Hemispheric Dominance of Language Comprehension in Subacute Stroke Patients

COGNITIVE NEUROSCIENCE MASTER THESIS

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Abstract

The field of cognitive neuroscience has benefited considerably from single- and multiple subject analyses, as well as qualitative methods. The current study has performed a multiple subject analysis alongside a group analysis and discussed the data in a quantitative and qualitative manner. Ten stroke patients and four healthy controls performed a context-driven picture naming task while their brain activity was recorded using electroencephalography. They listened to audio recordings of sentences that were played in normal temporal order, in one condition, and in a reversed temporal order in another. The comparison of the two resulted is a measure of language comprehension. Using a cluster-based permutation analysis after a frequency analysis, no significant results were found. Nonetheless, some descriptive tendencies were found: A higher electrophysiological power around 10Hz in the normal condition compared to the reversed condition, accounted to production-based prediction, and a higher electrophysiological power in the alpha (8-12Hz), interpreted as the focus on an auditory stimulus, and beta (15-25Hz) frequency range, interpreted as auditory stimulus novelty. The findings indicate an added value of qualitative- and multiple subject analyses when performed collectively with quantitative- and group analyses.

Contents

1 Introduction

In the history of cognitive neuroscience, many groundbreaking findings came about by single- or multiple subject analyses. Patients with lesions, for instance, Tan (Selnes & Hillis, 2000) or H.M. (Squire, 2009), have left a lasting mark on the field. However, the ubiquity of large scale group-level studies have overshadowed the current contributions of these methods. Rosenbaum et al., 2014 demonstrated that single or multiple subject studies advance the field of cognitive neuroscience. According to them, its function is two-fold, on the one hand they could threaten accepted conclusions and on the other they could generate new hypotheses. They focused on the hippocampus and described recent case studies that link the region to episodic memory and recollection. In general, stroke research is benefited by single- or multiple subject analyses (Jefferies & Lambon Ralph, 2006). The specific and unique stroke pattern of each patient will not be considered when grouped, therefore leading to a loss of valuable information. On top of this, there is a distinction between quantitative and qualitative methods. In quantitative methods the researcher only discusses the outcomes based on the statistical tests, whereas qualitative methods allow for the researcher to look at the data and discern information based on that. Like single-and multiple subject analyses, qualitative methods are beneficial for stroke data (Beis et al., 2004; Thompson-Butel et al., 2019). Statistical significance is hard to reach for a very heterogeneous sample, therefore, qualitative methods allow the researcher to find patters of effect in the stroke data that lead to new hypotheses. The current study touched upon language comprehension and in which hemisphere that function is predominantly processed in sub-acute stroke patients. It will demonstrate the value of additional individual analysis and qualitative analysis for stroke patient data. The topics of aphasia, plasticity and comprehension are introduced below.

1.1 Aphasia

Most research on stroke patients for brain function localisation was conducted using functional magnetic resonance imaging (fMRI) (Li et al., 2022; Sreedharan et al., 2020), using a stable blood oxygen level dependent (BOLD) response curve in analyses. This method is an indirect measure of brain activity and it is still debated what the BOLD response actually measures (Ekstrom, 2010) . Particularly for stroke patients, the fMRI signal requires appropriate analysis. Using the BOLD response, the conventional method, could result in invalid conclusions on the grounds that their BOLD response was lower in affected areas, leading to wrong conclusions about location and activity (Mazzetto-Betti et al., 2010). Other papers also questioned the validity of conclusions drawn with the conventional fMRI paradigm for stroke patient data (Geranmayeh et al., 2015; Kim et al., 2005; Murata et al.,

2006). Veldsman et al. (2015) explained that a set of assumptions made for the BOLD-fMRI analysis is no longer met in stroke patients: Perilesional ischemic changes, remodeling in regions distant from the stroke damage and diffuse perfusion changes all influence the validity of the BOLD analysis negatively. On the other hand, electrophysiological methods offer great potential to the topic of neuroplasticity of language after stroke (Meechan et al., 2021). They are direct and not dependent on a response that might be altered after stroke (Traut et al., 2019). Nevertheless, fMRI should not be put aside, for it is beneficial to look at the different methods as measuring different things.

Language is mainly a left-lateralized brain function. Therefore, most aphasia research focused on that hemisphere, disregarding right unilateral lesioned patients. However, there were recorded cases of aphasia due to right-hemisphere stroke, either demonstrating a nuance in the assumption of language being solely left-lateralized, or a different mechanism that allows this result (Dewarrat et al., 2009). On top of this, the right hemisphere could provide a valuable condition in the analysis. Normally left hemisphere patients would be compared to healthy controls to find a certain effect. However, one cannot be certain that the effect is actually due to the specific stroke profile. The possibility that the effect is caused by the fundamental presence of the lesion is never resolved. On top of that, with age, language functions have been found to be based on more bilateral networks (Tyler et al., 2010). Thus, the assumption of left-lateralized language processing could be wrong for a stroke patient sample that tend to be older. Right hemisphere patients could provide evidence for whether a laterality shift is due to the initial bilateral network or due to neuroplasticity. Thus, the inclusion of right hemisphere data in analyses could improve the validity of the conclusions made.

1.2 Plasticity

Little is known about longitudinal changes of language function in the brain and the research that is available is based on fMRI. Saur et al., 2006 have demonstrated that the brain, after an aphasia inducing stroke, often exhibits a specific pattern of functional reorganization for language. They used fMRI to measure brain activity during an auditory comprehension task. According to their theory, language is a predominantly left-lateralized function, pre-morbidly, which means that more brain activity occurs in the left hemisphere compared to the right hemisphere during language tasks. Immediately after stroke, the acute phase (i.e. the first 2 weeks after stroke), the unaffected language areas in the left hemisphere show a reduced activation. In the subacute phase (i.e. 3-11 weeks post-stroke), a high increase in activation occurs, particularly in right hemisphere areas that are homologous to the language areas in the left hemisphere. In the chronic phase (i.e. more than 11 weeks post-stroke) the language processing returns to pre-morbid intensity and occurs mostly in the left

hemisphere once more.

