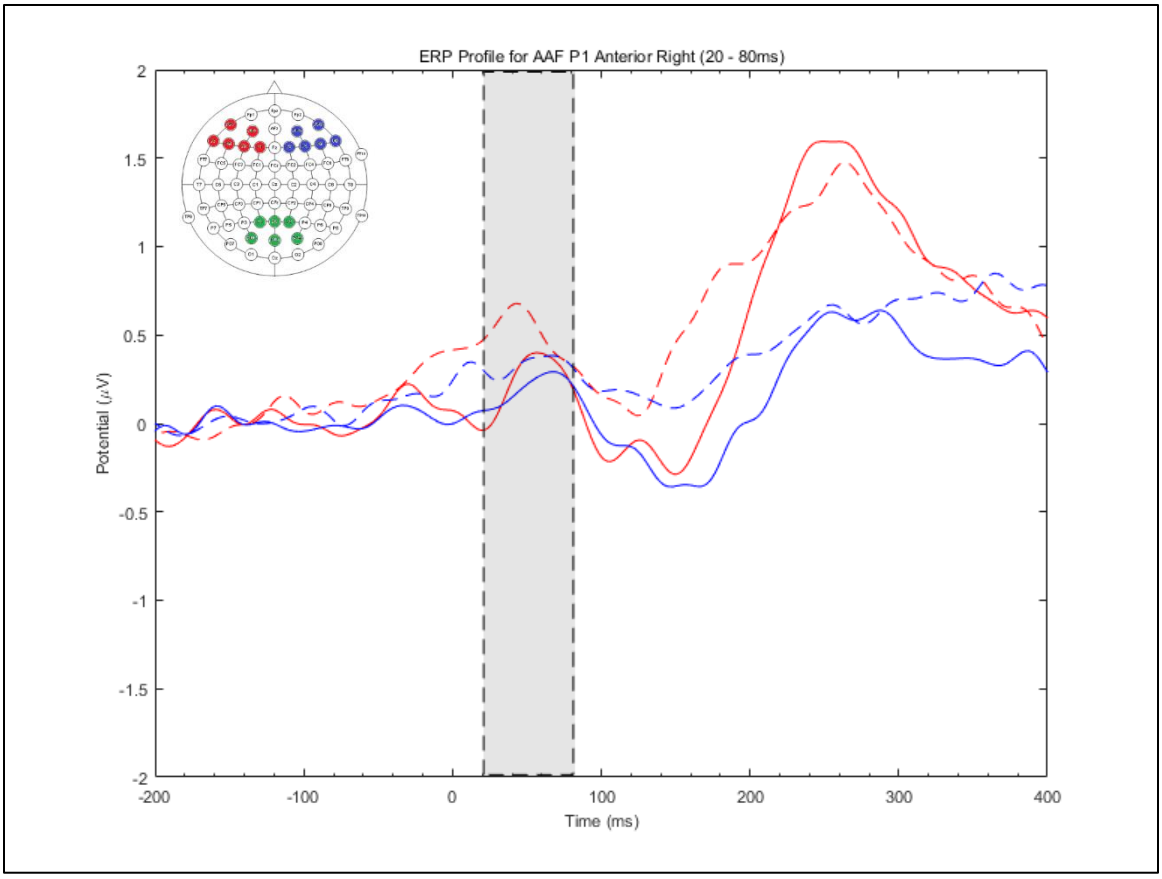


Figure 3.12 Overlaid profiles of ERP responses to AAF during vocalization (solid lines) and listening (dashed lines) for the control (red) and LHS (blue) groups at the AAF P1 Anterior Right ROI. The gray shaded rectangle indicates the ERP activity at the time window submitted for statistical analysis.

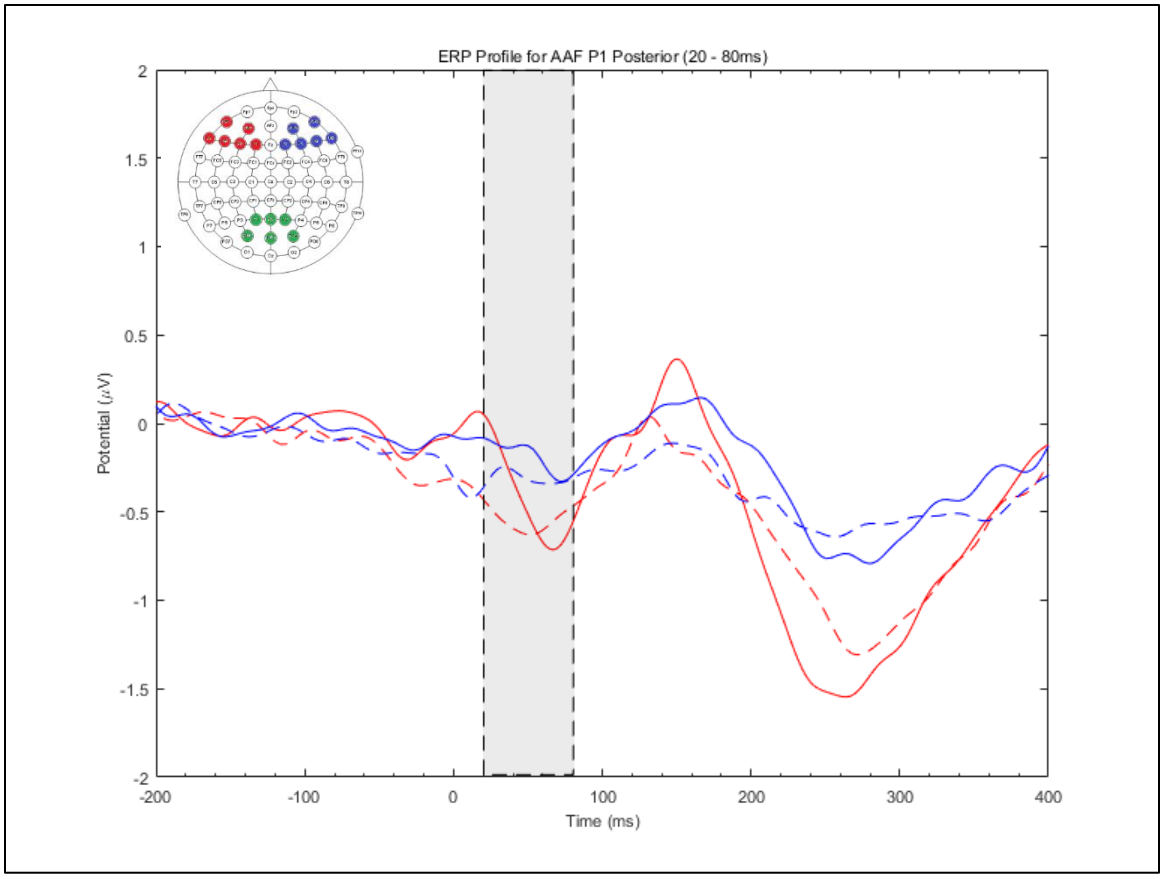


Figure 3.13 Overlaid profiles of ERP responses to AAF during vocalization (solid lines) and listening (dashed lines) for the control (red) and LHS (blue) groups at the AAF P1 Posterior ROI. The gray shaded rectangle indicates the ERP activity at the time window submitted for statistical analysis.

