



# *Neurodevelopmental impact of early-life ultrafine carbon nanoparticles exposure in mice*

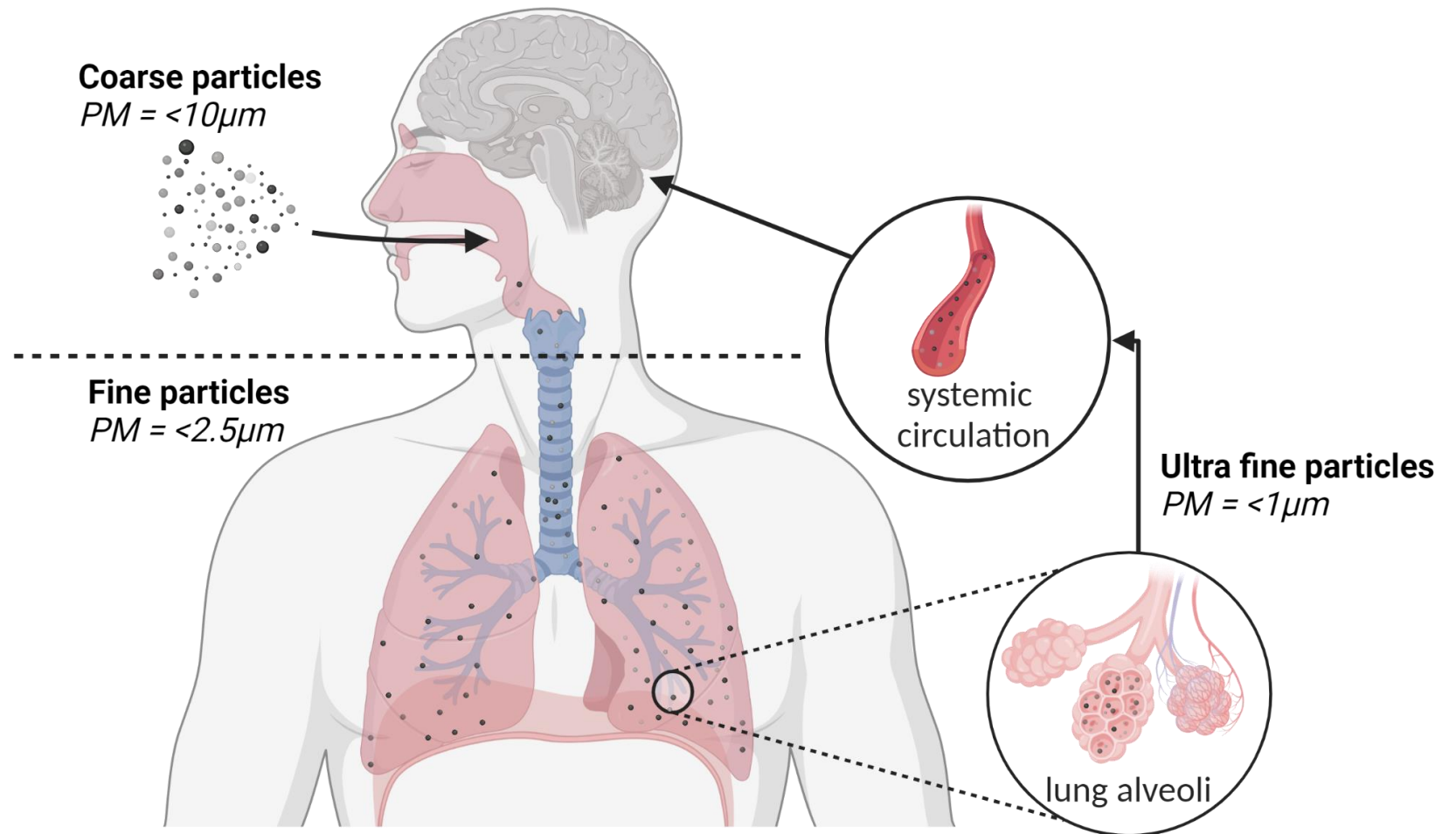
