Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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the effects of stress. However, how correlated astrocyte and oligodendrocyte changes account for activity and connectivity alterations in depression and stress remains largely unknown. Our research aims to understand those changes in human subjects, and in animal and cell culture models relevant to depression pathophysiology.

**Methods:** In postmortem brain from human subjects with depression and control subjects, and rodent models of chronic stress (CUS), we used immunohistochemistry, morphometry, western blots and mRNA determinations of glutamate transporters, connexins and myelin markers. In mixed cultures of rat astrocytes, oligodendrocytes and neurons we observed effects of high corticosteroids on expression of connexins, astrocytes, oligodendrocytes and neurons we reported. Western blots and mRNA determination of glutamate transporters demonstrated increased expression of glutamate transporters and connexins in high corticosterone (CORT) conditions (ANOVA, p < 0.001, Dunnett’s test p < 0.01 CORT to control), immuno-reactivity of myelin proteins and extent of myelination, effects blocked by GC receptor antagonist mifepristone (univariate tests were p < 0.01 for CORT compared to control or to mifepristone), suggesting that the effects of stress depended on reduced gap junction communication and disruption of myelin.

**Conclusions:** In summary, correlated disturbance of astrocytes and oligodendrocytes may be a mechanism accounting for anomalous activity and connectivity of the prefrontal cortex in depression and stress-related psychiatric disorders.

**Funding Source:** Funded by R56MH113828 and R21MH118675 from NIH, and University of Mississippi Medical Center IRSP grants

**Keywords:** Astrocytes, Gap Junctions, Glucocorticoid Receptor, Oligodendrocytes, Chronic Stress

**SYMPOSIUM**

**The COVID-19 Generation**

Co-Chairs: Dani Dumitriu, Catherine Monk

**Chasing the Footprints of COVID-19-RELATED STRESS: Behavioral and Epigenetics Effects in Pregnant Women and Their Infants**

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**Background:** During 2020, the COVID-19 pandemic dramatically hit Italy and rapidly emerged as a collective trauma. Pregnancy is a sensitive period during which prenatal stress may result in epigenetic signatures (e.g., increased DNA methylation) and altered infants’ developmental programming. The serotonin transporter gene (SLC6A4) is a well-known locus of epigenetic regulation by adverse environmental exposures.

**Methods:** In April 2020, the MOM-COPE project was launched. One-hundred-eight mother-infant dyads were enrolled from ten neonatal units in Northern Italy. Retrospective maternal self-report measures of COVID-19-related prenatal stress were obtained at birth. SLC6A4 methylation was estimated in 13 Cpg sites using NGS in buccal cells of mothers and infants obtained at from 6 to 12 hours after delivery. Infants’ temperament was assessed at 3-month-age through the IBQ-R questionnaire.

**Results:** No effects emerged for maternal SLC6A4 methylation. COVID-19-related prenatal stress significantly and positively associated with infants’ SLC6A4 methylation in 7 out of 13 Cpg sites (rs > .24, all ps < .05). These sites loaded on a single principal component (PC1) accounting for 35% of total variance. PC1 methylation was significantly and positively associated with COVID-19-related prenatal stress (RR = 0.07, F = 7.71, p = 0.007, B = 0.16) as well as with infants’ temperament at 3 months (RR = 0.05, F = 5.05, p = 0.027, B = – 0.45).

**Conclusions:** Prenatal pandemic-related stress was significantly associated with less-than-optimal temperament in 3-month-old infants, partly due to stress-induced epigenetic regulation of the SLC6A4 gene. Appropriate policy and clinical actions are needed to promote timely preventive strategies.

**Funding Source:** Italian Ministry of Health; Fondazione Roche per la Ricerca Indipendente

**Keywords:** COVID-19, Prenatal Maternal Stress, Infant Temperament, DNA methylation, Serotonin Transporter Gene

**The Impact of Covid-Related Stress on Maternal Sleep During Pregnancy**

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**Background:** Poor sleep during pregnancy is very common and is associated with increased risk of adverse maternal and infant outcomes. Maternal psychosocial stress has been found to negatively impact sleep. The recent outbreak of COVID-19 has exposed many individuals to an unprecedented level of stress, that will continue for an unknown period of time. Studies are showing that all these factors may not only increase levels of stress, but also influence sleep health.

**Methods:** From March 2020–May 2021, participants were recruited as part of the COVID-19 Mother Baby Outcomes (COMBO) study at Columbia University. Survey data on maternal depression (PHQ-9), perceived stress (PSS),
COVID-related stress, and sleep health (Pittsburgh Sleep Quality Index, PSQI) were collected. For this analysis, we excluded mothers identified as depressed based on PHQ9. Regressions analyses were implemented to estimate the associations between PSS and COVID-related stress and multiple domains of sleep, accounting for covariates (maternal age, education, gestational age cvid infection in pregnancy, time of the pandemic).

