Understanding the Processing of Degraded Speech:

Electroencephalographic Measures as a Surrogate For Recovery From Concussion

by

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ABSTRACT

The recent spotlight on concussion has illuminated deficits in the current standard of care with regard to addressing acute and persistent cognitive signs and symptoms of mild brain injury. This stems, in part, from the diffuse nature of the injury, which tends not to produce focal cognitive or behavioral deficits that are easily identified or tracked. Indeed it has been shown that patients with enduring symptoms have difficulty describing their problems; therefore, there is an urgent need for a sensitive measure of brain activity that corresponds with higher order cognitive processing. The development of a neurophysiological metric that maps to clinical resolution would inform decisions about diagnosis and prognosis, including the need for clinical intervention to address cognitive deficits. The literature suggests the need for assessment of concussion under cognitively demanding tasks. Here, a joint behavioral- high-density electroencephalography (EEG) paradigm was employed. This allows for the examination of cortical activity patterns during speech comprehension at various levels of degradation in a sentence verification task, imposing the need for higher-order cognitive processes. Eight participants with concussion listened to true-false sentences produced with either moderately to highly intelligible noise-vocoders. Behavioral data were simultaneously collected. The analysis of cortical activation patterns included 1) the examination of event-related potentials, including latency and source localization, and 2) measures of frequency spectra and associated power. Individual performance patterns were assessed during acute injury and a return visit several months following injury. Results demonstrate a combination of task-related electrophysiology measures correspond to changes in task performance during the course of recovery. Further, a discriminant function analysis suggests EEG measures are

more sensitive than behavioral measures in distinguishing between individuals with concussion and healthy controls at both injury and recovery, suggesting the robustness of neurophysiological measures during a cognitively demanding task to both injury and persisting pathophysiology.

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CHAPTER 1

CORTICAL CHARACTERIZATION OF THE PERCEPTION OF INTELLIGIBLE AND UNINTELLIGIBLE SPEECH MEASURED VIA HIGH-DENSITY ELECTROENCEPHALOGRAPHY

Introduction

The speed and accuracy with which individuals comprehend speech belies the complexity of the underlying cognitive perceptual processing. It also supports a guise of homogeneity of processing strategies among healthy listeners. Based on our previous work in the perception of degraded speech, we have found that healthy young listeners exhibit a wide range of performance accuracy when faced with moderately degraded speech intelligibility [1, 2]. This begs the question of whether differences in processing strategies can be ascertained at the cortical activation level. In the present report, we employ speech of diminished intelligibility to tax speech comprehension and reveal cortical activation patterns that link with behavioral performance on the speech comprehension task. If cortical activation differences are found between the more and less successful listeners (as defined by accuracy in a sentence verification task), this would be the first demonstration of the associated patterns of neural processing.

Our interpretive framework for this study is the dual stream model of speech perception proposed by Hickok and Poeppel [3, 4, 5]. Briefly, the dorsal stream contains the articulatory/ motor networks of the frontal lobe and the ventral stream contains the conceptual/ semantic networks of the temporal lobe. It is proposed that these two pathways converge, resulting in understanding speech. Previous research, utilizing fMRI, has demonstrated that when processing pseudowords, individuals show activity in the

dorsal stream (frontal), and listening to complex phrases shows language processing in the ventral stream (temporal) [6]. This artificial dichotomy of phonemic and semantic information demonstrates the delineation of these pathways; however, in natural speech, where listeners utilize both pieces of information in perception, we see activation of both the dorsal and ventral streams. Activations are seemingly bidirectional and simultaneous. As deciphering degraded speech requires problem solving and the use of both bottom up and top down strategies to segment the speech signal [7], it is expected that relative activations of the dual streams provide a proxy to the nature of the processing taking place.

Despite the abundance of detailed anatomical data (see [8] for a detailed overview), the temporal sequence of activation of these cortical structures remains to be established. What we do know about the temporal sequence of processing speech is through the examination of event-related potentials (ERPs). It is critical to make the distinction that among event-related potentials, exist both induced and evoked potentials. While both induced and evoked potentials occur relative to the onset of an event, there are differences in the degree to which the response is locked in time and phase over a series of trials. This is an important notion when examining the processes that underlay more complex processes, such as the perception of sounds and more complex speech.

There are several speech-related evoked potentials documented throughout the literature. Primarily, these are examined via short speech sounds, not connected speech and do meet the requirements of phase coherence to be considered an evoked potential. By examining the timing, amplitude, and location of peak activity, we glean a great deal of information about the neural generators underlying these basic processes that subserve

more complex speech perception. Namely, the relevant responses that are time-locked to processing sound include the P1- N1- P2 complex and the P300. For a comprehensive literature review, see [9].

It is important to note that when listeners are confronted with a speech signal that is difficult to understand, they actively problem-solve to decipher it [10]. This involves lower level processing of the degraded acoustic stream to decipher the sounds, as well as higher order (top-down) processing to map the degraded sounds to words in the mental lexicon and to extract meaning. Because speech perception involves integration across multiple cortical and subcortical areas, degraded speech can be used to magnify integrated approaches to perception, or identify problems that are subtle and/or diffuse. The task also serves as a proxy for integrative cortical function. Unfortunately, much progress is yet to be made in understanding the brain activation patterns associated with processing a given speech stimulus (see [11] for a comprehensive overview of current literature). Many functional imaging technologies (i.e., fMRI and PET) have poor temporal resolution. In fact, these imaging techniques yield rather gestalt snapshots in that the pictures portray all activation associated with the perception. This provides a problem for discerning the processes particularly associated with the mapping from auditory representation to semantic representation. As an example, Scott et al., 2006, examined PET data from listeners presented with intelligible or unintelligible speech. Unfortunately, when listeners hear intelligible speech, brain activation is present not only in the regions involved in spoken language perception, but also the regions involved in auditory representation and in the conceptual representation of the meaning of the speech.

What we are interested in are those processes that *make* the speech intelligible, especially if it is degraded in some form.

As mentioned previously, brain-imaging techniques that provide the spatial resolution necessary to delineate important cortical regions have not provided the necessary temporal resolution to develop a timeline of the processes involved in the comprehension of speech. Fortunately, emerging capabilities in high- density electroencephalography (EEG) can provide a tool with which to obtain both temporal and spatial resolution to address these issues [12]. This technology can achieve temporal and spatial resolution necessary for the mapping of brain activation patterns before, during, and after the perception of spoken language. While not utilized in many previous studies of speech perception, full advantage will be taken of these tools in the current studies while examining the strategies used by young, normal hearing listeners to understand degraded speech, including the profiles of cortical activity for both "good" and "poor" listeners, as determined by performance in a sentence verification task.

Methods

Participants

Listeners were 24 undergraduate and graduate students (21 female) recruited from Arizona State University. Ages ranged from 20- 48, with a mean of 25 years old. Listeners had no history of language or hearing disorders and were native speakers of English, per self-report. All listeners were right handed and had hearing thresholds within normal limits (detection of 125Hz- 4000Hz < 15dB), per pure tone screening conducted before the experiment. All listeners received $20 for their participation.

Speaker and Stimuli

Speech samples from one female speaker were used. The speaker was a healthy 46-year-old female, with acoustic characteristics in the range of normal, according to age and gender (i.e. F0 and formant values of corner vowels). The speaker recorded 240 phrases, 120 of which were "true" (e.g. zebras have stripes) and 120 of which were "false" (e.g. donkeys have wings). In a sound-attenuating booth, the speaker was fitted with a head-mounted microphone (Plantronics DSP-100), and read stimuli presented on the computer screen. Recordings were made using TF32 ([13]; 16-bit, 44kHz) and saved for editing (using [14]). All phrases were three words (3-5 syllables), with the last word determining the veracity of the phrase. On average, the phrases were 1959ms in duration (SD= 213ms). Sound files were RMS normalized prior to vocoding. A third of the phrases were vocoded using a 1-channel (unintelligible), 6-channel (moderately intelligible), or 16-channel (intelligible) noise vocoder, using PRAAT [15]. There were an equal number of 1-, 6-, and 16- channel vocoded phrases that were true and false (i.e. 40 of each combination of intelligibility level and veracity).

Task

Data were collected, analyzed, and interpreted at Arizona State University, in accordance with approved IRB protocols. Participants were seated in a hard-backed chair and situated at a comfortable distance from the computer screen. STIM2 [16] was used to

deliver the stimuli through inter-aural headphones (90dB) and the STIM audiobox system ensured synchronization of audio delivery to the participant and EEG recording [17].

On-screen visual prompts were used to guide the participants through the experiment. After the phrase played, participants were asked to press a keyboard button to indicate whether statements were true or false. Participants were given a practice period to demonstrate understanding of the instructions and ensure timelines of their responses and sufficient relaxation, as evidenced by minimal artifact in the EEG recording. Multiple practices were provided, as necessary. Each participant listened to six blocks of 40 stimuli, for a total of 240 items. Within each block, order of presentation was randomized and order of blocks (1-6) was partially counterbalanced amongst participants. Breaks were allowed during testing to reduce participant fatigue.

Electroencephalographic Recording

Electroencephalographic (EEG) recordings were made via Neuroscan Acquire (v4.5), using a 128-channel QuickCap. Positioning was assured through measurement and positioning of Cz, Fz, and Pz, in accordance with the 10-20 system. Recordings were acquired with a 1000 Hz-sampling rate and low-pass filtered below 200 Hz. After recording, a 60 Hz notch filter was used to minimize effects of electrical artifact. Impedance of all electrodes was well below 5kΩ. For each participant, continuous recordings were examined for physiologic and non-physiologic artifact. Artifact reduction through linear derivation was utilized to minimize the presence of blinks. All recordings were deemed high quality and used in subsequent epoching.

The continuous file for each individual was epoched for each condition- the 40 phrases of each 1-, 6-, and 16- channel intelligibility levels. Epochs were created for 300ms prior to the onset of the phrase to 1500ms following onset. Each individual epoch was examined for artifact and those with high levels of muscle artifact or a large number of blinks were removed. On average, 80% of recorded epochs were utilized to create an average file for each condition for each participant. The selected files were concatenated to create a grand average for all listeners, for each condition. Ten electrodes were omitted from the average due to high artifact. Only averaged files were utilized moving forward, to facilitate stronger signal to noise ratios.

Data Analysis

Behavioral Data. STIM2, which was utilized to present stimuli, also recorded participant response and response latency (recorded from offset of the stimulus to the time a response was entered). The data were transferred to Microsoft Excel for subsequent analyses. All participant data were reviewed; incorrect and no response items were considered together, as the response may have occurred outside the allowable response interval.

Given performance on the behavioral data, two groups of listeners were created: High Performing (HP) and Low Performing (LP) listeners. These designations were based on response accuracy in the 6-channel condition (< 80%). Descriptive statistics were calculated for each group and one-way analysis of variance (ANOVA) was utilized to determine if significant differences in behavioral performance existed. These

designations were utilized in follow-up EEG analyses, where analyses described below were repeated for HP and LP groups.

Event-related potentials. Utilizing CURRY 7 Multi-Modality Imaging Suite [18], average files were examined for transient activity, as indicated by peaks in the mean global field power (MGFP), representative of the power of activity, across all electrodes. Once a time interval of interest was identified, independent components analysis (ICA) was utilized to assess the transient. Following, current density reconstruction (CDR), via sLORETA, was utilized on the identified component of interest. This allows for the localization of the source of the component, or the underlying neural generator responsible for the transient activity. sLORETA computes minimum norm least squares (MNLS) current density amplitudes (dipole moments) and divides them by their error bars (and squares the result), taking into account the amplitude of activity; therefore, the F-values provided by sLORETA can be interpreted as magnitudes of activity. CURRY assigns a Brodmann's area to the solution to the MNLS problem, which was subjectively validated by the authors.

Frequency Analysis. Utilizing SCAN (v4.5), the frequency spectra for average files were examined. The time-domain averages were spline fit to ensure the average waveforms consisted of a power-of-2 number of points (2048 points). Each average file was analyzed via Fourier transform to obtain the power spectrum at each electrode, from the offset of the "early ERP" (see Table 2), to 1500ms, capturing the later processing associated with understanding the stimuli. After which, average power of each frequency band was calculated for traditional frequency bands: delta (0-3.5Hz), theta (4-7.5Hz), alpha (8-12.5Hz), and beta (13-30Hz), across all electrodes, for each condition. With the

given paradigm, a traditional event-related (de)synchronization approach was not deemed appropriate, as the pre-stimulus interval is likely not a passive baseline from which to conduct the analyses (i.e. there is ongoing cortical activity). Further, raw values can be utilized here, allowing for a more straightforward comparison across conditions.

Results

Behavioral Data

Accuracy. Using the performance of all listeners, overall accuracy scores were subjected to a one-way analysis of variance (ANOVA) to determine if a significant difference existed in performance between conditions. The main effect of intelligibility level was significant [F (2,69) = 120.32, p = .00]. Pairwise comparisons reveal differences between all levels of intelligibility ($p < .05$). Group descriptive statistics, along with individual accuracy are reported in Table 1.

According to the behavioral task, HP (n = 9) and LP (n = 14) listener groups were created. Descriptive statistics were calculated for each group (reported in Table 1). A one-way ANOVA, with Bonferroni adjustment, was conducted to evaluate the effect of being a HP or LP listener on overall understanding of varying intelligibility levels. The main effect of listener-type was significant [F (5,66) = 61.53, p = .00]. This difference was driven by significant differences in performance in the 6- and 16-channel accuracy scores ($p < .05$). Test of the 1-channel data did not reveal a significant difference in performance ($p = .15$) between LP and HP listeners.

Response Latency. Following a change in protocol, response latencies (RL) were recorded for 10/24 participants. For these individuals, RL were examined in relationship

with accuracy. When all listeners' data were examined, no strong correlations were found between accuracy and RL (r = -.13, -.22, -.1 for 1-, 6-, and 16- channel data, respectively). Separate examination of HP (n=4) and LP (n=6) groups revealed meaningful correlations. For 6-channel stimuli, a strong negative relationship existed for HP listeners (r = -.8; increased RL, decreased accuracy); however, a positive relationship existed between the accuracy of LP listeners and RL (r = .44; increased RL, increased accuracy). This relationship between RL and accuracy for LP listeners was also seen with 16-channel stimuli (r = .47), but is not maintained for the HP listening group (r = .11). While statistical analyses were not conducted because of insufficient power and unequal sample sizes, the correlations support a relationship between RL and accuracy. This information informs the formation of listener profiles, to be developed further in future work.

EEG Data

Event-related potentials. The grand average files for each condition were examined for transient activity. Two event-related potentials were noted, with varying latencies and amplitudes, hereafter referred to as the "late ERP" (L-ERP) and "early ERP" (E-ERP). Comparisons are made between the timing, location, and power associated with each, comparing different levels of intelligibility, as well as HP and LP listeners. Latencies and source localization areas for all comparisons are reported in Table 2.

When examining the E-ERP, several differences appear between listening conditions and listening performance groups. Results provide support this E-ERP is consistent with the P3b, more commonly known as the P300 [19]. For HP listeners, the superior parietal is localized as the neural generator responsible for the activity, as determined by CDR via sLORETA; this is consistent in timing and location with the P3b, documented in the literature when listening to intelligible (16-channel) speech. However, for LP listeners, this activity occurs later and is localized to the angular gyrus, an area which theory relates to internal monologue of written words, but perhaps also includes repetition of the stimulus item as a strategy for resolving content [20]. This speculation warrants further investigation with an approach yielding higher spatial specificity, particularly as activation occurs bilaterally.

Looking at the L-ERP seen when processing 1-channel speech stimuli, all listeners and listener sub-groups demonstrated an event-related potential with a diffuse distribution, suggesting nonspecific attentional activation, with no clear focal activation. As this speech is unintelligible, diffuse activity is expected. Still, the timing of this transient activity is shorter, occurs later (585-630ms; 45ms in duration), and has lower amplitude for LP listeners, when compared to HP listeners (540-600ms). When examining 6-channel data, differences in source localization reveal an underlying difference in listening strategy, likely responsible for high or low performance. Via CDR, it is revealed that the neural generator underlying this potential for LP listeners is the left transverse temporal gyrus, or Heschl's gyrus (Figure 1.a). This area of the brain is strongly associated with speech encoding, namely semantic tasks. This suggests a strategy that may work for nondegraded speech, which falls short when processing

speech that is degraded. For HP listeners, activity in the inferior frontal gyrus is seen bilaterally when processing 6-channel speech (see Figure 1.b). This suggests involvement of cortical areas traditionally utilized in speech production, consistent with the dual stream model of speech processing [3]. This supports the notion of a more successful listening strategy, appropriate for degraded speech. Again, this ERP occurs later for LP listeners (680- 705ms after onset of the stimuli) when compared to HP listeners (565-595ms following onset). Finally, the L-ERP present in response to 16-channel data is noted among LP listeners, but not HP listeners. This is consistent with previous studies of peripheral hearing disorders that show late or small responses when speech processing is degraded [see 21].

