Fingerprint propagation and the epileptogenic zone localization using cortico-cortical evoked potentials

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Introduction

Cortico-cortical evoked potentials (CCEPs) measured by low-frequency electrical stimulation allow in-vivo measures of network interactions in the brains of patients undergoing invasive presurgical stereo-electroencephalography (SEEG) monitoring for epilepsy[1,2]. In combination with other modalities, the CCEPs technique provides additional insight into brain regions involved in epileptic networks, thus helping in localization of the epileptogenic zone (EZ). Recently, we identified a "fingerprint" pattern from ictal SEEG signals that can be used as a reliable biomarker of the EZ[3]. In this study, we explore the relationship between CCEP responses and propagation of the ictal fingerprint. We show that the strength of the CCEP responses is strongly correlated with the fingerprint prediction scores when the EZ areas are stimulated.

Methods

: Five patients who underwent SEEG evaluation and had CCEPs recorded at the Cleveland Clinic were recruited for this retrospective study. All five patients had surgical resection and were seizure-free 12 months after surgery. From the CCEP recordings, we averaged trials corresponding to the responses for each stimulated contact pair for each polarity (odd and even) to improve the SNR. We then computed the root-mean-square (RMS) values of the averaged signals at all other contacts for three canonical periods: Early (10ms – 60ms), Late (60ms – 250ms) and VeryLate (>250ms) to represent the strength of CCEP responses. We also applied the fingerprint method[3] to the ictal data and generated a prediction (epileptogenicity) score for each contact. A positive score indicates higher probability of a contact being an EZ contact; a negative score indicates a very low probability. We then computed the Pearson correlation coefficients between the CCEP's RMS values from each stimulated contact pair to all other electrodes and the fingerprint prediction scores at the corresponding electrodes. We repeated this for each period for all five patients. In addition, we tested whether the (mean) correlation values were significantly higher when EZ contacts were stimulated than that when other non-EZ contacts were stimulated across all patients using the Wilcoxon rank sum test.

Results

Fig. 1 (a) – (e) shows the correlation matrices under the odd polarity for each period of CCEP response (x-axis) for all five patients when different contacts were stimulated (y-axis). The blue contacts in the y-axis were identified as the EZ contacts by the fingerprint method[3]. In contrast to the non-EZ contacts, higher correlations were observed consistently across patients when the EZ contacts were stimulated, indicating the concordance between the network identified using CCEPs and the network along which the fingerprint pattern propagated. Examples of the CCEP responses are shown in Fig. 2. Higher RMS values were observed at contacts that have higher fingerprint prediction scores and vice versa. Moreover, Fig. 1 (f) shows box-plots of the mean correlation values across five patients and two polarities when the EZ and non-EZ contacts were stimulated in different period of CCEP responses. The correlations were significantly higher (p-value was 9.13×10^{-5}, 1.23×10^{-4}, 2.91×10^{-4}, 9.13×10^{-5} for the four periods, respectively) when the EZ contacts were stimulated than when the non-EZ contacts were stimulated, regardless of the period of responses.

Conclusion

Higher correlations between the CCEP response and fingerprint scores were observed when the EZ contacts were stimulated, suggesting that interictal propagation of evoked potentials follows a similar propagation network as does ictal propagation as reflected in the characteristic 'fingerprint'. This result is consistent with the use of CCEPs for mapping ictal propagation networks as part of a presurgical evaluation of candidates for targeted ablation.