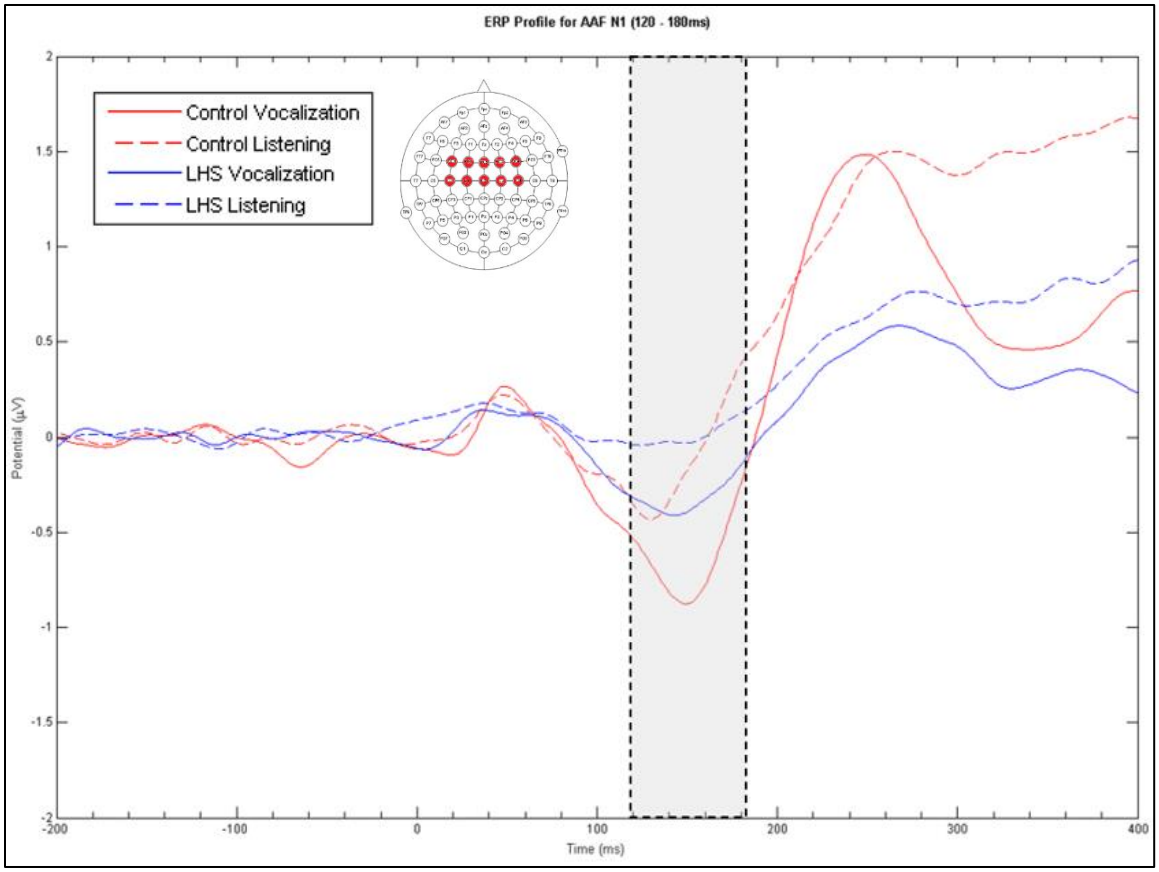


Figure 3.14 Overlaid profiles of ERP responses to AAF during vocalization (solid lines) and listening (dashed lines) for the control (red) and LHS (blue) groups at the AAF N1 medial ROI. The gray shaded rectangle indicates the ERP activity at the time window submitted for statistical analysis.

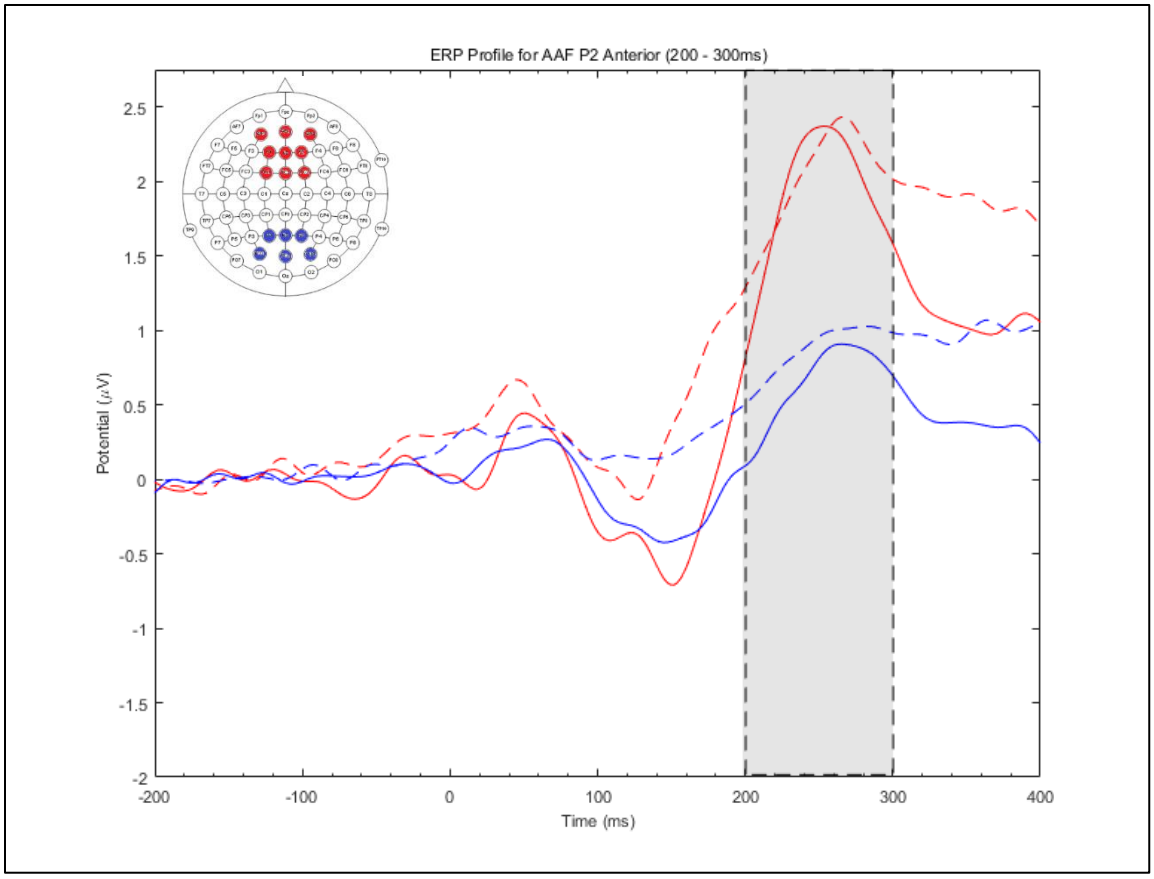


Figure 3.15 Overlaid profiles of ERP responses to AAF during vocalization (solid lines) and listening (dashed lines) for the control (red) and LHS (blue) groups at the AAF P2 Anterior ROI. The gray shaded rectangle indicates the ERP activity at the time window submitted for statistical analysis.

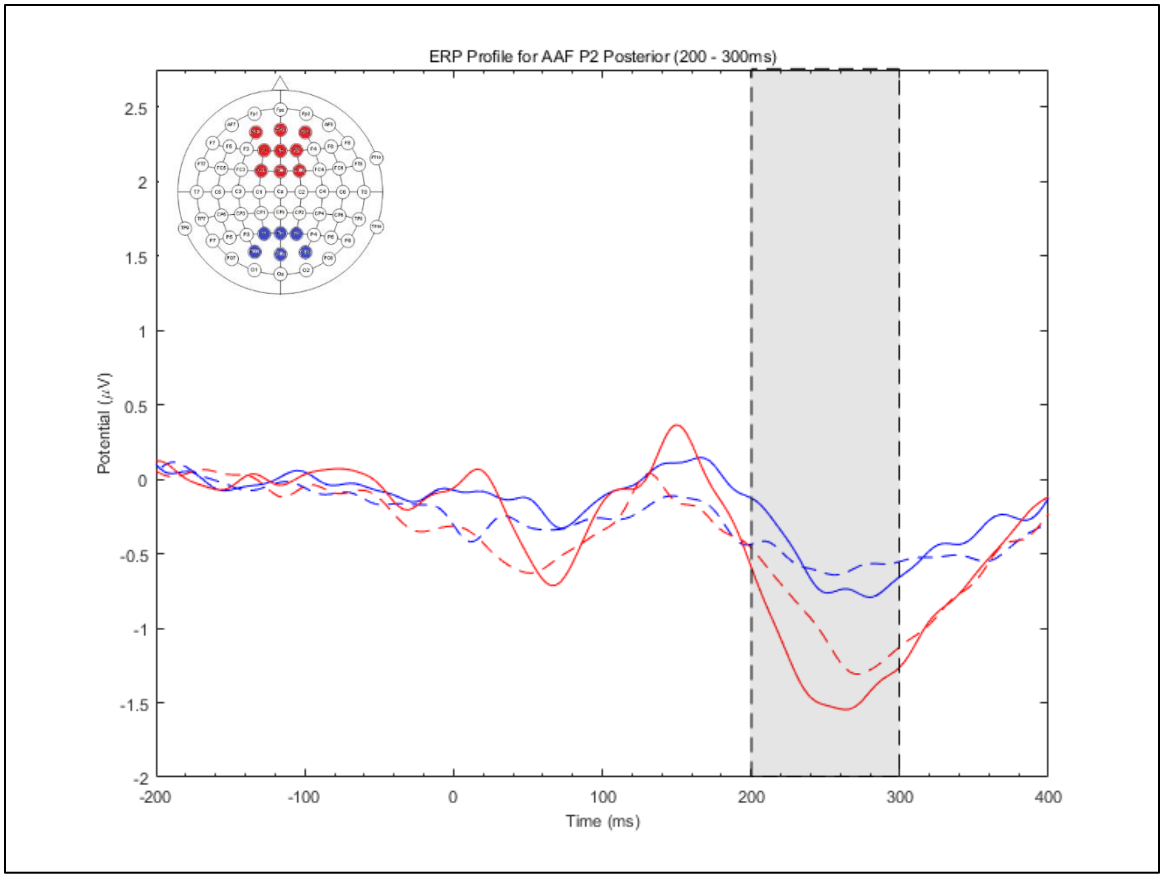


Figure 3.16 Overlaid profiles of ERP responses to AAF during vocalization (solid lines) and listening (dashed lines) for the control (red) and LHS (blue) groups at the AAF P2 Posterior ROI. The gray shaded rectangle indicates the ERP activity at the time window submitted for statistical analysis.

