There are around 50 million people with epilepsy worldwide and 30%-40% do not respond well to antiepileptic drugs. Electrical stimulation, as an alternative treatment for patients with refractory epilepsy, has received increased attention over the last decades. However, the efficiency of these electrical therapies is still relatively low. For example, only a 50% of reduction of seizures was obtained in 50% of the patients receiving for vagus nerve stimulation (VNS). One possibly way to improve the antiepileptic efficacy of such electrical stimulation treatments is to optimize the stimulation. The present thesis hypothesized that the antiepileptic effect of VNS and spinal cord stimulation (SCS) can be improved by using a higher stimulation frequency than currently used in the clinic and proposed in the literature.

An acute spike and wave rat seizure model was developed (seizure induction by pentylenetetrazole (PTZ)). Based on this model, three studies were conducted to test the hypothesis:

• Study 1 explored the effect of high frequency SCS (up to 180 Hz) in inhibiting spike-and-wave seizures.

• Study 2 explored the effect of high frequency VNS (up to 180 Hz) in inhibiting spike-and-wave seizures.

• In Study 3, the effect of VNS and SCS conducted at frequencies investigated in study 1 and 2 were further analysed by investigating the change of fast ripple (FR) activity (i.e. high frequency oscillations in the range of 250-600 Hz). FRs are thought to play an important role in seizure generation and propagation.

This thesis work demonstrated that VNS and SCS conducted at high frequencies (i.e. 130 Hz and 180 Hz) obtained a higher degree of control than lower stimulation frequencies. A higher reduction of FR was also achieved at these stimulation frequencies. Study 3, for the first time, evaluated how electrical stimulation at different frequencies influence the FRs under the seizure condition.

The results suggest that the antiepileptic effect of clinically used VNS and the potential new antiepileptic tool SCS may be improved by using a higher stimulation frequency in an animal model. Further studies will be needed to verify if similar results may be obtained in chronic animal epilepsy models and in patients.
To fulfill the requirements for the Ph.D. degree, Jianhang Jiao has submitted the thesis: Functional Electrical Stimulation for Control of Epileptic Seizures, to the Faculty Council of Medicine at Aalborg University.

The Faculty Council has appointed the following adjudication committee to evaluate the thesis and the associated lecture:

**Chief Physician** Troels Wesenberg Kjær  
Roskilde Hospital  
Denmark

**Academic Advisor** Jean Delbeke  
University of Gent  
Belgium

**Chairman:**  
Associate Professor Carsten Dahl Mørch  
SMI, Aalborg University  
Denmark

**Moderator:**  
Professor Winnie Jensen  
SMI, Aalborg University  
Denmark

The Ph.D. lecture is public and will take place on:

**Monday 14 December 2015 at 13:00**  
Aalborg University – Room D2-106  
Fredrik Bajers Vej 7 D2  
9220 Aalborg East

---

**Program for Ph.D. lecture on**

**Monday 14 December 2015**

**by**

Jianhang Jiao

---

**Functional Electrical Stimulation for Control of Epileptic Seizures**

**Chairman:**  
Associate Professor Carsten Dahl Mørch

**Moderator:**  
Professor Winnie Jensen

13.00 Opening by the Moderator

13.05 Ph.D. lecture by Jianhang Jiao

13.50 Break

14.00 Questions and comments from the Committee  
Questions and comments from the audience at the  
Moderator’s discretion

16.00 (No later than)  
Conclusion of the session by the Moderator

---

After the session a reception will be arranged