**Kenneth Vanbrabant**

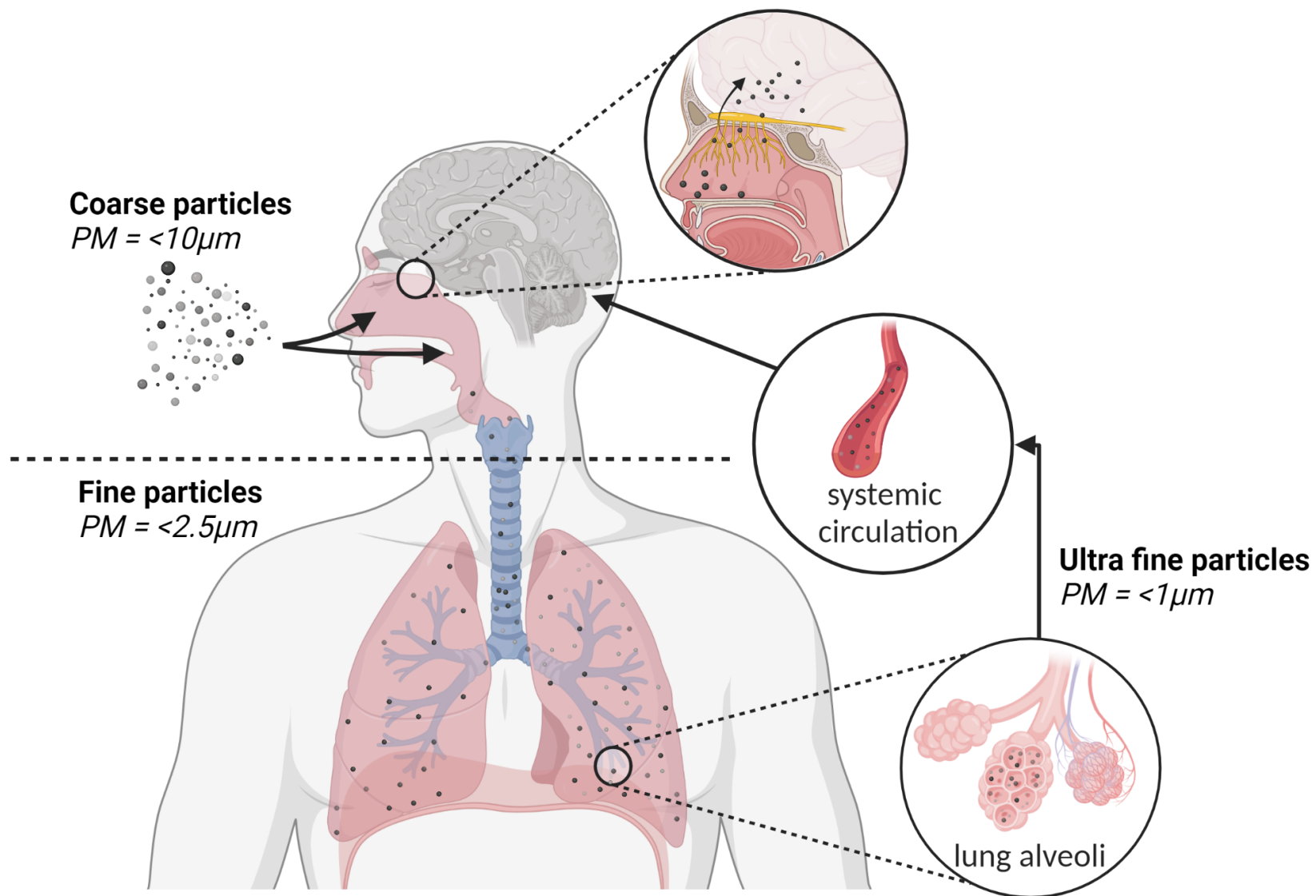
Center for Environmental Sciences

Hasselt University

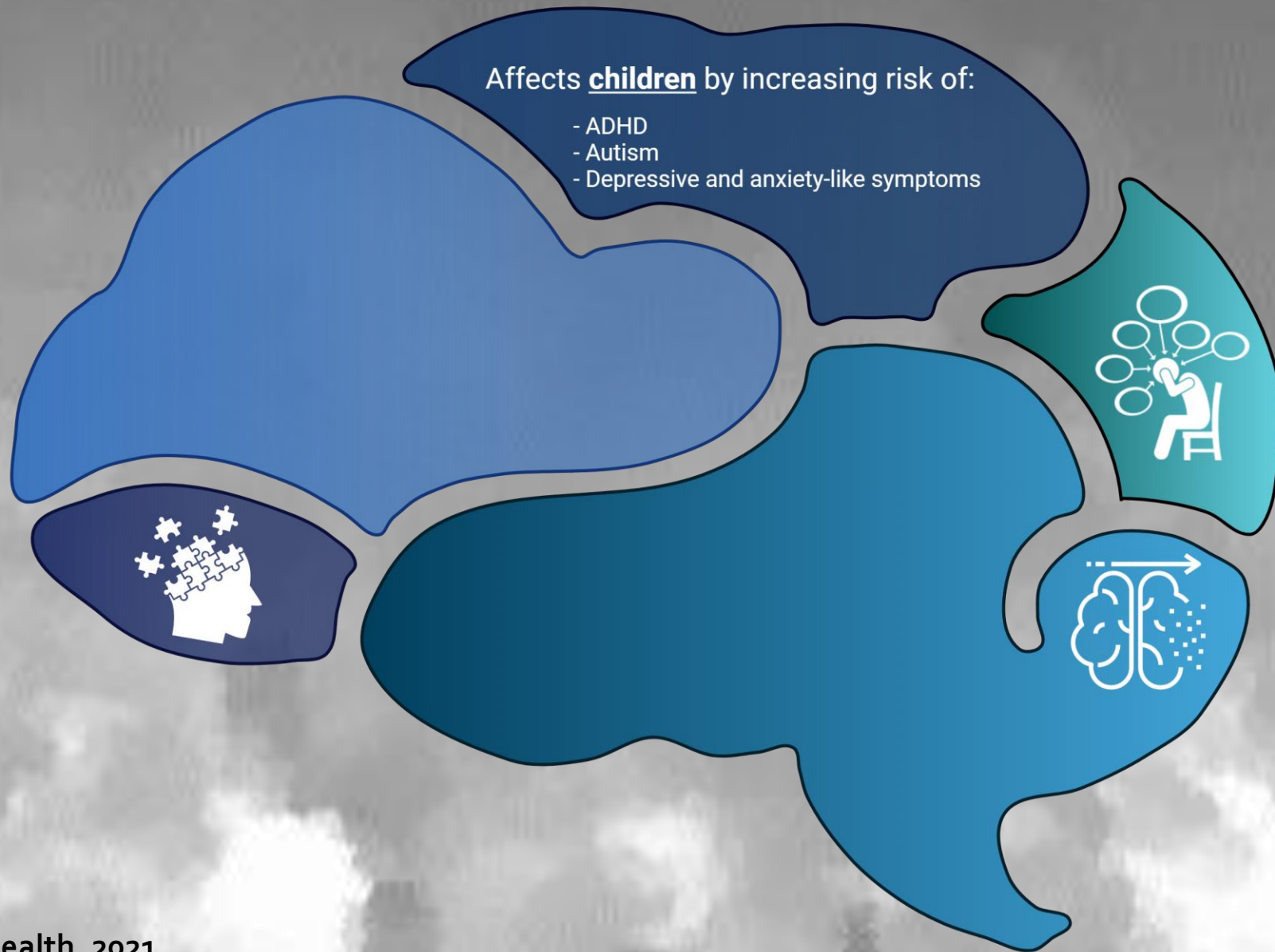