Frequency Analysis. The frequency spectra for average files were examined for each condition, separately for all listeners, HP listeners, and LP listeners. While no statistics were performed to determine statistical significance, differences appear in overall levels of delta and theta activity, when comparing HP and LP listeners. As cortical activity is measured on the small scale of microvolts, a difference of more than 2 microvolts may be substantial. Further, differences in the ratio of theta to alpha activity appear between HP and LP listeners across all three levels of intelligibility. For 6-channel processing intervals, the theta/alpha power ratio is 1 for HP listeners and .73 for LP; for 16- channel processing intervals, this difference is magnified with theta/alpha power ratios of 2.8 for HP listeners and .78 for LP listeners. Higher levels of theta activity seen in HP listeners drive these differences. While difficult to interpret, this identifies potential relationships between theta activity and degraded processing, to be explored further in future research.

Individual listener profiles

In addition to the group analyses, exemplars from each group were identified to assess whether the group average reflected individual performance characteristics. Figure 2 shows the average EEG response for both 6- and 16-channel stimuli. The individual's response is reflective of the group of high-performing listeners as a whole: 1) there is the presence of an L-ERP for the response to the 6-channel stimuli, but not the 16-channel stimuli, 2) there ERPs are of higher amplitude in response to the 16- compared to 6-channel stimuli, and 3) there is a poorer signal-to-noise ratio for the 6- compared to 16-channel response, suggestive of a more variable response to a degraded stimuli.

For the LP group, a larger degree of variability is expected in cortical responses, given the degree of variability among the behavioral data. Despite this, the individuals do reflect the group in that there is both an early and late ERP in response to both the 6- and 16- channel stimuli (see Figure 3 for individual exemplar of ERP).

Discussion and Conclusions

This study has presented evidence for different listener strategies that correspond to speech comprehension performance and underlying cortical activity. This includes an interesting relationship between accuracy and RL, where HP listeners demonstrate a decreased accuracy with increased RL, and LP listeners demonstrate a benefit from an increased RL, coinciding with improved levels of accuracy. This is consistent with timing of transient activity in the EEG recording, with longer RL associated with later ERPs.

We see evidence for an event-related potential, related to the processing of degraded speech, occurring approximately 600ms following the onset of the degraded speech signal. It is important to note that we see this potential earlier for more degraded speech (i.e. 1-channel occurs earlier than 6-channel) and, within that relationship, this potential is induced later for LP listeners, with lower amplitude (i.e. less accurate). This induced potential *is* seen when LP listeners are processing 16-channel speech, which is largely intelligible; however, this is not noticeably present for HP listeners, consistent with better processing of expectedly intelligible speech (i.e. less effort to understand). Noticeably present is defined as transient activity with an appreciable signal-to-noise ratio (i.e. above 1) and substantive component associated with such activity (i.e. accounting for nearly half of the variance). This supports the notion that this induced

potential may be related to either processing degraded speech, or a degraded processing of intelligible speech.

In line with theoretical hypotheses, different cortical locations are noted as the neural generators involved in the presence of this activity. Strong support comes from source localization of prominent cortical activity associated with 6-channel stimuli. Here, we see a strong temporal activation pattern for LP listeners, associated with attempts at semantic processing, where we see a strong frontal-dominated activation patterns for HP listeners. This suggests listeners who perform well here are engaging the motor aspects of their language system, and utilizing perhaps an acoustic-phonetic based strategy to help resolve the phrase.

Examination of the frequency components of the activity associated with processing degraded speech revealed a relationship between the ratio of theta activity to alpha activity and task performance. A higher theta/alpha ratio is seen for HP listeners compared to LP listeners. We see noticeable changes in theta activity, with higher levels of theta activity present when listeners perform well responding to 6- and 16-channel stimuli. Previous research shows associations between theta oscillations and processing rhythmic aspects of speech [22]; perhaps in addition to attention being paid to the acoustic-phonetic details, HP listeners are also focusing on the amplitude envelope of the speech signal, preserved in noise-vocoded speech. This study supports the notion that HP listeners present with a more complex and effective listening profile than LP listeners. Importantly, it suggests that behavioral performance is an important component to consider in neurophysiological studies of speech perception and comprehension.

Table 1

Performance on behavioral task, including % accuracy and number of no responses (NR) recorded for each type of stimuli (1-channel, 6-channel, or 16- channel). Group data are also reported, for high performing (HP), low performing (LP), and all listeners.

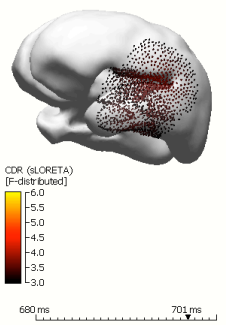
Subject	**1 Ch. Acc.**	**# of NR**	**6 Ch. Acc**	**# of NR**	**16 Ch. Acc.**	**# of NR**
HP listeners						
KP	56.25%	0	77.50%	0	93.75%	0
JM	43.21%	0	81.01%	0	91.25%	0
EL	49.37%	0	82.50%	0	92.50%	0
SR	45.45%	14	84.06%	9	97.10%	10
RP	47.50%	1	84.62%	1	90.00%	0
RS	47.50%	1	84.81%	0	98.75%	0
CL	51.85%	0	85.90%	1	93.59%	2
MV	70.00%	21	88.73%	8	94.59%	6
RU	85.02%	0	89.61%	2	95.00%	0
Average	55.13%	4	84.30%	2	94.06%	2
St. Dev.	13.75%	8	3.73%	4	2.73%	4
LP listeners						
AA	52.08%	32	90.57%	26	96.72%	19
AB	51.25%	1	59.49%	0	86.25%	0
AF	50.62%	0	63.29%	0	73.75%	0
AL	51.28%	2	70.00%	0	71.25%	0
AM	50.00%	7	73.85%	14	93.06%	8
CG	50.98%	30	72.22%	25	82.98%	33
CK	51.35%	6	73.68%	3	84.93%	7
DM	41.27%	18	64.06%	14	79.37%	18
JL	56.52%	35	80.49%	38	95.12%	39
KR	48.98%	32	82.00%	29	98.21%	24
LC	52.08%	28	77.78%	28	95.31%	16
LM	52.35%	2	65.79%	5	81.82%	2
MG	47.37%	27	76.74%	37	93.88%	27
SJ	56.67%	51	84.62%	40	90.91%	36
SL	42.50%	1	71.43%	1	80.00%	0
Average	50.35%	18	73.73%	17	86.90%	15
St. Dev.	4.19%	16	8.58%	15	8.59%	14
All listeners						
Average	51.95%	13	77.86%	12	89.71%	10
Min.	41.27%	0	59.49%	0	71.25%	0
Max.	85.02%	51	90.57%	40	98.75%	39
Range	43.75%	51	31.07%	40	27.50%	39

Table 2

Latency and % variance accounted for the by each independent component identified via independent component analysis (ICA). Signal-to-noise ratio (SNR) is also reported, along with the F-value reported by the current density reconstruction, sLORETA. "Late" and "early" event-related potential (ERP) details are reported for all listening groups, for each level of intelligibility. HP = high performing; LP = low performing listeners

Group	**Time (ms)**	**ICA (% Var.)**	**SNR**	**F-Value**
		"Late ERP"		
1- Channel				
All listeners	540- 600	49.9	2.9	35
LP Listeners	585-630	49.4	2.6	25
HP Listeners	540-600	52.2	3.5	60
6- Channel				
All listeners	630-675	40.6	1.9	40
LP Listeners	680-705	41.4	1.4	5
HP Listeners	565-595	50.9	2.3	25
16- Channel				
All listeners	685- 715	55.2	2.4	30
LP Listeners	685-715	47.9	1.9	15
HP Listeners	None Noted	N/A	N/A	N/A
		"Early ERP"		
1- Channel				
All listeners	215-255	48.4	2.9	40
LP Listeners	229-259	48	2.1	25
HP Listeners	220-254	56.8	3.1	60
6- Channel				
All listeners	225-280	51.5	3.9	500
LP Listeners	260-305	43.5	2.1	100
HP Listeners	225-270	52	3.3	65
16- Channel				
All listeners	215-275	42.7	2.7	750
LP Listeners	240-270	48.1	1.9	200
HP Listeners	225-270	49.6	2.8	500

a. LP 6 channel



b. HP 6 channel

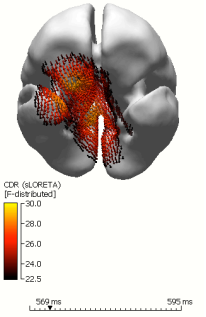


Figure 1. Demonstration of source localization, provided via sLORETA. Figure 1.a shows localization to the transverse temporal gyrus when listener's with LP encounter 6-channel speech; Figure 1.b shows HP listeners, for whom activity is seen in the inferior frontal lobe.

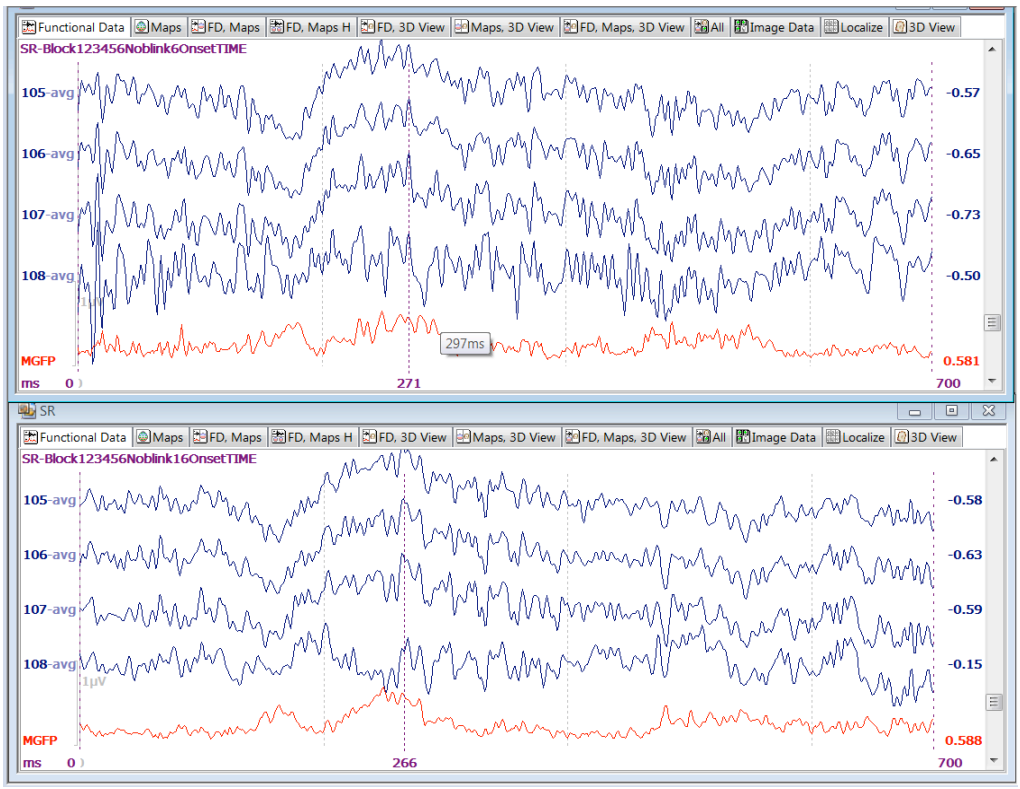


Figure 2

Exemplar of individual member of HP listening group. Top: 6-channel ERPs; Bottom: 16-channel ERP (Scale: 0.053 microvolts/ mm; view from 0 to 700ms; View: frontotemporal electrodes). Not marked is the later-ERP in the 6-channel response, occuring at approximately 500ms.

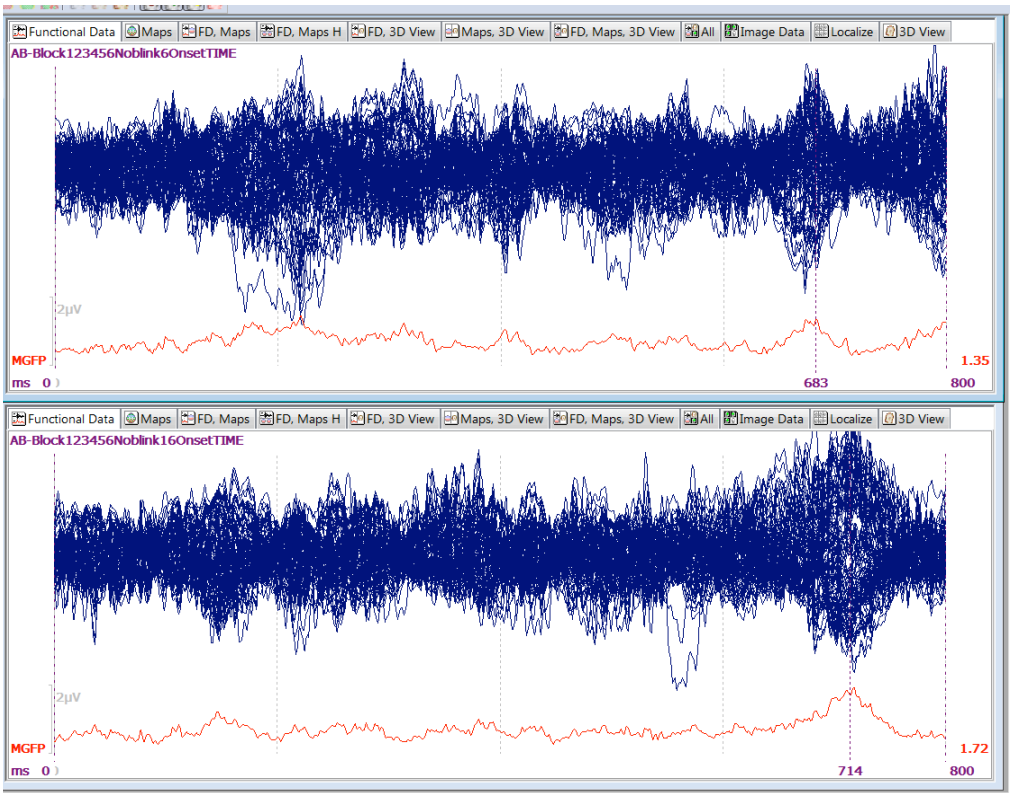


Figure 3

A different view: utilizing butterfly plot (all eleectrodes laid on top of one another)

Exemplar of individual member of LP listening group. Top: 6-channel ERPs; Bottom: 16-channel ERPs (Scale: .13 microvolts/ mm ; view from 0 to 700ms)

CHAPTER 2

BEHAVIORAL AND ELECTROENCEPHALOGRAPHIC CORRELATES OF: CONCUSSION INDUCED SPEECH PERCEPTION DEFICITS

Introduction

Sports-related concussion, especially among young athletes, is a public health problem worldwide. Concussion, also known as a mild traumatic brain injury (mTBI), refers to the clinical syndrome resulting from trauma. Despite lack of agreement about the clinical manifestation of concussions, the brain injury itself has been well characterized in terms of the initial biomechanics, and subsequent metabolic and neurochemical changes that occur. Bridging the knowledge gap between the signs/symptoms and the underlying physiology is a critical goal. There urgent need for a sensitive measure of brain activity that corresponds with the deficits resulting from concussion to verify that physiological recovery has occurred.

Concussion pathophysiology

In trauma, the fast-slow motion and rotation of the head result in concussion [23]. It is possible for injury to occur in the area of direct impact, the *coup*, or the opposite side of the brain from impact, the *contrecoup*. While this can occur in any area of the brain, the most common site of impact are the temporal lobes on the side of impact. The biomechanics of initial injury are far better understood than the underlying pathophysiology of concussion. With this, we lack a complete understanding of the lasting effects from even mild traumatic injuries and the mechanisms of prolonged vulnerability to subsequent damage. However, research has demonstrated that cerebral

blood flow is disrupted following concussion. A lack of blood flow is coupled with a disruption in the balance of glucose metabolism, as increased glucose demands offset these reductions in perfusion [24, 25]. This results in an offset of available energy supply and subsequent inefficiencies. At the level of the neuron, there are disruptions in depolarization, which affect the inhibition and excitation surrounding action potentials. Particularly, there is evidence of increased levels of extracellular potassium, which results from disruptions in opening of the potassium channel. This excess potassium leads to increased excitation, and plummeting deactivation (also referred to as "spreading depression"). Work by Giza and colleagues provide support that disruption of cognition, memory, and even loss of consciousness are direct manifestations of posttraumatic *spreading depression,* supporting the notion that there is a relationship between underlying neurophysiology and subsequent signs and symptoms [24]. It is of note that these changes, and potentially lasting disruptions in neurobiological mechanisms of the brain, may undercut our current guidelines for returning to play shortly after receiving a concussion. An understanding of these basic functions are critical for understanding the "cascade" effect of such dysfunction that ultimately results in the diffuse nature of these injuries. While the details of these mechanisms are outside the scope of the current paper, a thorough overview of metabolic and neurochemical changes are presented in several papers [26, 27, 28].

