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Dynamic Functional Connectivity During a Dual-Stream Auditory Attention Task

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A dissertation
submitted in partial fulfillment of the
requirements for the degree of

Doctor of Philosophy

University of Washington

2023

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Program Authorized to Offer Degree:
Electrical and Computer Engineering

University of Washington

Abstract

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Navigating conversations in complex auditory environments requires dynamic control of attention - switching and maintaining attention across multiple auditory objects. Several brain regions, some traditionally considered auditory and others non-auditory, have been highlighted as part of the cortical networks that contribute to the ability to switch and maintain attention between multiple talkers. M/EEG data was collected during a dual-stream auditory attention task from three separate experiments, in which the listener was asked to attend to one of two speech streams that differed in location or pitch. In each trial, the listener was cued to either maintain their attention on one talker, or switch their attention to the second talker during an interstimulus interval in which no speech was presented. A state-space model and a novel statistical approach were applied to the brain imaging data, to elucidate the differences in the dynamic functional connectivity across brain regions when maintaining and switching attention across different auditory cues.

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ACKNOWLEDGMENTS

The author wishes to express sincere appreciation to several funding sources who have supported the duration of this work: The Office of Graduate Student Equity and Excellence, the Auditory Neuroscience Training Grant, and the Department of Electrical and Computer Engineering at the University of Washington. The author also acknowledge the past and present members of the Laboratory for Auditory Brain Sciences and Neuroengineering (LABSN) for supporting me in running experiments, writing, and signal processing: Rahul Nadkarni, Eric Larson, and the members and PI of the Atlas lab. Finally I acknowledge Adrian KC Lee for his advising, mentorship, and friendship - your support is the foundation of my success, thank you.

DEDICATION

To my family and friends who believed in me, even when I didn't believe in myself - thank you, I could not have done this alone.

Chapter 1

INTRODUCTION

This dissertation is structured in the following way: Chapter 1 introduces ideas about auditory attention, or attending a single auditory object in the presence of competing auditory stimuli. It continues on to introduce functional connectivity, or how distinct brain regions work together to accomplish a behavioral task, and various ways to measure this relationship. Chapter 1 concludes with the motivation behind completing the research projects discussed. Chapter 2 outlines the research methods across 3 experiments, highlighting the differences and similarities across experimental paradigms. The remainder of the methods (including neuroimaging data collection and processing, and how functional connectivity was inferred) are presented collectively as these methods were consistent across experiments. This chapter also includes a measurement of the temporal dynamics of the functional connections as a deeper dive into the timing of these connections as they relate to the stimulus intervals. Chapter 3 discusses the various results for each of the experiments. The structure of Chapter 4 reflects Chapter 3 as the results are discussed and interpreted for meaning from a neuroscience perspective. Chapter 5 concludes this dissertation by discussing the significance of this work as it pertains to the fields of engineering and neuroscience, and by discussing possible future directions for this work.

1.1 Auditory Attention

Communication propels our society forward. Accurately transmitting information is essential to bringing ideas into fruition, forming relationships, and self-expression. Unfortunately, many of the social environments in which humans gather with the intention of communicating our thoughts and ideas are crowded and noisy. This collective noise makes holding a simple conversation a challenging task. The challenges we face in communicating in these types of environments are referred to in the literature as the “cocktail party problem,” where the overlapping spectrotemporal cues of several auditory streams make it challenging to perceive a single sound of interest [10]. Fortunately for us, the healthy, neurotypical auditory system has the extraordinary capability to effectively tune out non-salient auditory stimuli, and selectively enhance an attended sound stream, in a process frequently referred to as “auditory scene analysis” [10].

Alone, and at a reasonable loudness level, a single auditory stream would typically be perceived without any strain or challenge. When overlapping in time and space, multiple streams may be perceived as noise by the listener, making it challenging to process meaningful information from any single auditory stream. However, each of these streams has distinct spectral and temporal features that listeners can use as cues to distinguish one sound source from the remainder. Some of the primary cues used to isolate these mental auditory images include pitch and spatial location [6]. Systems neuroscientists are still investigating the role of selective attention in navigating complex auditory scenes. These questions surround the complex dynamics of neural activity as listeners pay attention to one of the many auditory sources in their environment.

While research in the visual domain has made strides in elucidating the cortical regions involved in executing visual attention, the coordination of said brain regions in executing selective attention in audition is underexplored. The few existing auditory studies so far suggest that visual and auditory selective attention rely on many of the same cortical regions. From the auditory neuroscience viewpoint, understanding how auditory areas interact with these cortical regions is a necessary path to understanding this attention-oriented cortical network. The collection of work discussed in this dissertation outlines the computational tools necessary for the analysis of high dimensional time series data from neuroimaging recordings across several regions, required to quantify these cortical interdependencies.

1.2 Neuroimaging

Depending on the scientific question, there are several methods that can be implemented in order to estimate the neural activity of the brain. One of the most common methods in the neuroscience community is magnetic resonance imaging (MRI). This method uses large magnets to align the protons of the water in the body, and a strong radiofrequency to knock those protons out of alignment. The time and energy it takes for those protons to realign are used to create a static image of the brain's structure. A similar method, known as functional MRI (fMRI) uses the blood oxygen level dependent (BOLD) measurement to observe how blood flows through biological tissue by detecting the paramagnetic signal from deoxygenated blood. The idea is that after a group of neurons fire, blood flow increases in the surrounding area to replenish nutrients of those neurons. While this method provides high spatial resolution, the fact that the blood flow occurs after the neural response means this method has low temporal resolution, working at a time scale of around one second. For scientific questions regarding neurons that respond to auditory stimuli, a neuroimaging technique that can record at a sub-second timescale is necessary. Fortunately, methods such as magneto- and electroencephalography (M/EEG) can yield datasets with the timescale of a millisecond (Figure 1.1a). MEG uses a very large sensor array structured around the head to record changes in magnetic field near the scalp. EEG uses a large sensor array to record changes in electric current at the scalp. While these methods are high in temporal resolution, they are limited to recording changes in magnetic field and electric current at the scalp, resulting in poor spatial resolution. Since magnetic fields and electric current are orthogonal in nature, these two methods can be used in combination to maintain the high temporal resolution while increasing spatial resolution (Figure 1.1b; [30, 39, 46]). While M/EEG recordings are traditionally used to quantify the dynamic behavior of separate brain regions, this data alone cannot elucidate how these brain regions work together in everyday scenarios.

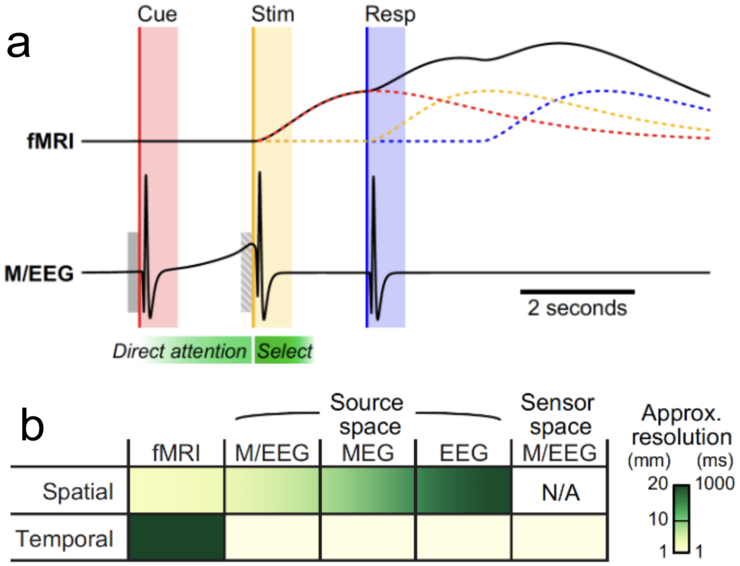

Figure 1.1: M/EEG Has Preferred Spatiotemporal Resolution for Measuring Neural Responses of Auditory Stimuli (borrowed from Lee et al., 2014 [31]). (a) M/EEG has better temporal resolution compared to fMRI and better spatial resolution compared to MEG or EEG alone. (b) M/EEG is more appropriate than fMRI to record neural responses from stimuli occurring on a sub-second scale.

Several more recent studies in auditory neuroscience make use of M/EEG recordings to discern the neural mechanisms involved in flexibly attending to competing auditory stimuli. While the cortical dynamics of attention are well studied and documented in the visual domain [13], the auditory attentional network is not as well characterized. In previous studies, many of the cortical regions outlined in the visual attention literature have been shown to be active in auditory attention tasks (Figure 1.2). For example, when selectively attending to an auditory stream differentiated by its location, neuroimaging reveals that the Frontal Eye Fields (FEF) have significantly more activation compared to attending a stream differentiated by its pitch [32]. FEF is described as being involved in directing attention even independent of eye movement [5, 12, 55]. Additional experiments reveal that the Right Temporal Parietal Junction (RTPJ) was more activated when instructed to switch spatial attention compared to maintaining spatial attention [29]. The activation of RTPJ is also correlated with performance and is indicated in playing a role in filtering out distractions and redirecting attention to salient cues from visual areas as part of the ventral frontoparietal network [13]. In addition to confirming the activation of RTPJ when switching attention, Larson & Lee, 2014 [29] also revealed that the Left Inferior Parietal Supramarginal Part (LIPSP) showed more activation when maintaining attention to pitch compared to switching attention between streams differentiated in pitch. More recent experiments indicate a higher level of activation in the Dorsolateral Prefrontal Cortex (DLPFC) when switching attention from pitch cues to spatial cues when compared to switching attention across different pitches. The DLPFC has been indicated as a key component of higher cognitive function and is said to play a role in switching between different cognitive tasks [9, 37]. Within the audition and vision literature, the Intraparietal Sulcus (IPS) is said to contain an extraretinal map and to interact with the FEF in directing eye gaze as part of the dorsal frontoparietal network, sending top-down influences to visual areas [13, 31]. The IPS has also been implicated as part of this network in roles associated with auditory scene analysis, figure-ground segregation [14, 50], and identifying the location of sound in space along the azimuth [17, 16]. Outside of the sensory literature, the IPS is described to play a role in counting or analysis of magnitude [18], which in regards to auditory attention could be related to the mental demands of mentally segregating multiple auditory streams. The dorsal frontoparietal network for attention also includes anterior cingulate cortical regions [42], including the anterior cingulate cortex (ACC) which has been argued to play a role in signal enhancement in the presence of distractions [58, 33, 48]. How these cortical regions work together over time to accomplish auditory scene analysis, and how auditory regions interact with the dorsal and ventral frontoparietal networks for attention, is not well understood.

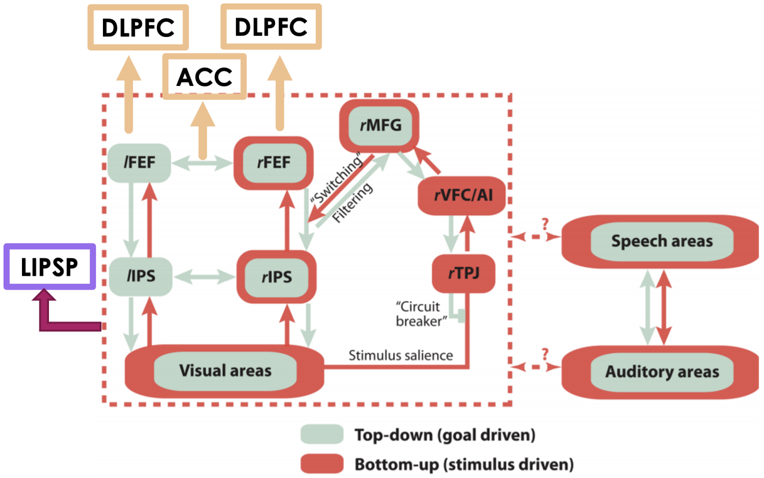

Figure 1.2: A priori Regions of Interest (modified from Lee et al., 2014 [31]). Connectivity between regions documented as part of the dorsal (goal driven) and ventral (stimulus driven) frontoparietal networks for attention is underexplored. Connections between these networks to speech and auditory areas are unknown.

1.3 Functional Connectivity

The field of neuroscience discusses multiple types of connectivity to describe the interaction between neurological entities, whether it be single neurons or cortical regions. Effective connectivity is defined by the most simple circuit of neurons needed to reproduce some experimentally observed temporal activity [23]. Structural connectivity explains how different regions of the brain are physically connected and can be measured via analysis of diffusion tensor imaging or other MRI-based tractography methods [57]. The focus of this body of work surrounds functional connectivity, whose definition varies depending on the neuroimaging techniques involved and analysis methods used.

Functional connectivity can be broadly defined as temporal dependencies or relationships between distinct neurophysiological areas that can account for some of the variance-covariances in neural activation patterns [21, 23]. More traditional measures of functional connectivity, such as Pearson's correlation, assume stationarity and thus capture primarily time-invariant linear dependencies between time series [38]. Multiple methods of coherence and phase-locking analyses in the frequency domain have also been implemented as alternatives to time domain analysis [44, 53], and provide a similarly static measure of connectivity. While both resting-state and task-based fMRI data can inform functional connectivity [35, 43], the temporal resolution prevents analysis on timescales shorter than about a second. Fortunately, M/EEG records brain activity with millisecond time resolution. This is useful for observing time-varying neural activity in response to many stimuli or conditions that involve rapid temporal processing (e.g., listening to auditory stimuli). However, the use of M/EEG introduces the inverse problem, where cortical activity must be localized in space. This localization is estimated per subject by mapping sensor data to specific cortical regions using data from a structural MRI. When computing functional connectivity across these estimated locations using frequency band coherence, a zero-lag coherence could provide false measurements of functional connectivity due to current spread across cortical regions and cross-talk across physical sensors.

Previous work [11] has used Pearson's correlation of the MEG signal's Hilbert envelope, as well as a measure of frequency band coherence to estimate resting state functional connectivity across hemispheres. To overcome issues regarding cross-talk, Guggisberg et al. [22] implemented a measure using imaginary coherence in order to eliminate coherent sources with zero-time lag. Even with the high temporal resolution of M/EEG, a simple correlation over time or coherence across frequency bands may not be sufficient in quantifying time-varying functional connectivity. In M/EEG accompanying behavioral tasks, inter-region connectivity is likely time-varying, as it may change as a function of time, stimulus, and the engagement of the subject (e.g., attention). Therefore, an ideal measure of connectivity would resolve the evolution of the connectivity structure over both space and time over the course of a fairly short time period of interest (e.g., one second).

To overcome these limitations, Yang et al. [60] developed a time-varying state-space model capable of characterizing the interregional dynamic connectivity between regions of interest (ROIs). The state-space model was used to estimate the time-varying functional connectivity of 2 ROIs for a single subject engaged in a visual task. Later, this model was modified in order to characterize the structured lagged dependence across multiple cortical ROIs during an auditory attention task [40, 41]. The resulting linear dynamic system incorporates a first-order multivariate autoregressive (AR) model whose AR coefficients indicate the lagged dependence between two ROIs (including an ROI with itself). The result is a time-varying matrix indicating the lagged ROI-to-ROI dependence as it changes over time (typically during a task of interest), for each ROI in time step t, compared with each ROI in time step $t + 1$ (Figure 1.3). These computed lagged dependencies, in addition to the robust statistical analysis presented in Section 2.4 , can be used to interpret the extent to which two regions are functionally connected. As the resulting data compares each ROI in both lead and lagged positions (t vs $t + 1$), the direction of information flow between two ROIs can be inferred. The use of the first-order AR model combats issues regarding current spread and volume conduction. Where analysis of a zero-lag interaction could mistake the activity of an ROI interacting with itself as an interaction with a neighboring ROI, effectively computing an autocorrelation, a single step time lag ensures that the signals of interest are from different sources.

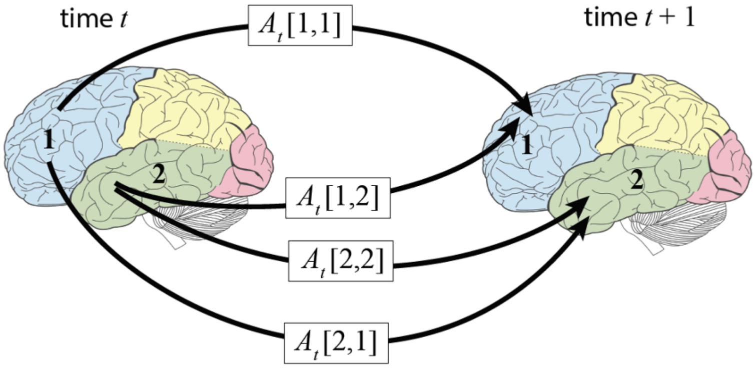

Figure 1.3: Connectivity Across Regions. Functional connectivity across regions is inferred from structured lagged dependence, as measured via first-order auto-regressive coefficients (borrowed from Nadkarni et al., 2019 [40]).

While typical approaches to computing functional connectivity estimate connectivity at the single-subject level and then make statistical inferences at the group level [11, 42, 51], the method presented here takes a different two-step approach. First, we jointly estimate connectivity across all subjects by incorporating the entire dataset into a single SNR-boosted "average subject" for each experimental condition. Second, we use a bootstrapping approach to avoid overfitting of the model and to determine the statistical significance of the model's output. The two-step approach implemented here is in response to the high dimensionality of the data. The large number of sensor recordings, the bank of 12 ROIs, and the length of the recordings across the duration of each trial, greatly increases the inherent noise of the dataset. By averaging several trials across subjects, the SNR-boosted "average subject" works to further de-noise the data and promote robust signals of interest. These SNR-boosted signals are then used as inputs to the linear dynamic system in order to infer which cortical regions are functionally connected.

1.4 Motivation

Although the cortical mechanisms behind visual attention have been more thoroughly studied, the mechanisms underlying the deployment of auditory attention are less understood. Corbetta et al., 2008 [13] discusses the dorsal and ventral frontoparietal networks as components of a larger supramodal attention network, a system of cortical regions that work together to execute attention across sensory modalities. The ventral network is more responsible for reorienting attention, in part due to the circuit-breaker-like behavior of RTPJ that works to filter out non-salient information. The dorsal network is said to be responsible for holding attention to some external stimulus. While some cortical regions from these networks have been shown to be engaged in the execution of auditory attention, it is unknown how auditory regions interact with this supramodal attention network when attending strictly auditory stimuli.

The objective of this study is to apply the previously mentioned state-space model to M/EEG data collected during a dual-stream auditory attention task in order to estimate the functional connectivity across the following 12 a priori selected attentional ROIs, listed from most highly executive regions, to dorsal and ventral regions, to sensory regions: left and right (l/r)DLPFC, ACC, (l/r) FEF, (l/r)IPS, LIPSP, RTPJ, (l/r) auditory regions (AUD), and the visual regions (Vis). The scientific contribution made here is the expansion of the model implemented in [60] to estimate functional connectivity across many ROIs for several jointly measured subjects. Additionally, this project implemented a novel approach for the statistical analysis of our SNR-boosted results. Although the measurement of connectivity is time-varying across the duration of the experimental trials, the cortical networks displayed here are representative of a snapshot in time, as they are derived from a small time window in which experimenters can assume the endogenous, or goal driven, actions of the listener.

This dissertation is the culmination of three experiments, each containing subjects completing a dual-stream auditory attention task while listeners partake in M/EEG recordings. Experiment 1 required normal-hearing subjects (i.e. had hearing thresholds $\leq$20 dB HL tested at octave frequencies between 250 and 8000 Hz) to attend 1 of 2 simultaneous speakers delivering brief speech tokens. Experiment 2 asked normal-hearing subjects to attend 1 of 2 simultaneous speakers delivering more realistic, yet still brief, speech streams. Experiment 3 recruited subjects with Autism Spectrum Disorder (ASD; as diagnosed by a clinical psychologist or supervised graduate student) as well as age- and sex-matched neurotypical (NT) subjects, to perform the same task as seen in Experiment 2. The motivation behind Experiment 1 was to determine if different ROIs were functionally connected when switching or maintaining attention to auditory cues in space or pitch. The motivation behind Experiment 2 was to expand on the results of Experiment 1 by removing any visual stimuli from the experimental paradigm, and to use more realistic speech stimuli. Experiments 1 and 2 were compared in a cross-validation analysis to determine if the functional connectivity and statistical analyses were robust enough to produce similar results across similar experimental paradigms. The motivation behind Experiment 3 was to determine if a difference in functional connectivity across subject populations could elucidate a cortical origin for the challenges that people with ASD experience in deploying attention.

This document aims to provide answers to several research questions across the 3 experiments. For Experiment 1: (1) Are the cortical regions of the dorsal and ventral frontoparietal networks functionally connected when deploying auditory attention? If yes, (2) how do the auditory regions connect to these frontoparietal networks? (3) Are different ROIs functionally connected when attending different auditory cues? For the cross-validation (i.e. Experiment 1 vs Experiment 2): (4) Are the presented functional connectivity and statistical analyses robust enough to produce similar results across similar experiments? (5) Is functional connectivity impacted as a function of the difference in stimuli across experiments? For Experiment 3: (6) Are differences in functional connectivity the origin of behavioral differences in attentional deployment across neurodivergent populations?

Chapter 2

RESEARCH METHODS

The following chapter outlines the research methods across experiments. Section 2.1 explains the experimental paradigm behind the dual-stream auditory attention task. The subsequent subsections highlight the differences of this paradigm across the three experiments. The remaining sections of this chapter discuss the methods that all three experiments had in common: the acquisition and preprocessing of M/EEG data, the functional connectivity analysis, the statistical analysis to determine which functional connections were significant, and finally the temporal dynamics of the functional connections between ROIs over the course of the analysis window.

2.1 Dual-Stream Auditory Attention Task

In order to investigate the cortical networks involved when executing auditory attention, a dual-stream auditory attention task was implemented. The foundation of this task involves two competing talkers who speak simultaneously. The two talkers are differentiated in either space or pitch. The talkers provide some speech stimuli over two stimulus intervals, separated by an interstimulus interval in which there is no speech. Throughout the entire trial duration, there is a dichotic presentation of white Gaussian noise to mask any ambient sound from the physical research space. The dual-stream auditory attention tasks described here start with cues, instructing the listener which of the two talkers to attend in each stimulus interval. Then, across two distinct stimulus intervals, both speakers provide their speech stimuli. The trial concludes with a response period in which the listener informs the experimenter what token was spoken by the attended listener. Responses that correctly matched both speech tokens of the attended speaker(s) were labeled as correct.

2.1.1 Experiment 1

This study used behavioral and neuroimaging data from 14 normal-hearing adults. Subjects completed a dual-stream auditory attention task where listeners were instructed to either maintain or switch their attention between two simultaneous talkers across two stimulus intervals. Spoken digits in the set of [‘1’, ‘2’, ‘3’, ‘4’] were presented in the MEG scanner using Tucker-Davis Technologies amplification hardware (RZ6 and HB7) and sound-isolation tubal insertion earphones (Nicolet Biomedical Instruments). Constant Gaussian white noise background (20 dB SNR) was presented in addition to the auditory stimuli in order to mask ambient noise. The white noise was inverted in one ear so that it seemed to come from in between the ears whereas a diotic presentation would've given the illusion of appearing distinctly at the center of the head. The simultaneous talkers differed in either location, spatialized to ± 50° azimuth using a generic head-related transfer function while pitch was held at 185 Hz; or in pitch, using speech stimuli monotonized to 185 Hz ± 4.25 semitones while the stimulus was presented at 0° azimuth. Speech stimuli was manipulated using Praat software [7]. In each stimulus interval, only one acoustic feature was manipulated, while the other was held constant so that cortical activity during the interstimulus interval (hereon referred to as the “switch gap”) could be analyzed to infer the cortical mechanics behind switching and maintaining attention across different auditory cues. The listening conditions shown in this study include: maintain attention to space, maintain attention to pitch, switch attention across space, switch attention across pitch, switching from space to pitch, and switching from pitch to space.

Each trial lasted for a duration of 6.5 seconds (Figure 2.1). At the start of each trial, listeners were given two visual cues each 200 ms in duration: arrows indicating which stimulus to attend. A left (right) arrow indicated to listen to the speaker to the left (right). An arrow pointing upward (downward) indicated to listen to the speaker with the higher (lower) pitch. The first cue indicated which speaker to attend in the first stimulus interval. The first cue was followed by a center fixation dot for a duration of 600 ms. The second visual cue indicated where the listener should switch their attention to during the switch gap. If the two cues were identical, the listener knew to maintain their attention on the first speaker for the duration of the trial. Visual cues were presented using Psychtoolbox (https://psychtoolbox.org; [8]). Following the presentation of the visual cues, there was a 600 ms gap before the listener was presented with the two simultaneous speech tokens, differing in location or pitch, for a duration of 350 ms. The first stimulus interval was followed by the switch gap, lasting 800 ms, while visually presenting the centered fixation dot. At the end of there was a 500 ms interval until the subject was prompted with an open circle around a centered fixation dot for 1500 ms, indicating the response period where subjects were to use a right-handed button box to report back the stimuli presented by the specified speaker(s). The circle around the fixation dot disappeared for 1400 ms before the start of the next trial.

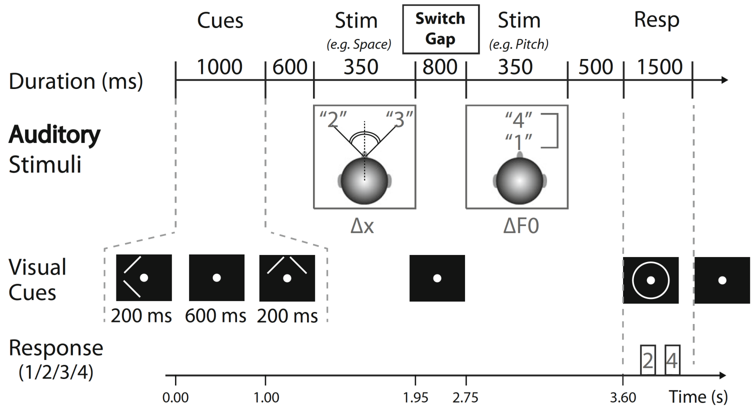

Figure 2.1: Experimental Paradigm of Experiment 1 (borrowed from McLaughlin et al., 2019 [37]). Example trial shows a switch of attention from left spatial cue in the first trial, to a high pitch cue in the second trial.

2.1.2 Experiment 2 (Cross-Validation)

Functional connectivity analysis was performed on M/EEG data collected during a separate but conceptually similar experimental paradigm as described for Experiment 1. The results of this dataset were used in order to help validate the reliability of the functional connectivity measurements. The major differences between Experiments 1 and 2 include a different set of subjects (16 normal-hearing subjects) and a difference in stimuli. The stimuli in the Experiment 2 were gendered, meaning the difference in stimuli was a male vs a female voice. Additionally, the stimuli from Experiment 2 came from a closed set of 2-syllable words: [football, footprint, headlight, headphones]. For the spatial conditions, speakers were separated ± 30° azimuth. Finally, there was a difference in the cues which instructed the listener which stimuli to attend, as well as the method of response. Experiment 2 began with auditory cues, where the voice in which the listener was meant to attend in the first stimulus interval spoke either "hold attention" or "switch attention." If the listener heard the "switch attention," they knew to attend to the other speaker in the second trial. The comparable listening conditions for the cross-validation include: maintain attention to space, maintain attention to pitch (gender for Experiment 2), switch attention across space, and switch attention across pitches (genders for Experiment 2). The paradigm for Experiment 2 also included maintaining attention to both space and gender, and switching attention across space and gender (Figure 2.2). As these conditions had no similar condition in Experiment 1, they were not part of the cross-validation.

