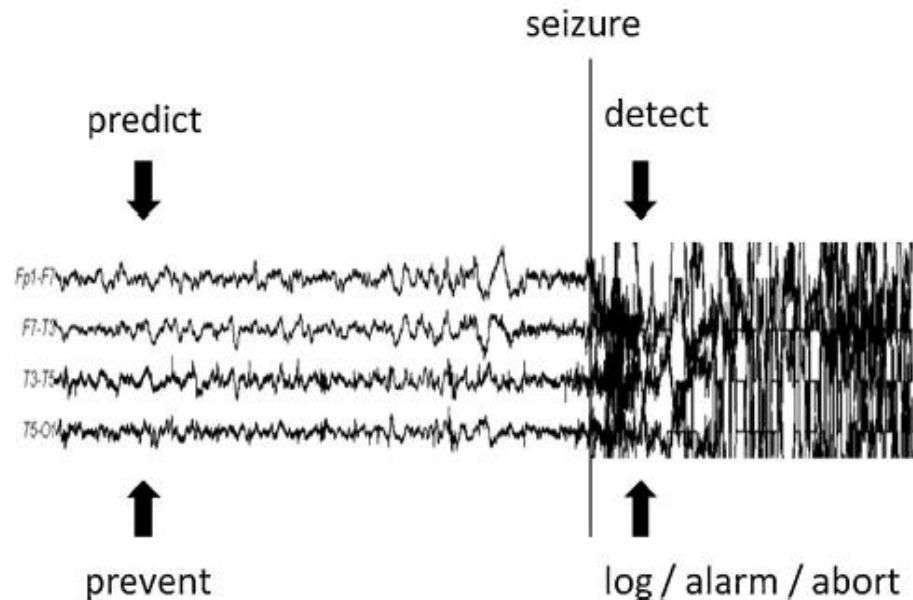
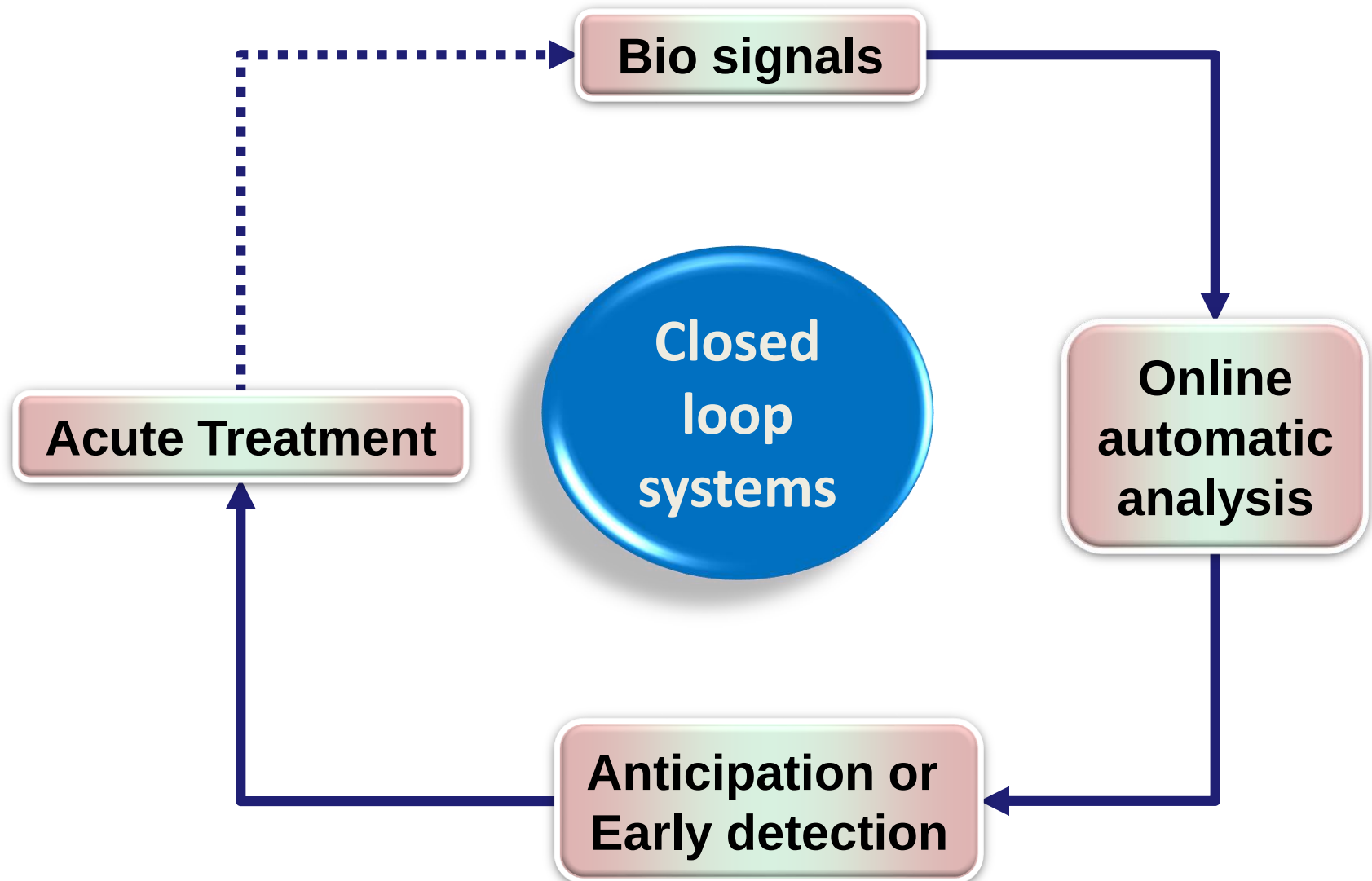


