Using Open Source Instruments wireless telemetry devices and software to monitor and analyse seizure activity in rodents.

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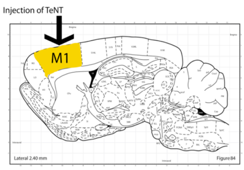
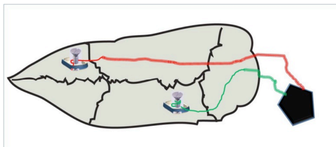
We are epilepsy researchers based in the department of Clinical & Experimental Epilepsy at the UCL Institute of Neurology, UK. We have been using a variety of implantable EEG devices and software scripts provided by Open Source Instruments to record and analyse EEG from epileptic rodents since 2010. Below we describe how their devices and software have aided some of our recent epilepsy research.

Implantable devices for long-term, wireless EEG recordings.

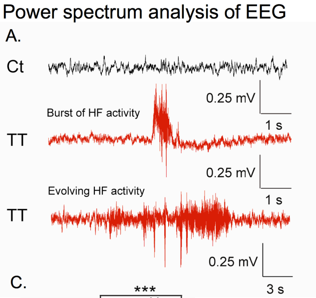


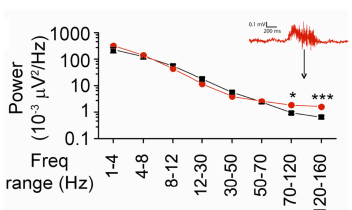


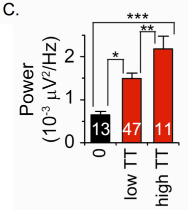
In our initial experiments we created an epileptic focus in the motor cortex (M1) of adult rats. An electrode was placed in this area to record epileptiform activity. A reference electrode was placed in the contralateral cortex. Epilepsy was induced by injection of tetanus toxin (TeNT) into layer 5 motor cortex. This resulted in short bursts of high frequency epileptiform activity.

Subcutaneous Transmitter A3019D with Screw electrodes. (20-mV range, 0.7-Hz HPF, 160-Hz 3-pole LPF, 512 SPS). Continuous EEG recording , non-tethered, allowing the animals to move around freely. Battery life >8 weeks.

Power spectrum analysis of EEG





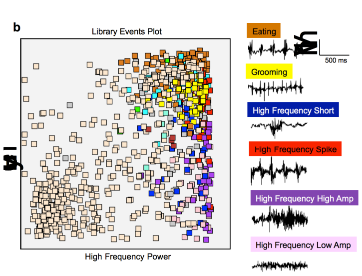


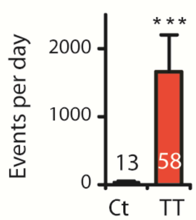
Tetanus toxin injection induces robust changes in EEG activity. Frequent bursts of high frequency epileptiform activity are observed. (A). Representative control EEG (Ct, black) and EEG after tetanus toxin injection (TT, red). A simple processor script was applied to the EEG which calculated power for different frequency bands. (B). Mean EEG power over a 24hr period for defined frequency bands 6-7 days post injection of TT. TT dose: 14.2 ± 0.6 ng n = 58; Ct (black): n = 13). (C). TT injection results in a dose-dependent increase in HF 70-160Hz power. Low TT = 10-15ng; high TT = 17.5-35ng.

Automated event classification program.

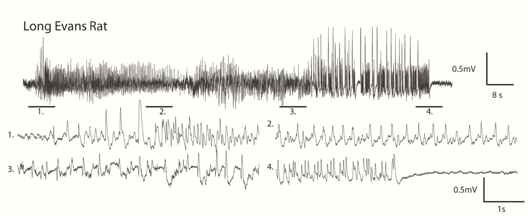
Because high-frequency power is not specific for seizures, we developed a complementary method, which relied on the detection of sudden increases in activity from a recent baseline. The features of such events were automatically compared to a library of EEG patterns, which was generated by a supervised learning algorithm that used concurrent video to identify increases that genuinely corresponded to seizures. In this way, we could distinguish electrographic seizure activity from EEG patterns related to normal behavior such as eating and grooming. The number of epileptiform events thus detected was greatly increased in tetanus toxin–injected animals. The program stepped through consecutive 1 s EEG epochs, and updated a running estimate of the baseline power as the lowest power between 4 and160 Hz in any 1 s epoch during the preceding 20 minutes. Epochs whose power exceeded 5 x baseline were defined as putative events. For each such event, 6 parameters were estimated. We applied a sigmoidal function to these 6 characteristics to obtain metrics bounded between zero and one. The event is thus represented as a point in a 6-dimensional hypercube.