Each trial lasted for a duration of 5.5 seconds (Figure 2.3), excluding the duration of the inter-trial interval. The auditory cue lasted for 1000 ms and was followed by a 500 ms gap. This was followed by the onset of the first stimulus interval which lasted a duration of 900 ms. The switch gap lasted for 600 ms and was followed by a second stimulus interval, also of 900 ms. The second stimulus interval was followed by another interval with no stimuli for 600 ms. Each trial concluded with a verbal response period of 1000 ms where the listener repeated back the attended stimulus from each stimulus interval. The stimuli of this experiment was also presented against constant dichotic white-noise background at 20 dB SNR.

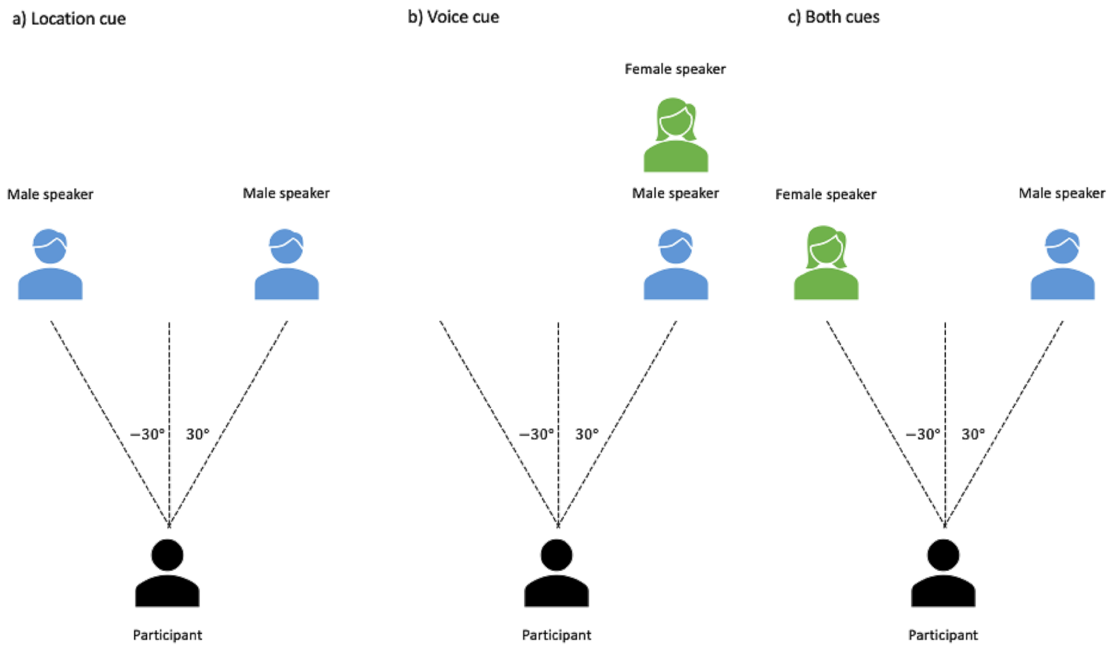

Figure 2.2: Experiment 2 - Listening Conditions. Experiment 2 has 3 types of listening conditions: (a) location cue - 2 speakers of same gender separated in space. (b) voice cue - 2 speakers of different genders co-located in space. (c) both cues - 2 speakers of different genders separated in space. Figure borrowed from Emmons et al., 2022 [19]

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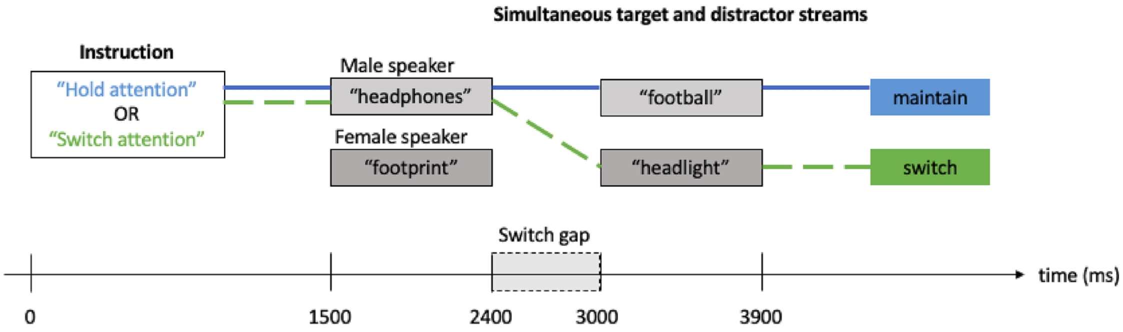


Figure 2.3: Experimental Paradigm of Experiment 2 (borrowed from Emmons et al., 2022 [19]). Blue stream shows example of maintaining attention across stimulus intervals, while green stream shows example of switching attention across stimulus intervals.

2.1.3 Experiment 3 (Neurodivergence)

The third and final experiment used as part of this dissertation used the exact paradigm as described for Experiment 2. The major difference between Experiments 2 and 3 were the subjects that participated in the study. The original study [19] determined that subject groups of 11 would suffice to determine significant differences between 2 groups of subjects. Using several screens for ASD, such as the Autism Diagnostic Observation Schedule (ADOS-2; [34]) and Wechsler Abbreviated Scale of Intelligence, Second Edition (WASI-II; [56]), the original study had a final sample size of 11 subjects with ASD and 11 NT subjects. Due to technical difficulties such as erroneous noise or a missing MRI, only 9 of those subjects per group made it to the functional connectivity analysis stage.

2.2 M/EEG Acquisition and Preprocessing

As in previous work [30] MEG and EEG data were simultaneously recorded for the duration of the behavioral task. A 306-channel dc-SQUID VectorView system (Elekta-Neuromag), combined with a 60-channel MEG-compatible EEG cap (Brain Products), was used to record M/EEG data inside a magnetically shielded room (IMEDCO). Additionally, electro-oculograms (EOG) and electro-cardiograms (ECG) electrodes were worn by the subject for later artifact removal. In preprocessing, environmental noise was removed using temporal signal space separation [49]. EOG and ECG artifacts were removed using signal space projection [52]. Neuroimaging data was low-pass filtered at 55 Hz as in previous work [30, 27, 29, 37]. Raw data from the M/EEG sensors was then epoched from -0.2 sec before cue onset to 5.1 sec after onset, and baseline corrected using the interval (-0.2, 0) seconds.

A total of 4096 dipoles, per hemisphere, were used to construct a cortical M-EEG source space. Individual subject MRIs were used to determine the gray/white matter boundary. Freesurfer (https://surfer.nmr.mgh.harvard.edu/) was used to constrain dipole orientation be normal to the cortical surfaces along the previously mentioned boundaries. An anatomically constrained minimum-norm linear estimation approach [15, 24, 25] was implemented, along with the sensor noise covariance estimated from baseline, to estimate dipole currents within source space from the preprocessed M/EEG data. A non-linear spherical morphing procedure was utilized to map source localization data to an average brain (“fsaverage” from Freesurfer), which aligns individual sulcal/gyral patterns [27, 29, 32, 37]. This process was used to map the 12 ROIs selected a priori (mentioned in the Section 1.2) to the “fsaverage” source space where each source within an ROI is assumed to have the same mean activity. Additional details regarding subjects and M/EEG preprocessing can be found in McLaughlin et al., 2019 [37].

2.3 Connectivity Analysis

In order to represent the activity from the selected ROIs within the source space, the observed (sensor) data is represented as a weighted sum of multiple latent sources, each representing a time series with a location on the cortical surface [60]:

$$y_t = Cu_t + \eta_t; \eta_t \sim \mathcal{N}(0, R) \tag{2.1}$$

$$u_t = A_t u_{t-1} + \epsilon_t; \epsilon_t \sim \mathcal{N}(0, Q), u_0 \sim \mathcal{N}(0, Q_0) \tag{2.2}$$

Equation (2.1) represents the sensor model where y_t is an array containing the time series of the observed data, or the sensor recordings. C represents the forward matrix transforming the unobserved data, or ROI data, u_t, into the sensor domain. η_t indicates the sensor noise, where R is the combined sensor noise covariance and source space noise covariance projected into sensor space via a forward matrix. Equation (2.2) represents how the ROI data are assumed to evolve over time, where A_t indicates the first-order time-varying auto-regressive coefficients indicating the lagged dependence across ROIs. ϵ_t represents the ROI activity noise, where Q is the ROI noise covariance. This mixed-membership representation [2] of the signals is augmented with a multiscale representation over space [59] allowing for regional interactions to be calculated across different spatial scales.

A maximum likelihood estimator (MLE) is implemented in order to determine the AR coefficients that best fit the relationship between the ROI activity at time t and the ROI activity at the previous time step, $t-1$. Since a MLE cannot function with latent or hidden variables, in this case the ROI activity, this computation requires a method to estimate these latent variables. Together, equations (1) and (2) represent a time-varying Kalman Filter, a state-space model commonly used for future predictions of latent variables based on the current and previous state measurements. The system, or space, being observed here is the collection of ROIs while the state is indicated by the ROI activity, where equation (2) is the state observer. The use of a MLE in combination with a latent variable estimator is known as an expectation maximization (EM) algorithm, which works in two steps: first, within the expectation step, the ROI activity is estimated given the sensor data. Second, the maximization step follows using Kalman smoothing to iteratively estimate the AR coefficients given hyperparameters that penalize the coefficient values from getting too large, and encourage temporal smoothness. These hyperparameters were determined for one listening condition for Experiment 1, then selected a priori for the remaining conditions and experiments. The process as described so far outlines the linear dynamic system used to estimate functional connectivity for M/EEG data.

Analysis began using all correct trials after removing sources of noise with traditional neuroimaging preprocessing techniques. For each subject, epochs were consolidated into the 6 listening conditions, per experiment, outlined above in Section 2.1. Additionally, for each subject, the number of trials per condition was made equal according to which condition had the least number of trials for a total of T trials per condition. This way, each subject contributed the same amount of data per condition. The analysis window for each experiment was 2.5 seconds in duration, centered around the middle of the switch gap. The end result was a connectivity analysis per condition for an SNR-boosted "average subject." This increase in SNR is necessary to implement higher order statistical analysis as low SNR data could be detrimental to the statistical computation of such a high-dimensional dataset. The analysis conducted here was combined with a bootstrapping procedure in order to avoid overfitting the EM algorithm. The bootstrapped analysis randomly selected T trials (using a seeded random number generator) with replacement from the T trials per condition. This can be thought of as each trial having a randomly weighted contribution to the analysis. Each bootstrapped analysis used a different random selection of trials. A total of 100 bootstraps were implemented per condition. Each bootstrap produced time-varying AR coefficients for each ROI-to-ROI pair. The values of these AR coefficients were used to infer the functional connectivity between ROIs.

Figure 2.4 shows the 12x12 connectivity analysis output, containing all of the time-varying AR coefficients across all ROI-to-ROI pairs for a single experimental condition. Note that some AR coefficients are negative while some are positive. Due to the complex nature of inverse imaging, the meaning of positive versus negative values cannot currently be explained. The sign of ROI activity is a function of the assigned dipole direction. This is a necessary step to ensure that averaging source activity within an ROI does not result in the cancellation of relevant signals. Therefore, the meaning of negative or positive correlation between ROI activity becomes ambiguous. As a result, our analysis is based on the absolute values of coefficients, rather than their sign. Therefore, AR coefficients with a confidence interval (± 2 standard deviations) not including 0 are the preliminary candidates for functionally connected regions. The diagonal is purposefully left blank as our analysis is not focused on a region's autoregression with itself. The AR model is of order 1, so the time series from ROIs in the rows lead the ROI time series in the columns by a single time step. This allowed us to infer the direction of functional connectivity, or to determine which ROIs were driving the activity in other ROIs.

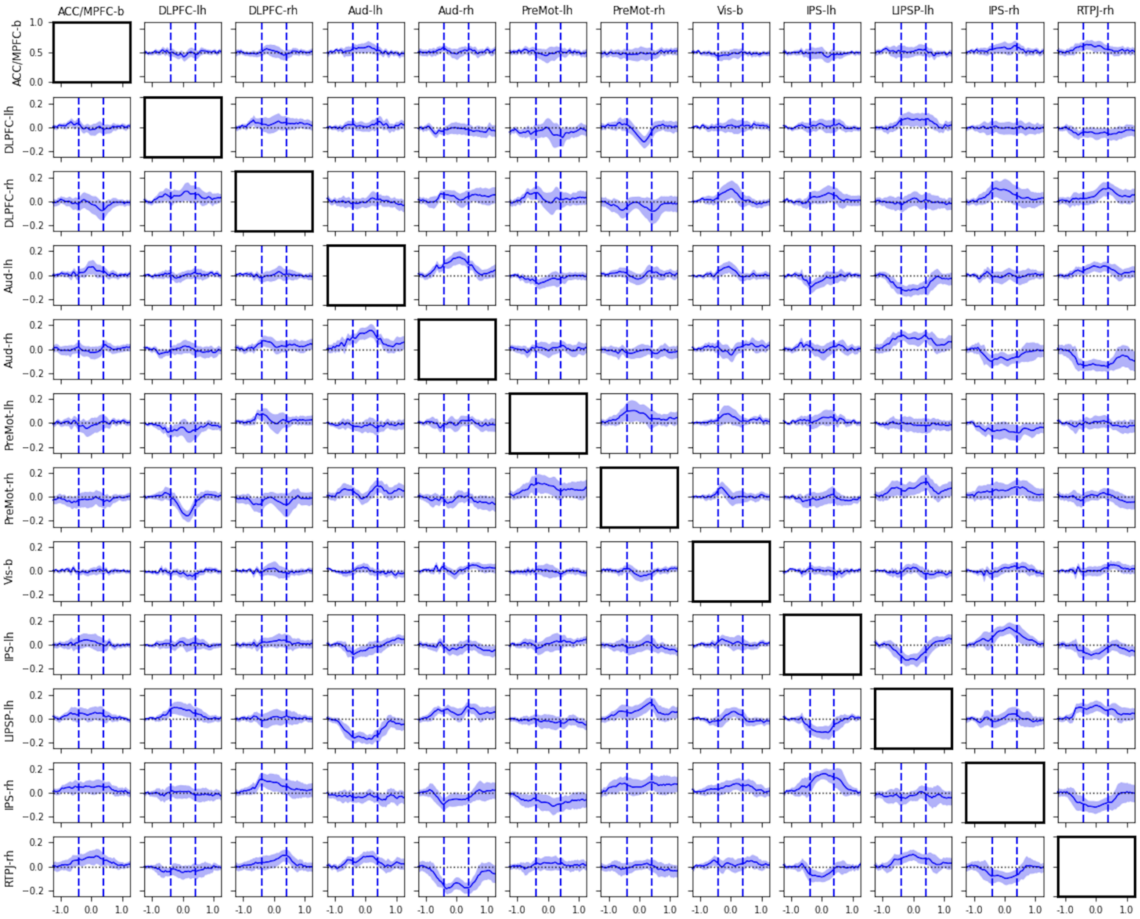


Figure 2.4: Connectivity Analysis Output. Output of connectivity analysis for single condition, showing connectivity curves (time-varying auto-regressive coefficients) for 12 ROIs over 2.5 seconds. Vertical lines indicate start and end of switch gap. Regions in rows lead (time $= t$) while regions in columns lag (time $= t + 1$).

2.4 Statistical Analysis (Significant Connections)

As previously mentioned, the switch gap indicates the time period between the two stimulus intervals per trial. The working assumption here is that during this time interval, the listener was preparing to either maintain their attention to the same talker attended in the first stimulus interval, or switch their attention to the second talker during the second stimulus interval. This switch gap period was the time of interest for our analysis. In order to determine if two regions were functionally connected, the time-varying AR coefficients during the switch gap were averaged across the duration of the switch gap so that each ROI-to-ROI pair had a single AR coefficient per condition per bootstrap. For the 12 ROIs selected for this analysis, excluding any ROI connecting with itself, there are a total of 132 ROI-pairs. For 6 conditions, and 100 bootstraps per conditions, this results in a total of 79,200 possible functional connections for a single experiment. For a single experiment, all of these values were pooled into a single histogram (Figure 2.5). The value at the 90th percentile was selected as the AR coefficient threshold. Whenever the average AR coefficient between ROIs during the switch gap was greater than or equal to the value at the 90th percentile of the experimental dataset, the 2 ROIs are labeled as potentially functionally connected for that bootstrap.

A graphical approach was implemented to develop a visual representation of functional connectivity between ROIs (Figure 3.1). Each node on the graph represents a ROI. Each edge indicates that at least 95 out of 100 (90 out of 100 for Experiment 3; see Section 3.1.3 for details) bootstraps contain an averaged AR coefficient value meeting or surpassing the designated threshold. Each solid edge on the graph represents a functional connection with an AR coefficient at or above the 90th percentile of AR coefficients - these edges are referred to as “significant connections.” Dashed edges indicate AR coefficients between the 75th and 90th percentiles - these edges are referred to as “near-significant connections.” A heatmap color scheme was used in order to visualize which connections were suprathreshold (meeting or exceeding the 90th percentile) and which edges were close to reaching threshold (meeting

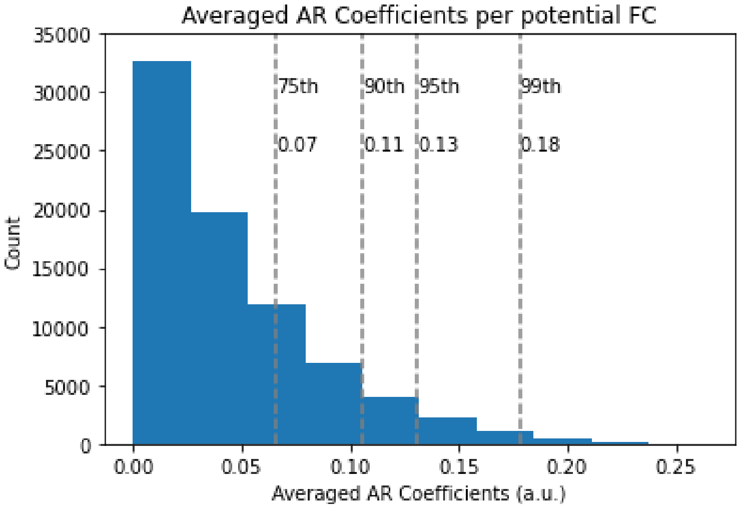
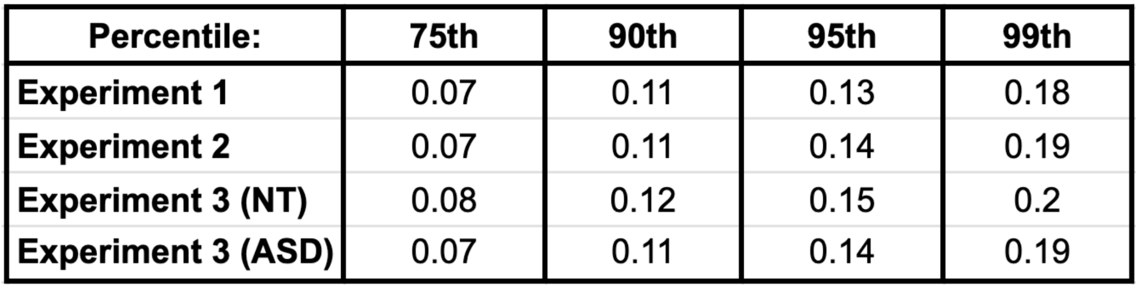


Figure 2.5: Averaged Auto-Regressive (AR) Coefficient Histogram. Histogram shows the collection of AR coefficients per potential functional connection, across listening conditions for a single experiment. Vertical lines indicate coefficient value at different percentiles.

or exceeding the 75th percentile). The nodes at the top of the figure represent ROIs that are the most anterior, while the nodes nearest the bottom are the most posterior. Table 2.1 contains the AR threshold values for the 75th, 90th, 95th, and 99th percentiles across the 3 experiments (4 subject groups).



Percentile:	**75th**	**90th**	**95th**	**99th**
Experiment 1	0.07	0.11	0.13	0.18
Experiment 2	0.07	0.11	0.14	0.19
Experiment 3 (NT)	0.08	0.12	0.15	0.2
Experiment 3 (ASD)	0.07	0.11	0.14	0.19

Table 2.1: Percentiles. Collection of several AR coefficient values and their corresponding percentiles for each experiment.

2.5 Temporal Dynamics

In order to better understand the endogenous response to the dual-stream auditory attention task, the temporal dynamics of each connectivity curve were investigated in relation to the timing of the auditory stimuli. In particular, the timing of the peak of the connectivity curve was compared to the time of the center of the switch gap. Additionally, the first and second points of inflection (over time) were computed and compared to the start and end of the switch gap, respectively. Each connectivity curve (per bootstrap) was fit to a cosine function of the form $A{*}cos(B{*}(x{-}c)){+}d$ using Python's scipy.optimize.curve_fit() function. Note that some connectivity curves (from some bootstraps) did not fit a cosine function (Figure 2.6b) according to Python's scipy.optimize.curve_fit() function. The first and second derivatives of the cosine function were computed. The peak point (green) was determined by finding the zero-crossing point of the first derivative. The points of inflection (red) were determined by finding the zero-crossing points of the second derivative. The standard deviations of each of these 3 points were also computed and compared to the difficulty of each task (Figure 2.6a).

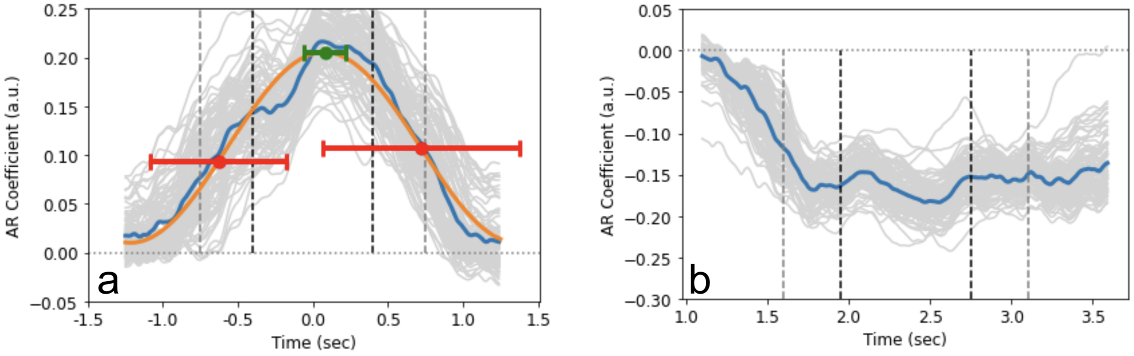


Figure 2.6: Connectivity Curves. Plots of the connectivity curves (time-varying AR coefficients) for 2 different ROI-pairs. Plots show 100 bootstraps (gray), mean of bootstraps (blue), (a) sinusoidal fit of the mean (orange), peak value (green), and points of inflection (red); (b) curve could not be fit to a sinusoidal function.

Chapter 3

RESULTS

The following subsections contain the results of the 3 experiments previously outlined. Section 3.1 outlines the results of the connectivity and statistical analyses from a graphical perspective. Section 3.2 summarizes the findings into tables that concisely describe the significant and near-significant connections depicted in the previous section. Section 3.3 discusses the temporal dynamics of the connectivity curves across the common connections, specifically, the difference in standard deviations of the peak and points of inflection of the connectivity curve across conditions or experiments.

3.1 Graphical Analysis

Figure 3.1 shows the significant and near-significant functionally connected ROIs as determined by the connectivity analysis and the statistical analysis described in Chapter 2. For each experiment, there are the primary figures that show the functional connectivity (or lack thereof) across the 12 ROIs for each experimental condition. The nodes of each graph are structured in a hierarchical fashion such that the ROIs of the frontal cortex are located at the top of the graph while the sensory ROIs are located at the bottom. Additionally, there are "comparison figures" that compare various conditions per experiment. For Experiment 1, the comparison figures compare the functional connectivity of switching attention across space vs pitch, maintaining attention across space vs pitch, maintaining vs switching attention in space, maintaining vs switching attention in pitch, and finally switching from space to pitch vs switching from pitch to space. For the cross-validation, the comparison figures compare similar conditions between the Experiments 1 and 2. Note that only 4 conditions are comparable across these 2 experiments, so the remaining 2 conditions from Experiment

2 are not compared to anything. For Experiment 3, the comparison figures compare the functional connectivity of 2 subject groups: the NT subjects and the ASD subjects.

3.1.1 Experiment 1

The significant connections, as defined above in Statistical Analysis, reveal sparse cortical networks for attending the different listening conditions of this experimental paradigm. Across the 6 conditions from Experiment 1, only 2-5 connections are significant per condition (out of the 132 possible connections) for an average of 3.33 significant connections per condition. For Maintain Space (Figure 3.1a), there are significant top-down connections from LIPSP to lAUD, and from RTPJ to rAUD. For Switch Space (Figure 3.1b), there are significant bilateral connections between the (l/r)FEF. For Maintain Pitch (Figure 3.1c), there are significant bilateral connections between (l/r)FEF, significant top-down connections from LIPSP to lAUD, and from the RTPJ to rAUD, and a significant lateral connection from rAUD to lAUD. For Switch Pitch (Figure 3.1d), there are significant bilateral connections between (l/r)DLPFC, and significant bi-directional connections between LIPSP and lAUD. For Space to Pitch (Figure 3.1e), there are also significant bi-directional connections between LIPSP and lAUD. For Pitch to Space (Figure 3.1f), there are the same significant connections as observed for Maintain Pitch: significant bilateral connections between the (l/r)FEF, significant top-down connections from LIPSP to lAUD, and from RTPJ to rAUD, and a significant connection from rAUD to lAUD.

The remaining figures (Figures g-k) are meant to compare the significant (sig) and near-significant (n.s.) connections across conditions. Each comparative figure compares “Condition 1” vs “Condition 2” where the conditions are indicated in the title. A solid red edge indicates that the connection was significant in condition 1 but not condition 2. A dashed red edge indicates that the connection was significant in condition 1 and near-significant in condition 2. A solid green edge indicates that the connection was significant in both conditions, while a dashed green edge indicates the connection was near-significant in both conditions. A solid blue edge indicates that the connection was significant in condition 2 but not condition 1. A dashed blue edge indicates that the connection was significant in condition 2 and near-significant in condition 1.

3.1.1.1 Space: Maintain vs Switch

In Maintain Space vs Switch Space (Figure 3.1i), the bilateral FEF connection is only significant in Switch Space, while the top-down connections from the LIPSP/RTPJ to the (l/r)AUD are significant in Maintain Space while near-significant in Switch Space. Both conditions had near-significant bilateral connections between (l/r)AUD, and a near-significant top-down connection between rIPS and RTPJ.

3.1.1.2 Pitch: Maintain vs Switch

In Maintain Pitch vs Switch Pitch (Figure 3.1j), the following connections were significant in Maintain Pitch and near-significant in Switch Pitch: bilateral connection between (l/r)FEF, the top-down connection between RTPJ and rAUD, and the lateral connection from rAUD to lAUD. The following connections were significant only in Switch Pitch: bilateral connection between (l/r)DLPFC and the bottom-up connection between lAUD and LIPSP. The following connections were near-significant for both Maintain and Switch Pitch: bilateral connection between LIPSP and RTPJ, the bottom-up connection from rAUD to LIPSP, and a lateral connection from lAUD to rAUD. Both conditions had a significant top-down connection from LIPSP to lAUD.

3.1.1.3 Maintain: Space vs Pitch

In Maintain Space vs Maintain Pitch (Figure 3.1g), the bilateral FEF connection is only significant in Maintain Pitch. Maintain Pitch also has a significant lateral connection from rAUD to lAUD while this connection is near-significant for Maintain Space. The following connections are significant across both conditions: top-down connections from LIPSP to lAUD and from RTPJ to rAUD. The following connections are near-significant across both conditions: bilateral connection between (l/r)IPS, top-down connection between IPS and LIPSP, bottom-up connection from rAUD to RTPJ, and lateral connection from lAUD to rAUD.

