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Characterization of Brain Regions Based on Event-related Potentials—N400 Component

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Abstract: *N400 is a typical event-related potential that reflects the degree of matching between words and context. A public dataset was selected to explore the effect of gender on N400 by performing statistical analysis, spectral analysis, and time-frequency analysis on the EEG of 40 subjects who participated in the lexical semantic relevance judgment task. The results showed that, although the gender difference was not significant, the mean and peak amplitudes of N400 in females were overall larger than those in males, and the latencies were shorter, which proved that the N400 responses of females were overall more sensitive. The time-frequency results showed that theta waves and low-frequency beta waves were active during the time window when the N400 appeared, reflecting cognitive processing of semantic mismatch. This study provides evidence for the use of the N400 to assess semantic processing, which is informative.*

Keywords: *EEG, N400, Statistical Analysis, Spectral Analysis, Time-frequency Analysis*

1. Introduction

Semantic processing, the process by which an individual comprehends and remembers linguistic information, is a core component of linguistic cognition[1]. This cognitive process encompasses the synergistic action of multiple brain regions and networks, and among them, N400 has become an important neural indicator that has received much attention. Specifically, in the field of brain cognitive processing, the N400 is categorized as an event-related potential (ERP), which is characterized by the generation of a negative potential waveform approximately 400 ms after stimulus presentation[2].

There are various forms of N400 experimental paradigms, a common one being the word pair judgment task proposed by Holcomb and Kutas[3]. Participants are required to judge whether the target word is semantically related or unrelated to the lead word. Semantically related word pairs trigger a smaller N400, while semantically unrelated word pairs trigger a larger N400.N400 has different characteristics and variations in different populations. Julie M. Schneider et al. collected EEG data from 226 children aged 8-15 years old and analyzed the N400 and theta waves triggered by content words while they read sentences word by word[4].

Researchers have also explored the characteristics of the N400 under different experimental equipment and experimental conditions. Johanne Tromp et al. combined virtual reality and EEG to simulate language processing in a natural environment and found that the N400 amplitude in the mismatched condition showed a more pronounced negative direction than the amplitude in the matched condition, which reflects the semantic processing of auditory information when it is mismatched with the visual environment[5]. MEG and EEG data collected by Sujoy Ghosh Hajra et al. demonstrated consistency with conventional N400 response results, which provides support for clinical translation[6].

Although there has been a considerable amount of research on the N400, many challenges and questions remain. For example, how to improve the reproducibility, consistency, and adherence to research standards of N400 studies[7]. Therefore, there is a need for a larger number of subjects, more in-depth and systematic studies of the N400 to reveal its neural mechanisms and applied value. In this study, we used publicly available EEG datasets to perform statistical analysis, one-way ANOVA, spectral analysis, and time-frequency analysis on the event-related potential N400 to provide objective electrophysiological indicators for the discovery of cognitive functions associated with N400.

2. Data sources and experiments

2.1 Data sources

This study used the N400 public dataset hosted on the Open Science Framework (OSF), which is motivated by the word pair association paradigm, as detailed at https://osf.io/29xpq/.

2.2 Subjects and Processes

The age range of the subjects was 18 to 30 years with a mean age of 21.5 (±2.837) years. The subjects consisted of 15 males and 25 females, 38 were right-handed and 2 were left-handed, and the ratio of dominant hands was 19:1.The dataset included 40 subjects, one of whom was excluded because of poor data quality.

The dataset was created using an open-access vocabulary, in which relevant cue words had a high mean positive association strength, while irrelevant cue words had a very low mean positive association strength. Each target word appeared twice in the trial, once followed by a relevant cue word and once by an irrelevant cue word, with the order of cue word pairs randomized. Different colors were used for cue words and target words to help participants determine which word to respond to.

3. Data preprocessing

To optimize the quality of EEG data, calibration, filtering, downsampling, re-referencing, electrode positioning, and artifact removal were performed to ensure accuracy and reliability of subsequent data analysis.The preprocessing flow is shown in Figure 1.

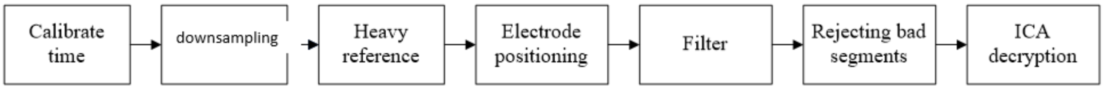


Figure 1: Pre-treatment flow chart

(1) The LCD monitor has a certain presentation delay and needs to be corrected for the stimulus event time. The stimulus event time was shifted forward by 26 ms from the light sensor measurement to ensure the accuracy of the event coding.

