of the stratified, trans-diagnostic, biological effects of childhood maltreatment may inform innovative treatment strategies.

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Telomere biology as a mechanism in developmental programming of health and disease risk

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Background: The long-term consequences of exposure to excess stress on the initiation and progression of many age-related diseases are well established. The effects of stress are particularly salient if exposure occurs during sensitive developmental windows such as intrauterine life and the early postnatal period. The elucidation of mechanisms underlying such effects is an area of intense interest and investigation. We propose that the integrity of the telomere system represents a candidate system of particular interest in this context, potentially underlying the observed effects of a disparate set of suboptimal early life exposures on various health and disease risk phenotypes of interest.

Methods: Data will be presented from several different longitudinal birth cohorts in which intrauterine conditions (including obstetric risk conditions, maternal stress- and nutrition-related processes) were assessed, and telomere length (TL) was subsequently measured in newborns and infants. In one of the cohorts, data from child follow-up assessments regarding temperament, developmental milestones and behavior problems are available.

Results: Obstetric risk conditions, maternal pre-pregnancy obesity, suboptimal maternal nutrition and maternal stress during pregnancy are each independently associated with offspring TL. Furthermore, newborn TL is associated with child behavioral problems related to attention deficit hyperactivity disorder (ADHD) at 3.5 years age.

Conclusions: Taken together, our findings provide evidence in humans that suboptimal conditions during pregnancy may exert a programming effect on the newborn and infant telomere biology system, and that newborn telomere length may be a predictor of later child behavioral problems. Telomere biology represents a potential molecular mechanism whereby different exposures in this critical developmental period before birth could impact subsequent health and disease susceptibility-related outcomes over the life span.

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Symposium 3: How Important is Sex/Gender in Personalized Medicine for Mental Health?

Time: Thursday, 08/Sep/2016: 3:00pm – 4:30pm
Session Chair: Mallory Elva Bowers
Session Chair: Sonia Lupien

A neural basis for sex-dependent fear expression

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An individual faced with a threatening stimulus may respond in many different ways. The selection of either an active or passive response can predict long-term outcomes in clinical populations, but what leads to the selection of one over the other is unknown. Using a classic rodent model of Pavlovian cued fear conditioning, we found that female rats were four times as likely as males to exhibit an active, escape-like "darting" response to the conditioned stimulus, even though escape was not possible. We have now begun to investigate the neural substrates of darting by examining c-fos activity in the medial prefrontal cortex (mPFC) and periaqueductal gray (PAG) after fear conditioning in darting and freezing subpopulations. Darters exhibited greater activity in the dorsolateral PAG, which is consistent with active response strategies. Freezers exhibited greater rostral mPFC activity compared to the ventral mPFC, and the rostral:ventral ratio was tightly correlated to freezing in both Freezers and Darters. These data suggest that darting may be mediated by a shift in the balance of mPFC activity, resulting in enhanced dlPAG activation.

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Association between estradiol and posttraumatic stress disorder in men and women military veterans

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Posttraumatic stress disorder (PTSD) manifests after a traumatic, typically life-threatening event and is characterized by four core clusters of symptoms – hyperarousal, intrusions ("flashbacks", e.g. nightmares), avoidance of trauma cues, and negative cognitions and mood. PTSD is twice as prevalent among women compared to men, even when normalizing for amount and type of trauma. Discordant prevalence of PTSD across genders could stem from biological factor(s) that are differentially expressed in women compared to men. Accordingly, the estrogen system is an appealing target for investigation. Using immunoassay, we observed a main effect of PTSD diagnosis on plasma estradiol levels in men and women military veterans with trauma in a combat zone. Specifically, PTSD+ veterans had lower levels of estradiol compared to PTSD-, trauma-control veterans. In men, an association between estradiol and PTSD diagnosis could be mediated by hyperarousal symptoms, as we found a significant negative correlation between