Interacting network dynamics of neural populations: synchrony and seizure prediction

Prelim Research Abstract

Epilepsy, one of the most common neurological disorders, is characterized by the sudden onset of recurrent seizures due to the synchronous firing of populations of neurons. Due to the debilitating nature of seizures and the fact that approximately 1% of the population suffers from epilepsy, much research has investigated the dynamics of the onset of seizures with the hopes of developing methods of seizure prediction [1]. This research relies primarily on the analysis of electroencephalogram (EEG) recordings which record the neural activity of epileptic patients. Many different types of electrodes can be used to record neural activity. The least invasive type of EEG is the scalp EEG in which electrodes are placed on the outside of the scalp, while the most invasive EEG procedure, which is generally reserved for patients awaiting surgery, involves the placement of depth electrodes into the brain itself. The recorded signal varies dependent upon the type of electrode used. For example, a scalp EEG records the signal after it has passed through the skull which likely attenuates and modifies the signal, although the details of this remain unknown. EEGs recorded from depth electrodes remove the effects of the skull, but still record the activity from a population of neurons, and the placement of the electrode with respect to the individual neurons determines how each neuron's activity contributes to the signal [2]. Thus, while EEG recordings give important information about neural activity, the recorded signal is not directly linked to the underlying dynamics of the brain, and while analysis of the EEG signal is essential in epilepsy research, it is understood that one is not gaining information about the true dynamics of seizure generation and propagation.

Through the analysis of EEG recordings, it has been shown that one can identify a preictal period before the onset of a seizure during which various properties of the EEG time series differ from those during interictal (normal activity between seizures) and ictal (seizure) periods [3]. This

change in the properties of the EEG signal is suggestive of changes in the underlying dynamics of the brain. Different types of analysis have been used depending of the type of EEG recording being studied, but one way of characterizing this preictal period is to examine measures of phase synchronization between different channels of intracranial EEG recordings from depth electrodes.

Phase synchronization refers to the state where the phases of two oscillators become locked but their amplitudes remain uncorrelated [4]. Measures of synchronization show that EEG channels exhibit high levels of phase synchronization during interictal and ictal periods [5, 6, 7, 8]. However, in patients who suffer from focal point epilepsy - a pathological condition in which seizure generation occurs in a specific location (focus) in the brain before spreading to encompass all neural activity - it has been found that there is a drop in the level of phase synchronization during the preictal period. While the cause of this decrease in synchronization is unknown, it has been hypothesized [5, 7] that the recordings are in separate regions of synchronization activity: one site has become involved in the synchronous activity associated with the focus and onset of the seizure, while the other site has yet to become enveloped in this activity. Testing this hypothesis at the neuronal level with EEG data cannot be done since EEG recordings do not give direct information about neuronal dynamics. We thus turn to a modeling approach to gain further insight into the possible mechanisms for the increased synchrony observed during interictal periods as well as the drop in synchrony during the preictal period.

We study a computational model in which two coupled networks of integrate-and-fire neurons model separate EEG recording sites. Both networks have a small-world (SW) topology [9], which is on the border of the transition between local and global synchrony and has been shown to mimic the transition from a non-bursting regime to the bursting regime observed during epilepsy [10]. Functional mappings of brain activity also exhibit a SW structure and suggest that the underlying topology is SW as well [11, 12]. Additionally, the rewiring done to create the SWN is suggestive of the rewiring of neural circuitry known as axonal sprouting which is common among epilepsy patients and involves the addition of excitatory synapses between different layers of the brain. The two networks are then coupled so that the dynamics of the networks are driven by the internal dynamics of each network and the external, mean-field type of signal from the other network.

