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.

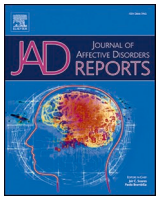
Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.

Journal of Affective Disorders Reports 6 (2021) 100213

Contents lists available at ScienceDirect

Journal of Affective Disorders Reports

journal homepage: www.sciencedirect.com/journal/journal-of-affective-disorders-reports



Correspondence

Anticipating the long-term neurodevelopmental impact of the COVID-19 pandemic on newborns and infants: A call for research and preventive policy

ARTICLE INFO

Keywords
COVID-19
Infant neurodevelopment
Maternal stress

ABSTRACT

It is estimated that 116 million children were born worldwide in the first nine months of the COVID-19 pandemic. Given the critical importance of early life for neurodevelopment, and evidence suggesting that prenatal maternal stress and early childhood adversity negatively impact neurodevelopment, it is alarming that many pregnant women and new mothers are experiencing high levels of pandemic-related stress. Research and proactive mental health policy is needed to minimize the impact of the COVID-19 pandemic on the future mental health of a global cohort of newborns and infants.

It is estimated that 116 million children were born worldwide during the first nine months of the COVID-19 pandemic (UNICEF, 2020). While important research has focused on the mental health of pregnant women coping with the pandemic (Berthelot et al., 2020; Thapa et al., 2020; Lopez-Morales et al, 2021), little attention has been given to the future long-term impacts that the pandemic will have on newborns and infants resulting from increased prenatal maternal stress and early childhood adversity.

Given previous research indicating the critical importance of fetal and infant neurodevelopment, it is alarming that many pregnant women and new mothers are experiencing high levels of stress as a result of the COVID-19 pandemic (Basu et al, 2021; Berthelot et al., 2020; Thapa et al., 2020). Like others, pregnant women and new mothers are experiencing increased stress due to social isolation, financial worry, grief for lost loved ones, and fear of illness or death from COVID-19 (Holmes et al., 2020). Additionally, they are confronted by difficulties accessing perinatal care, increased risk of pregnancy and birth complications, uncertainty regarding the need for – and safety of – vaccination during pregnancy, having to visit healthcare settings with perceived heightened risk of COVID-19 infection, and giving birth with shortages of medical personnel, supplies, and equipment (Ahlers-Schmidt et al., 2020; Basu et al, 2021; Hermann et al., 2020; Thapa et al., 2020). In some COVID-19 hotspots, containment policies have forced some women to give birth without a personal support person (Thapa et al., 2020). Some new mothers and primary caregivers to infant children have also been unable to share or outsource childcare responsibilities due to physical distancing and lockdown restrictions (Thapa et al., 2020). While many of these stressors are disproportionately affecting women in low-income settings, women in higher socioeconomic positions are also being impacted (Berthelot et al., 2020; Thapa et al., 2020; UNICEF, 2020). Altogether, these stressors are contributing to increased mental health problems among pregnant women and new mothers at the population level including depression, anxiety, post-traumatic stress symptoms, and suicidality, among others (Basu et al, 2021; Berthelot et al., 2020; Thapa et al., 2020). With subsequent waves of COVID-19 infection expected, many of these maternal stressors and corresponding psychiatric morbidities will likely be exacerbated.

Early life is a critically important and vulnerable period for neurodevelopment. The first 1000 days of life – i.e., from conception to approximately two years of age – is characterized by a unique period of rapid neuronal growth and refinement, which ultimately establishes the foundation for lifelong brain architecture (Cusick and Georgieff, 2016; Meredith, 2015). Infants and neonates exposed to environmental stressors during this timeframe are vulnerable to neurodevelopmental impairments that can remain across their lifespan. For example, prenatal maternal stress impacts fetal epigenetic and neurodevelopmental programming, which influences the expression of genes (e.g. *NR3C1*) that can predispose offspring to psychiatric disorders later in life (Berthelot et al., 2020; Beydoun and Saftlas, 2008; Cao-Lei et al., 2016). Maternal and infant bonding during the first 1000 days is also important to the long-term social and emotional wellbeing of children (Branjerdporn et al., 2017; Le Bas et al., 2020). "Serve-and-return" interactions – whereby primary caregivers provide consistent and appropriate reactions to infant babbles, gestures, or crying – promote healthy attachment and social and emotional development (Harvard University Center on the Developing Child August 2020). When caregivers experience mental health problems, the quality and quantity of such interactions can be impaired, thereby increasing their children's susceptibility to behavioral and psychiatric disorders in adulthood. Moreover, emerging research suggests that unresolved parental trauma can be inherited to children who were not exposed to the traumatic event themselves, which could impact not only the generation of infants born during the pandemic, but future generations to come (Yehuda and Lehrner, 2018).