PI: Prof. Dr. Michelle Plusquin



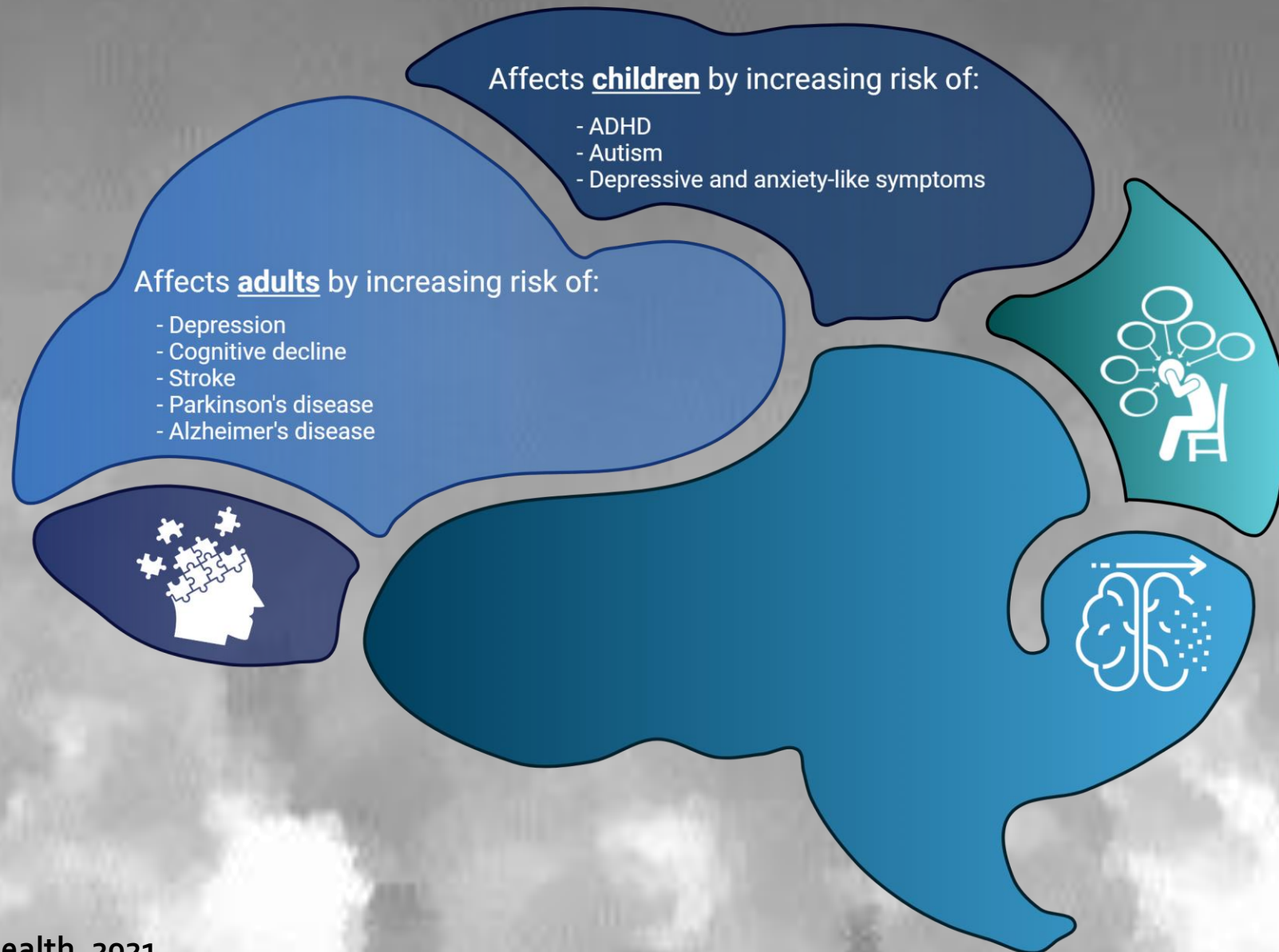




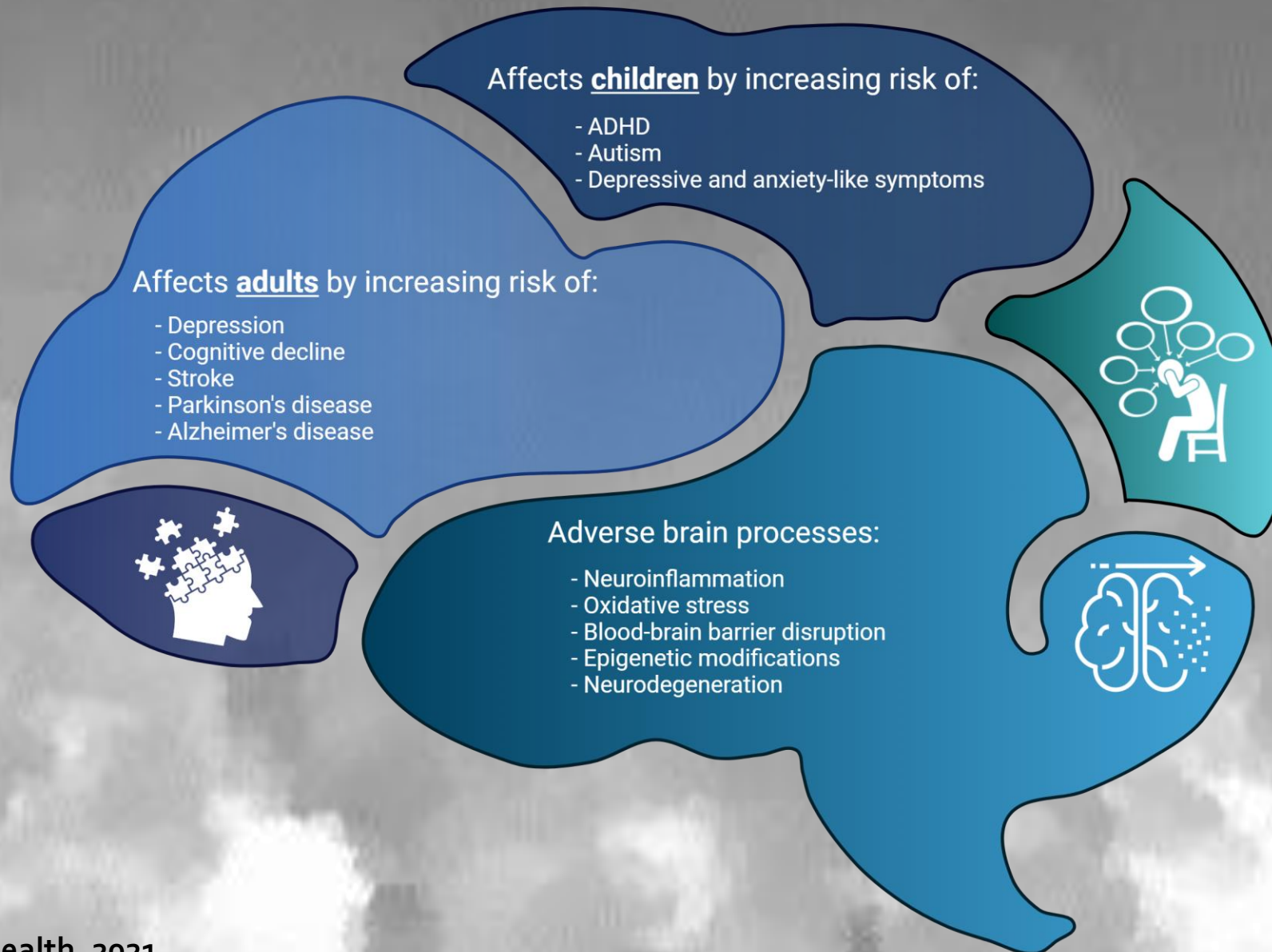
# Air pollution and brain