It is important to recognize that there is no universal clinical definition of concussion, however the American Association of Neurological Surgeons (AANS) recommends that *any* alteration of mental status or consciousness qualifies as concussion. This includes, but is not limited to headache, loss of consciousness, memory difficulties,

difficulty sleeping, mood swings, or increased anxiety. The exact prevalence of concussion is unknown because not all concussed individuals seek medical attention, nor do they necessarily recognize they have suffered a concussion. However, according to the AANS, more than 300,000 concussions occur annually in the United States alone. AANS also estimates that the likelihood of incurring a sports-related concussion is close to 20%. Among college football players in the US, 34% have had at least one concussion and 20% have had two or more [29].

This recent spotlight on concussion has illuminated glaring deficits in the current standard of care with regard to addressing acute and persistent cognitive signs and symptoms of mild brain injury. This stems, in part, from the diffuse nature of the injury, which tends not to produce focal cognitive or behavioral deficits that are easily identified, tracked, or targeted for therapy. Indeed it has been shown that patients with enduring symptoms have difficulty describing their problems [30] and one can presume this issue is of even greater magnitude in children with concussion. There is therefore an urgent need for a sensitive measure of brain activity that corresponds with higher order cognitive processing. The development of a neurophysiological metric that maps to clinical resolution would greatly enhance clinical practice to the extent it could inform decisions about diagnosis, prognosis, and return to play, including the need for clinical intervention to address cognitive deficits.

Critically, newer studies have concluded that people with concussions are more susceptible to widespread damage, and that neurologists *need to assess each patient on an individual basis* because neuronal impact is unknown [31]. Additionally, current

standards of care suggest focusing on focal concerns (e.g. the symptom of sleeping difficulties or memory loss). However, the most current concussion research shows that functional damage can occur resulting in *a breakdown of networked communicative activity between multiple areas of the brain* [31]. This can cause a loss of efficiency and coordination between diverse cognitive functions and the resulting complex symptomology cannot be easily addressed.

Overall, the current guidelines for clinical recovery carry no consensus. The American Speech-Language and Hearing Association (ASHA) states that there are up to twenty-two different guidelines currently used to assess the presence of injury and determine appropriateness of return to play post-injury [32]. These guidelines do not always factor in age, gender or other variables, which play a key role in recovery. The AAN created the most commonly used assessment for ***rating concussion severity***, which breaks down concussion into three subtypes, entirely dependent on time of lost consciousness [29]. Of course, the symptoms that result from different grades of concussion vary and the severity of resulting symptoms is not directly predicted by concussion-grade alone. Unfortunately, many concussions fall within a single grade of consciousness (grade 1, without loss of consciousness) and greatly vary on a continuum of severity. The most commonly used ***return to play guidelines*** were created by the Colorado Medical Society in 1991 [33]. These guidelines factor in concussion grade (determined by the AAN rating scale) and also number of concussions the person has endured. It is of note that these assessments do not take into account developmental factors and similar standards are utilized for children and adults when identifying concussion management strategies [34]. Due to this variability of both return to play and

severity guidelines, *The International Conference on Concussion in Sport* convened in both 2001 and 2004 to create recommendations for individualizing return to play and steadily increasing physical activity, working toward a complete return to play. However, the guidelines are only recommendations, and are not considered a rule, due to lack of standardization across athletic coaching and large inter-patient variability. According to public media, these recommendations are not being followed, resulting in a large disservice to athletes across the country [35].

A standard and reliable assessment of the severity of concussion is a critical first step in developing a gold standard of treatment. While there is not a single assessment that is used nationwide, there are several that are used, some of which require baseline testing and some that do not. Recognizing the impact of individual variability on the outcomes of concussion, and the range of "normal" behavior, it is important to recognize the critical need of a pre-injury point of comparison for test validity and reliability. It is similarly important to recognize the practical issues in obtaining pre-injury data. Without baseline data, we look to the most commonly seen symptoms across the continuum of concussion severity for ways to assess such deficits. With this, we can understand and utilize such deficits for sensitive detection of concussion and subsequent recovery.

Currently, clinical practice lacks standards for 1) defining severity of impairment and 2) objective concussion assessments that also incorporate subjective symptoms. This includes headaches, anxiety, depression, memory deficits, inability to concentrate, sleep problems, etc. Although many screeners and quick assessments are utilized, a large gap exists between current assessments and patient prognosis. Individuals who receive

treatment from speech-language pathologists post injury are among the minority, but if symptoms persist past the window with which the neurologist is comfortable, a referral is made. The main role of the SLP in concussion management is to provide treatment for post-concussive symptoms [32]. Most treatment services provided focus on cognition tasks (e.g. attention) to help the patient compensate for their cognitive difficulties. However, without a baseline measurement for comparison, an SLP may never know when a client has recovered. A person can fall within normal limits on a standardized test but still not be back to baseline (e.g. a person who used to perform at high-normal and now performs at low-normal). Similarly, an individual may be scoring poorly, but is performing as they would pre-injury.

Contributions of Electroencephalography to Concussion Research

Given the complex presentations of injury, and what is known about the underlying pathophysiology, electroencephalography (EEG) is a useful tool in the assessment of concussion. EEG allows for fine temporal resolution of processing, as well as global measures of cortical function and cohesion. With such diffuse damage and subsequent breakdowns of function, these measures offer sensitivity absent from current behavioral assessments and that present in a functional, rather than structural assessment of damage. In the literature, it has been demonstrated that acute differences occur in expected frequencies of the background rhythm (i.e. slowing occurs within the first two days post injury [36] and that the presence of diffuse slowing resolves in concussed injuries one to two months post injury [37]. There have been demonstrations of decreased power associated with given frequency bands in patients with mild traumatic brain injury

[38,39]. Interestingly, an increase in the ratio of alpha-theta power was identified as a lasting symptom of injury [40,41]. Recent research has compared clinical symptoms to neurophysiological metrics and revealed that the time course of physiological recovery is longer than that of behavioral recovery [42] and neurophysiological metrics may be more sensitive than EEG metrics [30]. Recently, some research has identified persisting difficulty with complex tasks following concussion, when basic symptoms covered in a concussion assessment battery appeared normal [43]. Sanchez and colleagues identified changes in amplitude and latency of event-related potentials in an auditory oddball task within patients with acute concussion [44].

Unfortunately, there are shortcomings with these studies as many utilized only resting EEG recordings or selective recording sites (e.g. only frontal electrodes). Cao and colleagues [45] found sensitivity of frequency power spectra values utilizing a support-vector machine for classification of concussion and non-concussed athletes. In Cao's study, postural instability is induced to provide challenging cortical situations; in the current study, a cognitive- linguistically demanding task is utilized, which addresses the diffuse areas of injury (i.e. frontal temporal lobe damage) often seen in concussion patients. See [46] for an overview of event-related potentials that have been explored with patients with concussion.

Theoretical Framework for Current Investigation

Critically, assessment of cognitive deficits post-concussion should efficiently tax higher-order processing. In the present study, this is accomplished through comprehension of spoken speech that is degraded. When listeners are confronted with a speech signal that is difficult to understand, they actively problem-solve to decipher it

[47]. This involves lower level processing of the degraded acoustic stream to decipher the sounds, as well as higher order (top-down) processing to map the degraded sounds to words in the mental lexicon and to extract meaning. Because speech perception involves integration across multiple cortical and subcortical areas, degraded speech can be used to magnify integration problems that are subtle and/or diffuse. Although the data can reflect frank issues with auditory-cognitive processing in concussion [48], the task also serves as a proxy for integrative cortical function in general. Our paradigm magnifies need for cognitive effort, so we can see deficits even when there is an apparent resolution of clinical symptoms.

In the last decade, the representation of understanding speech has moved toward of a dual model of processing [49], acknowledging the involvement of both temporal and frontal lobes in this complex process. In brief, the model states that acoustic information is mapped to both articulatory networks (via the dorsal stream, frontal lobe) and semantic networks (the ventral stream, temporal lobe). Activations are seemingly bidirectional [50] and simultaneous [51]. Functional imaging has captured the activity of these relationships, with differential involvement demonstrated in tasks using nonsense words (i.e. unintelligible speech) and complex sentences (i.e. intelligible speech) [52]. While theory of speech perception creates an artificial dichotomy to delineate these pathways, both phonemic and semantic information are utilized when processing natural speech; therefore, we expect to see both frontal and temporal lobe activation to converge on understanding speech.. Of course, there is a trade- off between the two such that, with improved semantic processing, little attention need be paid to phonetic information; however, in the case of noise-vocoded speech, this becomes increasingly more

challenging. It is expected that with injury resulting from concussion, we will see increased more diffuse cortical activation overall, suggestive of effortful and less efficient processing during the speech perception task. Throughout the course of recovery, however, we expect to see processing localized to frontal or temporal lobes, dependent on the strategy employed by the listener. Knowing that concussion patients often experience diffuse injury, often affecting the frontal and temporal lobes, it is important to acknowledge the necessity of these multiple areas of the brain in cognitive processing. The ability to use this paradigm to study the perception and recognition of speech by individuals post-concussion allows for the identification of persisting deficits.

In the current study, we present a design utilizing high-density EEG and, in addition to resting state EEG, assess frequency and associated power spectra during a cognitively demanding task. We tap into the diffuse nature of the injury, which tends not to produce focal cognitive or behavioral deficits that are easily identified, tracked, or targeted for therapy. Utilizing a sentence verification task in a joint EEG-behavioral paradigm, four specific aims were addressed: 1) assess the sensitivity of behavioral data from a speech perception task as a correlate of concussion recovery, 2) assess the relationship between performance changes and physiological measures of brain function during the task and at rest, 3) determine the cortical activation characteristics of speech perception during concussion recovery, and 4) test the sensitivity of task-related behavioral and physiology measures in distinguishing individuals with concussion from healthy individuals.

Methods

Participants

Concussed individuals were identified by treating neurologists and sports medicine physicians, and invited to participate in the present investigation. All procedures were approved by Institutional Review Boards of both ASU and Mayo Clinic. EEG and concurrent behavioral data were collected at Mayo Clinic Hospital and Arizona State University Health Services, by Arizona State University investigators. Analysis and interpretation were conducted at ASU in the Motor Speech Disorders Lab. A total of eight participants were recruited via the Mayo Concussion Program and ASU Student Health Services concussion referrals, who completed an initial visit and returned for a follow up visit several months following concussion. An additional six participants were recruited but were unwilling or unable to complete follow-up visits and their data are not included in the present report. Participants ranged from 15 to 31 years old, with a mean age of 18.5 years old (st. dev = 5.3 years). All participants were right-handed, per self-report. Participants were compensated $20 per visit. Overview of participant demographics and etiology of concussion are reported in Table 3.

The inclusion criterion for participation were: 1) a recent concussion (< 6-8 weeks post injury), 2) a native English speaker, and 3) between the ages of 14 and 65 years old. This age range was selected due reduce the influence of developmental and natural senescence related changes in neurophysiology. This protocol allowed for both feasible and reasonable assessment during the critical period of injury (average time between concussion and first visit was 23 days, with a range from 8 days to 60 days post-concussion). Participants who agreed to participate returned for an additional data collection session once they were deemed clinically back to baseline, including results of

cognitive testing by treating sports medicine doctor or neurologist, and self- and family-behavioral report. The length of time between initial meeting and second appointment was between 3 and 6 months. While age and education were not explicitly matched, the general sample from which participants were recruited was very similar for the participants in the current study and those in a previously reported study to which they were compared (namely, undergraduates at Arizona State University [54]). Additionally, data were collected from two healthy, control listeners (one female), to validate the paradigm and demonstrate intra-subject reliability across sessions. The intention of the current study was not to compare individuals with concussion with healthy controls, but rather to compare them to their own performance across time; however, a sense of how performance and neurophysiology changes over sessions may provide insight into the nature of the changes that occur.

Speaker and Stimuli

Speech samples from one female speaker were used in the present investigation. The speaker was a healthy 24-year-old female, with no history of neurological impairment and acoustic characteristics within the range of normal, according to age and gender (F0 and formant values for the corner vowels verified). The speaker recorded 800 phrases, 400 of which were "true" (e.g. zebras have stripes) and 400 of which were "false" (e.g. donkeys have wings). The speaker was seated in a sound-attenuating booth, and read stimuli from visual prompts presented on the computer screen. The recordings were made utilizing a pre-amp and external microphone; recordings were saved directly to disc for subsequent editing, using commercially available software [53] to remove any noise or extraneous silence before or after target utterances. The phrases were all three

words long (between 3 and 5 syllables), with the last word determining the veracity of the phrase. On average, the phrases were 1959 ms in duration (standard deviation = 213 ms). To systematically manipulate the intelligibility of the phrases, a random number was assigned to each of the 800 phrases, and then half of were processed using a 6-channel noise vocoder, making them difficult to understand without concentrating; and the other half were processed with a 16-channel noise vocoder, making them quite easy to understand without concentrating. All recordings were RMS normalized before vocoding. There were an equal number of 6- and 16- channel vocoded phrases that were True and False (i.e. 200 of each combination of intelligibility level and veracity).

Task

Data were collected, analyzed, and interpreted at Mayo Clinic-Arizona and Arizona State University, in accordance with approved IRB protocols. At the start of each appointment, a hearing screening was conducted to determine current hearing threshold. Participants were then fitted with a high-density electroencephalographic cap (64-channel QuickCap). Once fitted, they were played the 6- and 16- channel noise vocoded sentences. Participants were instructed to make a decision as to whether the statements are true or false, and respond with a keyboard button. This protocol, referred to as the "sentence verification" task, has been used in our previous research, which allows for assessment of cortical activation patterns, along with corresponding behavioral data [54].

E-prime [55] was used for delivery of the auditory stimuli through inter-aural headphones (90 dB to overcome ambient noise from computer systems), and

programmed for timed stimulus delivery and trigger mark indicators on the EEG recording, collected via CURRY 7 Multimodal Imaging Suite [56]. Each participant listened to eight blocks of 100 sentences, for a total of 800 stimulus items. Within each block, order of presentation was randomized and the order of blocks (1-8) was partially counterbalanced amongst participants. A 2000ms inter-stimulus interval was utilized to ensure completion of post-perceptual processing before presentation of the next stimulus. Breaks were allowed during testing in order to reduce participant fatigue. In some instances, participants fatigued before completing all eight blocks; regardless, the same number of blocks were administered in follow up visits to assure differences seen in follow-up were secondary to recovery versus differences in power associated with task completion. During follow up visits, the same protocol as above was followed. See Figure 4 for an overview of protocol.

Electroencephalographic Recording

Electroencephalographic (EEG) recordings were made via Compumedics CURRY 7 Multimodal Imaging Suite, using a 64-channel QuickCap. Positioning was assured through measurement and positioning of Cz, Fz, and Pz, in accordance with the 10-20 system. Recordings were acquired with a 1000 Hz sampling rate and low-pass filtered below 200 Hz. After recording, a 60 Hz notch filter was used to minimize effects of electrical artifact. Impedance of all electrodes was below 5 kΩ. For each participant, continuous recordings were examined for muscle and other physiologic and non-physiologic artifact. Artifact reduction was conducted via threshold detected and

covariance replacement to minimize the presence of blinks. All recordings were deemed a high quality recording and used in subsequent analyses.

Data were then analyzed separately for each condition, for each individual visit of each participant. The continuous file was epoched for each condition (the phrases of each 6- and 16- channel intelligibility levels). Epochs were created from 200ms before the onset of the phrase to 2000ms following the onset of the phrase, to allow for subsequent analyses on perceptual processing of the entire phrase, as the average duration of a phrase was 1900ms. Each individual epoch was further examined for artifact and those with high levels of muscle artifact or a large number of blinks were removed. On average, 80% of all recorded epochs were utilized to create an average file for each condition for each participant (for an average of 200 epochs per average file, given not all participants heard all 800 phrases). This provided a corpus of 32 averaged files for analysis, as there were eight participants, with two visits each, listening to two different levels of intelligibility. Only data on averaged files will be reported as they are associated with stronger signal to noise ratios.