A proposed explanation for this pattern of reorganisation is interhemispheric inhibition and collateral inhibition (Heiss & Thiel, 2006; Kinsbourne, 1998; Murase et al., 2004). Interhemispheric inhibition states that, initially, both hemispheres inhibit each other in the homologous areas. When a lesion occurs, that area is no longer able to inhibit its contralateral counterpart, leading to an increase in activation there. When more time has passed, the brain can adapt to the new situation and the perilesional areas can be recruited for the processing of the relevant function, resulting in the normalized activity in the initial hemisphere. Simultaneously collateral inhibition states that when an brain area is active, the surrounding areas are inhibited. Thus, after stroke, the surrounding areas will be activated more since they are no longer inhibited. Heiss and Thiel (2006) looked into the effects of the two inhibition types on aphasia outcome. The best outcomes were obtained with complete reactivation of the original system in the original hemisphere. This only occurs with a minor damaged area. More limited recovery is obtained when the brain recruits perilesional areas for language processing. This can occur due to the reduction of collateral inhibition. The continuous recruitment of the contralateral hemisphere, due to less interhemispheric inhibition, results in the worst outcome for language function. However, in instances of steady developing brain damage recruiting the right hemisphere can produce highly functional language processing.

1.3 Comprehension

Comprehension needs to be isolated for one to be able to study it. This isolation could be achieved by a simple subtraction of two EEG conditions; A baseline deducted from the presentation of normal speech. However, previous research showed multiple options for a baseline, for instance, pseudowords (Binder et al., 1994), a foreign language (Perani et al., 1996), reversed speech (Price et al., 1996) and signal-correlated noise (Rodd et al., 2005). The goal is to create a condition that overlaps with the presentation of normal speech as much as possible except that it cannot be comprehended. Stoppelman et al. (2013) have looked at signal-correlated noise and reversed speech. Signal-correlated noise is created by substitution of the frequency information by noise and maintaining the envelope of the original waveform, resulting in a sound fragment that maintains the onset features of speech but that lacks control over other features, for instance pitch and phonemic structure (Schroeder, 1968). Reversed speech is created by simply presenting a speech recording backwards. The result is unintelligible but still contains some of the factors of normal speech, like the presence of separate words. It is important to note that reversed speech has a different temporal pattern than normal speech. Where normal speech often starts with a fast plosive and ends with a slow decay

the opposite is true in reversed speech. Thus, apart from the absence of meaning in this baseline condition, there is also a difference in the processing of the temporal features (Narain, 2003). In their comparison of the two possible baselines, Stoppelman et al. (2013) concluded that the signal-correlated noise baseline was preferred over reversed speech. On the grounds that they were able to find more robust and higher activation during language tasks in the left inferior frontal gyrus by using signal correlated noise. Importantly, the left inferior frontal gyrus was found in some cases with the reversed speech baseline, but only when a semantic task was used. For stroke patients, there are some additional considerations for the baseline selection. Reversed speech has been found to sound ”bizarre or alien-sounding”(Galbraith et al., 2004), whereas signal-correlated noise, with a preserved envelope of normal speech, maintains the rhythm, tempo and syllabicity of the original fragment. Since people with aphasia can have trouble with speech comprehension, a baseline that sounds very similar to normal speech might be stressful, therefore it could be argued that reversed speech is preferred for these participants.

Previous research M/EEG research on language comprehension has presented neural oscillatory power signatures in the alpha (8-12 Hz) and beta (15-25Hz) frequency bands. Wöstmann et al., 2017 reviewed M/EEG papers on speech comprehension. Neural oscillatory power is one of the results they reported on. It is calculated for different frequency bands by squaring the amplitude of the Fourier or wavelet-transform coefficients. This is done for each trial and subsequently averaged. The review reports alpha power increases when participants pay attention to an auditory stimulus relative to a pre-trial baseline. They also report a beta power increase for auditory stimulus novelty.

The production-based prediction account entails an interpretation for brain activity in language comprehension processing. Ito et al., 2016 describe in their ERP study that participants generate a production-based representation of a sentence and predict the meaning and form of the subsequent word. The activation of the production network can explain a difference in brain activation during presentation of meaningful and meaningless sentences.

1.4 Current Study

The current study looked at functional laterality of speech comprehension in stroke patients. The patients were grouped based on the hemisphere in which the stroke occurred, resulting in a left and right hemisphere group (LH and RH respectively). The third group consisted of control participants without a stroke. The comprehension was measured by comparing the electroencephalography (EEG) signal during the processing of normal and reversed speech. A laterality index was calculated for each participant for the brain activity recorded with EEG to determine to which hemi-

sphere the function of language comprehension was lateralized. The data used for this study have been collected by Msc Natascha Roos for her PhD project. She used the context-driven picture naming paradigm, a method frequently applied for electrophysiological designs in our research group (Klaus et al., 2020; Piai et al., 2020; Piai et al., 2017; Piai et al., 2014; Piai et al., 2015; Piai et al., 2018; Roos & Piai, 2020). Her data was analyzed to answer the question: What is the influence of left- versus right hemisphere unilateral subacute stroke on the electrophysiological laterality index during comprehension? The results of this study were expected to match those of earlier studies on functional plasticity after stroke; I expected the left hemisphere patients with a significant lesion in an area related to speech processing, to have a shift of comprehension processing dominance to the right hemisphere. The right hemisphere patients would remain unaffected and maintain a left hemispheric dominance for speech comprehension, which would also be found in the control group.

Not only was the data from the reversed and normal speech conditions compared between LH, RH and control groups to obtain a measure of speech comprehension, but also on an individual level. The results were quantitatively statistically analyzed and later analyzed in a qualitative manner. The findings from all perspectives were compared and combined, which could inform us on the matter whether multiple subject analysis and qualitative analysis are an enhancement in stroke data analysis compared to quantitative- and group-level analysis alone.