3.7 ASSOCIATION BETWEEN VOCAL MOTOR AND NEUROPHYSIOLOGICAL RESPONSES

Linear regression models were run to examine associations between the magnitude of vocal motor responses and vocalization-induced ERP activity. Magnitude of vocal motor response was the response variable. Vocalization-induced ERP activity in NAF and AAF conditions and group (LHS versus control) were the predictor variables. The linear regression models showed no significant predictors of magnitude of vocal motor response. Results are reported in Tables 3.8 and 3.9.

Table 3.8 Results of linear regression analyses of vocal motor responses as a function of vocalization-induced ERP activity in the NAF condition.

Vocal Motor Response (VMR) Condition	**NAF ROI**	**Linear Regression Model Output**
Avg VMR 101-200 ms	NAF N1 Anterior	Coefficients: Estimate Std. Error t value Pr(>|t|) (Intercept) 4.7856 1.0010 4.781 1.27e-05 *** N1NAFant -0.7006 0.7144 -0.981 0.3309 Group 3.4000 1.4809 2.296 0.0254 N1NAFant:Group 0.6807 0.7441 0.915 0.3641 Residual standard error: 5.536 on 57 degrees of freedom Multiple R-squared: 0.12, Adjusted R-squared: 0.07367 F-statistic: 2.591 on 3 and 57 DF, p-value: 0.06159
	NAF N1 Posterior	Coefficients: Estimate Std. Error t value Pr(>|t|) (Intercept) 4.904 1.010 4.853 9.8e-06 *** N1NAFpost 1.229 1.027 1.196 0.2366 Group 3.294 1.496 2.202 0.0317 N1NAFpost:Group -1.187 1.102 -1.078 0.2858 Residual standard error: 5.514 on 57 degrees of freedom Multiple R-squared: 0.1271, Adjusted R-squared: 0.08113 F-statistic: 2.766 on 3 and 57 DF, p-value: 0.05003
	NAF P1 Anterior	Coefficients: Estimate Std. Error t value Pr(>|t|) (Intercept) 5.1165 0.9640 5.308 1.9e-06 *** P1NAFant -1.3665 0.6474 -2.111 0.0392 Group 3.0686 1.4303 2.145 0.0362 P1NAFant:Group 1.3996 0.6882 2.034 0.0466 Residual standard error: 5.376 on 57 degrees of freedom Multiple R-squared: 0.1702, Adjusted R-squared: 0.1265 F-statistic: 3.896 on 3 and 57 DF, p-value: 0.01332
	NAF P1 Posterior	Coefficients: Estimate Std. Error t value Pr(>|t|) (Intercept) 5.2309 0.9882 5.293 2e-06 *** P1NAFpost 1.6803 0.8143 2.063 0.0436 Group 2.9462 1.4476 2.035 0.0465 P1NAFpost:Group -1.6677 0.8885 -1.877 0.0656 Residual standard error: 5.385 on 57 degrees of freedom Multiple R-squared: 0.1672, Adjusted R-squared: 0.1234 F-statistic: 3.815 on 3 and 57 DF, p-value: 0.01463

Avg VMR 201-300 ms	NAF N1 Anterior	Coefficients: Estimate Std. Error t value Pr(>|t|) (Intercept) 13.515 1.654 8.172 3.56e-11 *** N1NAFant -2.983 1.180 -2.527 0.0143 Group 2.659 2.447 1.087 0.2818 N1NAFant:Group 3.071 1.229 2.498 0.0154 Residual standard error: 9.146 on 57 degrees of freedom Multiple R-squared: 0.1439, Adjusted R-squared: 0.09888 F-statistic: 3.195 on 3 and 57 DF, p-value: 0.03017
	NAF N1 Posterior	Coefficients: Estimate Std.Error t value Pr(>|t|) (Intercept) 13.540 1.690 8.012 6.56e-11 *** N1NAFpost 3.972 1.718 2.312 0.0244 Group 2.586 2.502 1.034 0.3057 N1NAFpost:Group -4.144 1.842 -2.249 0.0284 Residual standard error: 9.222 on 57 degrees of freedom Multiple R-squared: 0.1297, Adjusted R-squared: 0.08385 F-statistic: 2.83 on 3 and 57 DF, p-value: 0.04636
	NAF P1 Anterior	Coefficients: Estimate Std. Error t value Pr(>|t|) (Intercept) 13.531 1.623 8.338 1.89e-11 *** P1NAFant -3.017 1.090 -2.768 0.00759 Group 2.735 2.408 1.136 0.26071 P1NAFant:Group 3.167 1.158 2.734 0.00832 Residual standard error: 9.05 on 57 degrees of freedom Multiple R-squared: 0.1618, Adjusted R-squared: 0.1177 F-statistic: 3.669 on 3 and 57 DF, p-value: 0.01733
	NAF P1 Posterior	Coefficients: Estimate Std. Error t value Pr(>|t|) (Intercept) 13.608 1.687 8.065 5.36e-11 *** P1NAFpost 3.338 1.390 2.401 0.0196 Group 2.601 2.472 1.052 0.2971 P1NAFpost:Group -3.411 1.517 -2.249 0.0284 Residual standard error: 9.195 on 57 degrees of freedom Multiple R-squared: 0.1347, Adjusted R-squared: 0.08921 F-statistic: 2.959 on 3 and 57 DF, p-value: 0.03983
Avg VMR 301-400 ms	NAF N1 Anterior	Coefficients: Estimate Std. Error t value Pr(>|t|) (Intercept) 12.41556 1.42722 8.699 4.8e-12 *** N1NAFant -2.14431 1.01858 -2.105 0.0397 Group -0.09831 2.11152 -0.047 0.9630 N1NAFant:Group 1.98478 1.06095 1.871 0.0665 Residual standard error: 7.894 on 57 degrees of freedom Multiple R-squared: 0.07927, Adjusted R-squared: 0.03081 F-statistic: 1.636 on 3 and 57 DF, p-value: 0.1912

	NAF N1 Posterior	Coefficients: Estimate Std. Error t value Pr(>|t|) (Intercept) 12.5203 1.4478 8.648 5.84e-12 *** N1NAFpost 3.0830 1.4718 2.095 0.0406 Group -0.1414 2.1435 -0.066 0.9476 N1NAFpost:Group -2.8150 1.5784 -1.783 0.0798 Residual standard error: 7.901 on 57 degrees of freedom Multiple R-squared: 0.0776, Adjusted R-squared: 0.02905 F-statistic: 1.598 on 3 and 57 DF, p-value: 0.1998
	NAF P1 Anterior	Coefficients: Estimate Std. Error t value Pr(>|t|) (Intercept) 12.4190 1.4103 8.806 3.21e-12 *** P1NAFant -2.1524 0.9471 -2.273 0.0268 Group -0.1964 2.0925 -0.094 0.9255 P1NAFant:Group 2.1209 1.0068 2.107 0.0396 Residual standard error: 7.865 on 57 degrees of freedom Multiple R-squared: 0.08598, Adjusted R-squared: 0.03788 F-statistic: 1.787 on 3 and 57 DF, p-value: 0.1598
	NAF P1 Posterior	Coefficients: Estimate Std. Error t value Pr(>|t|) (Intercept) 12.528 1.453 8.623 6.42e-12 *** P1NAFpost 2.495 1.197 2.084 0.0416 Group -0.300 2.128 -0.141 0.8884 P1NAFpost:Group -2.522 1.306 -1.931 0.0584 Residual standard error: 7.918 on 57 degrees of freedom Multiple R-squared: 0.07367, Adjusted R-squared: 0.02492 F-statistic: 1.511 on 3 and 57 DF, p-value: 0.2214
Local Peak VMR 100 - 400 ms	NAF N1 Anterior	Coefficients: Estimate Std. Error t value Pr(>|t|) (Intercept) 16.976 1.687 10.064 2.97e-14 *** N1NAFant -2.758 1.204 -2.291 0.0257 Group 2.865 2.495 1.148 0.2558 N1NAFant:Group 2.688 1.254 2.143 0.0364 Residual standard error: 9.329 on 57 degrees of freedom Multiple R-squared: 0.1273, Adjusted R-squared: 0.08136 F-statistic: 2.771 on 3 and 57 DF, p-value: 0.04971
	NAF N1 Posterior	Coefficients: Estimate Std. Error t value Pr(>|t|) (Intercept) 7.051 1.716 9.934 4.8e-14 *** N1NAFpost 3.808 1.745 2.183 0.0332 Group 2.809 2.541 1.106 0.2736 N1NAFpost:Group -3.703 1.871 -1.979 0.0527 Residual standard error: 9.367 on 57 degrees of freedom Multiple R-squared: 0.1202, Adjusted R-squared: 0.07387 F-statistic: 2.595 on 3 and 57 DF, p-value: 0.06125