Event characteristics:
1. Power (in the 4 and 160 Hz band)
2. Transient Power (power in the 1 – 4 Hz band)
3. High Frequency Power (60 – 160 Hz)
4. Spikiness (voltage range/standard deviation)
5. Voltage Asymmetry (balance of points exceeding 2 standard deviations either side of the mean).
6. Intermittency (low-frequency power of the rectified high-frequency signal).



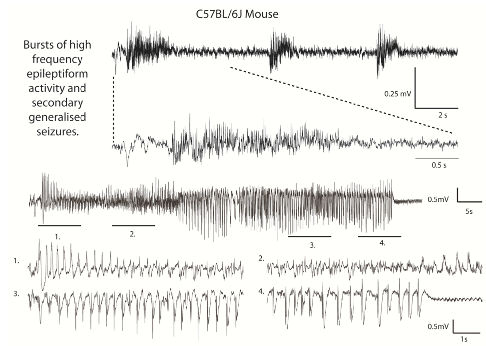


Seizures recorded following tetanus toxin injection into the rat visual cortex.

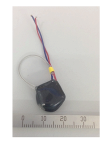


An epileptic focus was induced in layer 5 visual cortex and a recording electrode placed just above this. Displayed is a typical spontaneous seizure recorded using a A3019D transmitter .

Seizures recorded following tetanus toxin injection into the mouse visual cortex.



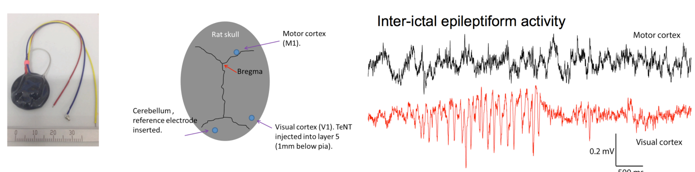
Open Source Instrument subcutaneously implanted mouse transmitters were used to record spontaneous secondary generalised seizures arising from an epileptic focus in the visual cortex in mice.



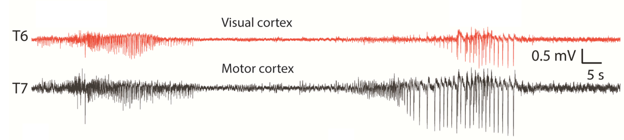
1.4ml volume, 20mV range, 512 SPS. Battery life ~ 3 weeks .

Dual channel EEG transmitters.

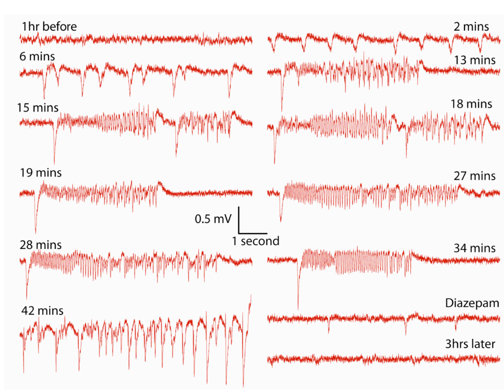
An epileptic focus was induced in the right hemisphere visual cortex. A rat dual channel transmitter was implanted with electrodes in the visual cortex and the contralateral motor cortex. This allows us to determine whether seizure activity remains localised or propagates across the cortex. A reference electrode was placed in the cerebellum. Inter-ictal epileptiform activity was detected only from the visual cortex electrode whereas a secondary generalised seizure was detected in both channels.



Secondary generalised seizure.



Recording epileptiform activity following acute injection of pilocarpine into layer 5 visual cortex of a mouse.



5M Pilocarpine injected into mouse layer 5 visual cortex results in robust epileptiform spiking correlated with behavioural manifestation (limb twitching and tail flicking). This evolves over time from simple spiking to trains of spikes to almost continuous spiking. Displayed are representative EEG traces at the time points indicated. This activity can be supressed by an i.p injection of diazepam.

Peer –reviewed publication using Opensourceinstruments EEG devices and analysis software.
Wykes RC *et al*. (2012) "Optogenetic and potassium channel gene therapy for focal neocortical epilepsy". *Science Translational Medicine* 4(161) 161ra152.

We are not employed by Open Source Instruments nor do we receive financial incentives from this company.

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