Table 1: Participant information

Participant	Group	Age	Gender
1	Control	69	M
2	Control	73	M
3	Left hemisphere	73	M
5	Right hemisphere	43	M
6	Control	80	M
7	Control	59	F
8	Left hemisphere	32	M
10	Right hemisphere	33	M
11	Left hemisphere	70	F
12	Right hemisphere	48	F
13	Right hemisphere	60	M
14	Right hemisphere	55	M

2 Methods

The data for this thesis have been collected for Natascha Roos's PhD project. Since her project is more extensive than the current study, only some aspects and conditions in these methods will be analyzed.

2.1 Participants

In total, 14 participants took part in the current study: eight unilateral ischemic or hemorrhagic cerebral infarction patients and four healthy controls. The two remaining participants could not be analyzed due to technical errors. Five of the patients have a right hemisphere stroke, and the three others a left hemisphere stroke (see table 1). Participant eleven was recruited after their second stroke, all other patients were analyzed for their first stroke. The patients' session was planned around 2 months post-stroke, in the subacute phase. Most patients were recruited from the RadboudUMC in Nijmegen, except for participant eleven, who was recruited from the CWZ in Nijmegen. All participants were native speakers of Dutch, pre-morbidly right handed and able to give written informed consent. The procedure includes MRI scans, so no participants with claustrophobia or large internal ferromagnetic metal parts could be included. Participants with neurological or psychiatric disorders other than the stroke or epilepsy as a consequence of the stroke were also excluded. All participants provided written informed consent and received monetary compensation for their participation.

2.2 Materials

The participants were presented with 234 trials, which were made up of spoken unfinished Dutch sentences and an image completing the sentence. The sentences were audio recordings of a female native Dutch actor. Some sentences entailed a strong constrained context (e.g. the farmer milked the ...) whereas others were unconstrained towards the following word (e.g. the child drew a ...). In one condition the sentences were altered to be played in reverse. The sentences were always short and had a simple syntactic structure. There were 117 different pictures, each shown twice in the unconstrained and constrained condition. They were simple and clear photos of mostly single objects (e.g. a Christmas tree) and a couple of more abstract concepts (e.g. a forest). Some pictures were scrambled, making them unrecognizable. The current study focuses on language comprehension and, therefore, I only analyzed the contrast between the reversed an unconstrained sentences. I analyzed 156 trials, 78 of the reversed condition and 78 of the unconstrained condition.

2.3 Procedure

Before participation, all participants signed an informed consent form. A session started with a structural MRI scan, after which a series of behavioural tasks were conducted: the Corsi Block-Tapping Task (Corsi, 1972), the Token Test (De Renzi & Vignolo, 1962), the Boston Naming Test (Kaplan et al., 1976), and the Amsterdam-Nijmegen Everyday Language Test (ANELT)(Blomert, 1992; Ruiter et al., 2011). In the current study, the Token Test and the Corsi Block-Tapping Test are included. The Token test is used to determine subtle auditory comprehension deficits that point to aphasia. We presented the participants with tokens in two shapes (circles and squares), in two sizes (big and small) and in five colors (black, white, green, red and yellow). The participant was asked to point at these tokens (e.g. tap the green square), but those questions become increasingly harder during the task (e.g. if there is a white circle, tap the green square). The Corsi task measures visuo-spatial working memory. Participants are presented with a board with scattered cubes on which the researcher taps specific sequences. After each sequence, the participant tries to repeat the sequence. The sequence becomes increasingly longer and more challenging until the participant fails. The Token test is used to determine language comprehension problems whereas the Corsi test is used as a control for aphasic patients. If the patient scores low on the Token test but high on the Corsi, it can be argued that the patient's deficit is language specific and not a broader issue.

Finally the participant performs a sentence completion task while the EEG signal is recorded. The participants were told to listen to the sentence and afterwards name a picture that was presented on computer screen. The sentences could be of three different types: unconstrained, constrained

or reversed. The pictures were either presented normally or scrambled. After each trial a fixation cross on the screen indicated a moment to blink. The 234 trials were divided in 9 blocks of 26 trials, and preceded by a familiarisation phase, to check and correct the understanding of the task by the participant. After each block there was an opportunity to take a break and continue when the participant indicated it. Each session took around three hours in total. All of the collection took place at the Donders Centre for Cognition and Neuroscience in Nijmegen.

2.4 EEG acquisition

Participants were seated in front of a PC for the sentence completion task on which the task was run using Presentation Software (Neurobehavioral Systems). EEG was recorded from 64 scalp electrodes from the Acticap system. The amplifyer used was the actiCHamp Plus by Brain Products and it sampled at 500Hz. Online referencing was done to electrode number 2 comparable to FCz in other caps. Four electrodes were placed on the face to control for movements of the eyes and mouth. To record the electrooculogram horizontally, an electrode was placed next to the left eye, which was compared to the nearest electrode in the cap on the left temple, to record it vertically an electrode was placed underneath the left eye and contrasted with the nearest forehead electrode in the cap, aligning vertically with the electrode underneath the eye. The remaining two electrodes were placed above and below the right corner of the mouth to record surface electromyogram from the orbicularis oris muscle. The electrode impedance of the ground and online reference were kept below $5k\Omega$, the rest were as low as possible given the time limit of 40 minutes for setting up the EEG cap and system. The response to the pictures was recorded with a microphone and there was an audio connection with the experimenters in the other room so that both could converse with each other when needed.

2.5 Analysis

The EEG signal was preprocessed and analyzed using Fieldtrip (Oostenveld et al., 2011) in MATLAB 2021a. In preprocessing, the trials were segmented from 0.8 seconds before sentence onset to picture onset. The trials were demeaned and corrected using a baseline from 0.8 seconds before each trial to trial onset. A lowpass filter was used to remove all frequencies above 50Hz. Bad channels were removed in its entirety before independent component analysis (ICA) to remove eye blinks and saccades. Afterwards the bad channels were interpolated and repaired. The data was re-referenced using the common average of all channels. In a final step, individual trials that still showed clear artifacts could be rejected based on visual inspection.

