

Health Impacts of Microplastics



Lindsay S. Cahill

Assistant Professor, Department of Chemistry

Cross-appointment, Discipline of Radiology

Physical Chemistry



Physics



Medical Physics



Advanced
Solid-State NMR

Rechargeable
Lithium Ion
Batteries

Develop
 ^{25}Mg NMR

Bioactive Glasses

^1H Conductors

Advanced
Medical Imaging

Mouse Models

Neurodegenerative
Diseases

Brain
Development

Placental
Dysfunction

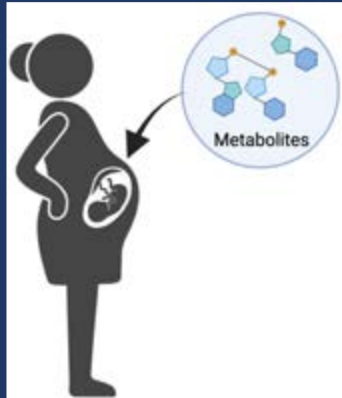




LINDSAY CAHILL

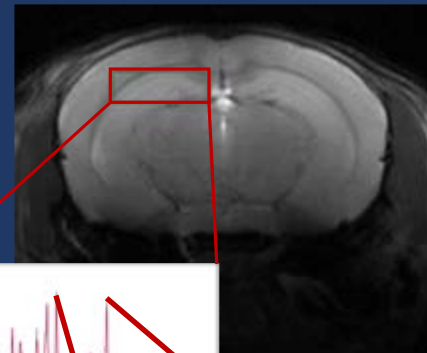
Magnetic resonance to study neurodevelopmental and pregnancy disorders

Email: lcahill@mun.ca Website: cahilllab.com



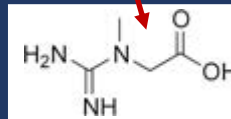
MAGNETIC RESONANCE IMAGING

- Study abnormal placental and brain development
- Improve understanding of pathophysiology
- Develop diagnostic procedures

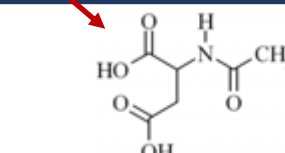


¹H MR SPECTROSCOPY

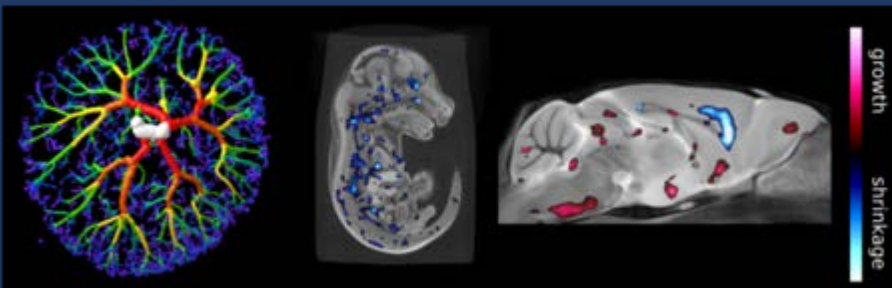
- Characterize brain and placental function
- Evaluate metabolic biomarkers of brain and placental injury



Creatine (metabolism)



N-acetyl aspartate (neuronal integrity)





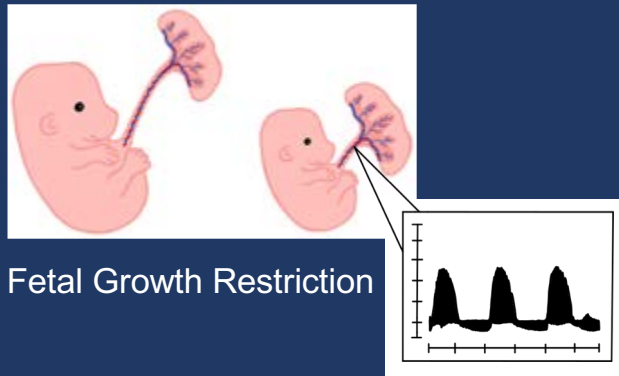
LINDSAY CAHILL

Environmental exposures and human health

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MICRO- AND NANOPLASTICS

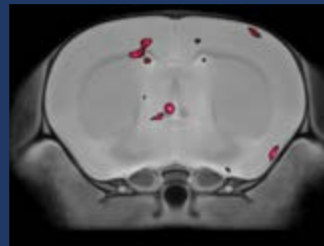
- Determine exposure levels in humans
- Establish causality between exposure and pregnancy outcomes using mice
- Are plastics a vector for harmful pollutants?



PERFLUOROALKYL SUBSTANCES

- Determine toxicity of novel, unregulated PFAS
- Understand why vulnerability to PFAS depends on fetal biological sex

Abnormal Placental Function



References:

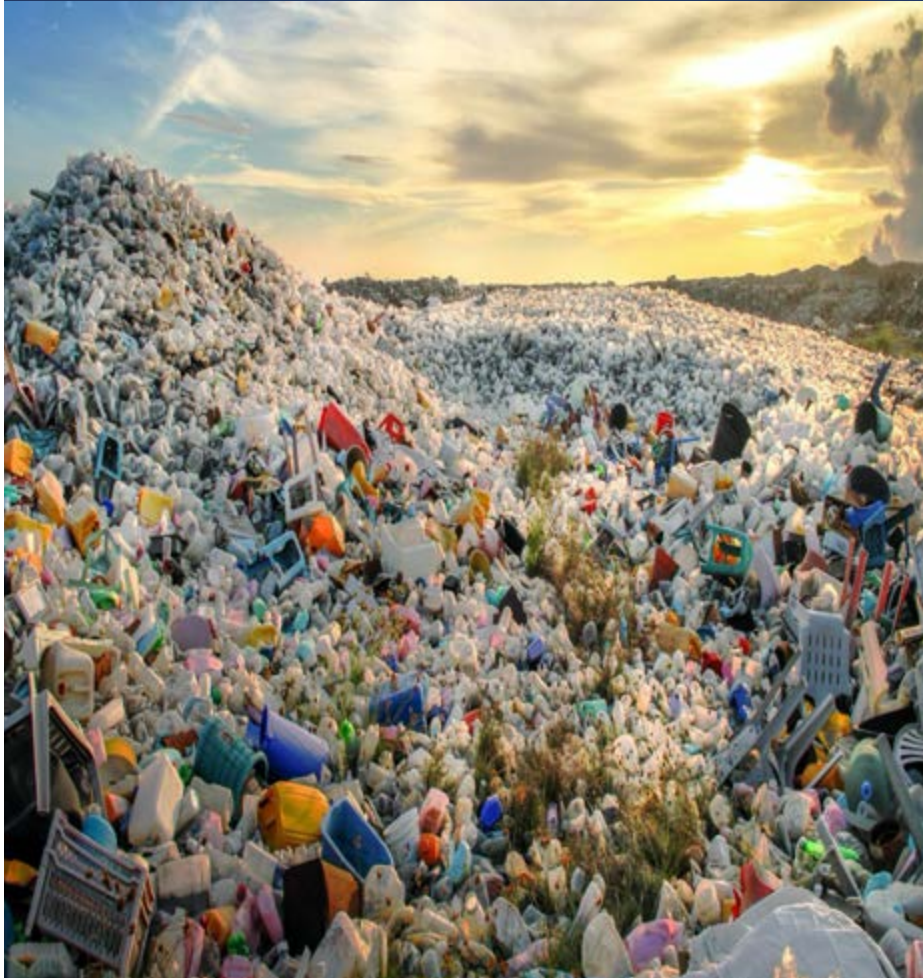


Plastics: The Bad



- Over 400 Megatons of plastics produced annually

Landrigan et al. *Ann Glob Health* 2023, 89:23



How much plastic is landfilled or left in the environment?

(a) < 10%

(b) 25%

(c) 50%

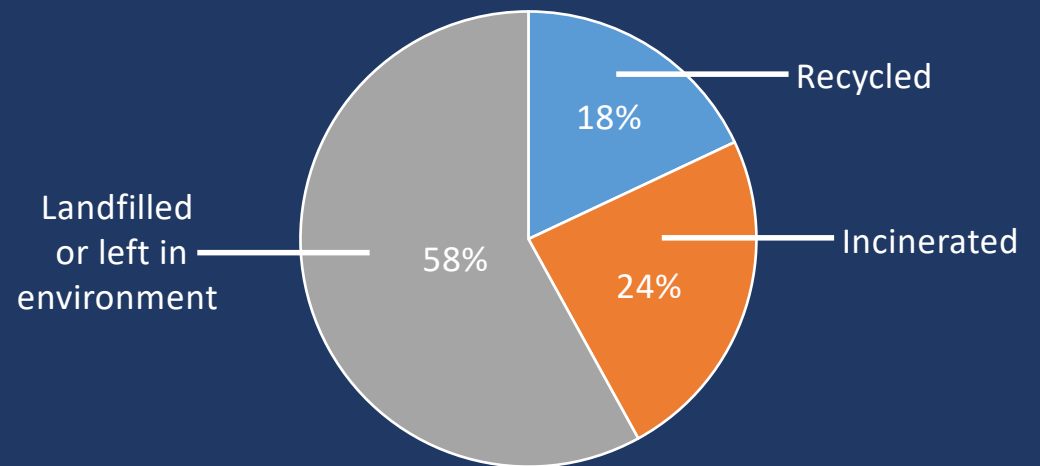
(d) > 50%

Plastics: The Bad



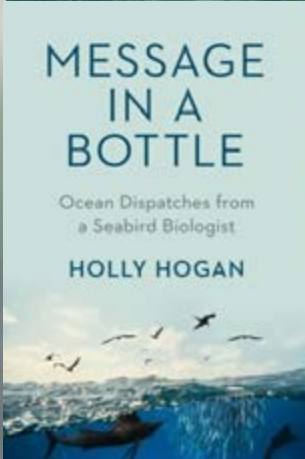
- Over 400 Megatons of plastics produced annually