3.1.1.4 Switch: Space vs Pitch

In Switch Space vs Switch Pitch (Figure 3.1h), there is a significant bilateral connection between (l/r)FEF in Switch Space, while this connection is only near-significant in Switch Pitch. The following connections are significant in Switch Pitch only: bilateral connection between (l/r)DLPFC and the bottom-up connection between lAUD and LIPSP. The top-down connection from LIPSP to lAUD was significant in Switch Pitch and near-significant in Switch Space. The following connections were near-significant for both Switch Space and Switch Pitch: bilateral connection between the LIPSP and RTPJ, a top-down connection from RTPJ to rAUD, a bottom-up connection from rAUD to LIPSP, and a bilateral connection between (l/r)AUD.

3.1.1.5 Space to Pitch vs Pitch to Space

In Space to Pitch vs Pitch to Space (Figure 3.1k), there was a significant lateral connection from rAUD to lAUD. The following connections were significant in Pitch to Space and near-significant in Space to Pitch: bilateral connection between (l/r)FEF, and the top-down connection from RTPJ to rAUD. The bottom-up connection from lAUD to LIPSP that was significant for Space to Pitch and near-significant for Pitch to Space. Both Space to Pitch and Pitch to Space had a significant top-down connection from LIPSP to lAUD.

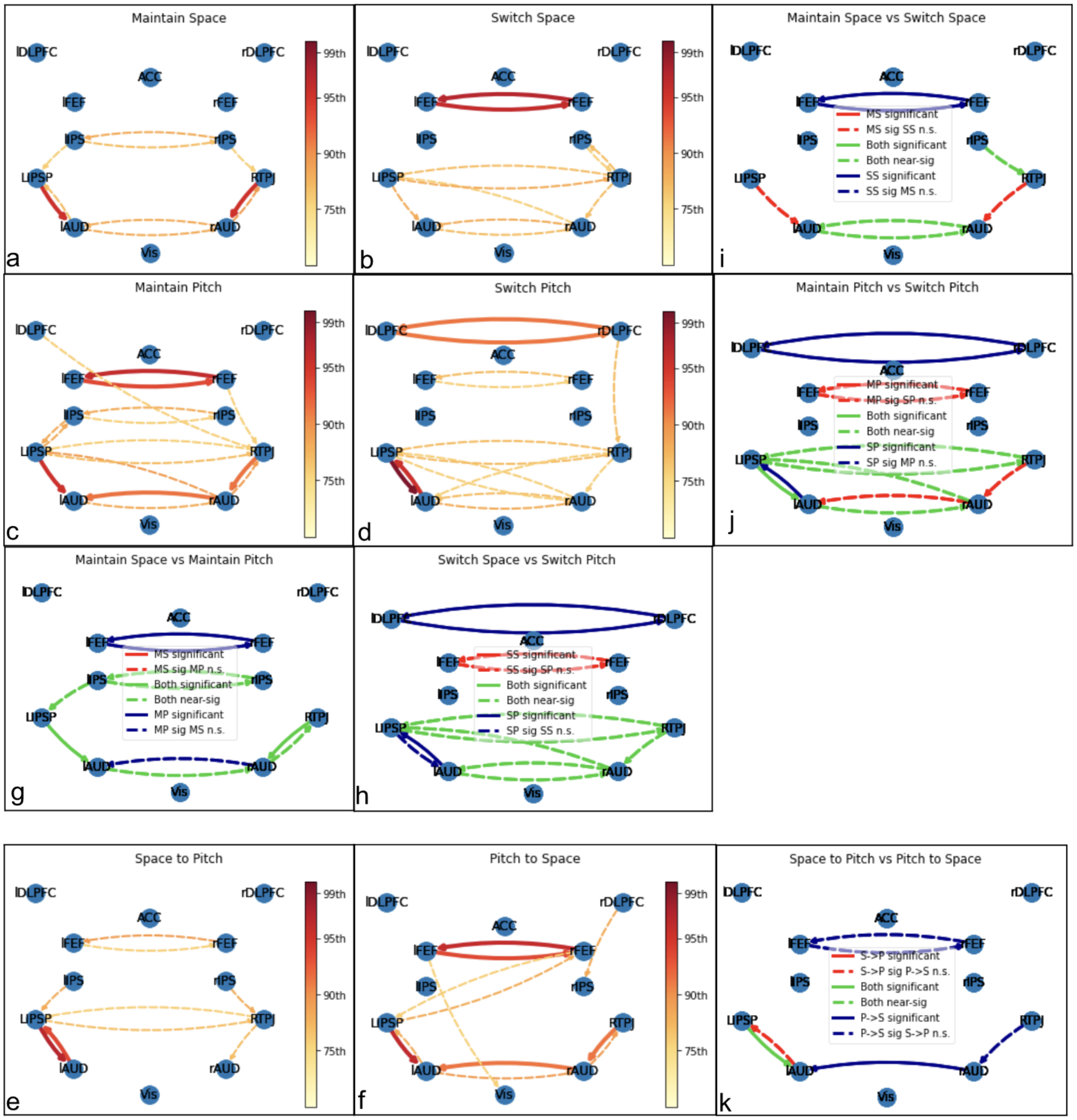


Figure 3.1: Experiment 1. (a-f) Graphical representation of significant (sig) and near-significant (n.s.) connections. Significant connections are bold (above 90th percentile), near-significant connections are dashed (between 75th and 90th percentiles). The colorbar indicates which percentile is met. Title indicates listening condition. (i-k) Graphical representation of similar and dissimilar connections across 2 listening conditions.

3.1.2 Experiment 2 (Cross-Validation)

Rather than repeating the investigative nature performed for Experiment 1 as outlined in the previous subsection, Experiment 2 was used as a cross-validation experiment. Recall that the experimental paradigms from Experiments 1 and 2 were similar in nature. Therefore, the hypothesis for the cross-validation was that similar regions of interest would be functionally connected for similar listening conditions. This section outlines the functional connections found in each condition, while the subsequent subsections will compare conditions across experiments. Note that for Experiment 2, conditions regarding pitch refer to gendered conditions with the presentation of either a male or female voice.

The significant connections, computed in the same manner as Experiment 1, across conditions were similarly sparse, when compared to the significant connections from Experiment 1. Each condition had 2-7 significant connections with an average of 4 significant connections per condition. For Maintain Space (Figure 3.2e), there are significant bi-directional connections between rIPS and RTPJ as well as LIPSP and lAUD. For Switch Space (Figure 3.2f) there are significant bi-directional connections between LIPSP and lAUD. For Maintain Pitch (Figure 3.1g), there are significant bi-directional connections between rIPS and RTPJ, LIPSP and lAUD, and RTPJ and rAUD. Additionally, there is a significant lateral connection from RTPJ to LIPSP. For Switch Pitch (Figure 3.1h), there are significant bi-directional connections between rIPS and RTPJ, and RTPJ and rAUD. For Maintain Both (Figure 3.2i), there are significant bi-directional connections between RTPJ and rAUD. For Switch Both (Figure 3.2j), there are the following significant connections: the lateral connection from rFEF to lFEF, bi-directional connections between LIPSP and lAUD, the top-down connection from rIPS to RTPJ, and the bottom-up connection from rAUD to RTPJ.

The remaining subfigures (Figures 3.2k-n) are designed to highlight the similarities and differences between the significant (sig) and near-significant (n.s.) connections of Experiment 1 (Exp1) and Experiment 2 (Exp2). A bold red edge indicates that the connection was significant only in Experiment 1. A dashed red edge indicates that the connection was significant in Experiment 1 and near-significant in Experiment 2. A bold blue edge indicates that the connection was only significant in Experiment 2. A dashed blue edge indicates that the connection was significant in Experiment 2 and near-significant in Experiment 1. A bold green edge indicates that the connection was significant for both experiments. A dashed green edge indicates that the connection was near-significant for both experiments.

3.1.2.1 Maintain Space

In Maintain Space (Figure 3.2k), Experiment 1 had a significant top-down connection from RTPJ to rAUD, while this connection was only near-significant in Experiment 2. Experiment 2 had a significant bottom-up connection from RTPJ to rIPS. The following connections were significant in Experiment 2 and near-significant in Experiment 1: top-down connection from rIPS to RTPJ and bottom-up connection from lAUD to LIPSP. For Maintain Space, both experiments had a significant top-down connection from LIPSP to lAUD as well as the following near-significant conditions: bilateral connections between (l/r)AUD and bottom-up connections from rAUD to RTPJ.

3.1.2.2 Switch Space

In Switch Space (Figure 3.2l), Experiment 1 had significant bilateral connections between (l/r)FEF. Experiment 2 had significant bi-directional connections between LIPSP and lAUD while Experiment 1 had a near-significant top-down connection from LIPSP to lAUD. The following connections were near-significant for both experiments: bilateral connections between LIPSP and RTPJ, bottom-up connection from rAUD to LIPSP, and a lateral connection from rAUD to lAUD.

3.1.2.3 Maintain Pitch

In Maintain Pitch (Figure 3.2m), Experiment 1 had significant bilateral connections between (l/r)FEF. Experiment 1 also had a significant lateral connection from rAUD to lAUD, while this connection was only near-significant in Experiment 2. The following connections were significant in only Experiment 2: bi-directional connections between rIPS and RTPJ, and a bottom-up connection from lAUD to LIPSP. The following connections were significant for Experiment 2 and near-significant for Experiment 1: a lateral connection from RTPJ to LIPSP and a bottom-up connection from rAUD to RTPJ. For Maintain Pitch, both experiments resulted in significant top-down connections from LIPSP to lAUD and from RTPJ to rAUD, as well as a near-significant lateral connection from LIPSP to RTPJ and a near-significant top-down connection from lIPS to LIPSP.

3.1.2.4 Switch Pitch

In Switch Pitch (Figure 3.2n), Experiment 1 had a significant bilateral connection between (l/r)DLPFC. Experiment 2 had significant bi-directional connections between RTPJ and rAUD while Experiment 1 had a near-significant top-down connection from RTPJ to rAUD. Both experiments had significant bi-directional connections between LIPSP and lAUD. Additionally, both experiments had the following near-significant connections for Switch Pitch: bilateral connections between (l/r)FEF, bottom-up connection from rAUD to LIPSP, and lateral connection from rAUD to lAUD.

3.1.2.5 Maintain/Switch Both

The two remaining conditions from Experiment 2 (Maintain Both and Switch Both; Figures 3.2i-j) were not comparable to the final two conditions of Experiment 1 (Space to Pitch and Pitch to Space). Therefore, these two conditions were not part of the cross-validation process.

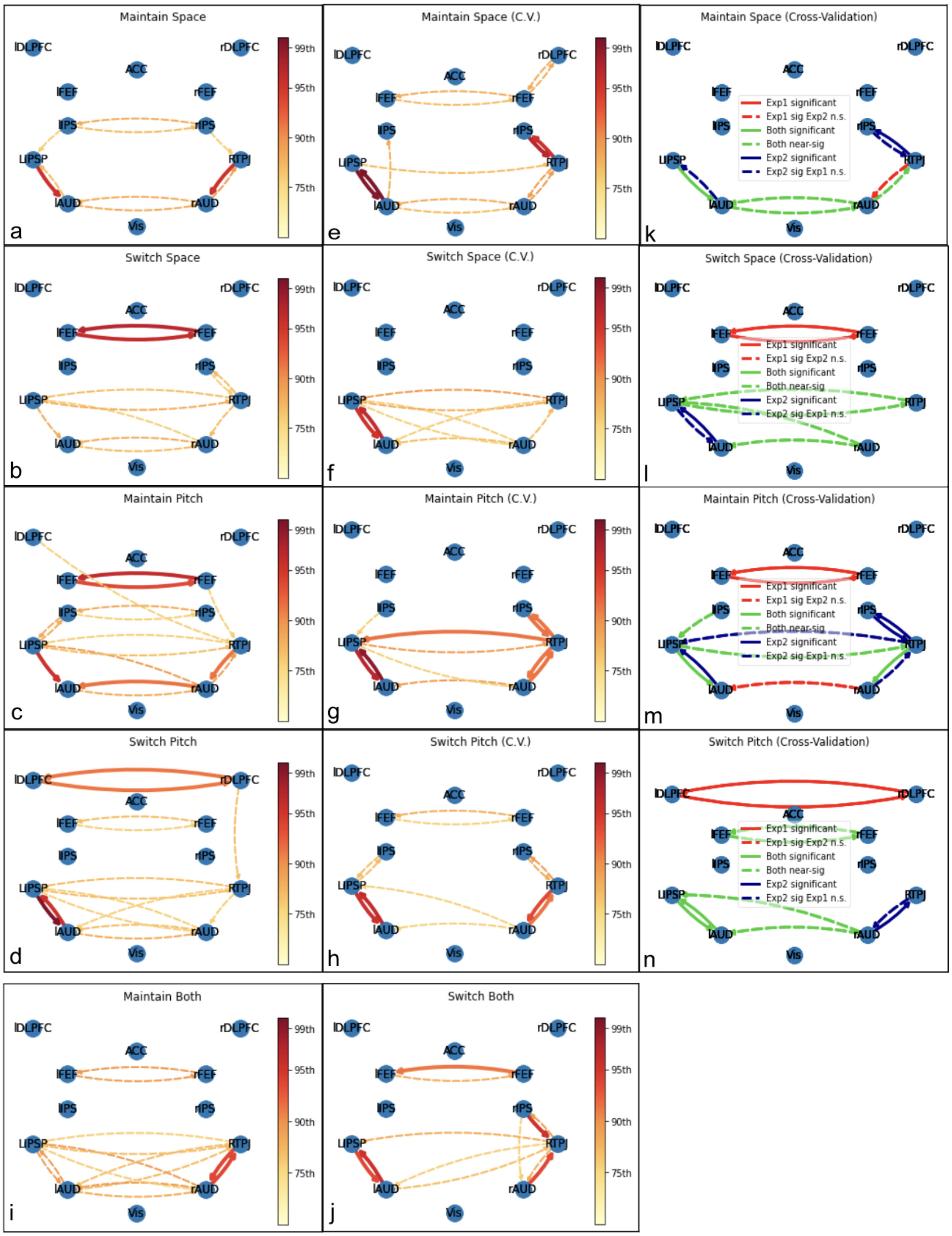


Figure 3.2: Experiment 2 (Cross-Validation). (a-d) Graphical representation of significant (sig) and near-significant (n.s.) connections from Experiment 1. (e-j) Graphical representation of significant and near-significant connections from Experiment 2. (k-m) Graphical representation of similar and dissimilar connections.

3.1.3 Experiment 3 (Neurodivergence)

The original study [19] determined that a sample size of at least 11 subjects per group was necessary to determine statistically significant differences across 2 groups. Since the functional connectivity analysis for Experiment 3 contained only 9 subjects per group, the statistical analysis was modified so that the criteria to determine a significant edge was less conservative. Where for previous experiments, 95 out of 100 bootstraps needed to meet the AR threshold, only 90 out of 100 bootstraps needed to meet the AR threshold in order to be deemed a significant edge. The purpose of this experiment was to investigate whether challenges in deploying auditory attention in subjects with ASD might relate to differences in functional connectivity when compared to NT subjects.

Even with the less conservative statistical analysis, significant connections were comparably sparse as seen with the previous 2 experiments. The NT subjects analysis resulted in 2-6 significant connections per condition with an average of 3.16 connections per condition. For Maintain Space (Figure 3.3a), the NT group had significant bilateral connections between (l/r)FEF and (l/r)IPS, as well as bi-directional connections between LIPSP and lAUD. For Switch Space (Figure 3.3b), the NT group had significant bilateral connections between (l/r)FEF. For Maintain Pitch (Figure 3.3c), the NT group had significant bilateral connections between (l/r)FEF and significant top-down connection from ACC to LIPSP. For Switch Pitch (Figure 3.3d), the NT group had significant lateral connection from lFEF to rFEF as well as a significant bottom-up connection from RTPJ to rIPS. For Maintain Both (Figure 3.3e), the NT group had significant bi-directional connections between rDLPFC and rFEF, as well as between rIPS and RTPJ. For Switch Both (Figure 3.3f), the NT group had significant bottom-up connections from rDLPFC to rFEF, as well as from RTPJ to rIPS.

The ASD subject analysis resulted in 0-5 significant edges per condition with an average of 2.16 edges per condition. For Maintain Space (Figure 3.3g), the ASD group had significant bi-directional connections between rIPS and RTPJ. For Maintain Pitch (Figure 3.3i), the ASD group had significant bilateral connections between (l/r)FEF, significant bottom-up connection from from rFEF to rDLPFC as well as from LIPSP to lAUD, and a significant lateral connection from rAUD to lAUD. For Switch Pitch (Figure 3.3j), the ASD group had significant bilateral connections between (l/r)FEF and a significant lateral connection from lIPS to rIPS. For Maintain Both (Figure 3.3k), the ASD group had significant bilateral connections between (l/r)FEF as well as a significant lateral connection from lIPS to rIPS. The ASD group had no significant connections for the Switch Space (Figure 3.3h) and Switch Both (Figure 3.3l) conditions.

Figures 3.3m-r depict the differences and commonalities between the 2 subject groups per listening condition. A bold red edge indicates that the connection was significant only for the NT group. A dashed red edge indicates that the connection was significant for NT and near-significant for the ASD group. A bold blue edge indicates that the connection was only significant for the ASD group. A dashed blue edge indicates that the connection was significant for ASD and near-significant for NT. A bold green edge indicates that the connection was significant for both subject groups. A dashed green edge indicates that the connection was near-significant for both subject groups. Note that the conditions regarding pitch for Experiment 3 are the same as described for Experiment 2, i.e., indicates gendered conditions (i.e., male vs female voice). The following subsections describe the differences in functional connectivity between the 2 subject groups per listening condition.

3.1.3.1 Maintain Space

For Maintain Space (Figure 3.3m), only the NT group had the following significant connections: bilateral connection between (l/r)IPS, and a bottom-up connection from lAUD to LIPSP. The following connections were significant for the NT group and near-significant for the ASD group: bilateral connection between (l/r)FEF, and a top-down connection from LIPSP to lAUD. The ASD group had significant bi-directional connections between rIPS and RTPJ, while the NT group had a near-significant bottom-up connection from RTPJ to rIPS. Both groups had near-significant bi-directional connections between rFEF and rDLPFC.

3.1.3.2 Switch Space

For Switch Space (Figure 3.3n), the NT group had significant bilateral connections between (l/r)FEF, while the ASD group only had a near-significant lateral connection from rFEF to lFEF. Both groups had the following near-significant connections: bottom-up connection from lFEF to lDLPFC, and a bottom-up connection from RTPJ to rIPS.

3.1.3.3 Maintain Pitch

For Maintain Pitch (Figure 3.3o), the NT group had a significant top-down connection from ACC to LIPSP. The ASD group had a significant bottom-up connection from rFEF to rDLPFC and a significant top-down connection from LIPSP to lAUD. A lateral connection from rAUD to lAUD was significant for the ASD group and near-significant for the NT group. Both groups had significant bilateral connections between (l/r)FEF, and both groups had a near-significant bottom-up connection from RTPJ to rIPS.

3.1.3.4 Switch Pitch

For Switch Pitch (Figure 3.3p), the NT group had a significant lateral connection from lFEF to rFEF, while only near-significant for the ASD group. The ASD group had the following significant top-down connections: from lDLPFC to lFEF and from rIPS to RTPJ. The NT group had a near-significant top-down connection from rIPS to RTPJ. Both subject groups had a significant bottom-up connection from RTPJ to rIPS, and a near-significant lateral connection from rFEF to lFEF.

3.1.3.5 Maintain Both

For Maintain Both (Figure 3.3q), the NT group had significant bilateral connections between rFEF and rDLPFC, and between rIPS and RTPJ. The ASD group had significant bilateral connections between (l/r)FEF and a significant lateral connection from lIPS to rIPS.

3.1.3.6 Switch Both

For Switch Both (Figure 3.3r), the NT group had a significant top-down connection from rDLPFC to rFEF and a significant bottom-up connection from RTPJ to rIPS. The ASD group had no significant connections and there were no common near-significant connections between groups.

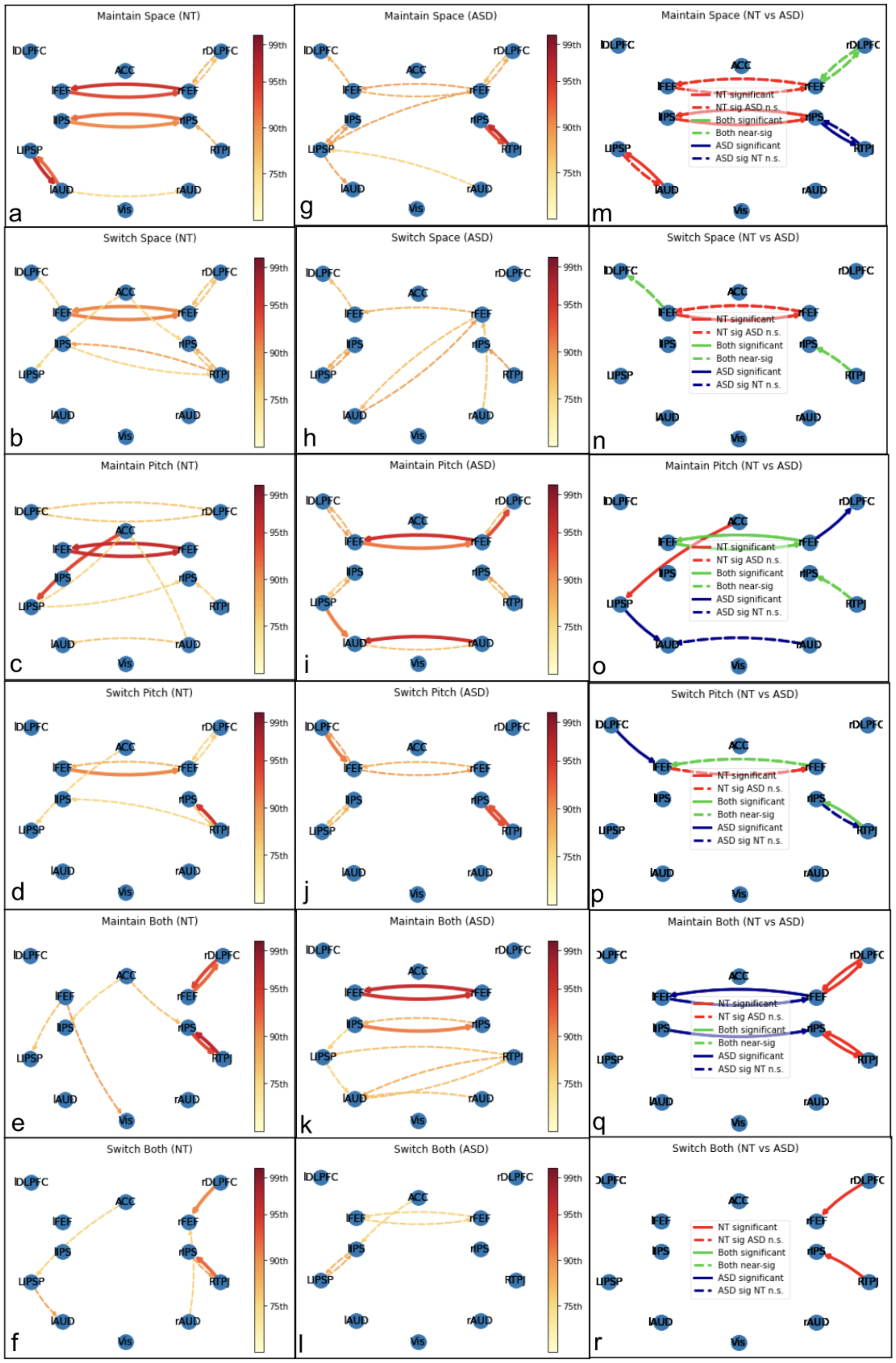


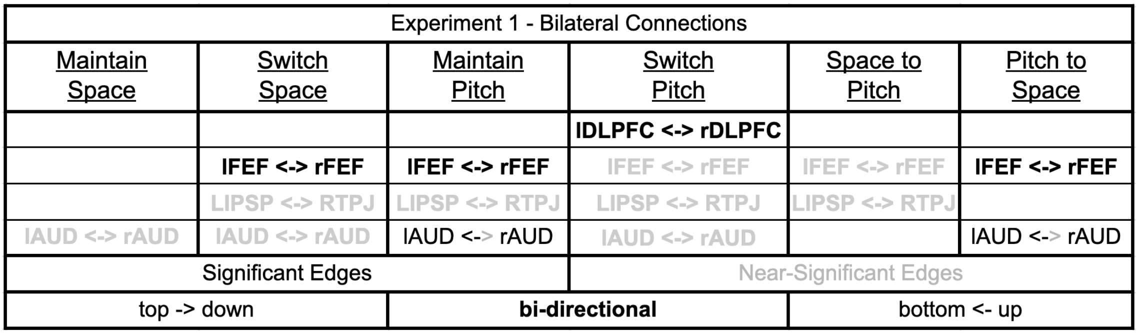
Figure 3.3: Experiment 3 (Neurodivergence). (a-f) Graphical representation of significant (sig) and near-significant (n.s.) connections from NT subject group. (g-l) Graphical representation of significant and near-significant connections from ASD subject group. (k-m) Graphical representation of similar and dissimilar connections.

3.2 Common Significant (and Near-Significant) Connections

The tables in this section show a collective summary of significant and near-significant connections across the 6 listening conditions used for each study. Tables titled “Bilateral Connections” consist of connections that cross hemispheres. Tables titled “Unilateral Connections” consist of connections that are confined to a single hemisphere. Bolded connections indicate significant connections while grayed connections indicate near-significant edges. Double-sided arrows indicate that the connection was bi-directional while a single-sided arrow indicates that the connection was unidirectional. Arrows pointing to the right indicate a top-down connection (according to the hierarchical structure previously described) while arrows pointing to the left indicate a bottom-up connection. Note that some bolded connections have a grayed arrow in one direction - this indicates that in one direction, this connection was significant while the other was near-significant. As described in Section 3.1, significant connections are sparse across all conditions of all experiments. The purpose of this section is to summarize the common significant (and comparable near-significant) connections across conditions and across experiments. If the same connection is observed across 3 or more conditions for a single experiment, that connection is labeled as a “common connection.” Note that near-significant edges are only included if that edge was significant in other conditions OR if 4 or more conditions contained that near-significant edge.

3.2.1 Experiment 1

Table 3.1, Bilateral Connections for Experiment 1, shows that there is 1 common significant bilateral connection between (l/r)FEF; observed in Switch Space, Maintain Pitch, and Pitch to Space conditions. Switch Pitch and Space to Pitch both contain this same connection but it is near-significant in these conditions. Switch Space, Maintain Pitch, Switch Pitch, and Space to Pitch all contain the near-significant bilateral connections between LIPSP and RTPJ. All conditions, excluding Space to Pitch, contain the near-significant bilateral connections between (l/r)AUD, although the lateral connection from rAUD to lAUD is significant in Maintain Pitch and Pitch to Space. Uncommon bilateral connections for Experiment 1 include the significant bilateral connection between (l/r)DLPFC.