The sentences offered two contrasts of interest: the contrast between constrained and uncon-

strained sentences and between reversed and normal sentences. In this study, only the latter contrast was examined. Since it is known that the constrained sentences have a large effect on the electrophysiological signal (Piai et al., 2014), I only considered the unconstrained condition versus the reversed condition. The participants were divided into a left hemisphere lesion, a right hemisphere lesion, and a healthy control group. On this basis the group-level analysis was run as well as a single subject analysis.

A frequency analysis was run for both the groups and the single subjects, disregarding the time dimension. On the grounds that normal speech and reversed speech no longer have the same entrainment. Entrainment is a process in which brain activity aligns in frequency and rhythm to a presented stimulus. This occurs when participants listen to normal speech. Since the temporal characteristics of reversed speech no longer matched those of normal speech, there were differences in entrainment between those conditions. These differences are a confound for research on comprehension if the data was analyzed in a time-frequency manner. Therefore, the data was only analyzed in a frequency analysis in the current research.

For both the group and single subject analyses, the power per frequency was calculated between 2 and 30 Hz in steps of 1Hz. A Hanning taper was multiplied with the data before the Fourier Transform was performed. Per participant the trials for the reversed and unconstrained conditions were selected. Subsequently the data was averaged over participants, for each group and for each condition, for the group analysis.

The effects of comprehension were statistically evaluated using non-parametric cluster-based permutation analyses (Maris & Oostenveld, 2007). Firstly, a t-statistic was obtained for the difference in electrophysiological power between the unconstrained and reversed condition. For the group analyses, a dependent samples t-tests were performed and an independent samples t-tests were performed for the individual analyses ($\alpha = 0.05$ in all t-tests). Similar t-values could occur in groups or clusters around adjacent frequencies and channels. A new statistic was generated by the sum of all t-values included in a cluster. The Monte Carlo method, a permutation test, then recreated all the t-values from the first part of the analysis, except that it randomized the conditions. This is done 500 times, resulting in normal distribution of statistical values from random permutations. The original statistic, obtained from a correct comparison between conditions, fell somewhere on this distribution. The significance was determined by its extremity compared to the random permutations: If it fell in either 2.5% extreme (two-tailed $\alpha = 0.05$) of the distribution it was considered significant.

The statistical analyses included all channels, however, only the frequencies between 5 and 25 Hz were included. This was decided since the frequencies below 5Hz are mostly based on the 1/f effect and syllable rate entrainment that was lost in the reversed condition.

In the individual analysis, instead of reporting on the electrophysiological power alone, the t-test statistics from the statistical analysis was reported. Between individual participants, the electrophysiological power can vary significantly, the t-statistic allowed for a measure that could be compared across each participant.

Finally, a functional laterality index was calculated for each participant(Traut et al., 2019 as an example) . This was calculated by averaging the t-statistics of the channels of either hemisphere individually, subtracting one from the other and dividing by the sum of the two hemispheres ((average t-values left hemisphere - average t-values right hemisphere) / (average t-values left hemisphere + average t-values right hemisphere)). Importantly, EEG results in a very distributed image of activity. There spatial blurring of the signal over the scalp. Therefore, an estimate of the scalp current density was computed using the surface Laplacian (the second order derivative) of the EEG signal using the finite-difference method. It was performed on the data before individual analysis to prevent any ”leaking” of activity from one hemisphere to the other.

Table 2: Results from the Token Test and Corsi Block-Tapping task

Participant	Group	Token test score	Corsi total	Corsi level	Corsi score
1	Control	35	7	5	35
2	Control	29,5	6	4	24
3	Left hemisphere	31	9	6	54
5	Right hemisphere	36	11	7	77
6	Control	29	7	5	35
7	Control	36	8	5	40
8	Left hemisphere	31	8	5	40
10	Right hemisphere	36	11	7	77
11	Left hemisphere	35	8	6	48
12	Right hemisphere	34	7	5	35
13	Right hemisphere	35	6	4	24
14	Right hemisphere	29	7	5	35

Note. Test scores per participant. The Corsi total is the total amount of correctly performed sequences. Corsi level is the highest amount of entries in a correctly performed sequence. Corsi score is a multiplication of the Corsi total and level.

3 Results

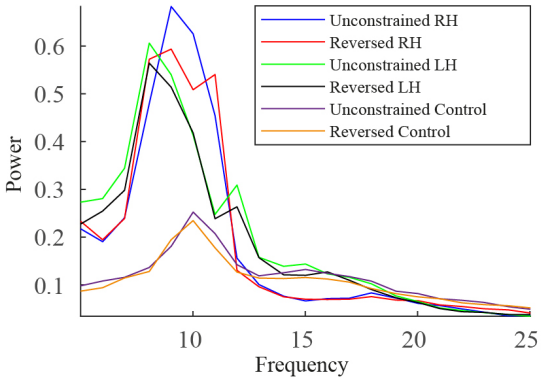
3.1 Behavioural results

Two tasks that were run are used for the current study: the Corsi Block-Tapping task and the Token Task. The results are presented in table 2. The Token Test scores entail the amount of correctly executed assignments out of a maximum of 36. Half points were appointed when the participant asked for the assignment to be repeated. Scores between 25 and 28 indicate mild comprehension problems, between 17 and 25 as moderate problems and below 17 as severe problems (Johnstone et al., 2010). The Corsi Test scores have three different components, one to display the amount of correctly performed sequences (i.e. Corsi total), one for the highest number of items in a correctly performed sequence (i.e. Cosi level) and one that is a multiplication of the other two numbers (i.e. Corsi score). The average Corsi level is 5-6. The Token test results in table 2 show that none of the participants has a mild, moderate or severe problem with language comprehension. The Corsi scores are average or above average for all participants except for two: participant 2 and 13 who both have scored to level 4.