Landrigan et al. *Ann Glob Health* 2023, 89:23

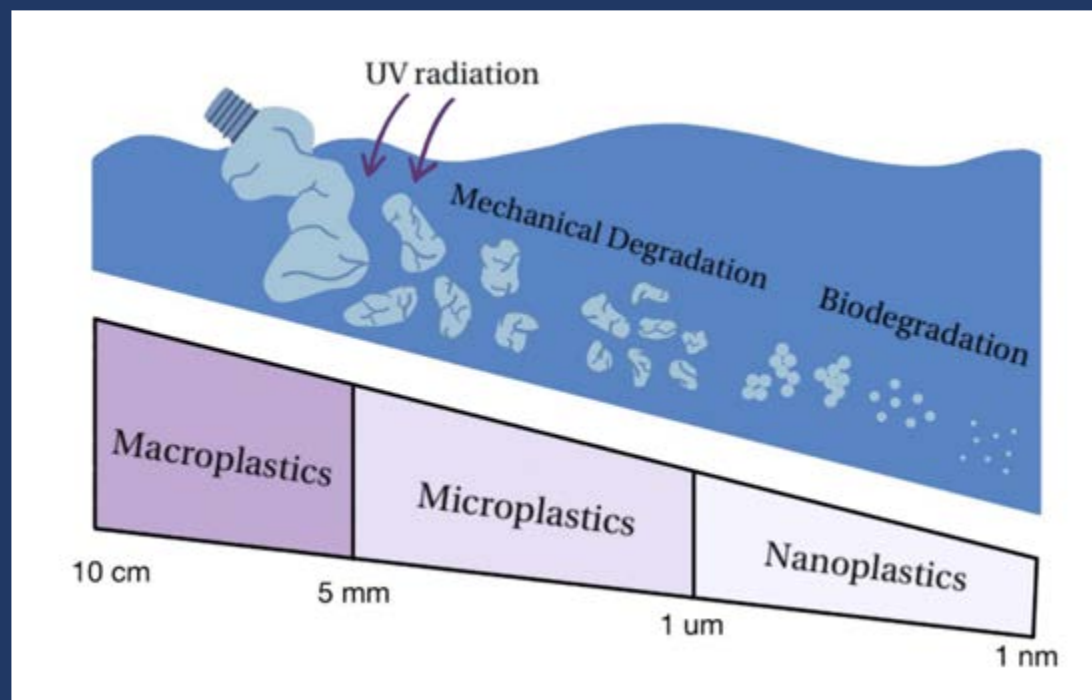


Chamas et al. *ACS Sustain Chem Eng* 2020, 8:3494

Plastics: The Ugly

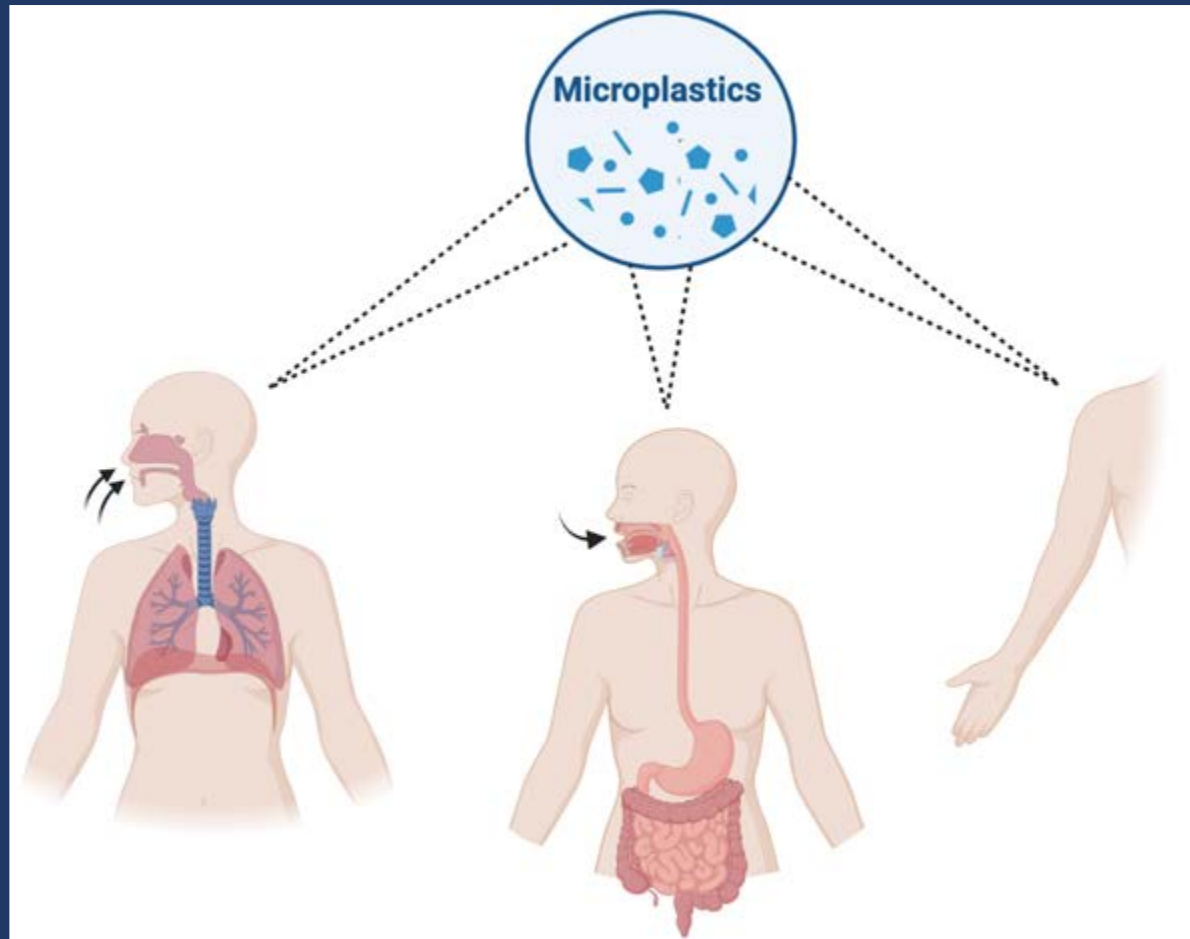


Micro- and Nanoplastics

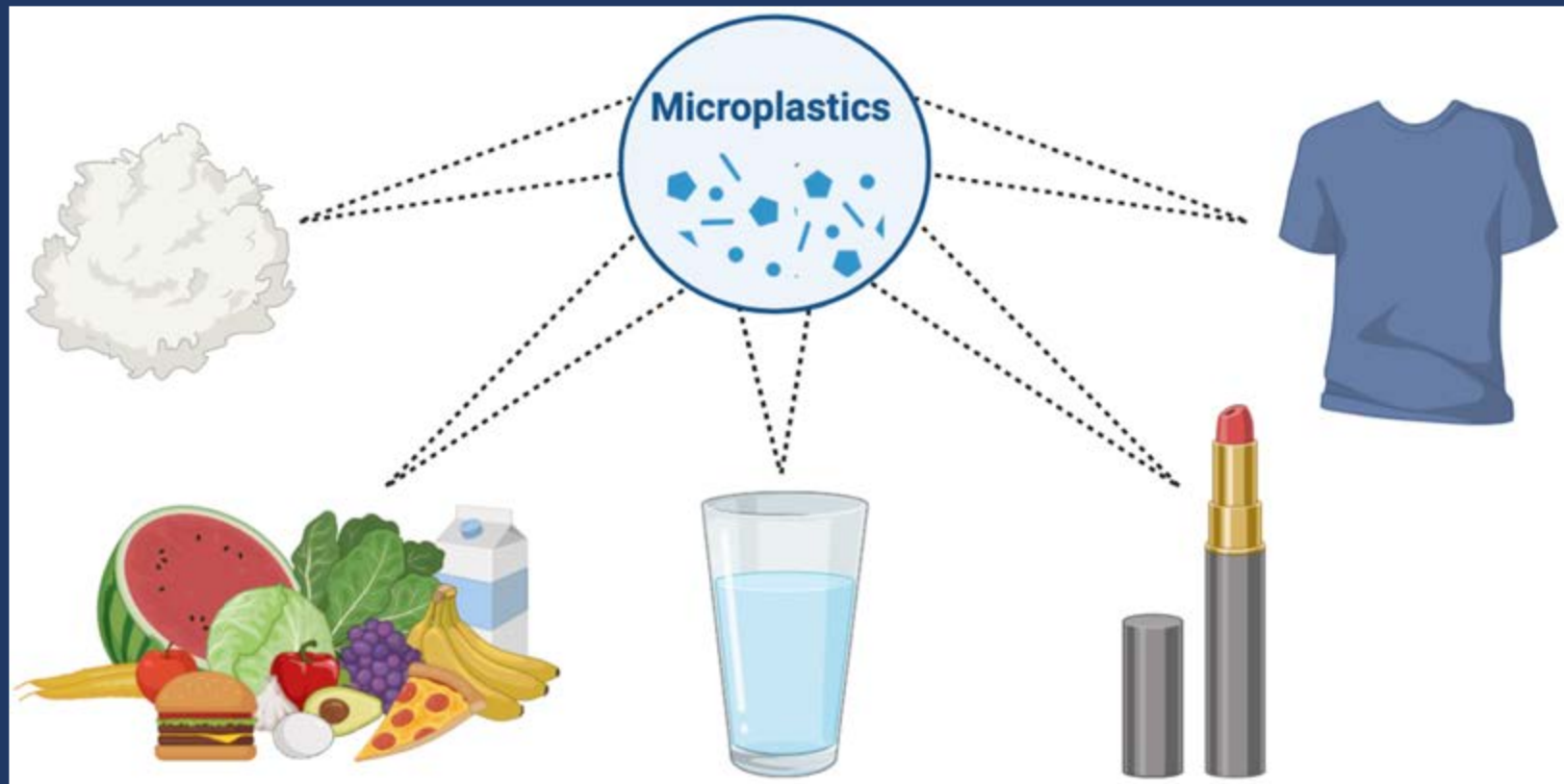


Gillibert et al. *Environ Sci Technol* 2019, 53:9003

Routes of Exposure



Sources of Exposure



Microplastics have been found in which of the following parts of the human body?

- (a) Carotid artery
- (b) Lung
- (c) Blood
- (d) Liver
- (e) Kidneys
- (f) Colon
- (g) Testes
- (h) All of the above

Micro- and Nanoplastics in Humans



Carotid artery: Marfella et al., 2024

Lung: Amato-Lourenço et al., 2021; Jenner et al., 2022

Blood: Leslie et al., 2022; Guan et al., 2023, Brits et al., 2024

Liver: Horvatits et al., 2022

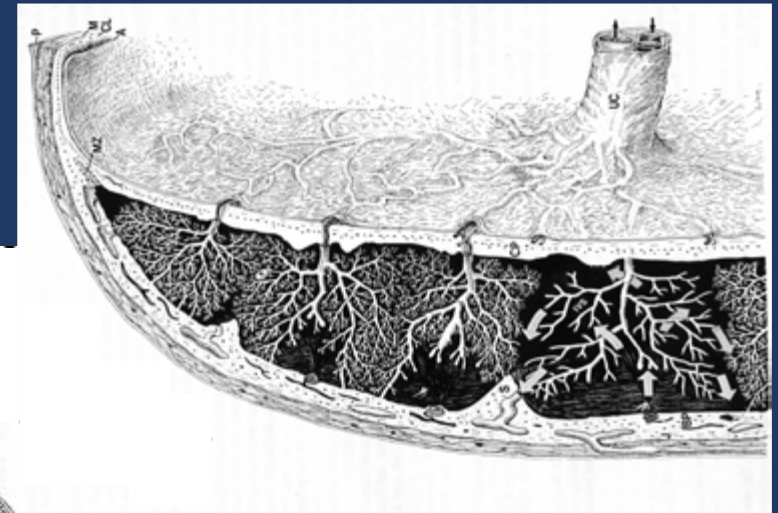
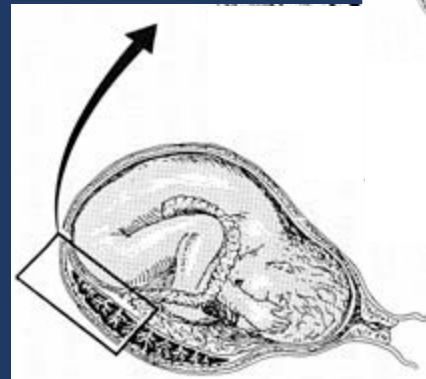
Kidneys: Massardo et al., 2024

Colon: Ibrahim et al., 2021

Testes: Zhao et al., 2023; Hu et al., 2024

The Placenta

- requirement for all mammalian pregnancies
- transient vascular organ with two distinct compartments (maternal and fetal)
- primary site of gas and nutrient exchange
- abnormal placental development can lead to:
 - maternal hypertension
 - preterm birth
 - fetal growth restriction
 - stillbirth



Plastics in the Placenta!

Environment International 146 (2021) 106274

Contents lists available at [ScienceDirect](https://www.sciencedirect.com)



ELSEVIER

Environment International

journal homepage: www.elsevier.com/locate/envint

Plasticenta: First evidence of microplastics in human placenta

Antonio Ragusa^a, Alessandro Svelato^{a,*}, Criselda Santacroce^b, Piera Catalano^b,
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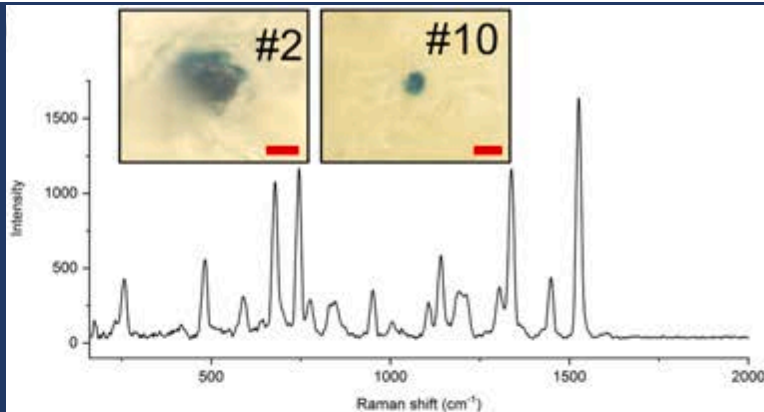
Plastics

Microplastics revealed in the placentas of unborn babies

Health impact is unknown but scientists say particles may cause long-term damage to foetuses

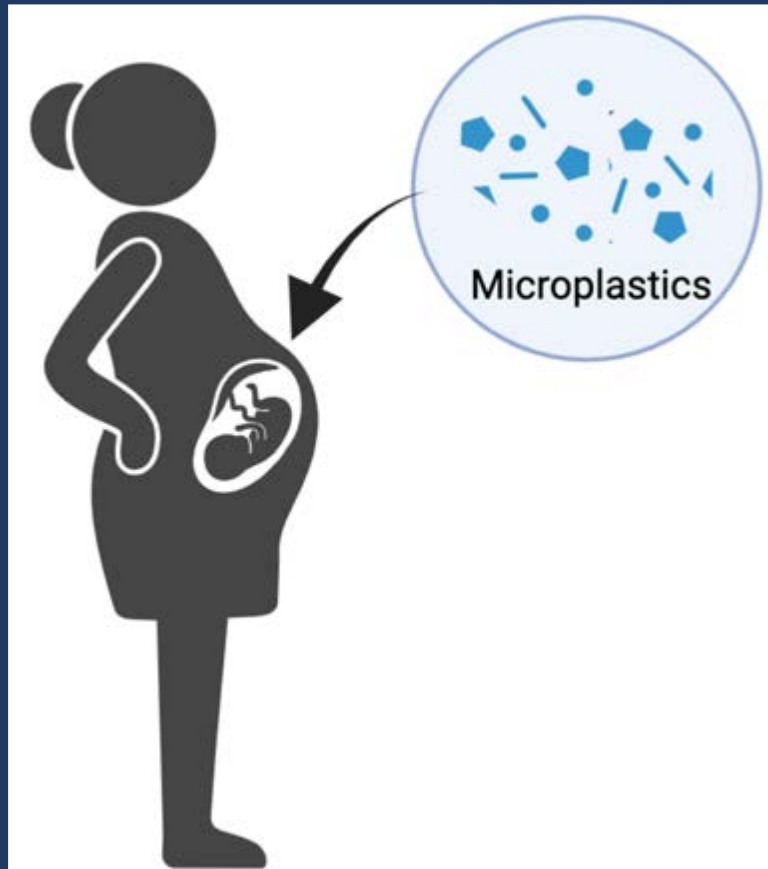
Damian Carrington
Environment editor

@dpcarrington
Tue 22 Dec 2020 10:55 GMT



- healthy pregnancies
- 5-10 micron polypropylene
- detected using Raman microspectroscopy

Plastics and Pregnancy



Placenta

Ragusa et al. *Int J Environ Res Public Health* **2022**, 19:11593.