(2) The original data is sampled at 1024 Hz in order to speed up the subsequent data processing, the sampling rate is downsampled from 1024 Hz to 256 Hz by means of the pop_resample function, which automatically applies an appropriate low-pass anti-alias filter.

(3) The reference electrode was modified to be the average of P9 and P10 (adjacent to bilateral papillae).

(4) The EEG data were subjected to electrode localization according to the 10-10 International Standard Electrode Localization System.

(5) The DC component was first removed, and a non-causal Butterworth high-pass filter (cutoff frequency of 0.1 Hz, order 2) was applied to remove extraneous noise interference.

(6) Intervals of more than 2000 ms between two consecutive stimulus event codes were designated as rest periods, and rest period data were excluded to minimize the effect of motion artifacts.

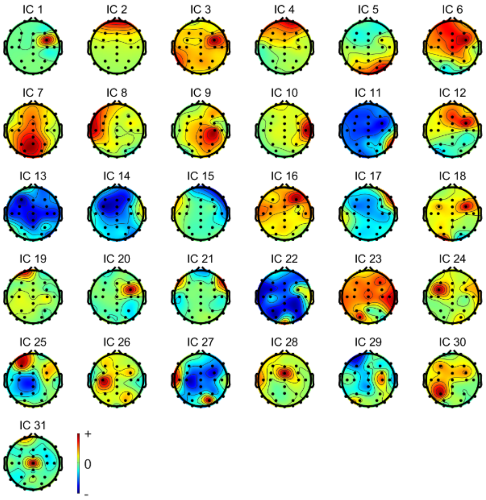


Figure 2: Scalp topography of ICA weights for subject 34

As can be seen in Fig. 2, there is a significant ocular electrical component in the IC2 component, and therefore in this component was removed in a subsequent step.

(7) The artifact components identified in the previous step are removed to further improve the quality of the data and reduce artifact interference.

4. Data processing and analysis

4.1 Data processing

The EEG data obtained in the previous step were imported, superimposed and averaged to obtain the group average ERP, and a time window of 300-500ms was selected to extract the N400 component features. According to the brain topography results, it was known that N400 was more obvious in the central region, so Pz, CPz, FCz and Cz electrodes were selected for subsequent analysis, as shown in Figure 3.

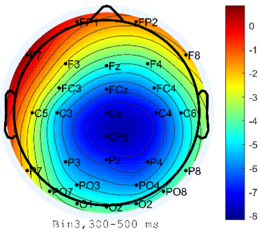


Figure 3: Brain topography with differential waves between 300 - 500ms

4.2 ERP waveforms

The group average ERP was calculated and plotted against the ERP of the four specific electrodes as shown in Figure 4.

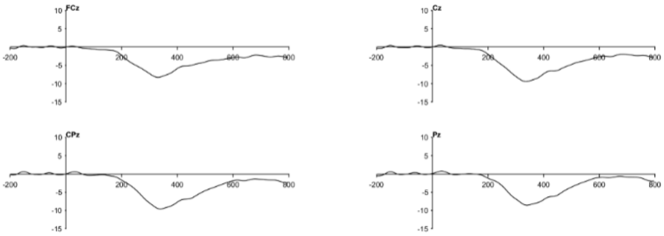


Figure 4: Channel-specific ERP waveforms

In neurolinguistic ERP studies, both specific time windows and their corresponding ERP components carry important cognitive information. As can be seen from the figure, the ERP curve is almost identical to the baseline for the time period from -200ms to 180ms, which implies that the brain does not respond significantly to a given linguistic stimulus during this period. However, on further observation, from 180ms to 350ms, the curve shows a significant decrease and peaks around 350ms. This characteristic waveform may represent the manifestation of the N400 component, which is considered to be a key indicator of semantic processing, especially when processing words that are out of context or violate semantic expectations, and its amplitude increases significantly. Subsequently, the ERP curve gradually rebounded from the time period of 350ms to 600ms and reached a steady state around 600ms, which may reflect the gradual weakening of the brain's response to semantically incongruent stimuli over time.

4.3 Statistical analysis

In this paper, the N400 of specific electrodes was statistically analyzed using SPSS statistical software, including the mean ± standard deviation ($\bar{x}$±s) of amplitude and latency, and was tested for significance using one-way ANOVA, and was considered to be statistically different at $p < 0.05$.