Data Analysis

Control listeners

Data from two control participants were recorded over two sessions to evaluate intersession stability of the dependent measures in this investigation. Correlations were used to assess consistency of behavioral performance and frequency power spectra between visits one and two. Consistency of PBR was assessed. While there is only a small number of control listeners with two visits, their data served as a point of reference

during visual inspection of neurophysiological measures and behavioral data (i.e. plotted in scatter plots to allow for interpretation of trends).

To address the first specific aim, a series of analyses were conducted to assess the sensitivity of the speech perception behavioral data as a correlate of concussion recovery. EPrime, which was utilized to present stimuli, also recorded participant response and response latency (recorded from offset of the stimulus to the time a response was entered). The data were transferred to Microsoft Excel for subsequent analyses. All participant data were reviewed; incorrect and no response items were considered together, to ensure penalty for responses that occurred outside of the allotted response interval. Performance for each condition was evaluation from first to second visit. Trends were assessed among the group, but individual performance was the primary indicator to which neurophysiological data are compared in the next portions of the study.

To address the second specific aim, both EEG and behavioral data were examined to assess the relationship between performance changes and physiological measures of brain function at rest and during the task. These included event-related potentials (ERPs) and frequency analysis, with subsequent comparison with the control data from the previous report.

Toward this end, predominant background rhythm (PBR) was calculated via epoching of a 5-minute recording of relaxed wakefulness. Epochs were created every 4 seconds to then create an average recording. From the average, the frequency value of the alpha rhythm with the strongest peak amplitude was deemed as the PBR for an individual. This was verified through visual inspection of the continuous waveform captured in the posterior electrodes. As no baseline data were available, comparisons

were made to expected values for PBR for the given age of the participant [57] to assess the presence of pathology. Comparisons were also made between first and second visits, to identify potential shifts toward higher PBR; differences were statistically assessed via a repeated measures ANOVA. Visual inspection was also completed relative to control listeners' PBRs across sessions.

Next, CURRY 7 Multi-Modality Imaging Suite [18] was utilized to examine average files for transient activity, as identified by peak activity in electrodes expected to reveal relevant activity (e.g. temporal regions). Once an interval of time was identified, independent components analysis (ICA) was utilized to assess the transient. The component of the ICA was examined for desirable signal to noise ratio, meaningful variance, as well as shape to verify its integrity (i.e. not a byproduct of artifact). The onset, duration, and peak amplitude of the early-ERP for the average 6-channel response and 16-channel response were recorded for both first and second visits.

Further, we used the offset of the early ERP, whenever it occurred for each individual in each condition, as the starting point for frequency analysis of post-perceptual processing. By post-perceptual processing, we mean the cognitive activity associated with comprehending the noise-vocoded sentence and rendering a true or false decision. The frequency spectra for each participant's average files were examined. Each individual's average file was analyzed via Fourier transform to obtain the power spectrum at each electrode, from the offset of the "early ERP" to 1900ms, capturing the later processing associated with understanding the stimuli. Average power of each frequency band was calculated for traditional frequency bands: delta (0-3.5Hz), theta (4-7.5Hz), alpha (8-12.5Hz), and beta (13-30Hz), across all electrodes, for each condition.

With the given paradigm, a traditional event-related (de)synchronization approach was not deemed appropriate, as the pre-stimulus interval is likely not a passive baseline from which to conduct the analyses. Further, raw values can be utilized here, allowing for a more straightforward comparison.

Further, frequency spectra values were compared from the first visit (acute concussion) to the second visit (clinical recovery); correlations were calculated to assess relationship of power spectra across sessions. This information was then used to characterize individual changes for patients across the course of their recovery from concussion (as measured by ERP and frequency spectra values at first and second visit).

Next, analyses were conducted to assess the cortical activation characteristics of speech perception during concussion recovery (third specific aim). First, the ERPs mentioned above were further analyzed. Following ERP ICA analyses, current density reconstruction (CDR), via sLORETA, was utilized on the identified component of interest. This allows for the localization of the source of the component, or the underlying neural generator responsible for the transient activity. sLORETA computes minimum norm least squares (MNLS) current density amplitudes (dipole moments) and divides them by their error bars (and squares the result), taking into account the amplitude of activity; therefore, the F-values provided by sLORETA can be interpreted as statistically significant magnitudes of activity. CURRY assigns a Brodmann's area to the solution to the MNLS problem, which was utilized in the interpretation of the ERPs.

Finally, a series classification analyses were conducted to test the sensitivity of task-related behavioral and physiology measures in identifying individuals with concussion from healthy individuals. In order to assess group differences before

proceeding with classification analyses, a series of tests were conducted. First, behavioral data from the concussion patients at first and second visit were evaluated relative to those from previous work, in which we examined performance patterns among healthy individuals of the same age cohort [54]. In this prior work, healthy listeners exhibited a wide range of accuracy, allowing for subdividing the groups into higher- and lower-performing cohorts. ANOVA of behavioral data from the first visit of the concussed participants were compared with both high- and low- performing groups (HP, LP) of control listeners. Then, the frequency spectra were calculated for each individual listener reported in previous research, utilizing the offset of the ERP for their respective group membership, HP or LP, to allow for use in classification analyses, described below. Next, a multivariate ANOVA was performed to assess if differences existed among the spectra of healthy, control listeners and concussed individuals.

Metrics from frequency analyses and behavioral performance were submitted to a series of stepwise discriminant function analyses (DFA). This analysis assessed the metrics' combined sensitivity to group membership (i.e. concussed individual, compared with younger individuals who had both high and low performance on the behavioral task). DFA is an ideal tool for the present purpose because it is known to be effective in determining which set of continuous variables (e.g., EEG metrics or accuracy) best discriminate between groups; the DFA has the opportunity to provide a quantitative composite index of group membership for each observation (e.g., listeners). Canonical functions, representing linear combinations of the selected (i.e., most powerful) predictor variables, were constructed by the DFA and were used to create classification rules for group membership. The accuracy with which these rules classify the members of the

group is expressed as a percentage. Because the classification rules are, in essence, tailored to the specific data set, it is necessary to invoke a more stringent test to assess reliability of the original classification results. Here, cross-validation (also called the "leave one-out method") is utilized. By this method, the DFA constructs the classification rules using all but one of the listeners. The excluded listener is then classified based on the functions derived from all other listeners. This is repeated for all listeners, and the resulting classification accuracy, which is usually lower than the original classification accuracy, provides an index of robustness of the original DFA results.

The DFAs conducted looked at sensitivity of classifying participants with concussion against 1) low performing young, healthy listeners, and 2) all healthy control listeners. The justification behind these separate DFAs is as follows: recognizing the large variability among healthy listeners, we can presume such variability exists among participants with concussion. Given the expectation that concussion will affect performance, the low-performing healthy group is a more appropriate comparison group to test sensitivity of pathological performance. Finally, the comparison with all control speakers tested the sensitivity of classification against a more heterogeneous listening group, providing another test of the robustness and sensitivity of measures to concussion classification. A third DFA attempted to replicate the sensitivity of classification, but this time against participants at the point of recovery from concussion from healthy listeners. This DFA was conducted with the metrics deemed sensitive in classifying individuals with concussion against a group of healthy listeners (delta and theta power associated with the processing of 6-channel stimuli). Here, we hypothesize poor classification

results, as there is evidence of both clinical and neurophysiological recovery at this juncture.

Results

Control listeners

In examining the performance of healthy control listeners on the behavioral task across sessions, correlations for Control One (C1) show a relationship of r = .95 for accuracy of responses, calculated across responses to 16- and 6-channel data. This suggests a strong consistency across sessions. Further, r = .99 for overall response time across conditions and .98 for response time of correct responses, demonstrating consistency of the speed with which responses are provided. Importantly, this demonstrates the likelihood that minimal learning occurred between the sessions, which were separated by several months. For Control Two (C2), there was a demonstration of inconsistent performance across sessions and improved accuracy and decreased response times, with correlations of r =.60 and r = .62, across sessions, respectively. This provides a healthy, control to which we can compare changes across sessions that we may see in concussion patients.

Additionally, EEG measures, including PBR, ERP, and frequency analyses were calculated for each control. EEG measures of C1 show a consistent 9.5 Hz PBR across sessions and a 9 Hz background rhythm was revealed during each visit for C2. As is expected, these measurements are considered within the healthy range of idle background rhythm. Further, frequency power spectra were calculated from the offset of the early

ERPs through 1900ms, or the average offset for the phrases heard. Average power across all electrodes was calculated for 6- and 16-channel stimuli and correlations were calculated between session 1 and two for all frequency bands. Correlations for C1 were at or exceeding r = + .90 (all responses (r = .9), 6-channel frequency power (r = .93), 16-channel frequency power (r = .9)), suggesting consistency of cortical task- related power across sessions. For C2, despite inconsistency of behavioral performance, correlations of frequency spectra values across sessions reveal strong correlations (r = .92 for all responses, 6-channel frequency power (r = .98), 16-channel frequency power (r = .94), ***suggesting consistency of cortical task- related power across sessions***. The changes seen in C2 serve as a point of comparison for changes seen in the participant population; while it does not lend to a straightforward interpretation of recovery versus learning, it does offer insight into the shifts in task-related neurophysiology.

With regard to the first specific aim, assessment revealed the behavioral data elicited in this task to be a modest correlate of concussion recovery. For the majority of concussed participants, higher accuracy was achieved on first visit as compared with their second visit. For the 6-channel condition, six participants demonstrated improvement in accuracy, while performance remained the same for one participant, and decreased for the final participant, who was the only participant younger than 16 years old. With regard to response latencies, results for the 6-channel condition were varied despite performance trends. Three of eight participants showed faster overall response latencies, with the remaining five showing slower overall response latencies; there was a decrease in the variability of overall response latency for three of eight individuals; and, yet again, three of eight showed faster response latencies for correct responses, with the remaining

showing a slower response latencies for correct responses when compared to the first visit. When examining the performance on 16-channel data for first and second visits, 6 of the 8 participants show improvement, with one performing the same at the first visit and one showing a decline in accuracy. Response latencies and variability of response latencies equally increased and decreased for half of the participants. For response latencies to correct responses, five participants showed a decrease in response latency and three participants showed an increase.

Frequency spectra and event-related potentials were examined and compared to behavioral performance, supporting the existing relationship between performance changes and physiological measures of brain function at rest and during task. The individual improvements in task performance coincide with changes in concurrent electrophysiological recordings. The relaxed wakefulness recording, taken before the start of the task at each visit, contains the predominant background rhythm (PBR) of cortical activity. Seven of eight participants exhibited an increase in background rhythm at the second visit. The PBR for both visits were subjected to repeated measures ANOVA, to assess if as a group, differences were revealed between visits. Overall, there was a significance difference [F (1,17) = 21.925, p = .002; partial Eta squared = .758). Despite being within the range of "normal" PBR at the first visit (average PBR = 10.06 Hz), there is evidence of change at second visit (average PBR = 10.65 Hz). This is clearly shown in Figure 5, which plots PBR at first and second visits, relative to performance in the 6-channel condition. Further, there is a noticeable shift of concussed participants toward the control participants across visits, or toward neurotypical-behavioral relationship between background rhythm and performance as they reach recovery.

Next, event-related potentials (ERPs) were first identified in the average response to 6-channel stimuli. Early ERPs, namely the P300 are related to speech processing and such localization verifies task-relevant areas of activation. Here, we identify a transient-induced potential - approximately 300ms after the onset of the phrase. Given the aforementioned ERPs, 4 participants presented with an ERP with an earlier latency at the second visit, when compared with the first. With regard to the trough-peak duration of the ERP related to 6-channel speech, four participants demonstrated an ERP of equal duration, two each with a longer or shorter transient. The overall power (MGFP) of interval associated with the ERP was decreased in six of eight participants, as was the relative power, or that associated with the electrode in which the ERP is most prominent. For the 16-channel condition, **all eight** participants demonstrate earlier ERP onsets, with four demonstrating a trough-peak duration that was longer and four demonstrating a trough-peak duration that is shorter in the second visit compared to the first visit. The overall power associated with the peak of the ERP was decreased for seven of the eight participants. With regard to relative power, half of the participants showed and increase and half showed a decrease from the first to second visit. Further examination of the individual data points across visits, demonstrate a shift toward control subjects in both amplitude and latency onset (see Figures 6 and 7 for respective comparisons for 6-channel data and Figures 8 and 9 for comparisons 16-channel; see Tables 2 and 3 for individual values).

For each individual, the offset of the early ERP, whenever it occurred (individual onset and offset values (ms) are listed in Table 4 for 6-channel responses and Table 5 for 16-channel responses), served as the starting point for frequency analysis of post-

perceptual processing. Frequency power spectra were calculated for each individual in the current study. Looking at the 6-channel responses, from first to second visit, seven of eight participants showed a reduction in power associated with each frequency band. The same trend holds for six of eight participants in response to the 16-channel stimuli. These power values are calculated as a global measure, using all electrodes; a reduction in overall power is suggestive of less diffuse, and more focal, processing. Similarly, examining the group as a whole, correlations between task-related frequency spectra values of first and second visits reveal relationships less strong than those demonstrated in control participants (see Table 6). This suggests the neurophysiology related to task has changed from first to second visit, coinciding with improved performance. This is further corroborated by the shift of active neural generators during the task, described below.

Cortical activation characteristics of speech perception, namely related to event-related potentials, track to individual changes during concussion recovery. Most interestingly, source localization of this event-related potential offers insight into the relationship of the nature of the injury and the behavioral performance. Localizations for five participants demonstrated an ERP localization from a diffuse or sub-cortical region; this likely results from poor localization secondary to overall diffuse activity. It is of note that there is activation seen in the frontal and temporal lobes, but its contribution is overshadowed with the surrounding activity. In the second visit, this ERP localization shifts to an interpretable, task-related area of activation (namely, frontal or temporal lobe

activity). See Figures 11-18 for figures of the source localizations of the EPR in each condition for each individual, in each visit.

Similar to the 6-channel data, at first visit, localizations of this ERP revealed diffuse activity; in the second visit, however, six of the eight participants revealed the neural generator underlying the ERP is in the frontal gyrus. This is consistent with both previous reports of individuals who performed well on the 16-channel task and these individuals' behavioral accuracy.

Individual Performance Patterns. Below are brief synopses of clinical histories, along with summaries of behavioral and electrophysiological changes from first to second visit for each participant.

1. AO is an 18- year- old college student, who plays lacrosse and received her concussion during training. She works as a hostess and has not yet declared a major. AO demonstrated improved performance across visits in the 6-channel condition, with increased response latencies and a delayed latency for the ERP, with diminished associated power. Across visits, a more focal localization, to the inferior frontal gyrus, was revealed. In the 16-channel condition, AO demonstrated increased response latencies, with a decreased latency for the ERP, and diminished associated power. Again, analyses reveal a more focal processing in the medial frontal gyrus. AO's PBR increased from first to second visit.

2. NG is a 24-year old hockey player, 5th year college student, who received his injury during a game. NG reported incapacitating headaches immediately following, that return intermittently, but he is largely feeling "back to normal."

NG showed an improvement of accuracy in the 6-channel task, accompanied with increased response latencies and an earlier ERP. Overall amplitude, as well as ERP amplitude increased. Localizations for both were to the frontal lobe. In the 16-channel condition, NG showed increased accuracy, with increased latencies and earlier ERP. Interestingly, there was an increase in overall and ERP amplitude. Localization shifted from the frontal to precentral gyrus. NG's PBR increased from first to second visit.

3. MR is 17-year-old female, was seen three months post- concussion with a history of two previous concussions. The patient complained of severe headache, anxiety, trouble sleeping, depression, poor grades, trouble concentrating and dizziness. Prior to her concussion, MR had an anxiety disorder and a troubled home life. Her brother recently became suicidal, and she is not close with her parents. After the concussion, MR stated that her symptoms have only worsened and that she is having an even harder time sleeping through the night, experiencing severe anxiety attacks daily. MR demonstrated improved accuracy with increased response latencies in the 6-channel condition. This is accompanied by earlier ERP and reduction in ERP and overall amplitude; localization shifted from a sub-cortical structure to the frontal gyrus. In the 16-channel condition, MR showed improvement of accuracy with increased response latencies. An earlier ERP was localized in the frontal gyrus at second visit that was previous localized sub-cortically. There is a reduction in ERP-related amplitude, yet increased in overall amplitude from first to second visit. MR demonstrated no shift in PBR,

and was the patient with the longest interval between injury and first visit. Interestingly, despite lack of shift in PBR, there are demonstrations of task-related changes.