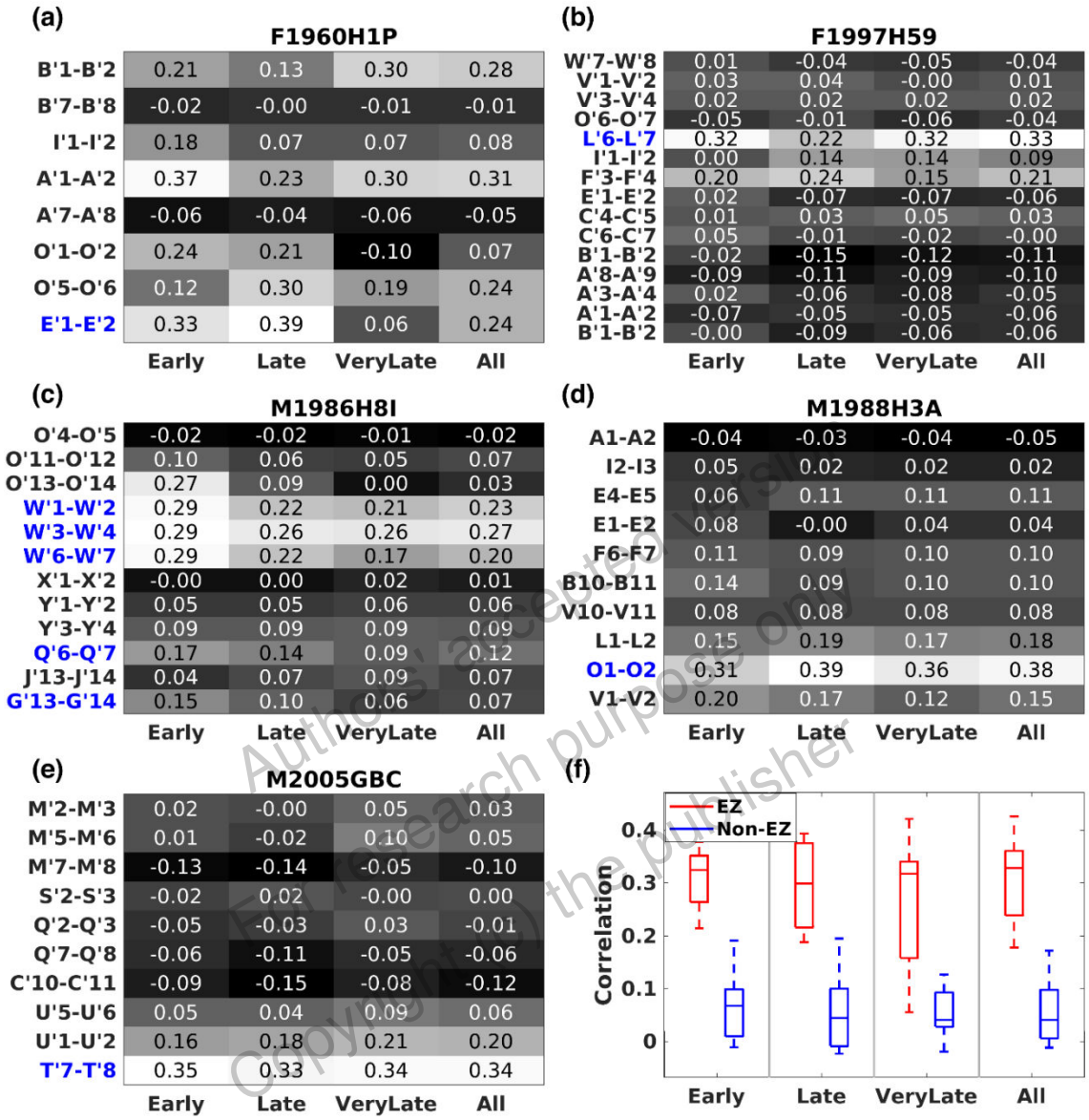

Figure 1: (a) – (e) The Pearson correlation coefficients between the RMS values measured in the CCEP responses and the fingerprint prediction scores for the five patients, respectively. Each column (x-axis, last column shows the correlation values when the entire response is used) represents different periods of the CCEP response and each row (y-axis) represents the stimulated pair of contacts. The EZ contacts identified by the fingerprint method are shown in blue; (f) Box-plots of the mean correlation values in EZ contacts (red) and non-EZ contacts (blue) across all patients and polarities.