health



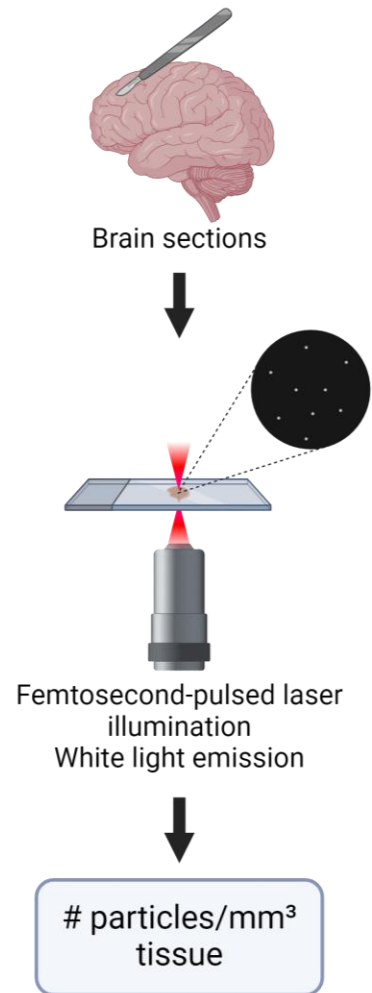
# Air pollution and brain health



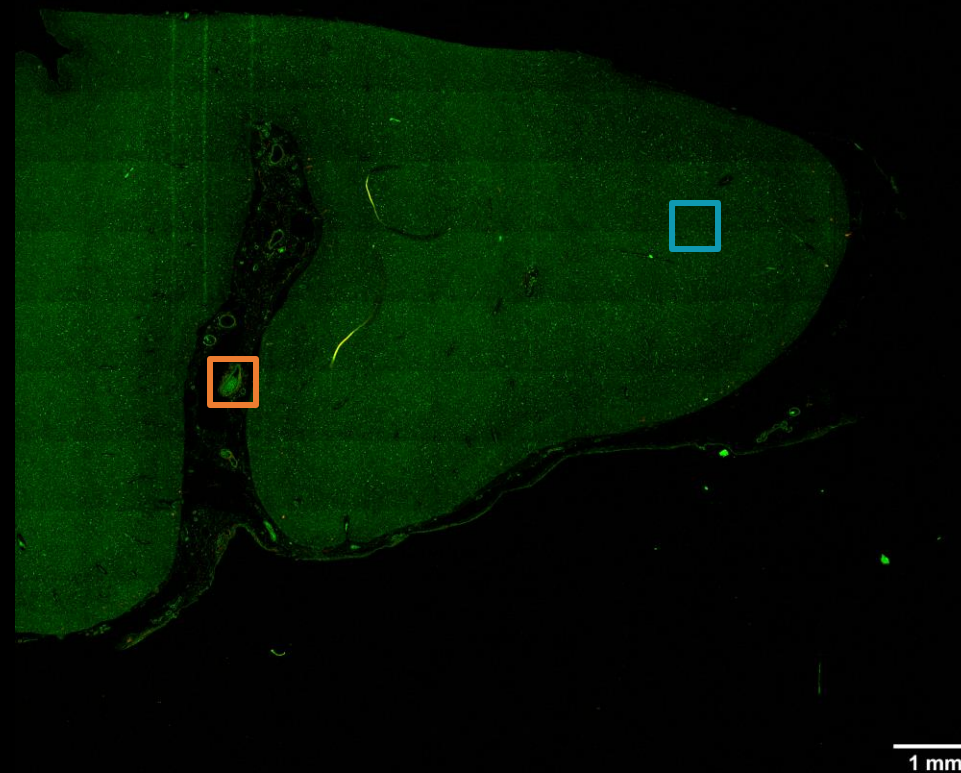
# Air pollution and brain health



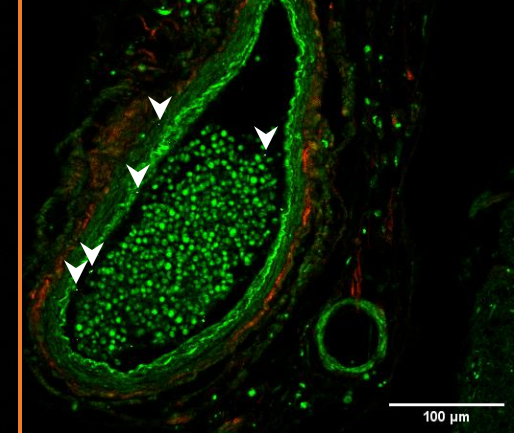
# Accumulation of ambient black carbon particles within key memory related brain regions