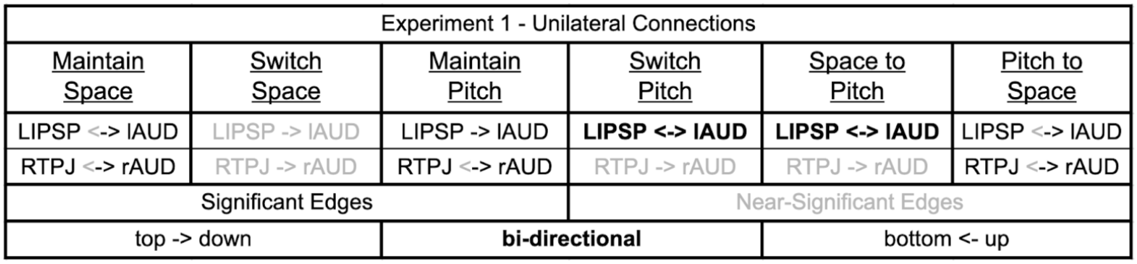
Experiment 1 - Bilateral Connections					
Maintain Space	Switch Space	Maintain Pitch	Switch Pitch	Space to Pitch	Pitch to Space
			lDLPFC <-> rDLPFC		
	lFEF <-> rFEF	**lFEF <-> rFEF**	**lFEF <-> rFEF**	**lFEF <-> rFEF**	**lFEF <-> rFEF**
	LIPSP <-> RTPJ	**LIPSP <-> RTPJ**	**LIPSP <-> RTPJ**	**LIPSP <-> RTPJ**	
lAUD <-> rAUD	**lAUD <-> rAUD**	lAUD <-> rAUD	**lAUD <-> rAUD**		lAUD <-> rAUD
Significant Edges			Near-Significant Edges		
top -> down		**bi-directional**		bottom <- up	

Table 3.1: Bilateral Connections for Experiment 1.

Table 3.2, Unilateral Connections for Experiment 1, shows that all conditions contain a significant top-down connection from LIPSP to lAUD, except for Switch Space where this connection is near-significant. The bottom-up connection from lAUD to LIPSP is significant in Switch Pitch and Space to Pitch, and near-significant in Pitch to Space and Maintain Space. The top-down connection from RTPJ to rAUD is significant in Maintain Space, Maintain Pitch, and Pitch to Space, while the bottom-up connection from rAUD to RTPJ was near-significant for the same 3 conditions. The remaining 3 conditions - Switch Space, Switch Pitch, and Space to Pitch - had near-significant top-down connections from RTPJ to rAUD.

3.2.2 Experiment 2 (Cross-Validation)

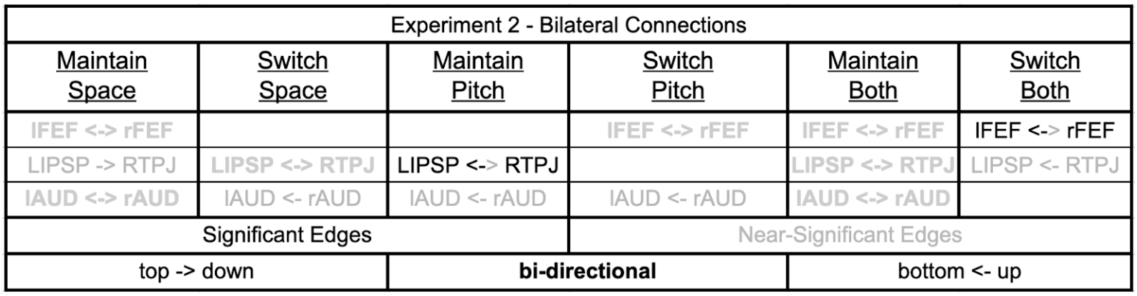
Table 3.3, Bilateral Connections for Experiment 2, shows many common near-significant connections. The bilateral connection between (l/r)FEF (although the lateral connection from rFEF to lFEF is significant for Switch Both) is common to Maintain Space, Switch Pitch, Maintain Both, and Switch Both. The near-significant bilateral connection between LIPSP and RTPJ (although the lateral connection from RTPJ to LIPSP is significant for



Experiment 1 - Unilateral Connections					
Maintain Space	Switch Space	Maintain Pitch	Switch Pitch	Space to Pitch	Pitch to Space
LIPSP <-> lAUD	LIPSP -> lAUD	LIPSP -> lAUD	**LIPSP <-> lAUD**	**LIPSP <-> lAUD**	LIPSP <-> lAUD
RTPJ <-> rAUD	RTPJ -> rAUD	RTPJ <-> rAUD	RTPJ -> rAUD	RTPJ -> rAUD	RTPJ <-> rAUD
Significant Edges			Near-Significant Edges		
top -> down		**bi-directional**		bottom <- up	

Table 3.2: Unilateral Connections for Experiment 1.

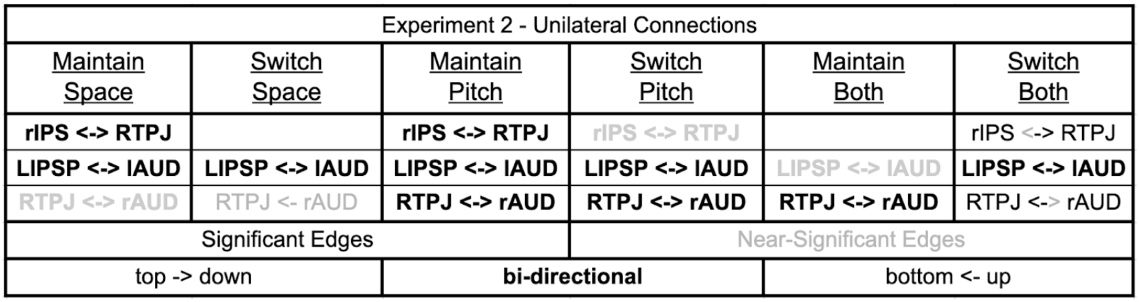
Maintain Pitch) is common to Switch Space, Maintain Pitch, and Maintain Both. There is a lateral near-significant connection from LIPSP to RTPJ in Maintain Space and a lateral near-significant connection from RTPJ to LIPSP in Switch Both. All conditions, excluding Switch Both, contain a near-significant lateral connection from rAUD to lAUD, while Maintain Space and Maintain Both also have lateral near-significant connections from lAUD to rAUD.



Experiment 2 - Bilateral Connections					
Maintain Space	Switch Space	Maintain Pitch	Switch Pitch	Maintain Both	Switch Both
lFEF <-> rFEF			**lFEF <-> rFEF**	**lFEF <-> rFEF**	lFEF <-> rFEF
LIPSP -> RTPJ	**LIPSP <-> RTPJ**	LIPSP <-> RTPJ		**LIPSP <-> RTPJ**	LIPSP <- RTPJ
lAUD <-> rAUD	lAUD <- rAUD	lAUD <- rAUD	lAUD <- rAUD	**lAUD <-> rAUD**	
Significant Edges			Near-Significant Edges		
top -> down		**bi-directional**		bottom <- up	

Table 3.3: Bilateral Connections for Experiment 2.

Table 3.4, Unilateral Connections for Experiment 2, shows significant top-down connections from rIPS to RTPJ for Maintain Space, Maintain Pitch, and Switch Both. Maintain Space and Maintain Pitch also have significant bottom-up connections from RTPJ to rIPS. This same connection is near-significant for Switch Both and Switch Pitch, while Switch Pitch also has a near-significant top-down connection from rIPS to RTPJ. All conditions for Experiment 2 show significant bi-directional connections between LIPSP and lAUD, excluding Maintain Both where this connection is near-significant. The conditions Maintain Pitch, Switch Pitch, and Maintain Both all have significant bi-directional connections between RTPJ and rAUD. The bottom-up connection from rAUD to RTPJ is significant for Switch Both and near-significant for Maintain Space and Switch Space. The top-down connection from RTPJ is near-significant for Maintain Space and Switch Both.



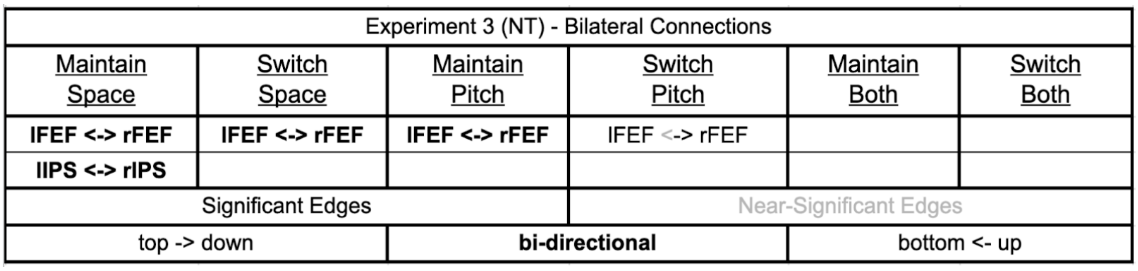
Experiment 2 - Unilateral Connections					
Maintain Space	Switch Space	Maintain Pitch	Switch Pitch	Maintain Both	Switch Both
rIPS <-> RTPJ		**rIPS <-> RTPJ**	rIPS <-> RTPJ		rIPS <-> RTPJ
LIPSP <-> lAUD	**LIPSP <-> lAUD**	**LIPSP <-> lAUD**	**LIPSP <-> lAUD**	LIPSP <-> lAUD	**LIPSP <-> lAUD**
RTPJ <-> rAUD	RTPJ <- rAUD	**RTPJ <-> rAUD**	**RTPJ <-> rAUD**	**RTPJ <-> rAUD**	RTPJ <-> rAUD
Significant Edges			Near-Significant Edges		
top -> down		**bi-directional**		bottom <- up	

Table 3.4: Unilateral Connections for Experiment 2.

3.2.3 Experiment 3 (Neurodivergence)

Table 3.5, Bilateral Connections for the NT subject group in Experiment 3, shows a common bilateral connection between (l/r)FEF for Maintain Space, Switch Space, and Maintain Pitch. Switch Pitch has a significant lateral connection from lFEF to rFEF and a near-significant lateral connection from rFEF to lFEF. Uncommon bilateral connections for the NT subject group include the significant bilateral connection between (l/r)IPS for Maintain Space.

Table 3.6, Unilateral Connections for the NT subject group in Experiment 3, shows a near-significant bi-directional connection between rFEF and rDLPFC for Maintain Space, Switch Space, and Switch Pitch, while this connection is significant in Maintain Both. Switch Both has a significant top-down connection from rDLPFC to rFEF. The near-significant top-down connection from ACC to LIPSP is common to Switch Space, Switch Pitch, and Switch Both, while this connection is significant in Maintain Pitch. Maintain Pitch also has a near-significant bottom-up connection from LIPSP to ACC. There is a significant bottom-up

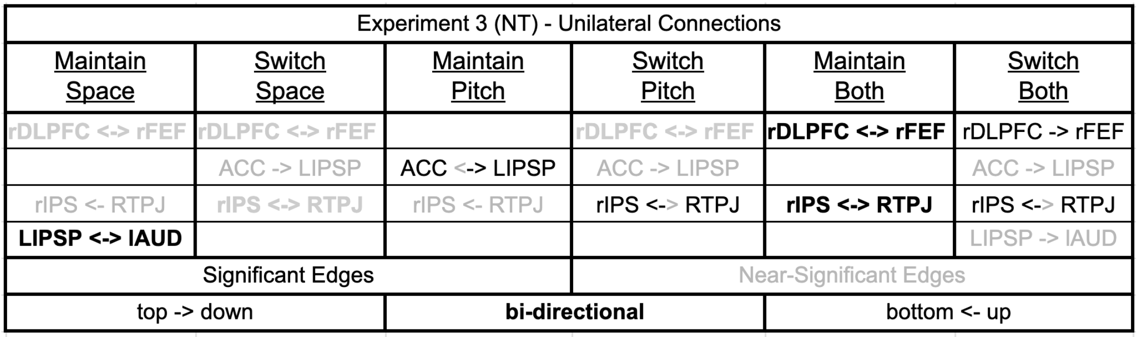


Experiment 3 (NT) - Bilateral Connections

Maintain Space	Switch Space	Maintain Pitch	Switch Pitch	Maintain Both	Switch Both
lFEF <-> rFEF	**lFEF <-> rFEF**	**lFEF <-> rFEF**	lFEF <-> rFEF		
lIPS <-> rIPS					
Significant Edges			Near-Significant Edges		
top -> down		**bi-directional**		bottom <- up	

Table 3.5: Bilateral Connections for NT Subject Group.

connection from RTPJ to rIPS for Switch Pitch, Maintain Both, and Switch Both. This connection is near-significant for Maintain Space, Switch Space, and Maintain Pitch. There is also a near-significant top-down connection from rIPS to RTPJ for Switch Space, Switch Pitch, and Switch Both. This connection is significant for Maintain Both. Uncommon unilateral connections for the NT subject group include the significant bi-directional connection between LIPSP and lAUD for Maintain Space, as well as the near-significant top-down connection from LIPSP to lAUD for Switch Both.



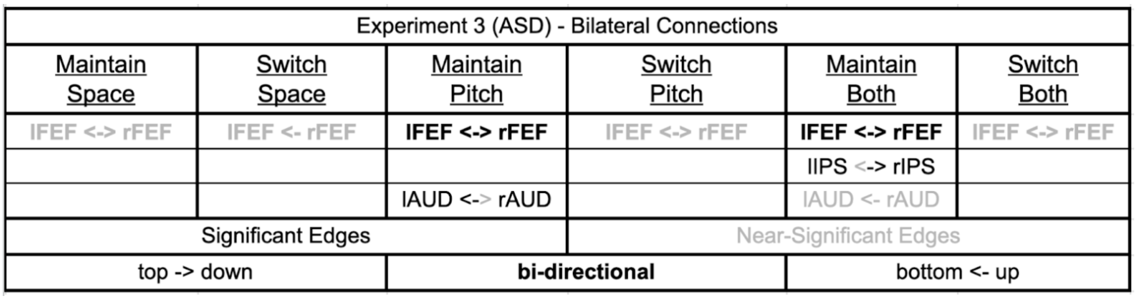
Experiment 3 (NT) - Unilateral Connections

Maintain Space	Switch Space	Maintain Pitch	Switch Pitch	Maintain Both	Switch Both
rDLPFC <-> rFEF	**rDLPFC <-> rFEF**		**rDLPFC <-> rFEF**	**rDLPFC <-> rFEF**	rDLPFC -> rFEF
	ACC -> LIPSP	ACC <-> LIPSP	ACC -> LIPSP		ACC -> LIPSP
rIPS <- RTPJ	**rIPS <-> RTPJ**	rIPS <- RTPJ	rIPS <-> RTPJ	**rIPS <-> RTPJ**	rIPS <-> RTPJ
LIPSP <-> lAUD					LIPSP -> lAUD
Significant Edges			Near-Significant Edges		
top -> down		**bi-directional**		bottom <- up	

Table 3.6: Unilateral Connections for NT Subject Group.

Table 3.7, Bilateral Connections for the ASD subject group in Experiment 3, shows a near-significant bilateral connection between (l/r)FEF for Maintain Space, Switch Pitch, and Switch Both. This bilateral connection is significant for Maintain Pitch and Maintain

Both. Switch Space has a near-significant lateral connection from rFEF to lFEF. Uncommon bilateral connections for the ASD subject group include a significant lateral connection from rAUD to lAUD and a near-significant connection from lAUD to rAUD for Maintain Space. Maintain both contains the following near-significant connections: lateral connection from rIPS to lIPS and rAUD to lAUD. Additionally, Maintain both contains the significant lateral connection from lIPS to rIPS.



Experiment 3 (ASD) - Bilateral Connections					
Maintain Space	Switch Space	Maintain Pitch	Switch Pitch	Maintain Both	Switch Both
lFEF <-> rFEF	lFEF <- rFEF	**lFEF <-> rFEF**	lFEF <-> rFEF	**lFEF <-> rFEF**	lFEF <-> rFEF
				lIPS <-> rIPS	
		lAUD <-> rAUD		lAUD <- rAUD	
Significant Edges			Near-Significant Edges		
top -> down		**bi-directional**		bottom <- up	

Table 3.7: Bilateral Connections for ASD Subject Group.

Table 3.8, Unilateral Connections for the ASD subject group in Experiment 3, shows a near-significant bottom-up connection from lFEF to lDLPFC for Switch Space, Maintain Pitch, and Switch Pitch. The top-down connection from lDLPFC to lFEF was near-significant for Maintain Pitch and significant for Switch Pitch. There was a near-significant bi-directional connection between lIPS and LIPSP for all conditions except for Maintain Both which contained a near-significant top-down connection from lIPS to LIPSP. Maintain Space and Switch Pitch both contained the significant bi-directional connection between rIPS and RTPJ. This bi-directional connection was near-significant in Maintain Pitch, while Switch Space only contained the near-significant bottom-up connection from RTPJ to rIPS. Uncommon unilateral connections for the ASD subject group include the following significant bi-directional connections for Maintain Space and Maintain Pitch: rFEF and rDLPFC, excluding the near-significant connection from rDLPFC to rFEF in Maintain Pitch. Finally, the top-down connection from LIPSP to lAUD is significant for Maintain Pitch and near-significant for Maintain Both.

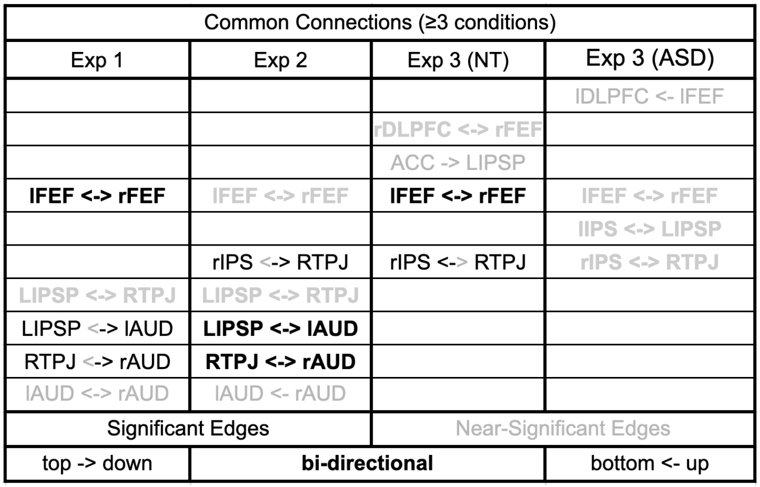
Experiment 3 (ASD) - Unilateral Connections					
Maintain Space	Switch Space	Maintain Pitch	Switch Pitch	Maintain Both	Switch Both
	lDLPFC <- lFEF	**lDLPFC <-> lFEF**	lDLPFC <-> lFEF		
rDLPFC <-> rFEF		rDLPFC <-> rFEF			
lIPS <-> LIPSP	**lIPS <-> LIPSP**	**lIPS <-> LIPSP**	**lIPS <-> LIPSP**	lIPS -> LIPSP	**lIPS <-> LIPSP**
rIPS <-> RTPJ	rIPS <- RTPJ	**rIPS <-> RTPJ**	**rIPS <-> RTPJ**		
		LIPSP -> lAUD		LIPSP -> lAUD	
Significant Edges			Near-Significant Edges		
top -> down		**bi-directional**		bottom <- up	

Table 3.8: Unilateral Connections for ASD Subject Group.

3.2.4 All Experiments

Table 3.9 summarizes the common connections for each Experiment. Common connections here are defined as a connection seen in at least 3 of the 6 conditions for that experiment. The purpose of summarizing these connections here is to determine if there are any connections that are consistent across experiments. The most common connection across experiments is the bilateral connection between the (l/r)FEF. This connection is significant in Experiments 1 and 3 for the NT subjects, and near-significant for Experiment 2 and 3 for the ASD subjects. The next most common near-significant connection is the bi-directional connection between rIPS and RTPJ. Note that for Experiment 3 for the ASD subject group, 2 of these connections are significant while the third is near-significant. The top-down connection from rIPS to RTPJ in Experiment 2 and the bottom-up connection from RTPJ to rIPS for Experiment 3 for the NT subjects are significant.

The remaining common connections are results of Experiments 1 and 2 only. First, there is the near-significant bilateral connection between LIPSP and RTPJ. Second, there is a significant bi-directional connection between LIPSP and lAUD, excluding the near-



<table>
<tr><th colspan="4">Common Connections (≥3 conditions)</th></tr>
<tr><th>Exp 1</th><th>Exp 2</th><th>Exp 3 (NT)</th><th>Exp 3 (ASD)</th></tr>
<tr><td></td><td></td><td></td><td>lDLPFC <- lFEF</td></tr>
<tr><td></td><td></td><td>rDLPFC <-> rFEF</td><td></td></tr>
<tr><td></td><td></td><td>ACC -> LIPSP</td><td></td></tr>
<tr><td>lFEF <-> rFEF</td><td>lFEF <-> rFEF</td><td>lFEF <-> rFEF</td><td>lFEF <-> rFEF</td></tr>
<tr><td></td><td></td><td></td><td>lIPS <-> LIPSP</td></tr>
<tr><td></td><td>rIPS <-> RTPJ</td><td>rIPS <-> RTPJ</td><td>rIPS <-> RTPJ</td></tr>
<tr><td>LIPSP <-> RTPJ</td><td>LIPSP <-> RTPJ</td><td></td><td></td></tr>
<tr><td>LIPSP <-> lAUD</td><td>LIPSP <-> lAUD</td><td></td><td></td></tr>
<tr><td>RTPJ <-> rAUD</td><td>RTPJ <-> rAUD</td><td></td><td></td></tr>
<tr><td>lAUD <-> rAUD</td><td>lAUD <- rAUD</td><td></td><td></td></tr>
<tr><td colspan="2">Significant Edges</td><td colspan="2">Near-Significant Edges</td></tr>
<tr><td>top -> down</td><td colspan="2">bi-directional</td><td>bottom <- up</td></tr>
</table>

Table 3.9: Common Connections Across All Experiments.

significant bottom-up connection from lAUD to LIPSP in Experiment 1. For Experiment 1, there are 2 significant and 2 near-significant bottom-up connections from lAUD to LIPSP. Third, there is a significant bi-directional connection between RTPJ and rAUD, excluding the near-significant bottom-up connection from rAUD to RTPJ in Experiment 1. Finally, Experiments 1 and 2 share a near-significant bilateral connection between lAUD and rAUD, excluding the insignificant lateral connection from lAUD to rAUD in Experiment 2. It's worth noting here that 2 of the 6 conditions from Experiment 2 contained the near-significant lateral connection from lAUD to rAUD.

Figure 3.4 shows the similarities of common connections across Experiments 1 and 2. A bold red edge indicates that the common connection was significant only in Experiment 1. A dashed red edge indicates that the common connection was significant in Experiment 1 and near-significant in Experiment 2. A bold blue edge indicates that the common connection was only significant in Experiment 2. A dashed blue edge indicates that the common connection was significant in Experiment 2 and near-significant in Experiment 1. A bold green edge indicates that the common connection was significant for both experiments. A dashed green edge indicates that the common connection was near-significant for both experiments.

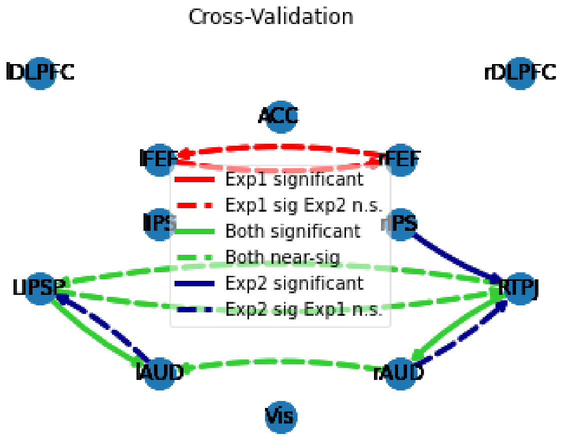


Figure 3.4: Common Connections. Graphical representation of similar and dissimilar significant common connections for cross-validation (Experiment 1 vs Experiment 2).

3.3 Temporal Dynamics

The purpose of this investigation was to determine how the timing of the stimulus intervals affected the functional connectivity curve, or the time-varying AR coefficients, between 2 ROIs over time. This investigation did not yield any enlightening results. The points of inflection were thought to represent the start and end of a window in time in which 2 ROIs were functionally connected, hereon referred to as the "connectivity window." There was no correlation between the connectivity window duration and task difficulty for each ROI-pair. The average window duration was computed by averaging the duration of the window across listening conditions per ROI-pair. There was no correlation between average window duration and ROI topology. There was also no correlation between the timing of the peak or points of inflection relative to the switch gap, and the task difficulty or topology. In many cases, there was a notable relationship between task difficulty and the standard deviation of the measured peaks and points of inflection. That relationship will be outlined per experiment across the following subsections.

Each of the figures of this section show the 100 bootstrapped connectivity curves plotted in gray, the mean of the 100 bootstrapped connectivity curves plotted in blue, the fitted sinusoidal curve of the mean bootstrapped curve plotted in orange, an audio file for the respective experiment plotted in light blue, the peak of the fitted curve with ±2 standard deviations plotted in green, and 2 points of inflection and their ±2 standard deviations plotted in red. Vertical gray lines indicate stimulus interval 1 onset and stimulus interval 2 offset, while the vertical black lines indicate the switch gap onset and offset. The x-axis in each figure is set so that the center of the "switch gap" is aligned at 0 seconds. The title of each figure indicates the listening conditions and the significant edge for which the data is shown. Titles containing "n.s." indicate that the connection is not significant, while titles containing "N.S." indicate that the connection is near-significant. The remaining connections are significant.

3.3.1 Experiment 1

The following subsections compare the standard deviations of the peak and points of inflection of the common significant connections for following conditions from Experiment 1: Maintain Space vs Switch Space, Maintain Pitch vs Switch Pitch, Maintain Space vs Maintain Pitch, Switch Space vs Switch Pitch, and finally, Space to Pitch vs Pitch to Space. The final subsection contains the few uncommon connections.

3.3.1.1 Space: Maintain vs Switch

The standard deviations of measured points for rFEF to lFEF are larger for Maintain Space (Figure 3.5a) than for Switch Space (Figure 3.5b). For lFEF to rFEF, the standard deviation of measured points are similar across listening conditions (Figures 3.5c-d) . Note that the bilateral connections between (l/r)FEF are not significant for Maintain Space. The standard deviations of measured points for the top-down connection from LIPSP to lAUD are smaller in Maintain Space (Figure 3.5e) compared to Switch Space (Figure 3.5f), excluding the second point of inflection which is similar for both conditions. The standard deviation of the second point of inflection measured from the top-down connection from RTPJ to rAUD is larger in Maintain Space (Figure 3.5g) than for Switch Space (Figure 3.5h), while the 2 remaining measured points are similar across conditions. Note that the top-down connections from LIPSP and RTPJ to lAUD and rAUD, respectively, are near-significant for Switch Space.