Closed Loop and monitoring Systems in the treatment of epilepsy



On-demand delivery of therapy



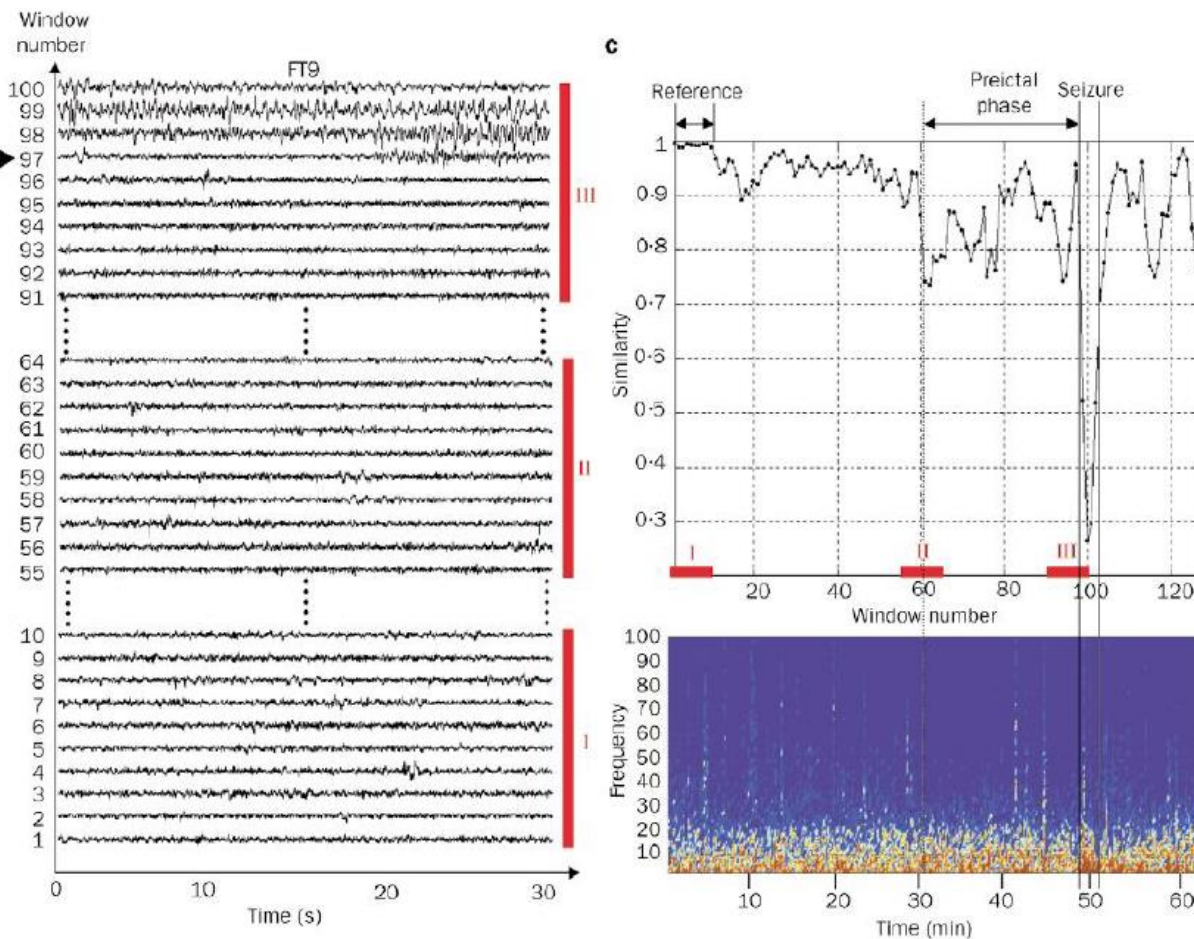
Afferent : measuring biosignals

The history of anticipation ; EEG based

ARTICLES

Anticipation of epileptic seizures from standard EEG recordings

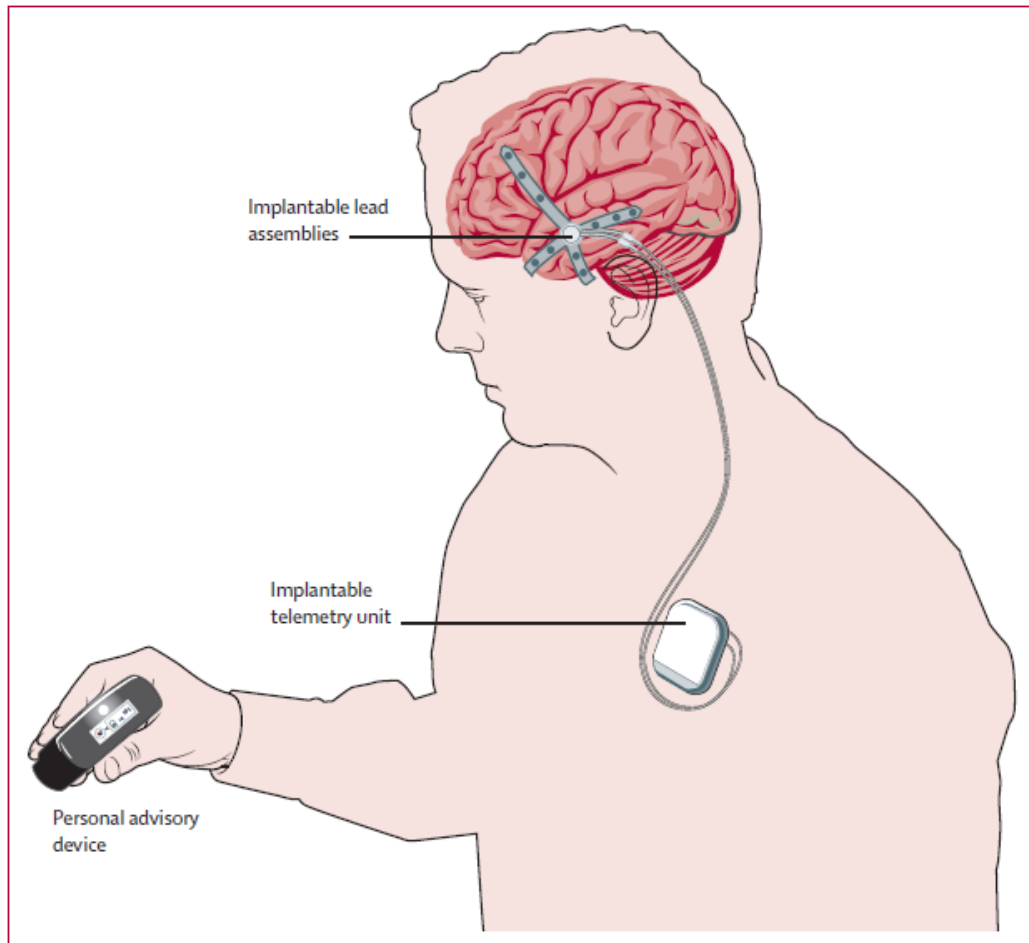
Michel Le Van Quyen, Jacques Martinerie, Vincent Navarro, Paul Boon, Michel D'Havé, Claude Adam, Bernard Renault, Francisco Varela, Michel Baulac



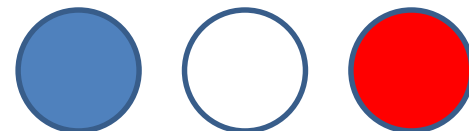
Prediction of seizure likelihood with a long-term, implanted seizure advisory system in patients with drug-resistant epilepsy: a first-in-man study

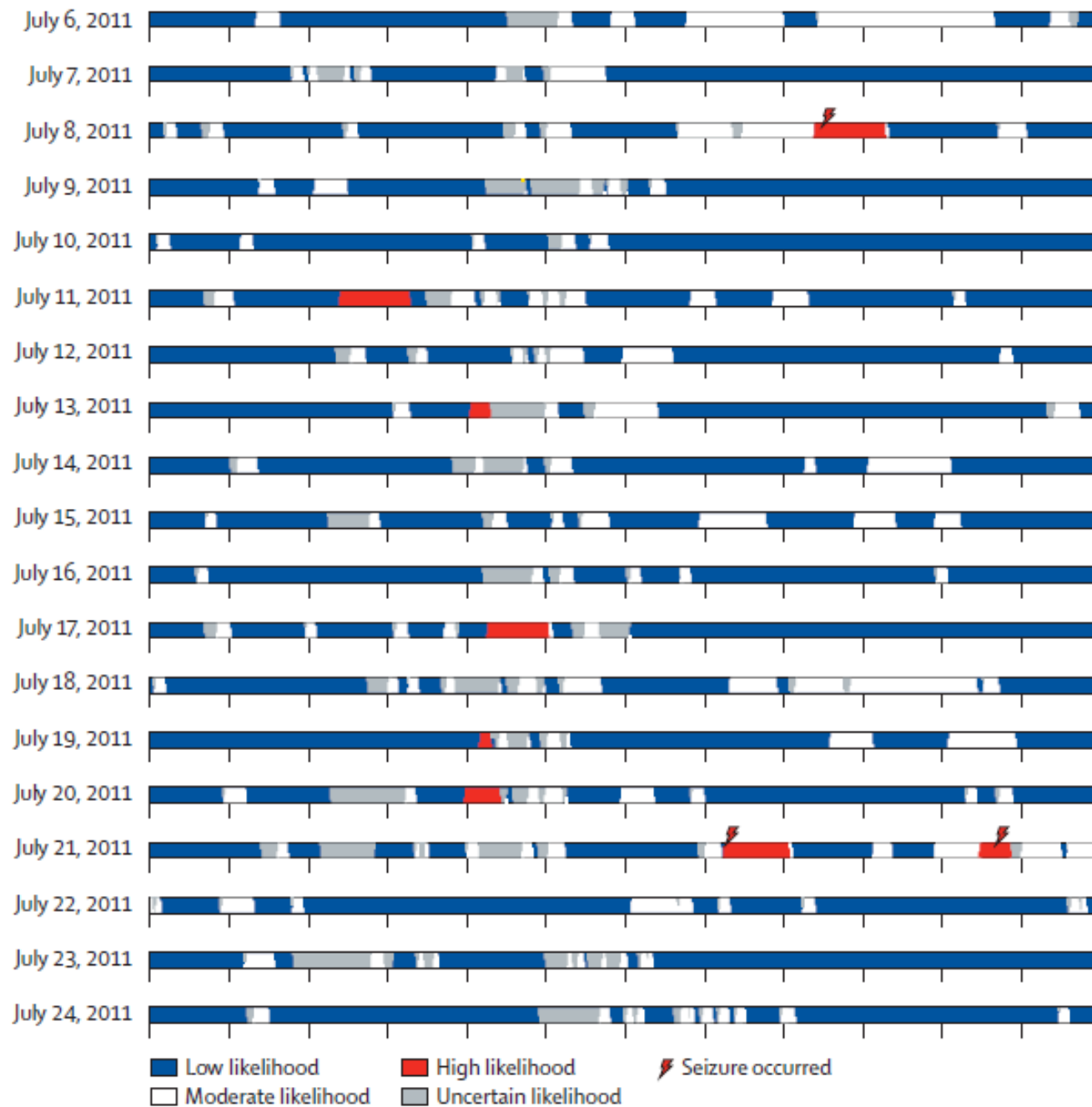


Mark J Cook, Terence J O'Brien, Samuel F Berkovic, Michael Murphy, Andrew Morokoff, Gavin Fabinyi, Wendyl D'Souza, Raju Yerra, John Archer, Lucas Litewka, Sean Hosking, Paul Lightfoot, Vanessa Ruedebusch, W Douglas Sheffield, David Snyder, Kent Leyde, David Himes



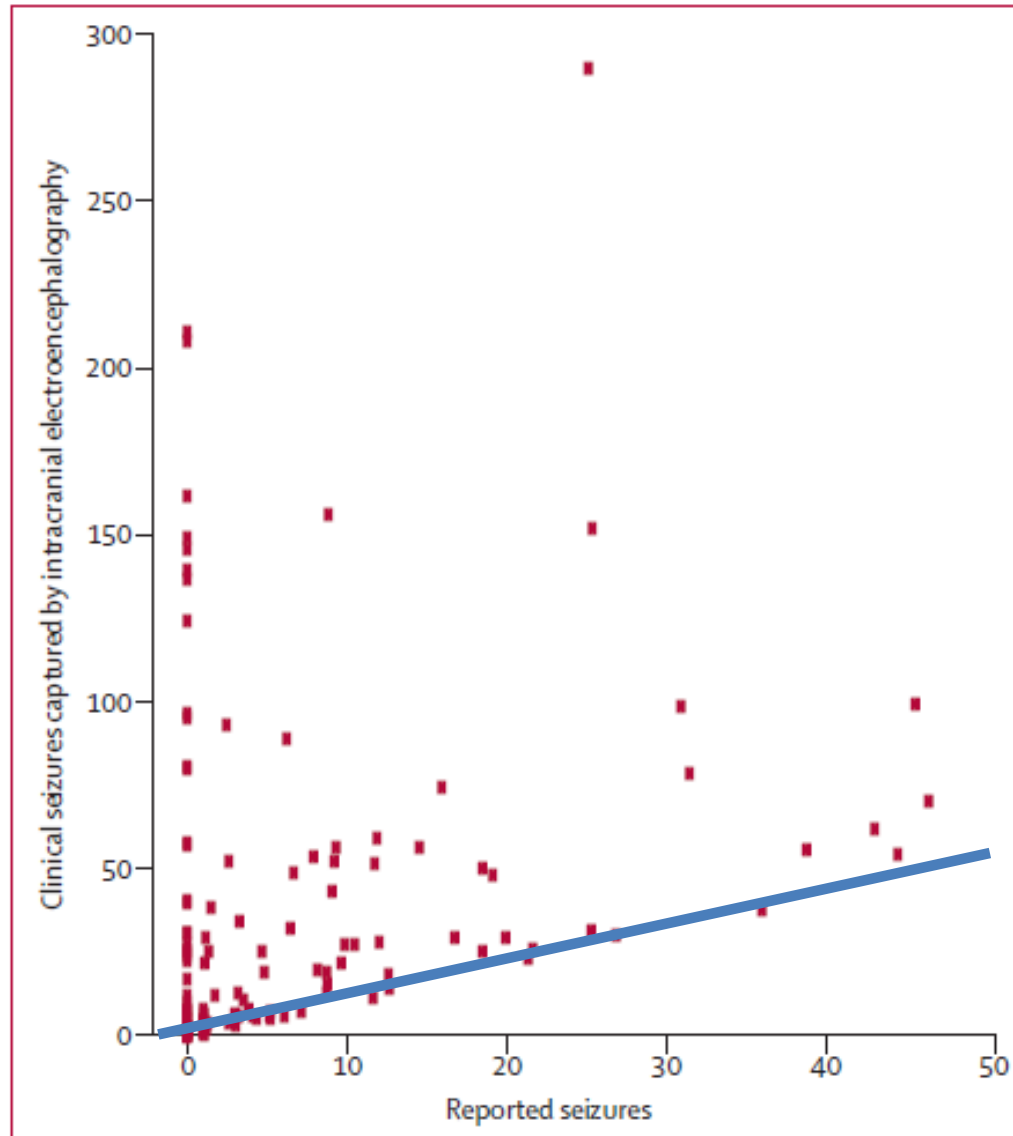
- Continuous EEG
- Online EEG analysis
- Warning device





Warning time
14 minutes
6 minutes
29 minutes

Seizure rates : patient reported versus intracranial analysis



Other biosignals

- Heart rate
- Respiration rate
- Movement
- Sweating
- ...

Combination of signals!

