



Applying recurrence time entropy to identify changes in event-related potentials

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Abstract The event-related potentials (ERPs) are an essential response of the human brain to environmental changes that correlate with behavior. They are thus widely used as indicators of brain activity in fundamental research and response sources in brain communication devices. The problem of their robust identification from single-trial EEG recordings or limited data sets is timely and challenging. The current study addresses this issue by evaluating the ERP-associated variations of EEG signals using the measures of complexity based on the recurrence quantification analysis (RQA). Specifically, we demonstrate that the recurrence time entropy (RTE) is a good indicator of ERP-associated changes in the course of successive discrimination of ambiguous visual stimuli. Using the distribution of recurrence times, we conclude why exactly this measure is sensitive to ERP-associated variations of EEG signal.

1 Introduction

Event-related potential (ERP) is an essential electrophysiological response of the brain to external stimulation or environmental changes. It manifests itself as a specific waveform of electrical cortical activity as recorded by an electroencephalogram (EEG) [1]. ERP waveform such as presented in Fig. 1 consists of components, i.e., positive and negative voltage deviations. Name of each component is comprised of the prefix indicating its polarity, i.e., P for positive and N for negative, and the time moment of its appearance in milliseconds (ms), i.e., component's latency. For example, a positive voltage peak around 300 ms after stimulus presentation would be referred as the P300 component. Usually, ERP covers EEG sensors located over the temporal, prefrontal, and somatosensory cortical areas and represents a short-term low-frequency modulation of local neuronal oscillations [2].

Variation of ERP components occurrence in both time and space domain allows to define which stage of neuronal processing is affected by experimental manipulation. ERP probe is, therefore, one of the widely used

methods in behavioral neuroscience and neuropsychology to test brain-behavior correlates in different experimental conditions [3, 4]. In neural engineering, ERP is exploited as a feedback source in brain-computer interfaces (BCIs) for rehabilitation and communication with patients whose motor and/or cognitive functions are limited or completely lost [5–7].

When detecting ERPs, one has to take into account that EEG signals suffer from a low signal-to-noise ratio. It means that the useful signal, i.e., the ERP waveform, is masked by high-intense random fluctuations of the brain's electrical activity. Extraction of useful ERP components, thus, requires an increase in signal-to-noise ratio which can be done in several ways. The most common one is averaging over a large number of trials (hundreds or more) under the same experimental conditions. The averaging removes all the random fluctuations uncorrelated between trials and leaves only a nonrandom EEG variation associated with ERP waveform phase-locked with the stimulus. However, such a procedure imposes restrictions on the duration of the experimental session, which should last for a considerable time to collect the required amount of data. Furthermore, applying such an approach is difficult in studies of rapid variations of neuronal activity, e.g. throughout the session, as well as in many practical applications, for example, online biofeedback-based BCIs.

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Alternatively, to extract ERP properties from the single-trial recordings or limited data sets, one can utilize some advanced filtering or nonlinear signal processing techniques. In this regard, recurrence quantification analysis (RQA) may be a good candidate [8, 9]. A growing number of studies points out the applicability of RQA in the different aspects of EEG analysis: from sleep and rest-state activity [10–13] to cognitive and motor brain functions [14–17]. In the context of ERPs, the pioneer works by Marwan et al. [18–20] have demonstrated the prospect of RQA in detecting P300 and N400 components, which are related to categorization and associations of presented stimuli, in the odd-ball paradigm (repetitive presentation of more and less expected stimuli). To this end, the authors have established that the meaningful variations of the vertical-line-based measure of laminarity (LAM) are related to the variation of above mentioned ERP components. This finding indicates that the ERP-associated brain dynamics become more laminar as compared with turbulent background activity. Our recent studies have established that another recurrence-based measure of complexity—the recurrence time entropy (RTE)—is also quite sensitive to ERP variations [21, 22]. It is not surprising, since RTE is a robust indicator of transitions between regular and chaotic dynamics [23].

