The connection between sleep spindles and epilepsy in a spatially extended neural field model

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Abstract

A connection between sleep spindles and epilepsy or in particular seizures has been stated in previous research. This is a project aiming to evaluate if this connection can be shown in a spatially extended cortical model. The model has earlier been used to generated spike and wave discharges, seizures, and it can therefore be thought to be able to show the wanted connection. The evaluation is made by changing the parameters in the cortical system when an external current is put into it. The external current is either a current of random spiking behavior or it has the pattern of sleep spindles. The conclusion of the evaluation is that this model is not sufficient enough to show the connection between sleep spindles and epilepsy.

1 Background

1.1 Sleep spindles

Sleep spindles are a type of oscillation that occur during one of the earlier stages of sleep, stage 2 in the sleep cycle. They are present in both the beginning and the end of stage 2, which is a non REM part of the sleep cycle. Sleep spindles have the feature of waxing and waning field potential at 7-14 Hz and they last for 1-3 seconds and reoccur every 5-15 seconds. [1] Sleep spindles are generated from the thalamus [2].

1.2 Epilepsy and seizures

Epilepsy is a neurological disorder which is defined by the occurrence and reoccurrence of seizures. A seizure was in 2005 defined by Fisher et al. as a ”transient of signs and/or symptoms due to abnormal excessive or synchronous neuronal activity in the brain”. Hence seizures are a result of abnormal, synchronized attacks of electrical activity in restricted area of connected neurons, called the epileptogenic focus. The neurons in the epileptogenic focus should also be fast in recruiting other parts of the brain to act them same. When seizures involve most part of the brain they can cause unconsciousness while if they are more localized, focal, they only affect single parts of the body. Epilepsy can be a result of inborn abnormalities in the brain, genetic alterations concerning brain metabolism, excitability-causing proteins or brain injury.[3]

While looking at the pattern of seizures a distinct feature is spike and wave oscillations. A spike and wave oscillation can be shown through EEG, as has been done in figure 1 below. The

frequency of the spike and wave oscillations are about 3 Hz in humans. This kind of pattern can be shown in one of the most common type of epileptic manifestations, absent seizures. This phenomenon, spike and wave discharges, is nonlinear and occur frequently in different kinds of epileptic disorders, especially in children. This type of seizures can also disappear with adolescence. Observation of similar seizures have been made in several animal models. [4]

1.2 The connection between sleep spindles and epilepsy

There are two descriptions concerning the connection between sleep spindles and seizures. One is that while a system is undergoing sleep spindle oscillations this pattern can turn in to seizures. This has been shown before in non-neural field models. [5] The other description is that sleep spindles and seizures originate from the same type of dynamical system. It has been shown that antagonizing manipulations made on sleep spindles have the same effect on seizures. [6]

2 The model

2.1 Background

Spike and wave discharges are not well understood in terms of their spatiotemporal features, how they behave in both space and time. In earlier models spike and wave discharges were modeled as oscillations being both periodic and homogenous on a macroscopic spatial scale and therefore space independent. In the model *A spatially extended model for macroscopic spike-wave discharges* by Peter Neal Taylor and Gerold Baier in March 2011 a model is made that take these spatial properties into account. [7]

Several experimental results point to the thalamus having a critical role in the generation of spike and wave discharges. It has been shown that if the thalamus is somehow inactivated these discharges disappear. [8] Even though, Taylor and Baier are able to generate spike-wave discharges in their cortical neural field model [9]. The cortex has also been shown having a critical role in modelling epilepsy [10].

2.2 Epilepsy and seizure

Spatially extended neural field models are systems of equations describing the spatiotemporal evolution of for example firing rate at tissue level. The Amari model is such a model. [11] Taylor and Baier simplified the Amari neural field model [12] to an ordinary differential equation of low dimension. They then extended this model and showed that it results in a model capable of generating spike and wave discharges. Further on they converted their model back to a neural field equation with three neural populations and they showed the existence of spike and wave discharges for the first time in such a model. [13]