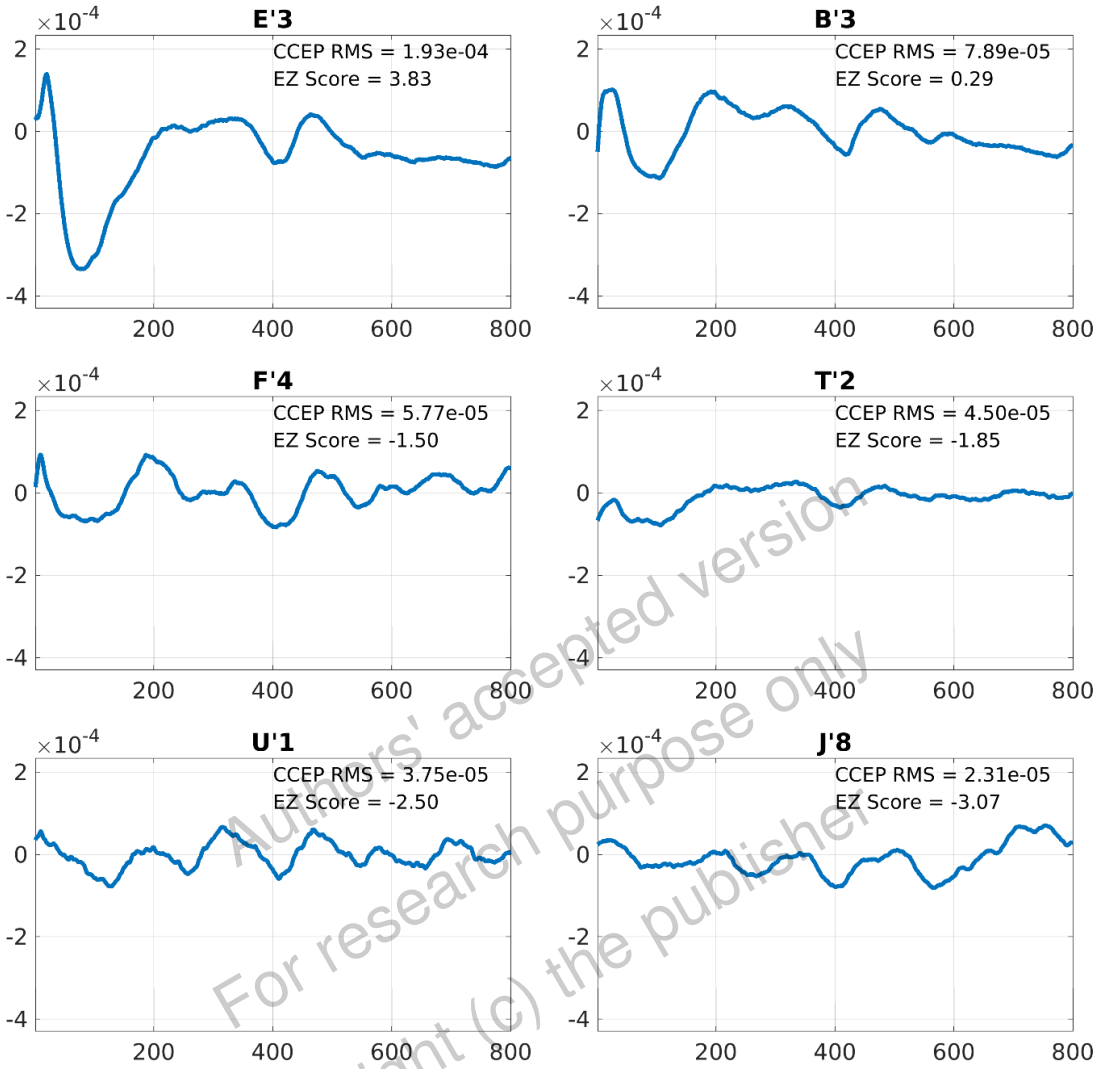

Figure 2: Examples of the CCEP response at different contacts for patient F1960H1P when the EZ contact pair E'1-E'2 is stimulated. In each sub-plot, the x-axis represents time in millisecond and the y-axis represents the magnitude of the response. The early RMS value of the CCEP response as well as the predicted EZ score are included in the top right corner for each plot.

References

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