S070

Identification of a long lasting stress signatures associated with enhanced vulnerability for depression by using 'omics and cross species approaches

A. Cattaneo

King's college London, psychological medicine, London, United Kingdom

Depression results from the interplay of vulnerability genes with environmental factors, a phenomenon named as 'gene-environment (GxE) interaction'. To date, GxE interaction studies have been limited to hypothesis-based candidate genes, since genome-wide (GWAS)-based GxE interaction studies would require enormous datasets with genetics, environmental and clinical variables. We used a novel, cross-species and cross-tissues "*omics*" approaches to identify genes predicting depression in response to stress in GxE interactions. We integrated the transcriptome and miRNome profiles from the hippocampus of adult rats exposed to prenatal stress (PNS) with transcriptome data obtained from blood mRNA of adult humans exposed to early life trauma, using a stringent statistical analyses pathway. Network analysis of the integrated gene lists identified the Forkhead box protein O1 (*FOXO1*), Alpha-2-Macroglobulin (*A2 M*) and Transforming Growth Factor Beta 1 (*TGFB1*) as candidates to be tested for GxE interactions, in two GWAS samples of adults either with a range of childhood traumatic experiences (Grady Study Project, Atlanta, USA) or with childhood emotional abuse only (Helsinki Birth Cohort Study, Finland). Six *FOXO1* SNPs showed significant GxE interactions with emotional abuse in the Grady Study that survived stringent permutation analyses and were all replicated in the Helsinki study. In addition, other SNPs in all the three genes showed significant GxE interactions with emotional, physical and sexual abuse in the Grady Study. We therefore provide a successful 'hypothesis-free' approach for the identification and prioritization of candidate genes for GxE interaction studies that can be investigated in GWAS datasets.

S071

Epigenetic signatures of early life adversities in animal models: A role for psychopathology vulnerability

M.A. Riva

University of Milan, Department of Pharmacological and Biomolecular Sciences, Milan, Italy

Stressful experiences early in life (ELS) represent one of the most relevant factors for the vulnerability to psychopathologies. Epigenetic changes, such as DNA methylation, have emerged as a major mechanism through which ELS can alter adult behaviour leading to persistent changes of gene regulation.

We performed DNA methylation analyses in the hippocampus and prefrontal cortex of adult rats exposed to stress during gestation (PNS), a model that is associated with persistent behavioral alterations relevant for psychiatric disorders.

Using an epigenome-wide analysis, an overlap of 893 differentially methylated genes was observed between hippocampus and prefrontal cortex of adult male and female rats exposed to PNS. The list includes several genes previously associated with schizophrenia and other psychiatric conditions, such as calcium and potassium voltage operated channels as well as GABA and glutamate receptor subunits. By restricting the overlap to genes that were modulated in the same direction, we identified miR-30a as being less methylated in PNS rats. Interestingly one of the targets for this miRNA is the neurotrophin BDNF, whose expression was indeed reduced as a consequence of the prenatal manipulation. Interestingly chronic treatment of PNS rats with the multi-receptor modulator lurasidone during adolescence was able to prevent the changes in miR30a and BDNF expression.

These results highlight the importance for the identification of methylation signatures through which stress exposure early in life could engrave on the outcome of the adult phenotype, and may allow the identification of novel genes and pathways that are affected as a consequence of ELS.

Symposium: Intergenerational transmission of parenting: Epigenetic, genetic, and psychological mechanisms

S072

Intergenerational transmission of well being–genetic and epigenetic mechanisms

E. Unternaehrer [1,*], K. Greenlaw [2], S. Hari Dass [1], L.M. Chen [1], A.A. Bouvette-Turcot [1], K. Cost [3], K.J. O'Donnell [1], H. Gaudreau [1], L. McEwen [4], J. MacIsaac [4], M.S. Kobor [4], A.S. Fleming [5], L. Atkinson [6], J.E. Lydon [7], M. Steiner [8], A. Ciampi [2], C.M.T. Greenwood [2], M.J. Meaney [1]

[1] *McGill University, Douglas Mental Health University Institute, Montreal, Canada*
[2] *Lady Davis Institute, Centre for Clinical Epidemiology, Montreal, Canada*
[3] *Sick Kids, Department of Psychiatry, Toronto, Canada*
[4] *University of British Columbia, Centre for Molecular Medicine and Therapeutics, Vancouver, Canada*
[5] *University of Toronto Mississauga, Department of Psychology, Toronto, Canada*
[6] *Ryerson University, Department of Psychology, Toronto, Canada*
[7] *McGill University, Department of Psychology, Montreal, Canada*
[8] *McMaster University, Department of Psychiatry & Behavioral Neurosciences, Hamilton, Canada*
* *Corresponding author.*

Introduction   Maternal mental well being influences offspring development. Research suggests that an interplay between genetic and environmental factors underlies this familial transmission of mental disorders.

Objectives   To explore an interaction between genetic and environmental factors to predict trajectories of maternal mental well being, and to examine whether these trajectories are associated with epigenetic modifications in mothers and their offspring.

Method   We assessed maternal childhood trauma and rearing experiences, prenatal and postnatal symptoms of depression and stress experience from 6 to 72 months postpartum, and genetic and epigenetic variation in a longitudinal birth-cohort study ($n = 262$) (Maternal adversity, vulnerability and neurodevelopment project). We used latent class modeling to describe trajectories in maternal depressive symptoms, parenting stress, marital stress and general stress, taking polygenetic risk for major depressive disorder (MDD),

a composite score for maternal early life adversities, and prenatal depressive symptoms into account.

