



Altered Chloride homeostasis in Reactive plasticity upOn BrAin Trauma, (ACRoBAT)

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Traumatic brain injuries are the main injury-related causes of permanent disability, and are the third leading cause of mortality in Europe. Worldwide, more than 10 million people are affected every year. Post-traumatic epilepsy is the most common cause of new-onset epilepsy in young adults; following penetrating brain wounds, the likelihood of developing epilepsy is more than 50%. 30 to 40% of patients with post-traumatic epilepsy have seizures that are incompletely controlled with currently available medication. Moreover, unnecessary treatment with currently available antiepileptic drugs may then impair neurorehabilitation after brain trauma. It is evident that this field desperately needs new therapeutically relevant targets. In order to find them, we need to understand in detail the mechanisms engaged upon brain trauma. In this proposal, five European groups, with expertise ranging from cellular to systems Neuroscience, will pursue a common aim: **to disclose the mechanisms and impact of trauma-induced changes in inhibitory neurotransmission in the cortex.** Our preliminary results allow us to propose a working hypothesis in which **a major component of altered inhibitory neurotransmission upon brain trauma is the malfunction of proteins involved in chloride transport in neurons.** Subsequent abnormalities in neuronal chloride regulation not only perturb inhibitory signals, but also appear to be crucial for post-traumatic neuronal survival and proliferation, leading to altered activity of neuronal networks. Thus, the multifaceted impact of chloride transport malfunction in neurons makes it a particularly promising target with strong potential for innovative therapeutic strategies to improve rehabilitation of brain trauma patients in the future.