Peri-ictal heart frequency

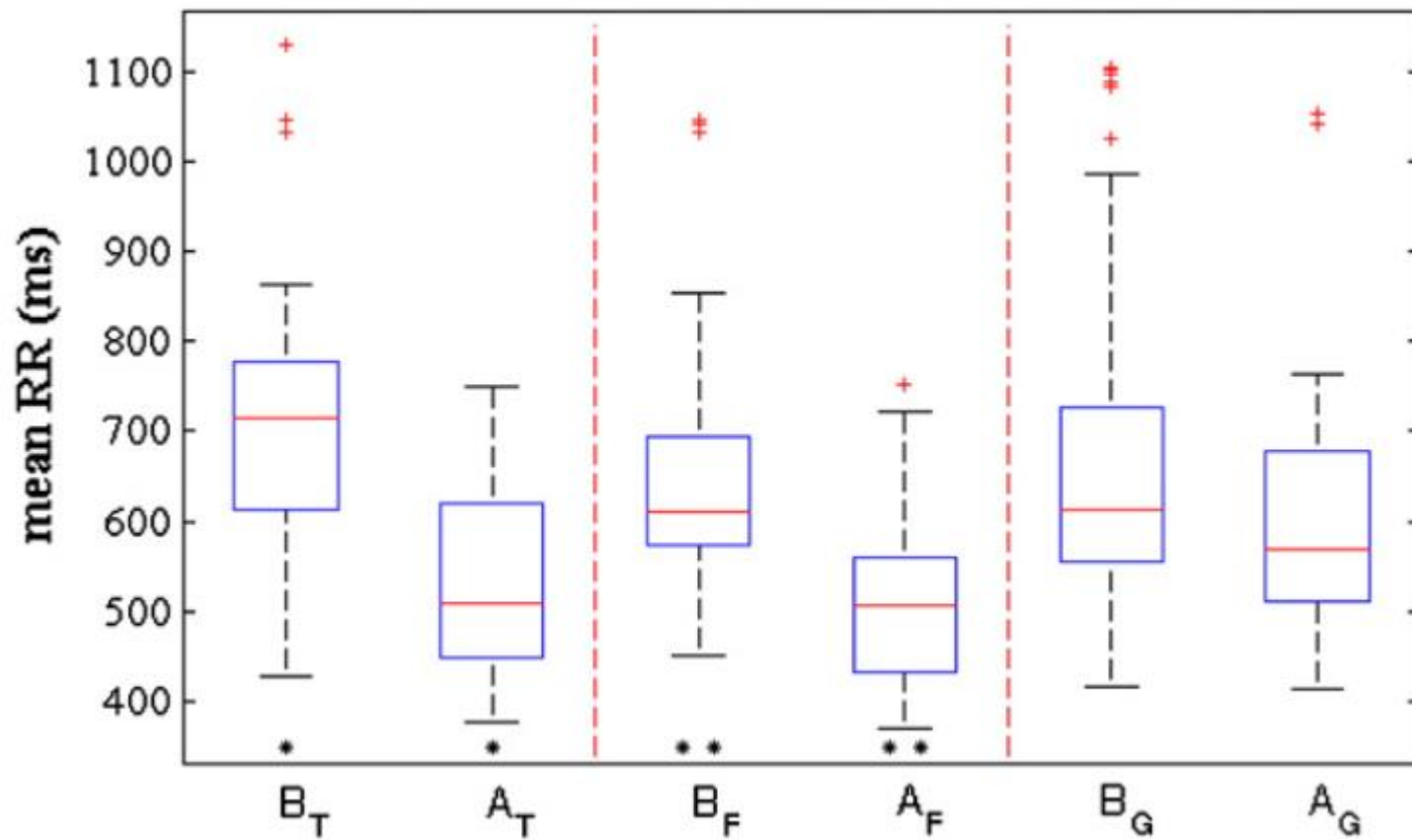
Peri-ictal ECG changes in childhood epilepsy: Implications for detection systems

Katrien Jansen ^a, Carolina Varon ^{b,c}, Sabine Van Huffel ^{b,c}, Lieven Lagae ^{a,*}

^a Pediatric Neurology, University Hospitals Leuven, Belgium
^b KU Leuven, Department of Electrical Engineering-ESAT, SCD-SISTA, Leuven, Belgium
^c iMinds Future Health Department, Leuven, Belgium

Studies on the presence of ictal/preictal tachycardia in patients with refractory epilepsy.

	Adults/children	Seizure type	Ictal findings	Preictal findings
Marshall et al. [10]	Adults	TLE	Ictal tachycardia 64%	
Blumhardt et al. [11]	Adults	TLE	Ictal tachycardia 92%	
Keilson et al. [12]	Adults	Refractory seizures	Ictal tachycardia 96%	
Galimberti et al. [13]	Adults	Partial seizures	Ictal tachycardia 49%	
Schemthaner et al. [14]	Adults	Partial seizures	Ictal tachycardia 82.5%	Preictal tachycardia 76.1%
Garcia et al. [15]	Adults	Partial seizures	Ictal tachycardia 32%	
Zijlmans et al. [16]	Adults	Refractory seizures	Ictal tachycardia 73%	Preictal tachycardia 23%
Leutmezer et al. [17]	Adults	Most pronounced TLE	Ictal tachycardia 86.9%	
Di Gennaro et al. [18]	Adults	TLE	Ictal tachycardia 92%	
Mayer et al. [8]	Children	TLE	Ictal tachycardia 98%	Preictal tachycardia 20/71
Moseley et al. [19]	Adults	Refractory seizures	Ictal tachycardia 57%	
Işik et al. [9]	Children	Refractory seizures	Ictal tachycardia 100%	

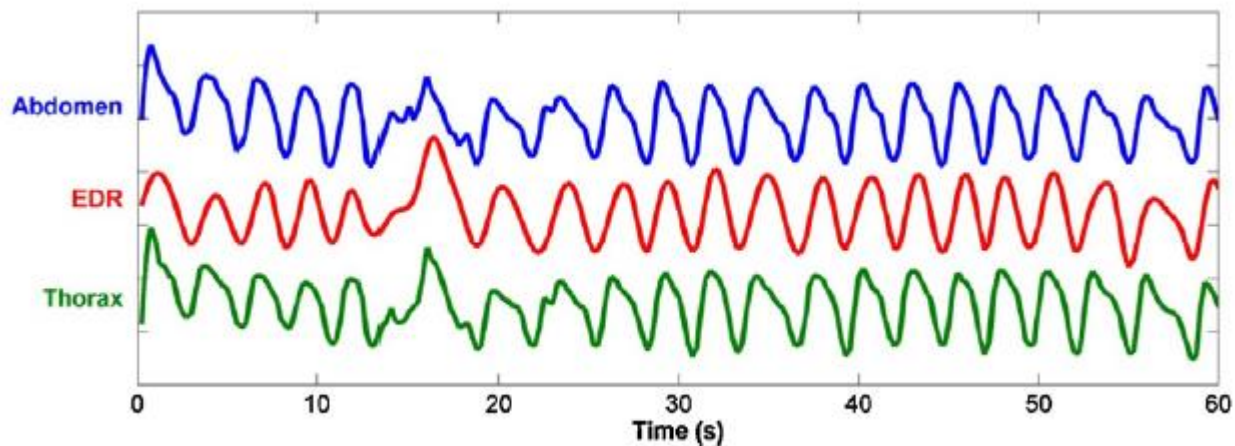


Significant changes in temporal and frontal lobe seizures , not in generalized seizures

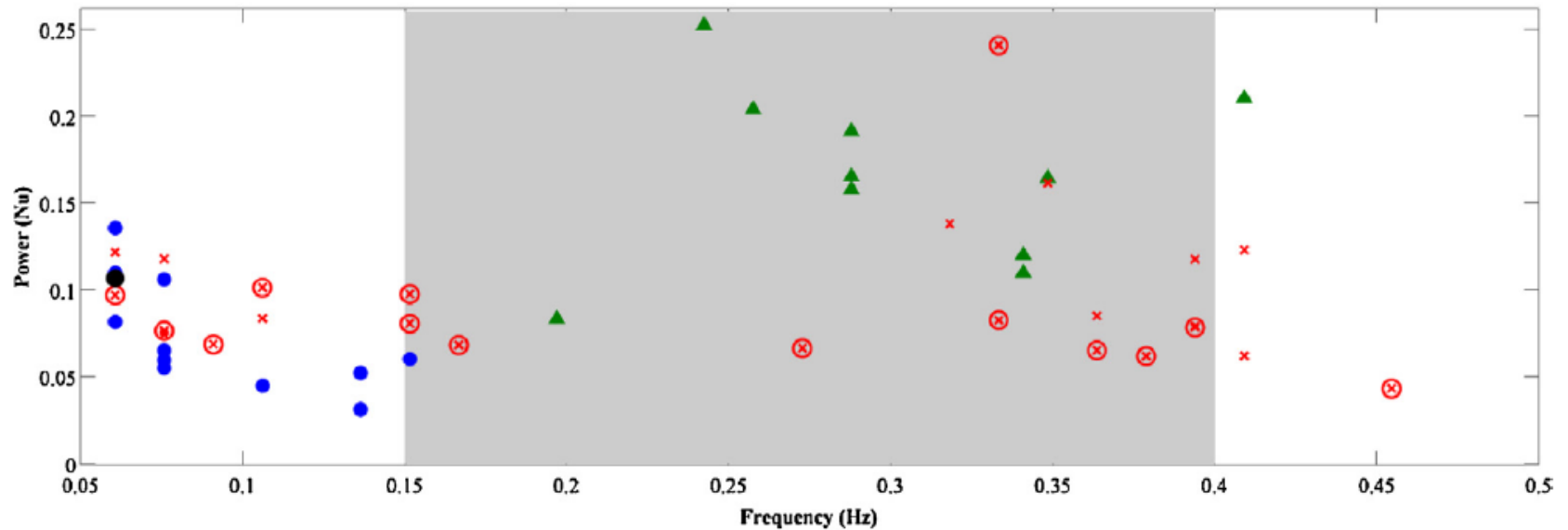
ECG derived respiratory frequency

Ictal and interictal respiratory changes in temporal lobe and absence epilepsy in childhood

Katrien Jansen^a, Carolina Varon^{b,c},
Sabine Van Huffel^{b,c}, Lieven Lagae^{a,*}