	NAF P1 Anterior	Coefficients: Estimate Std. Error t value Pr(>|t|) (Intercept) 17.012 1.657 10.269 1.41e-14 *** P1NAFant -2.833 1.112 -2.546 0.0136 Group 2.768 2.458 1.126 0.2648 P1NAFant:Group 2.759 1.183 2.333 0.0232 Residual standard error: 9.239 on 57 degrees of freedom Multiple R-squared: 0.1441, Adjusted R-squared: 0.09907 F-statistic: 3.199 on 3 and 57 DF, p-value: 0.03001
	NAF P1 Posterior	Coefficients: Estimate Std. Error t value Pr(>|t|) (Intercept) 17.112 1.713 9.988 3.93e-14 *** P1NAFpost 3.193 1.412 2.261 0.0276 Group 2.718 2.510 1.083 0.2833 P1NAFpost:Group -3.023 1.540 -1.962 0.0546 Residual standard error: 9.337 on 57 degrees of freedom Multiple R-squared: 0.1259, Adjusted R-squared: 0.07986 F-statistic: 2.736 on 3 and 57 DF, p-value: 0.05184
*** indicates a raw *p*-value of $p < .001$		

Table 3.9 Results of linear regression analyses of vocal motor responses as a function of vocalization-induced ERP activity in the AAF condition.

Vocal Motor Response (VMR) Condition	**AAF ROI**	**Linear Regression Model Output**
Avg VMR 101-200 ms	AAF P1 Anterior Left	Coefficients: Estimate Std. Error t value Pr(>|t|) (Intercept) 4.43815 0.94337 4.705 1.66e-05 *** P1aafAntL 0.01096 1.48765 0.007 0.9941 Group 3.36575 1.47451 2.283 0.0262 P1aafAntL:Group -1.58217 2.04971 -0.772 0.4434 Residual standard error: 5.523 on 57 degrees of freedom Multiple R-squared: 0.1241, Adjusted R-squared: 0.07798 F-statistic: 2.691 on 3 and 57 DF, p-value: 0.05464
	AAF P1 Anterior Right	Coefficients: Estimate Std. Error t value Pr(>|t|) (Intercept) 3.9669 0.9488 4.181 0.000101 *** P1aafAntR -2.9081 1.6058 -1.811 0.075405 Group 4.4197 1.4452 3.058 0.003389 P1aafAntR:Group 3.6133 1.8232 1.982 0.052321 Residual standard error: 5.399 on 57 degrees of freedom

		Multiple R-squared: 0.163, Adjusted R-squared: 0.1189 F-statistic: 3.699 on 3 and 57 DF, p-value: 0.01674
	AAF P1 Posterior	Coefficients: Estimate Std. Error t value Pr(>|t|) (Intercept) 4.4013 0.9642 4.565 2.72e-05 *** P1aafPost 0.2844 1.6054 0.177 0.8600 Group 3.8630 1.4905 2.592 0.0121 P1aafPost:Group -0.8908 2.6419 -0.337 0.7372 Residual standard error: 5.577 on 57 degrees of freedom Multiple R-squared: 0.1068, Adjusted R-squared: 0.05979 F-statistic: 2.272 on 3 and 57 DF, p-value: 0.08993
	AAF N1 Medial	Coefficients: Estimate Std. Error t value Pr(>|t|) (Intercept) 3.682 1.081 3.406 0.00121 N1aaf -2.185 1.660 -1.316 0.19346 Group 5.828 1.819 3.204 0.00222 N1aaf:Group 4.705 2.522 1.866 0.06721 Residual standard error: 5.419 on 57 degrees of freedom Multiple R-squared: 0.1567, Adjusted R-squared: 0.1123 F-statistic: 3.531 on 3 and 57 DF, p-value: 0.02036
	AAF P2 Anterior	Coefficients: Estimate Std. Error t value Pr(>|t|) (Intercept) 4.0045 0.9297 4.307 6.6e-05 *** P2aafAnt -2.1864 1.0688 -2.046 0.0454 Group 4.2571 1.4064 3.027 0.0037 P2aafAnt:Group 2.8061 1.2879 2.179 0.0335 Residual standard error: 5.356 on 57 degrees of freedom Multiple R-squared: 0.1762, Adjusted R-squared: 0.1329 F-statistic: 4.065 on 3 and 57 DF, p-value: 0.01097
	AAF P2 Posterior	Coefficients: Estimate Std. Error t value Pr(>|t|) (Intercept) 4.4389 0.9116 4.870 9.26e-06 *** P2aafPost 1.6267 1.3297 1.223 0.2262 Group 3.2954 1.4228 2.316 0.0242 P2aafPost:Group -3.0265 1.5886 -1.905 0.0618 Residual standard error: 5.393 on 57 degrees of freedom Multiple R-squared: 0.1649, Adjusted R-squared: 0.121 F-statistic: 3.752 on 3 and 57 DF, p-value: 0.01574
Avg VMR 201-300 ms	AAF P1 Anterior Left	Coefficients: Estimate Std. Error t value Pr(>|t|) (Intercept) 12.156 1.587 7.661 2.52e-10 *** P1aafAntL 1.373 2.502 0.549 0.5855 Group 2.916 2.480 1.176 0.2446 P1aafAntL:Group -6.235 3.448 -1.809 0.0758 Residual standard error: 9.29 on 57 degrees of freedom

		Multiple R-squared: 0.1168, Adjusted R-squared: 0.07032 F-statistic: 2.513 on 3 and 57 DF, p-value: 0.06754
	AAF P1 Anterior Right	Coefficients: Estimate Std. Error t value Pr(>|t|) (Intercept) 11.332 1.661 6.821 6.33e-09 *** P1aafAntR -4.325 2.812 -1.538 0.1295 Group 4.961 2.531 1.960 0.0549 P1aafAntR:Group 4.564 3.192 1.430 0.1583 Residual standard error: 9.454 on 57 degrees of freedom Multiple R-squared: 0.08538, Adjusted R-squared: 0.03724 F-statistic: 1.774 on 3 and 57 DF, p-value: 0.1624
	AAF P1 Posterior	Coefficients: Estimate Std. Error t value Pr(>|t|) (Intercept) 11.9926 1.6623 7.215 1.4e-09 *** P1aafPost 0.3051 2.7676 0.110 0.913 Group 3.8896 2.5695 1.514 0.136 P1aafPost:Group 1.9951 4.5545 0.438 0.663 Residual standard error: 9.615 on 57 degrees of freedom Multiple R-squared: 0.05393, Adjusted R-squared: 0.004133 F-statistic: 1.083 on 3 and 57 DF, p-value: 0.3637
	AAF N1 Medial	Coefficients: Estimate Std. Error t value Pr(>|t|) (Intercept) 10.521 1.887 5.577 7.02e-07 *** N1aaf -4.367 2.898 -1.507 0.1373 Group 6.143 3.175 1.935 0.0579 N1aaf:Group 5.205 4.401 1.183 0.2418 Residual standard error: 9.458 on 57 degrees of freedom Multiple R-squared: 0.08453, Adjusted R-squared: 0.03634 F-statistic: 1.754 on 3 and 57 DF, p-value: 0.1662
	AAF P2 Anterior	Coefficients: Estimate Std. Error t value Pr(>|t|) (Intercept) 11.221 1.605 6.993 3.27e-09 *** P2aafAnt -4.094 1.845 -2.220 0.0304 Group 4.924 2.427 2.029 0.0472 P2aafAnt:Group 3.554 2.223 1.599 0.1153 Residual standard error: 9.244 on 57 degrees of freedom Multiple R-squared: 0.1255, Adjusted R-squared: 0.07949 F-statistic: 2.727 on 3 and 57 DF, p-value: 0.05238
	AAF P2 Posterior	Coefficients: Estimate Std. Error t value Pr(>|t|) (Intercept) 12.036 1.577 7.632 2.82e-10 *** P2aafPost 4.085 2.300 1.776 0.0811 Group 3.754 2.462 1.525 0.1327 P2aafPost:Group -5.453 2.748 -1.984 0.0521 Residual standard error: 9.33 on 57 degrees of freedom