The present paper shows the suitability of RTE in tracing changes in the brain response throughout a prolonged experimental session based on a limited number of EEG trials. Specifically, a conducted experiment involved a large number of repetitions of ambiguous visual stimulus discrimination. As the image becomes more and more familiar to the participant throughout the experiment, we expected an improvement in behavioral response and a change in the task-related ERP components associated with it. As anticipated, we observed a reduction of the N400 amplitude, i.e., its deflection from zero-level, from the beginning to the end, which was correlated with the changes in reaction time. Further, we witnessed a significant N400-associated variation of RTE. Finally, complementing our previous results, we explain why the RTE measure appears to be sensitive to the variations of ERPs by analyzing the recurrence time distributions.

2 Materials and methods

2.1 Participants

Twenty healthy individuals with normal or corrected-to-normal visual acuity have been recruited among the employees of Innopolis University aged 26–35 ($n = 20$, 9 females) to participate in this experiment. All of them have been familiarized with the experimental procedure and have signed written informed consent in advance. The experimental design has been approved by the local ethics committee of Innopolis University and has been conducted following the Helsinki Declaration.

2.2 Procedure and EEG acquisition

The experimental study aimed at identifying behavioral and neural responses to repetitive discrimination of ambiguous visual stimuli. For approximately 40 minutes, 400 images of the Necker cube of randomly chosen ambiguity and orientation have been presented to each participant. Each stimulus has been shown on the monitor in front of the participant for a time interval randomly picked from the interval 1.0–1.5 s with the interval between stimuli of 3.0–5.0 s. The participant has been instructed to respond as fast as possible to each stimulus by pressing either the left or right button on the keypad if the presented image of the Necker cube has been identified as left- or right-oriented. Behavioral response is thus evaluated as the reaction time (RT), i.e., the time interval between the stimulus onset and button pressing.

During the experiment, we measured the electrical activity of the brain cortex using the whole-brain EEG. The electrodes have been placed over the scalp according to the extended 10–20 International system and the signals have been acquired using the electroencephalograph “Encephalan-EEG-19/26” keeping the level of impedance within 2–5 k Ω . The EEG signals have been sampled at the frequency of 250 Hz and presented in μV . Raw EEG has been band-pass filtered using the 5th order Butterworth filter in the band 1–100 Hz to exclude low-frequency artifacts and high-frequency noise. Additionally, undesired physiological artifacts have been removed using the independent component analysis (ICA). EEG trials have been collected from artifact-free recordings according to the experimental protocol. Each trial has been centered at the stimulus onset and contains 2 s of pre-stimulus (baseline) electrical activity and 2 s of post-stimulus activity.

To test the hypothesis of neural and behavioral adaptation throughout the experiment we have considered two samples of EEG trials picked from the beginning (condition Begin) and end of the experimental session (condition End). Each sample contains 40 trials such that all combinations of stimulus orientation and ambiguity are equally presented.

2.3 Event-related potentials

With such a paradigm we expect a perceptual priming to underlie the neural adaptation to subsequently presented visual stimuli [24, 25]. With this aim we have assessed the variation of ERP amplitudes from the early phase (Begin) to late phase (End) of the experiment. The ERP waveforms have been evaluated by reducing a signal-to-noise ratio via averaging EEG signals across trials in both experimental conditions for each participant.

2.4 Recurrence quantification analysis

Multichannel EEG recordings naturally pave the way to a multidimensional analysis of the brain’s electrical activity without exploiting additional embedding

procedures. Consider a set of m EEG signals $X(t) = \{x_1(t), x_2(t), \dots, x_m(t)\}$. It describes the dynamics of a certain brain area as a motion of the vector $\mathbf{x}(t_i) = (x_1(t_i), x_2(t_i), \dots, x_m(t_i))^T$ along the trajectory in the m -dimensional state space. The recurrence matrix R_{ij} for such a trajectory is constructed as:

$$R_{ij} = \begin{cases} 1, & D_{ij} < \epsilon, \\ 0, & \text{otherwise,} \end{cases} \quad (1)$$