3.2 Group-level analysis results

In the group-level analysis, no significant results were found. The three groups consisted of right hemisphere patients, left hemisphere patients, and control participants. Both for reversed sentences and unconstrained sentences the power per frequency was calculated for each group, as displayed in figure 1. There are no significant clusters in the group level data according to the non-parametric cluster-based permutation test. ($P > 0.05$) Descriptively, the results in figure 1 show an almost constant higher electrophysiological power for the unconstrained condition compared to the reversed condition in each group. The control data seem to have lower power than both RH and LH patients. Five clusters that did not reach statistical significance were found using non-parametric cluster-based permutation analysis comparing reversed to unconstrained conditions. Four insignificant negative clusters(i.e. reduced power for reversed sentences compared to constrained) were found in the control group. One positive cluster was found in the RH group, but no negative ones. No clusters were found for the LH group. The group-level analysis shows a general tendency for less electrophysiological power for a reversed sentence compared to an unconstrained sentence.

Figure 1: Power per frequency of each condition for the group analysis



Note. Power by frequency of unconstrained and reversed conditions in right hemisphere patients (RH), left hemisphere patients (LH) and control participants. Averaged over all scalp channels.

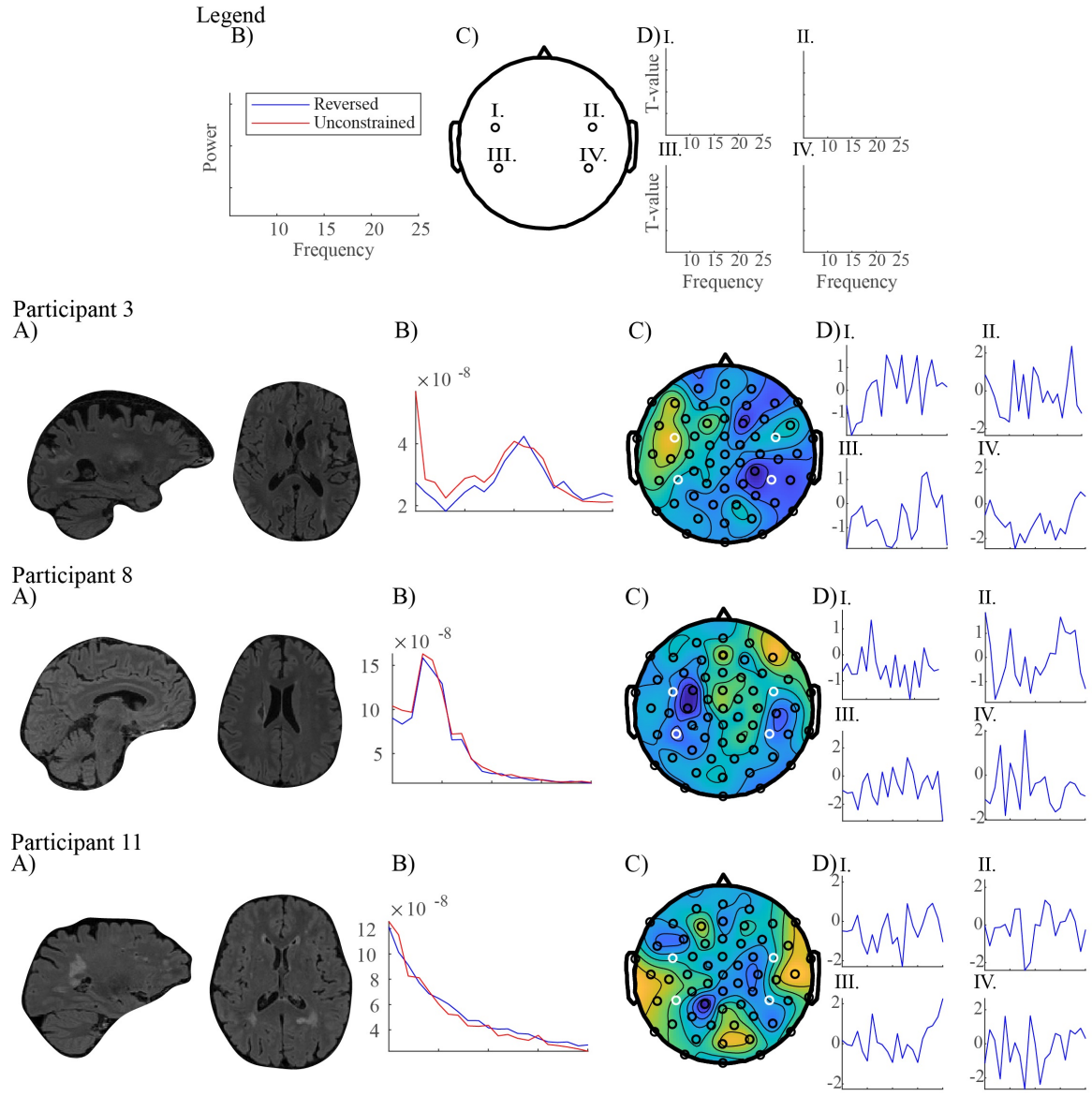
3.3 Individual analysis results

Because of the variability of the data set and the small sample size, an individual analysis was performed. An MRI fluid attenuated inversion recovery (FLAIR) image of the brain lesion, or the lack thereof, is presented in A) and the power per frequency of reversed and unconstrained conditions are

shown in B) of figures 2, 3, and 4. For each participant a non-parametric cluster-based permutation analysis was run, but no significant clusters were found. A topographical overview of the t-statistic averaged between 5 and 25 Hz is provided for each participant in C) of the figures 2, 3, and 4. D) shows the t-statistic per frequency in 4 different channels, 33, 22, 30, and 25 as depicted by the white markers in C). I. is the top left marked channel, II. the top right, III. the bottom left and IV. the bottom right. Some inferences can be made by looking at the figures. Descriptively, two different peaks can be observed in the frequency plots in B): a clear peak around 10 Hz, for instance, participant 5 in figure 3, and a peak around 18 Hz, participant 3 in figure 2. Only the peak around 10Hz shows up in the group level analysis in figure 1. Interestingly, participant 11 in 2 is not showing any peaks in electrophysiological power. The identified clusters, which did not reach statistical significance, were often negative, except for participant 14 in 3.