To minimize the impact of the COVID-19 pandemic on the neurodevelopment of a global cohort of newborns and infants, proactive mental health policies are needed. For example, telephone- and internet-based provision of empirically-supported clinical interventions such as cognitive behavioral therapy should be expanded to facilitate access for mothers and new parents in need. The migration of reproductive and pediatric health services online may also reduce maternal stress by reducing the number of clinic and hospital visits where perceived risk of COVID-19 infection is high. Public health authorities should also

https://doi.org/10.1016/j.jadr.2021.100213
Received 13 November 2020; Received in revised form 25 August 2021; Accepted 27 August 2021
Available online 1 September 2021
2666-9153/© 2021 The Author(s). Published by Elsevier B.V. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

conduct outreach for new parents to promote these services and provide essential information on COVID-19 risk and transmission for fetuses and infants. There is also evidence that self-guided non-clinical interventions can be helpful. Exercise, both during and after pregnancy (Davenport et al., 2018; Poyatos-León et al., 2017), and self-help materials, such as books, videos, computer software packages, and websites (Lin et al., 2018), have been demonstrated to prevent and manage maternal depressive symptoms. In addition to psychological resources, social support networks are effective at managing depression and anxiety, especially in high-trauma conflict settings (World Health Organization, 2016). Moreover, with many new parents losing their jobs, the pandemic also adds economic uncertainty. Governments' should provide sufficient childcare support and protect against price gouging for childcare essentials.

The COVID-19 pandemic also presents a unique opportunity to better understand psychiatric epigenetics. Previous epigenetic studies have largely examined stressful and traumatic events as natural experiments (e.g. genocide, famine, violent relationships, etc.); the COVID-19 pandemic is an unprecedented natural experiment in scope and size, offering researchers a chance to examine the epigenetic impact of pre- and post-natal maternal stress and intergenerational transmission of maternal stress on infant neurodevelopment. Large-scale baseline data collection is needed now to conduct this longitudinal research (Cao-Lei et al., 2016). It is crucial that we use this moment as a time for research and learning while doing all we can to reduce the mental health effects of the COVID-19 pandemic on mothers and children.

Declaration of Competing Interest

The authors declare no conflicts of interest.

References

Ahlers-Schmidt, C.R., Hervey, A.M., Neil, T., Kuhlmann, S., Kuhlmann, Z., 2020. Concerns of women regarding pregnancy and childbirth during the COVID-19 pandemic. Patient Educ. Couns. 103, 2578–2582.

Basu, A., Kim, H.H., Basaldua, R., Choi, K.W., Charron, L., Kelsall, N., Hernandez-Diaz, S., Wyszynski, D.F., Koenen, K.C., 2021. A cross-national study of factors associated with women's perinatal mental health and wellbeing during the COVID-19 pandemic. PLoS ONE 16, e0249780.

Berthelot, N., Lemieux, R., Garon-Bissonnette, J., Drouin-Maziade, C., Martel, É., Maziade, M., 2020. Uptrend in distress and psychiatric symptomatology in pregnant women during the COVID-19 pandemic. Acta Obstet. Gynecol. Scand. 99 (7), 848–855.

Beydoun, H., Saftlas, A.F., 2008. Physical and mental health outcomes of prenatal maternal stress in human and animal studies: a review of recent evidence. Paediatr. Perinat. Epidemiol. 22, 438–466.

Branjerdporn, G., Meredith, P., Strong, J., Garcia, J., 2017. Associations between maternal-foetal attachment and infant developmental outcomes: a systematic review. Matern. Child Health J. 21, 540–553.

Cao-Lei, L., Laplante, D.P., King, S., 2016. Prenatal maternal stress and epigenetics: review of the human research. Curr. Mol. Biol. Rep. 2, 16–25.

Cusick, S.E., Georgieff, M.K., 2016. The role of nutrition in brain development: the golden opportunity of the "first 1000 days". J. Pediatr. 175, 16–21.