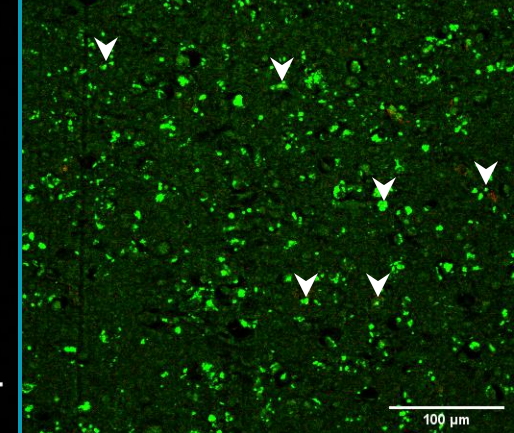
Overview



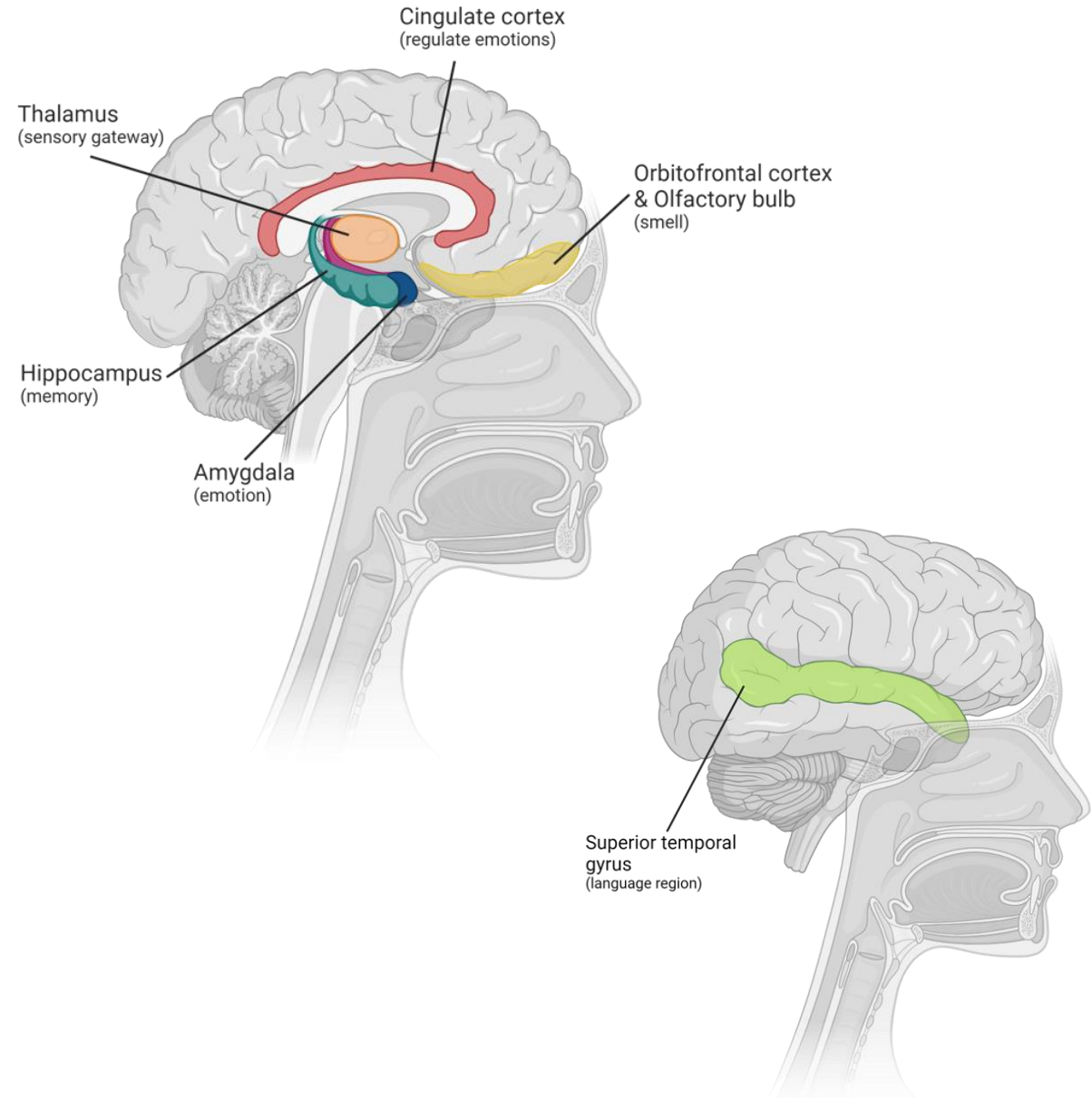
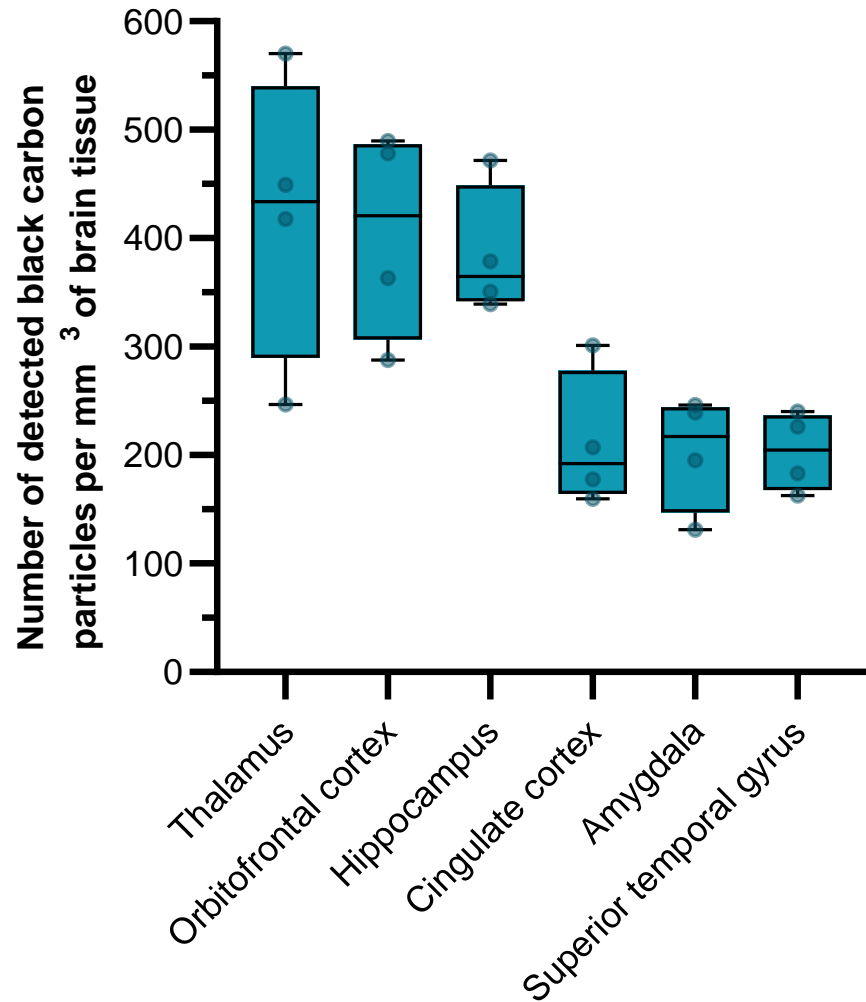
Blood vessel