For each participant, a functional laterality index was calculated by separating the channels of the left and right hemisphere. For each hemisphere separately, the t-values, average over 5 to 25 Hz, were averaged. The resulting number was compared to the other hemisphere, resulting in the laterality index. It indicates in which hemisphere speech comprehension is mostly processed. The results of the laterality index calculation is shown in figure 5. No conclusive evidence of a specific pattern or tendency can be found in these results. For all three groups the laterality indices are distributed over both positive and negative values.

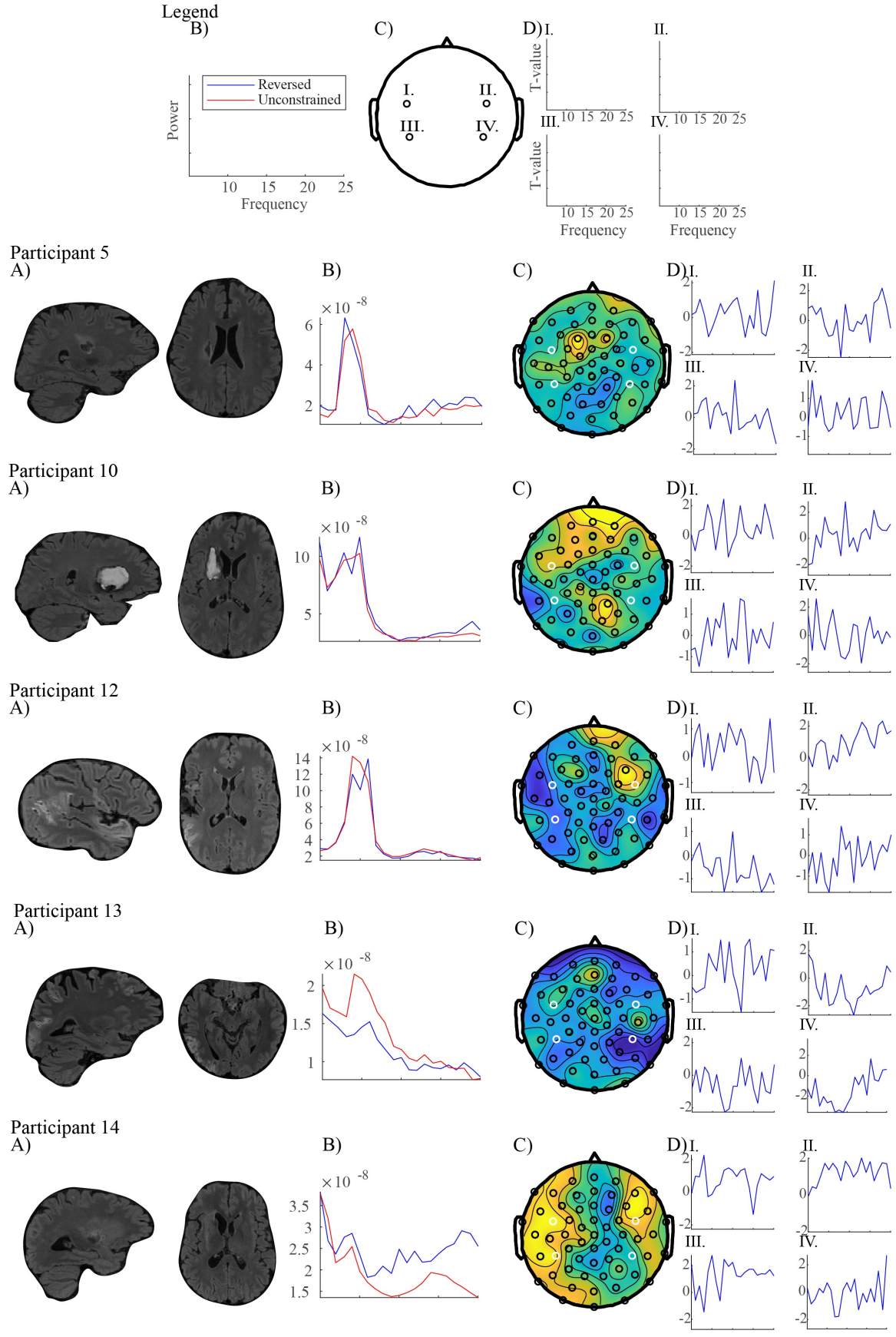
Figure 2: Left hemisphere patients



Note. A) FLAIR MRI structural images of the participant's brain. B) Power per frequency for the reversed and unconstrained conditions, averaged over all scalp channels. C) Topographical distribution of the t-values averaged over 5-25Hz. D) Four single channel representations of t-value per frequency.