$$D_{ij} = \|\mathbf{x}(t_i) - \mathbf{x}(t_j)\|, \quad (2)$$

where D_{ij} is a pairwise distance matrix calculated using the Euclidean norm $\|\bullet\|$ defined on the m -dimensional space and ϵ is a predefined recurrence threshold. There are several ways to define the recurrence threshold. To increase robustness of the recurrence matrix construction, which is crucial when analyzing experimental data, we use the approach proposed by Krämer et al. [23], which suggests choosing the threshold as a fixed percentile (sufficiently low) of the distance distribution to reduce the dependence of recurrence characteristics on the embedding dimensions. Without the loss of generality, we have chosen the 3^{rd} percentile of the pairwise distances distribution, i.e., $\epsilon : \Pr(D_{ij} < \epsilon) = .03$, as a suitable recurrence threshold.

The matrix R_{ij} can be visualized as a recurrence plot (RP). It consists of several elementary patterns—solitary dots, black diagonal and vertical lines, and white vertical lines—that constitute the global structure of the system's recurrences. This structure reflects the dynamical properties of the process evolving along the considered trajectory. Recurrence quantification analysis (RQA) offers a set of measures to estimate the complexity of the system's dynamics through the structure of RP. We are interested in the tracking of the changes of RQA measures associated with ERP along the time series, thus we apply windowed RQA, i.e., estimate complexity measures in a floating window over the global RP of size $w = 50$ d.p. (200 ms) with step $\delta w = 1$ d.p. (4 ms).

To trace the transitions from irregular and noisy background EEG to coherent oscillation associated with ERP we primarily exploit the recurrence time entropy (RTE)—the RQA measure of complexity based on the distribution of recurrence times (white vertical lines in the RP). It is defined as:

$$\text{RTE} = - \sum_{t_w}^w t_w P(t_w), \quad (3)$$

where $P(t_w)$ is a distribution of recurrence times t_w .

We compare the sensitivity of RTE to ERP-related changes in EEG with the other relevant RQA measures. Alongside, we use the diagonal-line-based measure of determinism (DET):

$$DET = \frac{\sum_{l=2}^w lP(l)}{\sum_{l=1}^w lP(l)}, \quad (4)$$

where $P(l)$ is a distribution of diagonal lines of length l , and the vertical-line-based measure of laminarity (LAM):

$$\text{LAM} = \frac{\sum_{v=2}^w vP(v)}{\sum_{v=1}^w vP(v)}, \quad (5)$$

where $P(v)$ is a distribution of vertical lines of length v .

To better illustrate the deviation of the RQA measures associated with the ERP, we have explicitly considered their variations from the pre-stimulus (baseline) level:

$$\text{dRTE}(t) = \text{RTE}(t) - \overline{\text{RTE}}_b, \quad (6)$$

$$\text{dDET}(t) = \text{DET}(t) - \overline{\text{DET}}_b, \quad (7)$$

$$\text{dLAM}(t) = \text{LAM}(t) - \overline{\text{LAM}}_b. \quad (8)$$

In the above equations, $\overline{\text{RTE}}_b$, $\overline{\text{DET}}_b$, and $\overline{\text{LAM}}_b$ are the baseline levels of the respective RQA measures, calculated as the mean across the time interval $[-500, 0]$ ms prior visual stimulus onset.

The RQA has been performed via the `pyunicorn` package for Python [26].

2.5 Statistical Inference

Cluster-based permutation test. Since we evaluate the effect of interest on a large number of (sensor, time)-pairs in the case of ERP or time points in the case of associated RQA measures variations, the multiple comparisons problem naturally arises. To control for the emerging family-wise error rate we employ a non-parametric cluster-based permutation test (details in [27]). Briefly, this approach implies computation of the relevant test statistic, which quantifies the effect for each pair of samples. Those (sensor, time)-pairs or time points for which the evaluated statistic exceeds the predefined significance level α_{cl} are clustered according to their spatial and/or temporal adjacency. The sum of pairwise test statistics C is then calculated for each cluster. Then the samples are permuted among the clusters and the sum of the test statistics on permuted samples C_p is collected. The latter randomized procedure is repeated for a sufficient time N , and the histogram of collected statistics C_p is constructed. The fraction of the random partitions whose statistics if larger (smaller) than the statistics for original samples $C_p > C$ ($C_p < C$) results in a desired cluster-based p -value.

