## POS-C01

*PD en Neurociencias*

### NEURAL BASIS OF COGNITIVE ENHANCEMENT IN AN ANIMAL MODEL OF SCHIZOPHRENIA.

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The function of N-methyl-D-aspartate receptor (NMDAR) is critical for the processes underlying learning, memory and synaptic plasticity. The hypofunction of NMDAr is currently the most accepted hypothesis for the pathophysiology of schizophrenia. This condition is induced in animal models using NMDA antagonist drugs, such as MK801, that provoke long-term structural brain changes and behaviors reminiscent of schizophrenia. Disturbances in glutamartergic transmission are especially relevant to mimic negative and cognitive symptoms of the disease. Schizophrenia is considered a neurodevelopmental disorder, although symptoms usually emerge during late adolescence/early adulthood, coinciding with GABAergic circuit maturation. It has been suggested that NMDA hypofunction preferentially affects GABAergic interneurons and perturbs the maturation of GABAergic circuits, including disrupted synaptic integration in early brain development and modified network activity and plasticity in adulthood. One of the major challenges in schizophrenia research is trying to modify brain circuits that present long lasting aberrant synaptic wiring. Enriched Environment (EE) is a combination of sensory stimulation, physical exercise and social interaction, and it is a powerful strategy to overcome cognitive deficits in several neurological diseases. Furthermore, the enrichment induces an overexpression of neurotrophic factors such as NGF, GDNF, BDNF or VEGF, which in turn act as response pathways. Given the etiopathogenic features of schizophrenia, we propose an animal model of schizophrenia based on the antagonism of NMDA receptors. In this context, we expect to find changes in molecular, cellular and behavioral levels that could be at least partially reverted in adulthood by enriched environment. We propose that this improvement could be largely mediated by the neurotrophic factor VEGF, and its inhibition would prevent the beneficial effects o environmental enrichment.