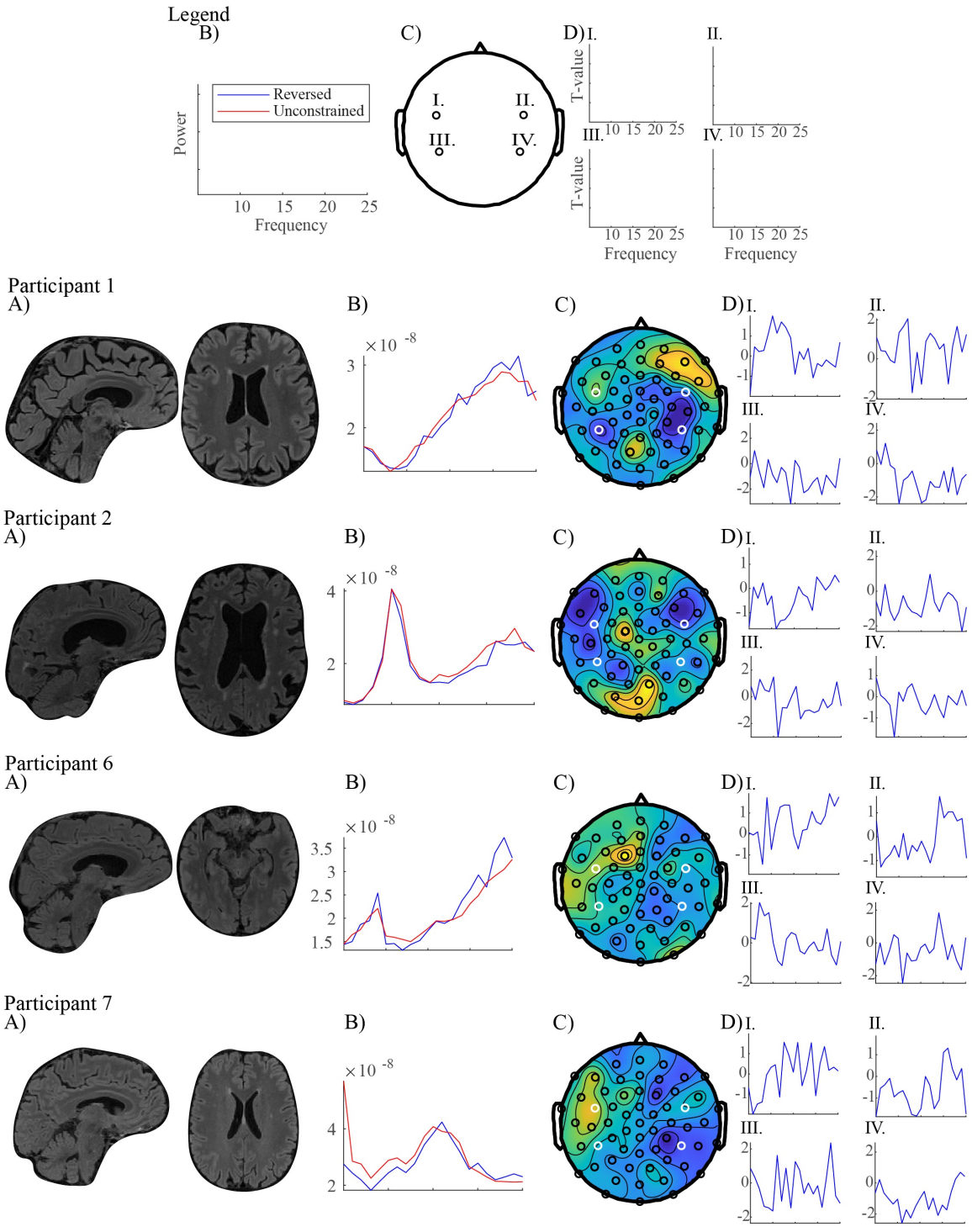
4 Discussion

The aim of the current study is to determine the influence of a unilateral subacute stroke on the electrophysiological laterality index during speech comprehension and to determine if the method of the laterality index and qualitative analysis is meaningful for research on language in stroke patients. We tested 14 participants with a context-constrained sentence completion task, while EEG was measured. The sentences were presented in reverse as one of the conditions. The comparison



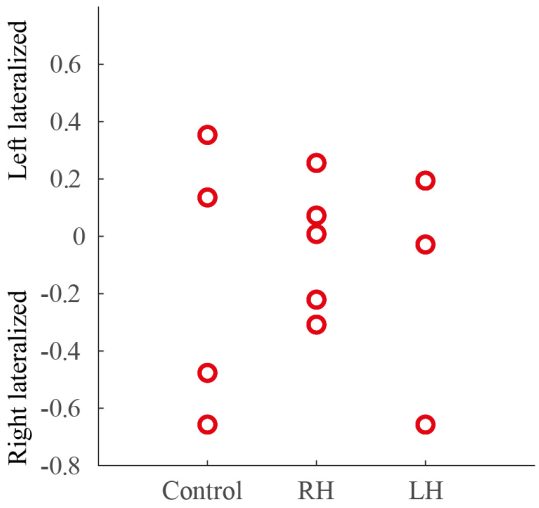
Note. A) FLAIR MRI structural images of the participant's brain. B) Power per frequency for the reversed and unconstrained conditions, averaged over all scalp channels. C) Topographical distribution of the t-values averaged over 5-25Hz. D) Four single channel representations of t-value per frequency.

Figure 4: Control patients



Note. A) FLAIR MRI structural images of the participant's brain. B) Power per frequency for the reversed and unconstrained conditions, averaged over all scalp channels. C) Topographical distribution of the t-values averaged over 5-25Hz. D) Four single channel representations of t-value per frequency.

Figure 5: Laterality index of each participant per group



Note. Laterality index per participant grouped by control particiapnts, right hemisphere patients (RH) and left hemsiphere patients (LH). Postive values denote a higher t-value in the left hemsiphere and negative values denote a higher t-value for the right hemisphere.

of the reversed and unconstrained sentences is the contrast of interest for this thesis. The data was analyzed in a group-level basis and on an individual basis. The laterality index was calculated for each participant individually.

The behavioural results did not show expected deviations between the groups. Two scores were reported on in the current study: the Corsi Block Tapping test and the Token test. The Corsi test was used to measure visuo-spatial working memory. Two participant's scored below average (level 4 where average is 5-6), one is a right hemisphere patient and one a healthy control. The Token test is used as a measure of language comprehension and for aphasia diagnosis. It was expected that some left hemisphere patients would score low, however, none of the scores in all groups indicate a problem with comprehension. The hypothesis of the current research entails a shift in hemispheric dominance, but it is based on aphasia research by Saur et al., 2006. There seems to be a discrepancy between the patients of the current research and the patients in the research that the hypothesis is based on. After all, the left hemisphere patients do not show aphasia scores on the Token test. Therefore, to test this hypothesis, future research should include only aphasic patients in the left hemisphere group.