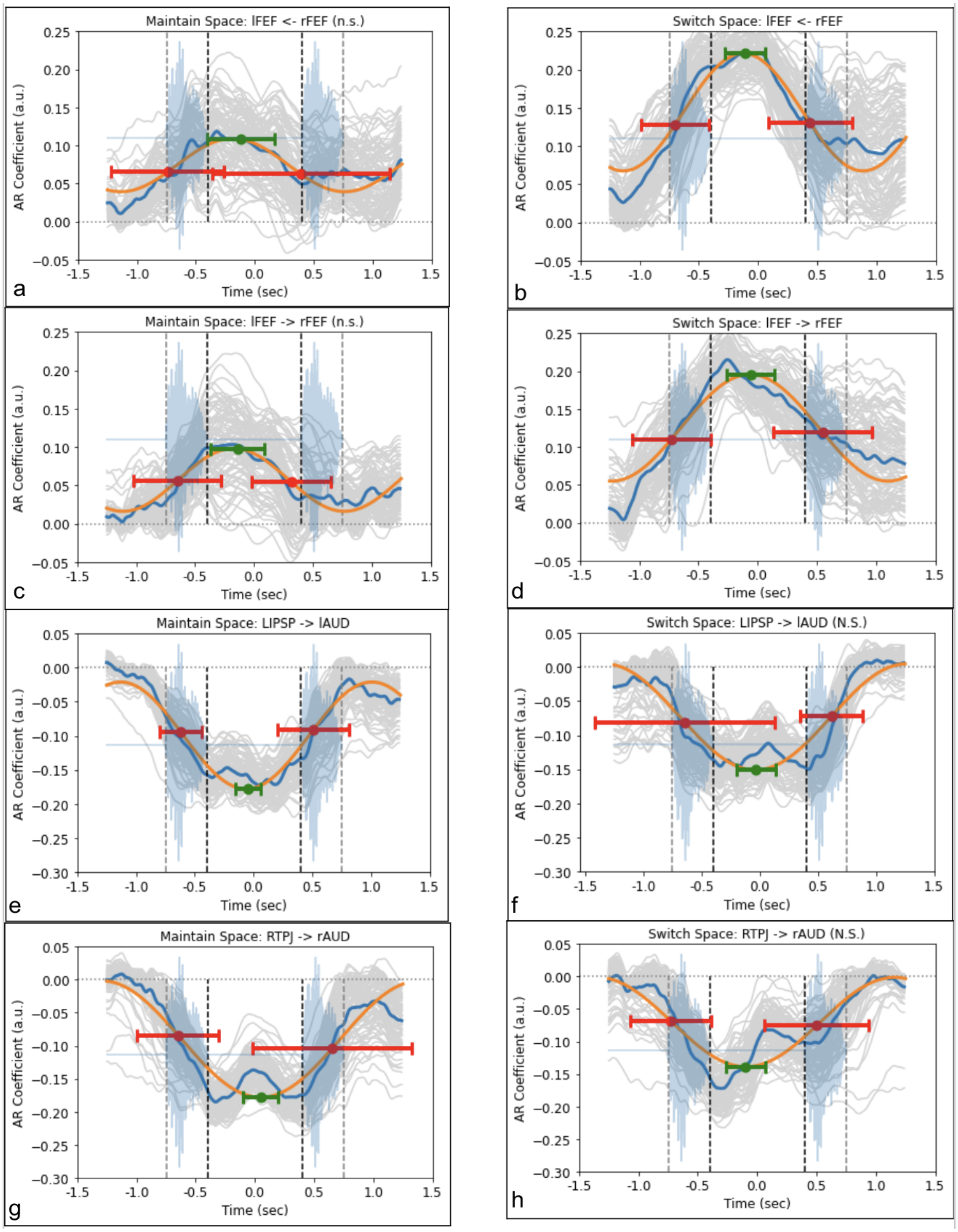


Figure 3.5: Experiment 1 - Connectivity Curves for Common Connections: Maintain Space vs Switch Space.

3.3.1.2 Pitch: Maintain vs Switch

The standard deviations of the measured points of inflection for rFEF to lFEF are larger for Maintain Pitch (Figure 3.6a) compared to Switch Pitch (Figure 3.6b), while the standard deviations of the peak points are similar across conditions. For lFEF to rFEF, the standard deviation of the first point of inflection is greater for Maintain Pitch (Figure 3.6c) relative to Switch Pitch (Figure 3.6d), while the standard deviations of the remaining measured points are similar across conditions. Note that the bilateral connection between (l/r)FEF is near-significant for Switch Pitch. The connectivity curve for LIPSP to lAUD for Maintain Pitch (Figure 3.6e) could not be fit to a sinusoidal function, thus the points of inflection could not be measured or compared to the measurements of the connectivity curve for Switch Pitch (Figure 3.6f). The standard deviation for the first point of inflection for the top-down connection from RTPJ to rAUD is similar across conditions, but the standard deviations of the peak and second point of inflection are larger for Maintain Pitch (Figure 3.6g) than for Switch Pitch (Figure 3.6h). Note that the top-down connection from RTPJ to rAUD is near-significant for Switch Pitch.

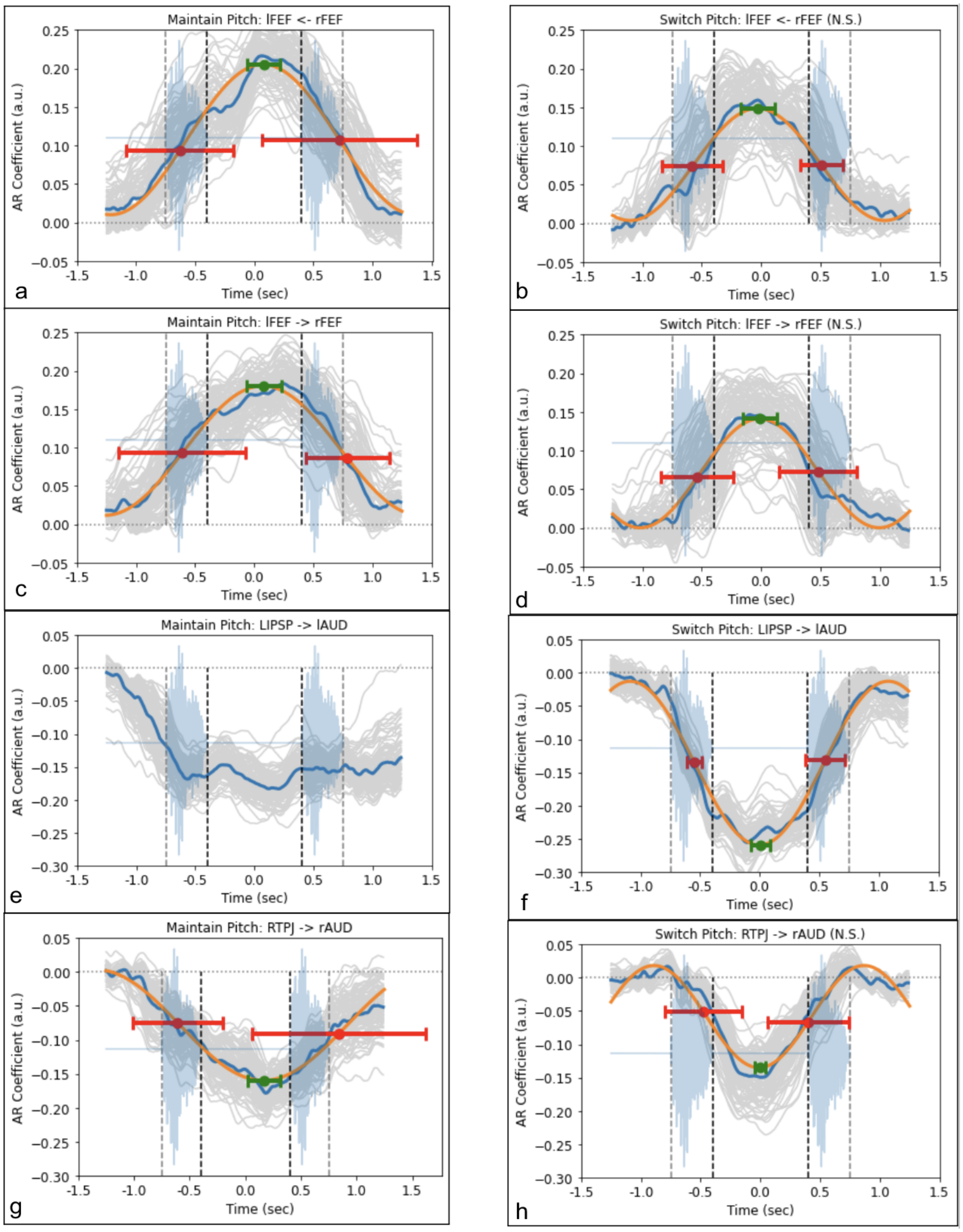


Figure 3.6: Experiment 1 - Connectivity Curves for Common Connections: Maintain Pitch vs Switch Pitch.

3.3.1.3 Maintain: Space vs Pitch

The standard deviation of the first point of inflection for rFEF to lFEF is similar for Maintain Space and Maintain Pitch. The standard deviations of the peak and second point of inflection are greater for Maintain Space (Figure 3.7a) compared to Maintain Pitch (Figure 3.7b). For lFEF to rFEF, the standard deviation of the first point of inflection is smaller for Maintain Space (Figure 3.7c) compared to Maintain Pitch (Figure 3.7d), while the standard deviation of the peak is larger for Maintain Space than in Maintain Pitch, and the standard deviation of the second point of inflection is similar across conditions. Note that the bilateral connection between (l/r)FEF is not significant. The connectivity curve for LIPSP to lAUD for Maintain Pitch (Figure 3.7f) could not be fit to a sinusoidal function, thus the points of inflection could not be measured or compared to the connectivity curve for Maintain Space (Figure 3.7e). For the top-down connection from RTPJ to rAUD, the standard deviations of the measured points are similar across both conditions (Figures 3.7g-h).

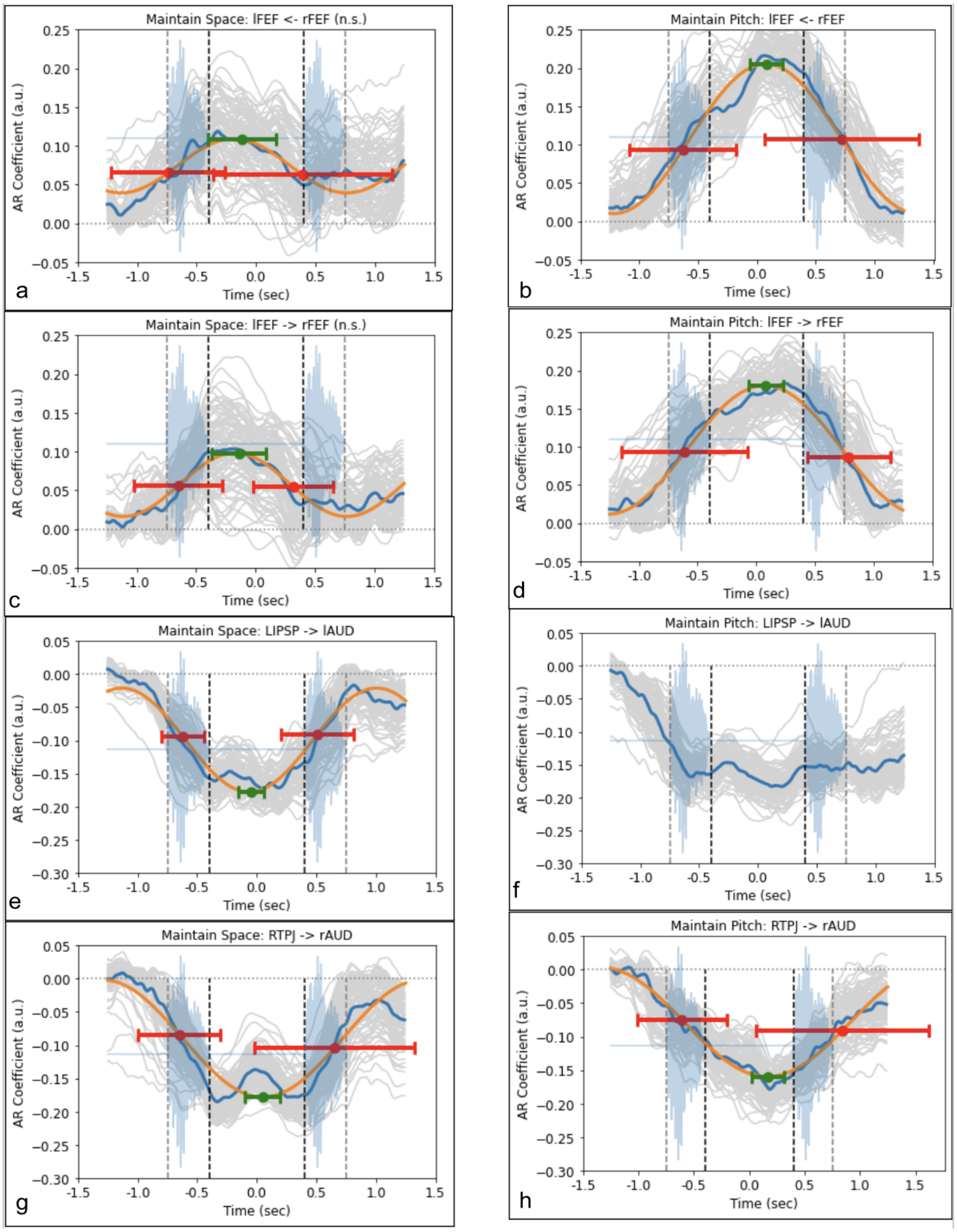


Figure 3.7: Experiment 1 - Connectivity Curves for Common Connections: Maintain Space vs Maintain Pitch.

3.3.1.4 Switch: Space vs Pitch

For the lateral connection from rFEF to lFEF, the standard deviation for the first point of inflection is similar for Switch Space compared to Switch Pitch. The standard deviations of the peak and second point of inflection are greater for Switch Space (Figure 3.8a) compared to Switch Pitch (Figure 3.8b). For the connection from lFEF to rFEF, the standard deviations of the measured points are similar across both conditions (Figures 3.8c-d). Note that the bilateral connections between (l/r)FEF are near-significant for Switch Pitch. The standard deviations for all measured points for the top-down connection from LIPSP to lAUD are greater for Switch Space (Figure 3.8e) compared to Switch Pitch (Figure 3.8f). For the top-down connection from RTPJ to rAUD the standard deviation of the first point of inflection is similar across both conditions, while the standard deviations of the peak and the second point of inflection are greater for Switch Space (Figure 3.8g) compared to Switch Pitch (Figure 3.8h). Note that the top-down connections from RTPJ to rAUD, are near-significant for both conditions, while the top-down connection from LIPSP to lAUD is near-significant for Switch Space.

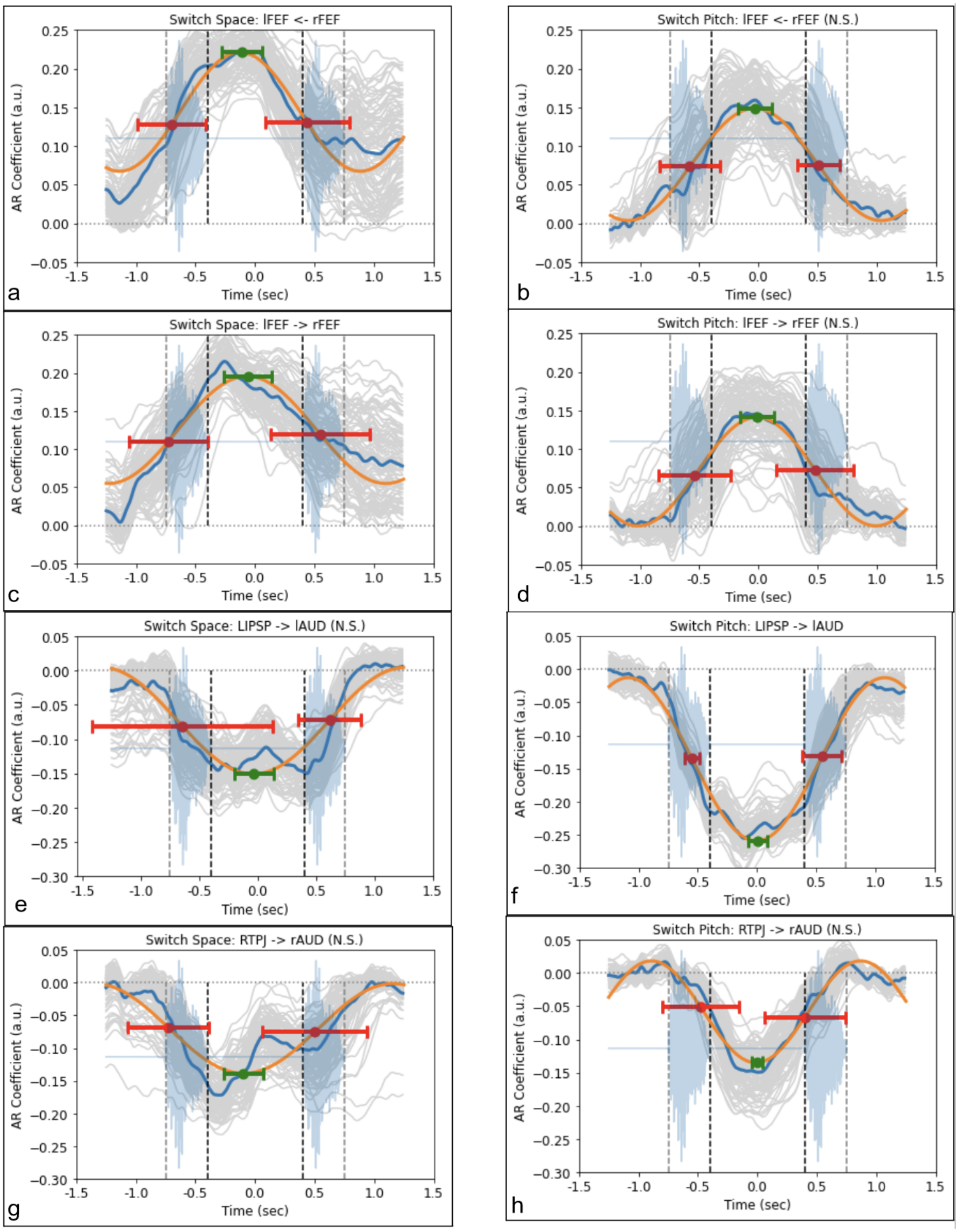


Figure 3.8: Experiment 1 - Connectivity Curves for Common Connections: Switch Space vs Switch Pitch.

3.3.1.5 Space to Pitch vs Pitch to Space

For the lateral connection from rFEF to lFEF, the standard deviation of the first point of inflection is greater for Space to Pitch (Figure 3.9a) compared to Pitch to Space (Figure 3.9b). The standard deviations of the peak and second point of inflection are similar across conditions. For the lateral connection from lFEF to rFEF, the standard deviations of the measured points are larger for Space to Pitch (Figure 3.9c) compared to Pitch to Space (Figure 3.9d). Note that the bilateral connections between (l/r)FEF are near-significant for Space to Pitch. For the top-down connection from LIPSP to lAUD, the standard deviations of both points of inflection were larger for Space to Pitch (Figure 3.9e) relative to Pitch to Space (Figure 3.9f), while the standard deviation of the peak was similar across both conditions. For the top-down connection from RTPJ to rAUD, the standard deviation of the 3 measured points are smaller for Space to Pitch (Figure 3.9g) compared to Pitch to Space (Figure 3.9h). Note that the top-down connection from RTPJ to rAUD is near-significant for Space to Pitch.

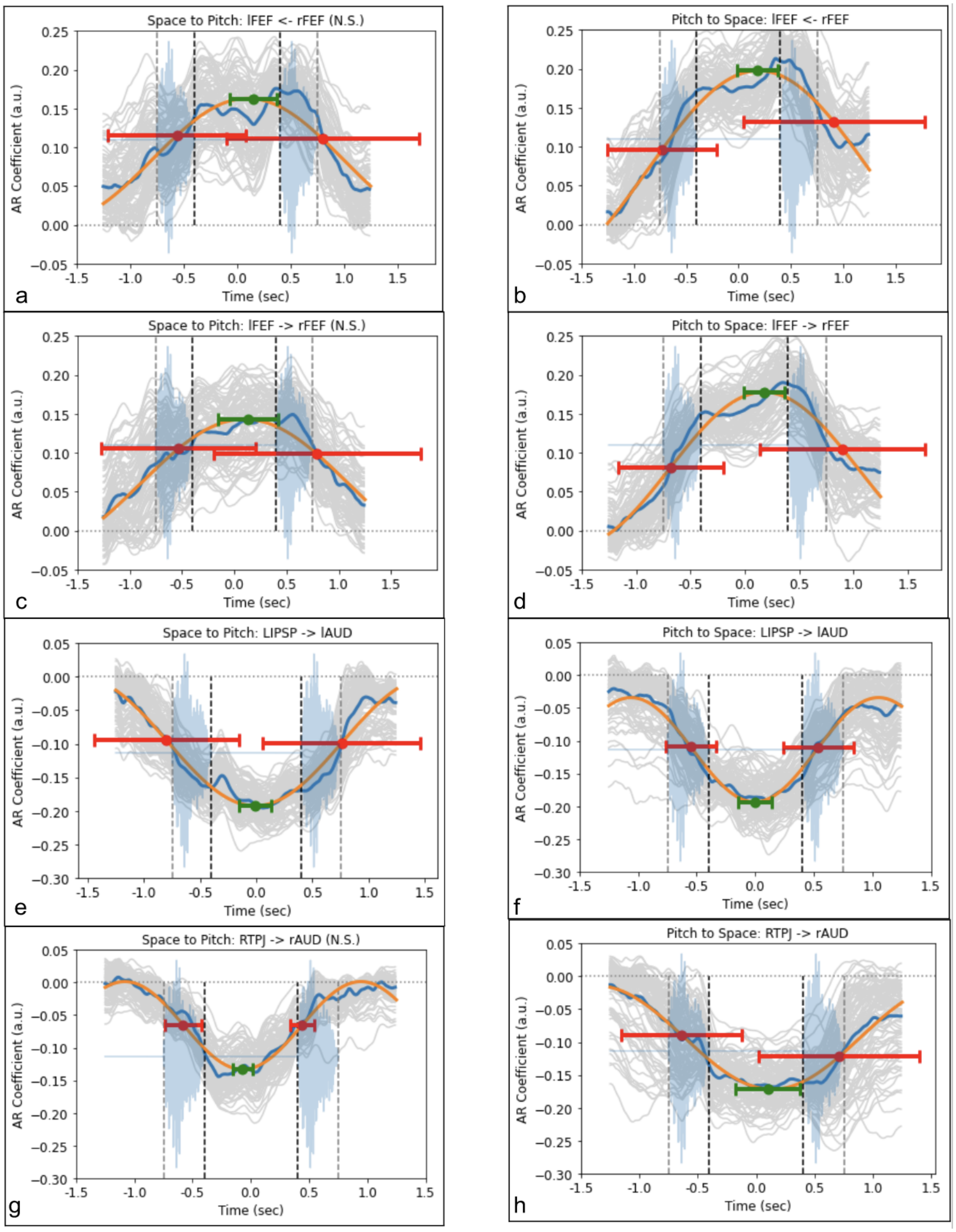


Figure 3.9: Experiment 1 - Connectivity Curves for Common Connections: Space to Pitch vs Pitch to Space.

3.3.1.6 Uncommon Significant Connections

This subsection contains 6 significant connections that were not commonly seen across experimental conditions. Out of the 6 connections across experiments, only 2 were common to at least 2 listening conditions: the lateral connection from rAUD to lAUD in Maintain Pitch and Pitch to Space, as well as the bottom-up connection from lAUD to LIPSP in Switch Pitch and Space to Pitch. The significant bilateral connections between (l/r)DLPFC were only observed in Switch Pitch (Figures 3.10e-f) and thus have no connectivity curves to be compared to. This section compares the standard deviation of measured points for the 2 uncommon significant connections mentioned previously, that were common to at least 2 experimental conditions.

For the lateral connection from rAUD to lAUD, while the standard deviation of the peak is similar between Maintain Pitch and Pitch to Space, the standard deviations of the points of inflection are larger in Maintain Pitch (Figure 3.10a) than in Pitch to Space (Figure 3.10b). For the bottom-up connection from lAUD to LIPSP, the standard deviation of the peaks are similar across conditions, while the standard deviations of the points of inflection are smaller for Switch Pitch (Figure 3.10c) than for Space to Pitch (Figure 3.1d).

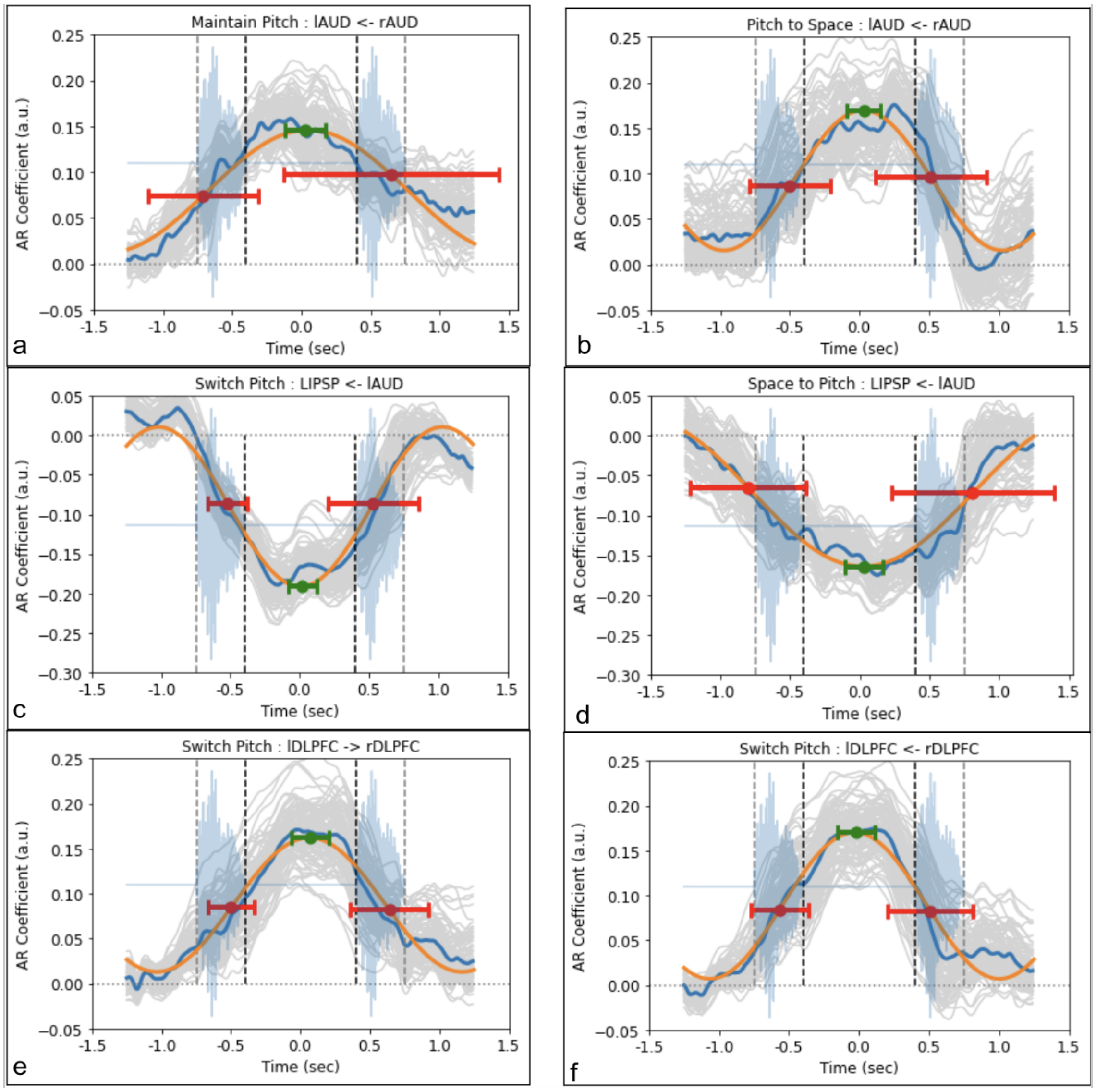


Figure 3.10: Experiment 1 - Connectivity Curves for Uncommon Significant Connections.

3.3.2 Experiment 2 (Cross-Validation)

In regards to the temporal dynamics across Experiments 1 and 2, there were more notable differences than commonalities. Since the duration and nature of the stimuli differed across experiments, comparing the standard deviations of the measured points, as conducted for Experiment 1, may not provide a picture of the difference in difficulty per task between experiments. However, there are still a few aspects worth observing that came up while analyzing the temporal dynamics across experiments. As a reminder, the first step in measuring the temporal dynamics was to fit the connectivity curve to a sinusoidal function. The first observation made here is that only 75% of bootstrapped curves from the Experiment 2 could be fit to a sinusoidal function, while 86% of the bootstrapped curves from the Experiment 1 were fit using the same method. Second, across conditions, the average frequency of the fit cosine functions was larger in Experiment 2 than in Experiment 1. Finally, the standard deviation of measured points was much larger for significant connections in Experiment 2 compared to Experiment 1. All of these findings are consistent with the difference in stimuli and will be discussed further in the Discussion section. Since the bilateral connection between (l/r)FEF was not a common significant connection in this experiment, the connectivity curves for (l/r)FEF are not part of this analysis.