Respiratory **ictal** changes in temporal lobe seizures versus absence seizures

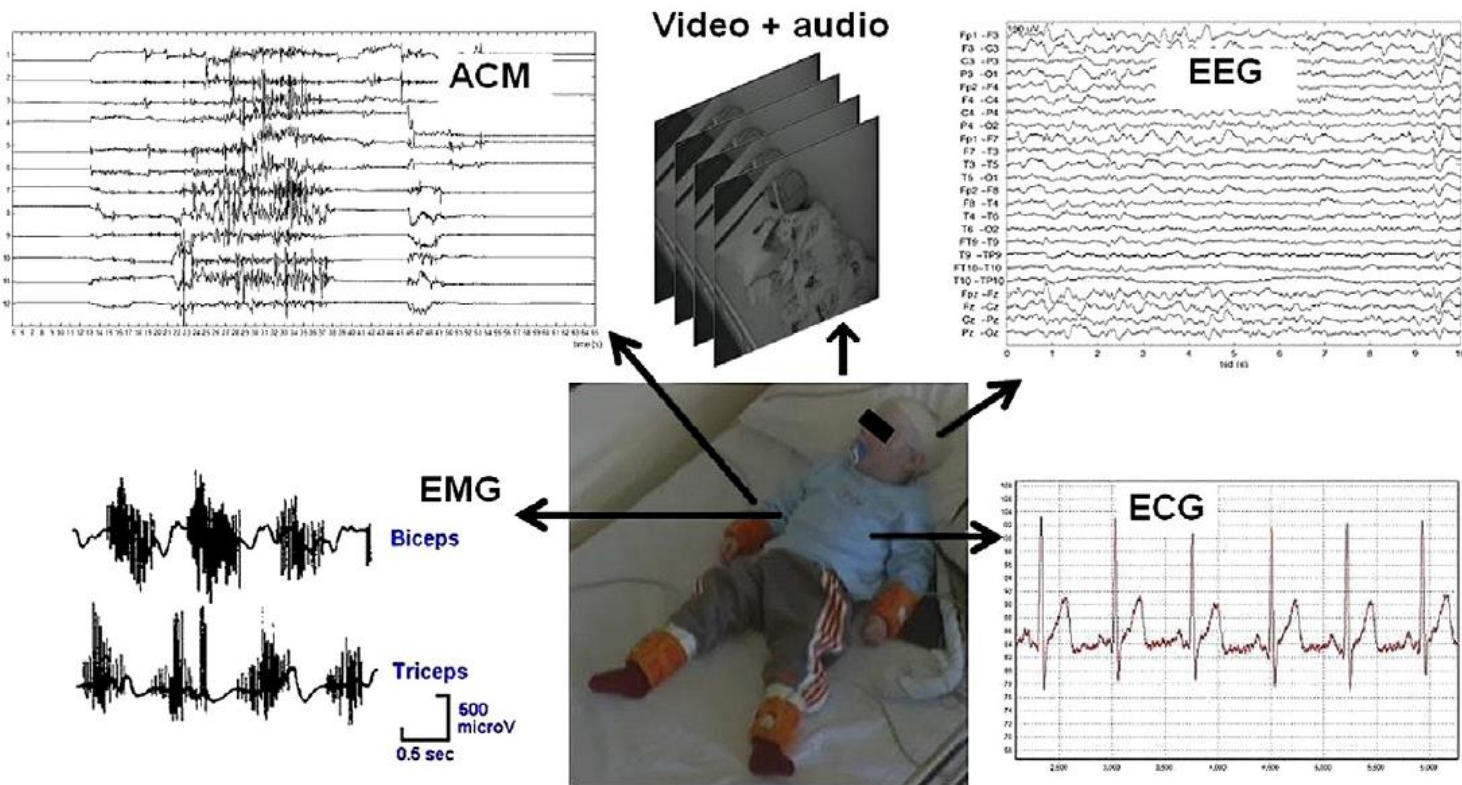


- Temporal lobe seizures
- Absence seizures

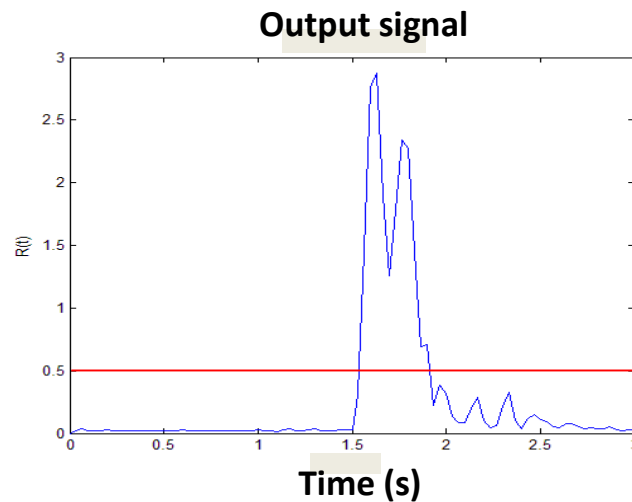
Accelerometers

Long-term home monitoring of hypermotor seizures by patient-worn accelerometers

Anouk Van de Vel ^{a,*}, Kris Cuppens ^{b,c}, Bert Bonroy ^b, Milica Milosevic ^c, Sabine Van Huffel ^c,
Bart Vanrumste ^{b,c}, Lieven Lagae ^{d,e}, Berten Ceulemans ^{a,e}



Automatic video detection



Movement detection performance
Sensitivity of 100%
Positive predictive value 92%

“Proguardian” system : alert system



Sensor connects to patch and analyzes **changes in heart rate and motion** associated with epilepsy during periods of sleep.

The Hub

- Communicates with Sensor via BLE (Bluetooth Low Energy)
- Records seizures based on Movement or HR Change confirmed by caretaker
- Logs Manual seizure entered by caretaker
- Communicates with Mobile App via in Home Wi-Fi network
- Seizure reports downloadable to supplied USB Stick
- Sensitivity settings customizable for heart rate change and movement

Community faster than academia

- Many (expensive) devices on the market
Who is responsible ?
Who owns the information?
- No rigorous research
- False alarms accepted by parents
- False negatives ?

		Audio	Video	Electromag- netic waves	ACM/ gyro/ magneto	Electrodes	Plethys- mograph (volume)	Pressure	Tempera- ture
Motor	Body	X (bed noise)	X (optical camera)	X (e.g. radio waves)	X (bed or body)	X (EMG)		X (pressure mat for bed vacancy)	X (thermal camera)
	Eye(lid)		X (optical camera)			X (EOG/EMG)			
Auto- nomic	HR/ BP/ SpO ₂			X (micro waves)		X (ECG)	X (oxi- meter)		
	Respira- tion	X (neck)	X (optical or thermal camera)	X (micro waves chest or infrared waves of oximeter/ capnograph)	X (ACM/ magneto chest)	X (EMG/ impe- dance pneu- mograph chest, electrodes for pO ₂ /CO ₂)	X (RIP chest)	X (pneumo- tachograph airflow)	X (thermo- couple airflow/ thermal camera)
	Sweating					X (ohm/ galvanometer)			
	Vomiting/ salivation/ coughing	X(audio phone)				X (humidity meter)			
	Incontin- ce					X (humidity meter)			
	Vocalizations	X(audio phone)							
	Fever		X (thermal camera)	X					X (sticker)

Company	Device name	Detection method	Contact(less)	Seizures/events	Article	Website
Adris Technologies (UK)	Pulse-Guard	PPG for heart rhythm	Watch coupled to iPad	Unspecified	npf	http://www.pulseguard.org
Alert-It (UK)	Ep-It Companion Monitor (S1029)	Unspecified movement sensor, audio, moisture sensor, body pressure	Under mattress (mat) and on mattress or under pillow sheet	TC and S, urination and vomiting, prolonged bed vacancy	npf	http://www.alert-it.co.uk
	Ep-It Guardian Monitor (P139)	Unspecified movement sensor that can also detect respiration, audio, moisture sensor, body pressure	Under mattress (mat) and on mattress or under pillow sheet	TC, S and complex seizures, abnormal breathing, urination and vomiting, prolonged bed vacancy, allows monitoring of up to 32 patients	npf	
Aremco (UK)	Aremco	Respiration, audio, moisture, body pressure	Under mattress plate	S	npf	http://www.disabilityworld.com/co/company.php?ID=3460
BioLert (Israel)	EpiLert	ACM for movement	Watch-like	TC, T, C	Kramer et al., 2011 ⁶⁹	http://www.biolertsys.com
Bioserenity (France)	Neuro-naute	ECG?, ACM?, EEG	Smart t-shirt & cap (the latter for EEG) coupled to smart phone	Unspecified	npf	http://www.bioserenity.com
Brain Sentinel (US)	Brain Sentinel	EMG	Device worn with strap on biceps	TC	Szabó et al., 2015 ⁵⁷	https://www.brainsentinel.com
Danish Care (Denmark)	Epi-Care Free	ACM for movement	Bracelet	TC in adults and teenagers	Beniczky et al., 2013 ⁶⁸	http://danishcare.dk/dk
	Epi-Care 3000	ACM for movement	Affixed to mattress	Convulsions such as TC, S mainly in small children	npf	
D.C.T. Associates Pty Ltd (Australia)	Vigil-Aide	Unspecified vibration detection	Affixed to bed or worn in pouch/belt during day	Convulsions	npf	http://www.dctassociates.com.au/convul.htm
Emfit Ltd (Finland)	Emfit Seizure Monitor	ACM for movement and respiration (even heart beating according to website), body pressure	Under mattress mat	Convulsions such as TC and S, micro movements caused by breathing and heart beating, prolonged bed vacancy	Narechania et al., 2013 ⁶⁷ ; Van Poppel et al., 2013 ⁶⁵	http://www.emfit.com

Empatica (US)	Embrace	PPG for heart rhythm, EDA, temperature, ACM	Watch coupled to smart phone	TC, non-convulsive seizures such as CPS	Poh et al., 2012 ²⁸	https://www.empatica.com/embrace-watch-epilepsy-monitor
IctalCare A/S (Denmark)	Eddi	EMG	ePatch attached to upper arm or leg	TC, T	Conradsen et al., 2012 ⁵⁴ ; Larsen et al., 2014 ⁵⁶	http://www.ictalcare.dk
LivaNova (former Cyberonics, US)	ProGuardian	ECG + ACM	Chest worn patch & bedside hub	CPS, H	Sabesan et Sankar, 2015 ²⁴	http://ir.livanova.cyberonics.com/releasedetail.cfm?releaseid=728198
Livassured (Netherlands)	Night-Watch	PPG for heart rhythm + ACM	(Upper) arm band	Nocturnal TC	npf	http://www.livassured.nl
Medpage (UK)	MP5	Audio for movement (bed noises) and vocalizations, movement sensor	Under mattress	TC in patients weighing ≥ 12.7 kg	Carlson et al., 2009 ⁶⁰ ; Fulton et al., 2013 ⁶¹	http://www.medpage-ltd.com
	ST-2 (outdated)	Unspecified movement sensor (audio?) and body pressure	Under mattress mat	TC & prolonged bed vacancy in patients weighing ≥ 12.7 kg	Fulton et al., 2013 ⁶¹	
RTI International (US)	RTI	ECG, respiration, temperature, body orientation, EDA, (EMG)	Torso band & bracelet (the latter for EDA)	TC (to a lesser extent T & M)	npf	http://www.rti.org/newsroom/news.cfm?obj=5C9D1803-AE4A-EE86-58351084319AA948
SAMi Alert (US)	SAMi	Video based movement detection, audio	Camera coupled to iPhone or iPad	Unspecified nocturnal motor seizures	npf	http://www.samialert.com
Sensorium (UK)	Sensalert (200/SPT X-EP200)	Unspecified movement sensor and optional moisture sensor	Under mattress	TC	npf	http://www.sensorium.co.uk
Smart Monitor Corp. (US)	Smart-Watch	ACM for movement	Watch coupled to Android smart phone	Convulsive seizures mainly TC, C	Lockman et al., 2011 ⁵² ; Patterson et al., 2015 ⁶⁶	http://www.smart-monitor.com
Vahlkamp (Netherlands)	Epi-Watcher	Unspecified movement sensor	Under mattress mat	TC	npf	http://www.vahlkamp.nl

Using	Application	Smart device and OS	Website
Smart phone only	EpDetect	Android or Microsoft phone	http://www.epdetect.com
	EpilepsyApp	Android or iOS phone	https://epilepsyapp.wordpress.com
Pebble watch detecting movement	Open Seizure Detector	Android phone	http://www.openseizuredetector.org.uk/?page_id=415
	Pebilepsy	Android phone	http://www.medgadget.com/2014/09/pebilepsy-uses-fitness-tracker-to-monitor-night-time-seizures.html
SmartWatch detecting movement	SmartWatch	Android or iOS phone	http://www.smart-monitor.com
MIO Alpha watch detecting HR	EpSyDet	Android phone	http://www.salvasoftware.com/epsydet
PulseGuard detecting HR	PulseGuard	iOS tablet (iPad)	http://www.pulseguard.org
Apple watch detecting movement and HR	EpiWatch	iOS phone (iPhone)	http://www.hopkinsmedicine.org/epiwatch#.VITQm62FP4g
	SeizAlarm	iOS phone (iPhone)	http://www.seizalarm.com
Any watch detecting movement and/or HR	Neutun	Android or iOS phone	http://neutun.com
Embrace detecting movement, HR, EDA and temperature	EmpaticaAlert	Android or iOS phone	https://www.empatica.com/embrace-watch-epilepsy-monitor
SAMi camera detecting movement and sound	SAMi	iOS phone (iPhone) or tablet (iPad)	http://www.samialert.com

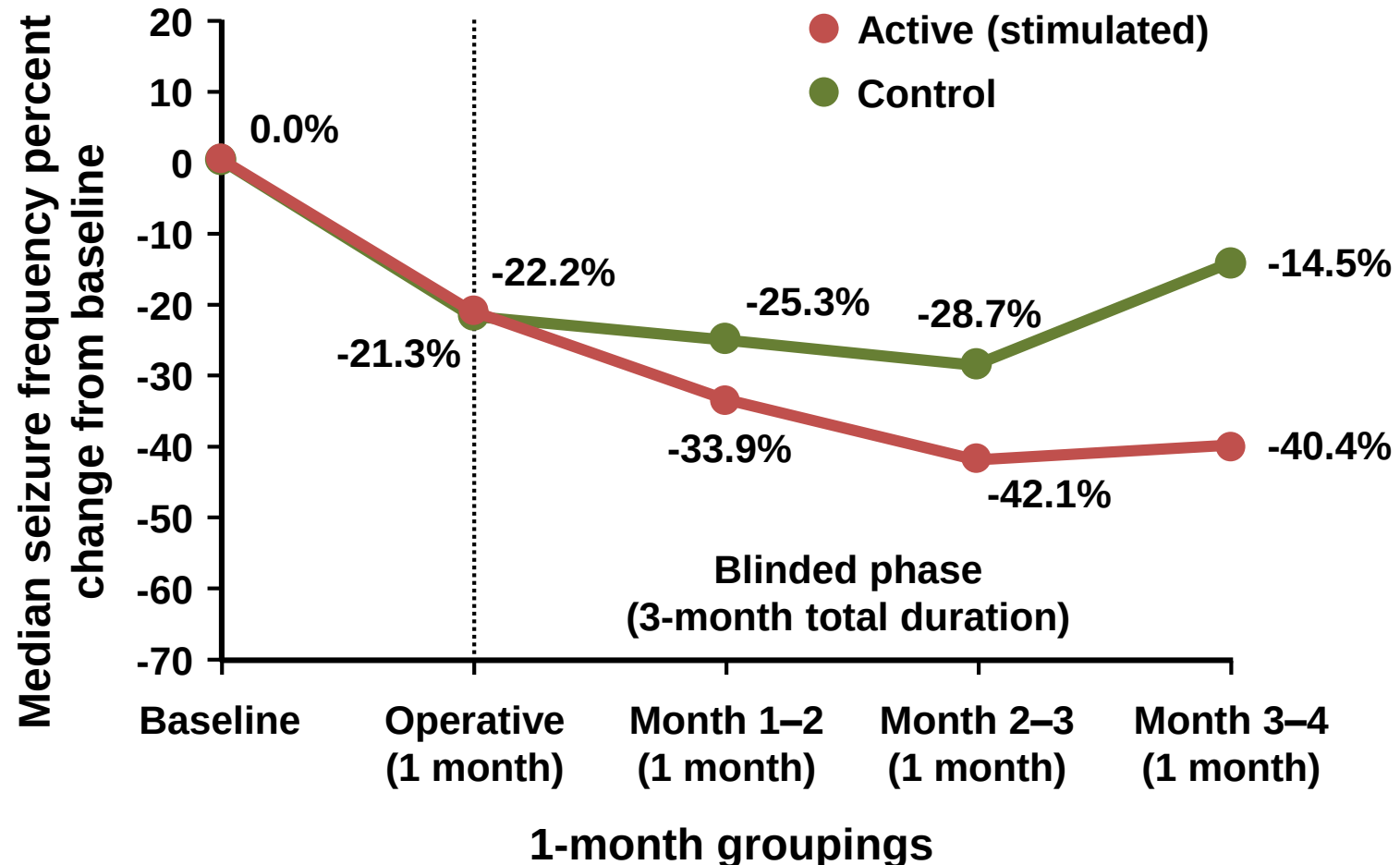
Table 4: Seizure detection applications for smart devices. HR = heart rate, OS = operating system.

Efferent side

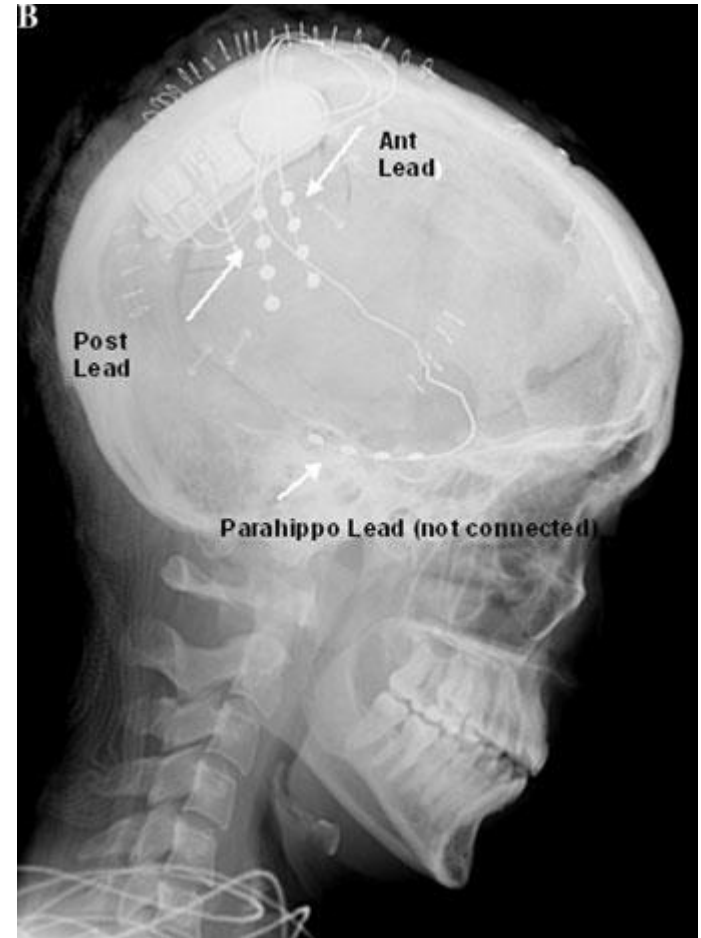
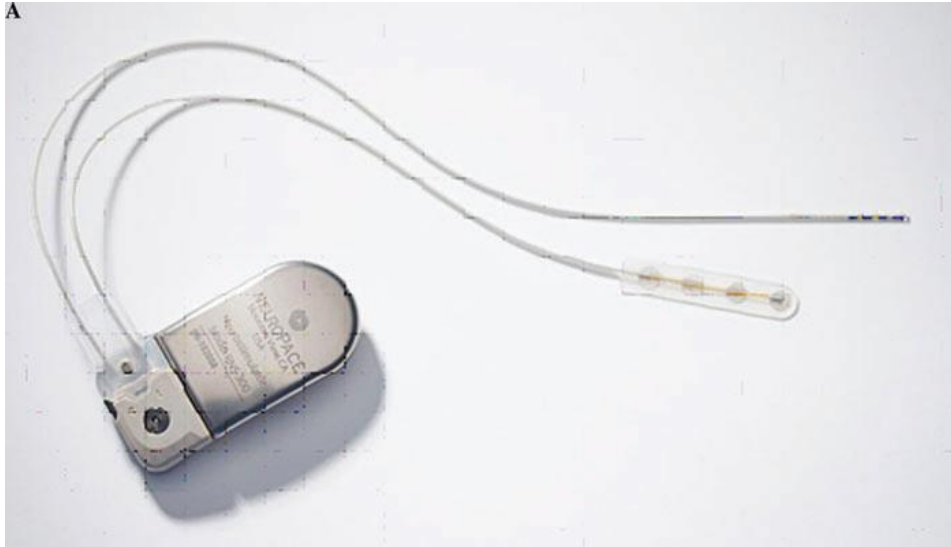
- alarming
- Brain stimulation
- (Rescue) medication