Both the group level analysis and the individual analysis did not return significant results. Thus, there is no evidence of a difference between processing unintelligible reversed speech and meaningful

unconstrained sentences for each of the group analyses and within each participant. Nonetheless, analyzing the data descriptively, some aspects stand out that are discussed below.

The higher power for unconstrained compared to reversed conditions during sentence comprehension can be explained by the production-based prediction account. In the results for the group analysis and in most individual cases, the electrophysiological power for the unconstrained condition appears higher than the reversed condition particularly around 10 Hz. The main difference between the two conditions is the presence of meaning. In the reversed sentences meaning is absent, but it is present in the unconstrained sentences. Production-based prediction entails a processing system of language comprehension in which the language production system is used. It states that people generate a production-based representation of the presented sentence and try to predict subsequent words (Ito et al., 2016). Only the meaningful unconstrained conditions can elicit prediction. I interpret this difference in power between the two conditions to be due to the prediction that is only present for unconstrained sentences.

The descriptive results included an increase in electrophysiological power around 10 Hz and sometimes around 20 Hz, usually in both conditions. The peak around 10Hz could be seen in both the group and in most individual analyses. However, the increase of power around 20 Hz could only sometimes be seen in the individual analyses. Wöstmann et al., 2017 have created a review on M/EEG language comprehension research. They state that the power in the alpha (8-12Hz) frequency band increases when a participant focuses on an auditory stimulus. Therefore the increase in power in the alpha frequency band in the current study is interpreted as directing attention to the incoming auditory stimulus. Wöstmann et al., 2017 also reported a beta (15-25Hz) power increase for auditory stimulus novelty. Thus, I interpret the results for the beta frequency band as such.

In previous research, a typical pattern of language activation was found for patients recovering from aphasia. Pre-morbidly, language would be a predominantly left functionally lateralized function, shifting to the right hemisphere in the subacute phase of the stroke. In the chronic phase, the function is predominantly left lateralized once again. Thus, according to this pattern and the subacute phase of the patients in the current research, one would expect the left hemisphere patients to be right lateralized for speech comprehension and the controls and right hemisphere patients to be left lateralized. A laterality index was calculated for each participant, it was a weighted index of the averaged t-values for the channels on the left and right hemisphere and it demonstrates in which hemisphere the function of language comprehension was mainly processed. The laterality index did not show the expected pattern of hemispheric dominance. The laterality indices were distributed in similar fashion for the left- and right hemisphere patients and controls alike and therefore supports the conclusion that there is no evidence for a difference in functional laterality between the groups

in the subacute phase of stroke. However, the left hemisphere group does not control for patients with aphasia and without. Previous research was solely based on aphasia patients, whereas here all patients with a left hemisphere damage are grouped together. Future research should control for this difference.

The current study included right hemisphere stroke patients as a reference point to the left hemisphere patients. Previous research has described a pattern of aphasia recovery that includes a shift of left hemispheric dominance of language to the right hemisphere. In studies that find this effect in left hemisphere stroke patients, it can always be claimed that the shift of laterality is not necessarily due to the specific stroke damage and its resulting impairment, but due to the presence of stroke damage in general. Right hemisphere patients were included in the current research to control for the presence of a stroke. It would be expected that the right hemisphere patients would have the same results as the controls. However, the current research did not find a significant difference between the three groups, as hypothesized the right hemisphere group and control group do not differ. However, in contrast to previous research, the right hemisphere patients and left hemisphere patients did not differ significantly.

For EEG research on stroke, qualitative- and individual analyses can be an informative addition to quantitative- and group-level analysis. In the current study, quantitative analysis entailed the statistical tests and their outcome, whereas the qualitative analysis was the inspection of the data plots and the descriptive tendencies. The field of cognitive neuroscience is predominantly a quantitative field with group-level analyses. However, studying stroke patients entails a heterogeneous sample and calls for a method that is sensitive to those details. The current study is an example: The results are not significant but do show interesting aspects for future research. Particularly the beta frequency increase, which is not visible in the group analysis. As well as the power increase for the unconstrained compared to the reversed condition. These methods provide meaningful insights because of the individual interpretation of the data, which would be overlooked by quantitative group analysis alone. On top of that the sample size for stroke research is often small. Recruitment of patients is a time-consuming task, there are only a limited amount of patients available and time is of the essence when research is done on the acute or subacute phase. The small sample size is often inadequate for statistical testing for small effects. Moreover, some aspects of the data are lost when grouped. Quantitative group-level research has the potential to be reliable and reproducible, able to present results that have impacted the data in a significant manner. A more qualitative method and multiple subject analysis, however, allows subtleties and effects to be shown that are overshadowed in a solely quantitative group analysis. For future research, a combination of the two is advised.

5 Conclusion

In this study, I examined the hemispheric dominance of language comprehension using EEG. In a sentence completion and picture naming task, sentences were presented in either an unconstrained or reversed manner. These two conditions were compared within groups of participants. The groups consisted of patients with a stroke lesion in the left hemisphere, patients with a stroke in the right hemisphere and healthy controls. Afterwards, all participants were analyzed on an individual basis. No significant results were found in the quantitative analyses, thus, no evidence was found for differences between the processing of unconstrained and reversed sentences.

However, I discussed the data in a descriptive manner. There is a difference between the unconstrained and reversed conditions in both the group analysis, and in the individual analyses, which could be explained by the prediction of following words according to the production-based prediction account. The unconstrained sentences produced a higher electrophysiological power across all frequencies, which portrays the extra mental effort required for prediction. The individual analysis also showed an increase in the alpha and beta frequency bands. The increase in alpha was interpreted as the focus on the presented sentence and the increase in beta for stimulus novelty. These aspects and interpretations of the data would be missed if only a quantitative group-level analysis was performed. Thus, to reach the full potential of the data, future stroke research would benefit from additional qualitative- and individual analyses.

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