Toward a molecular biology of conscious processing: consequences for drug design

Jean-Pierre Changeux
Kavli Institute for Brain & Mind UCSD, San Diego, USA
Institut Pasteur & Collège de France, Paris, FRANCE

Comparative analysis of the anatomy and psychophysics of brain development and evolution has led to the identification of features related to the emergence of conscious processing, in particular the development and maturation of the long-range connections between the prefrontal, parieto-temporal, and cingulate areas of the cerebral cortex. This network of long range connections has been hypothesized to contribute to the Global Neuronal Workspace for conscious processing (Dehaene et al 1998, Dehaene & Changeux 2011). In parallel, the analysis of gene-expression time-series data of rodent & human brain development has led to the detailed description of hierarchical networks of transcription factors (TFs), controlling coherent gene groups expression at several nested hierarchical levels of cortical development (Tsigelny et al. 2012). Attempts are being made in the identification in silico of the gene sets concerned with the long period of postnatal maturation which characterizes the Human brain and the synaptic selection (stabilization and pruning) that controls long-range connectivity development which takes place during this period through spontaneous and evoked activity and/or by endogenous/pharmacological modulators. The occurrence of possible allosteric switches mediated by the TFs and various allosteric receptors under the control of threshold concentration of orthosteric and allosteric modulatory agents possibly resulting into the discrete emergence of defined conscious processes is investigated. Last, analysis of the gene-expression patterns of the receptors for neurotransmitters (acetylcholine, glutamate, GABA) and neuropeptides (NGF, BDNF, etc.) engaged in regulation of the various states of conscious processing during brain development by pharmacological agents such as nicotinic compounds, benzodiazepine, and general anesthetics are currently under investigation.

References: