M175. BRAIN STRUCTURAL CORRELATES OF FUNCTIONAL CAPACITY IN FIRST-EPIODE PSYCHOSIS

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Background: Impaired functional capacity is a core feature of schizophrenia and present even in first episode psychosis (FEP) patients. Impairments in daily functioning tend to persist despite antipsychotic therapy but their neural basis is not clear. Previous studies suggest that volume loss in frontal cortex might be an important contributor but findings are inconsistent. We aimed to comprehensively investigate the brain structural correlates of functional capacity in first episode psychosis using MRI and a reliable objective measure of functioning (University of California, San Diego Health (CRASH), which is a scale developed to measure CR specifically for psychosis patients with severe mental illness). Correlations between CRASH scores and the remainder variables were performed.

Results: For the present study we included only the subjects who had CRASH score, a total of 112 patients, 42.7% female, aged 40.61±12.4 (mean±SD). Substance use was present in 44.3%. The CRASH score was 33.30±15.72 (mean±SD) and was associated with negative (but not positive) psychotic symptoms assessed using the Clinical Global Impression (CGI) scale and functioning was assessed using the Global Assessment of Functioning (GAF) scale. The intestinal-permeability was estimated with the “Permeable-Intestine-syndrome questionnaire”. The diet was assessed with the “Mediterranean-diet-adherence questionnaire”. Exercise was measured with the “International Physical Activity Questionnaire (IPAQ)”. Cognition was measured with the SCIP-S scale. CR was assessed with the Cognitive Reserve Assessment Scale in Health (CRASH), which is a scale developed to measure CR specifically for psychosis patients with severe mental illness. No significant associations were found with Mediterranean-diet scale (rs=0.195; p=0.056), IMC (rs=-0.192; p=0.063), C-reactive protein (rs=-0.104; p=0.278) and the IPAQ-resting scale and permeability-scale (rs=0.119; p=0.244).

Discussion:
1. High CR in SCZ-spectrum disorders is associated with low intestinal permeability, probably mediated by low-grade chronic inflammation through exercise and diet, although the latter was not significantly associated in this analysis.
2. A higher CR in SCZ-spectrum disorders may contribute to less negative psychotic symptoms, better functioning, a lower severity of illness, and better cognitive outcomes.
3. The complex inflammation-intestinal-permeability may play a role in the pathophysiology of SCZ-spectrum disorders, mediated by daily-life factors (exercise and diet).
4. Focused interventions on the modification of daily-life factors could reduce the influence of the complex inflammation-intestinal-permeability and secondarily reduce symptoms, and improve cognition, CR and functioning in SCZ-spectrum disorders.
5. Specific programs addressed to improve CR and functioning conducted at the early stages of the psychotic illness may be helpful in order to prevent cognitive and functional decline.

M177. THE PROTEOME OF OLIGODENDROCYTES DIFFERENTIATED FROM NEURAL STEM CELL DERIVED FROM SCHIZOPHRENIA PATIENTS

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Background: Oligodendrocytes constitute the majority of the cells in white matter and alterations in this region have been reported in patients with schizophrenia. The myelin sheath is produced exclusively by mature oligodendrocytes. Thus, a dysfunction during the maturation of these cells could lead to a change in normal myelination processes, causing the hypomyelination observed in patients with schizophrenia. In this manner, functional studies are needed for a better connection of these different aspects of the disease in order to understand the pathophysiology of schizophrenia in an integrated manner. Thus, our aim was to evaluate the differences between the proteome of oligodendrocytes derived from neural stem cells (NSCs) from patients with schizophrenia and controls.

Methods: The cells were differentiated using the protocol described by Yan, Shin, Jha and collaborators (Yan, Shin, Jha, et al., 2013). After 14 days, the proteins were extracted and proteomic analyses were performed in a two-dimensional microUPLC coupled to nano ESI-Q-IM-TOF mass spectrometer. Progenesis® QI software was used in order to identify and quantify the proteins.