4. JH is a 20-year old rugby player, who received his concussion hitting the sidewalk while out with friends; he has a history of 1 concussion 2 years prior. He reported difficulty feeling a “fogginess” that reportedly cleared up within a week of concussion, but difficulty sleeping that persisted even to second visit. He performed equally well on the 6-channel task from first to second visit, with decreased response latency and an earlier onset of task-related ERP. There was a decreased in ERP amplitude and overall amplitude during processing; localization remained within the temporal lobe. During the 16-channel task, performed increased with a decrease in response latency and earlier onset of task-related ERP; data show a decrease in both task-related and overall amplitude. Localization shifted from the temporal to frontal lobe from first to second visit. JH’s PBR increased from first to second visit.

5. LW is 16-year-old male hockey player, was assessed two weeks post-concussion. The patient self- reported memory and concentration problems secondary to his concussion at first visit that he reported as resolved at follow up visit. LW is also the lowest performing patient seen, demonstrated a dramatic increase in performance from first to second visit on the 6-channel task, accompanied by decreased response latency, ERP onset, ERP amplitude, and

overall amplitude. Localization shifted from sub-cortical to medial frontal. On the 16-channel task, the improvement in task performance was accompanied with an increase in average response latency, and decrease in overall and ERP amplitude. Localization for both ERPs went from a diffuse, sub-cortical localization to the frontal lobe. PBR increased from first to second visit.

6. WA is 32 year-old male, who received a concussion at the driving range. He reported having trouble sleeping and was experiencing mild headaches. He was observed to be very pleasant, explained his recovery very openly and seemed focused with high concentration to the task. Focus remained in second visit, during which time he reported symptoms were resolved. WA demonstrated improved accuracy with shorter response latencies and an earlier ERP in the 6-channel condition. In the 16-channel condition, WA demonstrated improved accuracy, with decreased response latencies and a corresponding earlier ERP. For both visits, ERP power was diminished from first to second visit, but overall amplitude increased. Sub-cortical localizations remain from first to second visit. WA's PBR increased from first to second visit.

7. AF is 15- year old high school cheerleader who received her concussion at a pool party with friends; practicing stunts, she hit the deck. AF is a diligent student on the honor roll with aspirations to become a cardiac surgeon for the armed forces. AF demonstrated decreased accuracy in 6- channel condition, with

increased response latencies and an earlier onset of event-related potential. She did however, demonstrate localizations in the frontal gyrus in both visits. There was an associated decrease in amplitude at the site where the ERP was most prominent. In the 16-channel task, however, she demonstrated decreased accuracy, accompanied by decreased response latencies and an earlier ERP, with localization occurring more focally, in the medial frontal gyrus. Amplitude at the point where the ERP was prominent remained equivalent across visits. AF's PBR increased from first to second visit 1.

8. MG is a 19-year old rugby player, who received his injury during a game. He reports all headaches and feelings of nausea have cleared and returned to play by the time of his second visit. MG's performance in the 6-channel task showed a slight decrease from first to second visit, but performance was impressively near ceiling to start. He demonstrated increased response latencies, corresponding to a delayed ERP from first to second visit. ERP amplitude and overall power were diminished. Localization shifted from the occipital to parietal lobe. On the 16-channel task, performance was equivalent, with shorter response latencies, consistent with the earlier appearance of the ERP. Localizations shifted from occipital to frontal lobe, consistent with his high performance. MG's PBR increased from first to second visit.

Finally, ***classification analyses demonstrate task-related physiology measures have a greater sensitivity in identifying individuals with concussion from healthy individuals, compared to behavioral performance.*** Statistical analyses were conducted

on the behavioral and electrophysiological data of concussion patients at injury and recovery to healthy controls, to determine if differences between the two exist. At the point of the first visit, ANOVA revealed no significant differences of group performance against that of high- and low- performing (HP; LP) healthy, control listeners on either 6- or 16- channel; as reviewed above, this is due to the large- intra-group variability. See Figure 10 for group mean group performance.

To assess the group's performance at the point of clinical recovery, an ANOVA of the return-visit performance, against that of HP or LP listeners demonstrated a significant group difference in 6-channel performance [F (2,29) = 6.107, p = .006]. Descriptive statistics (see Table 7; average performance of all groups is presented in Figure 11) reveal this is secondary to the concussion group now performing better than the LP group (further demonstrated by significantly different pairwise comparison, p = .049). There was no significant difference in 16- channel performance across groups [F (2,29) = 2.821, p = .076]. It is unclear whether this is due to learning or recovery, but it provides impetus for exploring the underlying neurophysiology responsible for changes in performance. *Even if related to learning, this provides evidence for potential of continued improvement over the course of recovery.* More important is recognition of the potential for combined sensitivity of behavioral and EEG metrics.

As described above for concussion patients, frequency spectra were also calculated for healthy listeners in a previous investigation. The multivariate test of all frequency power values support the hypothesis that differences exist between healthy listeners and individuals who 1) have acutely had a concussion (first visit; [F (8,23) =

3.498, p = .009, Partial Eta Squared = .549]), with significant differences in delta power associated with 6 channel processing, and 2) those who have clinically recovered from concussion (second visit; [*F* (4,27) = 22.724, p = .00, Partial Eta Squared = .771]), with significant differences between all frequency parameters.

Next, a series of discriminant function analyses (DFAs) were conducted. The first DFA was to identify those variables sensitive to classifying participants with acute concussions against those healthy participants who were low performing (LP) on the behavioral task. One canonical function was created, utilizing the delta power related to the processing of 6-channel speech (p = .041; standardized canonical discriminant function coefficient = 1). This function was then used to classify the data, accounting for 100% of the total variance; the test of the function was significant ($\chi^2(1) = 4.176$; p = .041). The canonical correlation of the classification function was .429. Correct classification was obtained for 87% of the originally grouped listeners and 87% of the cross-validated speakers. More specifically, 62.5% of the participants with concussion were correctly classified (5/8 participants), and 100% of the LP younger listeners were

correctly classified as such. Impressively, accuracy does not decline in cross-validation, suggesting the robustness of these measures to group membership.

The second DFA was conducted to assess sensitivity of EEG and behavioral measures to classify participants with concussion from the larger set of control listeners, who demonstrated a wide range of performance and profiles of cortical activation. One canonical function was created, utilizing the delta power related to the processing of 6-channel speech (p = .009; standardized canonical discriminant function coefficient =

1.971) and theta power related to the processing of 6-channel speech (p = .004; standardized canonical discriminant function coefficient = -1.4). This function was then used to classify the data, accounting for 100% of the total variance; the test of the function was significant ($\chi^2(2) = 11.287$; p = .004). The canonical correlation of the classification function was .568. Correct classification was obtained for 90.6% of the originally grouped listeners and 87.5% of the cross-validated speakers. Specifically, 62.5% (50% on cross-validation) of the participants with concussion were correctly classified (5/8 participants of original classification)), and 100% of the healthy, younger listeners were correctly classified as such. While accuracy does decline in cross-validation, a large degree of variability in the control group is still suggestive of the robustness of these measures to group membership. Consistently, previous attempts to use behavioral data only to classify individuals with concussion from healthy controls, utilizing traditional tests of cognition, demonstrated poor sensitivity [58].

A final DFA utilized the data from return-visits, to test sensitivity of classification from healthy control subjects. This DFA was conducted with the metrics deemed sensitive in classifying individuals with concussion against a group of healthy listeners, namely delta and theta power associated with the processing of 6-channel stimuli. One canonical function was created, utilizing the delta power related to the processing of 6-channel speech (standardized canonical discriminant function coefficient = 1.882) and theta power related to the processing of 6-channel speech (standardized canonical discriminant function coefficient = -1.205). This function was then used to classify the data, accounting for 100% of the total variance; the test of the function was significant ($\chi2(2) = 30.362$; p = .00). The canonical correlation of the classification function was

.806. Correct classification was obtained for 100% of the originally grouped listeners and 100% of the cross-validated speakers. Interestingly, the sensitivity and specificity of classifying participants recovered from concussion was higher than those in the stage of acute injury.

Discussion and Conclusions

The current study makes several contributions to the literature on concussion. These include the introduction of a novel paradigm for the study of concussion; new and corroborating evidence of physiological recovery over time that has behavioral correlates; and preliminary evidence of the sensitivity of electrophysiological patterns to distinguish concussed from healthy participants. Each of these contributions is described in turn.

The paradigm used in the current study uses two conditions of degraded speech allowed for interpretation of brain activation patterns relative to cognitive effort. The use of degraded speech to elicit higher-order cognitive processing in concussion was based on the premise that deciphering such speech is resource intensive, particularly when an accurate response is required. Overall, the wide variety of behavioral performance patterns among these 8 concussed individuals is not surprising, given that learning and recovery are not the only influences that affect performance. Participants had varying levels and types of symptoms; they were studied at different intervals post- concussion; and they were not of similar ages or, likely, intellectual levels. Further, concussion often gives rise to impulsivity [59] and compromised vigilance. It is possible that the demonstrated increases in response time during the second visit may have been associated with improvement in such symptoms. Interestingly, in the more taxing 6-

channel condition, only one participant exhibited reduced accuracy at second visit; this participant was the only participant younger than 16 years old; previous studies have demonstrated young athletes' cognitive performance is significantly different from performance of older athletes [60]; perhaps these results translate to course of recovery.

The simultaneously collected electrophysiological data further demonstrates the need for cortical integration and extra cognitive resources during the more challenging task of listening to 6-channel vocoded speech. The discovery of differential changes in brain activity during this task demonstrate disruptions in speech perception secondary to concussion that, to our knowledge, have not been previously reported in the EEG literature on concussion (or speech perception, for that matter). The data of the present investigation demonstrate there is a relationship between performance changes and physiological measures of brain function during the speech perception task. Looking to the frequency spectra during the period of perceptual processing in each condition, there is evidence of change across sessions. In tandem with improvements of behavioral performance, this overall reduction of power in each frequency band is consistent with the need for less effort, or resources, to reach the resulting improvement in performance. For control subjects, despite potential learning evidenced by changes in behavioral data, there was strong consistency among neurophysiological measures in correlations of frequency across sessions and consistent PBR. In contrast, for individuals with concussion, improvements in performance were accompanied by shifts in neurophysiological patterns (as demonstrated by poorer correlations of frequency distributions across sessions), suggesting improved electrophysiological efficiency, rather than listening strategy, is responsible for behavioral improvements among the clinical

population. Further, there is a reduction in overall global power in the period of processing during the task; this activity outside of the resources dedicated to speech perception is consistent with extra cognitive effort necessary to employ an effective listening strategy. As such, the diminished power at second visit supports the notion of an overall more efficient processing strategy.

Most impressive are the changes and improvements seen in cortical integrations across recovery. That there are consistent improvements in localizations of transient task-related potentials is another impressive demonstration of the change in electrophysiology over the course of recovery from concussion. The data highlight the importance of longitudinal studies of individual participants, as recovery patterns show considerable variation. A particularly compelling finding is the evidence of physiological recovery after the widely held cutoff of 45 days [30]. Knowledge of the algorithm used in the localization of ERPs allows for a strict assessment of their result; in other words, if a sub-cortical neural generator is identified, caution can and should be taken in its interpretation. These do not explicitly suggest the involvement of a sub-cortical neural generator, but rather are the byproduct of back propagation of such diffuse neural activity. This is the framework in which these results are interpreted in the current investigation. A shift from a sub-cortical localization via sLORETA in the first visit, to a hypothesized region of interest, suggests more focal activation related to efficient task-related processing. ***There is a sub-cortical localization for the ERP during the processing of 6-channel speech for one patient at their second visit; this may be an indication of persisting sub-clinical deficits or deficits only seen in challenging listening situations and warrants further study.*** The consistency with which this shift

occurs in line with improved behavioral performance is a demonstration of the change in electrophysiology. These results confirm the importance of both behavioral and neurophysiological data and support the notion that breakdowns occur during cognitively demanding tasks, which might not be noticeable during tasks that require little higher-order processing.

The data of the current study are consistent with previous research that the resting background rhythm in the EEG recording does change across the course of recovery. This global measure of integrity of electrophysiological activity suggests improvements in the overall network and coherence necessary to solve cognitively taxing tasks, such as the task in the current investigation. While initial recordings of PBR were in the range of "normal," change over the course of time demonstrates sensitivity of improvements in the cortical network. For seven of the eight participants, we see an increase in background rhythm, suggesting their resting frequency was lowered following injury. This is consistent with findings of McCrea and colleagues, who saw recovery over the course of a few days. It is of note that in the current study, recordings were made several weeks post injury and there was still evidence of improvement several months later. This is contrary to McCrea's findings of resolved EEG patterns 45 days post-injury [30]. It is of note that the one participant who did not demonstrate a change in PBR is the one who had the first visit two months out of concussion (versus within two weeks for the majority of other participants). Taken together, this suggests there may be an interval in which detection is possible, but also provides evidence that the acute state of symptomatic concussion is likely beyond the initial 48 hours post-injury and detection of change is possible outside of 45 days. As there is resolution of PBR, but still residual differences in

frequency distribution of activity during the cognitively demanding task, it is of interest to discern if this indicates the likelihood or possibility for continued issues.

It is also the case that the EEG measures elicited during the cognitively taxing speech task are more sensitive for distinguishing concussed participants from healthy controls than are the more coarse-grained behavioral measures alone (e.g. accuracy). This finding would not be attainable from fMRI or other imaging that does not provide temporal resolution. Utilizing a DFA, EEG metrics are selected to successfully separate individuals with concussion from healthy individuals over seemingly robust behavioral measures. Behavioral performance was not sensitive enough to discern the difference during acute injury. Overall, there is evidence of a change in neurophysiology over time, but also lasting neurophysiological effects that remain after concussion resolves.

Further research is necessary to clarify electrophysiological patterns post-concussion, as related to recovery, before implementation in the clinical setting with individual participants; however, this study offers potential methodological concerns and cautions as well as promise for the sensitivity of electrophysiological changes to injury that result from concussion. The limitations of this study include the small number of individuals with concussion who participated and the small number of healthy control individuals who returned for follow up visits. Larger sample sizes will help validate the clinical utility of these findings and larger samples of control listeners will allow for a robust assessment of sensitivity and specificity to changes over time.

Given these findings, there is a strong foundation on which to lay new research questions. For instance: What is the threshold of change for an induced speech potential across sessions that corresponds to a meaningful shift in processing? What are the

constellations of neurophysiology measures that identify the need for intervention? Or suggest a greater vulnerability for repeat concussion? Is a discrepancy between measures of global network efficiency and task-related measurements indicative of continued deficits? Further research will focus on applying our understanding of physiological recovery following concussion, as seen during cognitively demanding tasks. It is essential to examine individual patterns of performance and critical to recognize that simple tasks may not allow for demonstration of residual deficits; this is paramount for developing methods to protect athletes and other individuals from future injury and identifying the need for cognitive-rehabilitation.

Table 3

Participant demographic information, and predominant background rhythm (PBR) at first visit (acute concussion) second visit (clinical recovery).

Participant	**Age**	**Date of Concussion**	**Time b/w injury & first visit**	**Months b/w first & second**	**Etiology of Injury**	**PBR 1st Visit**	**PBR 2nd Visit**
WA	31	6/24/12	36 days	3	Golf club	11.2	**11.72**
MR	16	10/12/12	60 days	6	Soccer	9.5	9.5
LW	16	8/31/12	14 days	5	Hockey	10.5	**11**
MG	19	10/15/13	8 days	4	Rugby	10	**11**

NG	24	10/12/13	22 days	4	Hockey	10.25	**11**
AO	18	9/1/13	15 days	6	Lacrosse	8.79	**9.0**
AF	15	10/31/2013	10 days	4	Horseplay	10.25	**11**
JH	20	10/19/2013	17 days	4	Horseplay	10	**11**

Table 4
Individual ERP parameters, and behavioral data for 6-channel responses, for each concussion patient, at first and second visits. RT and duration are reported in ms; power and frequency spectra values are reported in microvolts^2. Red indicates a change that is lower (in accuracy, latency, or duration) or later (in latency); green indicates improvements in accuracy or earlier latency.

