ECoG-based Short-range Recurrent Stimulation Techniques to Stabilize Tissue At Risk of Progressive Damage: Theory based on Clinical Observations

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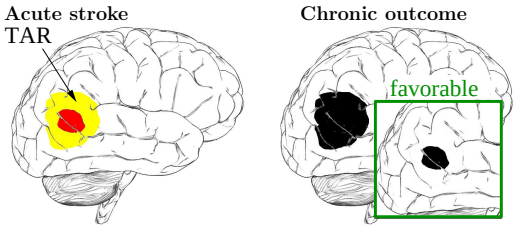
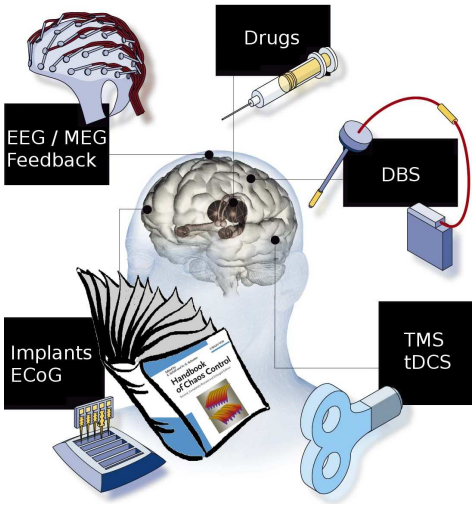
Problem

How to stabilize in acute stroke the tissue at risk (TAR, yellow region surround red infarct core) by preventing adverse effects of waves of mass neuronal depolarization, i. e., spreading depolarization (SD)?



The emergence of re-entrant SD waves in the TAR region is believed to worsen outcome. We present theoretical concepts based on chaos control [1] to prevent such events:



SD and haemodynamic responses

In aneurysmal subarachnoid haemorrhage (aSAH, see box), SD waves have a high incidence and cause hypoxia in tissue at risk, and, importantly, the haemodynamic response is the inverse of that seen in healthy tissue. Below SD shown by functional magnetic resonance imaging (fMRI) in a migraine patient [2].

Non-invasive recordings

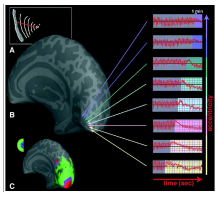
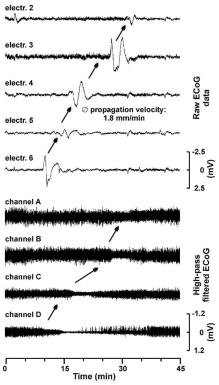
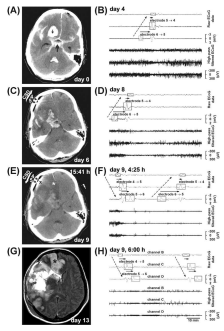


Figure courtesy of Nouchine Hadjikhani [2]

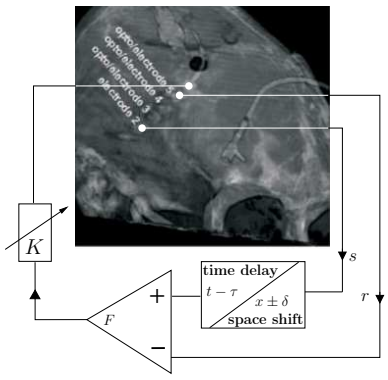
Invasive recordings

Clinical electrocorticography (ECoG) recordings of relevant signals suggested for the feedback control.





Solution



In theoretical studies[3, 4, 5], a mechanism was presented suggesting how a failure of internal feedback could be a putative mechanism of SD patterns in acute stroke. This failing internal feedback control is now suggested to be replaced by ECoG-based short-range recurrent functional stimulation that initiates the normal hyperperfusion haemodynamic response in a demand-controlled way and stabilizes the tissue at risk during the critical phase of SD passage.

Extended Hodgkin-Grafstein model

$$\frac{\partial u}{\partial t} = u - \frac{u^3}{3} - v + D\frac{\partial^2 u}{\partial x^2}$$
$$\frac{\partial v}{\partial t} = \epsilon(u + \beta - \gamma v) \quad + K(u(x,t) - u(x-\delta, t-\tau))$$

The suggested method has three key features:

(i) it is short-range, i.e., in the order of the distance of the ECoG electrode strip,

(ii) it is demand-controlled, and

(iii) it uses no prior knowledge of the target state, in particular, it adapts to conditions in the healthy physiological range.

On-demand type stimulation provides minimal invasive feedback as the control force is off when the target state is reached, i.e., when the TAR region is without SD wave or the parameters of TAR are back to their physiological range (out of risk). These last two features (ii-iii) are shared with classical methods of chaos control, where major progress was made in the last years with respect to extensions for spatio-temporal wave patterns.

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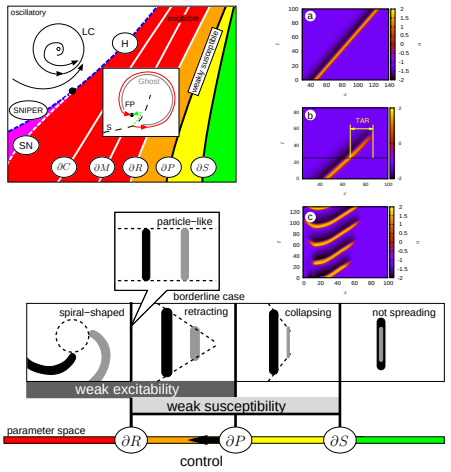
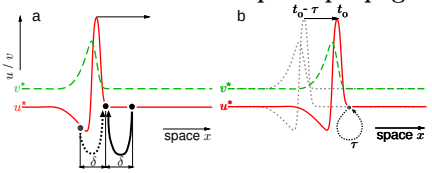
Parameter space of excitability



Nonlocal feedback on pulse propagation



Objective: Investigation of the influence of the system parameters (ϵ, β and γ) on the emergence of SD waves.

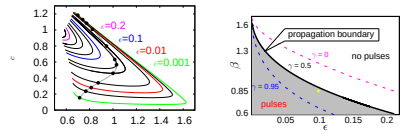
Method: Continuation of homoclinic orbits in the co-moving frame using AUTO

- co-moving variable $\xi = x - ct$
- searching for stationary solutions $\Rightarrow \partial_t = 0$

Profile equations to study shape dynamics

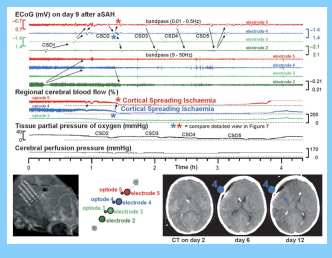
$$\partial_\xi u(\xi) = w(\xi)$$
$$\partial_\xi w(\xi) = \frac{1}{D}(-u(\xi) + \frac{u^3(\xi)}{3} + v(\xi) - cw(\xi))$$
$$\partial_\xi v(\xi) = \frac{\epsilon}{c}(-u(\xi) - \beta + \gamma v(\xi))$$

For each ϵ a saddle node bifurcation of fast and slow homoclinic orbits mark the maximum β for which stationary pulses can occur.



Aneurysmal subarachnoid haemorrhage

The recordings are performed in combination with novel subdural opto-electrode technology for simultaneous laser-Doppler flowmetry in patients with aneurysmal subarachnoid haemorrhage (aSAH). In previous clinical studies, clusters of prolonged SDs have been measured in aSAH patients in close proximity to structural brain damage as assessed by neuroimaging [6, 7]



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