		Multiple R-squared: 0.1092, Adjusted R-squared: 0.06233 F-statistic: 2.329 on 3 and 57 DF, p-value: 0.08397
Avg VMR 301-400 ms	AAF P1 Anterior Left	Coefficients: Estimate Std. Error t value Pr(>|t|) (Intercept) 11.28939 1.35087 8.357 1.76e-11 *** P1aafAntL -0.65362 2.13025 -0.307 0.760 Group -0.05616 2.11144 -0.027 0.979 P1aafAntL:Group -3.57491 2.93511 -1.218 0.228 Residual standard error: 7.909 on 57 degrees of freedom Multiple R-squared: 0.07567, Adjusted R-squared: 0.02702 F-statistic: 1.555 on 3 and 57 DF, p-value: 0.2102
	AAF P1 Anterior Right	Coefficients: Estimate Std. Error t value Pr(>|t|) (Intercept) 10.923 1.427 7.652 2.6e-10 *** P1aafAntR -2.631 2.416 -1.089 0.281 Group 1.186 2.174 0.545 0.588 P1aafAntR:Group 2.222 2.743 0.810 0.421 Residual standard error: 8.123 on 57 degrees of freedom Multiple R-squared: 0.025, Adjusted R-squared: -0.02631 F-statistic: 0.4873 on 3 and 57 DF, p-value: 0.6925
	AAF P1 Posterior	Coefficients: Estimate Std. Error t value Pr(>|t|) (Intercept) 11.0809 1.3879 7.984 7.31e-11 *** P1aafPost 2.1257 2.3108 0.920 0.361 Group 0.5507 2.1454 0.257 0.798 P1aafPost:Group 1.9542 3.8027 0.514 0.609 Residual standard error: 8.028 on 57 degrees of freedom Multiple R-squared: 0.04765, Adjusted R-squared: -0.002477 F-statistic: 0.9506 on 3 and 57 DF, p-value: 0.4224
	AAF N1 Medial	Coefficients: Estimate Std. Error t value Pr(>|t|) (Intercept) 10.6611 1.6261 6.556 1.74e-08 *** N1aaf -1.9892 2.4973 -0.797 0.429 Group 0.8348 2.7361 0.305 0.761 N1aaf:Group 0.5993 3.7929 0.158 0.875 Residual standard error: 8.152 on 57 degrees of freedom Multiple R-squared: 0.01803, Adjusted R-squared: -0.03365 F-statistic: 0.3489 on 3 and 57 DF, p-value: 0.7901
	AAF P2 Anterior	Coefficients: Estimate Std. Error t value Pr(>|t|) (Intercept) 10.9888 1.4009 7.844 1.25e-10 *** P2aafAnt -1.8198 1.6104 -1.130 0.263 Group 1.1106 2.1191 0.524 0.602 P2aafAnt:Group 0.8707 1.9406 0.449 0.655 Residual standard error: 8.07 on 57 degrees of freedom

		Multiple R-squared: 0.03755, Adjusted R-squared: -0.01311 F-statistic: 0.7412 on 3 and 57 DF, p-value: 0.5319
	AAF P2 Posterior	Coefficients: Estimate Std. Error t value Pr(>|t|) (Intercept) 11.353 1.354 8.383 1.59e-11 *** P2aafPost 3.285 1.975 1.663 0.102 Group 1.038 2.114 0.491 0.625 P2aafPost:Group -2.781 2.360 -1.178 0.244 Residual standard error: 8.011 on 57 degrees of freedom Multiple R-squared: 0.05155, Adjusted R-squared: 0.001635 F-statistic: 1.033 on 3 and 57 DF, p-value: 0.385
Local Peak VMR 100 - 400 ms	AAF P1 Anterior Left	Coefficients: Estimate Std. Error t value Pr(>|t|) (Intercept) 15.6460 1.6130 9.700 1.13e-13 *** P1aafAntL 0.4607 2.5436 0.181 0.857 Group 3.0530 2.5211 1.211 0.231 P1aafAntL:Group -5.1339 3.5046 -1.465 0.148 Residual standard error: 9.443 on 57 degrees of freedom Multiple R-squared: 0.1057, Adjusted R-squared: 0.05867 F-statistic: 2.246 on 3 and 57 DF, p-value: 0.09268
	AAF P1 Anterior Right	Coefficients: Estimate Std. Error t value Pr(>|t|) (Intercept) 14.844 1.673 8.872 2.5e-12 *** P1aafAntR -4.702 2.832 -1.661 0.1023 Group 5.062 2.548 1.986 0.0518 P1aafAntR:Group 5.046 3.215 1.570 0.1221 Residual standard error: 9.521 on 57 degrees of freedom Multiple R-squared: 0.09106, Adjusted R-squared: 0.04322 F-statistic: 1.904 on 3 and 57 DF, p-value: 0.1393
	AAF P1 Posterior	Coefficients: Estimate Std. Error t value Pr(>|t|) (Intercept) 15.4281 1.6763 9.204 7.19e-13 *** P1aafPost 1.3950 2.7909 0.500 0.619 Group 4.0297 2.5912 1.555 0.125 P1aafPost:Group 0.9498 4.5929 0.207 0.837 Residual standard error: 9.696 on 57 degrees of freedom Multiple R-squared: 0.05724, Adjusted R-squared: 0.007618 F-statistic: 1.154 on 3 and 57 DF, p-value: 0.3355
	AAF N1 Medial	Coefficients: Estimate Std. Error t value Pr(>|t|) (Intercept) 14.415 1.922 7.499 4.69e-10 *** N1aaf -3.439 2.952 -1.165 0.2490 Group 5.634 3.234 1.742 0.0869 N1aaf:Group 3.904 4.484 0.871 0.3876 Residual standard error: 9.637 on 57 degrees of freedom

		Multiple R-squared: 0.06875, Adjusted R-squared: 0.01973 F-statistic: 1.403 on 3 and 57 DF, p-value: 0.2514
	AAF P2 Anterior	Coefficients: Estimate Std. Error t value Pr(>|t|) (Intercept) 14.865 1.635 9.091 1.1e-12 *** P2aafAnt -3.733 1.880 -1.986 0.0518 Group 4.870 2.473 1.969 0.0538 P2aafAnt:Group 3.251 2.265 1.435 0.1567 Residual standard error: 9.42 on 57 degrees of freedom Multiple R-squared: 0.1101, Adjusted R-squared: 0.06329 F-statistic: 2.351 on 3 and 57 DF, p-value: 0.08181
	AAF P2 Posterior	Coefficients: Estimate Std. Error t value Pr(>|t|) (Intercept) 15.609 1.589 9.824 7.19e-14 *** P2aafPost 4.624 2.318 1.995 0.0508 Group 3.903 2.480 1.574 0.1210 P2aafPost:Group -5.546 2.769 -2.003 0.0499 Residual standard error: 9.4 on 57 degrees of freedom Multiple R-squared: 0.1139, Adjusted R-squared: 0.06727 F-statistic: 2.442 on 3 and 57 DF, p-value: 0.07342
*** indicates a raw *p*-value of $p < .001$		

3.8 ASSOCIATION BETWEEN AVERAGE CORRECT RATES AND NEUROPHYSIOLOGICAL RESPONSES

Linear regression models were run to examine associations between average correct rates and vocalization-induced ERP activity. Average correct rate was the response variable. Vocalization-induced ERP activity in NAF and AAF conditions, task (vocalization versus listening), and group (LHS versus control), were the predictor variables. The linear regression models showed that group was positively and significantly correlated with average correct rate, indicating that the control group had higher average correct rates than the LHS group. Results are reported in Tables 3.10 and 3.11.

Table 3.10 Results of linear regression analyses of average correct rates as a function of vocalization-induced ERP activity in the NAF condition, task, and group.