4.3.1 N400 Amplitude

The average and peak amplitudes between Pz, CPz, FCz and Cz electrodes were statistically analyzed as shown in Table 1.

Table 1: Comparison of mean and peak amplitude of N400 between genders ($\bar{x}$±s,μV)

Electrode position		N400 average amplitude					N400 peak amplitude				
		average value	standard deviation	standard error	F	significance	average value	standard deviation	standard error	F	significance
Pz	males	-5.43	2.44	0.65	0.93	0.33	-8.14	2.99	0.80	1.90	0.17
	females	-6.28	2.72	0.54			-9.95	4.35	0.87		
CPz	males	-6.25	2.63	0.70	0.48	0.49	-8.74	3.48	0.93	1.60	0.21
	females	-6.92	3.07	0.61			-10.61	4.82	0.96		
FCz	males	-4.97	3.11	0.83	0.22	0.63	-7.42	3.94	1.05	1.06	0.30
	females	-5.51	3.53	0.70			-8.75	3.81	0.76		
Cz	males	-6.32	3.12	0.83	0.10	0.75	-8.72	4.09	1.09	0.65	0.42
	females	-6.68	3.50	0.70			-9.74	3.58	0.71		

The analysis shows that during the 300-500 ms time window corresponding to N400, the mean and peak amplitudes of N400 at Pz, CPz, FCz, and Cz electrodes for males were smaller than those for females, but there was no statistically significant difference. This result suggests that the female N400 response may be slightly stronger when confronted with semantically mismatched word pairs.

4.3.2 N400 latency

The mean latencies and peak latencies between Pz, CPz, FCz and Cz electrodes were statistically analyzed as shown in Table 2.

Table 2: Comparison of mean latency and peak latency of N400 between genders ($\bar{x}$±s,μV)

Electrode position		N400 average latency					N400 peak latency				
		average value	standard deviation	standard error	F	significance	average value	standard deviation	standard error	F	significance
Pz	males	291.29	48.70	13.01	0.03	0.85	373.88	33.58	8.97	0.08	0.77
	females	288.43	45.18	9.03			369.37	51.92	10.38		
CPz	males	285.71	49.64	13.26	0.03	0.85	371.09	44.00	11.76	0.01	0.89
	females	282.81	44.36	8.87			369.06	45.47	9.09		
FCz	males	295.97	54.92	15.23	2.98	0.09	376.11	51.74	13.82	0.05	0.81
	females	265.00	51.13	10.22			371.71	57.82	11.56		
Cz	males	273.43	31.91	8.53	0.02	0.86	366.62	42.64	11.39	0.06	0.79
	females	275.93	49.89	9.97			371.24	57.41	11.48		

From the results, it can be seen that, except for the Cz electrode, the mean latency and peak latency at the Pz, CPz and FCz electrodes were longer for males than for females, and although there was no statistically significant difference, the between-group difference in mean latency at FCz was $p = 0.09$, which is close to the significant difference of $p = 0.05$. When confronted with semantically mismatched word pairs, the results at the Pz, CPz, and FCz electrodes suggest that the N400 response may be slightly earlier in females, i.e., cognitive processing may be faster in females.

4.4 Spectral analysis

In this experiment, for the four electrodes of Pz, CPz, FCz and Cz, 300 to 500 ms after the stimulation occurred was selected as the time window for spectral analysis, and the Fourier transform was calculated with a target frequency range of 0 to 45 Hz, and the results are shown in Fig. 5.