We choose one network to be associated with the focal point of the seizure and slowly drive this network into a bursting (seizing) state by increasing the excitability of the neurons within that network over time. The neural excitability determines the amount of synaptic input needed to cause the neurons to spike. A neuron with a higher excitability needs less synaptic input in order to spike and thus will have a higher mean firing rate. Once the excitability (and therefore mean

firing rate) is increased beyond a threshold value, the network enters the bursting state in which the entire population of neurons fire synchronously. This method of transition into a seizure is chosen to mimic the increased excitability measured in neurons which have been induced into an epileptic state under laboratory conditions [13]. The increase in neuronal excitability is believed to be due to an imbalance between activity in excitatory and inhibitory synapses. By summing the synaptic activity of all of the neurons within a given network, we create a signal representative of the behavior of the network as a whole. A model of this type allows for analysis of the levels of synchronization over the total population of the networks (similar to that done using intracranial EEG) as well as at the level of the individual neurons.

We can relate the excitability parameter to the natural frequency of the network since this parameter gives information about the firing rates of the neurons. We observe increased levels of synchrony between the summed signals of each network around the region of parameter matching between the two networks. Here, the neurons in the networks share the same distributions of frequencies but are not yet in the bursting state, and we associate this state with the interictal regime. As the excitability of one network is increased and the natural frequencies of the networks no longer match, we see a drop in the synchrony as found during the preictal stage. Once the networks enter the bursting regime, we again observe high levels of synchrony as the bursting network drives the other near different frequency locking patterns, dependent on the frequency of the bursting network. Interestingly, examination of the firing rates of the individual neurons within the driven network indicates that the behavior of the network as a whole is not necessarily reflective of the behavior of the neurons but is instead a combined result of their firing rates and relative phases. We observe that during the preictal period the neurons in the focus exhibit increased frequency locking. However, this locking does not lead to increased synchrony in that network.

We thus postulate that the preictal period marks the beginning of the transition from normal neural dynamics into bursting dynamics, which is characterized by the steady increase and locking of neuronal frequencies that leads eventually to an increase in neural activity (bursting). This transition in the focus is accompanied by an initial lack of a similar transition in the “normal” network, which causes the divergence of intrinsic network properties and a drop in the phase synchrony. We associate this effect with a resonance effect similar to that of stochastic resonance which is known to play an important role in other neural systems such as the electroreceptors of paddlefish [14, 15] and the photoreceptors of crayfish [16, 17].

Therefore, we hypothesize that the observed drop of phase synchrony in EEG recordings is in fact an early signature of the pathological changes in the dynamics of the focus that eventually lead

to seizure-type dynamics. Assuming that the realization of this pathological process could vary significantly from patient to patient (i.e. a different rate of transition to ictal dynamics and/or a different distance in terms of the necessary parameter change needed to reach the bursting threshold) but should be relatively constant from seizure to seizure within the same patient, we predict the length of the preictal drop of the phase synchrony should show large inter-patient and reduced intra-patient variability. To illustrate this we have varied the rate of change in neuronal excitability and observe that repeatable realizations of the interictal - ictal transition for the same rate of change of excitability generate relatively repeatable preictal lengths. However, these preictal lengths vary widely for different rates of change in the excitability.

It is also worth noting that different realizations of the same network topology (the same rewiring parameter for both networks and the same number of inter-network connections) generate different amounts of variance in the preictal lengths for the same rates of change of excitability. This again indicates that the variance in the length of the preictal period could differ from patient to patient. We hope to further explore the effects of specific realizations of the network topology in future research.

In conclusion, we have created a simple model which demonstrates changes in synchrony consistent with those observed in EEG recordings from epilepsy patients. Through analysis of our model, we propose a possible mechanism for the dynamics of seizure generation and propagation in which changes in the firing frequency of neurons in the focus cause the system to move out of a resonance state as the focus transitions from a normal to bursting regime. This bursting behavior then acts as a driving force, recruiting neurons in a previously unaffected area into the bursting state. This difference in network dynamics during the transition from resonance to bursting leads to the observed drop in phase synchrony, and differences in the rate of this transition between patients could explain the large variance in the observed preictal lengths in different patients suffering from focal epilepsy.

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