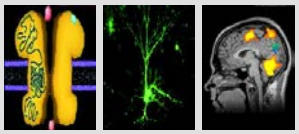

EXTINCTION LEARNING: THE NEURAL, BEHAVIOURAL, ONTOGENETIC, EDUCATIONAL, AND CLINICAL MECHANISMS

April 24 - 25, 2018 Veranstaltungszentrum, Ruhr University Bochum

Tuesday April 24, 9:25 – 12:35

Session 1 **Brain-Immune-Interactions**

ULRIKE WEBER-STADLBAUER

Institute for Pharmacology and Toxicology, University of Zurich, Switzerland

Transgenerational transmission of behavioral deficits induced by prenatal immune activation

Background: Non-genetic transgenerational transmission of behavioral traits has gained increasing recognition in view of its potential importance in the etiology of multi-factorial psychiatric disorders. Here, we explored whether maternal immune activation (MIA), which is a known risk factor for various neurodevelopmental and psychiatric disorders, can induce pathological effects across multiple generations.

Methods: We used an established MIA model that is based on maternal exposure to the viral mimetic poly(I:C) in mice (C57BL6/N). First-generation (F1) MIA offspring and control offspring were either assigned to behavioral testing when they reached adult age, or they were used as breeders to obtain second- (F2) and third- (F3) generation offspring. Adult F2 and F3 offspring were then also assigned to behavioral testing.

Results: Compared to F1 control offspring, F1 MIA offspring showed a number of behavioral abnormalities, including reduced sociability in the social interaction test, impaired sensorimotor gating in the prepulse inhibition test, and increased sensitivity to the dopamine-stimulating drug, amphetamine. While F2 and F3 offspring of MIA-exposed ancestors similarly showed deficits in sociability, they developed novel phenotypes that were not seen in F1 MIA offspring, including blunted amphetamine sensitivity and behavioral despair in the forced swimming test.

Conclusions: Prenatal immune activation leads to a modification of pathological phenotypes across generations. While the spectrum of behavioral abnormalities emerging in F1 MIA offspring recapitulates “psychosis-like” phenotypes, their subsequent generations develop “depression-like” phenotypes that were initially not present in the F1 generation.