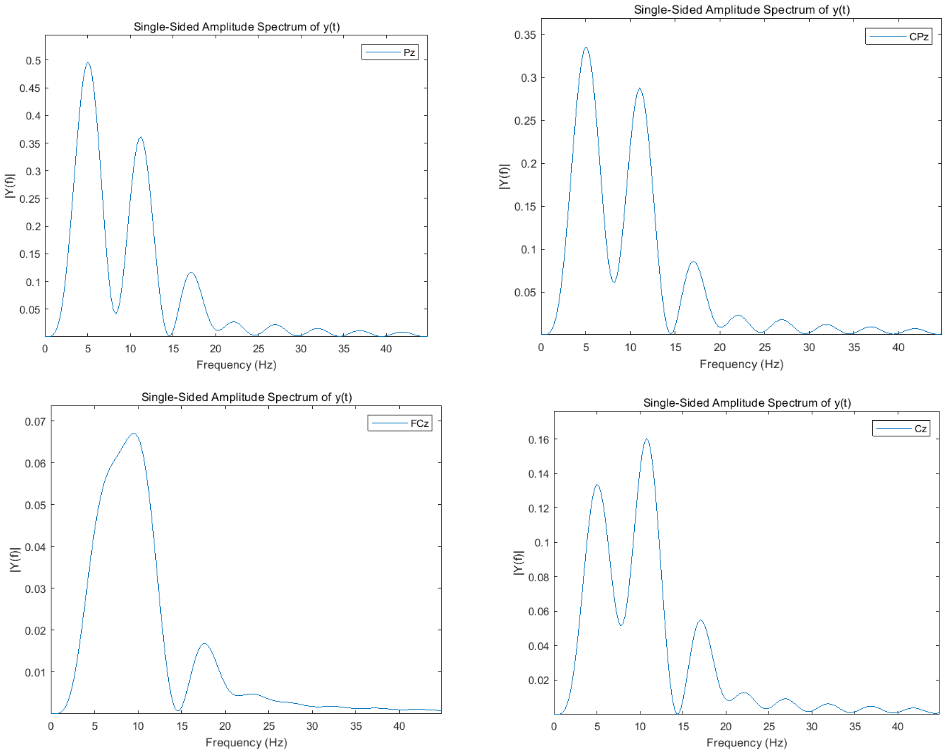


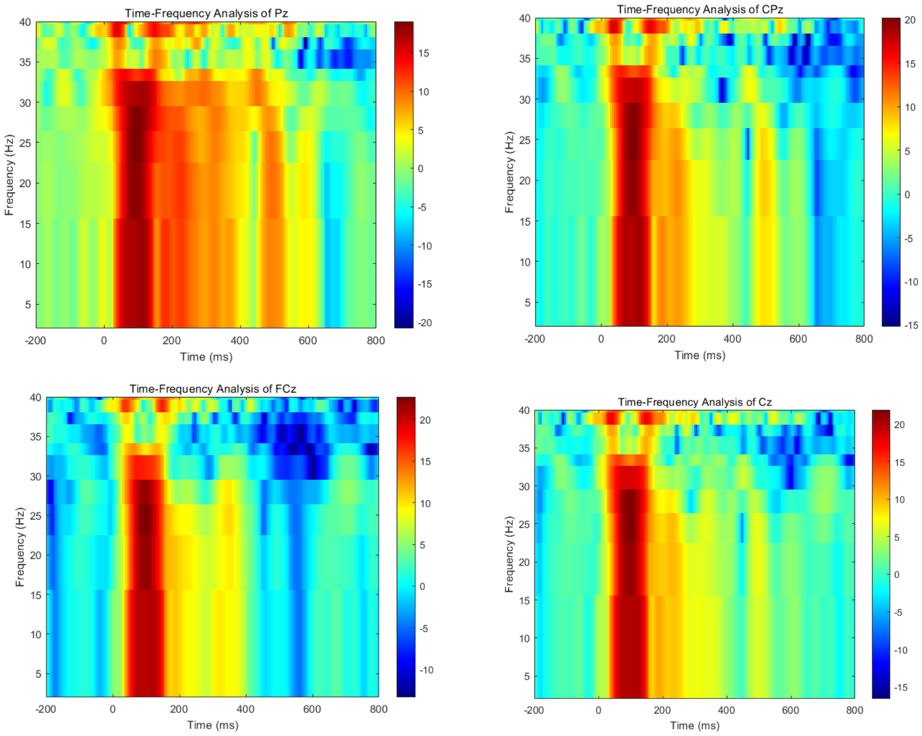
Figure 5: Spectrograms for specific channels

In the electrophysiological activity of the brain, different frequency ranges reflect different stages of the brain in processing information. For CPz, Cz, and Pz electrodes, the relatively high theta wave power in the range of 1 to 8 Hz, i.e., the brain activity, showed a higher intensity of brain activity, which may be related to the appearance of cue words. This is because when the cue words appeared, the participants' brains needed to make preliminary comprehension, especially when there was a semantic mismatch between the target word and the cue word, this theta wave activity might be enhanced. In the range of 8 to 14 hz, i.e., the enhanced alpha wave may reflect the participant's state of relaxation during the processing of the cue word and waiting for the target word to appear. However, when the target word appears, the alpha wave activity may temporarily decrease, which represents a shift in attention. The relatively low brain activity in the range of 14 to 20 Hz may represent participants' logical and analytical processing of the target word. Both before and after the appearance of the N400, beta wave activity may be enhanced due to the need for deeper thinking and decision making about the mismatched information.

