

Does prenatal exposure to SSRI antidepressants 'protect' against the effects of maternal stress?

Tim Oberlander, MD, FRCP Professor, Department of Pediatrics, University of British Columbia, Canada Jodi Pawluski, Ph.D., University of Liège GIGA -Neurosciences Liège, Belgium Veronika Kiryanova, Ph.D., Candidate, Neural Development and Plasticity Lab (Richard Dyck), University of Calgary, Canada

Selective serotonin reuptake inhibitor (SSRI) antidepressants are the most common antidepressant treatment used during pregnancy and the postpartum period. Up to 10% of pregnant women are prescribed SSRIs. SSRIs inhibit the reuptake of a key neurodevelopmental signal, serotonin (5HT), via 5HT transporter blockade at presynaptic neurons, thereby increasing synaptic 5HT concentrations. Serotonin plays an integral part in neurodevelopment, and questions have been raised about the placental transfer of SSRIs and the effects of increasing presynaptic 5HT levels during critical periods of fetal brain development.

To date, much attention has focused on increased risks for poor or delayed development associated with prenatal exposure to SSRIs, however, recent data are now showing that under specific developmental circumstances, SSRIs may protect against the effects of early exposure to maternal stress. Preclinical data is beginning to show no effects or potentially even protective effects associated with developmental exposure to SSRI medication (akin to the human 3rd trimester) on specific neurobehavioral outcomes at critical stages of development (i.e. puberty).

Emerging clinical data is also now indicating that among some infants and children, prenatal SSRI exposure may protect against the effects of maternal mood disturbances in social settings and/or in response to a stressful event.

This symposium will review recent clinical and preclinical research that is beginning to reveal a potentially protective effect of perinatal SSRI exposure on neurobehavioural outcomes and will serve to stimulate a broader discussion about the risks and benefits associated with the use of these antidepressants during the perinatal period.



Development of Limbic-Based Learning in Humans (Sackler Symposium)

Chairs: Nim Tottenham, Columbia University, USA; Adriana Galvan, UCLA, USA Rasmus Birn, Ph.D., University of Wisconsin at Madison, USA Adriana Galvan, Ph.D., University of California, Los Angeles, USA Tanja Jovanovic, Ph.D., Emory University, Georgia, USA Leah H. Somerville, Ph.D., Harvard University, Cambridge, Massachusetts, USA Mattijs Vink, Ph.D., Utrecht University, The Netherlands

> Although the basic neuroanatomical architecture is established during early postnatal life, large developmental changes occur during childhood and adolescence in limbic---cortical connections and function. The protracted period of development between birth and adulthood in humans is characterized by significant changes in affective learning, which is supported by the maturation of these limbic---cortical circuits. The goal of this symposium is to present the current state of the science on human limbic---cortical development as measured by functional neuroimaging, while considering how these findings translate across species. Invited speakers include Adriana Galvan (University of California, Los Angeles), Rasmus Birn (University of Wisconsin---Madison), Tanja Jovanovic (Emory University), Leah Somerville (Harvard University), and Mattijs Vink (Utrercht University), with Nim Totteham (Columbia University) as moderator. These speakers conduct programs of research that examine basic amygdala and striatal development in humans as they relate to learning across development. A consistent theme across presentations involves both the search for sensitive periods, when the environment can greatly influence developmental trajectories, as well as the search for age---specific function, when the circuitry operates to meet the unique developmental needs of that organism. The presentations will identify principles regarding human limbic---cortical circuitry development that allow for translation across species.



Diverse Perspectives on Social Development: Genes, Experience, and Neural Mirroring Systems

Chair: Kimberly Cuevas, University of Connecticut, USA; Discussant: Nathan A. Fox, University of Maryland, USA Nathan A. Fox, Distinguished Prof., University of Maryland, College Park, USA

Raphael Bernier, Assc. Prof., University of Washington; Clinical Director, Seattle Children's Autism Center, USA Pier F. Ferrari, Asst. Prof. in Biology, University of Parma, Italy; Adjunct Prof. at the University of Maryland, College Park, USA Jules Panksepp, Postdoctoral Research Assc., Oregon Health and Science University, Dept. of Behavioral Neuroscience, USA Julia M. Stephen, PhD., The Mind Research Network, Albuquerque, New Mexico, USA

Social learning and vicarious experiences are theorized to serve socio-emotional, cognitive, and survival functions. The aim of this symposium is to provide in-depth, cross-species analyses of the neural, genetic, and experience-based factors that contribute to optimal outcomes in the developing social organism. To this end, we incorporate social development in four distinct populations: preterm human infants, rhesus macaque monkeys, adolescent mice, and individuals with Autism Spectrum Disorders (ASD). Neuroscience evidence indicates that rhesus macaques and humans have a neural mirroring system (NMS) that responds similarly when executing an action as compared to observing another perform the same action. Ferrari and Fox provide evidence of NMS activity in newborn macaques, including the negative impact of adverse social experience on the NMS developmental trajectory. Likewise, Stephen has found that premature birth is associated with abnormal NMS activity and cognitive deficits at 3 and 6 months of age as compared to age-matched controls. Bernier's research highlights the link between NMS activity and imitation in children and adults regardless of ASD status, with potential differences in NMS activity between genetically defined ASD subgroups. To provide a broader perspective of the developing social organism, we also consider the role of vicarious experiences in non-primate species. Using adolescent mice, Panksepp has found evidence of vicarious experience as a function of genetic background and social deprivation, while also identifying the underlying brain substrates linked with particular phenotypes. This symposium integrates the multiple levels of organization that contribute to social development—an essential step in the field.



Neuronal, Hormonal, and Epigenetic Mechanisms of Maternal Behavior

Catherine J. Peña, PhD, Icahn School of Medicine at Mount Sinai, USA *Oliver J. Bosch*, PhD, University of Regensburg, Germany *Christina M. Ragan*, PhD, Michigan State University, USA *Danielle S. Stolzenberg*, PhD, University of California, Davis, USA

Early mother-neonate interactions are crucial for the proper neurobiological and social development of mammalian offspring. It is well-known that variability in mother-neonate interactions exists and can have consequences for the offspring later in life. Several neuronal and hormonal systems are involved in regulating maternal behavior, however many of the mechanisms driving this behavior, and the variability of maternal behavior across individuals, are unknown.

To explore some of the molecular contributors to maternal behavior we propose a symposium entitled, "Neuronal, Hormonal, and Epigenetic Mechanisms of Maternal Behavior." Our diverse symposium speakers will discuss various molecular mechanisms contributing to initiation, maintenance, and dysregulation of maternal behavior including neuronal, hormonal, and epigenetic factors. Our first speaker, Dr. Catherine Peña, will explain how variability in maternal care received is associated with estrogen receptor-alpha levels and can affect adult female rat maternal behavior. Our second speaker, Dr. Oliver Bosch, will discuss how vasopressin and corticotropin-releasing factor mediate maternal care and maternal aggression. Our third speaker, Dr. Christina Ragan, will present how variability in tryptophan hydroxylase-2 (TPH2) protein expression (enzyme involved in serotonin synthesis) in brain regions associated with maternal behavior is related to females' experiences with pups and the role that delta FosB may have on TPH2 plasticity. Our last speaker, Dr. Danielle Stolzenberg, will highlight how "natural" rearing conditions influence gene expression related to maternal behavior in dams compared to standard laboratory conditions. Together, these speakers will elucidate environmental, neuronal, and hormonal factors to better understand the regulation of maternal behavior.