Tissue



# Accumulation of ambient black carbon particles within key memory related brain regions



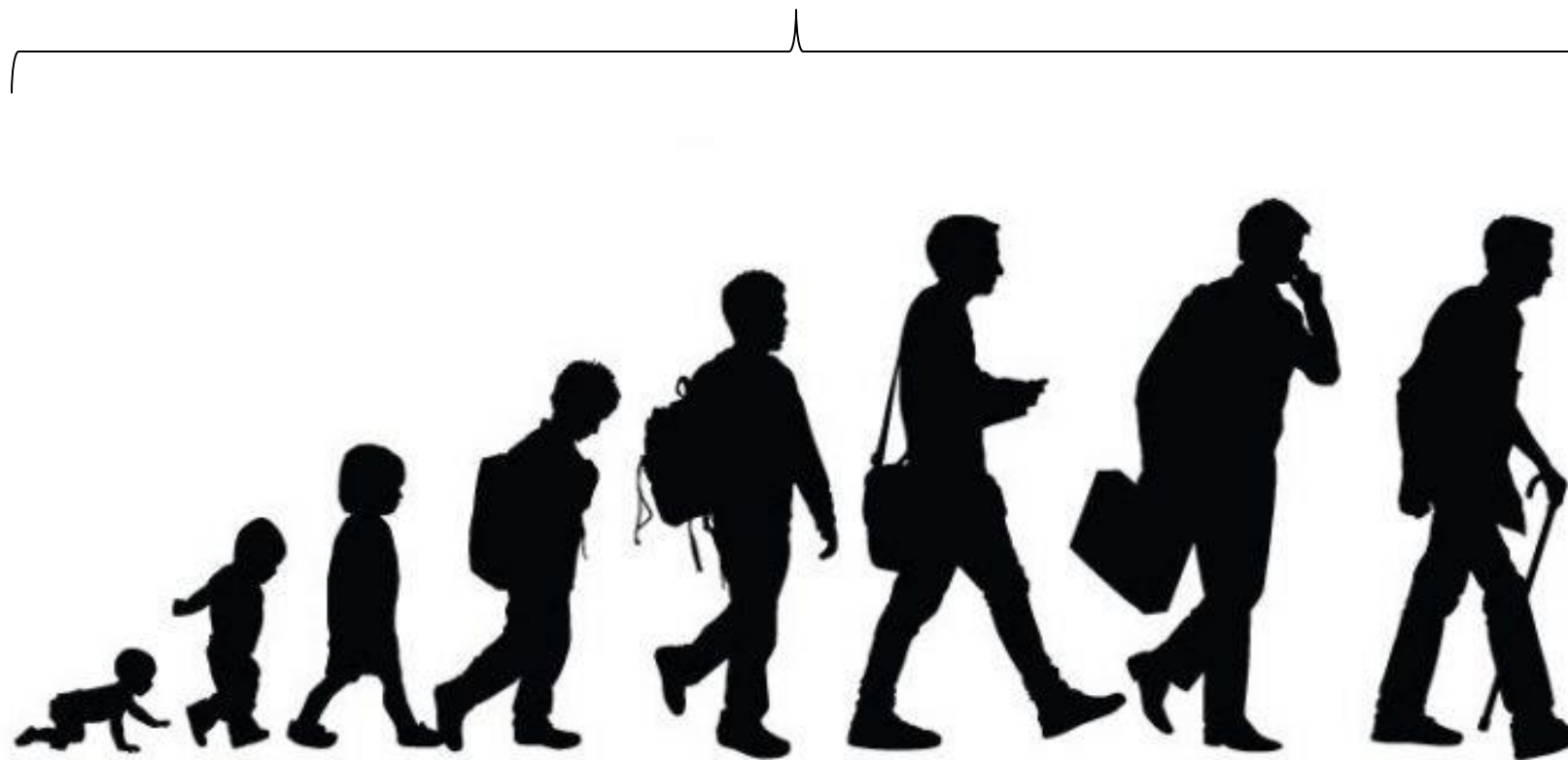


# Developmental origins of health and disease (DOHaD)

What happens here



Can influence health here



# ASPaNO

## Airborne Soot Particles and Neurobiological Outcomes

### Objective

#### **Early life exposure**

***In utero***



**Pup**



Impact of early life exposure to CNP's on  
brain development?

# ASPaNO

## Airborne Soot Particles and Neurobiological Outcomes

### Objective

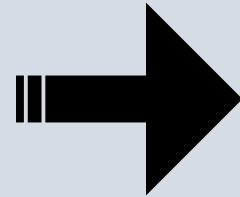
#### Early life exposure

*In utero*



Impact of early life exposure to CNP's on brain development?

**Pup**



#### Adult re-exposure



Is there a priming effect of CNP's exposure on cognitive behavior?