	AF		**AO**		**JH**		**LW**	
Visit	***1***	***2***	***1***	***2***	***1***	***2***	***1***	***2***
% Correct	79%	**62%**	84%	**87%**	92%	**92%**	24%	**77%**
Avg. RT	597.21	**616.39**	838.50	**855.86**	782.27	**524.26**	503.75	**490.32**
SD of RT	445.59	**530.15**	301.92	**339.66**	440.65	**413.71**	280.45	**317.48**
RT Corr.	631.72	**688.90**	796.89	**842.50**	776.46	**523.22**	619.25	**458.85**
ERP Onset	312	**200**	218	**296**	329	**306**	307	**204**
Duration	61	**41**	43	**19**	24	**54**	48	**47**
Power	0.424	**0.395**	0.948	**0.499**	1.01	**0.861**	0.558	**0.365**
Rel. Power	1.0	0.468	1.73	0.7	2.66	1.25	1.39	1.12
Localization	Inferior Frontal	Medial Frontal	Sub-cortical	Inferior Frontal	Inferior Temp.	Inferior Temp.	Sub-cortical	Middle Frontal
PBR	10.25	**11**	8.79	**9**	10	**11**	10.5	**11**
6_Delta	0.0284	0.0174	0.0853	0.0175	0.0305	0.0314	0.0310	0.0247
6_Theta	0.0141	0.0107	0.0529	0.0187	0.0313	0.0246	0.0411	0.0228
6_Alpha	0.0071	0.0057	0.0404	0.0153	0.0309	0.0185	0.0257	0.0197
6_Beta	0.0049	0.0041	0.0136	0.0052	0.0086	0.0079	0.01556	0.0079

MG	**NG**	**MR**	**WA**

1	*2*	*1*	*2*	*1*	*2*	*1*	*2*	**Visit**
92%	**88%**	77%	**91%**	70%	**78%**	72%	**86%**	**% Correct**
685.62	**671.18**	623.43	**792.76**	458.53	**600.51**	1065.7	**756.53**	**Avg. RT**
379.95	**434.77**	557.15	**464.31**	358.14	**518.40**	563.65	**378.03**	**SD of RT**
671.46	**687.41**	718.67	**814.05**	404.05	**482.74**	946.40	**718.36**	**RT Corr.**
209	**219**	309	**302**	174	**185**	372	**338**	**ERP Onset**
20	**21**	48	**48**	20	**30**	20	**23**	**Duration**
0.369	**0.301**	0.157	**0.537**	1.16	**0.7**	1.07	**0.762**	**Power**
0.71	0.62	0.201	1.18	1.69	0.83	1.4	1.4	**Rel. Power**
Middle Occ.	Inf.Parietal	Middle Frontal	Middle Frontal	Sub-cortical	Medial Frontal	Sub-cortical	Sub-cortical	**CURRY Localization**
10	**11**	10.25	**11**	9.5	**9.5**	11.2	**11.72**	**PBR**
0.00538	0.01754	0.01880	0.02460	0.06357	0.02616	0.07307	0.04610	**6_Delta**
0.00489	0.01260	0.01818	0.01806	0.06641	0.03021	0.05962	0.05125	**6_Theta**
0.00496	0.01154	0.01348	0.01545	0.06387	0.03611	0.04783	0.03765	**6_Alpha**
0.00177	0.00449	0.00620	0.00504	0.02744	0.01479	0.03466	0.02012	**6_Beta**

Table 5

Individual ERP parameters, and behavioral data for 16-channel responses, for each concussion patient, at first and second visits.

	AF		**AO**		**JH**		**LW**	
Visit	***1***	***2***	***1***	***2***	***1***	***2***	***1***	***2***
% Correct	0.82	0.75	0.95	0.96	0.94	0.98	0.13	0.89
Avg. RT	526.99	489.67	728.32	844.91	687.48	415.20	463.59	584.04
SD of RT	434.93	483.44	275.83	343.77	377.19	285.38	155.95	526.36
Avg. RT Corr.	599.09	574.26	722.99	843.90	679.01	422.84	547.29	451.87
ERP Onset	284	233	255	230	311	291	214	203
Duration	76	24	16	26	33	19	31	53
Amplitude	0.48	0.22	0.72	0.20	0.69	0.44	0.62	0.34
Rel. Power	0.85	0.86	1.65	0.40	2.19	1.19	0.85	0.66
CURRY Localization	Sub-cortical	Medial Frontal	Post central	Medial Frontal	Middle Temp.	Inferior Frontal	Sub-cortical	Inferior Frontal
6_Delta	0.0315	0.0143	0.0888	0.0124	0.0281	0.0324	0.0268	0.0314
6_Theta	0.0121	0.0071	0.0509	0.0155	0.0310	0.0220	0.0297	0.0231
6_Alpha	0.0064	0.0050	0.0429	0.0097	0.0315	0.0212	0.0193	0.0197
6_Beta	0.0043	0.0031	0.0122	0.0037	0.0078	0.0085	0.0121	0.0081

MG		**NG**		**MR**		**WA**		
1	***2***	***1***	***2***	***1***	***2***	***1***	***2***	**Visit**
0.95	0.95	0.75	0.93	0.80	0.84	0.88	0.91	**% Correct**
668.95	587.67	487.62	709.03	410.11	637.40	947.94	619.20	**Avg. RT**
365.79	336.36	532.61	458.91	313.44	606.46	492.03	380.55	**SD of RT**
663.09	591.75	524.63	733.44	368.59	464.29	864.37	579.69	**Avg. RT Corr.**
199	176	289	237	283	137	246	200	**ERP Onset**
35	49	71	24	17	28	48	37	**Duration**
0.42	0.17	0.14	0.34	1.72	0.80	1.55	0.80	**Power**
1.10	0.39	0.49	1.01	1.77	2.01	1.78	2.34	Relative Power
Middle Occ.	Middle Frontal	Sup. Frontal	Pre central	Sub-cortical	Medial Frontal	Sub-cortical	Sub-cortical	**CURRY Localization**
0.0195	0.01602	0.00519	**0.02016**	0.08489	**0.19839**	0.10297	0.0562	**6_Delta**
0.0183	0.01257	0.00440	**0.01691**	0.06682	**0.18683**	0.07138	0.0514	**6_Theta**
0.0138	0.01033	0.00436	**0.01214**	0.06934	**0.11155**	0.05466	0.0379	**6_Alpha**
0.0063	0.00493	0.00170	**0.00466**	0.02841	**0.08672**	0.03659	0.0205	**6_Beta**

Table 6

Correlations (Pearson's r) between frequency spectra values obtained from participants with concussion across visits 1 and 2 (n = 8) and control listeners for first and second visits (n = 2).

	Overall	**Delta**	**Theta**	**Alpha**	**Beta**
Concussion	0.73	0.35	0.73	0.87	0.95
Control	.95	0.93	0.98	0.95	0.99

Table 7

Mean and standard deviation of performance in each level of intelligibility for concussion participants at first and second (n = 8) and for the cohort of younger, healthy listeners (n = 24).

Visit	Intelligibility	Mean	Std. Deviation
First	***16 Channel***	.78	.272
	6 Channel	.74	.217
Second	***16 Channel***	.90	.075
	6 Channel	.83	.100
Healthy Listeners	***16 Channel***	.90	.077
	6 Channel	.78	.09

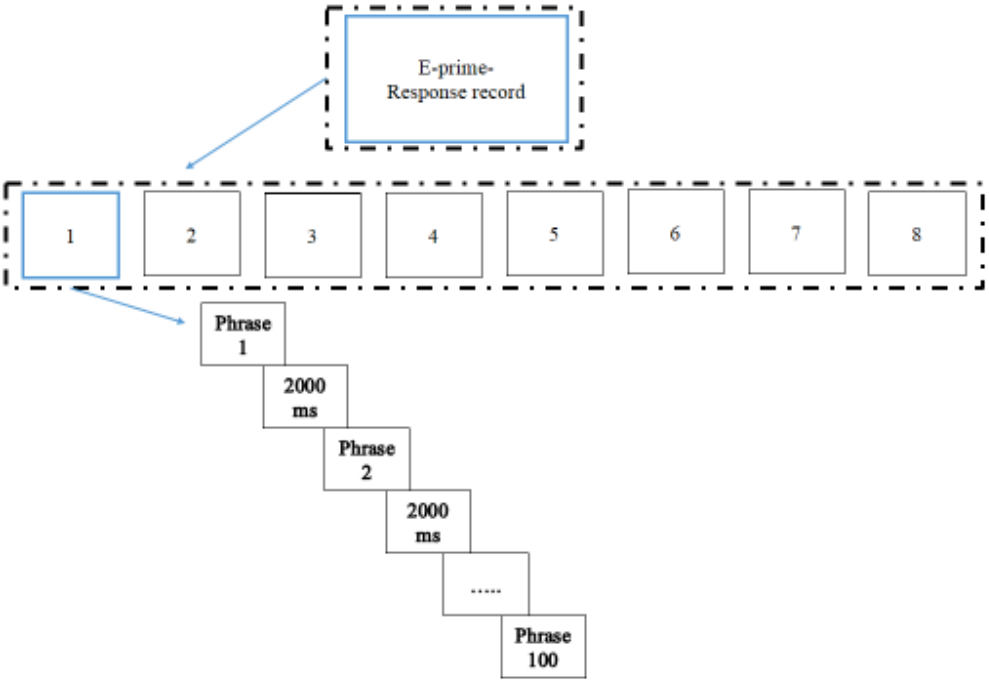


Figure 4

Block diagram of protocol; viewed as a nested representation of blocks and stimuli. The E-prime program has 8 blocks, each of which contains 100 phrases, with a 2000ms interstimulus interval between each phrase.

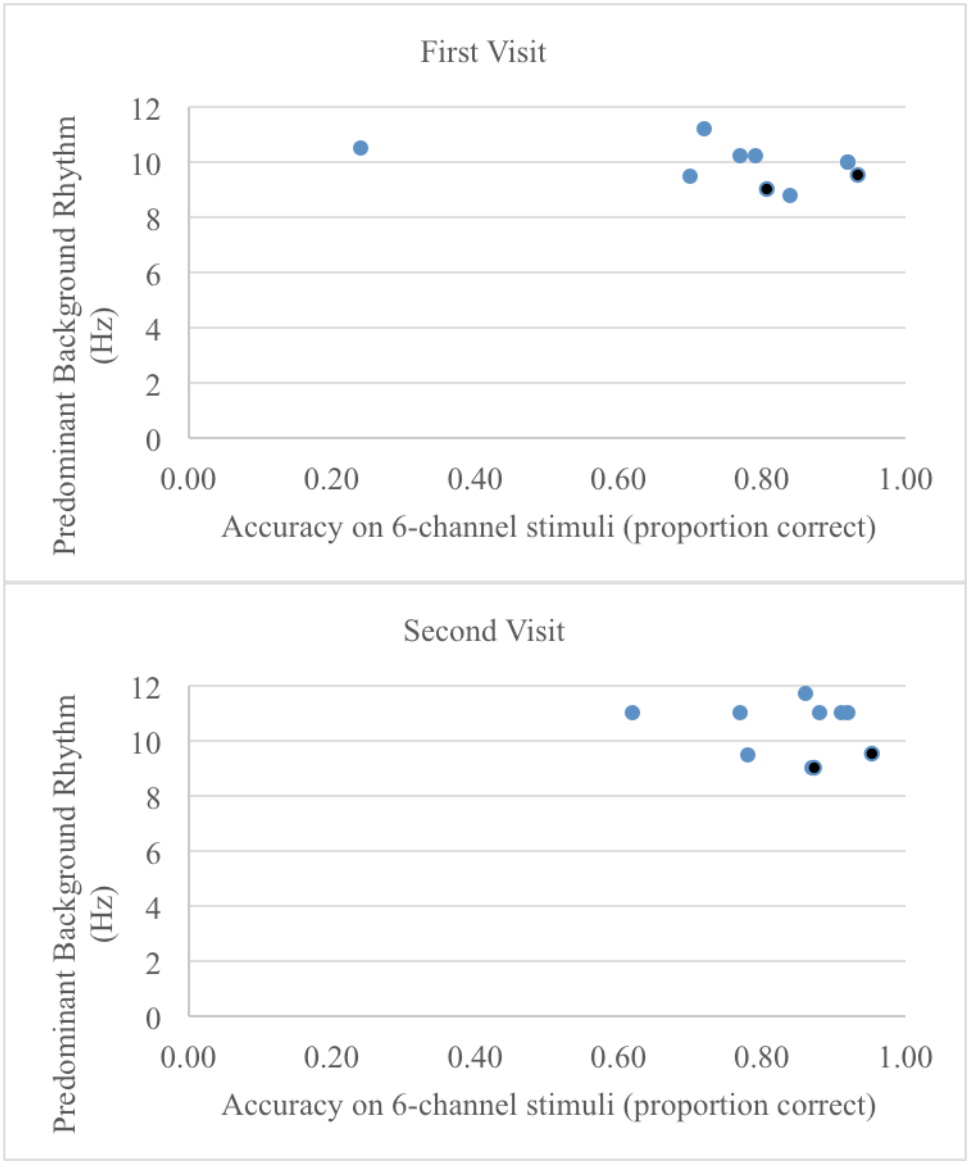


Figure 5

Top: Scatterplot of Predominant Background Rhythm (PBR; Hz) during an awake-relaxed recording, against accuracy of responses to 6-channel stimuli in the first visit. Bottom: Scatterplot of Predominant Background Rhythm (PBR; Hz) during an awake-relaxed recording, against accuracy of responses to 6-channel stimuli in the second visit (clinical recovery).

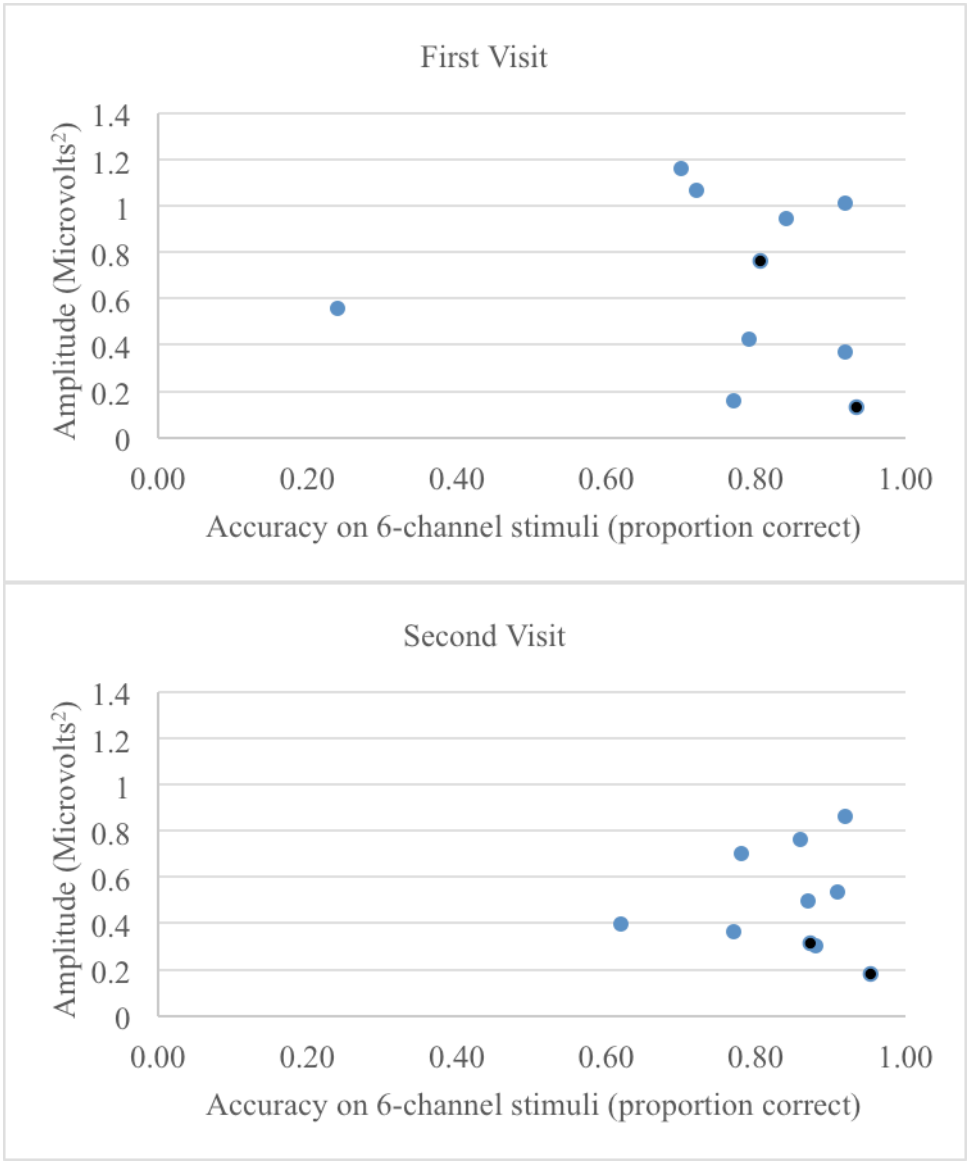


Figure 6

Top: Scatterplot of early ERP peak amplitude (microvolts^2) against accuracy of responses to 6-channel stimuli in the first visit (acute injury).

Bottom: Scatterplot of early ERP peak amplitude (microvolts^2) against accuracy of responses to 6-channel stimuli in the second visit (clinical recovery).