For pairwise comparisons of ERP, dRTE, dDET, and dLAM between conditions we have used a two-tailed t -test for paired samples. The one-sample t -test has been used to reveal if the baseline corrected RQA measures significantly deviate from the zero-level. A desired level of significance for t -tests has been set as $\alpha_{cl} = .005$, which results in the critical value $t_{cr} = \pm 3.174$ given $df = n - 1 = 19$. Cluster-level p -values

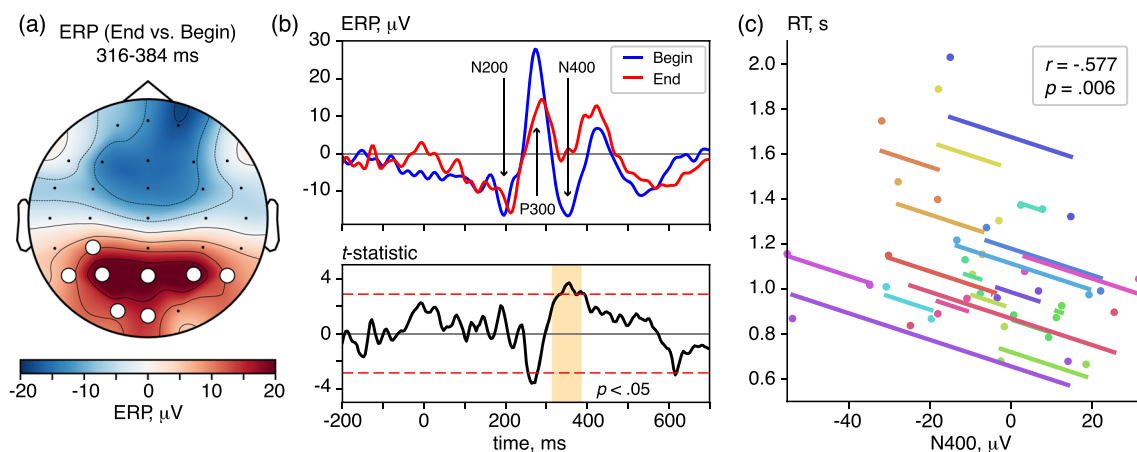


Fig. 1 Analysis of event-related potentials. **a** The topogram of ERP amplitude difference between the End and Begin conditions (red – higher in the End, blue—higher in the Begin). White circles indicate the electrodes demonstrating a statistically significant difference ($p < 0.05$ via the non-parametric permutation test, see Methods). **b** ERP waveforms in the Begin and End conditions averaged across trials and selected electrodes (upper panel) and corresponding t -value (lower panel). **c** Rm-corr plot illustrating a significant subject-wise negative correlation between the RT and the amplitude of the N400 component

have been achieved under $N = 1024$ permutations. The non-parametric cluster-based permutation test has been performed via the `MNE.statistics` package for Python [28].

Correlation analysis. To uncover a within-individual brain-behavior association as the relationship between the behavioral characteristic of RT and the ERP amplitude, we exploit a statistical technique called a repeated measures correlation (rm corr) [29]. Unlike the traditional correlation/regression analyses, this approach does not account for between-subject variability and evaluates the common slope shared among the individuals. Rm-corr, thus, exhibits greater statistical power and is especially applicable in repeated measures designs, which is the case in the current study. Rm-corr analysis and visualization have been performed via the `pingouin` statistical package for Python [30].

3 Results and discussion

3.1 ERP and behavioral response

A non-parametric cluster-based permutation test has revealed a significant reduction of the N400 component's amplitude between conditions “Begin” and “End” in occipital and parietal electrode sites ($p = 0.013$). Topogram in Fig. 1a shows a spatial distribution of the ERP difference. Figure 1b presents the ERP waveforms averaged over occipital and parietal sensors along with the corresponding t -statistic. No significant differences in the amplitude have been identified for the rest ERP components.

The inferred suppression of N400 amplitude is correlated with the behavioral response measured in terms of RT as identified by rm corr ($r = -0.577$, $p = 0.006$).