3.3.2.1 Maintain Space

For the top-down connection from LIPSP to lAUD, the standard deviation of the peak is similar across experiments, while the standard deviations of the points of inflection are much smaller in Experiment 1 (Figure 3.11a) compared to Experiment 2 (Figure 3.11b). The near-significant connectivity curve for the top-down connection from RTPJ to rAUD in Experiment 2 (Figure 3.11d) could not be fit to a sinusoidal function, thus the standard deviation of measured points could not be compared to the measurements of Experiment 1 (Figure 3.11c).

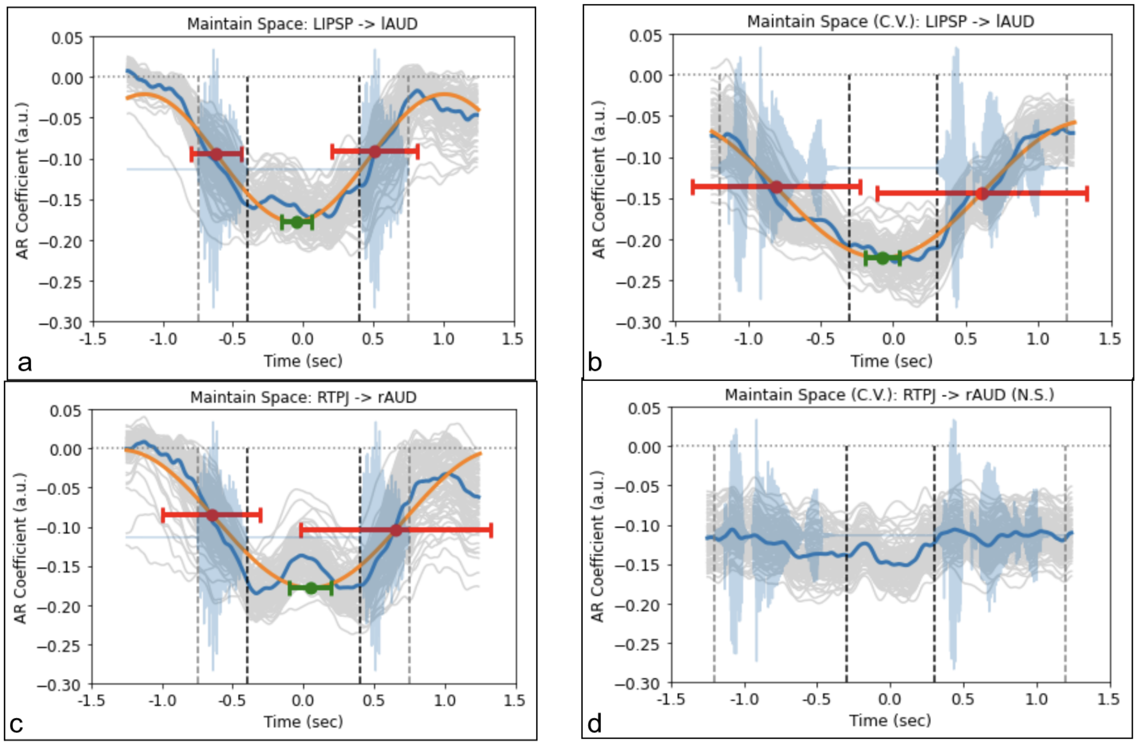


Figure 3.11: Experiment 2 (Cross-Validation) - Connectivity Curves for Common Connections: Maintain Space.

3.3.2.2 Switch Space

The standard deviations of all 3 measured points, for the top-down connection from LIPSP to lAUD, were smaller in Experiment 1 (Figure 3.12a) compared to Experiment 2 (Figure 3.12b). For the top-down connection from RTPJ to rAUD, the standard deviation of all 3 measured points was similar across the 2 experiments (Figures 3.12c-d). Note that the connections for Experiment 1 were near-significant, while the connection from RTPJ to rAUD was not significant for Experiment 2.

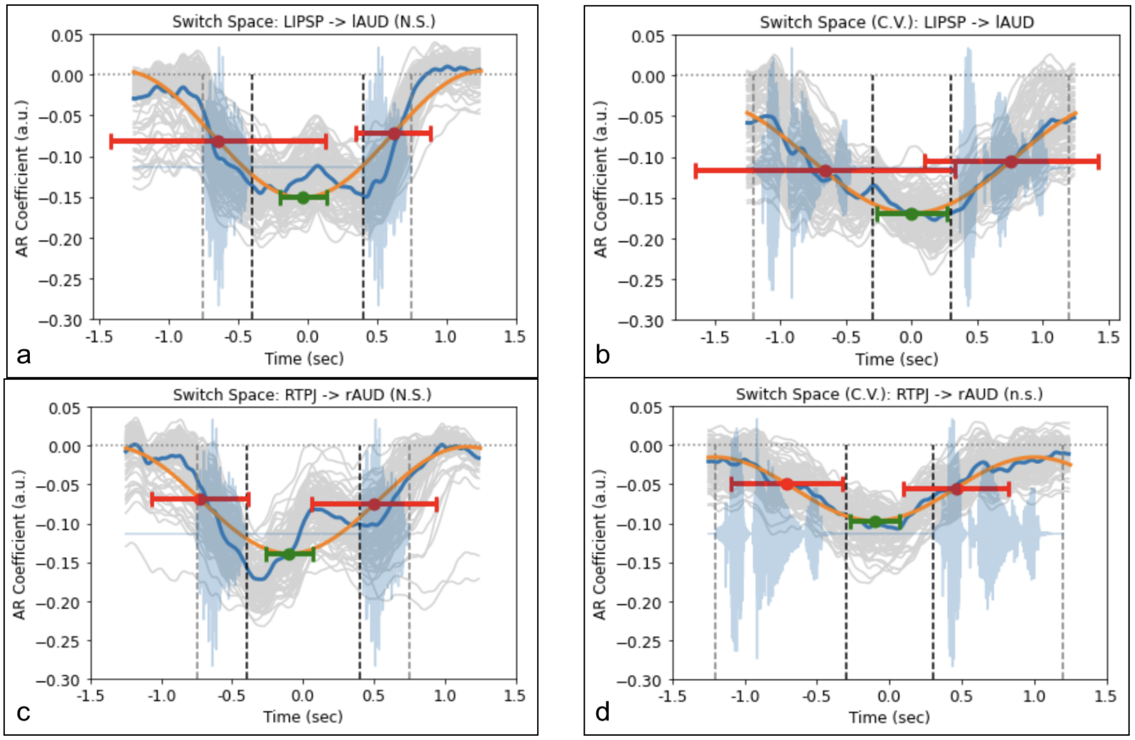


Figure 3.12: Experiment 2 (Cross-Validation) - Connectivity Curves for Common Connections: Switch Space.

3.3.2.3 Maintain Pitch

Direct comparisons across experiments could not be made for this listening condition since 2 of the 4 connectivity curves, LIPSP to lAUD for Experiment 1 (Figure 3.13a) and RTPJ to rAUD for Experiment 2 (Figure 3.13d), could not be fit to sinusoidal functions.

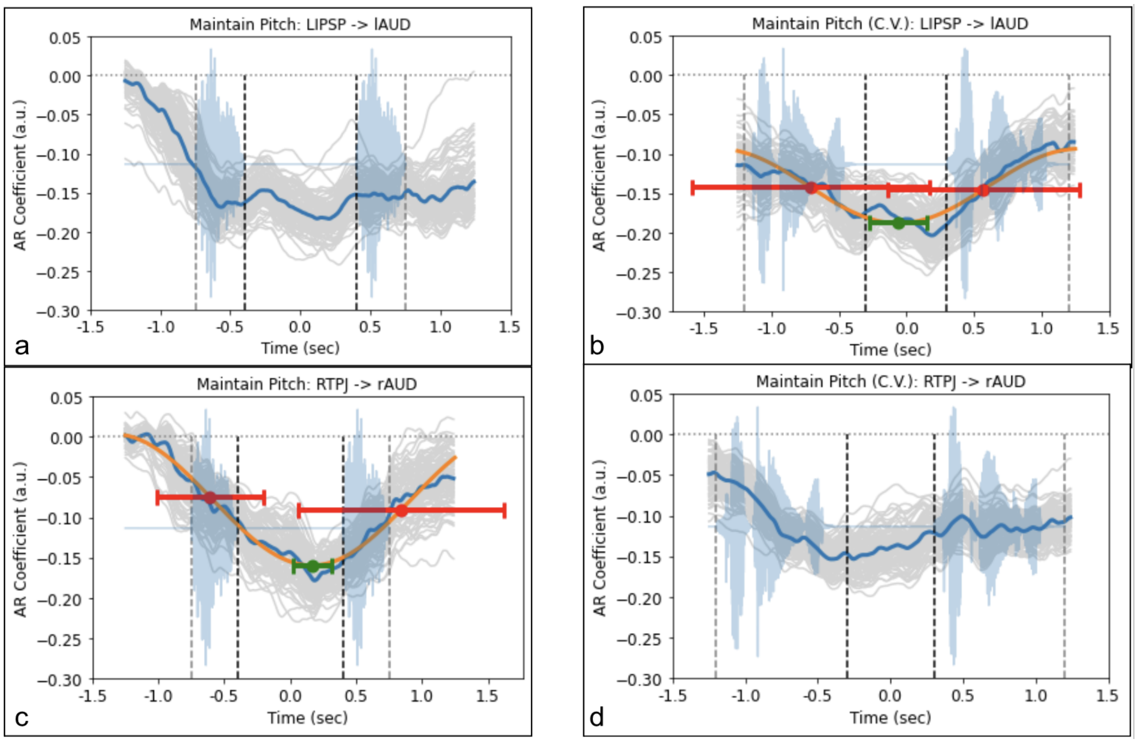


Figure 3.13: Experiment 2 (Cross-Validation) - Connectivity Curves for Common Connections: Maintain Pitch.

3.3.2.4 Switch Pitch

The standard deviations of the 3 measured points for the top-down connection from LIPSP to lAUD were smaller for Experiment 1 (Figure 3.14a) than for Experiment 2 (Figure 3.14b). For the top-down connection from RTPJ to rAUD, the same relationship was observed, where the standard deviations of the 3 measured points were much smaller for Experiment 1 (Figure 3.14c) compared to Experiment 2 (Figure 3.14d).

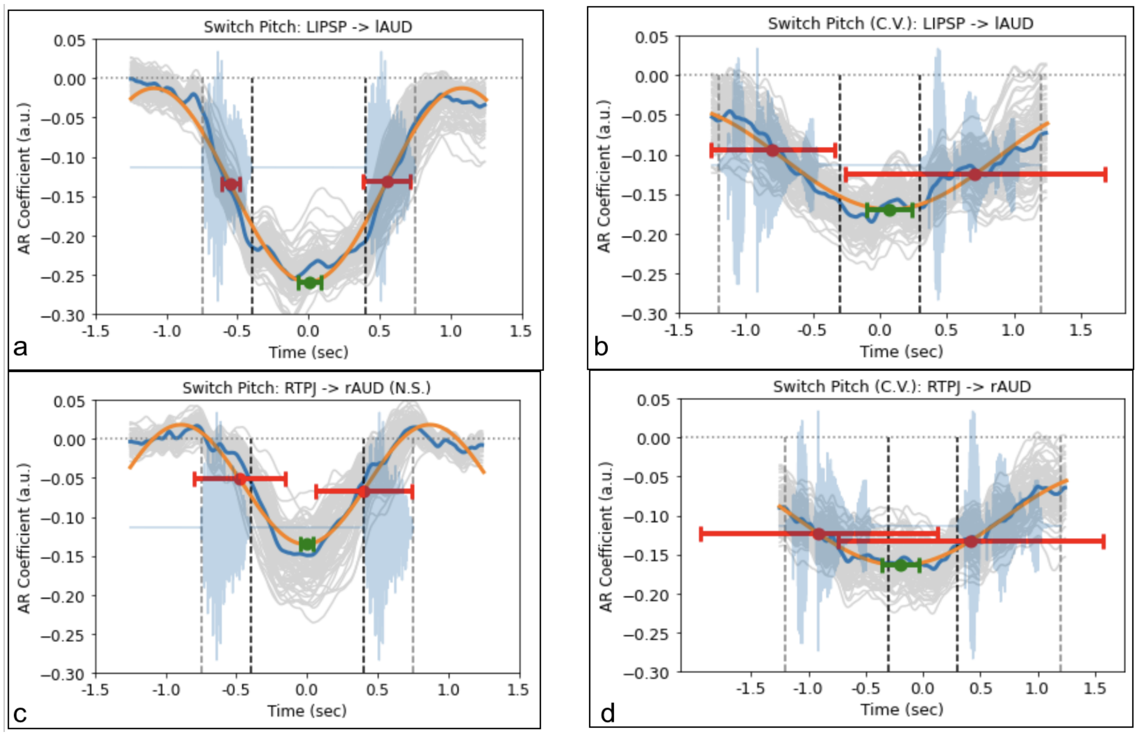
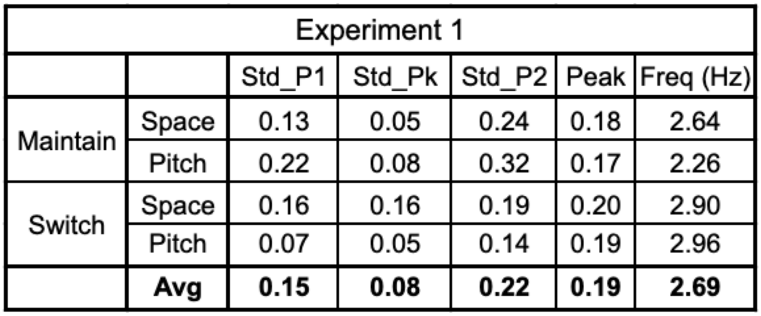


Figure 3.14: Experiment 2 (Cross-Validation) - Connectivity Curves for Common Connections: Switch Pitch.

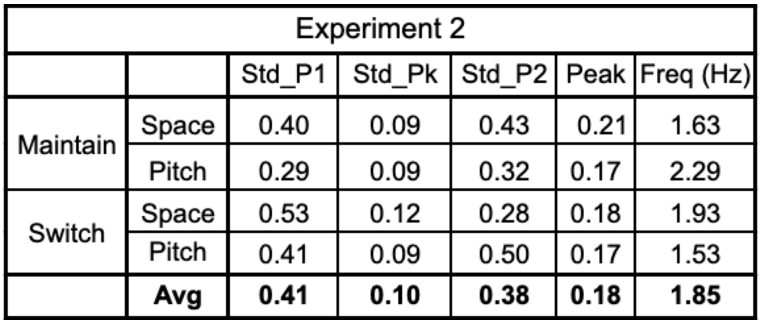
3.3.2.5 Summary of Measurements

Tables 3.10 and 3.11 show a summary of measurements for the 4 comparable conditions of Experiments 1 and 2, respectively. The first 3 columns of each table contain values representing the average standard deviations of the first point of inflection, the peak, and the second points of inflection, respectively. The last 2 columns contain the average peak value, measured as the maximum point of the mean bootstrapped connectivity curve, and the average frequency, as output by the optimization function providing the sinusoidal fit. The "averages" contained in these tables are computed across significant connections for each experimental condition, where each row is a different experimental condition. The final row of each table, averages the values across experimental conditions, providing a summary of measured values for each experiment. Each of these measurements excluded cases where the connectivity curve could not be fit to a sinusoid, except for the peak measurements which used the mean bootstrapped connectivity curve instead of the peak of the sinusoidal fit.



Experiment 1						
		Std_P1	Std_Pk	Std_P2	Peak	Freq (Hz)
Maintain	Space	0.13	0.05	0.24	0.18	2.64
	Pitch	0.22	0.08	0.32	0.17	2.26
Switch	Space	0.16	0.16	0.19	0.20	2.90
	Pitch	0.07	0.05	0.14	0.19	2.96
	Avg	**0.15**	**0.08**	**0.22**	**0.19**	**2.69**

Table 3.10: Experiment 1. Average of measurements from connectivity curves (dynamic AR coefficients) across significant connections: standard deviation of first point of inflection, peak, and second point of inflection, peak value, and frequency of connectivity curves.



Experiment 2						
		Std_P1	Std_Pk	Std_P2	Peak	Freq (Hz)
Maintain	Space	0.40	0.09	0.43	0.21	1.63
	Pitch	0.29	0.09	0.32	0.17	2.29
Switch	Space	0.53	0.12	0.28	0.18	1.93
	Pitch	0.41	0.09	0.50	0.17	1.53
	Avg	**0.41**	**0.10**	**0.38**	**0.18**	**1.85**

Table 3.11: Experiment 2. Average of measurements from connectivity curves (dynamic AR coefficients) across significant connections: standard deviation of first point of inflection, peak, and second point of inflection, peak value, and frequency of connectivity curves.

While the average standard deviations for the peak are similar across experiments, the standard deviations of both points of inflection are smaller for Experiment 1 compared to Experiment 2. The average peak values are similar across experiments, resulting in a similar range of signal-to-noise ratios across experiments (Figure 3.15). The measured average frequency of the sinusoidal connectivity curves were greater in Experiment 1 compared to those of Experiment 2. Although there were many notable differences in the different aspects of the connectivity curves across experiments, none of these results suggest that the connectivity and statistical analyses implemented here are unreliable, just that the experimental stimuli were different in nature.

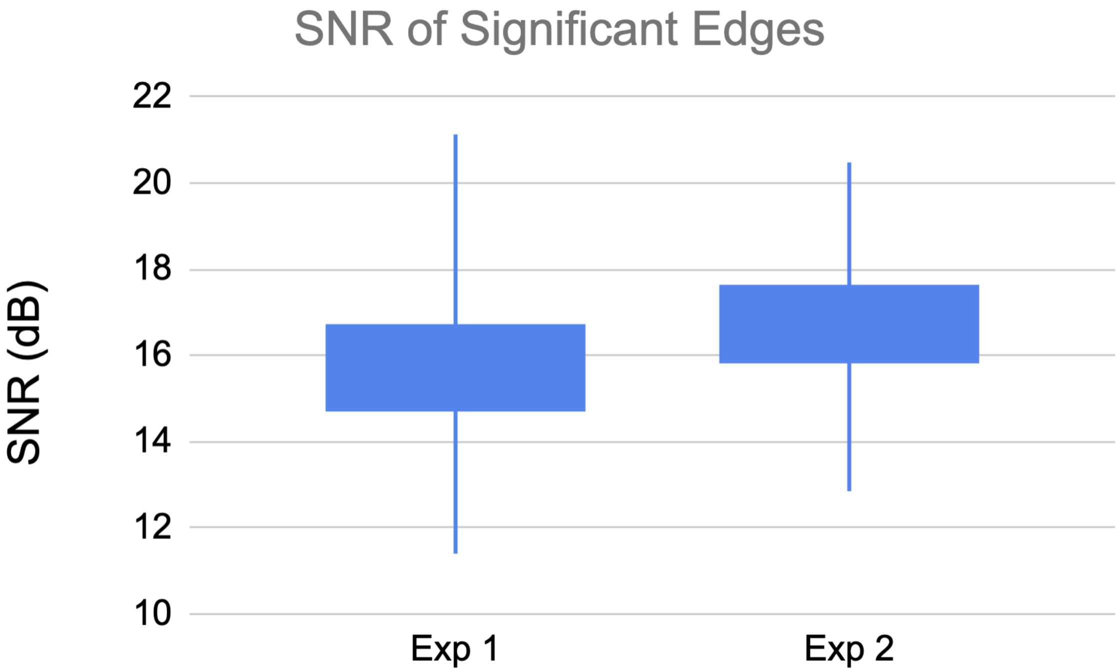


Figure 3.15: SNR of Significant Edges from Experiments 1 and 2.

3.3.3 Experiment 3 (Neurodivergence)

The relatively small number of subjects for this experiment resulted in very noisy connectivity analysis output. For the NT subject group, only 13 of 19 (68%) connectivity curves of the significant connections could be fit to a sinusoidal function. For the ASD subject group, only 8 of 13 (61%) of the significant connections could be fit to a sinusoidal function. As a result, the peak and points of inflection could not be measured for many of the significant connections. As seen in Section 3.2.4, the NT and ASD subject groups had 2 functional connections in common across subject groups: the bilateral connection between (l/r)FEF and the bi-directional connection between rIPS and RTPJ (significance varies across subject groups and listening conditions; see Tables 3.5 - 3.9). The following subsections discuss the differences in standard deviations for the measured peaks and points of inflection across subject groups for various listening conditions. Since so many of the connectivity curves for these ROI-pairs could not be fit to a sinusoidal function, most of the data is not shown here and only connectivity curves for the following are presented: Maintain Space, Switch Space, Maintain Pitch, Maintain Both, and Switch Both. It's also worth mentioning here that Switch Both was the only condition which had sinusoidal fits for the lateral connection from lFEF to rFEF. None of the other conditions had sinusoidal fits for either of the bilateral connections between (l/r)FEF. Additionally, Switch Both is the one condition listed in the following subsections that does not have sinusoidal fits for either of the bi-directional connections between rIPS and RTPJ.

3.3.3.1 Maintain Space

The standard deviation for the first point of inflection for the top-down connection from rIPS to RTPJ is much larger for the NT subject group (Figure 3.16a) compared to the ASD subject group (Figure 3.16b). The standard deviations of the peak and second point of inflection are similar across subject groups for the top-down connection from RTPJ to rIPS. For the bottom-up connection from RTPJ to rIPS, the standard deviations of all measured points are larger for the NT subject group (Figure 3.16c) compared to the ASD subject group (Figure 3.16d). Note that the top-down connection from rIPS to RTPJ is not significant, while the bottom-up connection from RTPJ to rIPS is near-significant.

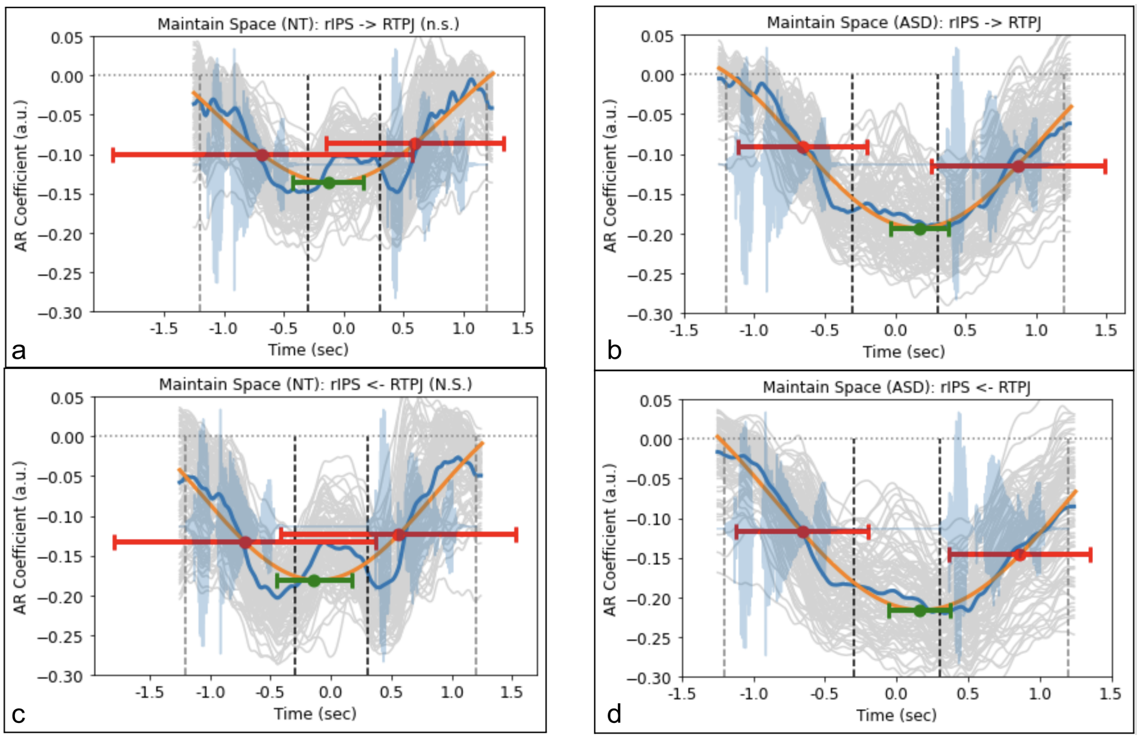


Figure 3.16: Experiment 3 (Neurodivergence) - Connectivity Curves for Common Connections: Maintain Space.

3.3.3.2 Switch Space

The standard deviation of all measured points of the connectivity curve for the top-down connection from rIPS to RTPJ are larger for the NT subject group (Figure 3.17a) relative to the ASD subject group (Figure 3.17b). In regards to the bottom-up connection from RTPJ to rIPS, the standard deviations of the measured points are similar when comparing the NT subject group (Figure 3.17c) to the ASD subject group (Figure 3.17d). Note that all connections mentioned here are near-significant, excluding the top-down connection from rIPS to RTPJ in the ASD subject group which is not significant.

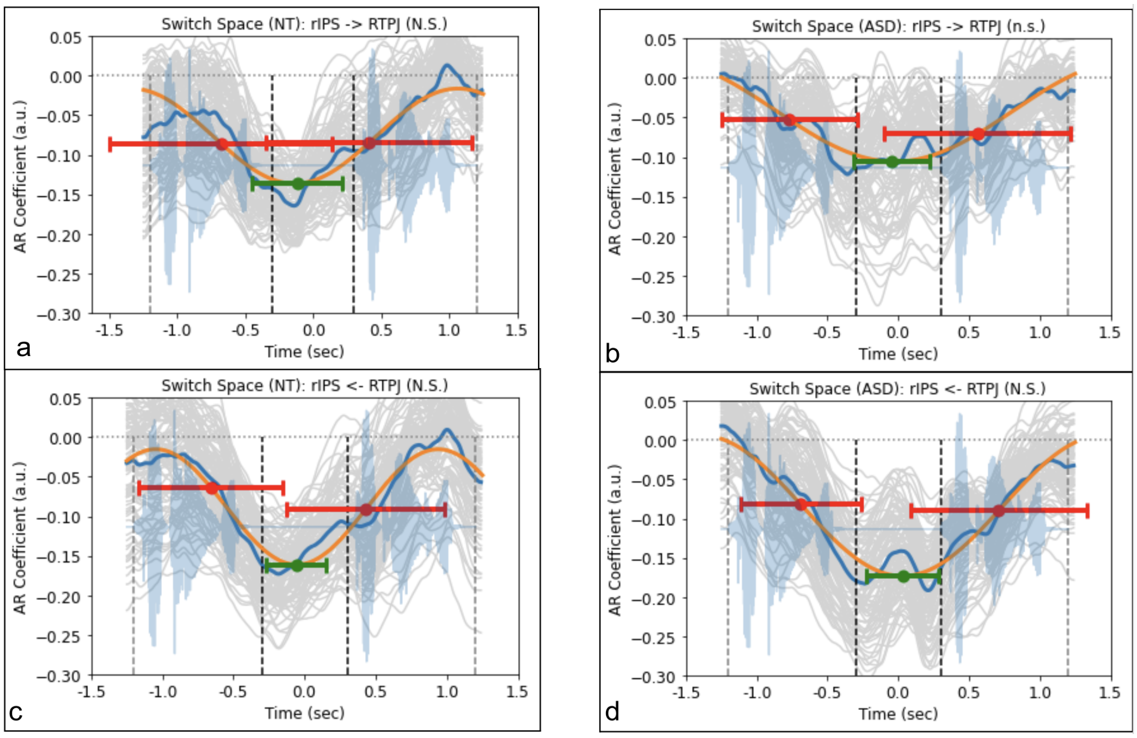


Figure 3.17: Experiment 3 (Neurodivergence) - Connectivity Curves for Common Connections: Switch Space.