NAF ROI	Linear Regression Output
NAF N1 Anterior	Coefficients: Estimate Std. Error t value Pr(>|t|) (Intercept) 65.3137 3.1167 20.956 < 2e-16 *** N1NAFant 0.5931 2.0413 0.291 0.772 Task 4.4858 4.4077 1.018 0.311 Group 20.4821 4.7518 4.310 3.32e-05 *** N1NAFant:Task -1.2982 2.8868 -0.450 0.654 N1NAFant:Group -1.1683 2.1565 -0.542 0.589 Task:Group -4.0244 6.7201 -0.599 0.550 N1NAFant:Task:Group 0.7581 3.0498 0.249 0.804 Residual standard error: 18.57 on 122 degrees of freedom Multiple R-squared: 0.2199, Adjusted R-squared: 0.1751 F-statistic: 4.912 on 7 and 122 DF, p-value: 6.499e-05
NAF N1 Posterior	Coefficients: Estimate Std. Error t value Pr(>|t|) (Intercept) 64.475 3.280 19.655 < 2e-16 *** N1NAFpost -2.538 3.156 -0.804 0.423 Task 5.115 4.639 1.103 0.272 Group 21.895 4.892 4.476 1.72e-05 *** N1NAFpost:Task 2.696 4.463 0.604 0.547 N1NAFpost:Group 4.066 3.426 1.187 0.238 Task:Group -4.526 6.918 -0.654 0.514 N1NAFpost:Task:Group -2.019 4.845 -0.417 0.678 Residual standard error: 18.48 on 122 degrees of freedom Multiple R-squared: 0.2275, Adjusted R-squared: 0.1831 F-statistic: 5.131 on 7 and 122 DF, p-value: 3.874e-05
NAF P1 Anterior	Coefficients: Estimate Std. Error t value Pr(>|t|) (Intercept) 64.883 3.203 20.254 < 2e-16 *** P1NAFant 1.337 2.080 0.643 0.522 Task 5.247 4.530 1.158 0.249 Group 20.567 4.832 4.257 4.1e-05 *** P1NAFant:Task -2.560 2.942 -0.870 0.386 P1NAFant:Group -1.530 2.228 -0.687 0.493 Task:Group -5.304 6.833 -0.776 0.439 P1NAFant:Task:Group 1.969 3.150 0.625 0.533 Residual standard error: 18.69 on 122 degrees of freedom Multiple R-squared: 0.2093, Adjusted R-squared: 0.164 F-statistic: 4.614 on 7 and 122 DF, p-value: 0.0001316
NAF P1 Posterior	Coefficients: Estimate Std. Error t value Pr(>|t|) (Intercept) 63.490 3.360 18.894 < 2e-16 *** P1NAFpost -3.521 2.567 -1.371 0.173 Task 5.942 4.752 1.250 0.214 Group 22.172 4.904 4.521 1.44e-05 ***

	P1NAFpost:Task 3.366 3.631 0.927 0.356 P1NAFpost:Group 4.343 2.844 1.527 0.129 Task:Group -5.619 6.936 -0.810 0.419 P1NAFpost:Task:Group -2.676 4.021 -0.666 0.507 Residual standard error: 18.54 on 122 degrees of freedom Multiple R-squared: 0.2224, Adjusted R-squared: 0.1778 F-statistic: 4.985 on 7 and 122 DF, p-value: 5.475e-05
*** indicates a raw *p*-value of *p* <.001	

Table 3.11 Results of linear regression analyses of average correct rates as a function of vocalization-induced ERP activity in the AAF condition, task, and group.

ROI	**Linear Regression Output**
AAF P1 Anterior Left	Coefficients: Estimate Std. Error t value Pr(>|t|) (Intercept) 65.5374 3.0905 21.206 < 2e-16 *** P1aafAntL -0.0864 5.0029 -0.017 0.986 Task 4.2865 4.3705 0.981 0.329 Group 20.2004 4.8676 4.150 6.19e-05 *** P1aafAntL:Task 3.0476 7.0752 0.431 0.667 P1aafAntL:Group 0.9951 6.9033 0.144 0.886 Task:Group -3.9063 6.8838 -0.567 0.571 P1aafAntL:Task:Group -2.3169 9.7628 -0.237 0.813 Residual standard error: 18.79 on 122 degrees of freedom Multiple R-squared: 0.2011, Adjusted R-squared: 0.1552 F-statistic: 4.386 on 7 and 122 DF, p-value: 0.0002262
AAF P1 Anterior Right	Coefficients: Estimate Std. Error t value Pr(>|t|) (Intercept) 65.297 3.142 20.781 < 2e-16 *** P1aafAntR -1.558 5.156 -0.302 0.763 Task 4.079 4.444 0.918 0.360 Group 21.070 4.849 4.346 2.89e-05 *** P1aafAntR:Task 0.639 7.291 0.088 0.930 P1aafAntR:Group 4.513 5.954 0.758 0.450 Task:Group -3.989 6.857 -0.582 0.562 P1aafAntR:Task:Group -1.109 8.421 -0.132 0.895 Residual standard error: 18.69 on 122 degrees of freedom Multiple R-squared: 0.2094, Adjusted R-squared: 0.1641 F-statistic: 4.617 on 7 and 122 DF, p-value: 0.0001307
AAF P1 Posterior	Coefficients: Estimate Std. Error t value Pr(>|t|) (Intercept) 65.4091 3.1390 20.837 < 2e-16 *** P1aafPost 0.9736 5.3563 0.182 0.856 Task 4.3850 4.4393 0.988 0.325 Group 20.2132 4.8620 4.157 6.01e-05 *** P1aafPost:Task -2.8985 7.5750 -0.383 0.703 P1aafPost:Group -1.6353 8.7145 -0.188 0.851 Task:Group -3.6841 6.8759 -0.536 0.593

	P1aafPost:Task:Group -0.9880 12.3242 -0.080 0.936 Residual standard error: 18.78 on 122 degrees of freedom Multiple R-squared: 0.2017, Adjusted R-squared: 0.1559 F-statistic: 4.404 on 7 and 122 DF, p-value: 0.0002165
AAF N1 Medial	Coefficients: Estimate Std. Error t value Pr(>|t|) (Intercept) 65.51893 3.60276 18.186 < 2e-16 *** N1aaf -0.07931 5.65695 -0.014 0.98884 Task 1.69441 5.09507 0.333 0.74004 Group 19.84179 6.20105 3.200 0.00175 N1aaf:Task -6.64567 8.00014 -0.831 0.40777 N1aaf:Group -0.24915 8.58468 -0.029 0.97689 Task:Group 0.50802 8.76961 0.058 0.95390 N1aaf:Task:Group 10.26052 12.14057 0.845 0.39969 Residual standard error: 18.7 on 122 degrees of freedom Multiple R-squared: 0.2086, Adjusted R-squared: 0.1632 F-statistic: 4.594 on 7 and 122 DF, p-value: 0.0001379
AAF P2 Anterior	Coefficients: Estimate Std. Error t value Pr(>|t|) (Intercept) 65.331 3.146 20.768 < 2e-16 *** P2aafAnt -0.909 3.643 -0.250 0.803 Task 3.517 4.449 0.791 0.431 Group 20.285 4.779 4.245 4.29e-05 *** P2aafAnt:Task -1.938 5.152 -0.376 0.707 P2aafAnt:Group 1.639 4.407 0.372 0.711 Task:Group -3.043 6.758 -0.450 0.653 P2aafAnt:Task:Group 4.415 6.232 0.708 0.480 Residual standard error: 18.65 on 122 degrees of freedom Multiple R-squared: 0.2134, Adjusted R-squared: 0.1683 F-statistic: 4.729 on 7 and 122 DF, p-value: 0.0001002
AAF P2 Posterior	Coefficients: Estimate Std. Error t value Pr(>|t|) (Intercept) 65.5187 2.9933 21.888 < 2e-16 *** P2aafPost 2.1512 4.2885 0.502 0.617 Task 3.9749 4.2332 0.939 0.350 Group 19.0789 4.7218 4.041 9.36e-05 *** P2aafPost:Task 0.1569 6.0648 0.026 0.979 P2aafPost:Group -5.4155 5.2083 -1.040 0.301 Task:Group -4.3700 6.6776 -0.654 0.514 P2aafPost:Task:Group -2.2920 7.3657 -0.311 0.756 Residual standard error: 18.45 on 122 degrees of freedom Multiple R-squared: 0.2299, Adjusted R-squared: 0.1857 F-statistic: 5.204 on 7 and 122 DF, p-value: 3.266e-05
*** indicates a raw *p*-value of $p < .001$	

CHAPTER 4

DISCUSSION AND CONCLUSIONS

The purpose of this study was to identify behavioral and neural correlates of impaired speech auditory feedback processing in people with a history of left-hemisphere stroke. More specifically, we wanted to answer these five questions: Are there differences in perceptual error detection ability between groups (LHS versus neurologically intact controls) and tasks (vocalization versus listening)? Are there differences in magnitude of vocal response to AAF during vocalization between groups? Is there a strong relationship between magnitude of vocal response and perceptual error detection ability during a motor task? What are the differences in neural processing of pitch-shifted AAF and NAF between groups? Is there a strong relationship between neural activity and behavioral measures? Findings from this research will inform our understanding of sensorimotor processing involved in speech perception, error detection, and motor correction, as well as our knowledge of how impacted brain networks following left-hemisphere injury affect expressive and receptive speech processing which is vital for the spoken communication system. Understanding the impacts and underlying sources of sensory, motor, and/or sensorimotor deficit on speech error detection and correction is important for the development of targeted, efficacious diagnostic and treatment tools to improve communication and quality of life of people with speech disorders.