Figure 1c shows that the tendency for the “less negative” N400 component to be associated with shorter RT is shared among the participants.

These results are consistent with our hypothesis that behavioral adaptation during a long-term experiment is most probably connected with perceptual priming. There is evidence that the amount of N400 amplitude reduction reflects the degree of positive priming. As the images of the Necker cube are repeatedly presented, the participants unconsciously recognize that the stimuli share the same shape despite having different orientations and ambiguity. The stimuli presented earlier activate specific brain regions to store their representation in the memory. Regarding the later phase, the representations are already preactivated, and less neural activation is required for stimulus perception, resulting in increased processing speed.

3.2 Recurrence quantification analysis of ERPs

Now, we consider if the RQA measures of complexity exhibit the ERP-associated variations. The pioneer works by Marwan and Meinke [18] have identified that DET and LAM quantifiers indicate P300-related changes in brain dynamics. Further attempts exploiting more sophisticated order pattern recurrence plots have also shown potential for discrimination of ERPs from single-trial EEG data.

Currently, the study complements the existing knowledge by testing the applicability of the RTE measure as a promising technique to trace the transition from chaotic to regular dynamics. Figure 2 shows the pipeline of RQA applied to single trials in the frame of current research. In this example, we analyze a randomly picked EEG trial from the “Begin” condition. We consider a multivariate set of EEG signals from 8 EEG sensors (Fig. 2a) exhibiting the most pronounced variation

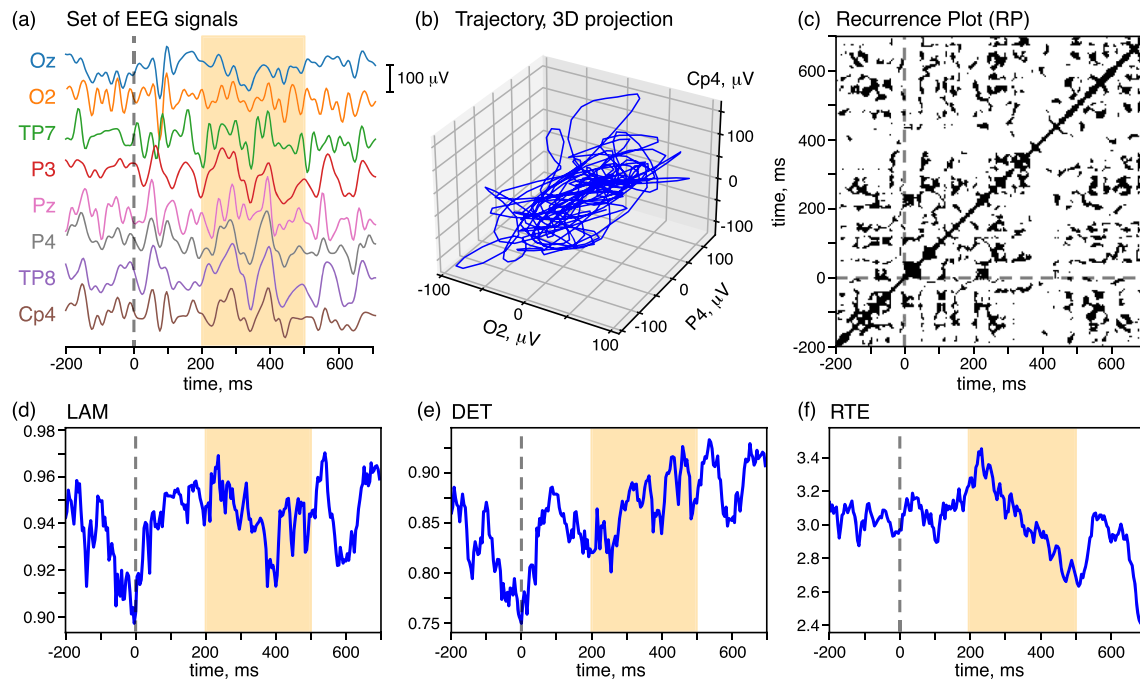


Fig. 2 The pipeline of recurrence quantification analysis. **a** Given single-trial EEG recordings from the selected set of electrodes. **b** The 3D projection of the constructed trajectory on the state space is formed from the multivariate EEG signals. **c** Constructed recurrence plot of the trajectory. Time-dependent measures of LAM (**d**), DET (**e**), and RTE (**f**) were calculated using windowed RQA of the constructed recurrence plot