**Results:** Our sample consisted of N=155 women; Gestational age at assessment: 30.6±5.8 weeks; Age: 32.2±5.0 years; non-Hispanic White=66, non-Hispanic Black=12, Hispanic=56, Asian=16, Other=5; 69% 4-year college/graduate degree. Mean PSS was 18.3±5.8. COVID-related stress was 3.9±0.4. COVID-related stress negatively affected subjective sleep quality ($\beta$=-0.3±0.1, $p<0.01$), latency ($\beta$=-0.4±0.1, $p<0.001$) and sleep disturbances ($\beta$=-0.5±0.2, $p<0.003$). Increased PSS negatively affected sleep duration ($\beta$=-0.09±0.2, $p<0.001$), efficiency ($\beta$=-0.08±0.02, $p<0.001$), and daytime dysfunction ($\beta$=-0.08±0.03, $p<0.01$).

**Conclusions:** Our results suggest that stress related to the current COVID-19 pandemic is uniquely affecting maternal sleep health during pregnancy.

**Funding Source:** R01MH126531; Eunice Kennedy Shriver National Institute of Child Health and Human Development under grant number P2CHD058486, awarded to the Columbia Population Research Center

**Keywords:** Sleep, Perceived Stress, COVID-19, Pregnancy

Birth During the COVID-19 Pandemic, but Not Maternal SARS-CoV-2 Infection in Pregnancy, is Associated With Lower Neurodevelopmental Scores at 6-Months

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**Background:** Associations between in utero exposure to maternal SARS-CoV-2 infection and neurodevelopment are widely speculated, but currently unknown. Here, we sought to determine the associations between maternal SARS-CoV-2 infection during pregnancy, being born during the COVID-19 pandemic regardless of maternal SARS-CoV-2 status, and neurodevelopment at 6-months.

**Methods:** Infants exposed to maternal SARS-CoV-2 infection during pregnancy and unexposed controls were enrolled into the COVID-19 Mother Baby Outcomes (COMBO) initiative at Columbia University Irving Medical Center (CUIMC) in New York City. Of 1706 women approached, 596 enrolled and 70.6% of 385 women invited to a 6-month assessment completed the Ages and Stages Questionnaire, 3rd Edition (ASQ-3) at 6-months of age. Data were available for 255 COMBO infants (114 in utero exposed, 141 unexposed). Data on the ASQ-3 was also available from a historical cohort of 62 infants born at CUIMC prior to the pandemic.

**Results:** In utero exposure to maternal SARS-CoV-2 infection was not associated with differences on any ASQ-3 subdomain regardless of infection timing or severity. However, infants born during the pandemic had significantly lower scores on gross motor (mean difference -5.63, 95%CI[-8.75; -2.51], F1, 267=12.63, $p<0.005$), fine motor (mean difference -6.61, 95%CI[-10.00; -3.21], F1, 267=14.71, $p<0.005$), and personal-social (mean difference -3.71, 95%CI[-6.61; -0.82], F1, 267=6.37, $p<0.05$) subdomains when compared to the historical cohort.

**Conclusions:** Birth during the pandemic, but not maternal SARS-CoV-2 infection, was associated with differences in neurodevelopment at 6-months. These early findings suggest significantly higher public health impact for the generation born during the COVID-19 pandemic than previously anticipated.

**Funding Source:** R01MH126531

**Keywords:** COVID-19 Pandemic, Neurodevelopment, ASQ-3

Impact of the COVID-19 Pandemic Environment on Early Child Brain and Cognitive Development

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**Background:** Since the first reports of the novel coronavirus in the US in early 2020, public health organizations have advocated preventative policies including stay-at-home orders that closed businesses, daycares, schools, playgrounds, and limited child learning activities. The impact of these policies on child neurodevelopment is unknown but may have significant long-term consequences.

**Methods:** Leveraging a large and ongoing longitudinal study of child neurodevelopment, we examined general childhood cognitive scores (assessed using the Mullen Scales of Early Learning) in 672 children between 0 and 3 years of age born between 2020 and 2021 (n=118) vs. the preceding decade from 2011 to 2019 (n=554). Brain neuroimaging (MRI) was also performed on each child. Using longitudinal mixed-effects models, we compared longitudinal trends of voxel-wise brain cognitive domain measures before and during the pandemic.

**Results:** We find that children born during the pandemic (Since July 2020) have significantly reduced verbal, motor, and overall cognitive performance compared to children born pre-pandemic; and that skills have continued to decline as the pandemic has progressed. Moreover, we find that children from lower socioeconomic families have been most affected. These neurocognitive findings are supported by neuroimaging data, which also shows reduced brain white matter development in children born since July 2020 compared to their counterparts from 2011 to 2019.

**Conclusions:** Results highlight that even in the absence of direct SARS-CoV-2 infection and COVID-19 illness, the environmental changes associated COVID-19 pandemic is negatively affecting infant and child development.

**Funding Source:** U01 OD023313

**Keywords:** COVID-19 Pandemic, Child Cognition, Early Neurocognitive Development, Longitudinal Neuroimaging, Developmental Neuroimaging