

TARGETING THE BRAIN FROM A NEUROBIOLOGICAL POINT OF VIEW: A CHALLENGE FOR THE PHARMACOTHERAPY

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Neuropsychiatric diseases are characterized by their variety of symptoms and the complexity of their pathophysiology. In fact, approved medications to treat these diseases present, in general, low efficacy and a high profile of provoking adverse side effects. And, why are we still far away from developing safe and effective medications to treat neuropsychiatric diseases? In this talk, we will analyze different reasons that might underly this problem, from the anatomical and functional complexity of the central nervous system (CNS) to the poor access of drugs to the specific altered brain areas. We will also address the lack of knowledge of the pathophysiology and neural mechanisms of these diseases that also contributes to the difficulty to develop new medications. The brain, spinal cord and brainstem are parts of the CNS that are formed by glial cells and neurons. Moreover, neurons are very diverse in the molecules expressed and the functions that they develop. Increasing the complexity of the system, the neurons that, i) express same neurotransmitters, ii) are located in same brain areas and iii) apparently regulate very same functions, can be differently connected to other neurons. As a consequence, the transmission of the information might be unique at neuronal level and this fact, ultimately, can condition the physiological functions and the behavioral output of the individuals. In addition, glial cells participate very actively in regulating not only the homeostasis of the extracellular environment, but also the function of the neural networks. This very complex structure, which is not completely known, has diffculted our ability to disentangle the neural mechanisms that underly neuropsychiatric disorders as for example addiction, schizophrenia, depression or anxiety. However, and even after decades of scientific effort, we have been able to identify new pharmacological targets to treat some neuropsychiatric diseases, but these targets are usually effective when pharmacologically restricted to specific brain areas or neuron type. As a consequence of the complexity of the biology of the CNS, the administration of pharmaceutical agents that modify the activity of the new identified target, very probably impacts its function at several other levels and brain areas leading to unwanted side effects. We will provide specific examples of these problems. We will also review the difficulties of several pharmaceutical agents to trespass the blood brain barrier and the different pathways to arrive to the CNS. Finally, we will summarize the challenges that the pharmaceutical technology is facing to overcome the biological difficulties that present the treatment of the neuropsychiatric diseases.

Short Curriculum Vitae:

Lucia Hipólito is Associate Professor of Pharmacy and Pharmaceutical Technology in the University of Valencia. Since the start of her scientific career, she has been working on the field of neuropharmacology of addiction. During the PhD, under the direction of L. Granero and A. Polache, she investigated a new mechanism underlying alcohol addiction. She has also completed research stays at the University of Cambridge and the Rutgers University in New Jersey. After finishing the PhD, she joined the Dr. Morón laboratory at Columbia University to start a project involving the study of pain and opioid addiction. Data obtained in this project had showed for the first time a dose dependent pain-increased heroin intake, being crucial in understanding the factors that contribute to the opioid epidemic that has been declared in the United States. Indeed, her research had a high impact in the field and Dr. Hipolito has received in 2016 the ESBRA Young Investigator Award, the Pain Award from the Valencian Society for the Studies and Treatment of Pain in 2017 and the Valencian Young Investigator Award in 2018. Currently she is developing her investigation in the University of Valencia as leader of the DOREAL lab (www.uv.es/doreal). Doreal lab is focused in the research of alcoholism, opioid signaling and neuroinflammation and pain neuropsychiatry comorbidities. Moreover, Dr. Hipólito has recently started a collaboration with Dr. A Melero to develop new pharmaceutical dosage forms to improve access to the central nervous system of drugs to treat these neuropsychiatric conditions.