of ERP between conditions as assessed by statistical analysis (Fig. 1a). These signals describe the trajectory of electrical brain activity on an 8-dimensional space, whose 3D projection is presented in Fig. 2b. Next, we construct an RP of this trajectory by choosing a threshold ϵ that yields the recurrence rate of the global RP equal to 0.03 (Fig. 2c). Time-dependent measures of LAM, DET and RTE for this RP are presented in

Fig. 2d–e. In contrast with [18], both *LAM* and *DET* measures do not show clear ERP-associated variations in single-trial recordings. Possibly for better detection these measures require averaging across multiple EEG trials. However, the RTE demonstrates a visually distinct peak at approximately 200 ms. This observation is in the favor of RTE sensitivity to ERP-associated variations.

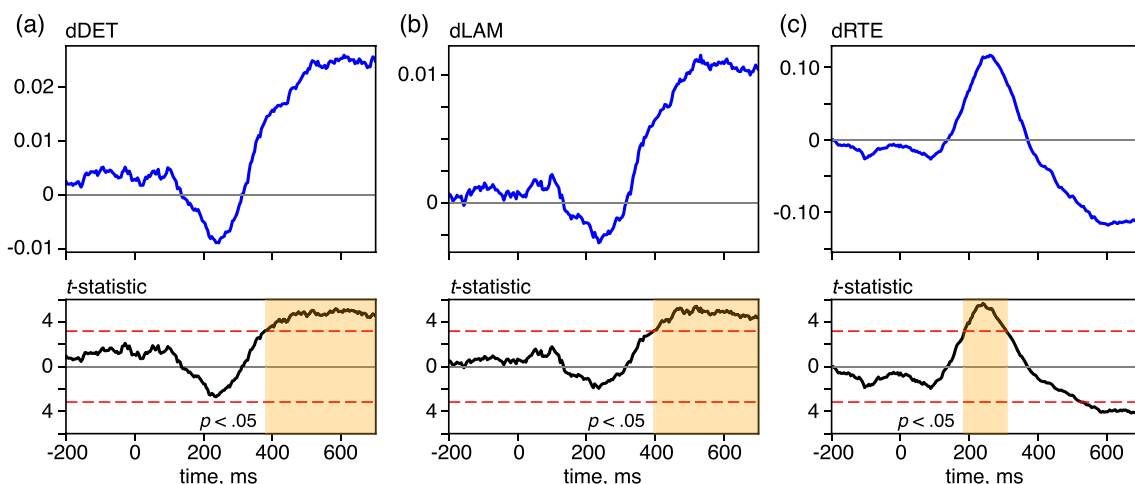


Fig. 3 Windowed RQA in the condition Begin. Upper panels illustrate the grand average of variations $dDET(t)$, $dLAM(t)$, and $dRTE(t)$, and lower panels present corresponding t -values computed via the one-sampled t -test. Shadings highlight the time intervals on which DET, LAM, and RTE significantly deviate from their baseline level ($p < 0.05$ via the non-parametric permutation test, see Methods)

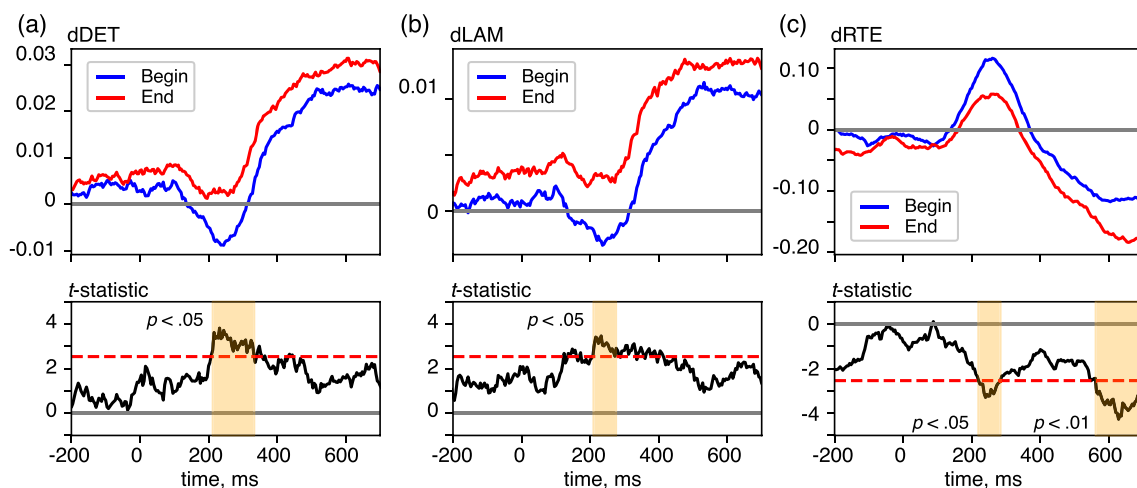


Fig. 4 Windowed RQA between experimental conditions. Upper panels illustrate the grand average of variations $dDET(t)$, $dLAM(t)$, and $dRTE(t)$, and lower panels present corresponding t -values computed via the paired t -test. Shadings highlight the time intervals on which $dDET$, $dLAM$, and $dRTE$ significantly differ between experimental conditions ($p < 0.05$ via the non-parametric permutation test, see Methods)

Employing a non-parametric cluster-based permutation test, we evaluate the group-level variations of RQA measures from their zero-level in condition “Begin”. Figure 3 reports the grand average of $dLAM$, $dDET$ and $dRTE$ along with the respective values of t -statistics. One can see that both $dLAM$ and $dDET$ exhibit a statistically significant increase after 400 ms, $p < 0.001$ in both cases, that indicates the transition from chaotic and turbulent dynamics to more periodic and laminar one. One can interpret this result as a stimulus-related attenuation of intrinsic brain noise. In contrast, the variation of $dRTE$ is more specifically related to ERP yielding significant group-level growth in the interval 188–304 ms ($p < 0.001$). This observation reflects an ERP-associated complication of the brain dynamics in terms of recurrence times. Given that ERP is a coherent and phase-locked brain response to external stimulus, one would expect quite the opposite result, and it may seem counter-intuitive at first sight. However, we will further provide a reasonable explanation of this finding.

Next, we evaluated the effect of interest by comparing the RQA measures between conditions (“End” vs. “Begin”). A non-parametric cluster-based permutation test has indicated that all considered quantities, i.e., $dDET$, $dLAM$ and $dRTE$, exhibit significant ERP-associated changes between conditions (Fig. 4). Compared with the “Begin”, both $dDET$ and $dLAM$ demonstrate an increase in the “End” on the intervals 208–332 ms ($p = 0.009$) and 208–284 ms ($p = 0.03$) respectively. Besides, $dRTE$ is reduced on approximately the same time interval 236–268 ms ($p = 0.048$) between the conditions. One may conclude that the suppression of N400 potential is reflected as a local reduction of EEG signal complexity expressed in terms of the recurrence times.

