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Poster sessions P.100–P.199

P.100 Effects of perinatal cannabis exposure on transcriptional regulation of dopamine receptor d2 and cannabinoid receptor 1 in rats at adulthood

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Background and aim: Exposure during the gestational and perinatal period to different adverse environmental insults can increase the risk of developmental disorders and disease manifesting in childhood, over the lifecourse, or even transgenerationally [1]. In particular, prenatal development represents a vulnerable period for epigenetic disruption and insults during this critical phase induce short- and long-term effects on brain structure and function through epigenetic mechanisms, such as DNA methylation and histone modifications [2].

Delta-9-tetrahydrocannabinol (THC) is the major psychoactive component in Cannabis Sativa and its exposure has been found to lead to persistent abnormalities resembling schizophrenia [3]. Moreover, cannabis is the most commonly used illicit substance among pregnant woman and studies on long-term effects of his use during pregnancy show its detrimental impact on offspring cognitive development from childhood until later in life and it appears to be a contributing factor to psychosis [4].

The aim of this study is to evaluate the involvement of transcriptional regulation of endocannabinoid and dopaminergic system genes in the development of psychotic-like symptoms in a rat model of prenatal and perinatal THC exposure.
Methods: Time Pregnant Sprague-Dawley rats were treated with THC (5 mg/kg/day, per os) or Vehicle (Sesame Oil, 5 mg/mL, per os) from gestational day (GD) 15 to postnatal day (PND) 9. At adulthood (PND$>$180) genomic DNA and total RNA were isolated from selected brain regions (Prefrontal Cortex, Nucleus Accumbens and Ventral Tegmental Area). Quantitative Real-Time RT-PCR and Pyrosequencing were performed to quantitatively assess the state of gene expression and DNA methylation at gene promoters, respectively.
Results: Selective changes in CNR1 (Cannabinoid Receptor type 1) and D2 (Dopaminergic Receptor type 2) genes expression were observed in the Prefrontal Cortex of prenatal exposed THC rats (1.75 ± 0.19 CNR1; 2.38 ± 0.23 D2) when compared with the control animals (1.06 ± 0.18, $p<0.05$ CNR1; 1.02 ± 0.09 $p<0.002$ D2). No alterations have been observed in other brain regions as well as in the other genes investigated (CB2, TRPV1, FAAH, MAGL, DAGL). No significant changes in DNA methylation levels at gene promoters have been detected.
Discussion: Our data suggest that a dysregulation of endocannabinoid and/or dopaminergic system induced by perinatal THC exposure could play a role in the development of schizophrenia-like alterations at adulthood. Further studies are needed to evaluate the epigenetic regulation of these receptors such as histone modifications and miRNA (microRNA). A number of miRNA and site-specific modifications of the nucleosome core histones, in fact, are of particular interest and could be the key to understand and explain the observed THC effects on the CB1 and D2 expression. Studying how the environment factors might induce the development of psychosis would be helpful to better understand what happens in the central circuits and to select new treatment strategies.

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P.101 White matter structural connectivity abnormalities in subjects with deficit schizophrenia: A diffusion tensor imaging study

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Introduction: Since schizophrenia represents a clinically heterogeneous disorder, the identification of the neurobiological correlates of the disease is made difficult [1]. Deficit schizophrenia (DS) has been proposed as a separate disorder with respect to non-deficit schizophrenia (ND). It is characterised by the presence of primary and enduring negative symptoms and by different course, risk factors and clinical features. In particular, it is associated to poor response to pharmacological treatment, worse functional outcome and greater impairment of neurocognitive functions [2].
Aims: Our primary aims, using probabilistic analysis of diffusion tensor imaging data [3], were 1) to investigate differences of white matter connectivity within several brain areas in subjects with DS compared to ND and healthy controls (HC); 2) to investigate the relationships between white matter connectivity and clinical variables.
Methods: We acquired diffusion tensor imaging (DTI) data in forty-six subjects with chronic schizophrenia (SCZ) and 35 age- and gender-matched HC. Probabilistic tractography was applied to examine the connectivity index [CI] (% of the probabilistic streamlines originating from a region that reach a second one) and Fractional Anisotropy (FA) of pathways connecting dorso-lateral prefrontal cortex (DLPFC), nucleus accumbens (NAcc), amygdala (AMY) and insular cortex (IC). We used the Schedule for the Deficit Syndrome (SDS) to subdivide patients in DS and NDS and to assess negative symptoms, the Positive and Negative Syndrome Scale to assess positive symptoms, disorganisation and depression, the MATRICS Consensus Cognitive Battery to evaluate neurocognition. Statistical analyses were carried out by linear regression analysis using SPSS (version 15.0, SPSS Inc, Chicago, IL). General linear model was fitted separately for each measure to assess differences between groups and correlations with clinical scores.
Results: Using the SDS, nine patients were classified as DS and 37 as ND. There was no significant group difference in sex ($p = 0.136$) and age ($p = 0.116$) between SCZ and HC and, also, between DS and NDS as regard sex ($p = 0.51$) and age ($p = 0.22$). While the CI between right AMY and DLPFC was reduced in SCZ compared to HC (Beta In 0.311; $p = 0.0044$), we did not find any differences between DS and ND as regard to this measure. CI between right AMY and dorsal-anterior IC was increased in DS compared to ND (Beta In 0.434; $p = 0.0036$). Finally, in the whole group of SCZ, the FA of right NAcc-DLPFC connections was correlated with PANSS disorganization score (Beta In 0.441; $p = 0.0031$).
Conclusions: Our data are in line with previous results showing that different symptom dimensions and clinical subtypes of schizophrenia are underpinned by distinct neurobiological substrates. In addition, our findings concerning the increased Connectivity Index between right amygdala and dorsal-anterior insular cortex in DS as compared to ND demonstrate that primary and persistent negative symptoms are related to connectivity abnormalities within brain regions involved in guiding goal-directed behavior based on experienced value [4,5].

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P.102 Relationship between antipsychotic compliance and malondialdehyde in acute and stabilized paranoid schizophrenia

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