Davenport, M.H., McCurdy, A.P., Mottola, M.F., Skow, R.J., Meah, V.L., Poitras, V.J., Jaramillo Garcia, A., Gray, C.E., Barrowman, N., Riske, L., Sobierajski, F., James, M., Nagpal, T., Marchand, A.A., Nuspl, M., Slater, L.G., Barakat, R., Adamo, K.B., Davies, G.A., Ruchat, S.M., 2018. Impact of prenatal exercise on both prenatal and postnatal anxiety and depressive symptoms: a systematic review and meta-analysis. Br. J. Sports Med. 52, 1376–1385.

Harvard University Center on the Developing Child, Serve and return. http://developingchild.harvard.edu/science/key-concepts/serve-and-return (accessed August 2020).

Hermann, A., Fitelson, E.M., Bergink, V., 2020. Meeting maternal mental health needs during the COVID-19 pandemic. JAMA Psychiatry 78 (2), 123–124.

Holmes, E.A., O'Connor, R.C., Perry, V.H., Tracey, I., Wessely, S., Arseneault, L., Ballard, C., Christensen, H., Cohen Silver, R., Everall, I., Ford, T., John, A., Kabir, T., King, K., Madan, I., Michie, S., Przybylski, A.K., Shafran, R., Sweeney, A., Worthman, C.M., Yardley, L., Cowan, K., Cope, C., Hotopf, M., Bullmore, E., 2020. Multidisciplinary research priorities for the COVID-19 pandemic: a call for action for mental health science. Lancet Psychiatry 7, 547–560.

Le Bas, G.A., Youssef, G.J., Macdonald, J.A., Rossen, L., Teague, S.J., Kothe, E.J., McIntosh, J.E., Olsson, C.A., Hutchinson, D.M., 2020. The role of antenatal and postnatal maternal bonding in infant development: a systematic review and meta-analysis. Soc. Dev. 29, 3–20.

Lin, P.Z., Xue, J.M., Yang, B., Li, M., Cao, F.L., 2018. Effectiveness of self-help psychological interventions for treating and preventing postpartum depression: a meta-analysis. Arch. Women's Mental Health 21, 491–503.

López-Morales, H., del Valle, M.V., Canet-Juric, L., Andrés, M.L., Galli, J.I., Poó, F., Urquijo, S., 2021. Mental health of pregnant women during the COVID-19 pandemic: a longitudinal study. Psychiatry Res. 295, 113567.

Meredith, R.M., 2015. Sensitive and critical periods during neurotypical and aberrant neurodevelopment: a framework for neurodevelopmental disorders. Neurosci. Biobehav. Rev. 50, 180–188.

Poyatos-León, R., García-Hermoso, A., Sanabria-Martínez, G., Álvarez-Bueno, C., Cavero-Redondo, I., Martínez-Vizcaíno, V., 2017. Effects of exercise-based interventions on postpartum depression: a meta-analysis of randomized controlled trials. Birth 44, 200–208.

Thapa, S.B., Mainali, A., Schwank, S.E., Acharya, G., 2020. Maternal mental health in the time of the COVID-19 pandemic. Acta Obstet. Gynecol. Scand. 99 (7), 817–818.

UNICEF, 2020. Pregnant mothers and babies born during COVID-19 pandemic threatened by strained health systems and disruptions in services. https://www.unicef.org/press-releases/pregnant-mothers-and-babies-born-during-covid-19-pandemic-threatened-strained-health (accessed July 2020).

World Health Organization, 2016. WHO behavioral intervention shows promise for treating depression and anxiety in conflict-affected areas. https://www.who.int/mental_health/emergencies/behavioral-interventions-conflict-areas/en/ (accessed October 2020).

Yehuda, R., Lehrner, A., 2018. Intergenerational transmission of trauma effects: putative role of epigenetic mechanisms. World Psychiatry 17, 243–257.

André J. McDonald[a,b,1], Emma J. Mew[c,1,*], Nicola L. Hawley[c], Sarah R. Lowe[d]

[a] *Centre for Addiction and Mental Health, Institute for Mental Health Policy Research, Toronto, Ontario, Canada*

[b] *Epidemiology Division, Dalla Lana School of Public Health, University of Toronto, Toronto, Ontario, Canada*

[c] *Department of Chronic Disease Epidemiology, Yale School of Public Health, Yale University, New Haven, CT, United States*

[d] *Department of Social and Behavioral Sciences, Yale School of Public Health, Yale University, New Haven, CT, United States*

[*] Corresponding author.
E-mail address: emma.mew@yale.edu (E.J. Mew).

[1] These authors contributed equally to this work.