For FCz electrodes, in the frequency range of 1 to 14 Hz, which contains theta and alpha waves, the power of brain activity in this range is relatively high, showing that the intensity of brain activity in this frequency interval is relatively significant. In this experiment, the enhanced theta wave may be a reflection of the brain's initial comprehension and interpretation of the cued words. Comparatively, the enhanced alpha wave may reflect the relaxed state of the participants during the processing of the cued words until responding to the target words. The frequency range of 14 to 21 hz included a low-frequency beta wave, and this low-frequency beta wave may be related to the brain's activity in performing logical and analytical processing.

4.5 Time-frequency analysis

The time-frequency analysis was performed for four electrodes, Pz, CPz, FCz and Cz, and the results are shown in Fig. 6.


Time-Frequency Analysis of Pz

Time-Frequency Analysis of CPz

Time-Frequency Analysis of FCz

Time-Frequency Analysis of Cz

Figure 6: Channel-specific time-frequency diagrams

For the Pz electrodes, the intensity of brain activity in the range of 0 to 400 ms, 0 to 34 Hz, showed a color change from dark to light, indicating a significant enhancement of brain activity during this time period. This enhanced activity may be related to the cue words that appeared during this time period, as the brain needs to initially recognize and process this new stimulus. During this period, theta wave activity is associated with mild to moderate relaxation and creative thinking, possibly reflecting the fact that the brain is trying to understand and interpret the meaning of the cued word. Meanwhile, alpha waves and low-frequency beta waves were associated with a state of relaxation and resting with eyes closed, suggesting that the brain may be in a state of readiness for the next target word. Between 450ms and 540ms, in the range of 0 to 30 HZ, a darker red color appeared in this frequency range compared to the baseline color, marking a further increase in brain activity. This time period overlapped with the typical appearance of the N400, suggesting that the brain may be processing information related to semantic mismatches between cued and target words. Theta wave activity may be related to the brain's attempts to parse such mismatches. At the same time, low-frequency beta-wave activity was enhanced, possibly reflecting the brain engaging in more active thinking.

For CPz, FCz, and Cz electrodes, the brain activity showed a deep to shallow change in the frequency range from 0 to 35 Hz during the time period from 0 to 350 ms, which indicates that the brain activity changed from strong to weak during this time period. Considering that this period of time may be associated with the appearance of cued words, the brain may be in the process of initial recognition and processing of the emerging information. During this period, theta wave activity may be related to the brain's understanding and interpreting the meaning of the cued words. At the same time, alpha wave activity is enhanced, which may be an indication that the brain is preparing for the upcoming target word. And the low-frequency beta-wave activity indicates that the participants maintained an alert state during this period to prepare for responding to the next stimulus.

5. Discussion and conclusion

In recent years, the N400, as an important component of the ERP, has received much attention in the field of neurolinguistically related brain sciences.The N400 is generally regarded as a key neural indicator of lexical semantic processing.Laszlo and Federmeier's study found that the N400 is able to accurately capture real-time information in interactive processing, which provides important clues to reveal how the brain instantly decodes and processing linguistic information provides important clues[8]. In addition, Junge et al.'s study further revealed the role of the N400 in infant vocabulary learning, providing new perspectives for understanding the process of language acquisition in humans at early developmental stages. Notably, Ihara et al. showed that there is a significant difference between the N400 responses elicited by handwriting and keyboard typing when learning new words[9]. This not only provides us with a new research perspective, but also implies that the N400 may also have a unique role and significance in other cognitive domains of nonverbal processing, such as perception and motor coordination.

Although significant progress has been made in the study of N400, there are still some urgent problems to be solved[10]. For example, the specific neurobiological mechanisms of N400, the interrelationships with other ERP components, and the differences in performance in different cultural and linguistic contexts are all hot and difficult issues in current research[11].

Along with continued advances in neuroscience techniques, such as functional magnetic resonance imaging and near-infrared spectroscopy, research on the N400 is expected to enter a more in-depth and innovative phase[12]. It is expected that future studies will focus more on the deep neural mechanisms of the N400, its interaction with other cognitive functions, and its specificity in specific populations (e.g., bilinguals, people with language disorders, etc.). In conclusion, the N400 provides a powerful tool for neurolinguistic research and helps to deepen our understanding of the complex mechanisms of the brain in language processing.

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