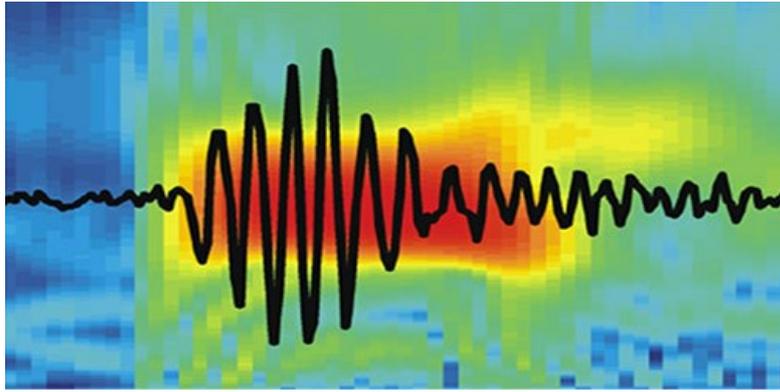


Epilepsy Research Group



Group leader: **Professor John Jefferys**
[\(/staff/profiles/cem/NN/Jefferys-John.aspx\)](/staff/profiles/cem/NN/Jefferys-John.aspx)

Overview

In epilepsy brain function is suddenly, and usually transiently, disrupted by the excessive activity of seizures. The fundamental problem is in the organisation and dynamics of networks of neurons and glia. Our goal is to discover how neural networks change in epilepsy with a view to help improving treatment and our understanding of normal brain function.

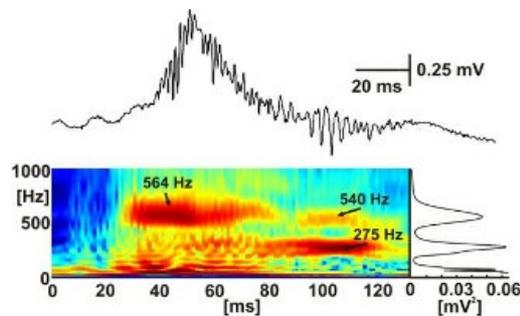
Our research group

Temporal lobe epilepsy is one of the most common classes of epilepsy. Up to 40% of cases do not gain adequate seizure control with currently available drugs, which presents a major unmet clinical need. Most cases of temporal lobe epilepsy are thought to result from non-traumatic precipitating events, and most experimental models use some means of inducing the epileptic focus. A latent period (weeks to months or longer) follows the precipitating event, during which the normal brain circuitry transforms into an epileptic focus ("epileptogenesis"). One of the major goals of the field is to develop disease-modifying treatments that can prevent epileptogenesis, although the ambiguity of the identity of the precipitating events makes it difficult to know when any such treatment could be administered.

Our aims are to understand how neural circuitry is disrupted in epileptic foci and how the dynamics of neuronal activity change both during seizures and during the prolonged "interictal" periods between them.

Cellular and network mechanisms of epileptic foci. Chronic experimental models, corroborated by the limited data available from clinical cases, show that multiple aspects of cellular structure and function change in each epileptic focus. This poses a major challenge to distinguish the causes of the epilepsy from the consequences of repeated seizures. We are using a range of electrophysiological (electrical) and histological methods to identify cellular and network changes in a model of temporal lobe epilepsy which lacks any obvious damage to the brain (about one third of clinical temporal lobe cases are known as non-lesional). Ultimately this work could lead to improvements in treatment by drugs or therapeutic stimulation.

Dynamics of neuronal activity during and between seizures. Seizures are the most dramatic feature of epilepsy. Between seizures activity may be changed in more subtle ways, such as the interictal discharge shown in the banner to this page. Interictal epileptiform activity can have subtle effects on brain function, but can help with diagnosis. Surgery to remove the epileptic focus can be very effective in carefully selected cases. The challenge is to find the "epileptogenic zone" which by definition is the brain tissue that needs to be removed to stop the seizures. We have been particularly interested in "high frequency oscillations" between, preceding and during seizures. In the hippocampus (see drawing of a brain with hippocampus exposed) those faster than ~250 per second seem to be much more common in the epileptic focus and may provide a viable marker for the epileptogenic zone. We always are interested in basic mechanisms, and in 2003 reported that these high frequency oscillations depended on clusters of individual neurons firing at much lower rates.



Fast ripples mark the primary epileptic tissue in experimental temporal lobe epilepsy.

Modified from Jiruska et al 2010, *Brain* 133:1380-90
<http://brain.oxfordjournals.org/content/133/5/1380>

Clinical implications. Translation into clinical practice of our work currently is mainly on helping refine the identification of the epileptogenic zone before surgery, which now is impacting on some patients and contributing to major reviews. We also are committed to teaching about epilepsy at all levels, including a special study module on epilepsy for our medical students which is delivered by epilepsy researchers and clinicians from across our campus and Health Trusts.