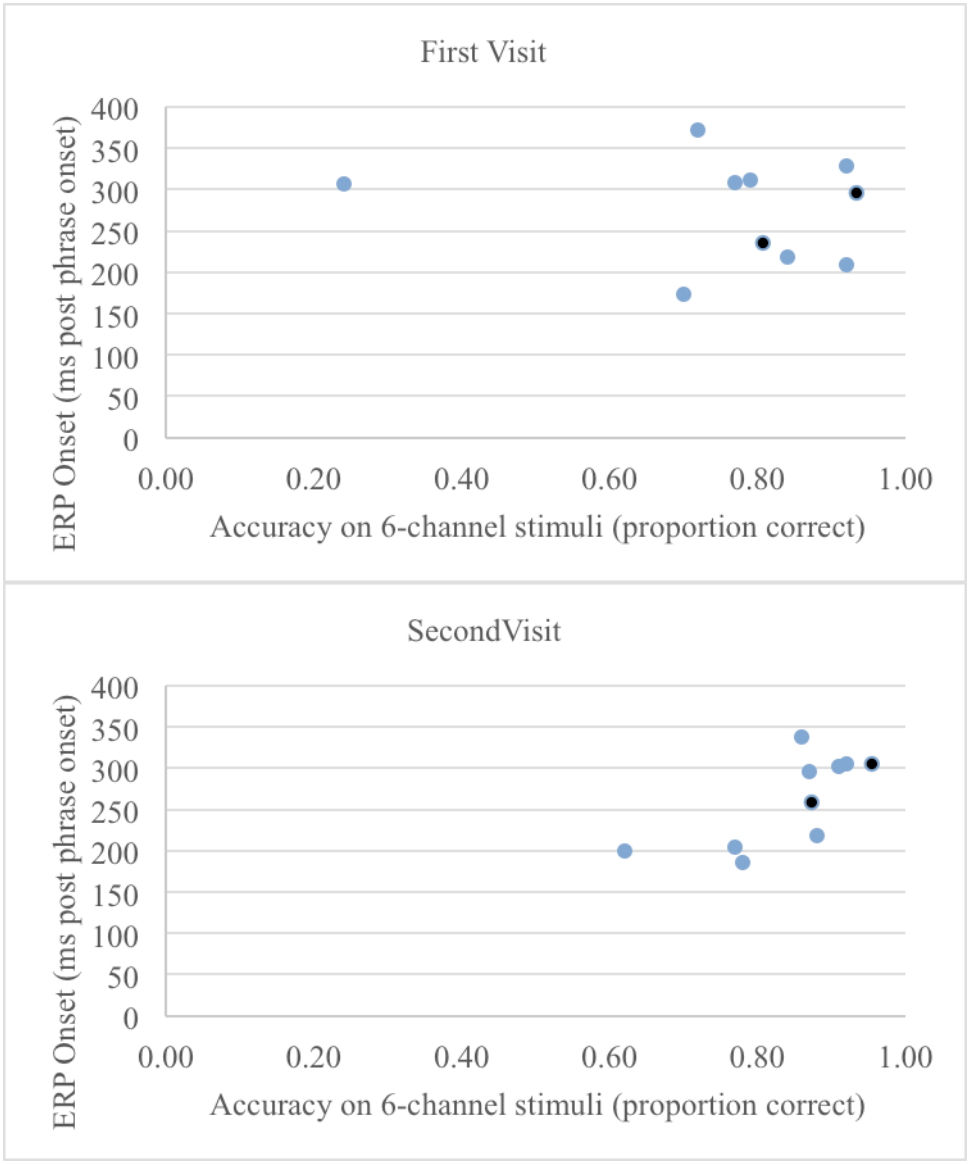


Figure 7

Top: Scatterplot of early ERP onset (ms) against accuracy of responses to 6-channel stimuli in the first visit (acute injury).

Bottom: Scatterplot of early ERP onset (ms) against accuracy of responses to 6-channel stimuli in the second visit (clinical recovery).

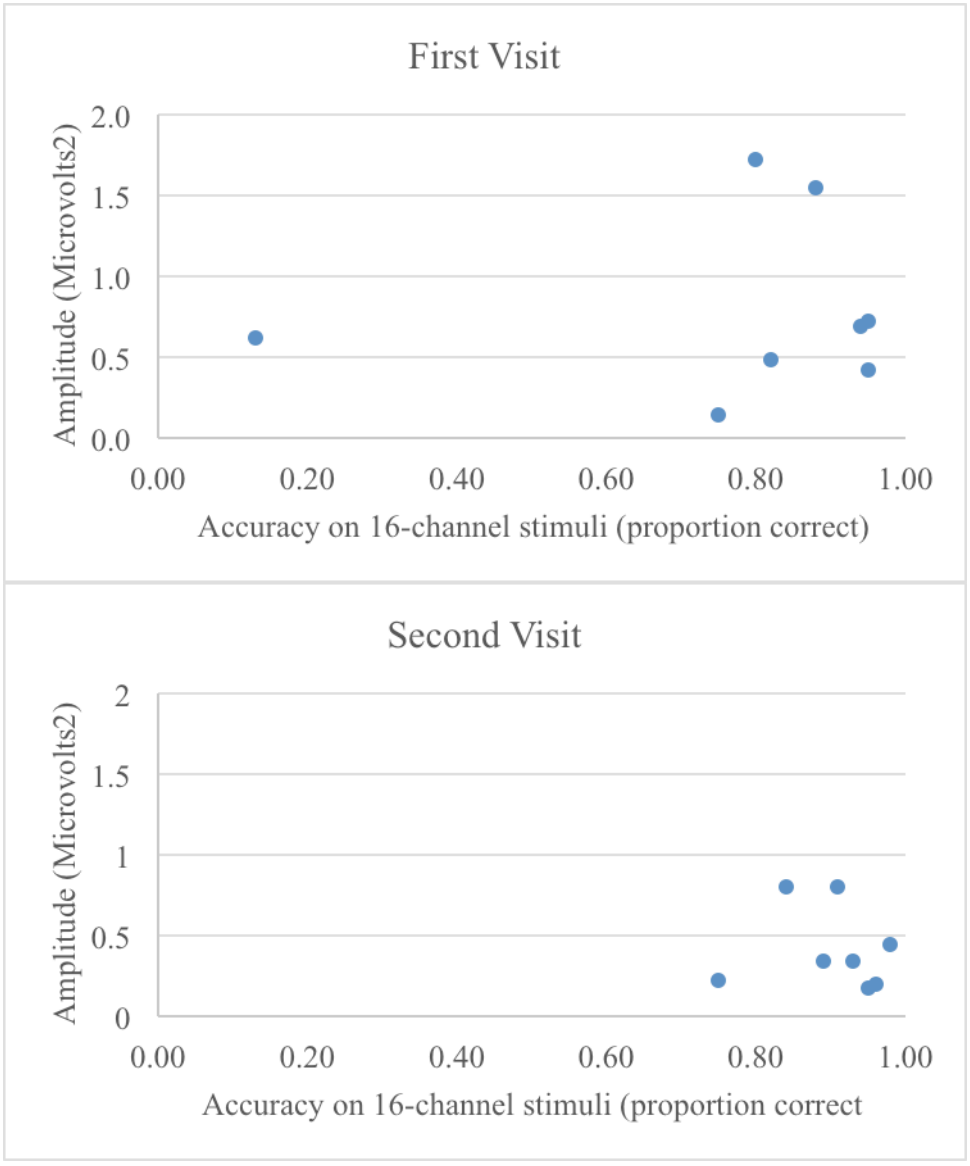


Figure 8

Top: Scatterplot of early ERP peak amplitude (microvolts^2) against accuracy of responses to16-channel stimuli in the first visit (acute injury).

Bottom: Scatterplot of early ERP peak amplitude (microvolts^2) against accuracy of responses to 16-channel stimuli in the second visit (clinical recovery).

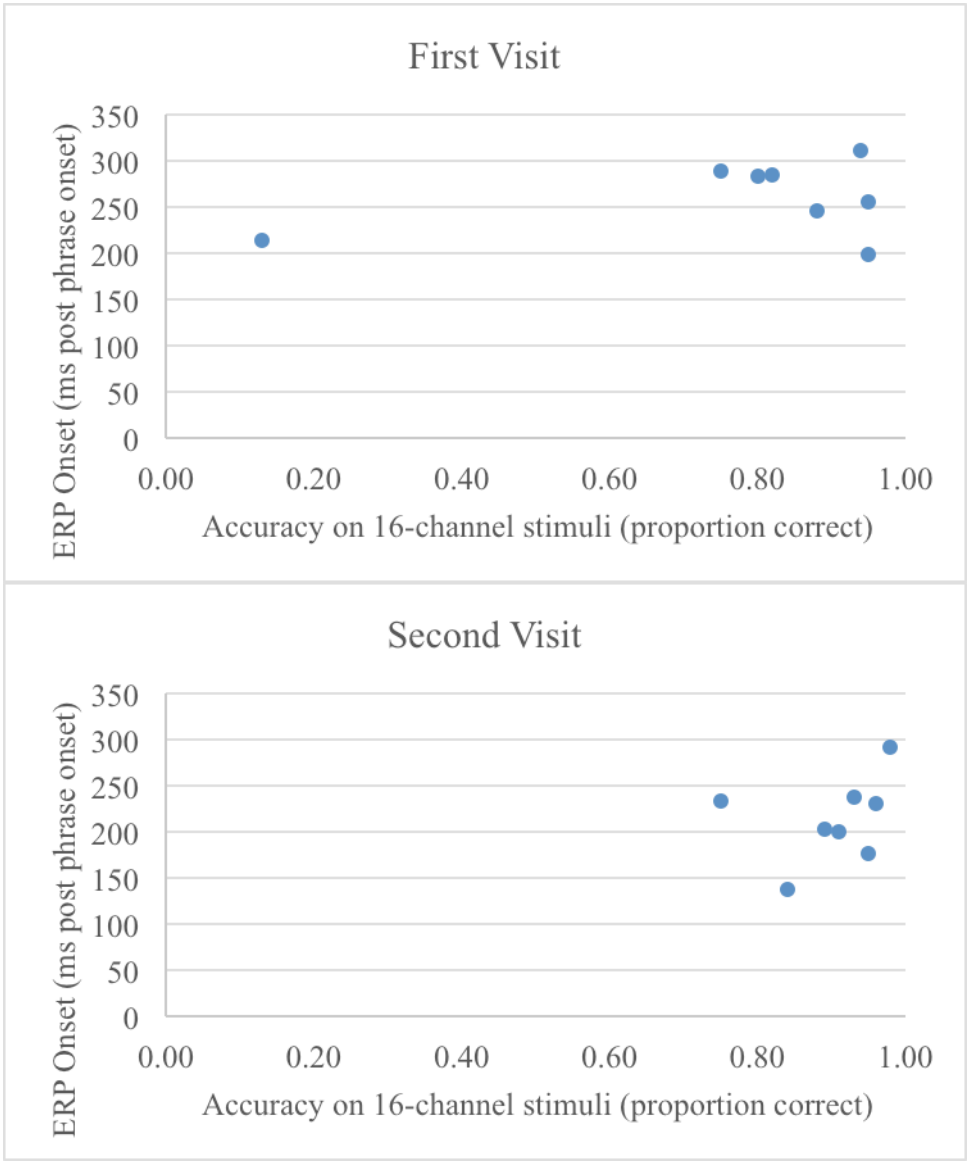


Figure 9

Top: Scatterplot of early ERP onset (ms) against accuracy of responses to 16-channel stimuli in the first visit (acute injury).

Bottom: Scatterplot of early ERP onset (ms) against accuracy of responses to 16-channel stimuli in the second visit (clinical recovery).

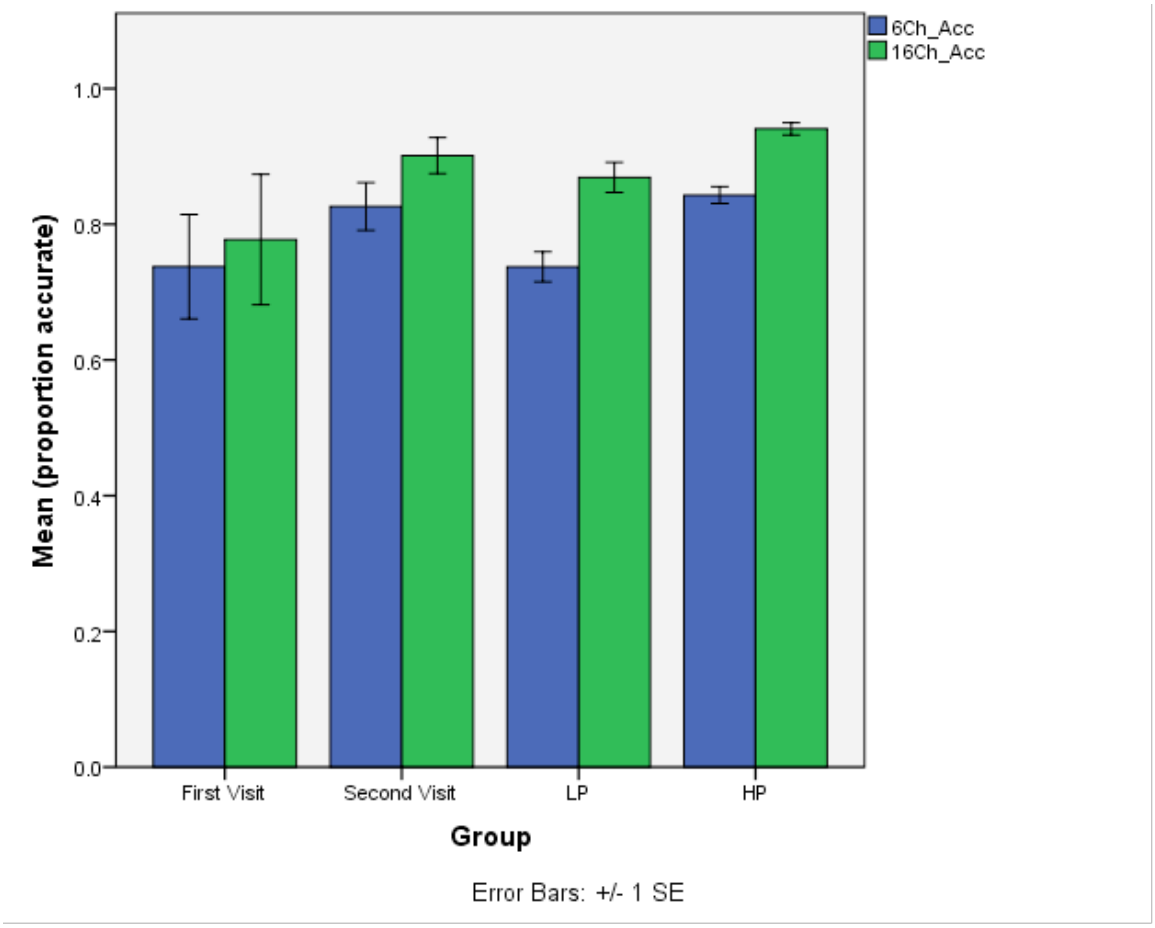
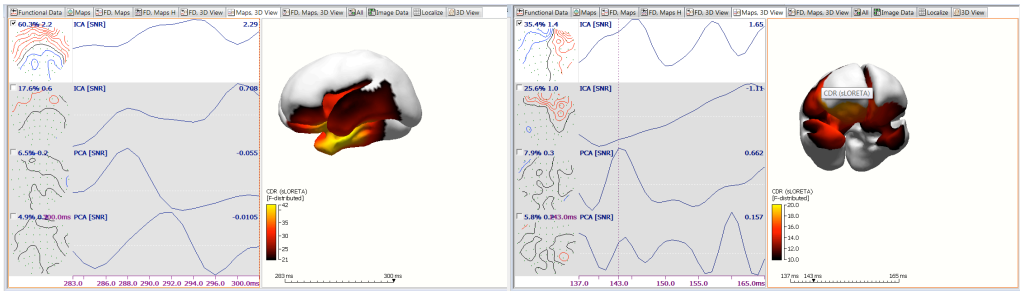
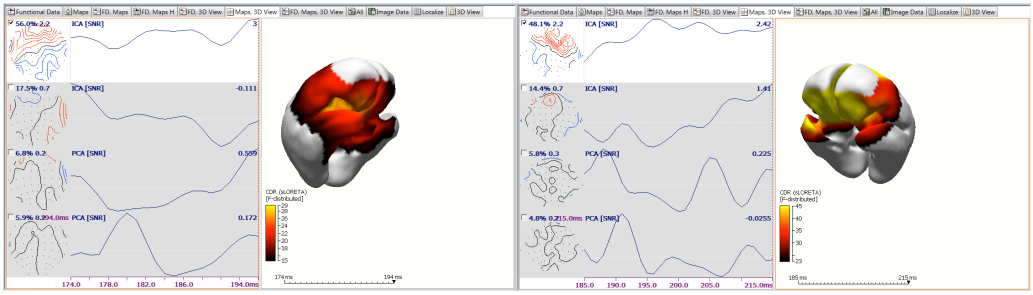


Figure 10

Mean intelligibility on the sentence verification task for 1) participants with concussion (first visit), 2) patients at second visit, 3) healthy, younger listeners from a previous investigation who performed 3) poorer than expected (LP) or 4) performed well (HP).