Their model is these ordinary differential equations with three variables

$$\dot{E}(t) = h_1 - E + w_1 f[E] - w_2 f[I_1] - w_3 f[I_2]$$

$$\dot{I_1}(t) = (h_2 - I_1 + w_4 f[E])/T_1$$

$$\dot{I_2}(t) = (h_3 - I_2 + w_5 f[E])/T_2$$

Where E stands for the excitatory population of the model while $I_1$and I_2 stand for the two inhibitory populations of the model. h_i are the constants arising from the Amari model, w_i are the connectivity parameters and T_1 and T_2 are time scale parameters, for which it holds that $T_1 < T_2$.

f is the piecewise linear function with the behaviour:

$$f = 0 \quad if \quad v \leqslant -1$$

$$f = \frac{v + l}{2 \cdot l} \quad if \quad -1 < v < 1$$

$$f = 1 \ if \quad v \geqslant 1$$

where $l > 0$ determines the steepness of the transition and v is defined as either E, I_1or I_2. f is replacing the Heaviside step function in the original model by Amari, which has been shown to not be generating spike and wave discharges. In addition to the piecewise linear function a sigmoid function is also used.

If $w_i, i = 1,..,5$ are left as constants the model is a spatially homogenous version of the Amari model with an additional inhibitory population operating in a different time scale than the first inhibitory population. The model is also using the piecewise linear function or the sigmoid function. If $w_i, i = 1,..,5$ instead are set to the form of a "Mexican hat" connectivity, as in the original Amari model, a modified version of it is constructed with an additional inhibitory population as following:

$$\left.\begin{aligned} \dot{E}(i) &= h_1 - E + \textstyle\sum_{j=1}^{n} w_1(i-j) f[E(j)] - \sum_{i=1}^{n} w_2(i-j) f[I_1(j)] - \sum_{i=1}^{n} w_3(i-j) f[I_2(j)] \\ \dot{I}_1(i) &= (h_2 - I_1(i) + w_4 f[E(i)])/T_1 \\ \dot{I}_2(i) &= (h_3 - I_2(i) + w_5 f[E(i)])/T_2 \end{aligned}\right\} \quad (1)$$

where n is the number of spatial locations.

The result is spike and wave discharges for many combinations of connectivity values w_i when simulating this model with periodic boundary conditions for one dimension. In figure 2 below the simulation of the model is shown for the following values for the parameters; $h_1 = 5$, $h_2 = -0.9$, $h_3 = -1.6$, $w_4 = 4$, $w_5 = 3$, $T_1 = 0.66$and $T_2 = 200$. Where $w_i, i = 1..3$ are built up by mexican hat functions. [14]

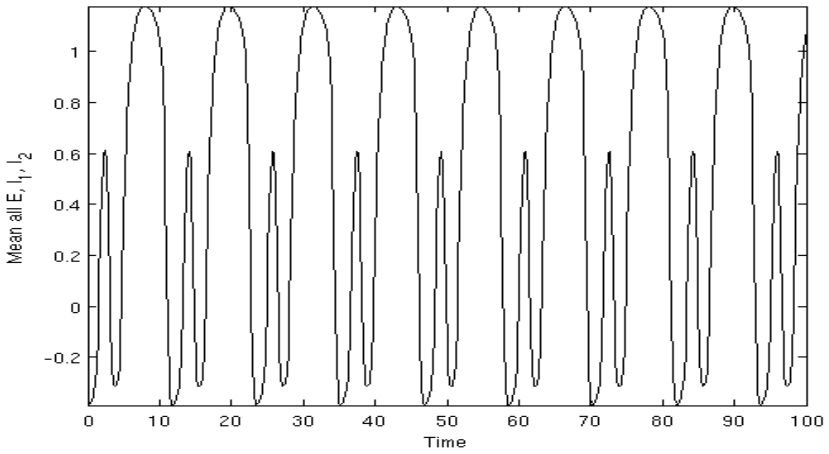

Figure 2. Spike and wave discharges

3 The method

The goal is to analyse if the connection between sleep spindles and epilepsy that is described in section 1.3 can be shown in this cortical model.

3.1 Injecting an external sleep spindle current

A model of sleep spindles can be done by the following function in time [15]:

$$g(t) = \frac{c}{\sqrt{s}} g(\frac{t-u}{s}) e^{iwt} \quad (2)$$

where $s > 0$, $g(x) = \mathrm{e}^{-x^2/2\sigma^2}$ is a gaussian function and σ, c, u and w are constants.

