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NEMESIS - NEurological MEchanismS of Injury, and Sleep-like cellular dynamics

Focal brain disorders, including stroke, trauma, and epilepsy, are the main causes of disability and loss of productivity in the world, and carry a cumulative cost in Europe of about 500 billion euro/year. Now, physicians diagnose and treat these conditions as if they were caused by local dysfunction due to the pathological process. However, there is growing evidence that, in most neurological and psychiatric disorders, clinical symptoms reflect widespread network abnormalities. Normalization of such network abnormalities through “circuit-based” stimulation would therefore improve function. However, this form of therapy is currently limited by numerous factors: lack of knowledge about the underlying mechanisms and their behavioural relevance; inability to map these abnormalities onto single patients; and, most importantly, a principled understanding of where and how to stimulate the brain to produce functional recovery. ‘NEMESIS’, from Ancient Greek as “give what is due”, aims to “give an injured brain what is missing”, i.e., restore through stimulation normal activity in dysfunctional brain circuitries. By synergizing people, concepts, and technologies, NEMESIS will first characterize the effects of focal injury at multiple spatial and temporal scales (from whole brain to local circuits). Through the combination of observational (e.g., fMRI, EEG, calcium imaging, LFPs) and causal methods (e.g., electro-magnetic stimulation, optogenetics) NEMESIS will test the hypothesis that disconnected networks lie in a “sleep-like state” that impairs communication. Thirdly, NEMESIS will create whole brain models of structure/function to predict the effect of individual lesions and simulate novel stimulation protocols aimed at “re-awakening” the disconnected brain. Finally, proof-of-concept interventions that combine circuit-based stimulation and behavioural training, guided by modelling and animal studies, will be tested to restore normal activity, and so give back what is due.

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