Amereh et al. *Environ Pollut* **2022**, 314:121074.

Zhu et al. *Sci Total Environ* **2023**, 856:159060.

...

Meconium

Zhang et al. *Environ Sci Technol* **2021**, 8:989.

Liu et al. *Environ Sci Technol* **2022**, In press.

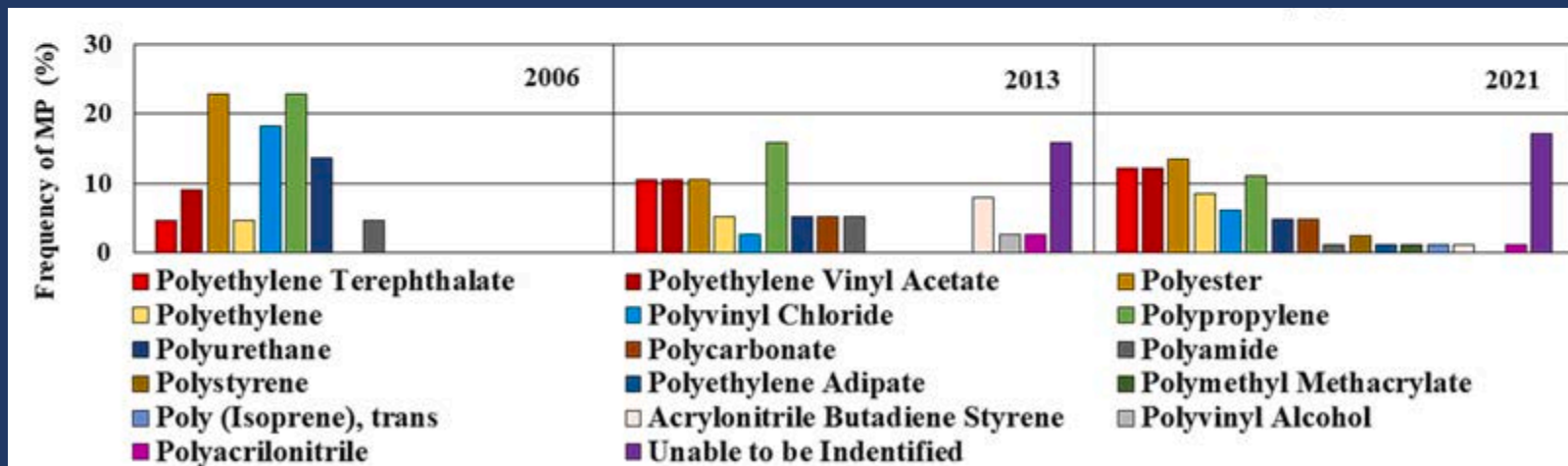
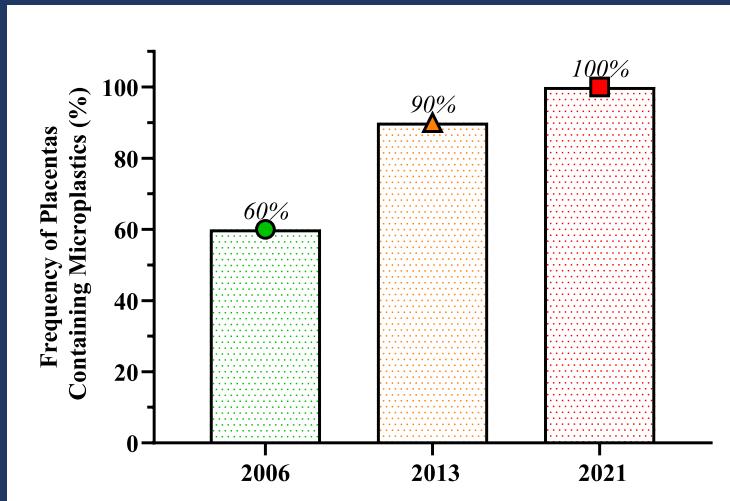
Braun et al. *Pharmaceutics* **2022**, 13:921.

Breastmilk

Ragusa et al. *Polymers* **2022**, 14:2700.

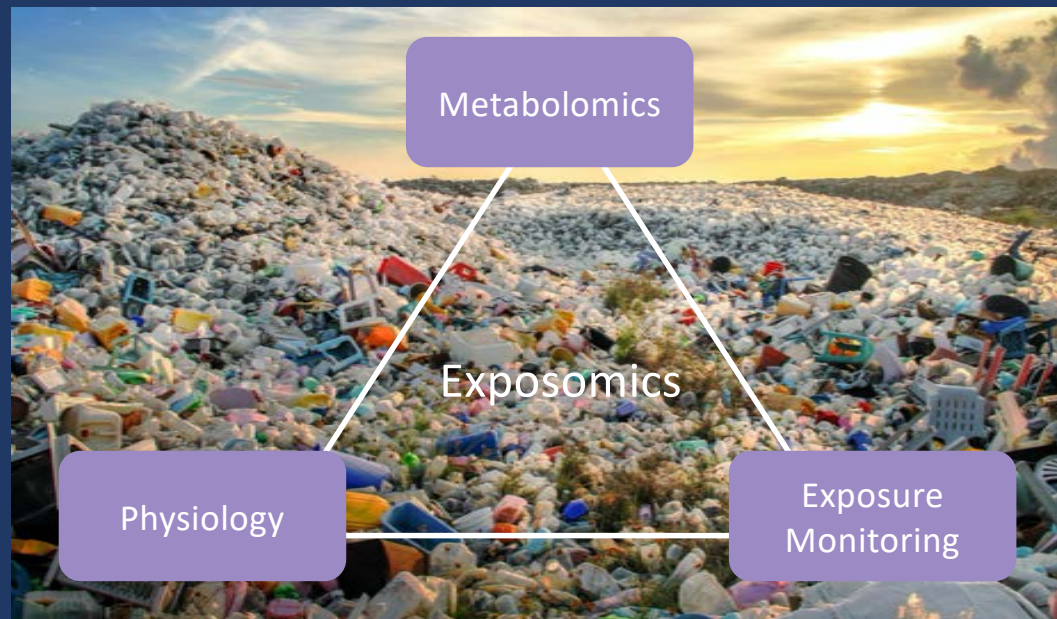
Liu et al. *Sci Total Environ* **2023**, 13:158699.

Is human exposure to microplastics increasing?



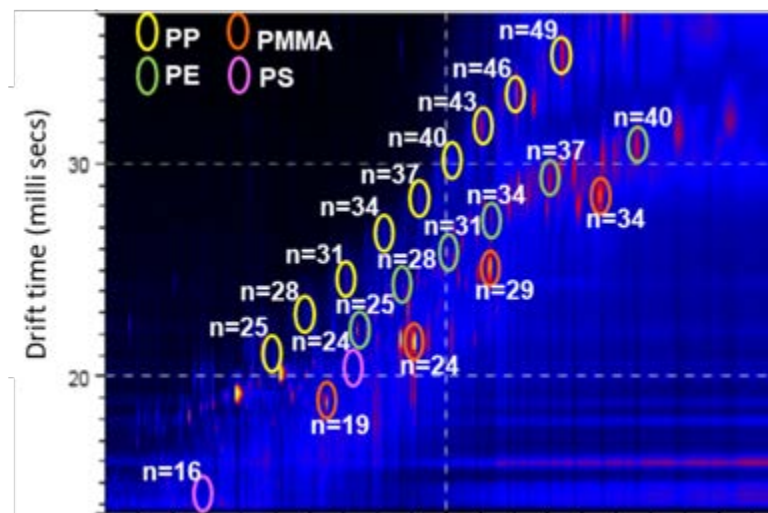
Knowledge Gaps

1. What concentration of sub-micrometer plastics are humans exposed to?
2. What are the impacts of micro-/nanoplastics exposure to human health?



Plastics in Indoor Environment and Human Tissue

- Pyrolysis gas chromatography x cyclic ion mobility mass spectrometry (Pyr-GCxcIMS-MS)
 - allows for quantitative analysis





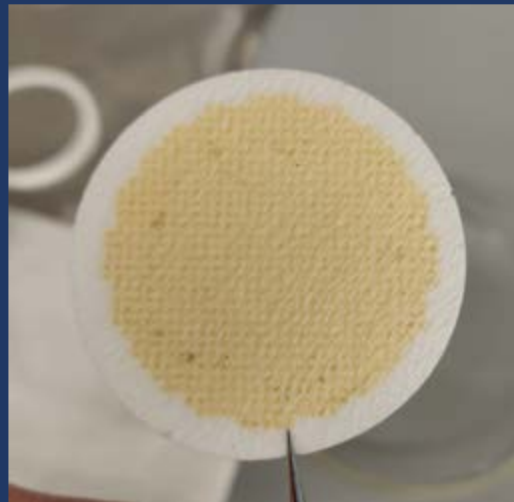
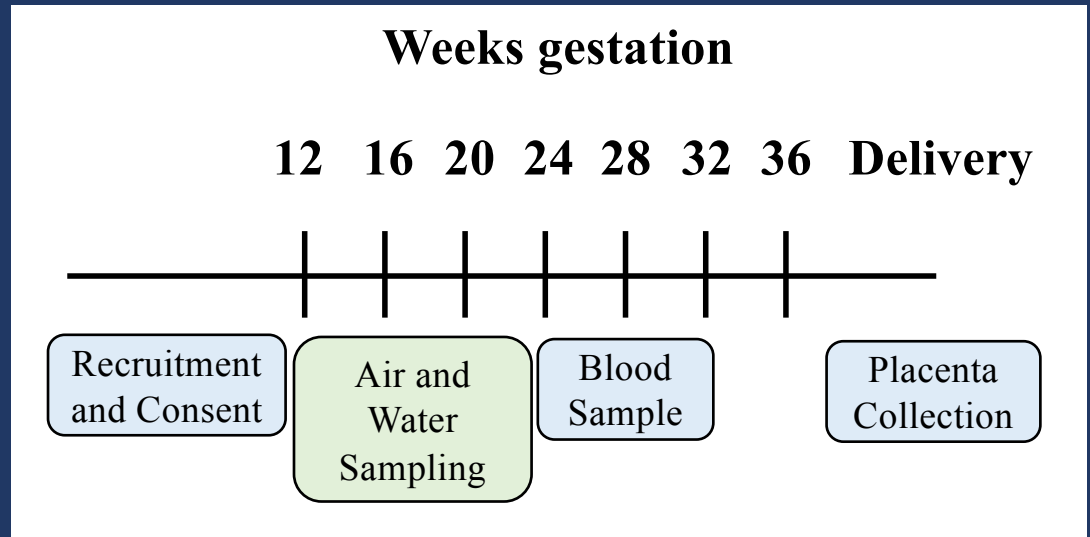
Health
Canada



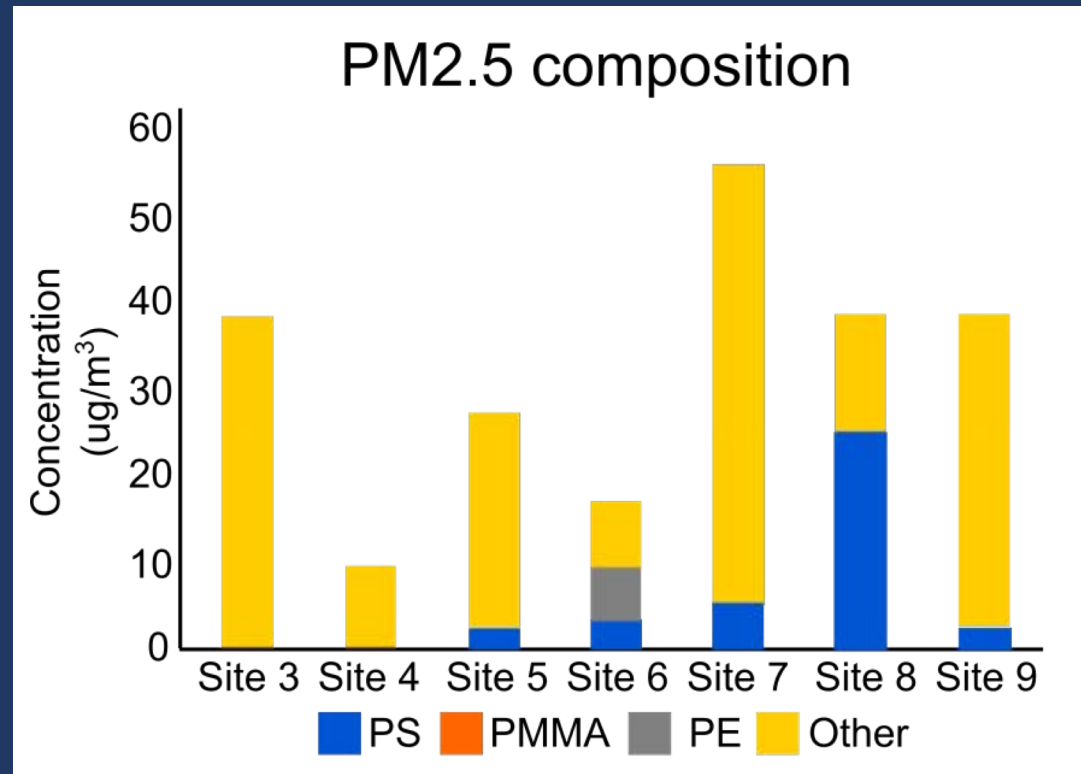
St John's, Newfoundland and Labrador



Toronto, Ontario



Plastics in the Indoor Environment



- Between 9-65% of indoor particulate matter consists of plastic
- Most of the plastic detected is polystyrene (less dense!)



Contents lists available at [ScienceDirect](#)

Journal of Hazardous Materials Letters

journal homepage: www.sciencedirect.com/journal/journal-of-hazardous-materials-letters



Ingested microplastics: Do humans eat one credit card per week?

Martin Pletz

5 g/week

Senathirajah et al. *J Hazard Mater*
2021, 404:124004


4.1 μg /week

Mohamed Nor et al. *Environ Sci Tech*
2021, 55:5084

One million
times less!


Based on our estimates (160 $\mu\text{g}/\text{day}$), it would take 85 years to inhale a credit card worth of plastic ($\sim 5\text{ g}$)

Payment cards are made up of several layers of plastic. Traditionally PVC has been used but increasingly new sustainable plastics are being used either for individual layers or for the whole card. This allows us to reduce the amount of first use PVC in the card.



- Chip
silicon, gold, nickel
- Transparent overlay
PVC
- Offset printed front
PVC, additives, inks
- Core with antenna
PVC, aluminum or copper
- Offset printed back
PVC, additives, inks
- Transparent overlay with magnetic strip
PVC, barium

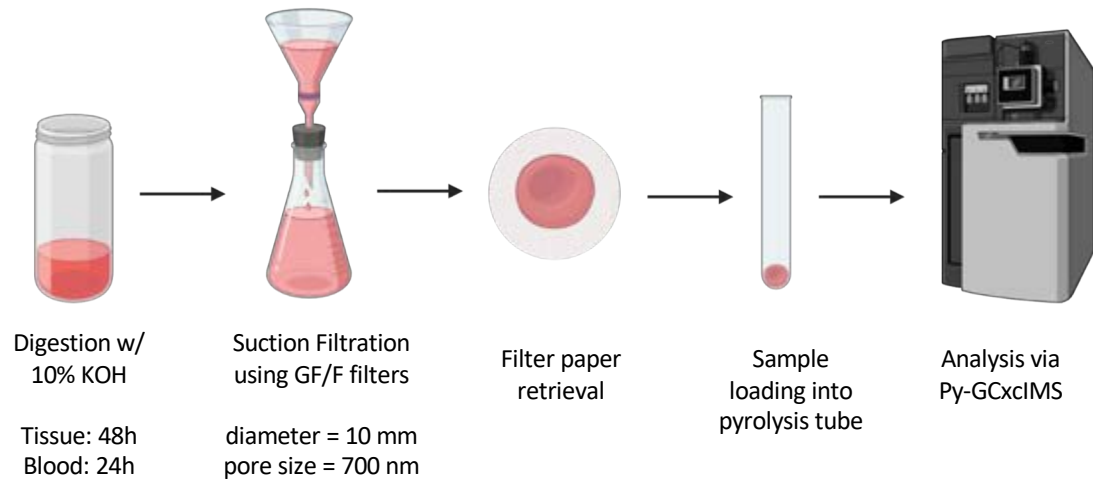
Mastercard has developed a sustainable card program to make sustainable choice the preferred option for all financial institutions. At the center of this is the world's first sustainable card badge for cards made from recyclable, recycled, bio-sourced, chlorine-free, degradable or ocean plastics.



© 2021 Mastercard. All rights reserved.

Plastics in Placental Tissue

- 46 pregnant people recruited from St John's, Newfoundland, Canada.
- All placentas collected were brought out directly from the OR in sterile metal dishes.
- 4 biopsy punches from four corners of placenta collected (~1 g).
- 1 vial of blood scooped from inside the placenta (~1 mL).
- Placenta samples are then stored in glass scintillation vials at -80°C.
- Blood samples are stored in glass heparinized vacutainer at -20°C.



Vacuum filtration is done in an ISO Class 6 clean room

Large differences between studies

Environment International 146 (2021) 106274

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Elisabetta Giorgini^c

^a Department of Obstetrics and Gynecology, San Giovanni Calibita Fatebenefratelli Hospital, Isola Tiberina, Via di Ponte Quattro Capi, 39, 00186 Rome, Italy
^b Department of Pathological Anatomy, San Giovanni Calibita Fatebenefratelli Hospital, Isola Tiberina, Via di Ponte Quattro Capi, 39, 00186 Rome, Italy
^c Department of Life and Environmental Sciences, Università Politecnica delle Marche, via Brecce Bianche, 60131 Ancona, Italy
^d Department of Obstetrics and Gynecology, ASST Bergamo Est, Bolognini Hospital, Seriate, Via Paderno, 21, 24068 Bergamo, Italy
^e Harvey Medical and Surgery Course, University of Pavia, Corso Strada Nuova 65, 27100 Pavia, Italy

12 microplastic fragments in 4 of 6 placentas

Quantitation and identification of microplastics accumulation in human placental specimens using pyrolysis gas chromatography mass spectrometry

Marcus A. Garcia,¹ Rui Liu,¹ Alex Nihart,¹ Eliane El Hayek,¹ Eliseo Castillo,² Enrico R. Barrozo,³ Melissa A. Suter,³ Barry Bleske,⁴ Justin Scott,⁵ Kyle Forsythe,⁵ Jorge Gonzalez-Estrella,⁵ Kjersti M. Aagaard,³ Matthew J. Campen^{1,*}

¹Department of Pharmaceutical Sciences, College of Pharmacy, University of New Mexico Health Sciences, Albuquerque, New Mexico 87106, USA
²Division of Gastroenterology and Hepatology, Department of Internal Medicine, University of New Mexico School of Medicine, Albuquerque, New Mexico 87106, USA
³Division of Maternal-Fetal Medicine, Department of Obstetrics and Gynecology, Baylor College of Medicine and Texas Children's Hospital, Houston, Texas 77030, USA
⁴Department of Pharmacy Practice and Administrative Sciences, College of Pharmacy, University of New Mexico Health Sciences, Albuquerque, New Mexico 87106, USA
⁵School of Civil & Environmental Engineering, Oklahoma State University, Stillwater, Oklahoma 74078, USA

*To whom correspondence should be addressed at Department of Pharmaceutical Sciences, MSC09 5360, 1 University of New Mexico, Albuquerque, NM 87131-0001. E-mail: mcampen@salud.unm.edu

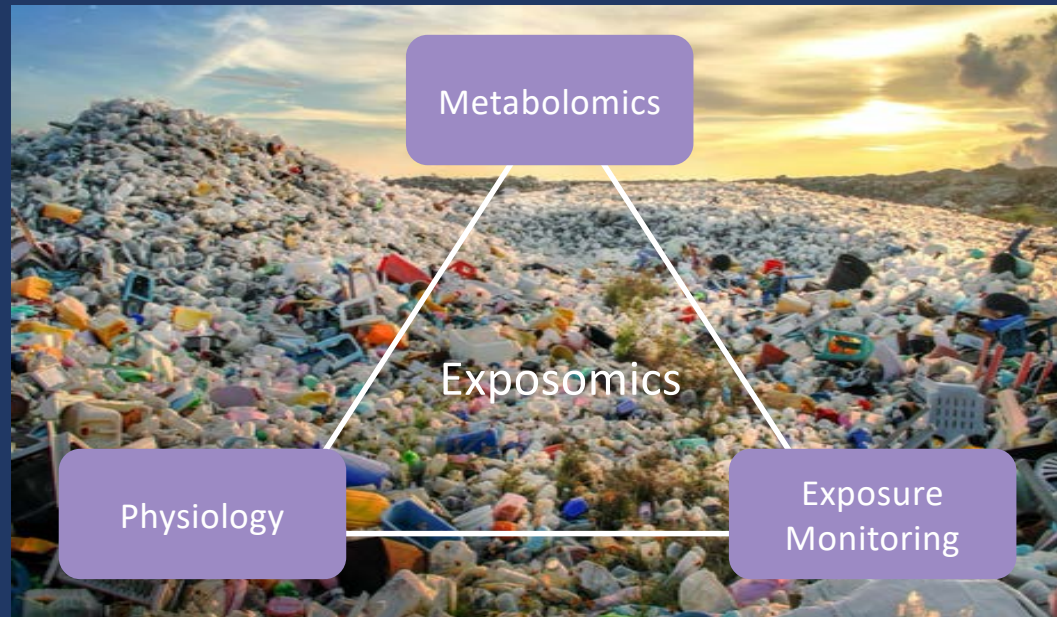
The authors certify that all research involving human subjects was done under full compliance with all government policies and the Helsinki Declaration.

Toxicological Sciences, 2024, 199(1), 81–88
<https://doi.org/10.1093/toxsci/kfae021>
Advance Access Publication Date: February 17, 2024
Research article

Quantitative analysis: concentrations range from 6.5 to 685 µg/g ! (mean = 127 µg/g)

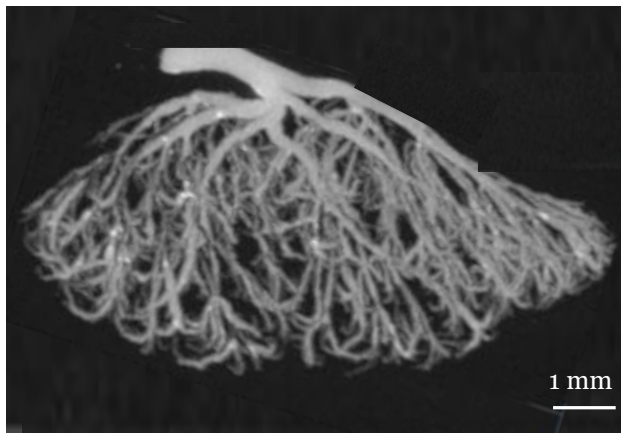
Knowledge Gaps

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2. What are the impacts of micro-/nanoplastics exposure to human health?

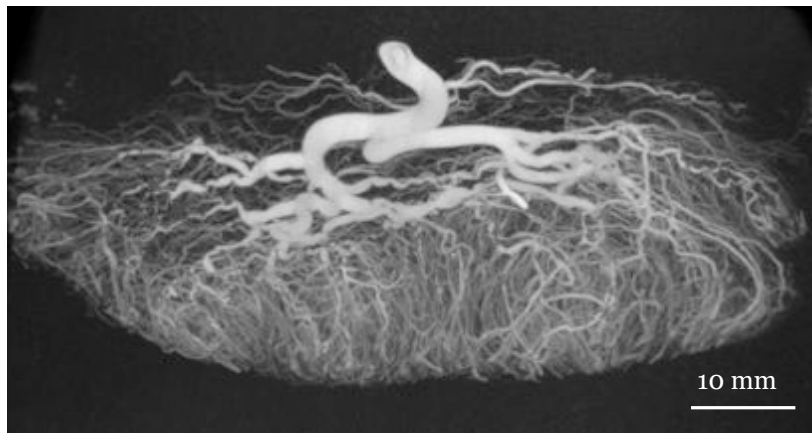


Animal Research in Pregnancy

- The benefits of mice include:
 - the placenta in both mice and humans have a similar vascular and cellular structure
 - efficient for research (low cost, rapid gestation, large litter sizes, reproducible pathology)
 - used to establish causal relationships between exposure and early life development



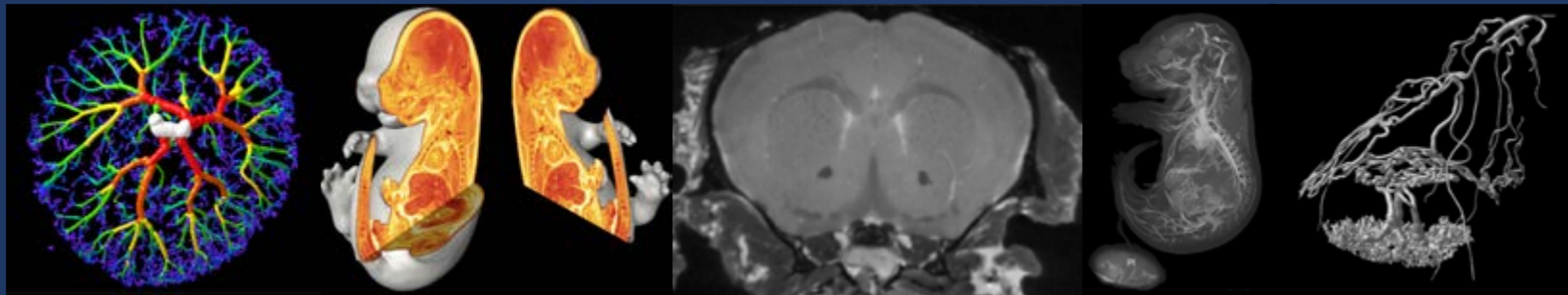
Mouse placenta



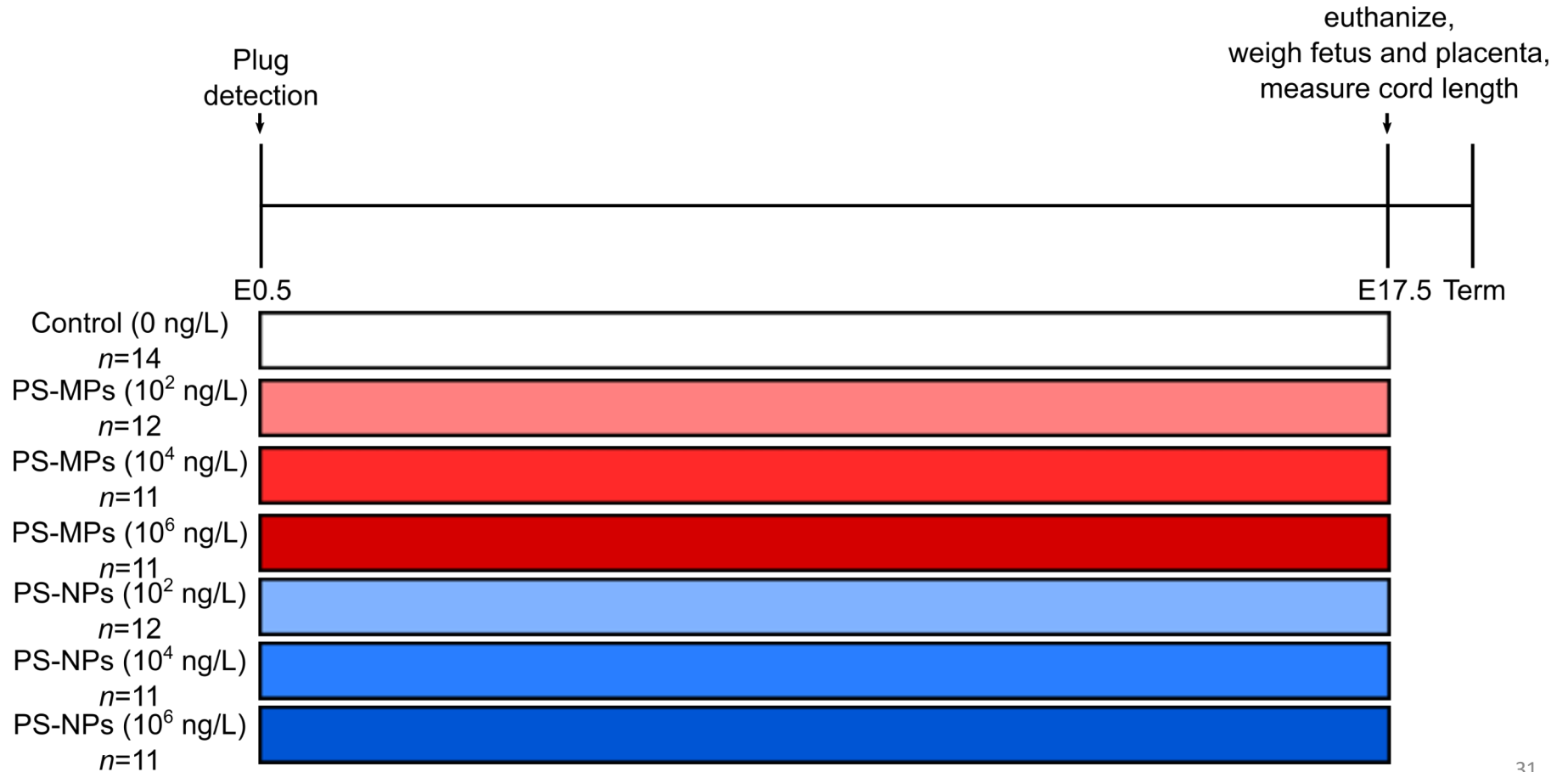
Human placental cotyledon

Biomedical Imaging in Mice

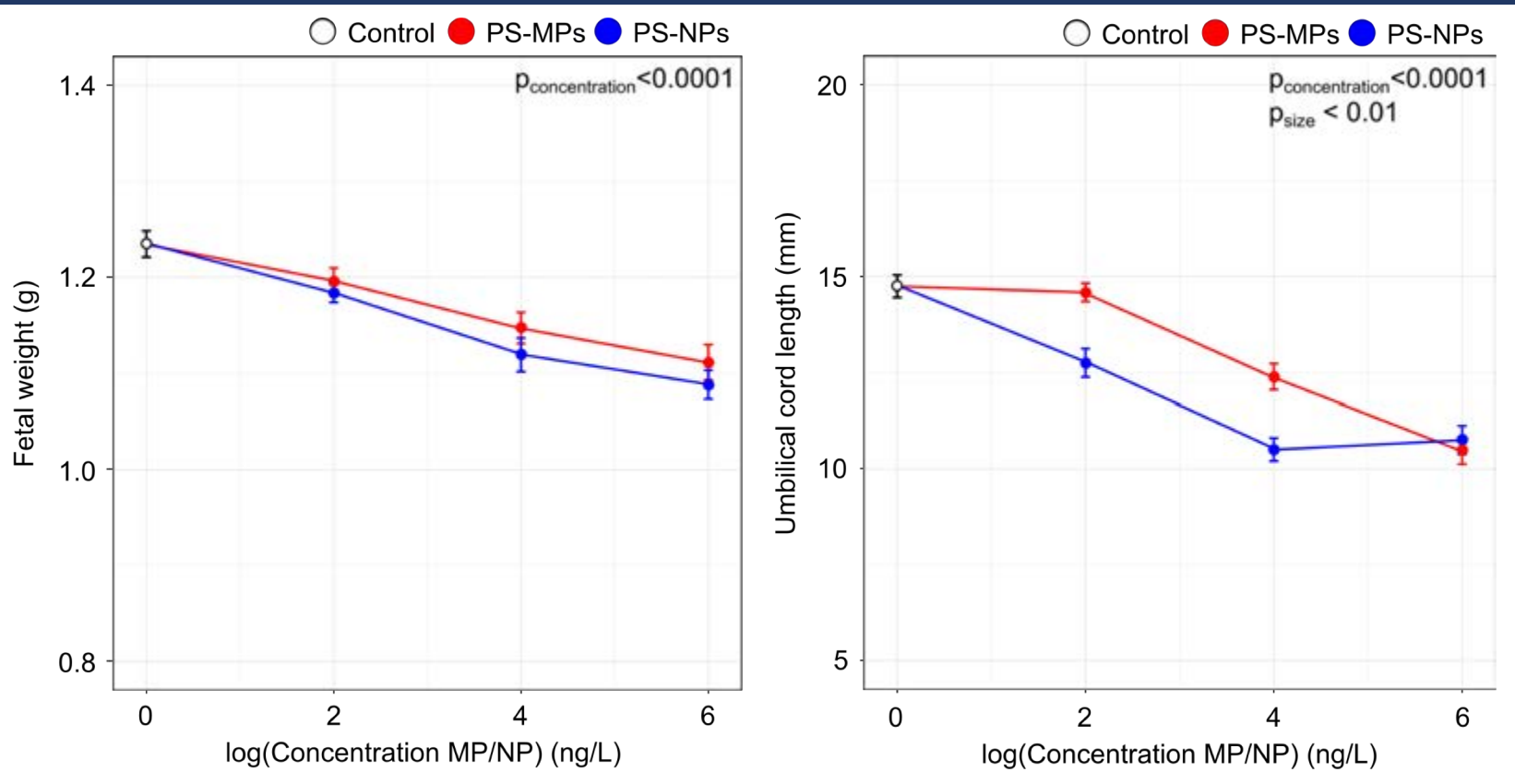
- imaging technologies used to study animals are the same as those used clinically
- possible to study the same animal in real time throughout its life
- full animal coverage and rich quantitative data sets



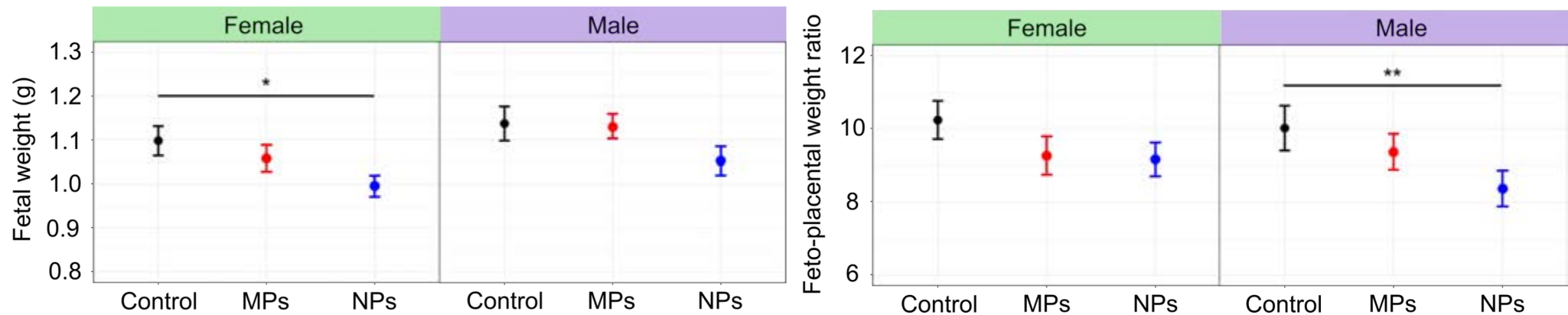
Study Design



Maternal Exposure Causes Fetal Growth Restriction

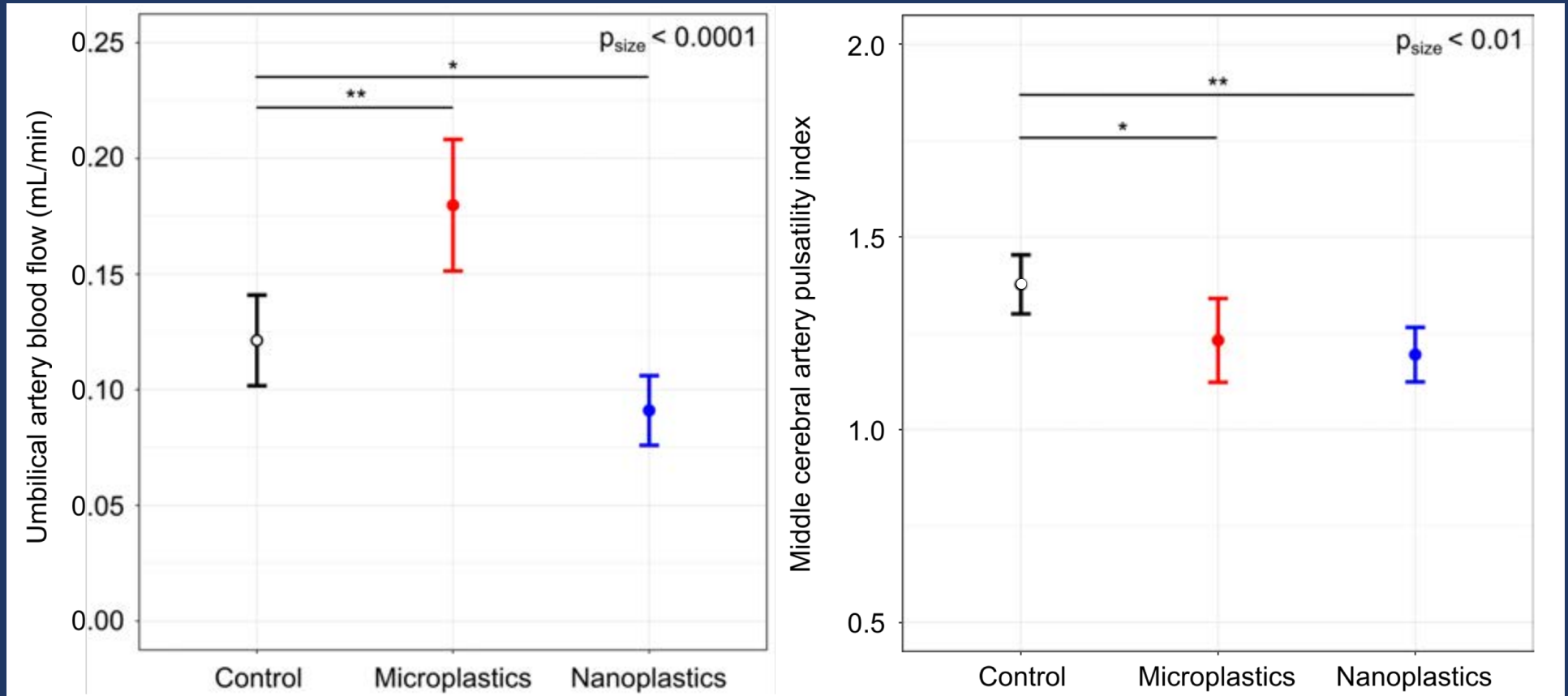


Biological Sex Differences in Growth

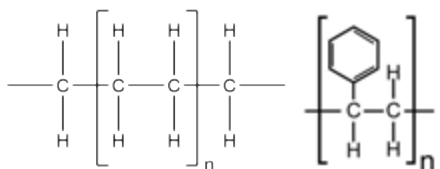
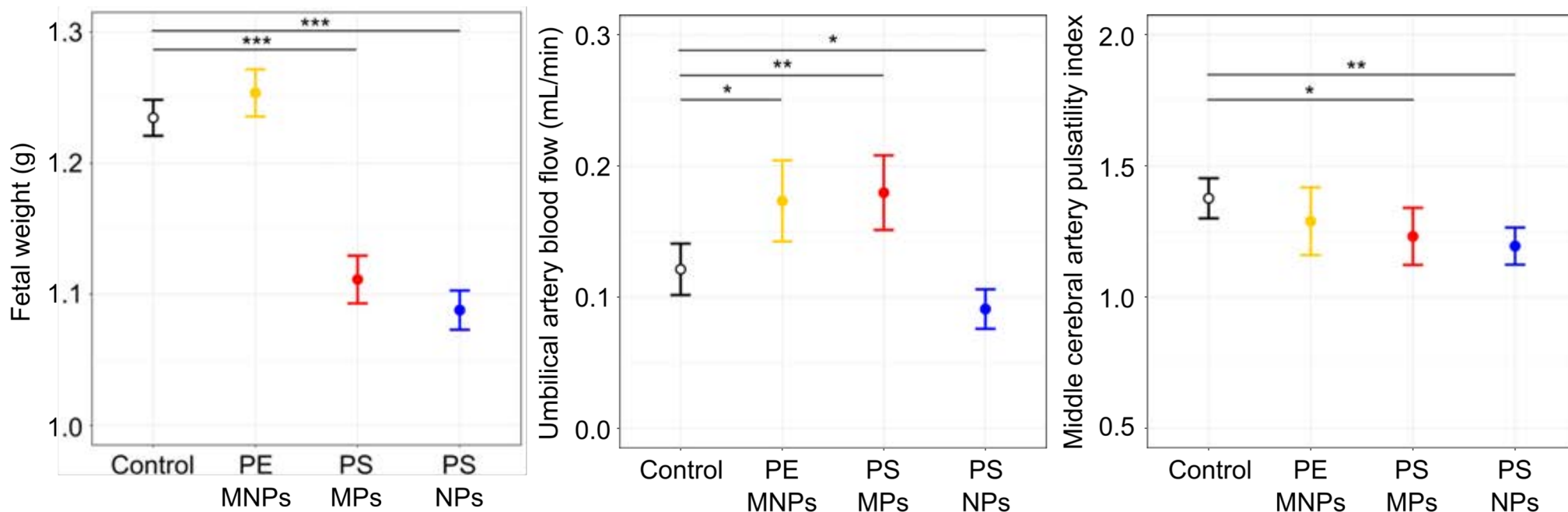


- **Female** fetuses may slow growth in response to plastics exposure, maintaining a healthy balance of nutrient transfer from the placenta and growth
- **Male** fetuses have a less effective nutrient transfer capacity but maintain similar growth to controls which may be harmful

Maternal Exposure Causes Placental Dysfunction



Developmental toxicity depends on polymer type

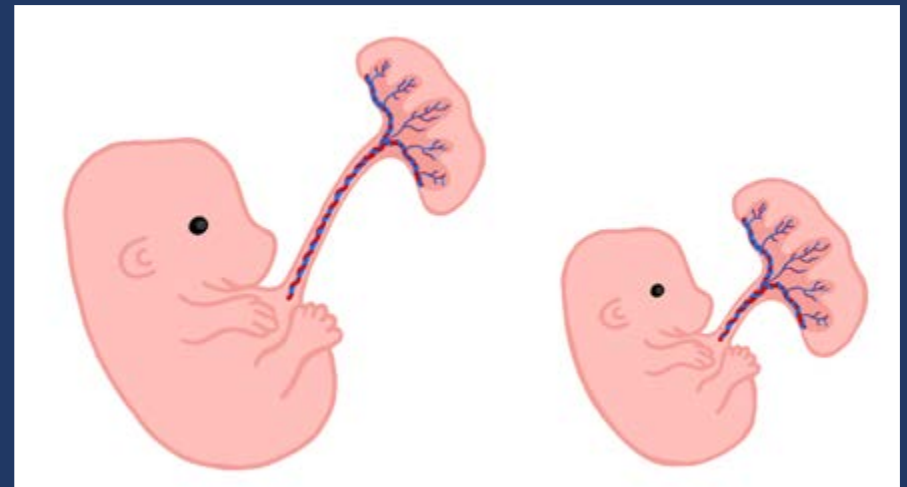


* $p < 0.05$, ** $p < 0.01$, *** $p < 0.0001$, $n = 11-14$ dams/group

Hanrahan et al. *Sci Rep* 2024, 14:399

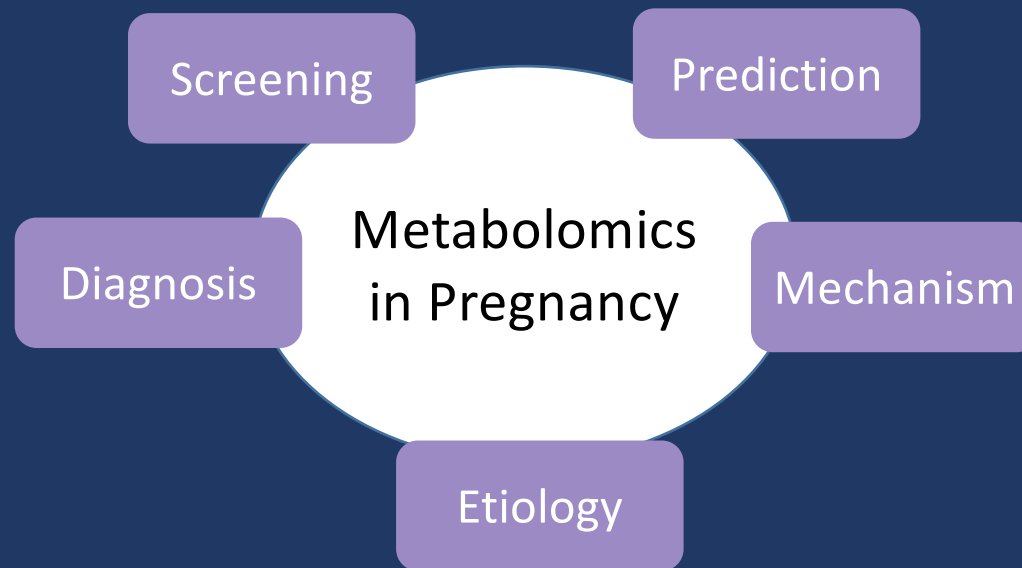
Is the fetal growth restriction associated with micro-/nanoplastics exposure partially the result of alterations in placental metabolism?

What is the impact on fetal brain metabolism?



Placental Metabolism

- fetuses depend on appropriate metabolic responses of the placenta to reach their growth potential
- “application of metabolomics in pregnancy research is an *embryonic* science”



Magic Angle Spinning Magnetic Resonance Spectroscopy

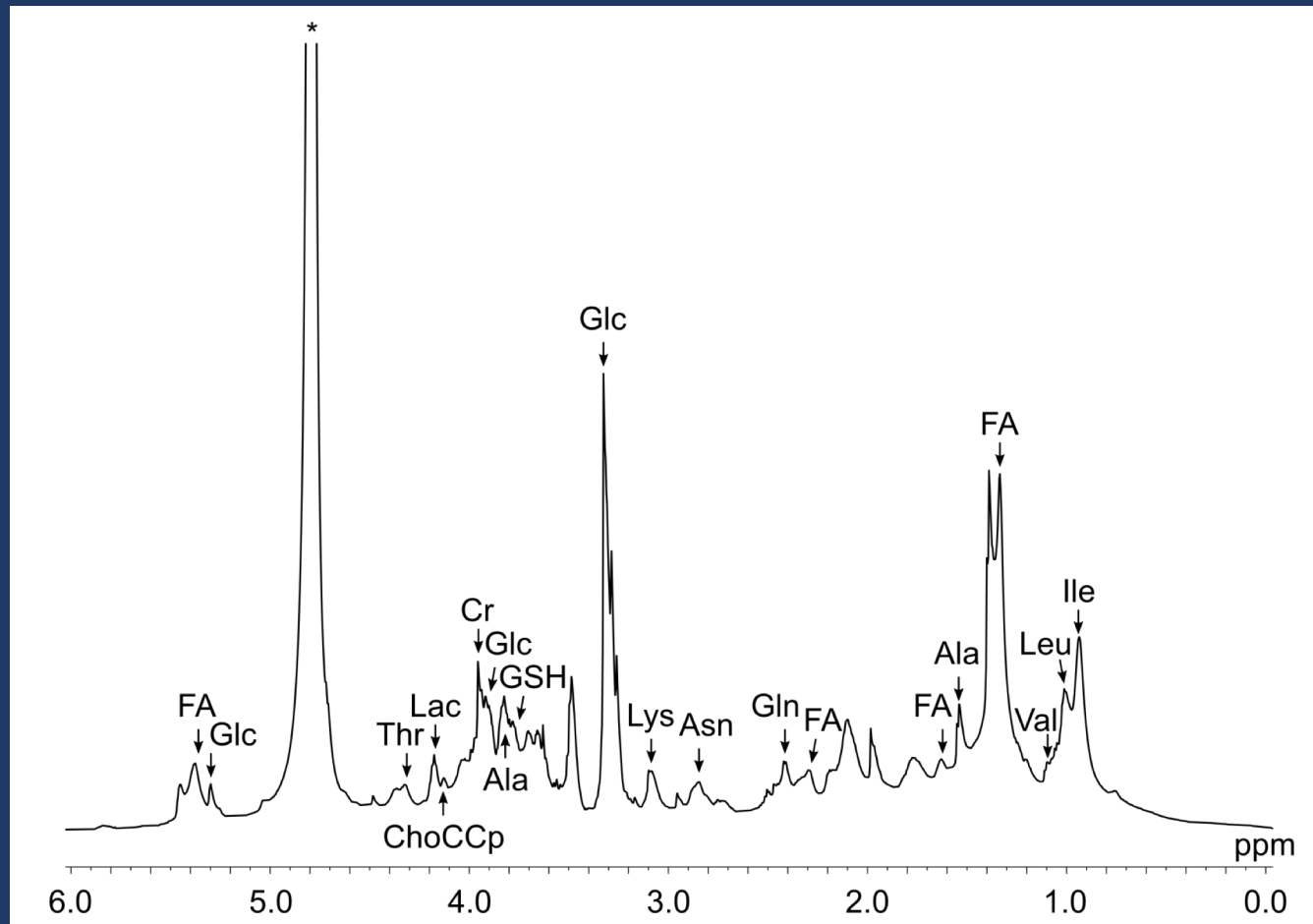
- freezing in liquid N₂ for rapid inactivation of enzymes
- intact, unprocessed tissue samples:
 - avoid extraction procedures
 - minimize impact of solvent effects
 - better represent molecular integrity of *in vivo*



Weybright et al. *Magn Reson Med* **1998**, 39:337.

Davila et al. *Magma* **2012**, 25:401.

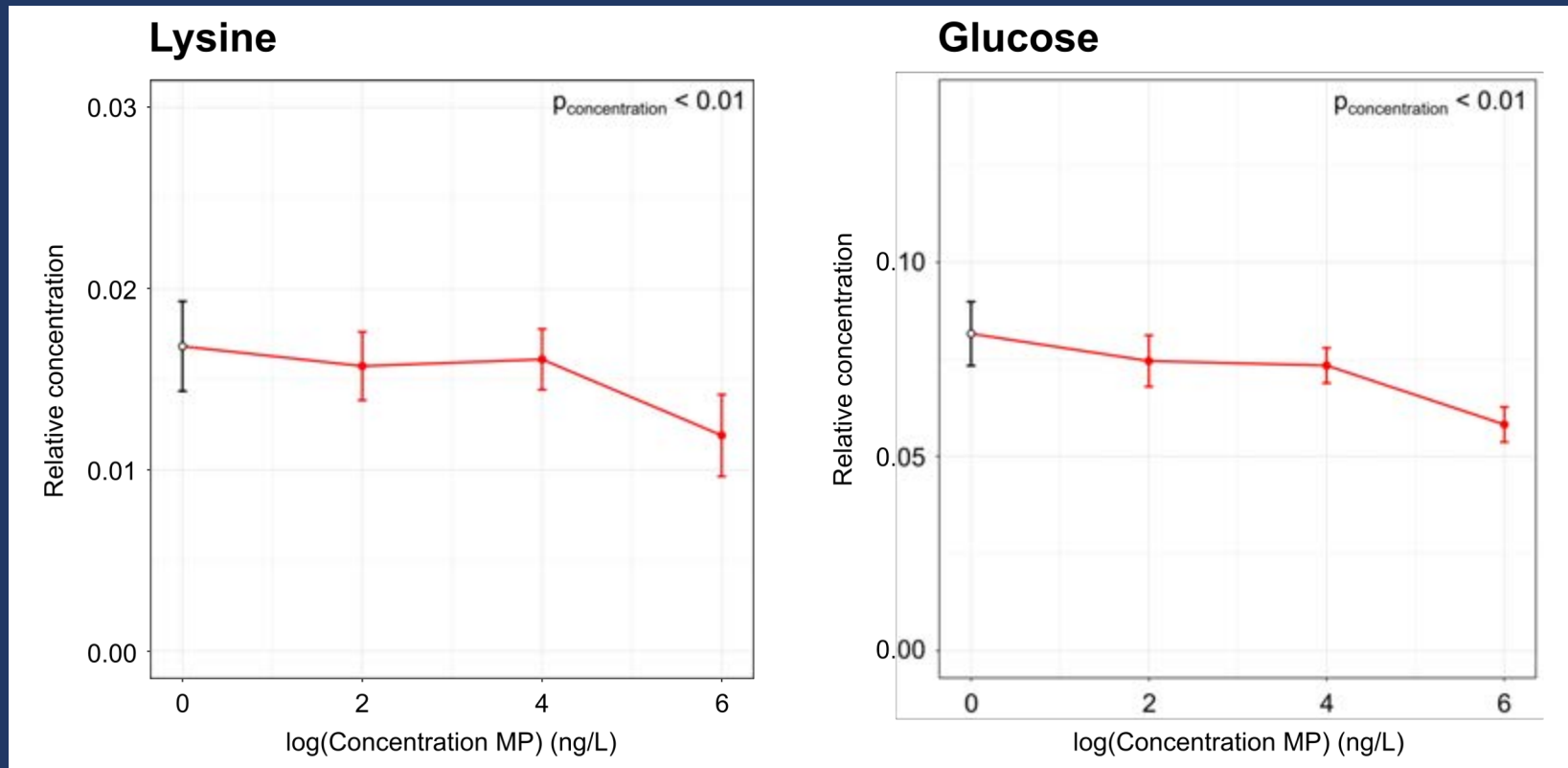
^1H HRMAS MRS of the Mouse Placenta



MAS = 4 kHz
Temp = 310 K
n = 32 scans

Schneider et al. *Metabolomics* 2022, 18:10

Effect of plastics exposure on placental metabolomics

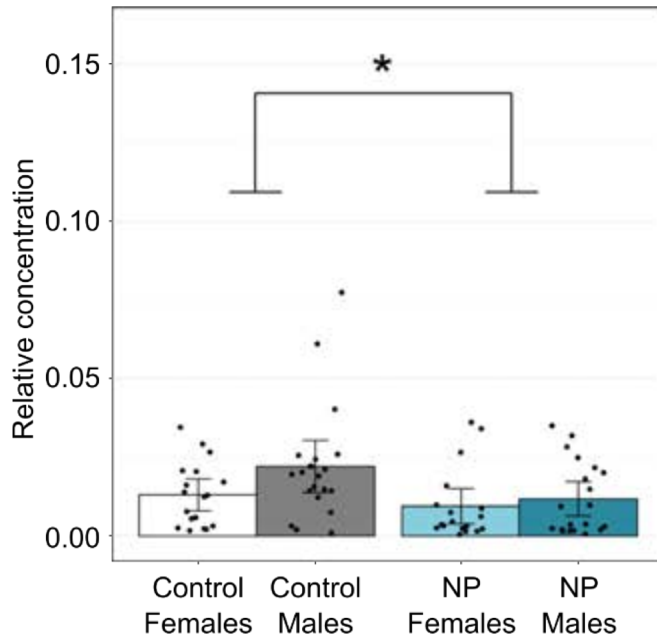


n = 28-44 placentas/group

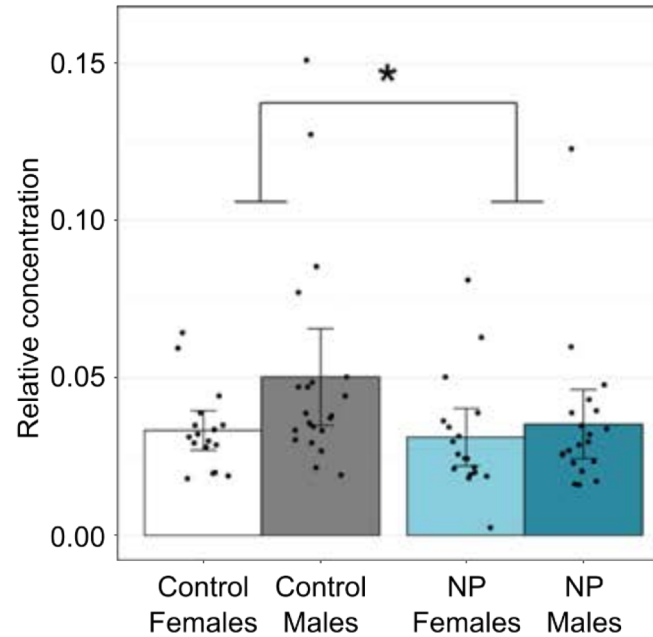
Aghaei et al. *Metabolomics* 2023, 19:1

Fetal Brain Metabolites

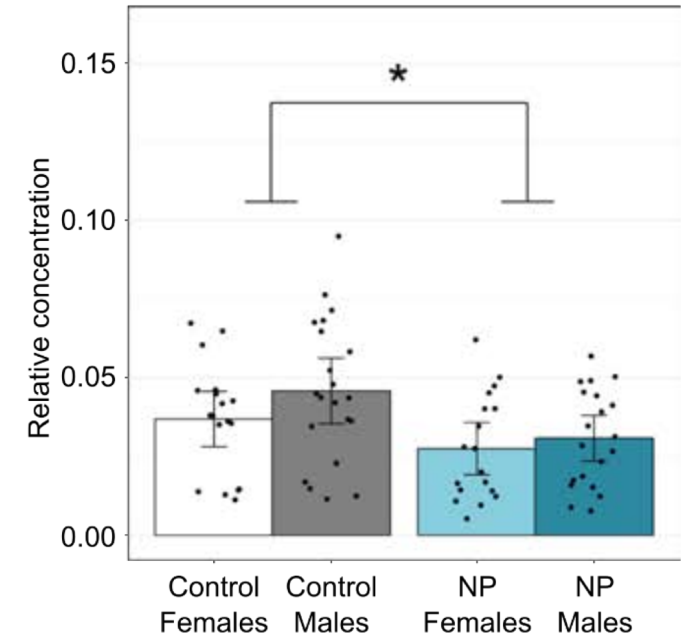
GABA



Creatine



Glucose



Essential neurotransmitter
for brain maturation

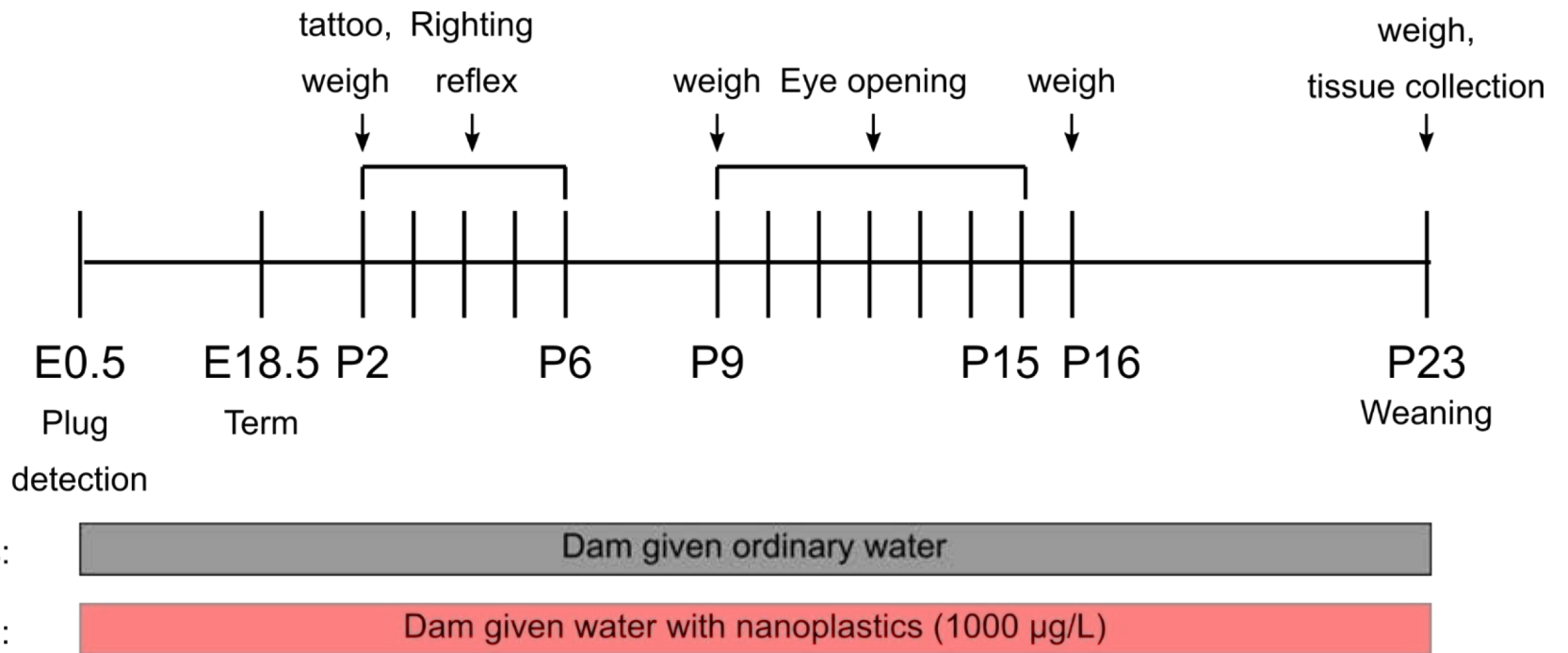
Important for production
of ATP

Main source of energy for
brain function

* $p < 0.05$, $n = 18-21$ brains/group/sex

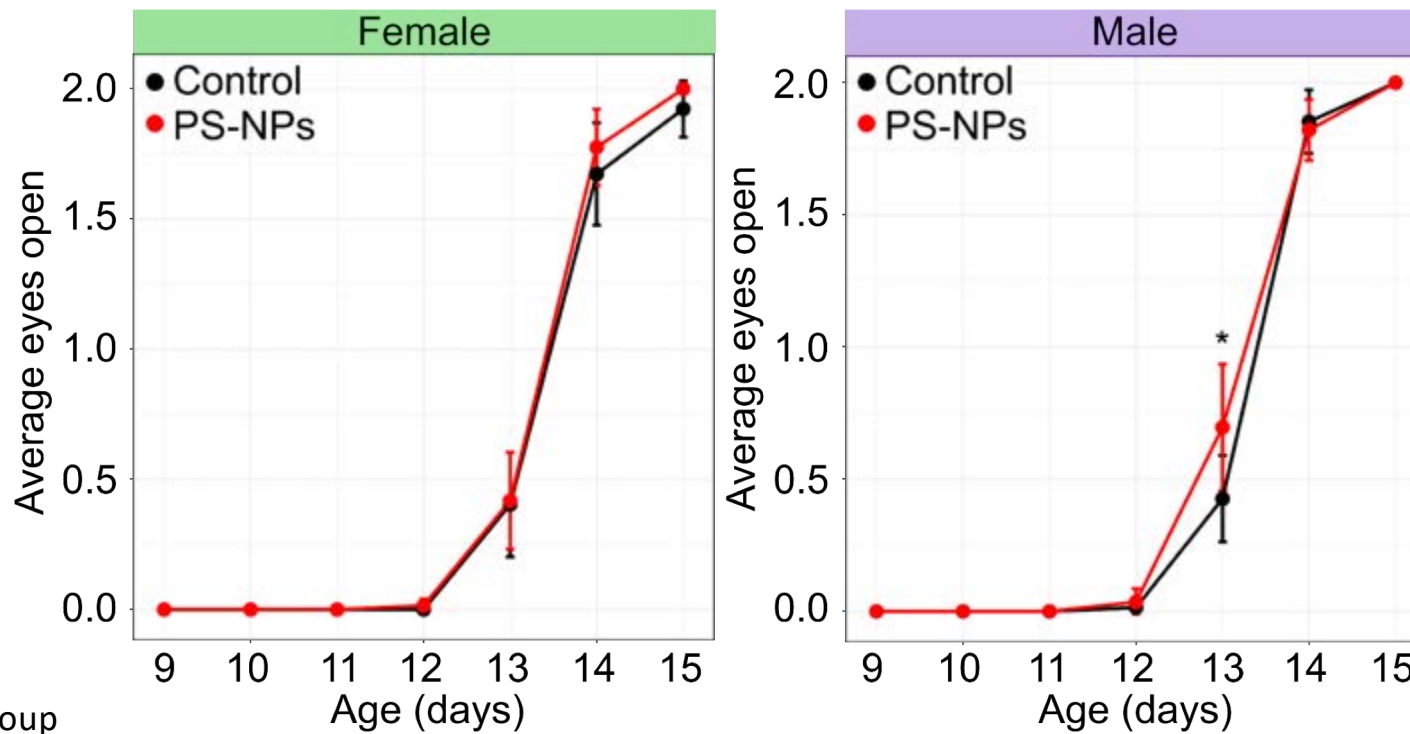
Mercer et al. *Metabolomics* 2023, 19:96

Study Design



n = 10 dams/group

Impact of nanoplastics exposure on postnatal development



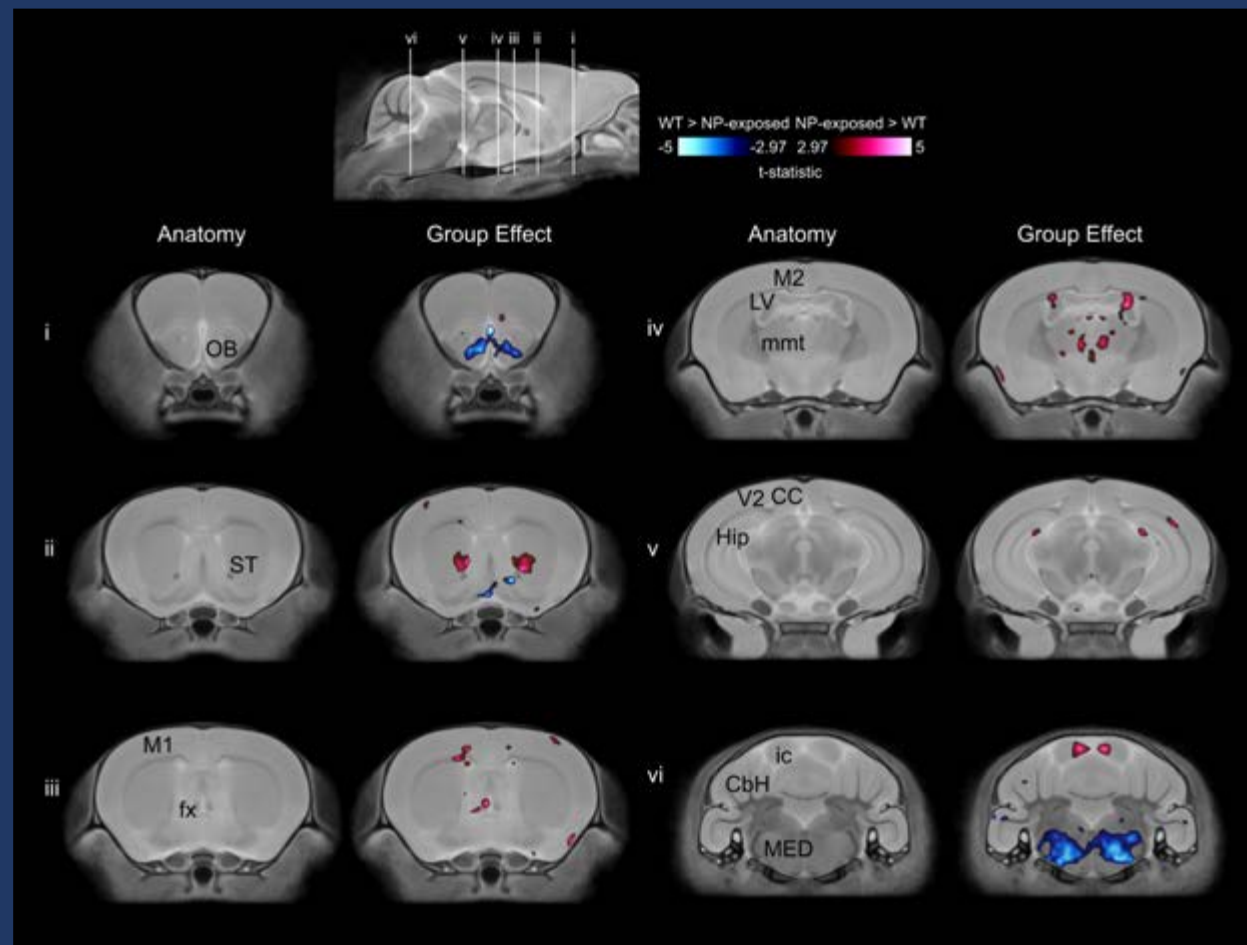
*p<0.05
n =10 litters/group

Impact of nanoplastics exposure on neuroanatomy

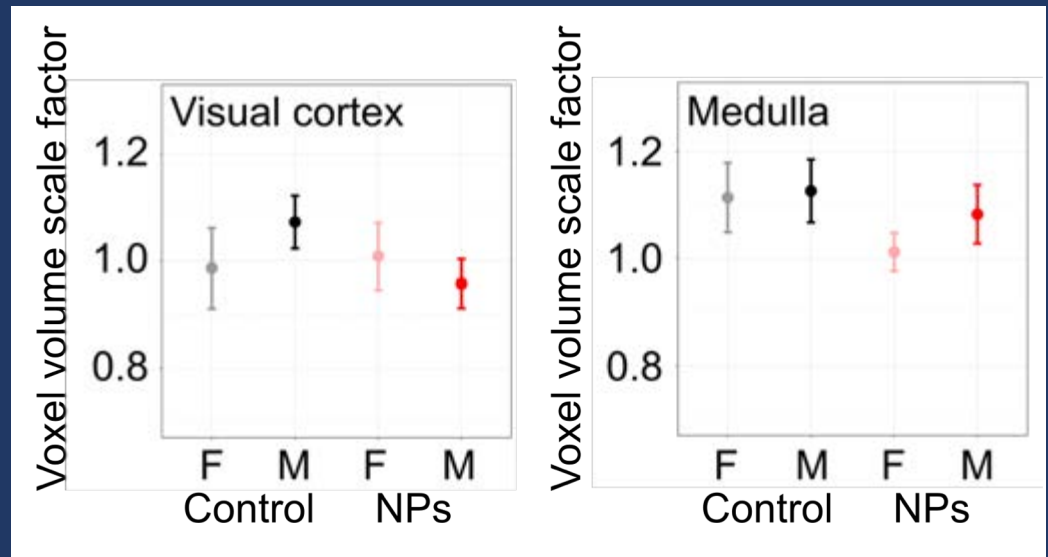
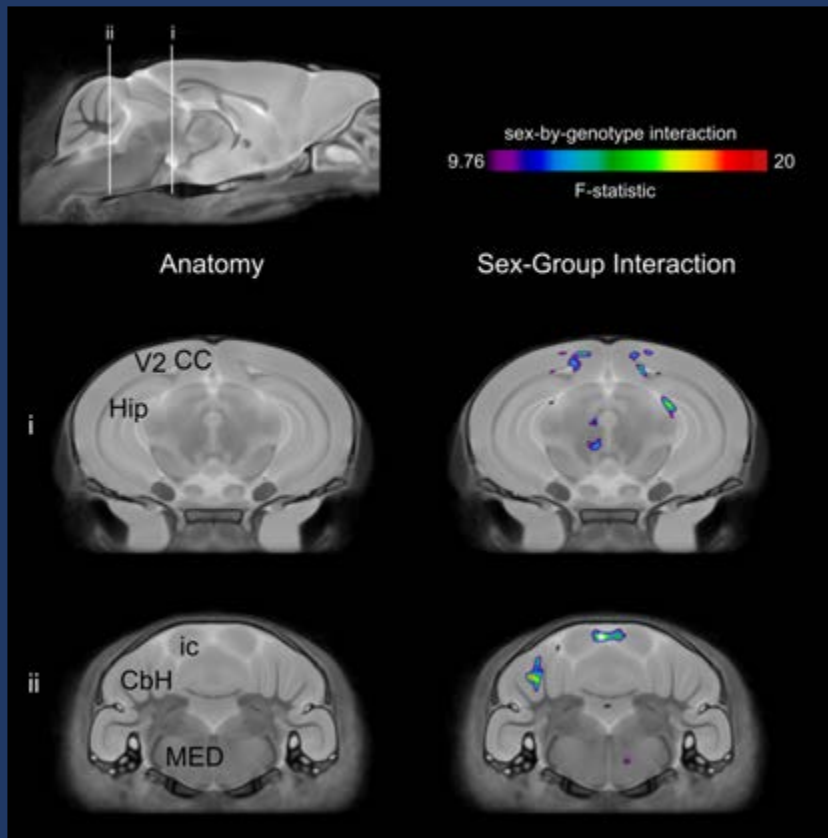
- Region-specific effects on brain structure:

- Olfactory bulb
- Motor cortex
- Hippocampus
- Hypothalamus
- Medulla
- Striatum

10% FDR, $n = 11$ brains/group/sex



Impact of nanoplastics exposure on neuroanatomy



n = 11 brains/group/sex

Summary



www.ciel.org/plasticsandclimate

Center for International Environmental Law

1. Humans: Micro-/nanoplastics are in the human placenta with a large variation in concentration
2. Mice: Maternal exposure to micro-/nanoplastics significantly impacts early life development (growth restriction, abnormal placental metabolism, abnormal brain development)
3. Mice: Developmental toxicity depends on plastic type and size
4. Critical to better characterize exposure levels in healthy and complicated pregnancies

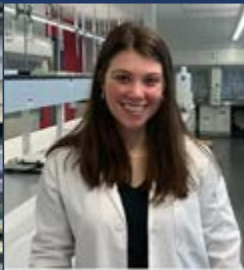
Acknowledgements



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Martin Van Velzen



Karl Jobst
Céline Schneider
Stacy Lambe
Nadine Burry
Jayne Simmons
Haley Adams
Katherine Steeves
Catherine Barrett
Caroline Ryan
Sophie Kieft
Drew Locke
Thomas O'Brien



Jenna Hanrahan



Grace Mercer



Justine Bissonnette



Miriam Diamond
Andre Simpson
Myrna Simpson



John Sled
Christopher Macgowan
Shoshana Spring



Ahmet Baschat

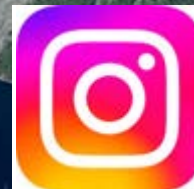


John Kingdom
Anjana Ravi-Chandran

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Questions?

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