If the parameters are chosen as follows; $s = 2$, $\sigma^2 = 100$, $u = 5$, $w = 50$ and $c = 1$, the following sleep spindle model can be produced in Matlab, se figure 3 below.

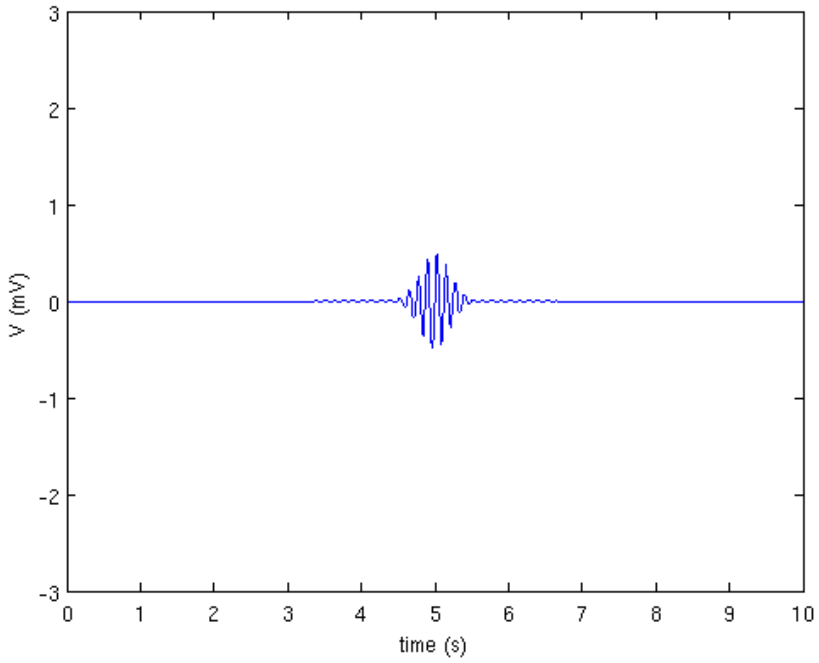

Figure 3. Model of sleep spindle with frequency 8 Hz and a duration of 1.4 sec

An external current is made of the sleep spindle formation in figure 3 above reoccuring every 5-15 seconds during 100 seconds. The effect of this external current, when being put into both the excitatory population and both of the inhibitory populations in system (1) in section 2.2 above, is then analysed while changing the parameters of the system. In addition, two other formations of the sleep spindle are used to generate the external current. These are of frequency 10 and 14 Hz and exist for 2.1 and 3 seconds, respectively.

3.2 Generating sleep spindle formation with the model

An external current with random spiking behavior (noise) is first inserted into the excitatory population and then to the two inhibitory populations respectively in the system (1) in section 2.2 above. The behavior of the system is analyzed while the parameters are changed in order to find a behavior of the system similar to that of a sleep spindle formation.

4 Results

In part 3.1 the system is showing spike and wave discharges while the parameters are set to values that are already showing this pattern without the external sleep spindle formatted current. Otherwise the external current is not turning in to seizure like behavior. In part 3.2 no parameters are found for which the system is generating a pattern similar to that of a sleep spindle.

5 Conclusions

Even though spike wave discharges, which is a phenomenon that is concerning the thalamus as well, can be shown in this cortical model the model is not sufficient enough to show the connection between sleep spindles and seizures. The model for sleep spindles that is used (2) is not taking into account the feedback the sleep spindle oscillations are given by the thalamus. What would be done in the future is expanding this model to include the thalamus and generate the sleep spindle oscillations from the thalamic neurons, injecting their output signal into the cortical model. This would be a feedback system which might would be sufficient enough to show the connection between sleep spindles and epilepsy.

References

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[4] http://www.scholarpedia.org/article/Spike-and-wave_oscillations (2011-11-17)

[5] see [2]

[6]http://www.scholarpedia.org/article/Thalamocortical_oscillations#Sleep_spindle_oscillations(2011-11-17)

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[8] see [2]

[9] see [7]

[10] see [6]

[11] http://www.scholarpedia.org/article/Neural_fields (2011-11-18)

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[13] see [7]

[14] see [7]

[15] see [1] p.5