Bridget Callaghan, Assistant Professor of Psychology, UCLA Brain Behavior Research Foundation, November 2024 @BABLab_UCLA @Dr_BCallaghan

Intergenerational Impacts of Adversity on Mind + Body Health

Pathways through the brain-gut axis



Adversity Exposure & Mental Health





Account for 30% of adult mental illnesses

(Kessler et al., 2018)

MENTAL



PHYSICAL

Increase the odds of many physical health problems, including heart disease and respiratory diseases

(Hughes et al., 2017)



Adversity Exposure & Mental Health



GENERATIONAL IMPACTS

Risk for worsened physical and mental health following adversity is carried forward to the next generation.

(Yehuda et al., 2005; Roth et al., 2013)



Priorities for Understanding Mental Illness After Adversity







The Brain-Gut Microbiome Axis

Communication is bidirectional and occurs through multiple pathways including vagal and spinal afferents, and chemical signaling.

Brain-gut-microbiome axis implicated in:

- Depression (e.g., Kelly et al., 2016)
- Anxiety (e.g., Bercik et al., 2011)
- Cardiovascular disease (e.g., Rahman et al., 2022)
- Irritable Bowel Syndrome (e.g., Menees et al., 2018)

Brain-gut-microbiome axis affected by early caregiving adversity (Callaghan et al., 2019; Reid et al., 2022; Hantsoo et al., 2019).







Part I

How does early caregiving affect **brain** development, and how is that associated with youth **mental health**?









Part II

How does early caregiving affect the **microbiome and brain-gut axis** function in ways important for mental health?











Part III

How does early caregiving affect brain and behavior, and the BGM axis in the **next** generation?



Overview of Talk







Part IV

one transitions into motherhood, and risk for perinatal depression?



Overview of Talk



Part I: Caregiving Adversity on Brain Function



Generation 1





Caregiving adversity has an outsized effect on limbic system development (Vannucci et al., 2023)

Likely because limbic regions (supporting emotional processing, learning, and responding) undergo rapid structural growth during childhood, a period of maximal dependence on parents









Gee, et al., 2014, Psychological Science







Callaghan et al., 2019 Biological Psychiatry: CNNI



Individual differences in amygdala buffering are relevant for affective function and could be targeted through parenting.



Callaghan et al., 2019 Biological Psychiatry: CNNI



Parent-teen interactions still shape amygdala patterns in ways that are relevant for mental health



Callaghan, Dandash et al., 2017, JAACAP



Part II: Caregiving Adversity & Brain-Gut Axis







Caregiving adversity and the brain-gut-microbiome axis

Caregiving adversity is known to impact the microbiome (Callaghan et al., 2019; Reid et al., 2022; Hantsoo et al., 2019)

Studies involve small samples, or retrospective reports of caregiving adversity.

All focus on the gut microbiome, while other microbial communities (e.g., oral microbiome) are neglected.





Postnatal adversity affects the community composition of the microbiome

Postnatal adversity (maternal anxiety and depression) was associated with a sharper increase in alpha diversity from birth to 2 years of age (N = 100) 4 time points

Fran Querdasi @fquerdasi Genesis Flores @gendflores

UNPUBLISHED DATA

Querdasi, Flores et al., (in prep)



Prenatal and postnatal adversity affect the community composition of the microbiome

Caregiving adversity (maltreatment + foster care) was associated with altered alpha diversity from 2-17

> years (N = 107)

Naomi Gancz @NGancz



Gancz et al., in prep



Maltreatment is associated with altered age-related change in single microbe abundance



12 microbes showed age related change in relative abundance that was moderated by adversity exposure

Gancz et al., in prep







Clostridium innocuum - typically pathogenic

Halli - butyrate producer

Butyricimonas - butyrate producer

Gancz et al., in prep



Nutritional interventions might be especially salutary for adversity exposed youth

Fiber was associated with enrichment of Butyricimonas in the adversity group, which was itself negatively associated with internalizing symptoms

> **Fiber** was also negatively associated with internalizing symptoms in the adversity group

> > t al., in prep



CA may also have an impact on the development of microbial communities outside the gut





Childhood adversity affects oral microbiome in adults

(Charalambous, et al., 2021)

Diurnal cortisol is dysregulated across childhood and adolescence after CA

(Van Tieghem et al., 2021)



Immune cells are less sensitive to the regulatory effects of cortisol after CA

(Kuhlman et al., 2017)



The oral microbiome of caregiving adversity exposed youth appears to be less responsive to tonic cortisol levels

Hair cortisol was negatively related to alpha diversity in comparison youth, but was not in CA (maltreatment + foster care) youth (N = 152)





Naomi Gancz @NGancz

Gancz et al., 2024 Brain, Behavior, Immunity: Health



Caregiving adversity and the brain-gut-microbiome axis

CA may also have an impact on the development of microbial communities outside the gut

Several taxa were associated with CA and one of those was associated with internalizing symptoms (N = 152)



Comparison Caregiving Adversity

Gancz et al., 2024 Brain, Behavior, Immunity: Health



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Interim Summary of Part II



Generation 1

Generation 2

Directly experienced childhood caregiving adversity impacts:

- The <u>development</u> of children's gut microbiome community composition and the differential abundance of microbes in the gut.
- The way that the oral microbiome responds to cortisol, and the differential abundance of microbes in the mouth.

