The urgent need for a systems biology approach to neurology

Dear Reader,

Biomedical research is traditionally based on the collection of numerous individual observations leading to a multitude of hypotheses on diagnosis and therapy. Without detracting from the fundamental role of this multiplicity of views and research studies, it has to be pointed out that collecting the many available observations into a coherent framework has often proved hard or even impossible. This holds even truer for brain diseases, since the connection between the molecular level and brain function is not immediate, but rather passes through several levels, including neuronal microcircuits and large-scale networks. Disease biomarkers are spread from the molecular to the anatomical level and often turn out to be unspecific. At the same time, therapeutic strategies often remain based on general schemes in the absence of precise knowledge of relevant etiopathogenetic factors. This situation has three main consequences. First, a solid basis for diagnosis has yet to be established for several neurological diseases. Second, in many cases prevention is difficult or even impossible, which increases the social costs related to hospitalizations and health care. Third, therapies are often imprecise and of limited utility, moreover at a time when pharmaceutical companies are showing less interest in drug development.

There is thus an urgent need for a new trend and this has been recognized by the major research agencies (Kandel et al., 2013). To address this challenge, the European Union, in 2013, launched the Human Brain Project (HBP), whose main aim is to define a new framework for *future medicine*. To this end, two approaches are crucial: developing advanced technologies to generate large-scale brain models, and federating data to generate new interpretative strategies. A year into the project and a year since *Functional Neurology* devoted a whole issue to this topic (Markram, 2013), the HBP consortium is generating a solid infrastructure that was illustrated at the recent HBP meeting in Heidelberg (https://www.humanbrainproject.eu/it/home). What was initially criticized by many as pure "utopia" is now becoming reality, indicating that this project can be fully implemented and has the real potential to bring systems biology approaches into clinical research and medical practice, opening up new avenues for personalized prevention, diagnostics and treatment of human diseases.

In this regard we may consider, for example, the need for new criteria for the prevention, differential diagnosis and treatment of dementia, a pathology that is generating increasing concern in modern society. In Alzheimer's disease (AD), neuropsychological tests give important but incomplete indications on the nature of the pathology. Genetic analysis can reveal familiarity while detection of specific patterns of β-amyloid on PET scans and of *tau*-protein in the cerebrospinal fluid provide important diagnostic information. The interpretation of standard MRI scans provides additional information on neurodegeneration, although distinguishing signs obtained using high-field MRI techniques have not yet entered clinical practice. AD is thus a typical example of a condition in which relevant information is spread over different levels, from genes to circuits and behavior, without the availability of a coherent interpretation framework (Redolfi et al., 2013). What is foreseen is that all these data could be integrated into a multi-level model of the brain in order to trace the development of the disease and identify biomarkers for early diagnosis and prevention and for more effective therapies.

Egidio D'Angelo, MD, PhD

Brain Connectivity Center, C. Mondino National Neurological Institute, Pavia, Italy
Department of Brain and Behavioral Sciences, University of Pavia, Italy
Editor-in-Chief, Functional Neurology

References

Kandel ER, Markram H, Matthews PM, et al (2013). Neuroscience thinks big (and collaboratively). Nat Rev Neurosci 14:659-664.
Markram H (2013). Seven challenges for neuroscience. Funct Neurol 28:145-151.
Redolfi A, Bosco P, Manset D, et al (2013). Brain investigation and brain conceptualization. Funct Neurol 28:175-190.