Electrical stimulation of the anterior nucleus of the thalamus

Scheduled specific stimulation



Responsive specific stimulation

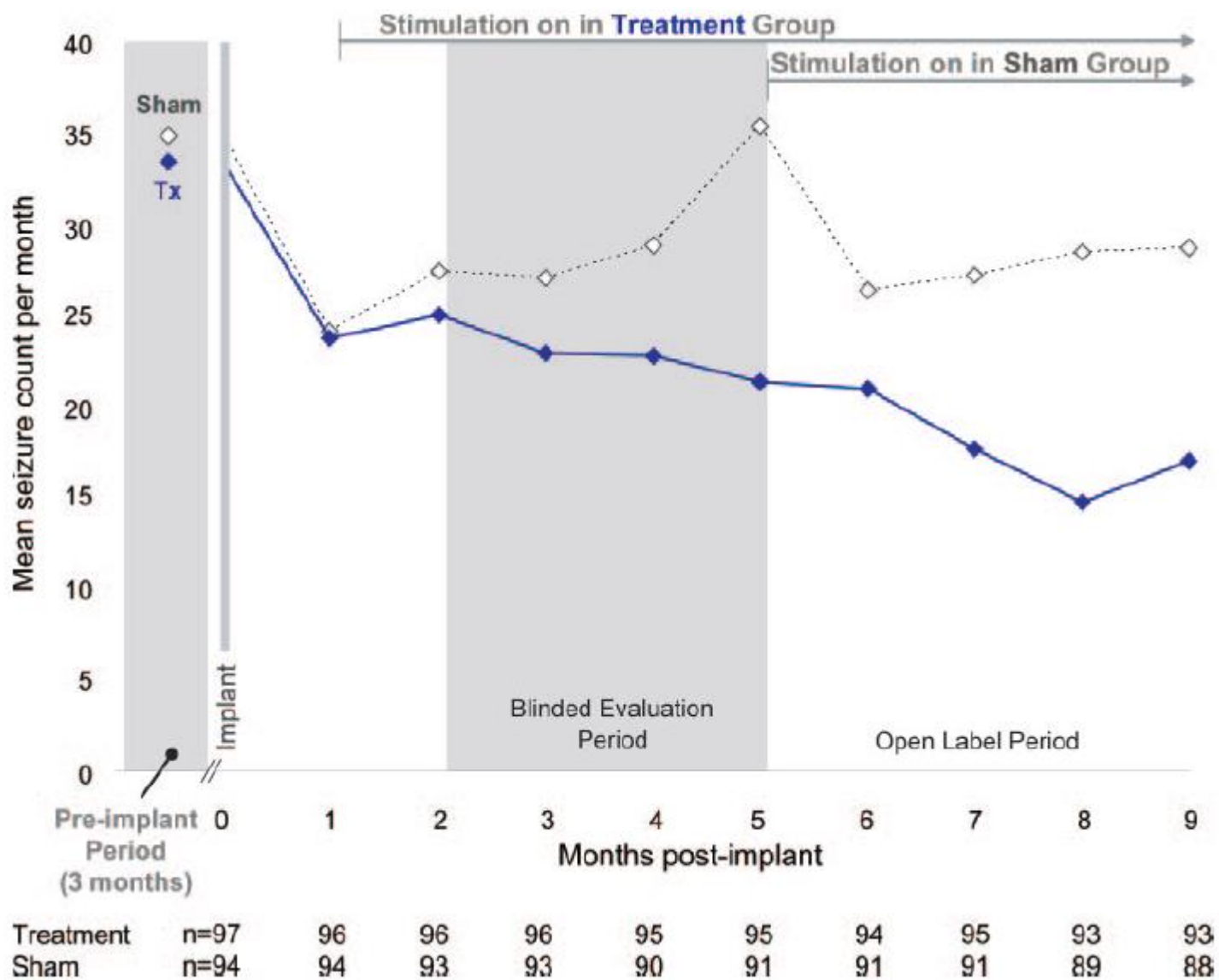


Neurology®

Responsive cortical stimulation for the treatment of medically intractable partial epilepsy

Martha J. Morrell

Neurology 2011;77;1295-1304 Published Online before print September 14, 2011
DOI 10.1212/WNL.0b013e3182302056



Responsive specific stimulation

AspireSR™

Non EEG based

Provides “standard” VNS Therapy stimulation

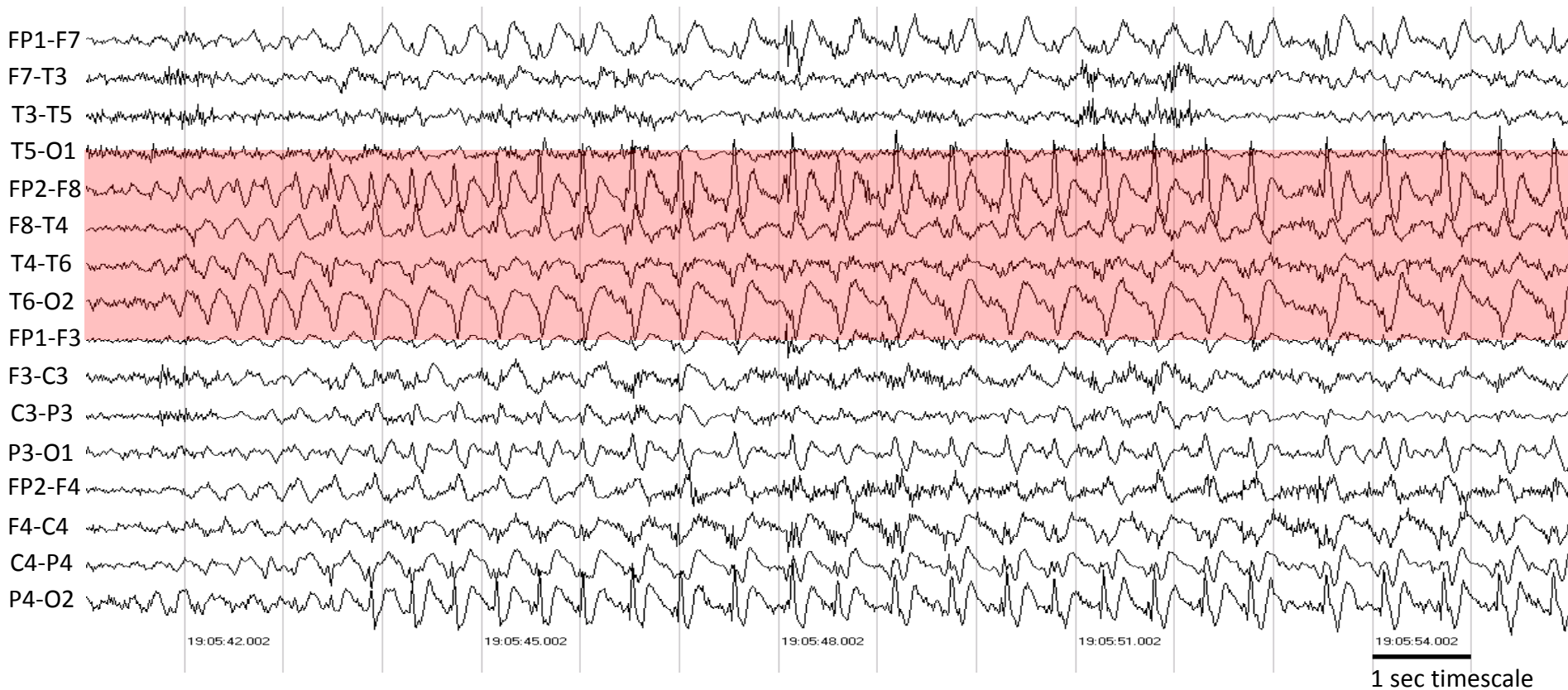
+

Automated magnet mode stimulation upon seizure
detection (**heart frequency changes**)



Clinical Observations: Stimulation-Associated Desynchronization

Focal Seizure (not stimulated in this view)

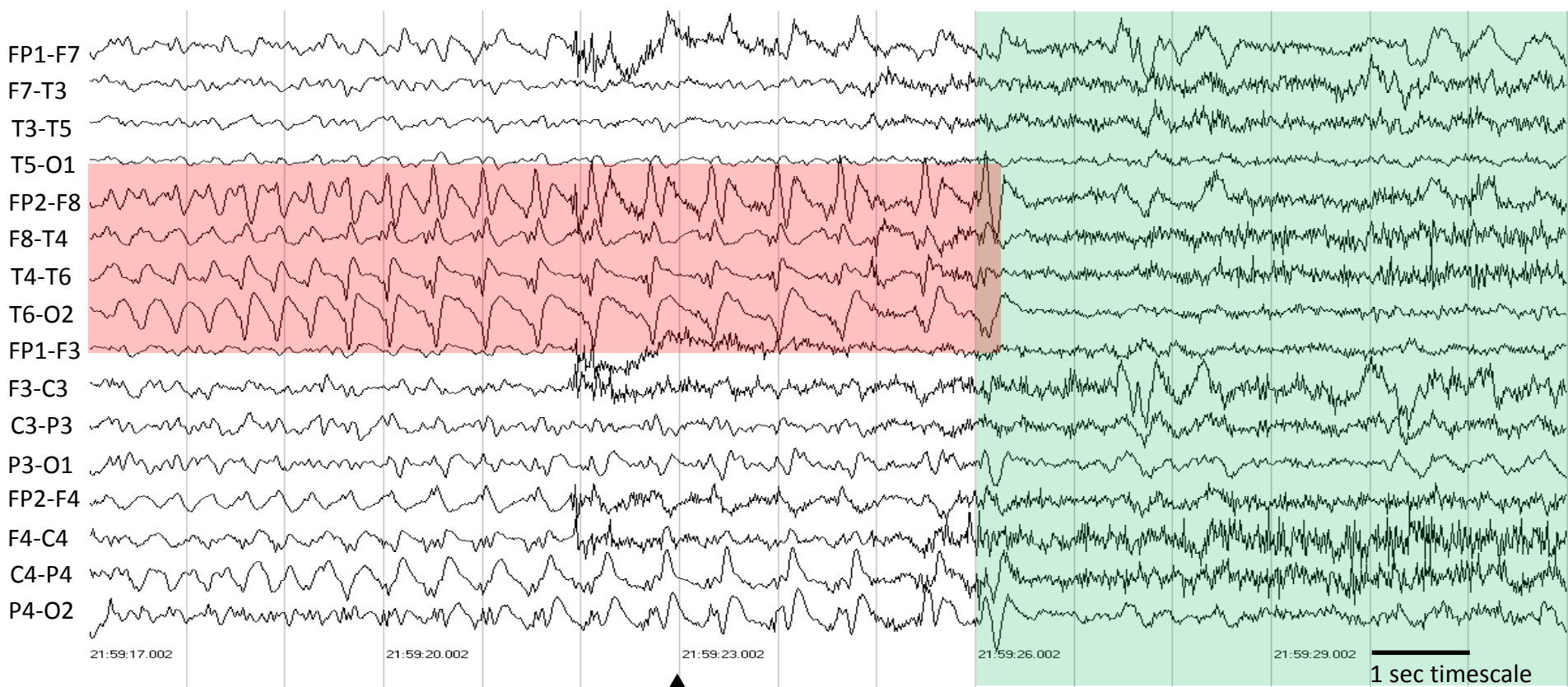


Typical seizure progression (without VNS Therapy Automatic Stimulation) for this patient

Clinical Observations: Stimulation-Associated Desynchronization

Focal Seizure (during sleep)