To answer these questions, participants completed a pitch-shift AAF paradigm while their voice feedback, perceptual error detection responses, and neurophysiological responses were collected. Behavioral results revealed that, as compared to controls, the LHS group had lower average correct rate; a significantly decreased average magnitude of vocal response in the 101-200 ms time window post pitch-shift onset; and a significantly longer time to local peak latency in the 100 to 400 ms time frame following pitch-shift onset. ERP analyses showed a decreased magnitude of ERP activity in the LHS group compared with controls and a significant expression of the SPRE effect in both control and LHS groups at the N1 component during the AAF condition. There was no interaction between task and group indicating no significant modulation of SIS or SPRE effects between groups. No significant relationships between the behavioral and neurophysiological measures were established in this study.

4.1 BUTTON PRESS RESPONSES

Analyses of button press responses revealed significantly lower average correct rates in the LHS group compared with controls with no significant differences in performance between vocalization and listening tasks for either group. This finding confirmed our first hypothesis of observing a group effect but not a task effect. This current study's lower average correct rates in the LHS group are consistent with findings from the Sangtian et al. (2021) study that was previously conducted on a subgroup of this current study's participant pool. In the Sangtian et al. (2021) study, the LHS group had lower speech error detection rates, lower speech error rejection rates, and decreased sensitivity to discriminate pitch-

shift alterations in auditory feedback compared with controls during both vocalization and listening tasks. From a neuroanatomical perspective, the lower perceptual accuracy rates in the LHS group may be explained by cortical damage to auditory networks vital to speech-auditory processing, such as the superior temporal gyrus, area Spt, STS, Heschl's gyrus, postcentral gyrus, (Chang et al., 2013; Greenlee et al., 2013; Hickok, 2012; Behroozmand et al., 2015 & 2016). We did not conduct a full lesion-symptom mapping analysis as part of the present study. However, in support of this speculative account, ~82% (31 out of 38) of LHS participants in the study had lesions to the left hemisphere in both the Heschl's and superior temporal gyri. Further, previous studies have shown that total lesion volume in stroke participants is strongly correlated with decreased behavioral performance (DeMarco and Turkeltaub, 2018; Price, Hope, & Seghier, 2017; Wiesen et al., 2019).

By contrast, our alternative hypothesis, which stated there would be no task effect in the control group but the LHS group would have a higher average correct rate during vocalization compared with listening due to activation of the efference copy, was not supported. The lack of task effect within the control group was expected given their presumably intact auditory processing mechanisms. Previous studies in neurotypical populations have shown enhanced auditory neural responses to pitch-shift stimuli during vowel vocalization versus passive listening, possibly attributable to activation of the efference copy mechanism (Behroozmand et al., 2009; Chang et al., 2013; Greenlee et al., 2013; Korzyukov et al., 2012). However, the lack of task effect was mirrored in the LHS group as well: the LHS

group showed no significant difference in performance during vocalization versus listening. The lack of a task effect in the LHS group does not negate the activation or existence of the efference copy. Rather, when considering the LHS group's overall lower average correct rate and lack of task effect, the implications of impairment to the cortical areas in the left hemisphere involved in sensory, motor, and/or sensorimotor networks must be considered. Damage to any one or more of these networks may impair perception and processing of the speech error and/or auditory-to-motor transformation of the vocal response involving activation of the efference copy. For example, it is possible that the efference copy may be intact, but impairment of the auditory (sensory) network may prevent its activation. Additionally, the overall lower average correct rates in the LHS group are not likely due to diminished peripheral perception of the pitch-shifts given the LHS group had pure-tone hearing screen measures comparable to the control group, and the local peak magnitude of vocal motor responses was comparable to the control group, as discussed in the next section.

4.2 VOCAL MOTOR RESPONSES

For the average vocal compensation during the 101 to 200 ms time bin, the LHS group had significantly decreased magnitude of vocal response. The decreased magnitude of vocal response in this early time bin was consistent with other studies on a subgroup of this current study's population (i.e., Behroozmand et al., 2022; Sangtian et al., 2021). The Behroozmand et al. (2022) and Sangtian et al. (2021) studies found decreased magnitude of vocal response in the LHS group compared with controls in an early time window of 150-200 ms after the

onset of pitch-shift stimuli. However, there are notable differences in further analyses conducted in this current study compared with the Behroozmand et al. (2022) and Sangtian et al. (2021) findings. Particularly, this current study explored both the magnitude and time latency of average local peak vocal responses in the full 100 to 400 ms time range, in addition to average vocal response analyses within separate 100 ms time bins. This current study's exploratory analyses showed no significant group difference in magnitude of local peak vocal responses over the longer time window post-pitch-shift. However, there was a significantly longer time latency of peak vocal response in the LHS group compared with controls (i.e., 307ms for LHS compared to 265ms for control). In other words, there is a delay in processing time within the LHS group, but their average local peak magnitude of vocal compensation in this sample is comparable to that of the control group. This peak, which is delayed in time but comparable in magnitude, suggests the auditory feedback signal takes more time to catalyze into a compensatory action in the LHS group. Similarly, Johnson et al. (2020) showed people with aphasia had slower vocal compensation response times to pitch-shift stimuli compared with controls. Moreover, Johnson et al. (2020) found no significant group difference in magnitude of vocal response when the timing variable was controlled.

The LHS group's time delay in reaching the average local peak magnitude is also reflected in the average vocal response magnitude group comparisons per 100 ms time bin. More specifically, a significant decrease in average vocal motor response magnitude was present in the early 101 to 200 ms time bin only, and not

for the later time bins from 201 to 400 ms. The LHS group's time delay in reaching peak is not completely surprising, given the supporting literature on both slowed motor reaction and slowed domain-general processing speed in stroke survivors, including some persons with aphasia (e.g., Meier et al., 2018; Faroqi-Shah & Gehman, 2021; Loranger et al., 2000; Rasquin et al., 2002; Su et al., 2015). Further, the majority of this current study's LHS group had lesions to cortical regions vital to speech auditory processing mentioned previously (e.g., STG, etc.) which have been shown to account for diminished speech error detection and correction ability (Behroozmand et al., 2018; 2022). What warrants further investigation is whether the time delay in reaching peak vocal compensation is affected specifically by speech sensorimotor impairment or whether it is a consequence of the stroke in general.

Analyses were additionally conducted to examine correlations between perceptual auditory measures during the vocalization task (i.e., button press responses) and vocal motor responses within the LHS and control groups. Contrary to our hypothesis, results indicated no statistically significant correlations between these two behavioral measures within any group. There are a few possible explanations for this lack of correlation. First, as previously mentioned, earlier studies provided evidence of a dissociation between perception and motor action in neurologically-intact controls where participants were able to compensate vocally for AAF without perceptual detection of the pitch shift (Franken et al., 2018; Hain et al., 2000). This dissociation appears to have been evidenced in this current study as well in both the control and LHS groups. Additionally, cognitive processes,

such as attention, are involved in overt awareness. Perhaps the measure of average correct rate was not a good predictor of vocal compensation magnitude because the average correct rate was not a measure that fully captured other cognitive processes that may drive the connection between overt auditory perception and vocal compensation response. Further, in the case of the LHS group, lesions to critical auditory-motor cortical areas may further obfuscate the association between auditory perception and motor response.

4.3 ERP RESPONSES

The second part of this study examined the neurophysiological data collected during the speech error detection task . We hypothesized that the LHS group would demonstrate a) diminished suppression of ERP responses to NAF during vocalization versus listening, and b) diminished enhancement of ERP responses to AAF during vocalization vs listening compared with the control group. First, we conducted two-way ANOVAs to assess the effects associated with task, group, and their interaction on ERP activity within each region of interest, separately. Then, we conducted t-tests to evaluate the group differences in the amount of motor-related activity at each ROI.

Results revealed significant group effects with reduced amplitude of ERP responses in the LHS group compared with controls in two ROIs. Within the NAF condition, this group effect was evidenced in P1 anterior ROI. Within the AAF condition, this group effect was evidenced in the P2 anterior ROI. Notably, this study used the Bonferroni method for multiple comparisons which is a relatively conservative criterion for statistical significance. Additional results trended toward

significance but did not reach the threshold for statistical significance after application of the Bonferroni method. These results included main effects of group at both N1 and P1 anterior and posterior ROIs in the NAF condition, and main effects of group at the P1 posterior, P2 anterior, and P2 posterior ROIs in the AAF condition. The group effect demonstrated in this study is in line with the Behroozmand et al. (2022) study which evidenced stronger ERP activity in the control group compared with aphasia at the N1 and P1 ERP components during NAF, and P1, N1, and P2 ERP components during AAF.