Some of the microbiome outcomes are associated with youth mental health



Caregiving adversity and the brain-gut-microbiome axis

Understanding how the gut microbiome is linked to internalizing symptoms requires an understanding of microbiome-brain communication



Microbiome @ 2 years



Inter- & Intra- Resting State Network Connectivity @ 6 years

Internalizing Symptoms @ 7.5 years



<u>Growing Up in Singapore Towards Healthy Outcomes</u>





Read more >





Caregiving adversity and the brain-gut-microbiome axis

Multivariate, data-driven, symptom informed, longitudinal approach





Fran Querdasi @frquerdasi Dr. Jess Uy @Jessica_Uy_PhD

Querdasi, Uy, Labus... Callaghan (in prep) using GUSTO study data





Generation 2

Final Summary of Part II

Directly experienced childhood caregiving adversity impacts:

- Gut and oral microbiome development
- Some of the microbiome outcomes are associated with youth mental health
- Working backwards from mental health we can identify relevant brain networks, and then microbes that are associated with those brain networks
- Those microbes are potential targets for therapy



Part III: Caregiving Adversity Impacts on the Next Generation



Generation 1





Generational impacts of adversity on brain and behavior

Maternal Prenatal Mental Health

Maternal Childhood Trauma



Dr. Jess Uy @Jessica_Uy_PhD

Uy et al., (2023) - Journal of Child Psychology & Psychiatry - GUSTO study data







Generational impacts of adversity on brain and behavior



Maternal Childhood Maltreatment

Maternal Prenatal Mental Health

Maternal Postnatal Mental Health



N = 89

Uy et al., (2023) - Journal of Child Psychology & Psychiatry - GUSTO study data



Generational impacts of adversity on brain and behavior



Maternal Childhood Maltreatment

Maternal Prenatal Mental Health

Maternal Postnatal Mental Health

Uy et al., (2023) - Journal of Child Psychology & Psychiatry - GUSTO study data

Child rs-fMRI @ 6 years



N = 89


Generational impacts of adversity on the microbiome



Maternal Childhood Maltreatment

Maternal Prenatal Mental Health

Maternal Postnatal Mental Health & Stressful Life Events from 0-2 years



Fran Querdasi @frquerdasi



N = 450



Generational impacts of adversity on microbiome





Querdasi et al., (2023) - Proceedings of the National Academy of Sciences



Sequencing Resolution Limits What is Known About the Microbiome







Generation 2

Summary of Part III

Maternal childhood adversity affected:

- Children's behavior and brain via impacts on maternal prenatal and postnatal mental health
- Children's microbiome via pathways that partially overlapped with those of prenatal and postnatal maternal mental health



Part IV: Caregiving Adversity Impacts on the Transition to Parenthood



Generation 1



Generation 2



- 12% of women will experience depression during their 2nd or 3rd trimester (Bennett et al., 2004)
- Women who have experienced childhood trauma are at greater risk (Tebeka et al., 2021)
- Peripartum depression could perpetuate cycles of adversity (Meaney, 2018; Sawyer et al., 2019)



Savoca et al., (2024) Neuroscience and Biobehavioral Reviews



Depression can be characterized as arising from disordered interoception

Depression involves dysregulation across numerous bodily systems, suggesting inefficient energy regulation (Barrett et al., 2014)

Energy regulation is supported by **interoception** (Quigley et al., 2021)

Interoception is impaired in depression (Eggart et al., 2019)



Savoca et al., (2024) Neuroscience and Biobehavioral Reviews



Interoception and metabolic demands in pregnancy







Savoca et al., (2024) Neuroscience and Biobehavioral Reviews



Interoception in pregnancy is moderated by maternal childhood trauma





Savoca et al., (2024) Archives of Women's Mental Health



Interoception in pregnancy is moderated by maternal childhood trauma



Savoca et al., (2024) Archives of Women's Mental Health





Generation 2

Summary of Part IV

Maternal childhood adversity affected:

 Mother's experience of interoception changes during pregnancy, in ways important for maternal mental health

Focusing on interoception during pregnancy may be an important way to address intergenerational patterns of trauma.



Priorities for Understanding Mental Illness After Adversity







Priorities for Understanding Mental Illness After Adversity







Acknowledgements



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