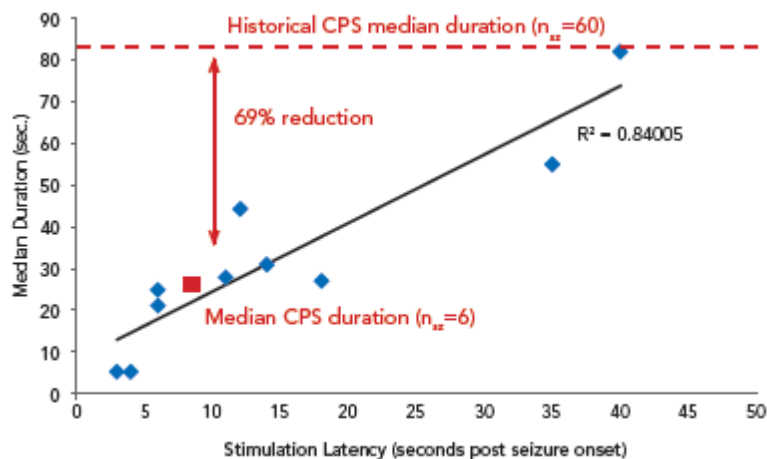
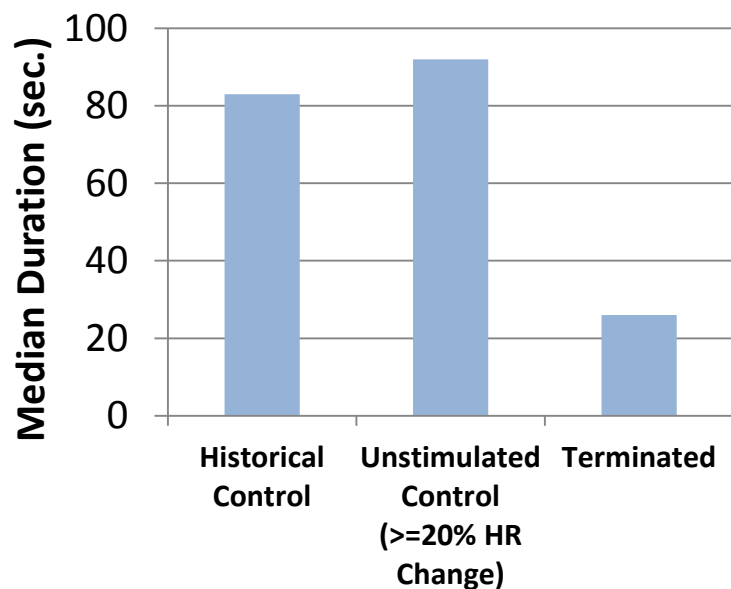
VNS Therapy Automatic Stimulation



Automatic Stimulation Latency = 6s
SDA = 6, Output Current: 0.75mA

Stimulation-Associated
Desynchronization
(+3s after Automatic Stimulation)

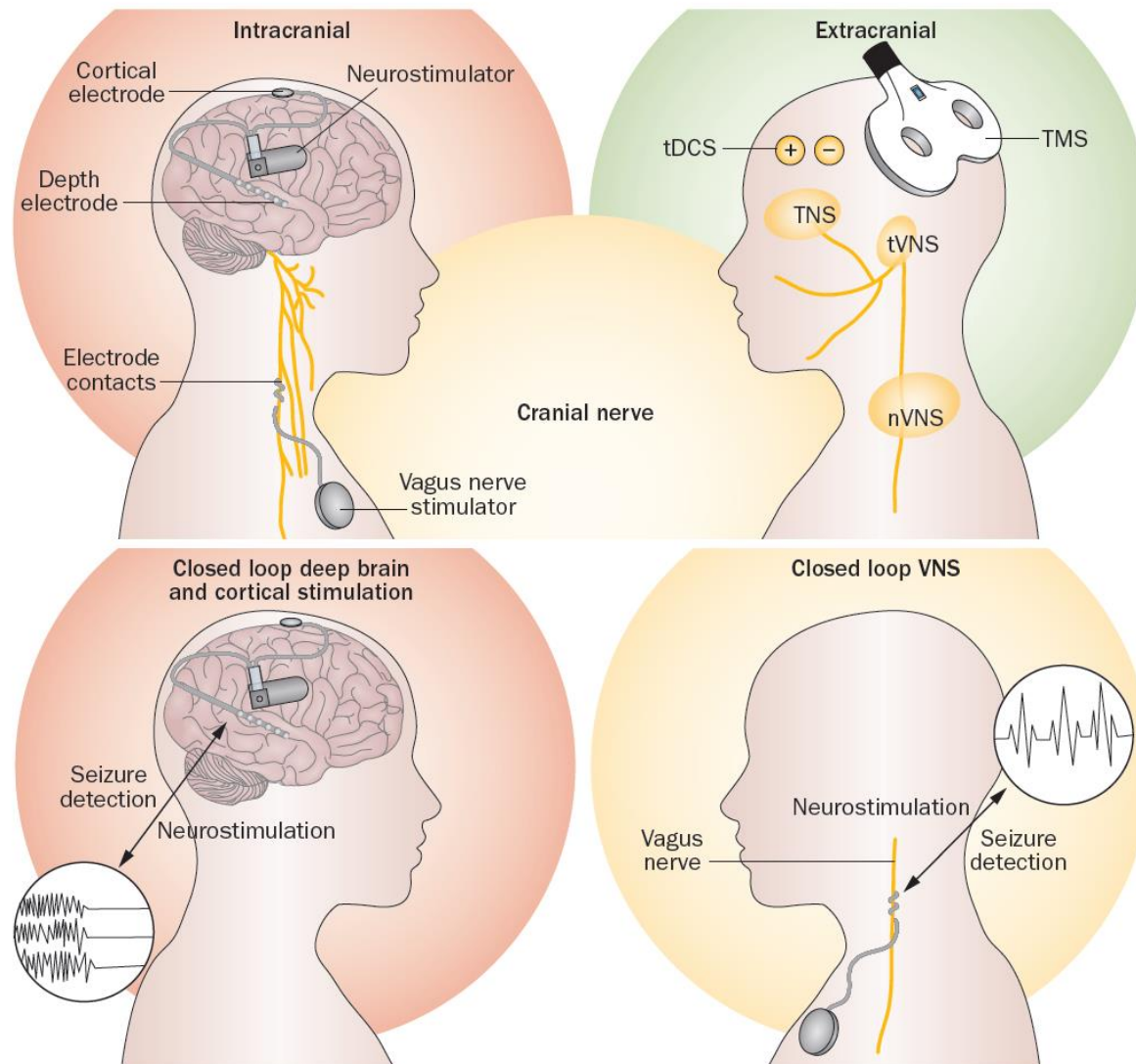
AspireSR[®] E36 Data: Key Results



EMU :

- 52% of seizures (45/86) had heart rate changes $\geq 20\%$ (above lowest SDA threshold)
- Efficacy:
 - ~60% of stimulated focal seizures ended during AutoStim
 - 69% reduction in median CPS duration vs. historical
 - Severity significantly lower (NHS3) at EMU discharge

Closed Loop Systems : responsive devices



The near future

ARTICLE

Received 26 Nov 2012 | Accepted 12 Dec 2012 | Published 22 Jan 2013

DOI: 10.1038/ncomms2376

OPEN

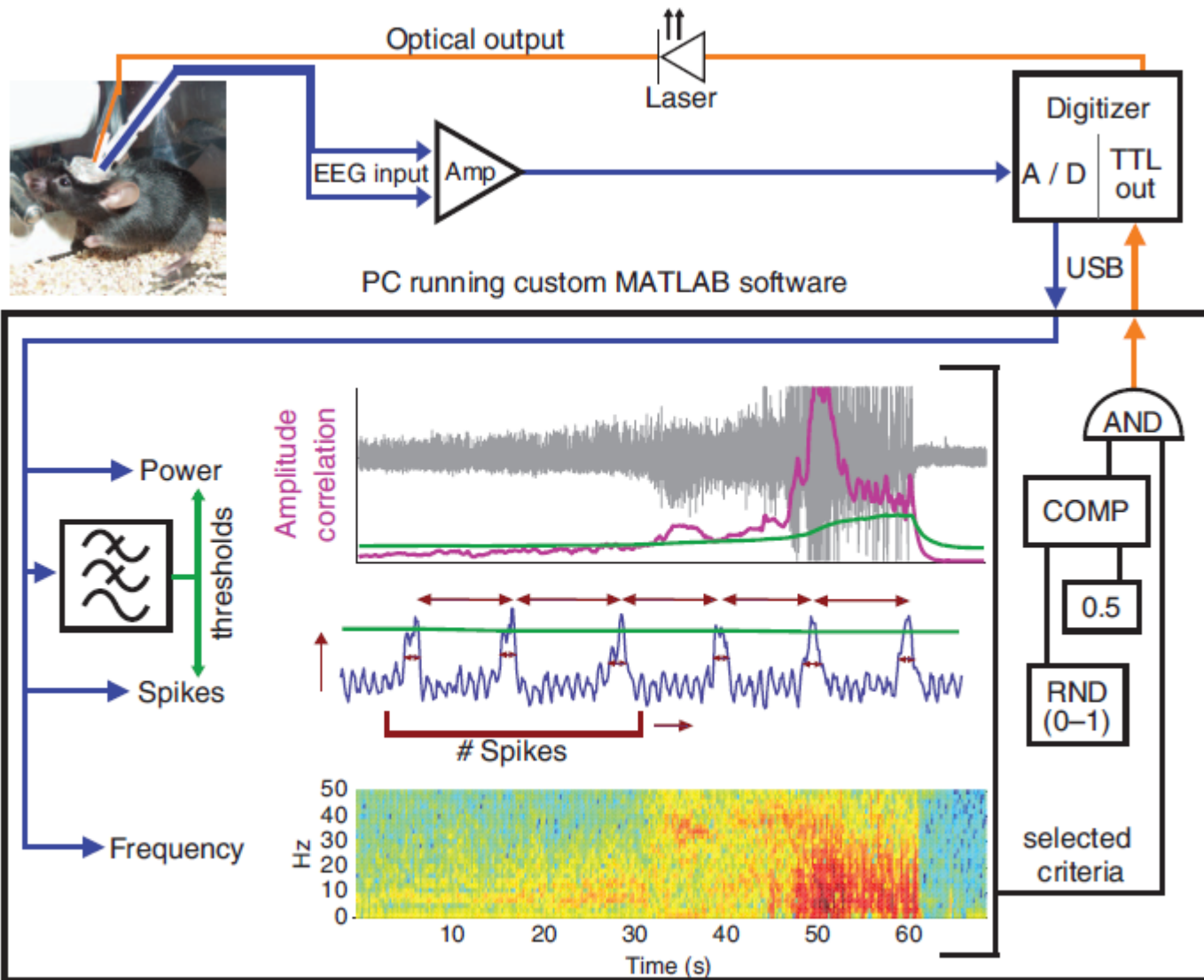
On-demand optogenetic control of spontaneous seizures in temporal lobe epilepsy