Results   Genetic risk for MDD associated with trajectories of maternal well being in the postpartum, conditional on the experience of early life adversities and prenatal symptoms of depression. We will explore whether these trajectories are also linked to DNA methylation patterns in mothers and their offspring. Preliminary analyses suggest that maternal early life adversities associate with offspring DNA methylation age estimates, which is mediated through maternal mental well being and maternal DNA methylation age estimates.

Conclusion   We found relevant gene-environment interactions associated with trajectories of maternal well being. Our findings inform research on mechanisms underlying familial transmission of vulnerability for psychopathology and might thus be relevant to prevention and early intervention programs.

Disclosure of interest   The authors have not supplied their declaration of competing interest.

S073

Once and again: Intergenerational transmission of parenting

K. Tombeau Cost [1,*], E. Unternaehrer [2], W. Jonas [3], H. Gaudreau [2], A.A. Bouvette-Tourcot [2], M. Steiner [4], J. Lydon [2], P. Szatmari [5], M. Meaney [2], A. Fleming [6]
[1] *Psychology, Canada*
[2] *McGill University, Psychology, Montreal, Canada*
[3] *Karolinska Institute, Department of Women's and Children's Health, Stockholm, Sweden*
[4] *McMaster University, Psychiatry and Behavioural Neurosciences, Hamilton, Canada*
[5] *The Hosptial for Sick Children, Psychiatry, Toronto, Canada*
[6] *University of Toronto Mississauga, Psychology, Mississauga, Canada*
* *Corresponding author.*

Introduction   Animal and human studies suggest that individual differences in maternal parenting behaviour are transmitted from one generation to the next.

Objective   This study aimed to examine potential psychosocial mechanisms underlying an intergenerational transmission of conceptualization of parenting, including affect, cognition, and parental support.

Methods   In a subsample of 201 first-time mothers participating in the Maternal Adversity, Vulnerability and Neurodevelopment (MAVAN) project, we assessed maternal childhood rearing experiences, using the Parental Bonding Instrument and the Childhood Trauma Questionnaire. At 6 months postpartum, mothers completed questionnaires on parenting stress, symptoms of depression, internalization of maternal care regulation and current relationship with mother and father.

Results   We found significant direct associations of maltreatment and rearing by the grandmother with parenting stress at 6 months. These associations were mediated through distinct psychosocial pathways: the association of maltreatment on higher parenting stress was fully mediated through more maternal symptoms of depression ($z = 2.297$; $P = 022$). The association between sub-optimal rearing provided by the mother and higher parenting stress was mediated through lower internalization of maternal care regulation ($z = -2.155$; $P = 031$) and to a lesser degree through more symptoms of depression ($z = -1.842$; $P = 065$). Finally, higher quality rearing by the grandfather was indirectly related to lower parenting stress through positive current relationship with the father ($z = -2.617$; $P = 009$).

Conclusions   There are distinct pathways by which early experiences manifest in parenting stress. By understanding the structure of dysregulated parenting, clinicians will have practical information to specifically target maternal motivation, social supports, and

depressed mood to disrupt maladaptive parenting cognitions and practices.

Disclosure of interest   The authors have not supplied their declaration of competing interest.

S074

Early adversity, symptoms of depression and breastfeeding

W. Jonas [1,*], A. Fleming [2], M. Steiner [3], M.J. Meaney [4], L. Atkinson [5], V. Mileva [2], M. Sokolowski [6], J. Kennedy [7]
[1] *Karolinska Institute, Department of Women's and Children's Health, Stockholm, Sweden*
[2] *University of Toronto, Department of Psychology, Toronto, Canada*
[3] *McMaster University, Departments of Psychiatry & Behavioural Neurosciences and Obstetrics & Gynecology, Hamilton-ON-CA, Canada*
[4] *McGill University, Departments of Psychiatry and Neurology and Neurosurgery, Montreal, Canada*
[5] *Ryerson University, Department of Psychology, Toronto, Canada*
[6] *University of Toronto, Department of biological Genetics, Toronto, Canada*
[7] *Centre for Addiction and Mental Health, Psychiatric Neurogenetics Section, Toronto, Canada*
* *Corresponding author.*

Backround   There is considerable variation in the prevalence of breastfeeding, which allows for investigation of factors that influence the initiation and duration of breastfeeding and its association with well being of the mother infant dyad.

Aims   To better understand factors that influence (1) maternal breastfeeding status and (2) the "effects" of breastfeeding on mothers and infants.

Methods   Participants ($n = 170$) derive from a longitudinal Canadian study "Maternal Adversity, Vulnerability and Neurodevelopment (MAVAN)", a project designed to understand the pre- and postnatal influences on maternal health and child social-emotional development. Mothers provided data on breastfeeding status, early life adversity, oxytocin gene and oxytocin gene receptor polymorphisms, depression/anxiety, infant temperament and maternal sensitivity.

Results   Early life adversity associated with a shorter breastfeeding duration and higher maternal depression levels. The relation between mothers' early adversity and the duration of breastfeeding was mediated by mothers' depression level, but only in women carrying one variant of the oxytocin rs2740210 gene marker (CC genotype). Mothers who breastfeed at 3 months acted more sensitively towards their infants when they were 6 months old and they in turn had infants who at 18 months showed reduced negative affectivity.

Conclusion   Women who have been exposed to early adversity are "living with the past" and they are, to certain extent, protected or more vulnerable to depression, depending on their genotype. Breastfeeding associated with higher maternal sensitivity, which associated with decreased negative emotionality in the infant at 18 months. Our results help to clarify associations between early life experiences, breastfeeding, and the mother-infant relationship.

Disclosure of interest   The authors have not supplied their declaration of competing interest.

S075

Perinatal stress, anxiety, and depression: Effects of a MBCP intervention on mother-infant interaction