cima
CENTER FOR APPLIED MEDICAL RESEARCH
UNIVERSITY OF NAVARRA

Schizophrenia: Animal Models

Schizophrenia is a severe and chronic mental disorder that affects approximately 1% of the population worldwide. Symptoms fall into three categories: positive (hallucinations, paranoia and movement disorders), negative (social withdrawal, poverty of speech and blunted affect) and cognitive (executive function, working memory and attention).

Although several genetic and environmental factors could contribute to the risk of developing schizophrenia, causes are still unknown and treatments focus on aleviating their symptomatology. Initaially, the most influential hypotheses concerning the neurobiology involved dopamine, but new theories suggest an origin related to misregulations in the glutamatergic system.

Animal models fit into four different induction categories: developmental, drug-induced, lesion or genetic manipulation; drug-induced, rat-based NMDA-receptor blockade models are available at CIMA.

NMDA-receptor blockade models (Rat)

DETAILS: Whilst dopaminergic dysfunction/models explain negative and cognitive symptoms, glutamatergic models (NMDA-receptor blockade) reproduce positive, negative and cognitive domains. ***Acute administration*** of non-competitive NMDA receptor antagonists (phencyclidine (PCP), dizocilpine (MK-801) and ketamine) leads to immediate psychological effects, which closely resemble symptoms that occur in ***acute schizophrenia***. ***Long-term, sub-chronic administration*** causes long-lasting deficits in set-shifting ability and produce cognitive deficits similar to those observed in ***chronic schizophrenia***. In addition, NMDA receptor antagonist administration causes neurotoxic changes in cortical brain and thalamic regions which are similar to reductions in brain volume seen inpatients with schizophrenia.

APPLICATIONS: This animal model is useful in the understanding the pathophysiology, etiology and neural correlates of schizophrenia. It also offers insights into molecular adaptations that follow acute/chronic NMDA blockade that could lead to identify new therapeutic targets. The NMDA antagonist approach ***does not***, however, address the developmental component of schizophrenia.

ANALYSIS: CIMA team has the know-how and facilities required to manage and characterize this model. Expertise includes chronic and acute administration of NMDA receptor antagonist, behavioral and electrophysiological characterization through simultaneous digital video and neurophysiologic signal acquisition in awake, freely moving animal. Complementary histological and biochemical analyses are also available.