3.3.3.3 *Maintain Pitch*

The standard deviation of the first point of inflection of the sinusoidal connectivity curve of the top-down connection from RTPJ to rIPS is smaller for the NT subject group (Figure 3.18a) relative to the ASD subject group (Figure 3.18b). The standard deviations of the peak are similar across subject groups, while the standard deviation of the second point of inflection is larger for the NT subject group compared to the ASD subject group. Note that this connection is near-significant for both subject groups.

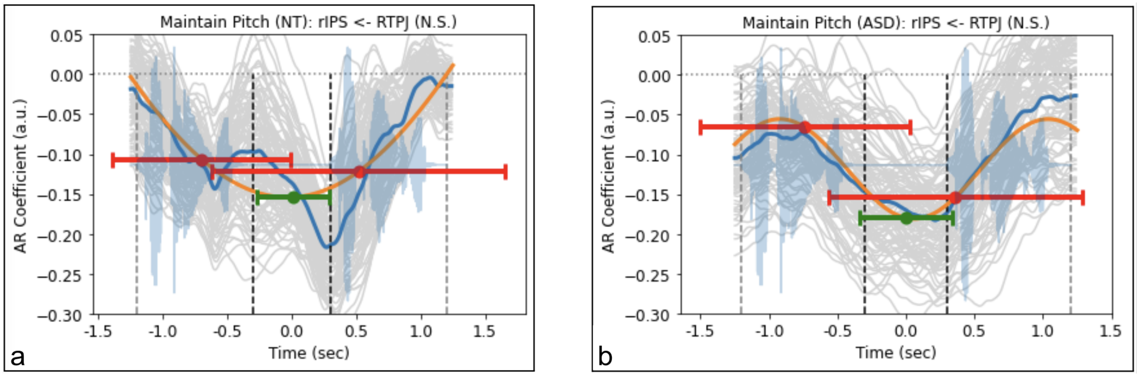


Figure 3.18: Experiment 3 (Neurodivergence) - Connectivity Curves for Common Connections: Maintain Pitch.

3.3.3.4 Maintain Both

The standard deviation of the first point of inflection for the sinusoidal connectivity curve for the top-down connection from rIPS to RTPJ is smaller for the first point of inflection for the NT subject group (Figure 3.19a) compared to the ASD subject group (Figure 3.19b). The standard deviations for the peak and second point of inflection are similar across subject groups. For the bottom-up connection from RTPJ to rIPS, the standard deviations of the first point of inflection and the peak are smaller for the NT subject group (Figure 3.19c) compared to the ASD subject group (Figure 3.19d). The second point of inflection is much larger for the NT subject group than for the ASD subject group. Note that both of these connections were not significant for the ASD subject group.

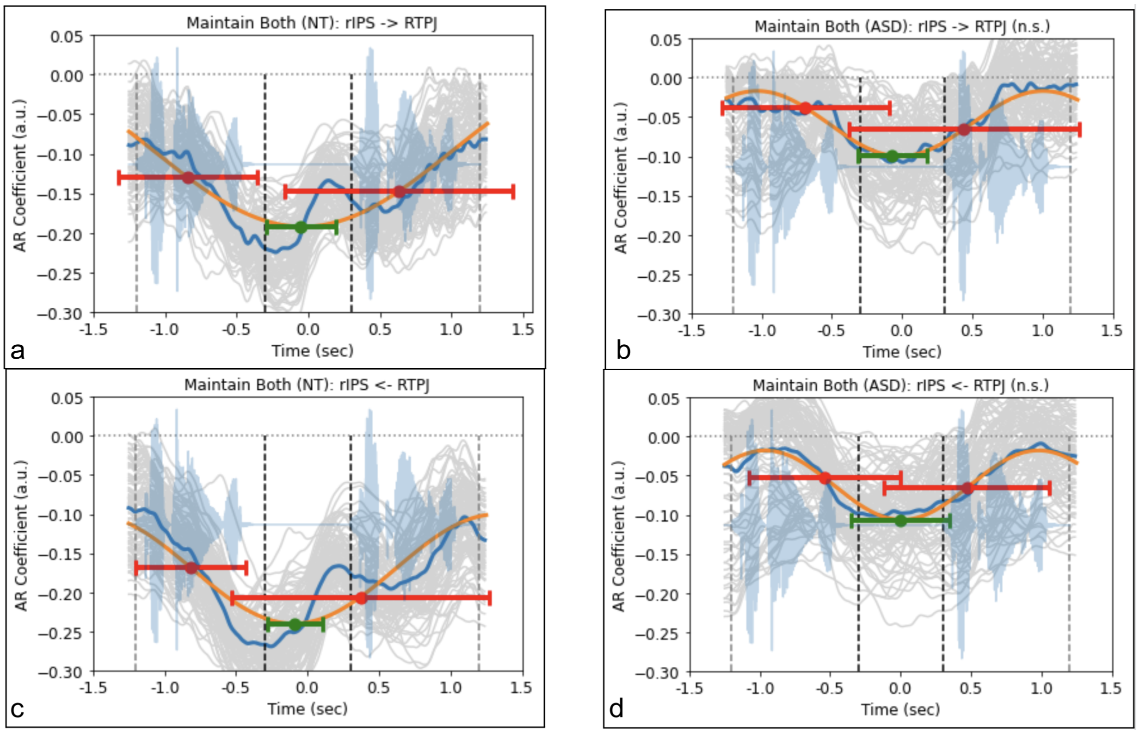


Figure 3.19: Experiment 3 (Neurodivergence) - Connectivity Curves for Common Connections: Maintain Both.

3.3.3.5 Switch Both

For the lateral connection from lFEF to rFEF, the standard deviations of all measured points are smaller for the NT subject group (Figure 3.20a) than for the ASD subject group (Figure 3.20b). Note that this connection is not significant for the NT subjects and near-significant for the ASD subjects

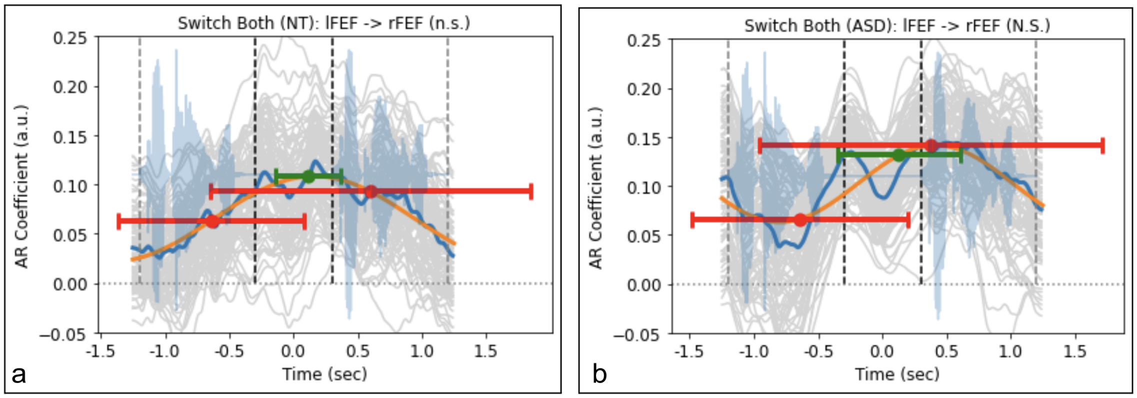


Figure 3.20: Experiment 3 (Neurodivergence) - Connectivity Curves for Common Connections: Switch Both.

Chapter 4

DISCUSSION

The following subsections discuss the results described in Chapter 3. The purpose of this section is to frame the results in regards to the hypotheses formed based on previous research and to begin to answer the research questions presented in Section 1.4. This chapter follows the structure of Chapter 3 by discussing the results one subsection at a time. Section 4.1 discusses the collective results from Sections 3.1 and 3.2, in particular which significant (and near-significant) connections met a priori expectations and which results were less expected. Section 4.2 discusses the relative difficulty across tasks and how the standard deviation of the measured points along the connectivity curves may relate to the relative task difficulties.

4.1 Significant (and Near-Significant) Connections

Overall, the results from the presented studies in Sections 3.1 and 3.2 did not meet expectations. Taking consideration of previous literature regarding active ROIs when switching and maintaining attention across various auditory cues, the hypothesis was that the results would show distinct cortical networks that correlate to the endogenous actions of the listener. Due to the conservative statistical analysis performed, the significant functional connections determined for each experiment were fairly sparse. In order to remain conservative but increase the impact of these results, near-significant connections were also computed. This was made in an effort to determine what ROIs may be functionally connected despite not meeting the stringent criteria of the outlined connectivity and statistical analyses.

4.1.1 Experiment 1

The following subsections describe which ROIs, one region per subsection, were determined to be functionally connected and how those results align (or misalign) within the context of the field's current literature. The final subsection discusses the collection of ROIs found across multiple listening conditions and how the functional connectivity of these regions may play an important role in auditory attention.

4.1.1.1 Left and Right FEF

Previous literature has described FEF in roles regarding directing attention, and directing eye movement in overt attention [13, 27, 32]. This led to the hypothesis that (l/r)FEF would be functionally connected to each other, and/or other ROIs, in listening conditions dealing with switching attention to auditory stimuli in space. Some of the results were aligned with this hypothesis: there was a significant bilateral connection between (l/r)FEF in Switch Space and Pitch to Space, and a near-significant bilateral connection between (l/r)FEF in Space to Pitch. Results show that this connection was also significant for Maintain Pitch and near-significant for Switch Pitch. One may argue that pitch has a spatial correlate, where higher pitches are perceived higher on a vertical axis while lower pitches are perceived lower to the ground. This would make the case that the (l/r)FEF should be involved when switching attention across different pitches. This theory supports the absence of this connection for Maintain Space. However, studies have also shown that FEF is involved in visual fixation [26], which supports the functional connection between (l/r)FEF for Maintain Pitch where there was no shift in attention between stimulus intervals.

4.1.1.2 LIPSP and lAUD

Previous investigations into the cortical dynamics of switching and maintaining attention [29] showed that LIPSP was more active when maintaining attention to pitch cues when compared to switching attention across spatial cues. This led to the hypothesis that LIPSP would be more functionally connected to ROIs in conditions dealing with pitch, and less connected in conditions regarding spatial cues. Results show a significant top-down connection from LIPSP to lAUD in all listening conditions, excluding the near-significant connection in Switch Space. While LIPSP may be more engaged when maintaining attention to pitch cues, the results presented here suggest that this ROI plays an important role in auditory attention regardless of auditory cue. Additionally, all conditions except Maintain Space and Pitch to Space show a near-significant bilateral connection between LIPSP and RTPJ. Although these 2 ROIs have been shown to have distinct roles when switching or maintaining attention across space or pitch, these results may indicate a functionally similar role when executing auditory attention.

4.1.1.3 RTPJ and rAUD

Multiple studies [13, 29] have described RTPJ as a "circuit breaker", or a filter of extraneous stimuli, allowing the dorsal frontoparietal network to only engage with salient information. Similar to the expectations regarding (l/r)FEF, it was hypothesized that RTPJ would be more functionally connected in listening conditions regarding a switch of attention compared to conditions regarding maintaining attention. Similar to the results described regarding LIPSP, results show a top-down connection from RTPJ to rAUD in every listening condition. The results may indicate a valid null hypothesis, where the RTPJ would be more functionally connected in conditions regarding maintaining attention, as this connection was significant in Maintain Space and Maintain Pitch and only near-significant for Switch Space, Switch Pitch, and Space to Pitch. Additional support for the null hypothesis is shown via the near-significant bottom-up connection from rAUD to RTPJ in Maintain Space and Maintain Pitch, the thought here being that a bi-directional connection may be stronger evidence for functional connectivity than a unidirectional connection. The same connectivity observed for the Maintain conditions was observed for Pitch to Space. It could be argued that since Pitch to Space is more challenging than Space to Pitch, the increased connectivity could be correlated with task difficulty. However, this argument does not align with the null hypothesis as argued in this paragraph.

4.1.1.4 Left and Right DLPFC

Most functional connections observed in this experiment were observed across multiple listening conditions. However, the significant bilateral connection between (l/r)DLPFC is only observed in Switch Pitch. One may argue that this is a function of task difficulty, where the spatial conditions and Maintain Pitch are easier conditions and thus require less recruitment of regions in the frontal cortex. However, since this connection, or any connections to regions of the frontal cortex, were not observed in the 2 of the more difficult conditions (switching attention across auditory cues) this argument is null. However, if we assume that since 2 of the more difficult conditions contained spatial cues, the challenges that accompany identifying and then switching attention across pitch cues is the only condition that requires functional connectivity of higher processing ROIs such as DLPFC.

4.1.1.5 Left and Right AUD

One final functional connection worth mentioning here is the bilateral connection between (l/r)AUD. As the entirety of the stimuli in this study were of auditory nature, it was hypothesized that these regions would be connected in every listening condition. This hypothesis was nearly valid as this connection was observed in every condition except Space to Pitch. These bilateral connections were near-significant (excluding the significant lateral connections from rAUD to lAUD), showing that the functional connectivity of these regions to each other and other regions, likely play an important role in executing auditory attention. It should be mentioned again here that our analysis window for measuring functional connectivity was during the switch gap period where no speech was present. Therefore, this connection is indicative of endogenous processing, rather than a direct response to auditory stimuli.

4.1.1.6 Cortical Network for Auditory Attention

According to the results presented in this study, several cortical regions are functionally connected regardless of the cue being attended, or if the listener is maintaining or switching their attention. This could be indicative of a functionally connected network for executing auditory attention that supersedes specifics regarding auditory cues or endogenous processing. Results show that 5 out of 6 listening conditions (all but Maintain Space) engage the bilateral connection between (l/r)FEF, with varying significance. All conditions show a near-significant bilateral connection between lAUD and rAUD (excluding Space to Pitch), as well as a near-significant bilateral connection between LIPSP and RTPJ (excluding Maintain Space and Pitch to Space). All 6 conditions analyzed in this study also show a significant, or near-significant, top-down connection to the left and right AUD from LIPSP and RTPJ, respectively. This symmetry may indicate some similarity between LIPSP and RTPJ in regards to their functional connectivity when executing auditory attention, even though previous studies have shown a functional double dissociation between these regions in regards to switching/maintaining attention to space/pitch [29]. This top-down connection between LIPSP and lAUD (as well as RTPJ and the rAUD) could be the primary connection(s) in which auditory stimuli influence this supramodal network, or the ventral frontoparietal network in particular.

4.1.2 Experiment 2 (Cross-Validation)

The cross-validation experiment was implemented in order to determine the reliability of the connectivity and statistical analyses described in Sections 2.3 and 2.4 for M/EEG data recorded during a dual-stream auditory attention task. Since Experiments 1 and 2 were similar in nature, with notable differences in stimuli, the results were expected to be comparable, per comparable condition. When taking into account both significant and near-significant functional connections for the 4 comparable conditions, these 2 experiments had twice as many connections in common (24 connections) as they had different (12 connections). The following subsections discuss how these results support previous claims regarding the cortical network for auditory attention, and additional regions that may be important for speech stimuli.

4.1.2.1 Cortical Network for Auditory Attention

The results from Experiment 2 support the claims made in Section 4.1.1.5. There were near-significant bilateral connections between (l/r)FEF for 4 of 6 conditions in Experiment 2 (all but Switch Space and Maintain Pitch). As stated previously, these ROIs are also part of the frontoparietal supramodal attention network, and as they are functionally connected in most conditions for both experiments under consideration, this finding is in support of these ROIs as part of this larger cortical network. Additionally, results of Experiment 2 show a near-significant bilateral connection between (l/r)AUD for all conditions except Switch Both and a near-significant bilateral connection between LIPSP and RTPJ for Switch Space, Maintain Pitch (excluding the significant bottom-up connection from RTPJ to LIPSP), and Maintain Both. Additionally, there were near-significant lateral connections from RTPJ to LIPSP for Switch Both and from LIPSP to RTPJ for Maintain Space, suggesting that these ROIs may be more or less functionally connected depending on the methods used to approach the task. Finally, the results of Experiment 2 show significant and near-significant connections connecting the LIPSP and RTPJ with the left and right AUD, respectively, for all 6 of the listening conditions. These findings support the theory discussed in Section 4.1.1.5 that auditory regions are functionally connected to the frontoparietal networks for supramodal attention when attending auditory stimuli.

Additionally, in comparing all common edges, results from Experiment 2 contain all the common connections (despite differences in significance level) that resulted in Experiment 1. These results successfully validate that the analyses performed here can reliably determine the functional connectivity across ROIs during a dual-stream auditory attention task.

4.1.2.2 rIPS and RTPJ

The most interesting result when observing the common connections in Experiment 2 was that most of the listening conditions for this experiment contained a bilateral connection between rIPS and RTPJ with varying significance (all conditions except Switch Space and Maintain Both). Both of these ROIs are suggested to be part of the ventral frontoparietal supramodal attention network [13]. Although they were suggested to be connected via visual areas, the results here suggest they are functionally connected to each other. For Experiment 2, this connection was significant for Maintain Space and Maintain Pitch, and near-significant for Switch Pitch. In Switch Both, the top-down connection from rIPS to RTPJ was significant while the bottom-up connection from RTPJ to rIPS was near-significant. The first theory is that these ROIs are connected in Experiment 2 and not Experiment 1 because of the difference in stimuli: Experiment 2 contained gendered 2 syllable words while Experiment 1 utilized monotonic single digit speech tokens. Therefore, these ROIs are functionally connected when attending realistic speech stimuli. Since this connection was not observed in 2 out of the 6 conditions, there may not be enough evidence to support this theory.

The second theory is that this bilateral connection is important for maintaining attention to the more realistic speech tokens of Experiment 2. The first piece of evidence is that this connection is significant in both Maintain Space and Maintain Pitch. Switching attention across space is a relatively easy task as you can simply ignore the speech stimulus from one direction. Switching attention across pitch (gender) is more challenging as these stimuli are colocated and may require the listener to keep in mind the pitch (gender) of the talker to be ignored in order to effectively attend to the other. As the IPS has been described to play a role in counting ([18]; in this case, counting the number of auditory stimuli in an environment) and in figure-ground segregation [14, 50], this connection could be important for distinguishing a single auditory source from a mixture of auditory sources. Although Switch Both also shows this connection, supporting this theory given that there is a pitch (gender) component, Maintain Both does not show this connection, which does not support this theory.

More likely than these two regions being connected as a function of stimulus, the connection between rIPS and RTPJ is likely one the means in which the dorsal and ventral frontoparietal networks interact. As part of the dorsal network, IPS works in conjunction with the FEF during a visual search. Unlike FEF, the IPS also responds to the target stimulus. When the visual search results in finding the target stimulus, the TPJ is activated [47]. Other studies suggest the connection between these two networks may be through the meidal frontal gyrus [20], FEF, or rIPS [54]. The results of this study suggest that one of the machanisms in which the dorsal and ventral networks interact is through the functional connection between rIPS and RTPJ. Additional differences between the functionally connected networks computed in the cross-validation experiment can be attributed to the differences in stimuli presented to the two separate groups of subjects.

4.1.3 Experiment 3 (Neurodivergence)

Keeping in mind that the experimental set up for Experiments 2 and 3 were exactly the same, it may come as a surprise that the results for the NT group in Experiment 3 were very different when compared to the results of Experiment 2. It should be noted that subjects for Experiment 2 were not screened for ASD and assumed to be from a NT population. Since there were fewer subjects in Experiment 3, there was no cross-validation process comparing the results of the NT group with the results of Experiment 2. Instead, Experiment 3 involved an internal investigation by comparing the results of the 9 sex- and age-matched subjects from the NT and ASD subject groups. Additionally, due to the small number of subjects per subject group, the statistical analysis for this experiment was made less conservative by reducing the number of bootstraps needing to meet the AR threshold in order to be deemed significant (or near-significant) from 95 to 90. The most notable difference between these two subject groups is that the significant connections for the ASD group were far more sparse (0-5 significant connections per condition for an average of 2.16 connections per condition) compared to the NT group (2-6 significant connections per condition for an average of 3.16

connections per condition). The following subsections are structured according to possible difficulties that ASD subjects might encounter when deploying attention to auditory stimuli.

4.1.3.1 Switching vs Maintaining Attention

A noteworthy observation is that the Switch Space and Switch Both conditions each had 0 significant connections for the ASD subject group. Previous studies have demonstrated that subjects with ASD have more difficulty switching their attention across stimuli compared to their NT counterparts [3, 45]. Even though Switch Pitch had 3 functional connections, this lack of significant connections in the 2 switch conditions previously mentioned could be due to this challenge ASD subjects face in switching attention. However, the original study in which the data for Experiment 3 was collected [19] indicated no significant difference in the correct responses between the switch- and maintain-attention trials for the ASD subject group. Although insignificant, the ASD subject group was about 10% less correct in trials involving switching attention compared to maintaining, which may be evidence that there is less coordination among cortical ROIs when switching attention compared to maintaining attention for ASD subjects. There is currently insufficient evidence to support this hypothesis.

4.1.3.2 Higher Cognitive Processing

Results for both subject groups showed functional connectivity between ROIs not observed in either of the first 2 experiments. For example, functional connectivity was observed between FEF and DLPFC for 3 or more conditions in both subject groups. For NT subjects, this connection was in the right hemisphere while the connection was in the left hemisphere for ASD subjects (2 conditions also had this right hemisphere connection for ASD subjects). As the DLPFC is thought to have a role in higher cognitive processing [9, 37], one might expect this ROI to be functionally connected in more challenging tasks such as those requiring attention across different cues as in Switch or Maintain Both. There are functional connections between FEF and DLPFC for these 2 conditions for the NT subject group but not the ASD subject group. This could indicate that subjects with ASD are less able to recruit regions of the frontal cortex necessary to complete these more complicated attention tasks. Since both NT and ASD subject groups have functional connectivity between FEF and DLPFC for 3 conditions not including Maintain Both or Switch Both, there is currently not enough evidence to support this theory.

There are also 4 conditions in which the NT subjects show near-signficant top-down functional connectivity between ACC and LIPSP (excluding the significant connection for Maintain Pitch which also includes a near-significant bottom-up connection from LIPSP to ACC). As stated in Section 1.2, ACC is thought to play a role in signal enhancement in noise [58]. For this study it could work to enhance the perception of the target speaker. The lack of ACC's functional connectivity in the ASD subject group could support the previous theory that subjects with ASD are less able to recruit more frontal regions engaged in higher processing, which could be why these subjects have increased difficulty in deploying auditory attention.

4.1.3.3 Cortical Network for Auditory Attention

Finally, when observing the common functional connectivity across all experiments, there are 2 common connections present in both NT and ASD subject group results that support previous discussion points regarding the frontoparietal supramodal attention network. The first is the bilateral connection between (l/r)FEF, observed in all conditions except Maintain Both and Switch both for the NT subjects, and observed in all 6 conditions for the ASD subjects, with varying significance. Results from the original study [19] state that ASD subjects showed the best performance when both auditory cues were available. It is possible that these subjects recruited more engagement from the FEF ROIs relative to the NT subject group which resulted in their improved performance for tasks where both auditory cues were present.

The second functional connection worth mentioning here is the bi-directional connection between rIPS and RTPJ. This connection was observed in 4 of 6 conditions for the NT subject group (Maintain Space and Maintain Pitch only showed bottom-up connections from RTPJ to rIPS), and in 3 of 6 conditions for the ASD group (Maintain Space, Maintain Pitch, and Switch Pitch, plus 1 additional bottom-up connection from RTPJ to rIPS for Switch Space). As the experimental paradigm for Experiment 3 was identical to that of Experiment 2, the functional connection between rIPS and RTPJ supports the hypothesis that these ROIs are functionally connected when attending more realistic speech stimuli, relative to the stimuli in Experiment 1. It should also be noted that 5 of 6 listening conditions for the ASD subject group resulted in a near-significant bi-directional connection between lIPS and LIPSP (Maintain Both showed a near-significant top-down connection from lIPS to LIPSP). As subjects with ASD were observed to have more difficulty across listening conditions, this connection between lIPS and LIPSP may suggest a neurological compensation in order to complete the tasks. Alternatively, since this connection was not seen in the NT subjects, it could suggest neurological dysfunction that takes away from the possibly similar functional connection between rIPS and RTPJ.

Overall, the preliminary results of Experiment 3 suggest that there are differences in functional connectivity across cortical regions in ASD subjects, compared to their NT counterparts, when deploying auditory attention. Since neither the NT or ASD group showed some of the connections deemed important to auditory attention from the cross-validation experiment, it cannot be determined where exactly the challenges ASD subjects face in deploying attention may originate. The low number of subjects per subject group suggests that these conclusions are likely to change and will hopefully provide more details into the cortical origin of these challenges. On a positive note, the observation of the functional connections between (l/r)FEF, as well as the functional connections between rIPS and RTPJ, support previous statements that these connections are part of the cortical networks engaged in executing auditory attention across different auditory cues.

4.2 Temporal Dynamics

Although measuring the peak point and points of inflection for the sinusoidal fit curve on the significant edges did not provide any insight into how the timing of functional connectivity is impacted by task difficulty or topology, there was a noticeable difference in the standard deviations of the measured points when comparing across listening conditions. Many of the observed results discussed here show evidence of a relationship between the standard deviation of the measured points and the task difficulty. According to previous literature, there is a behavioral deficit measured via response time and in accuracy for switching attention across stimuli of similar auditory cues (i.e., switching attention across locations or switching attention across pitches) compared to maintaining attention [28]. Additionally, pupillometry measures show an increased cognitive load when switching attention compared to maintaining attention across auditory stimuli [36], further supporting the behavioral costs seen in previous studies.

The stimuli of the experiments described here were constructed such that the pitch conditions were more challenging than the space conditions. Switching attention across pitch was a more challenging task because in order to switch their attention to the competing pitch, the listener first needed to take note of the first pitch to attend in order to make the relative switch to the competing pitch. For a musician or someone with perfect pitch, this task may have been relatively easy. For someone who does not have much experience differentiating pitch, this becomes a much more difficult task. However, for the spatial condition, the listener is likely very familiar with the difference between differentiating sounds located to the left versus the right. This allows the listener to have a more defined attentional focus and thus an easier time switching between attended stimuli. This decrease in difficulty would allow different listeners to switch their attention at different times depending on how they approached the task, resulting in a larger standard deviation for the points of inflection of the sinusoidal fit connectivity curves. Since the relative difficulty across less comparable listening conditions (i.e., Maintain Pitch vs Pitch to Space) is more ambiguous, the comparisons in this section (see Section 3.3.1) were made to investigate the relationship between the standard deviation of the measured points and the relative difficulty in switching vs maintaining attention, attention to space vs pitch, and finally attention to/across different auditory cues.

4.2.1 Experiment 1

The founding hypothesis for this section is that easier tasks would have a larger standard deviation of the measured peak and points of inflection. The following subsections describe whether this hypothesis was supported or opposed. The connectivity curves analyzed in this section include the common significant connections for Experiment 1: bilateral connection between (l/r)FEF, and the top-down connections from LIPSP and RTPJ to lAUD and rAUD, respectively for all listening conditions.

4.2.1.1 Space: Maintain vs Switch

Most of the standard deviations for the 4 connectivity curves outlined in Section 3.3.1.1 are similar across conditions. For the lateral connection from rFEF to lFEF, all standard deviations of measured points are larger for Maintain Space compared to Switch Space, supporting the hypothesis that Maintain Space is an easier task than Switch Space. The standard deviations of the measured points for the top-down connection from LIPSP to lAUD are smaller in Maintain Space relative to Switch Space, supporting the null hypothesis that maintaining attention in space is more difficult than switching attention in space. For the top-down connection from RTPJ to rAUD, the standard deviation of the second point of inflection is larger in Maintain Space, supporting the hypothesis that maintaining attention in space is easier than switching attention in space. Overall, the results of this subsection support the founding hypothesis.

4.2.1.2 Pitch: Maintain vs Switch

Similar to the previous subsection, most of the standard deviations for the 4 connectivity curves outlined in Section 3.3.1.2 are similar across conditions. For the lateral connection from rFEF to lFEF, the standard deviation of the measured points are larger for Maintain Pitch than for Switch Pitch. This supports the hypothesis that maintaining attention to pitch is an easier task than switching attention across pitches. For the lateral connection from lFEF to rFEF, the standard deviation of the first point of inflection is larger for Maintain Pitch, also supporting the given hypothesis. For the top-down connection from RTPJ to rAUD, the standard deviations of the peak and second point of inflection are greater in Maintain Pitch. Overall, these results strongly support the hypothesis that maintaining attention to pitch is an easier task than switching attention across pitches.

Something worth mentioning here is that the top-down connection from LIPSP to lAUD for Maintain Pitch is the only significant connection that could not be fit to a sinusoidal function in Experiment 1. A previous study found that LIPSP was most significantly activated when maintaining attention to pitch [29]. The functional connectivity between LIPSP and lAUD seems to be sustained beyond the switch gap. A possible theory for this sustained activity could be that the high engagement of LIPSP when maintaining attention to pitch, could prolong the connection between the 2 ROIs. The same study shows significant activation of the RTPJ when switching attention across space. This theory might be supported if the RTPJ to rAUD connection showed a similarly sustained connection. As of now, there is no support for or against the presented theory.

4.2.1.3 Maintain: Space vs Pitch

Since most of the standard deviations of the measured points of the sinusoidal connectivity curves for Maintain Space and Maintain Pitch are similar, this subsection will discuss only the differences in standard deviations of measured points. For the lateral connection from rFEF to lFEF, the standard deviations of the peak and second point of inflection are greater for Maintain Space. For the lateral connection from lFEF to rFEF, the standard deviation of the first point of inflection is smaller for Maintain Space, while the standard deviation for the peak is larger for Maintain Space. As previously stated, the top-down connection from LIPSP to lAUD could not be fit to a sinusoidal function. See the previous section for possible reasons why this significant connection could not be fit to a sinusoidal function.

Despite the standard deviation of the first point of inflection for the connectivity curve for lFEF to rFEF, the results discussed here support the hypothesis that maintaining attention to space is an easier task than maintaining attention to pitch. A possible explanation for the smaller standard deviation of the first point of inflection for the connectivity curve from lFEF to rFEF for Maintain Space could be in the difference in significance between the 2 conditions. The bilateral connection between (l/r)FEF is significant for Maintain Pitch while not significant for Maintain Space. This lack of significance is due to the amplitude of the sinusoidal connectivity curve. Since the amplitude of the sinusoidal connectivity curve is smaller for Maintain Space, there could be less variance in the measured points, although this theory is not supported by the results comparing the connectivity curves for the connection from rFEF to lFEF.

4.2.1.4 Switch: Space vs Pitch

When comparing the standard deviations of the measured points across Switch Space and Switch Pitch, most are similar. However, there are a handful of comparisons worth discussing. For the lateral connection from rFEF to lFEF, the standard deviations of the peak and second point of inflection are larger for Switch Space. For the top-down connection from LIPSP to lAUD, the standard deviations of all measured points are greater for Switch Space. For the top-down connection from RTPJ to rAUD, the standard deviations of the peak and second point of inflection are greater for Switch Space. All of the comparisons presented here support the hypothesis that switching attention across space is an easier task than switching attention across pitches.

4.2.1.5 Space to Pitch vs Pitch to Space

The hypothesis determining the more difficult task between Space to Pitch and Pitch comes from literature regarding “asymmetric task switching” [4, 61], which states that switching from a harder task to an easier task is more difficult than switching from an easier task to a harder task. This counter-intuitive conclusion is because of the time and effort it takes to disengage from a harder, more engaging task, and switch to the simpler task. Whereas disengaging from a simpler task takes less effort. This asymmetric switching cost was also observed in the auditory domain where switching attention from Space to Pitch (easier to harder) had less of a switch cost than switching attention from Pitch to Space (harder to easier). Therefore, Pitch to Space was the more challenging of the 2 tasks [37]. The hypothesis for this section is that the standard deviation of the measured points would be greater for Space to Pitch compared to that of Pitch to Space.

As with the previous subsections, when comparing the standard deviations of the 3 measured points, most were similar across the 2 listening conditions. For the lateral connection from lFEF to rFEF, the standard deviation of the first point of inflection was greater for Space to Pitch. For the lateral connection from rFEF to lFEF, the standard deviations of all 3 measured points are greater for Space to Pitch. For the top-down connection from LIPSP to lAUD, the standard deviations of both points of inflection were greater for Space to Pitch. For the top-down connection from RTPJ to rAUD, the standard deviation of the 3 measured points are smaller for Space to Pitch compared to Pitch to Space. Excluding this final point, the findings here are in support of the hypothesis that the standard deviation of the measured points are larger for the easier task of switching attention from space to pitch compared to switching attention from pitch to space. A possible explanation for the only piece of evidence in support of the null hypothesis is similar to the explanation given in Section 4.2.1.3: the smaller standard deviations of the measured points for the connection from RTPJ to rAUD in Space to Pitch is due to the difference in significance compared to Pitch to Space. Since this connection is only near-significant in Space to Pitch, this also means that the amplitude of the sinusoidal connectivity curve is less than that of the curve for Pitch to Space. Therefore, there was less variance across bootstraps as they all contained values closer to zero. Additionally, a visual observation of these 2 connectivity curves shows that the measurements for Pitch to Space were much noisier, resulting in a larger variance across bootstraps.

4.2.1.6 Uncommon Significant Connections

In an effort to report the temporal dynamics of the entire set of significant connections, Section 3.3.1.6 compares the standard deviations of the measured points for the significant connections observed in 2 or less listening conditions, referred to as the "uncommon significant connections." As described in Section 4.2 and Section 4.2.1.5, the literature has described that switching attention across stimuli is more challenging than maintaining attention [28, 36], and that switching attention from Pitch to Space is more challenging than switching attention from Space to Pitch [37]. It was also described in Section 4.2 that the stimuli for these experiments were designed such that the pitch conditions were more challenging than the spatial conditions. Due to these relative comparisons, the primary analysis only consisted of comparisons in switching vs maintaining attention, attention to space vs pitch, and attention across different auditory cues. This subsection deviates from this pattern so that comparisons can be made in regards to the uncommon significant connections. Based on the relative difficulties across listening conditions previously described, one might hypothesize the following order of difficulty across conditions from easiest to most difficult: Maintain Space, Switch Space, Maintain Pitch, Switch Pitch, Space to Pitch, and Pitch to Space.

For the lateral connection from rAUD to lAUD, the standard deviations of both points of inflection are larger in Maintain Pitch than in Pitch to Space. This supports the hypothesis that maintaining attention to pitch is an easier task than switching attention from pitch to space. For the bottom-up connection from lAUD to LIPSP, the standard deviations of both points of inflection are greater for Space to Pitch compared to Switch Pitch. This result supports the null hypothesis that switching attention from a spatial cue to a pitch cue is easier than switching attention across pitches. One might consider that since Space to Pitch contains one interval of spatial cues, this task is easier than a condition with 2 intervals of pitch cues, which would also be in support of the null hypothesis.

4.2.2 Experiment 2 (Cross-Validation)

The differences in the standard deviations of these measurements across experiments is likely due to the differences in stimuli across the 2 experiments. The stimuli in Experiment 2 were gendered (labeled as pitch conditions for consistency), meaning spoken by either a male or female voice. The stimuli in Experiment 1 were monotonized to a single pitch. Additionally, the stimuli in Experiment 2 were two-syllable words, versus the single digits speech tokens in Experiment 1, with a much longer stimulus duration (350 ms speech tokens in Experiment 1 vs 900 ms two-syllable words in Experiment 2). This difference in duration is most likely the reason for the decrease in frequency of the fit cosine curves and why less connectivity curves were able to be fit to a sinusoid in Experiment 2. This decrease in frequency is most simply observed as a flatter connectivity curve. It could be that having the same analysis window duration, despite the difference in stimulus interval durations, made it more challenging to see a dynamic connectivity window, observed as well fitting sinusoidal functions for Experiment 1 and flatter, less well fitting sinusoidal functions for Experiment 2. Also, the increased duration of stimuli from a closed set of two-syllable words may have allowed the resolution of the stimulus to be different across subjects, resulting in the larger standard deviations of the measured peaks and points of inflection when compared to Experiment 1.

The nature of the stimuli in the Experiment 2 allowed for a much larger time scale for shifting of attention and this is adequately represented in the larger standard deviation of measured time points. The working hypothesis for this section is that longer duration of the stimuli in Experiment 2 made it so the point in time in which a listener could resolve the speech token was more variable across experiments, resulting in larger standard deviations across measured points on the connectivity curve. Additionally, it could be argued that the nature of the stimuli in Experiment 2 compared to Experiment 1 (gendered instead of monotonized, longer in duration, two-syllable words instead of single syllable digits) make it so that the tasks of Experiment 2 are easier than in Experiment 1. The following subsections discuss the results that are either in support or against these hypotheses. Measurements of standard deviation that were similar across experiments are not discussed.

4.2.2.1 Maintain Space

The standard deviations of the points of inflection are much smaller for the top-down connection from LIPSP to lAUD in Experiment 1 than in Experiment 2. This supports the hypothesis that the same task in Experiment 2 was less difficult as a function of the stimuli.

4.2.2.2 Switch Space

For the top-down connection from LIPSP to lAUD, the standard deviations of all 3 measured points were smaller in Experiment 1 when compared to Experiment 2. This finding is in support of the hypothesis that this task was easier in Experiment 2 due to the nature of the stimuli. It is worth mentioning that the standard deviations of all 3 measured points for the top-down connection from RTPJ to rAUD were similar across experiments. This may be due to the difference in significance across experiments for this connection. While the connection in Experiment 1 was near-significant, the connection in Experiment 2 was not significant, meaning the connectivity curve was smaller in amplitude. A possible explanation for the smaller variance across bootstraps for this connection could be that these measurements were closer to zero for Experiment 2.

4.2.2.3 Maintain Pitch

As 2 of the 4 connectivity curves outlined in Section 3.3.2.3 could not be fit to a sinusoidal function, comparisons of the measured points could not be made. Possible reasons for the sustained connectivity curve for the top-down connection from LIPSP to lAUD in Experiment

1 are discussed in 4.2.1.2. The connectivity curve for the top-down connection from RTPJ to rAUD is similarly sustained as the previously mentioned curve. Unfortunately, due to the listening condition of this subsection, the same argument cannot be made to why a sinusoidal fit was unable to be made.

4.2.2.4 Switch Pitch

For the top-down connections from LIPSP to lAUD and RTPJ to rAUD, the standard deviations of all 3 measured points were smaller for Experiment 1 compared to Experiment 2. Each of these measurements support the hypothesis that the time point of resolving the speech tokens was more variable across listeners in Experiment 2, making it the less difficult of the 2 presented experiments.

4.2.2.5 Summary of Measurements

Two measurements of the elements of the connectivity curves were comparable across experiments: the standard deviation of the peak value across bootstraps, and the peak (or maximum) value of the mean bootstrap curve. The remaining values - the standard deviations of the first and second points of inflections and the frequency of the sinusoidal connectivity curves - were in support of the hypothesis that the nature of the stimuli made it so that the time point in which a listener could resolve the speech token was more variable across listeners. The values of the standard deviations of the points of inflection being larger for Experiment 2 also support the secondary hypothesis that it was the easier of the two experimental paradigms.

4.2.3 Experiment 3 (Neurodivergence)

As stated previously, this experiment contained an insufficient number of subjects needed to draw statistically significant conclusions. Therefore, all the findings presented in the following subsections are strictly preliminary and need additional data collected to be confirmed. First, given that the output of the connectivity analysis for this experiment were more noisy than for the previous 2 experiments, it was not surprising that less of the significant connections for this experiment were able to be fit to a sinusoidal function. In line with there being no significant connections for 2 of the 3 switch conditions (Switch Space and Switch Both) for the ASD subjects, the one switch condition that did yield significant connections (Switch Pitch) was unable to fit a sinusoidal function to any of the 3 significant connectivity curves. This provides further support that ASD subjects have an increased challenge in switching their attention relative to maintaining. In regards to the common connections observed in this section, only the lateral connection from lFEF to rFEF for Switch Both was able to fit to a sinusoidal function for both the NT and ASD subject groups.

Keeping in line with the theory that there is a negative correlation between the standard deviation of measured points and task difficulty, most of the results presented in Section 3.3.3 are as expected. As previous literature illuminates the challenges that subjects with ASD face in deploying attention compared to NT subjects [3, 45, 19] the hypothesis here is that the standard deviations of the peak and points of inflection will be larger for NT subjects compared to ASD subjects. The following subsections discuss the results from Section 3.3.3 and if they support the provided hypothesis.

4.2.3.1 Maintain Space

In regards to the top-down connection from rIPS to RTPJ, while the standard deviations of the peak and second point of inflection were similar across subject groups, the standard deviation of the first point of inflection being larger for the NT subject group is in support of the provided hypothesis. The hypothesis is further supported by comparing the standard deviations of all 3 measured points for the bottom-up connection, which are larger for the NT subject group compared to the ASD subject group. These results support the hypothesis that the ASD subject group had a more challenging time maintaining their attention in space.

4.2.3.2 Switch Space

For the top-down connection from rIPS to RTPJ, the larger standard deviations of the measured points support the hypothesis that the NT subjects had a less difficult time for this listening condition. For the bottom-up connection from RTPJ to rIPS, the standard deviations of the measured points are similar across subject groups. This finding does not support the provided hypothesis or the null hypothesis that subjects from the ASD group had less difficulty in switching their attention across space.

4.2.3.3 Maintain Pitch

For the bottom-up connection from RTPJ to rIPS, the standard deviation of the first point of inflection is smaller for the NT subject group compared to the ASD subject group. This result is in support of the null hypothesis that the ASD subject group had less difficulty in maintaining their attention to pitch than the NT subjects. The standard deviation of the peaks being similar across conditions is not in support of either the hypothesis or null hypothesis. The standard deviation of the second point of inflection is larger for the NT subject group which does support the hypothesis that the NT subjects had a less difficult time maintaining their attention in pitch. Overall, the aggregate of these results is neither in support of the hypothesis or null hypothesis when maintaining attention to pitch.

4.2.3.4 Maintain Both

For the top-down connection from rIPS to RTPJ, although the standard deviations of the peak and second point of inflection are similar across subject groups, the standard deviation of the first point of inflection is smaller for the NT subject group compared to the ASD subjects group. For the bottom-up connection from RTPJ to rIPS, while the standard deviation of the second point of inflection is larger for the NT subjects, the standard deviations of the peak and first point of inflection are smaller for the NT subjects compared to the ASD subjects. In aggregate, these results are in support of the null hypothesis, that the ASD subjects had less difficulty maintaining attention to both space and pitch when compared to the NT subjects.

This mismatch in expectation between the hypothesis and results could be attributed to the difference in significance, where this bi-directional connection is significant for the NT subjects and not significant for the ASD subjects. The significance makes it so that the amplitude of the connectivity curve is larger for the NT subjects, making the peak and points of inflection easier to measure, resulting in less deviation across bootstraps. Another possibility is that since ASD subjects performed better in listening conditions with both auditory cues present [19], the mixed bag of results here (standard deviation of first point of inflection being smaller for NT subjects while the second is larger) could indicate that ASD subjects faced similar difficulty compared to NT subjects when maintaining attention to both pitch and space, although this is not observed in the original study according to the percent of correct trials.

4.2.3.5 Switch Both

For the lateral connection from lFEF to rFEF the standard deviation of all measured points are smaller for the NT subject group compared to the ASD subject group, supporting the null hypothesis that the ASD subjects had a less difficult time switching their attention across both space and pitch cues. Similar to the previous subsection, this mismatch between expectation and results could be due to 1 of 2 reasons: first, the difference in significance could make it such that the peak and points of inflection are easier to measure for the near-significant connectivity curve for the ASD subjects compared to the NT subjects. Second, since both auditory cues were presented in this listening condition, it could be that an improvement in performance made the standard deviation of measured points more comparable across conditions. Since the error between the sinusoidal fit and the mean bootstrap curve is higher for the ASD subjects than the NT subjects, the more likely reason for the results here is that the ASD subject curves were noisier because of differences in approaching the task across listeners, resulting in larger deviation of measured points across bootstraps.

Chapter 5

CONCLUSIONS

This chapter concludes this dissertation by first discussing the significant contributions to the field of neuroengineering, as the work pertains to the fields of engineering and neuroscience. The next section is an executive summary, answering each of the posed questions in Section 1.4. The subsequent section discusses possible future directions of this work for future generations of researchers looking to continue to expand the field of neuroengineering. The final section of this dissertation reflects on this project from the perspective of a neuroengineer and how expertise in both neuroscience and engineering was necessary for the success of this project.

5.1 Significance

The culmination of this dissertation makes significant contributions to the fields of engineering and of neuroscience. In regards to engineering, the methods implemented here expand on previously proposed methods of measuring functional connectivity across ROIs as recorded from M/EEG data. In regards to neuroscience, these studies answer the question "how do auditory regions engage with the supramodal attention network described in literature during a dual-stream auditory attention task?" The following subsections dive into these contributions in more detail.

5.1.1 Contributions to Engineering

The state-space model described in Section 2.3 was originally developed by Yang et al., 2016 [60] to determine the functional connectivity between 2 ROIs, whose activity was recorded using a large array M/EEG sensors, for a single subject. This model was expanded by

Nadkarni et al., 2019 [40] to measure the functional connectivity across 12 ROIs, measured jointly across several subjects for multiple trials, providing results for a "SNR-boosted average subject." This SNR-boosting was a necessary step in denoising such a high-dimensional dataset. The work described in this dissertation used this state-space model to measure the functional connectivity across the 12 ROIs for each of the 3 experiments described in Section 2.1. A bootstrapping approach was implemented to avoid overfitting of the Expectation Maximization algorithm and to apply a non-traditional statistical analysis approach. The results of the state-space model (i.e. the auto-regressive coefficients) were applied to a novel conservative statistical model (Section 2.4) to estimate the functional connectivity across the 12 ROIs. The novel statistical analysis was necessary to compute statistical significance from our "average subject" dataset, as traditional methods require independent subject data. The linear dynamic system and statistical analysis described in this study provide feasible measurements of functional connectivity across ROIs recorded from via M/EEG.

5.1.2 Contributions to Neuroscience

The presented results show that the implemented linear dynamic system, in series with the presented statistical method, is robust. The results show consistently functionally connected regions, including auditory regions and regions described as being part of the supramodal attention network [13], across experiments and listening conditions. The primary research question presented here was: "how do auditory regions connect with the frontoparietal supramodal attention network?" The results presented from the cross-validation experiment (i.e. the comparison of Experiments 1 and 2, both with enough subjects for sufficient statistical power) suggest that the ventral frontoparietal network, responsible for filtering new stimuli into one's awareness, is connected to the auditory regions via a top-down connection from RTPJ to rAUD.

As the RTPJ is said act as a circuit breaker [13, 29] of external stimuli, the working theory becomes that the RTPJ is functionally connected to the rAUD in efforts to modulate what auditory information is filtered and which is salient enough to pay attention to. Interestingly, there is a symmetrical top-down connection from LIPSP to lAUD that is observed in the cross-validation experiment as well. Previous studies described a double dissociation between the function of RTPJ and LIPSP where the RTPJ was more active when switching attention across space and LIPSP was more active when maintaining attention to pitch [29]. The results shown via the cross-validation experiment show that these symmetrical top-down functional connections are present across several listening conditions and are not exclusive to either switching attention across space or maintaining attention to pitch. It should be noted that the while the authors of Larson & Lee, 2014 [29] show this double dissociation for LIPSP and RTPJ being more active for their respective conditions, the data presented in that publication shows that these regions are still active in the remaining conditions, just that there is no significant difference in their activation. These results suggest that there may be some functional similarity between LIPSP and RTPJ and their role in deploying auditory attention. Given that the RTPJ is part of the ventral frontoparietal attention network, one might conclude that this symmetric top-down functional connection is indicative of a top-down influence on auditory inputs first received by left and right auditory regions.

Additionally, results across the cross-validation experiment show that a bottom-up functional connection from lAUD to LIPSP and from rAUD to RTPJ may also be important when executing auditory attention. These results suggest that both top-down and bottom-up interactions between these symmetric connections play a role in determining the salience of auditory stimulus. Finally, cross-validation results suggest possible functional connections between left and right auditory regions, as well as between LIPSP and RTPJ. Overall, the results presented in this dissertation suggest that LIPSP, RTPJ, lAUD and rAUD work as a cortical network to determine the salience of auditory stimuli as part of the ventral frontoparietal network. Once determined to be of importance to the listener, the ventral network engages the dorsal frontoparietal network, where the left and right FEF work to direct attention toward salient stimuli. As 3 of the 4 experiments show functional connectivity between RTPJ and rIPS, results suggest that this connection is where the interaction between the ventral and dorsal networks takes place, i.e., where the stimulus is deemed salient and subsequently attended by the listener.

5.2 Executive Summary

This section consolidates the findings to the research questions posed in Section 1.4. For Experiment 1: (1) Are the cortical regions of the dorsal and ventral frontoparietal networks (Figure 1.2) functionally connected when deploying auditory attention? The results discussed here show that, yes, there is functional connectivity between some of these cortical regions when maintaining and switching attention across location and pitch cues. This includes connectivity between the (l/r)FEF, as well as the RTPJ and rIPS. (2) How do the auditory regions connect to these frontoparietal networks? The presented results show that there is functional connectivity between rAUD and RTPJ. As RTPJ is largely responsible for the reorienting of attention [13], the connection between rAUD and RTPJ is likely the connection in which new auditory information interacts with the ventral frontoparietal network. Additionally, the culmination of these and previous results [29] suggest that there may be functional similarity between LIPSP and RTPJ. Therefore, the functional connection between LIPSP and lAUD may also be a connection in which auditory information interacts with the frontoparietal networks, although LIPSP has not been determined to be a component of these networks. (3) Are different ROIs functionally connected when attending different auditory cues? As there was not a one-to-one mapping between functional connectivity and switching or maintaining attention to location or pitch, the current results suggest no. In fact, there seems to be symmetric functional connectivity across LIPSP, RTPJ, rAUD, and lAUD, that remains almost regardless of what cues are being attended. This dissertation refers to the network formed across these 4 ROIs as the "cortical network for auditory attention", and may be part of the ventral frontoparietal network when attending auditory stimuli.

For the cross-validation (i.e. Experiment 1 vs Experiment 2): (4) Are the presented functional connectivity and statistical analyses robust enough to produce similar results across similar experiments? The cross-validation experiment suggests yes, these analyses are robust as they produced similar results across two similar experimental paradigms. In addition to the same cortical network for auditory attention seen in Experiment 1, Experiment 2 also showed consistent connectivity between RTPJ and rIPS across all listening conditions. As this connection was also seen across conditions and subject groups for Experiment 3, these results suggest that this connection may be the interface between the dorsal and ventral frontoparietal networks. (5) Is functional connectivity impacted as a function of the difference in stimuli across experiments? The results of the temporal dynamics analysis showed larger variance of measured points for the stimuli with longer duration in Experiment 2 compared to that of Experiment 1. Additionally, the frequency of the connectivity curves were smaller in Experiment 2. While the shapes of the connectivity curves were different across experiments, the regions that were functionally connected were similar. However, the common connection of rIPS and RTPJ was exclusive to Experiment 2, which suggests that the difference in stimuli may impact which regions are functionally connected.

For Experiment 3: (6) Are differences in functional connectivity the origin of behavioral differences in attentional deployment across neurodivergent populations? The preliminary results of Experiment 3 suggest that there is likely a difference in functional connectivity between NT and ASD subjects when executing auditory attention. As there were less subjects for the analysis in Experiment 3, there is less statistical power in the analyses performed. Therefore, an increase in subjects and/or a modification of hyperparameters is necessary before this question can be answered with confidence.

5.3 Future Directions

From the current results, it is deemed that the implemented linear dynamic system does a sufficient job of elucidating significant functionally connected ROIs engaged in executing auditory attention. The sparsity of these cortical networks provides a strong indication that the outlined functional connections are the most important for switching or maintaining attention between auditory cues that differ in space or pitch. As presented, the current results do not show enough differences across conditions to determine precisely what cue a listener is attending from a cortical representation alone. In order to get this one-to-one cortical representation of auditory attention, future iterations of this study could reconsolidate conditions into categories such as switch attention from the left to the right, or maintain attention to higher pitch. As this would increase the number of listening conditions, it would also require an increase in the number of subjects completing the task while recording M/EEG. With enough data, this could turn into a machine learning classification problem where different functionally connected networks could indicate what specific cues a listener is attending.

In regards to Experiment 2, future iterations would begin with lengthening the time analysis time window. The current connectivity analysis used the same time window for Experiments 1 and 2 to implement a direct comparison across experiments. However, due to the nature of the stimuli in Experiment 2, the edges of the analysis window are hardly beyond the onset and offset of the first and second stimulus intervals, respectively. An increased time window may allow for more of the connectivity curves to be adequately fit to sinusoidal functions and possibly decrease the variance of measured time points. If expanding the time window of analysis for Experiment 2 yielded better results, that time window would also be used for analyzing the data in Experiment 3. The first next step for Experiment 3 would be to increase the number of ASD and age- and sex-matched NT subjects until the statistical power of the results are strong enough to make firm conclusions. Alternatively, the hyperparameters of the linear dynamic system could be adjusted which may provide better results for this dataset with less subjects. If investigation into this neurodiverse population proves fruitful, long-term applications of this model could include investigation into the cortical mechanisms of anyone diagnosed with hidden hearing loss or auditory processing disorder, where the origin of hearing difficulties may be cortical and therefore, more challenging to accurately diagnose.

5.4 Reflections on Neuroengineering

This project exists at the intersection of neuroscience and engineering. Having skills in just one of these areas would have made producing reliable results a much more challenging feat. As an engineer measuring dynamic functional connectivity, the most obvious method would have been a simple correlation over the time period of interest between 2 ROIs. As a neuroscientist, it was important to take into account the fact that the current spread of electrical signals from neighboring cortical regions might result in incorrect functional connectivity measurements. This knowledge informed the use of a non-zero lag auto-regressive model in order to exclude this possible confusion. Neuroscience also informed the use of an analysis window at a time when the endogenous actions of the subject could be assumed, instead of using the duration of an entire trial. Since neuroimaging provides an estimate of neural activity, a carefully designed experimental paradigm in which a small window of instructed endogenous activity took place was crucial to this analysis.

As a neuroscientist measuring functional connectivity, the tools used for these projects may have been unavailable. As an engineering project, there was necessary a balance between computational complexity and simplicity of the neuroscience model. In setting up the linear dynamic system there were options in regards to running more iterations of the EM algorithm, more bootstraps, a longer analysis window, or even a higher-order auto-regression. An increase in EM iterations and bootstraps were investigated and deemed to not provide significantly more information. A longer time window or higher-order auto-regression were not investigated. The time window was set so that the switch gap was centered in time, with enough time before and after to reach beyond the stimulus intervals. The increase to a second-order model would have doubled the already high-dimension output, making the results even more challenging to interpret. The state-space model used here implemented traditional signal processing methods in combination with machine learning to model a relationship between latent variables, a common engineering approach not often seen in neuroscience. Lastly, the use of a jointly measured SNR-boosted subject was an important step to reduce the dimensionality of a very large dataset.

The symbiosis between neuroscience and engineering made it possible to produce reliable measurements of functional connectivity. While neuroscience informs the engineering methods, the limitations on time and computation inform the construction of the experimental paradigm. Without knowledge in both of these fields, the important details of the analyses may have been missed.

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