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Bonn Lecture Series in Neuroscience

Different EEG seizure patterns and ictogenic mechanisms (from animal models to human studies)

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Clinic for Epileptology, Seminar Room, Ground Floor

Network mechanisms responsible for focal seizure initiation are still largely unknown. Two prevalent seizure patterns observed during diagnostic intracranial recordings performed in patients with focal epilepsy were identified by computer-assisted EEG analysis. Pattern A: long seizures (>50s) with low-voltage fast activity onset (125Hz) and bursting phase with following post-ictal depression at the end. Pattern B: shorter seizures (10-40s) with characteristic on-set / off-set high amplitude transients and "higher" low-voltage fast activity (190-200Hz) onset. These patterns were combined with epileptic zone (EZ) biomarkers low-voltage fast activity at 80-200 Hz and slow transient polarizing shift to improve EZ detection. We reproduced fast oscillations at seizure onset in the temporal lobe of in vitro isolated guinea pig brain to study cellular and network mechanisms involved in seizure generation. Intracellular, extracellular, and ion-selective electrophysiological recordings were performed simultaneously in the entorhinal cortex (EC) during interictal-ictal transition. Principal neurons in deep and superficial layers of the EC did not generate action potentials during fast activity at ictal onset, whereas sustained firing was observed in putative interneurons. Within 5 to 10 seconds from seizure initiation, principal neurons generated a prominent firing that was correlated with the appearance of extracellular hypersynchronous bursting discharges. In superficial neurons, fast activity correlated with rhythmic IPSPs that progressively decreased in amplitude during the development of a slow depolarization associated with an increase in extracellular potassium. We conclude that in an acute model of ictogenesis, sustained inhibition without firing of principal neurons correlates with the onset of a focal seizure. The progression of the ictal discharge is contributed by a potassium dependent change in reversal potential of inhibitory postsynaptic potentials. These findings demonstrate a prominent role of inhibitory networks during the transition to seizure. Similarity between the ictal patterns in animal models and human patients suggest that a comparable ictogenic mechanisms could play a role in focal patient's seizure generation.

Selected Publications

Uva L, Saccucci S, Chikhladze M, Tassi L, **Gnatkovsky V**, Milesi G, Morbin M, de Curtis M. A Novel Focal Seizure Pattern Generated in Superficial Layers of the Olfactory Cortex. J Neurosci. 2017 Mar 29;37(13):3544-3554. doi: 10.1523/JNEUROSCI.2239-16.2016. Epub 2017 Mar 6. PubMed PMID: 28264979.

Gnatkovsky V, de Curtis M, Pastori C, Cardinale F, Lo Russo G, Mai R, Nobili L, Sartori I, Tassi L, Francione S. Biomarkers of epileptogenic zone defined by quantified stereo-EEG analysis. Epilepsia. 2014 Feb;55(2):296-305. doi: 10.1111/epi.12507. Epub 2014 Jan 13. PubMed PMID: 24417731.

Gnatkovsky V, Francione S, Cardinale F, Mai R, Tassi L, Lo Russo G, de Curtis M. Identification of reproducible ictal patterns based on quantified frequency analysis of intracranial EEG signals. Epilepsia. 2011 Mar;52(3):477-88. doi: 10.1111/j.1528-1167.2010.02931.x. Epub 2011 Jan 26. PubMed PMID: 21269289.

de Curtis M, **Gnatkovsky V**. Reevaluating the mechanisms of focal ictogenesis: The role of low-voltage fast activity. Epilepsia. 2009 Dec;50(12):2514-25. doi: 10.1111/j.1528-1167.2009.02249.x. Epub 2009 Aug 8. Review. PubMed PMID: 19674056.

Gnatkovsky V, Librizzi L, Trombin F, de Curtis M. Fast activity at seizure onset is mediated by inhibitory circuits in the entorhinal cortex in vitro. Ann Neurol. 2008 Dec;64(6):674-86. doi: 10.1002/ana.21519. PubMed PMID: 19107991.

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