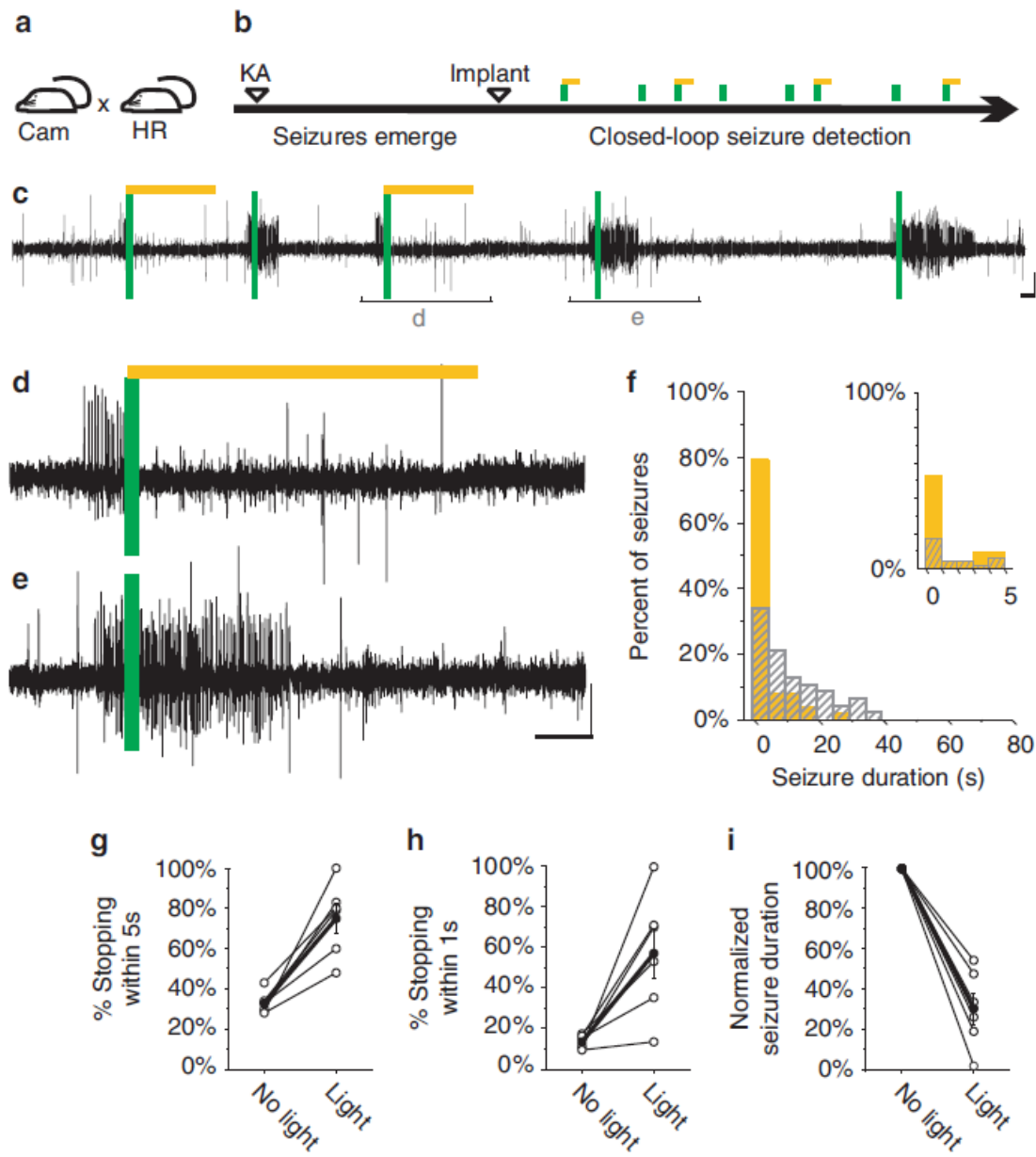
Esther Krook-Magnuson^{1,*}, Caren Armstrong^{1,*}, Mikko Oijala¹ & Ivan Soltesz¹

Gene therapy

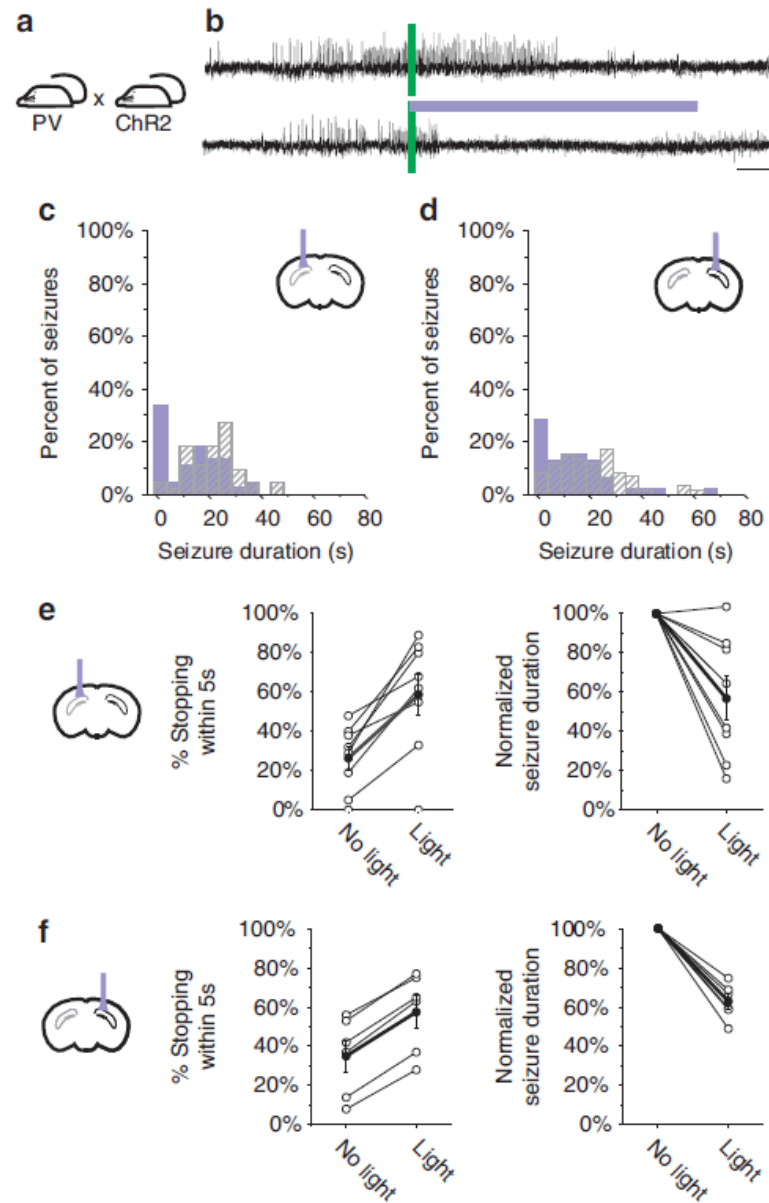
- Halorhodopsin transfection of pyramidal cells or GABA hippocampal cells
- Optic light stimulation inhibits excitability



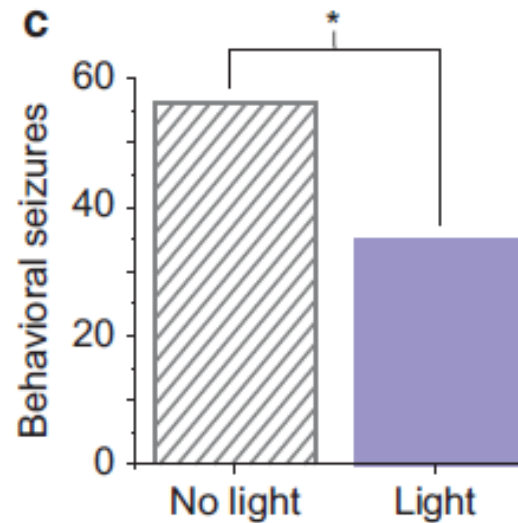
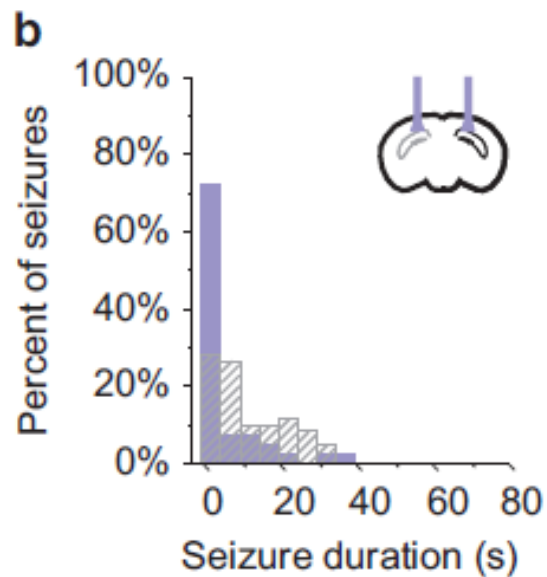
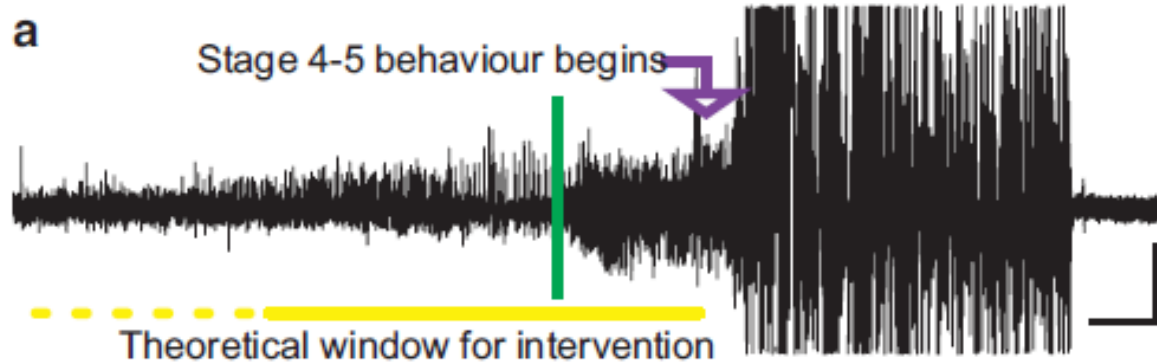




Inhibitory opsin HR in excitatory pyramidal cells



Excitatory opsin ChR2 in inhibitory GABA interneurons



Excitatory opsin ChR2 in inhibitory GABA interneurons

Closed loop optogenetic control of the thalamus in a model of a cortical lesion