Additionally, there was a significant main effect of task in the AAF condition at the N1 medial ROI which indicated larger ERP amplitude during vocalization compared with listening (i.e., expressed SPRE effect) in both groups. In other words, the demonstrated SPRE effect indicated both groups exhibited differences in sensory processing when presented with a pitch shift (speech error) during an active motor task compared with during a passive listening task. The demonstrated SPRE effect during an AAF task is consistent with findings of previous EEG (e.g., Behroozmand et al., 2009, 2022; Eliades and Wang, 2008) and ECog (Chang et al., 2013, Greenlee et al., 2013) studies in neurologically intact adults. Accordingly, Behroozmand et al. (2022) showed a significant SPRE effect at the N1 component in both PWA and control participants. The SPRE effect was again expressed in this study. The SPRE effect occurs when the motor system is active and there is a mismatch between the corollary discharge and actual auditory feedback. Thus, in the context of this study, presence of the SPRE effect suggests an at least partial activation of the efference copy in the LHS group.

While there was evidence of main effects of both group and task, we found no support for our hypotheses of diminished SIS and SPRE effects in LHS versus control groups. However, that is not to say that such effects cannot occur. For example, Behroozmand et al. (2022) evidenced diminished SIS and SPRE effects in the LHS group compared with controls. As previously mentioned, there is an overlap in the participants observed in both this current study and the Behroozmand et al. (2022) study. Alternate approaches between the analyses conducted in the Behroozmand et al. (2022) study versus this current study may have contributed to discrepancies in results. Additionally, the resources available for ERP analyses of the current data set differed from the tools used for the Behroozmand (2022) paper. More specifically, the Behroozmand et al. (2022) study did a TANOVA analysis that looked at ERP activity in a smaller number of electrodes in the left hemisphere in slightly different time ranges, and they calculated an ERP Modulation Index for the aphasia participants to determine between-group differences in vocalization-induced enhancement. In contrast, this current study analyzed ERP components in a larger number of electrodes that often spanned the left and right hemispheres and midline at different time bins, and difference waves values calculated for the LHS and control groups were submitted for between-group statistical analyses.

4.4 RELATIONSHIPS BETWEEN ERP AND BEHAVIORAL RESPONSES

The final analyses in this study sought to merge both areas of focus within the examination of speech auditory feedback processing by combining behavioral and neurophysiological data. We hypothesized there would be a) significant

associations between vocalization-induced ERP activity and average correct responses within the control group among both vocalization and listening tasks, b) a significant association between the vocalization-induced ERP activity and average correct rates during vocalization only for the LHS group, and c) a significant association between the vocalization-induced ERP activity and magnitude of vocal motor response in the control group, but not in the LHS group.

As mentioned before, an ECog study by Chang et al. (2013) revealed a relationship between ERP activity and behavioral response. In particular, Chang et al. (2013) found that the electrode sites with greater SPRE activity were more predictive of stronger correlations with vocal compensatory responses. Further, Behroozmand et al. (2022) found a positive correlation between vocalization-induced N1 ERP enhancement and stronger vocal compensation responses to pitch-shift stimuli in the AAF condition only in the control group and not PWA. Contrary to the Chang et al. (2013) and Behroozmand et al. (2022) studies, this current study's results revealed that the control group tended to have higher average correct rates than the LHS group (in line with the behavioral results previously discussed), but there were no statistically significant associations between behavioral and neurophysiological activity. In other words, there was no strong linear relationship between vocalization-induced ERP activity and behavioral responses in this current study. The lack of linear associations between vocalization-induced ERP activity and behavioral measures in the LHS group was not surprising. As described in section 4.1, damage to any one or more of the sensory, motor, and/or sensorimotor networks may impair perception and neural

processing of the speech error. Lesions to these cortical networks can weaken behavioral and neural responses and/or the associations between them. In this study, there was not a strong association between neural and behavioral measures in the control group as was seen in the Behroozmand et al. (2022) and Chang et al. (2013) studies. The discrepancy in results may also be related to the differences in ROIs selected and methods of calculation for vocalization-induced ERP activity. These factors are acknowledged in the limitations of this study as addressed below.

4.5 LIMITATIONS AND FUTURE DIRECTIONS

Several limitations should be considered in this study. First, we acknowledge the relatively small and heterogeneous sample size, particularly with respect to the LHS group. Participants with and without aphasia, and with different subtypes of aphasia as identified by the WAB-R clinical assessment, were grouped together despite the individuals' differing levels of impairment on receptive and expressive speech and language tasks. Moreover, some LHS participants had co-occurring motor speech disorders including dysarthria and/or apraxia of speech. The heterogeneity and small sample size of the LHS participants in this study would limit robust analyses if the participants were analyzed by subgroup, such as impairment type or level. The sample size will be expanded for future studies to enable further investigation of differences between aphasia subtypes, lesion locations, lesion sizes, age, and cognitive factors associated with performance on speech error processing and motor control tasks.

Like other studies using the pitch-shifted AAF paradigm, this study consisted of a nonlinguistic task which limits the translation of results to the language domain. Additional studies are warranted to better understand the similarities and differences between non-linguistic and linguistic speech sound processing.

Another possible limitation is the effect of fatigue on attention during testing. While breaks were given as needed, this experiment consisted of two 45-minute blocks and sought to obtain data from approximately 180 trials for each experimental condition. Because some participants experienced fatigue, their sessions were shortened. In those cases, we obtained less than 180 trials. In the future, analysis of possible variances in performance between each 45-minute block warrants further investigation.

As previously mentioned, the selection of the time range for the ERP components was based on visual inspection of the prominent ERP latency in the ERP profile at the Cz electrode. Consequently, the ERP amplitudes at the time windows submitted for analyses at varying ROIs may not have necessarily captured the true peak amplitude for each component across the electrode sites at each ROI. Further, EEG measurements for some of the participants were visually determined, which may have possibly led to discrepancies in neural data collected at targeted electrode sites between individuals.

Finally, since measures of pitch discrimination threshold were not obtained in this study, it is not possible to determine if variability in frequency difference limens contributed to performance variability on the experimental tasks. Further

investigations into the effects of pitch discrimination thresholds would be of interest in the future studies, as would an exploration of differences in perceptual performance based on the direction of pitch-shift stimuli.

4.6 CONCLUSIONS

In summary, our findings were consistent with previous studies showing decreased perceptual auditory error detection ability in LHS compared with controls; slowed motor response in stroke survivors; decreased magnitude of ERP activity in the LHS group compared with controls; and expression of the SPRE effect in the LHS and control groups. In the context of the speech sensorimotor system, the expression of the SPRE effect in the LHS group suggests an at least partially intact feedforward system, including the engagement of the efference copy mechanism. However, the slowed vocal motor response and decreased perceptual error detection ability in the LHS group indicate impairment within the sensory, motor, and/or combined sensorimotor mechanism. No significant linear relationships were detected between vocal motor response and perceptual error detection ability, vocalization-induced ERP activity and vocal motor response, or vocalization-induced ERP activity and perceptual error detection ability. The lack of significant relationships between the specific behavioral and neurophysiological measures selected in this study does not preclude the possibility of other behavioral and neurological measures as potential biomarkers of impaired speech auditory feedback processing and feedforward system impairment, such as latency of vocal motor response, auditory comprehension or verbal fluency behavioral scores, lesion location, or a number of other factors. Future studies are

necessary to further investigate the relationships between behavioral and neural responses in the left-hemisphere stroke population.

As this current study was a piece of a larger ongoing study, several limitations may be overcome as the larger project approaches completion, including an increased sample size that would allow for examination of more specific subgroups of clinical populations (e.g., participants grouped by lesion location, aphasia subtype, or motor speech disorder). Overall, this current study provided further supporting evidence of speech auditory feedback processing impairment in left-hemisphere stroke and identified additional areas warranting further investigation to advance our understanding of the extent to which the separate and integrated sensory and motor systems contribute to speech auditory processing deficit. A clear understanding of the etiology of speech auditory processing deficits in the brain and their consequences on everyday communication is of clinical importance for the development of targeted, efficacious diagnosis and treatment methods of speech and language disorders in people with neurological injuries. For example, identification of the specific cortical areas where damage results in speech error processing impairment may be informative for focused application of rehabilitative stimulation such as transcranial electric stimulation or transcranial magnetic stimulation. Accordingly, clinical application of these findings may be transferable to other acquired neurological disorders with motor speech impairment. Improving our understanding of the speech auditory processing network gives us the ability to improve the quality of life of people affected by motor speech disorders.

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