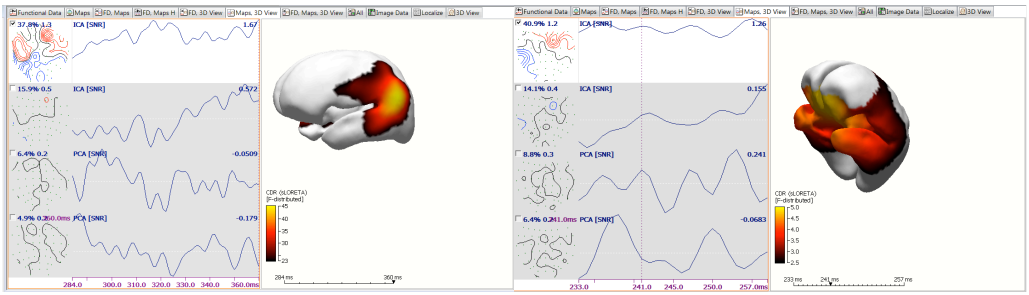
Above: 16 channel, first (left) and second (right) visit ICA components and localizations



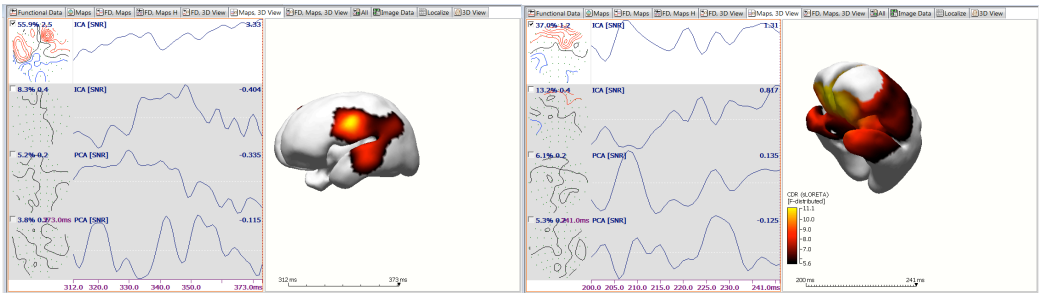
Above: 6- channel, first (left) and second (right) visit ICA components and localizations

Figure 11

Localizations of EPRs for MR. Orientations of cortex are adjusted to allow for visibility of maximal activity.



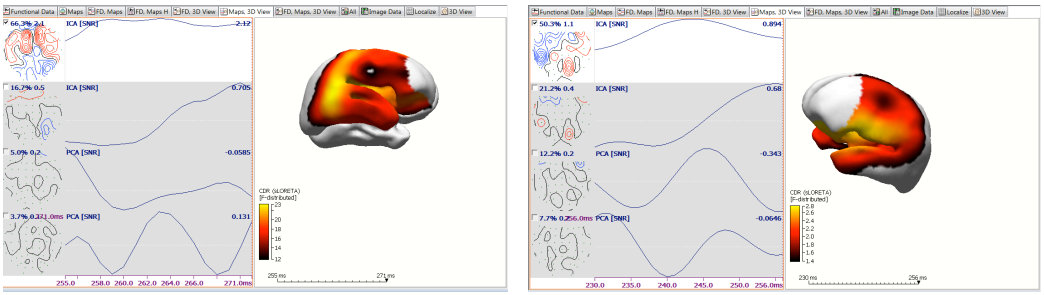
Above: 16- channel, first (left) and second (right) visit ICA components and localizations



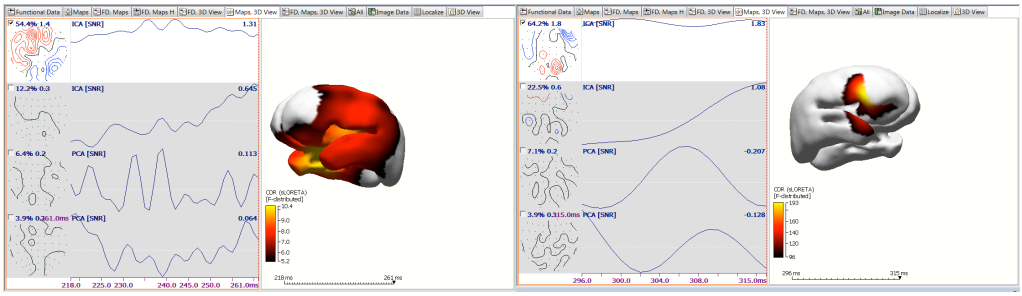
Above: 6- channel, first (left) and second (right) visit ICA components and localizations

Figure 12

Localizations of EPRs for AF. Orientations of cortex are adjusted to allow for visibility of maximal activity.



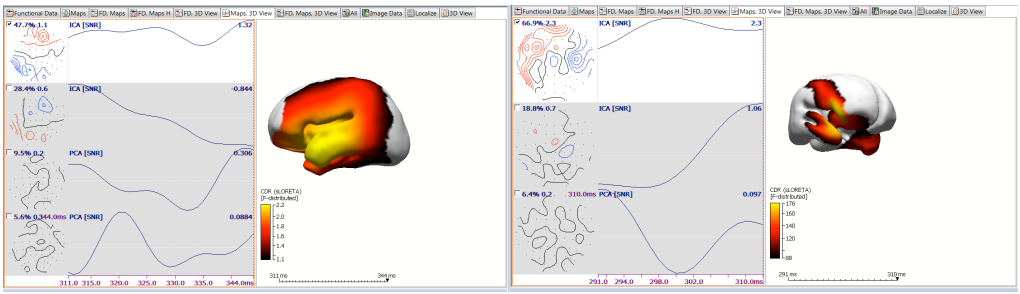
Above: 16 channel, first (left) and second (right) visit ICA components and localizations



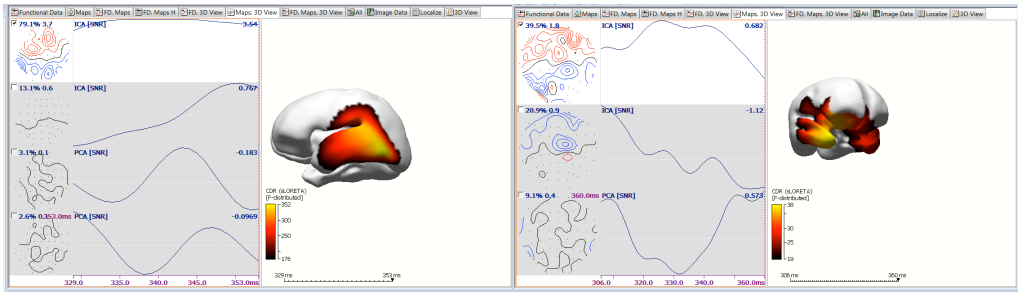
Above: 6 channel, first (left) and second (right) visit ICA components and localizations

Figure 13

Localizations of EPRs for AO. Orientations of cortex are adjusted to allow for visibility of maximal activity.



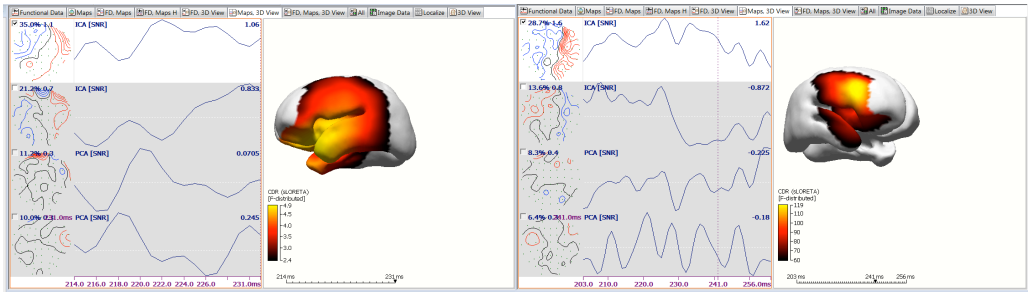
Above: 16 channel, first (left) and second (right) visit ICA components and localizations



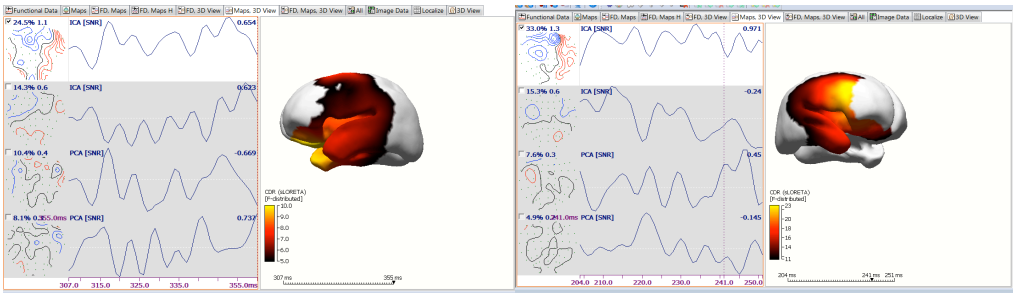
Above: 6 channel, first (left) and second (right) visit ICA components and localizations

Figure 14

Localizations of EPRs for JH. Orientations of cortex are adjusted to allow for visibility of maximal activity.



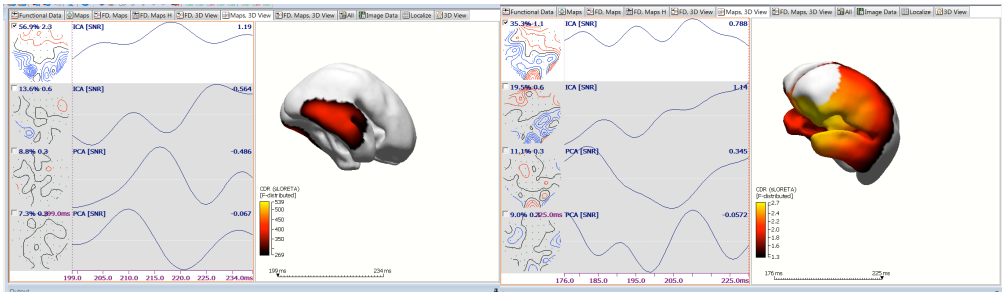
Above: 16 channel, first (left) and second (right) visit ICA components and localizations



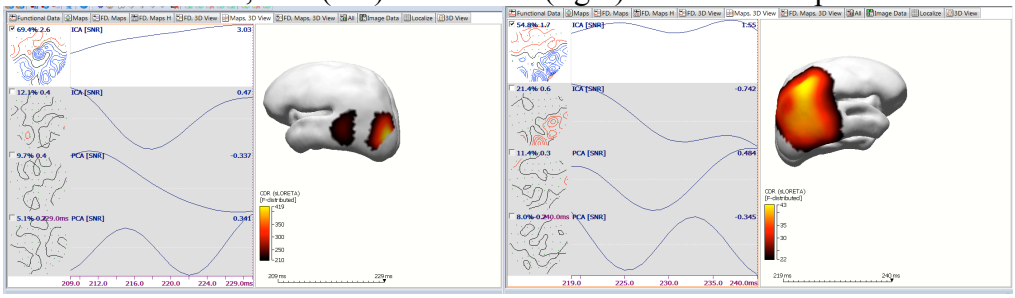
Above: 6 channel, first (left) and second (right) visit ICA components and localizations

Figure 15

Localizations of EPRs for LW. Orientations of cortex are adjusted to allow for visibility of maximal activity.



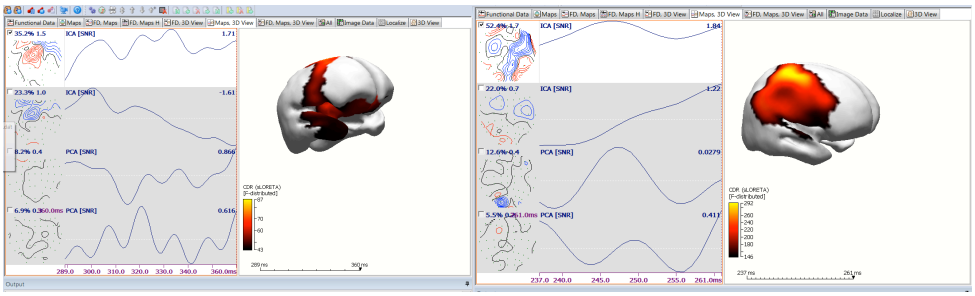
Above: 16 channel, first (left) and second (right) visit ICA components and localizations



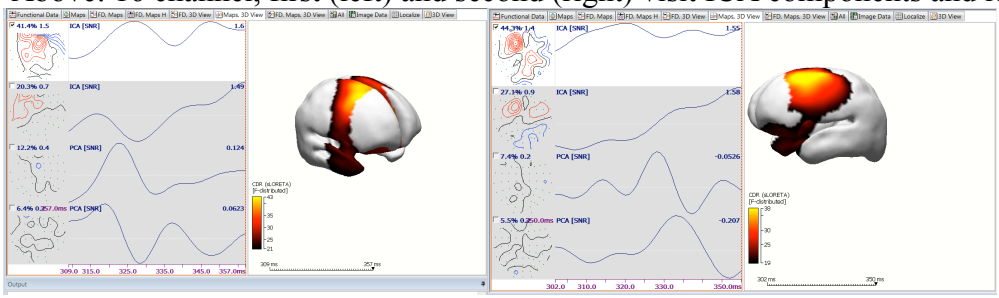
Above: 6 channel, first (left) and second (right) visit ICA components and localizations

Figure 16

Localizations of EPRs for MG. Orientations of cortex are adjusted to allow for visibility of maximal activity.



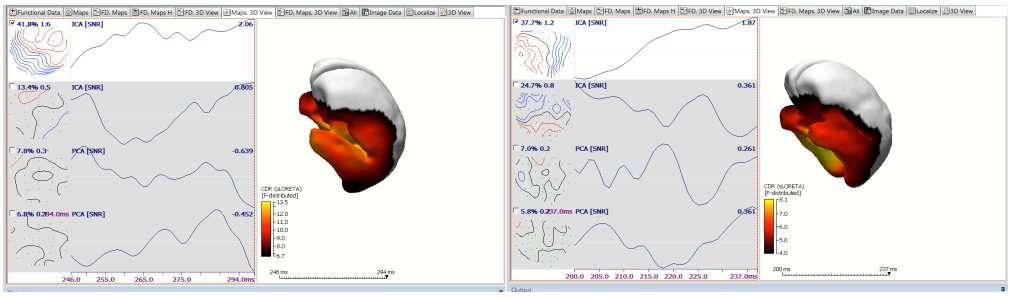
Above: 16 channel, first (left) and second (right) visit ICA components and localizations



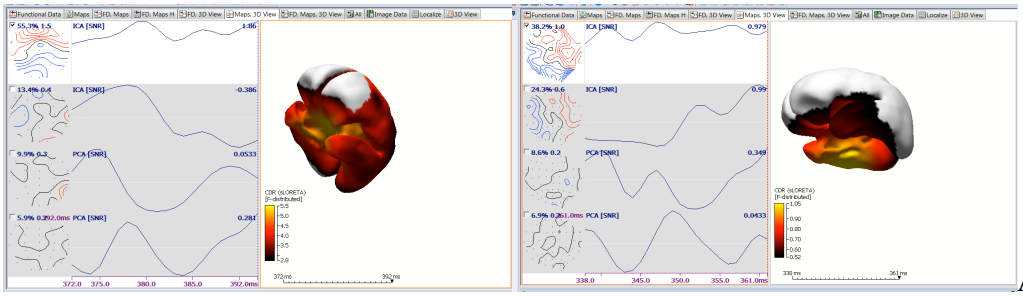
Above: 6 channel, first (left) and second (right) visit ICA components and localizations

Figure 17

Localizations of EPRs for NG. Orientations of cortex are adjusted to allow for visibility of maximal activity.



Above: 16 channel, first (left) and second (right) visit ICA components and localizations



Above: 6 channel, first (left) and second (right) visit ICA components and localizations

Figure 18

Localizations of EPRs for WA. Orientations of cortex are adjusted to allow for visibility of maximal activity.

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