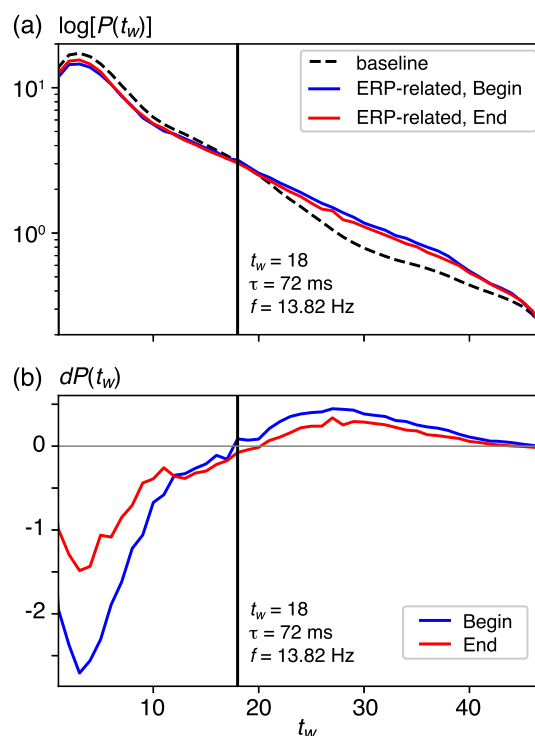


Fig. 5 Recurrence times distributions. **a** A semi-log presents the ERP-related distributions $\log P(t_w)$ of recurrence times in the Begin (blue) and End (red) conditions contrasted by the distribution during the baseline period. **b** The difference between ERP-related $P(t_w)$ and the baseline distribution for both experimental conditions. A vertical black line indicates the inflection point

3.3 ERP-associated recurrence times distributions

Figure 5a reports the semi-log plot of ERP-associated recurrence times distribution $P(t_w)$ in the “Begin” (blue line) and “End” (red line) conditions. These distortions are assessed on the interval 236–268 ms, where dRTE demonstrates a significant variation between experimental conditions and averaged across participants. They are contrasted by the distribution of the pre-stimulus (baseline) interval $[0, -500]$ ms (black dashed line). One can see that the ERP-associated positive variation of dRTE presented in Fig. 3c is determined by attenuation of the fast noisy recurrences ($t_w < 18$ d.p. or 72 ms) on the one hand and facilitated recurrences on the larger time scales ($t_w > 18$ d.p. or 72 ms) on the other hand. The time scales associated with the enhanced recurrences correspond to the period of the slow-wave ERP modulation (about 100 ms). It implies that the additional (slow) ERP-associated orbits emerge in the dynamical trajectory along with the fast motion corresponding to attenuated noisy fluctuations. The coexistence of several recurrence time scales determines a locally complicated pattern in the RP, thus causing local growth of the RTE with respect to its baseline level.

Regarding the changes between experimental conditions, Fig. 5b shows the difference between the ERP-associated and the baseline recurrence time distributions $dP(w)$ in “Begin” (blue line) and “End” (red line). It is seen that the difference $dP(w)$ is more prominent in the “Begin” condition than in the “End”. It implies a more pronounced ERP response at the beginning of the experiment that corresponds to Fig. 1b and explains the higher complexity of the trajectory expressed in the terms of recurrence times (Fig. 4).

4 Conclusion

To summarize, our study examines the variations of event-related potential during a successive ambiguous stimuli discrimination task using the recurrence quantification analysis. First, we have evaluated a significantly reduced amplitude of the N400 component from beginning to end of the experimental session. Moreover, on the group level, the amplitude of this ERP component is negatively correlated with the reaction time, which reflects a link between brain dynamics and behavior. Secondly, we have tested various RQA measures of complexity to quantify this observation in terms of dynamics. Our results establish that the recurrence time entropy is a good indicator of the ERP-associated variations in EEG signals. Surprisingly, the RTE locally increases in the ERP-associated time frame. This counterintuitive finding is, however, explained using the recurrence time distribution. While the baseline EEG signal is mostly defined by fast random fluctuations of electrical brain activity, the ERP constitutes a non-random slow modulation resulting in the additional time-scale of brain dynamics. The coexistence of fast

fluctuations and slow-wave causes an enhanced heterogeneity of recurrence times, thus locally increasing the value of RTE.

We hope that the demonstrated efficiency of the RTE in the evaluation of ERP-associated variations from a limited number of EEG trials could be useful in both further fundamental studies and neural engineering.

Author contribution statement

All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by NF, EP and VM. The study was supervised and coordinated by AH. The first draft of the manuscript was written by NF and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Data availability statement This manuscript has associated data in a data repository: <https://doi.org/10.6084/m9.figshare.12155343.v2>.

Declarations

Conflict of interest The authors have no relevant financial or non-financial interests to disclose.

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