Results: On average, 2046 proteins were identified and 444 had alterations in the expression levels. These differentially expressed proteins were related most with metabolism, RNA transport, spliceosome machinery, vesicular transport, and signal transduction.

Discussion: The proteins and canonical pathways found here may contribute to understanding the biochemical mechanisms involved in the disorder, which may provide new targets for the development of more effective treatments, improving the schizophrenic patient’s quality of life.

M178. PROTEOMIC EVIDENCES OF COMPROMISED ENERGY METABOLISM IN THE NEURODEVELOPMENTAL COURSE OF SCHIZOPHRENIA

Abstract not included.

M179. ALTERNATED BRAIN AND BEHAVIORAL DEVELOPMENT IN A NONHUMAN PRIMATE MODEL OF MATERNAL IMMUNE ACTIVATION

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Background: Children born to women who experience infection during pregnancy have an increased risk of brain disorders with neurodevelopmental origins, including both schizophrenia (SZ) and autism spectrum disorder (ASD). Rodent models of maternal immune activation (MIA) have identified the maternal immune response as the critical link between maternal infection and aberrant brain and behavior development in offspring. The nonhuman primate MIA model provides an opportunity to maximize the translational utility of this model in a species more closely related to humans. Our previous pilot study found that rhesus monkeys (Macaca mulatta) born to MIA-treated dams developed behavioral abnormalities and increased striatal dopamine during adolescence. Here we present emerging behavioral outcomes from a larger cohort of MIA-treated nonhuman primates.

Methods: A modified form of the viral mimic, Polyinosinic-polycytidylic acid (PolyIC), was delivered to a new cohort of pregnant rhesus monkeys (N=14) in the late first trimester (gestational days 43, 44, 46) to stimulate a maternal immune response. Control dams received saline injections at the same gestational time points (N=10) or were untreated (N=4). The offspring are undergoing ongoing comprehensive behavioral evaluations paired with longitudinal neuroimaging to quantify the emergence of brain and behavior pathology associated with prenatal maternal immune challenge.

Results: MIA-treated dams exhibited a strong immune response as indexed by transient increases in sickness behavior, temperature and inflammatory cytokines. Although MIA offspring developed species-typical milestones and showed no overt signs of atypical interactions with mothers or peers early in development, they had significantly smaller gray matter volume in the prefrontal and frontal cortices than control offspring at 6, 12 and 24 months of age (p < 0.05). At 24 months of age, the animals were tested in a reversal learning paradigm that requires a subject to flexibly adjust its behavior when the reward-related contingencies that it has previously learned are reversed. All animals advanced and performed similarly on the training and initial discrimination phases of the test. However, on the first day of the initial reward reversal, the MIA-treated animals more frequently failed to make a choice as compared to controls (Wilcoxon two-sample test p-value = .005). These emerging data suggest that MIA-treated animals exhibit subtle impairments in cognitive processing. Additional assessments of social and cognitive development, including non-invasive eye tracking data, will be presented to further explore the impact of MIA on primate behavioral development.

Discussion: These findings provide new insights into the emergence of brain pathology in MIA-exposed primates and have implications for the developmental pathophysiology of human psychiatric disorders associated with maternal gestational infection.

M180. SUSCEPTIBILITY AND RESILIENCE IN A MOUSE MODEL OF MATERNAL IMMUNE ACTIVATION

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Background: Epidemiological studies over the past decades have repeatedly implicated maternal immune activation (MIA) in the etiology of psychiatric illnesses, including schizophrenia and related psychotic disorders. Not all offspring exposed to MIA, however, develop overt pathologies, suggesting that some are susceptible while others are resilient to MIA. To elucidate susceptibility and resilience in MIA, we used a mouse model that is based on prenatal exposure to the viral mimic poly(I:C).

Methods: Poly(I:C)-based MIA was induced in C57BL/6J mice on gestation day 12. Control dams received vehicle solution only. Offspring of poly(I:C)- or vehicle-exposed dams were subjected to a comprehensive behavioral testing battery when they reached adulthood (12 weeks of age onwards). Next-generation mRNA sequencing and gene pathway analyses...