Current Projects

- Mechanisms of high frequency activity in chronic epileptic foci (Jefferys Powell and Jiruska, Epilepsy Research UK)
- Mechanisms of mesial temporal lobe epilepsy (Jefferys and Sik. Medical Research Council)
- Electrographic patterns in epileptogenesis (Jefferys and Kansas Medical Center Research Institute, USA)
- Cell controlling approaches to epilepsy research (Chang, MRC Centenary Award)

Recent Publications

- Jefferys JGR, Menendez de la Prida L, Wendling F, Bragin A, Avoli M, Timofeev I, da Silva FHL (2012) Mechanisms of physiological and epileptic HFO generation. *Prog.Neurobiol.* 98:250-264
- Jiruska P, Csicsvari J, Powell A, Fox JE, Chang WC, Vreugdenhil M, Li X, Palus M, Bujan AF, Dearden RW, Jefferys JGR (2010) High-frequency network activity, global increase in neuronal activity and synchrony expansion precede epileptic seizures in vitro. *J Neurosci* 30:5690-701
- Jiruska P, Finnerty GT, Powell AD, Lofti N, Cmejla R, Jefferys JGR (2010) High-frequency network activity in a model of non-lesional temporal lobe epilepsy. *Brain* 133:1380-90
- Jiruska P, Tomasek M, Netuka D, Otahal J, Jefferys JGR, Li X, Marusic P (2008) Clinical impact of high-frequency seizure onset zone in a case of bi-temporal epilepsy. *Epileptic.Disord.* 10:231-238
- Bikson M, Fox JE, Jefferys JGR. (2003)Neuronal aggregate formation underlies spatiotemporal dynamics of nonsynaptic seizure initiation *J.Neurophysiol.* 89:2330-2333

Staff

Principal Investigators

[Professor John Jefferys \(/staff/profiles/cem/NN/Jefferys-John.aspx\)](/staff/profiles/cem/NN/Jefferys-John.aspx)

[Professor Attila Sik \(/staff/profiles/cem/NN/Sik-Attila.aspx\)](/staff/profiles/cem/NN/Sik-Attila.aspx)

[Dr Martin Vreugdenhil \(/staff/profiles/cem/NN/Vreugdenhil-Martin.aspx\)](/staff/profiles/cem/NN/Vreugdenhil-Martin.aspx)

Internal Collaborators

[Dr Andrew Powell \(/staff/profiles/cem/PPT/Powell-Andrew.aspx\)](/staff/profiles/cem/PPT/Powell-Andrew.aspx) - School of Clinical and Experimental Medicine, College of Medicine and Dental Sciences

[Dr Andrew Bagshaw \(/staff/profiles/psychology/bagshaw-andrew.aspx\)](/staff/profiles/psychology/bagshaw-andrew.aspx) - School of Psychology, College of Life and Environmental Sciences and The Birmingham University Imaging Centre (**[BUIC \(http://www.buic.bham.ac.uk/\)](http://www.buic.bham.ac.uk/)**)

[Dr Amanda Wood \(/staff/profiles/psychology/wood-amanda.aspx\)](/staff/profiles/psychology/wood-amanda.aspx) - School of Psychology, College of Life and Environmental Sciences and The Birmingham University Imaging Centre (**[BUIC \(http://www.buic.bham.ac.uk/\)](http://www.buic.bham.ac.uk/)**)

External Collaborators

Dr Premysl Jiruska - Developmental Epileptology, Institute of Physiology Academy of Sciences of Czech Republic

Associate Professor Pedro Irazoqui - Purdue University, Indiana, USA

Professor Ivan Osorio - Kansas City Medical Research Institute, USA

Clinical Epileptologists

Dr Doug McCorry - Neurology, University Hospitals Birmingham NHS Trust, UK

Dr Manny Bagary - University Hospitals Birmingham NHS Trust, UK

[Dr Andrea Cavanna \(/staff/profiles/cem/NN/cavanna-andrea.aspx\)](/staff/profiles/cem/NN/cavanna-andrea.aspx) - University Hospitals Birmingham NHS Trust, UK

Dr Colin Shirley - Neurophysiology, University Hospitals Birmingham NHS Trust, UK

Mr Ramesh Chelvarajah - Neurosurgery, University Hospitals Birmingham NHS Trust, UK

Postdoctoral Researcher

[Dr Wei-Chih Chang \(/staff/profiles/cem/NN/chang-wei-chih.aspx\)](/staff/profiles/cem/NN/chang-wei-chih.aspx)

PhD Students

Gareth Morris

Lucy Foss

Funding Bodies

- **[Epilepsy Research UK \(http://www.epilepsyresearch.org.uk/\)](http://www.epilepsyresearch.org.uk/)**
- **[Medical Research Council \(http://www.mrc.ac.uk/index.htm\)](http://www.mrc.ac.uk/index.htm)**
- **[The Wellcome Trust \(http://www.wellcome.ac.uk/\)](http://www.wellcome.ac.uk/)**