# Early life exposure

***In utero***

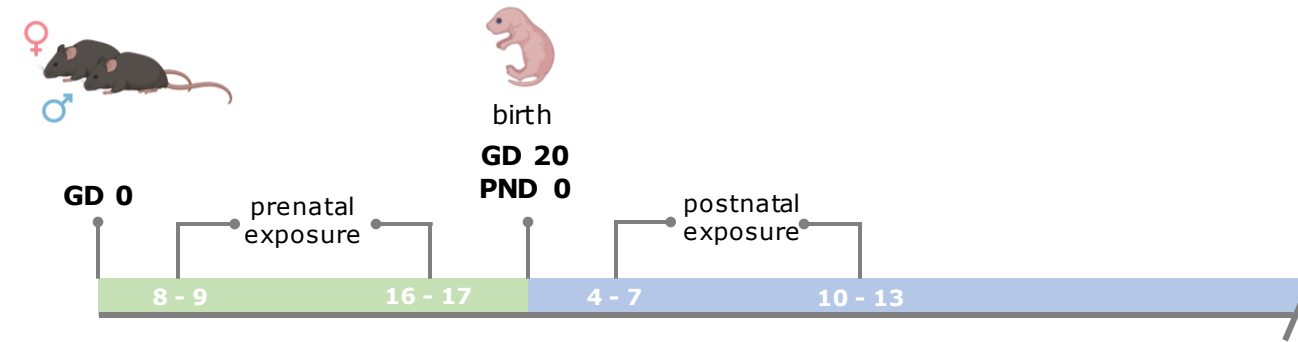


**Pup**



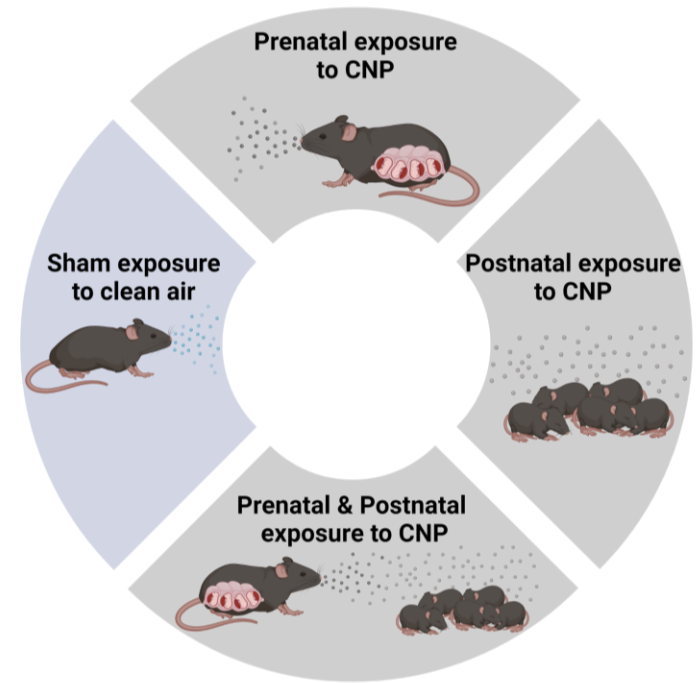
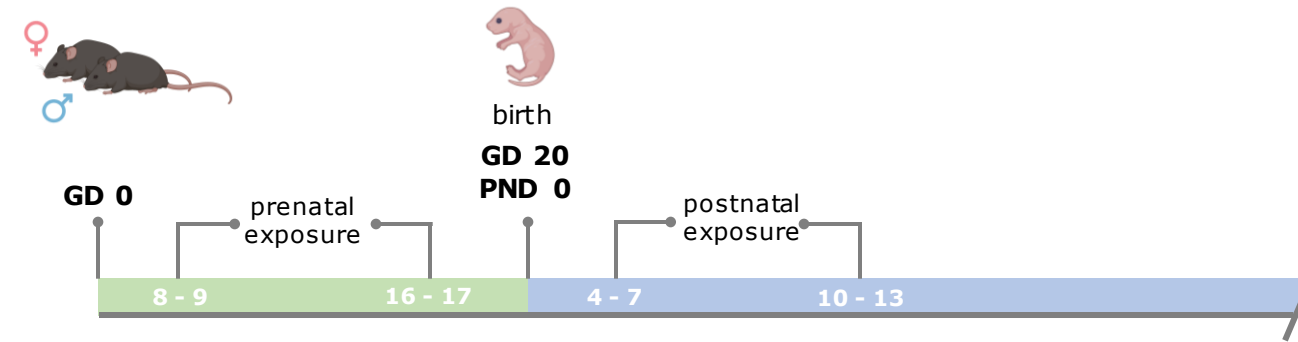
Impact of early life exposure to CNP's on brain development?

# Experimental timeline



GD = gestational day (mating = day 0), PND = postnatal day (birth = day 0)

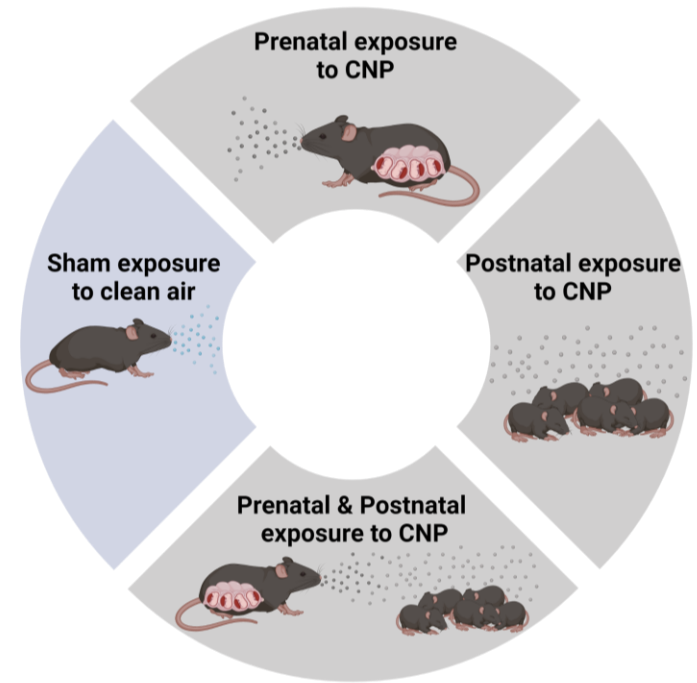
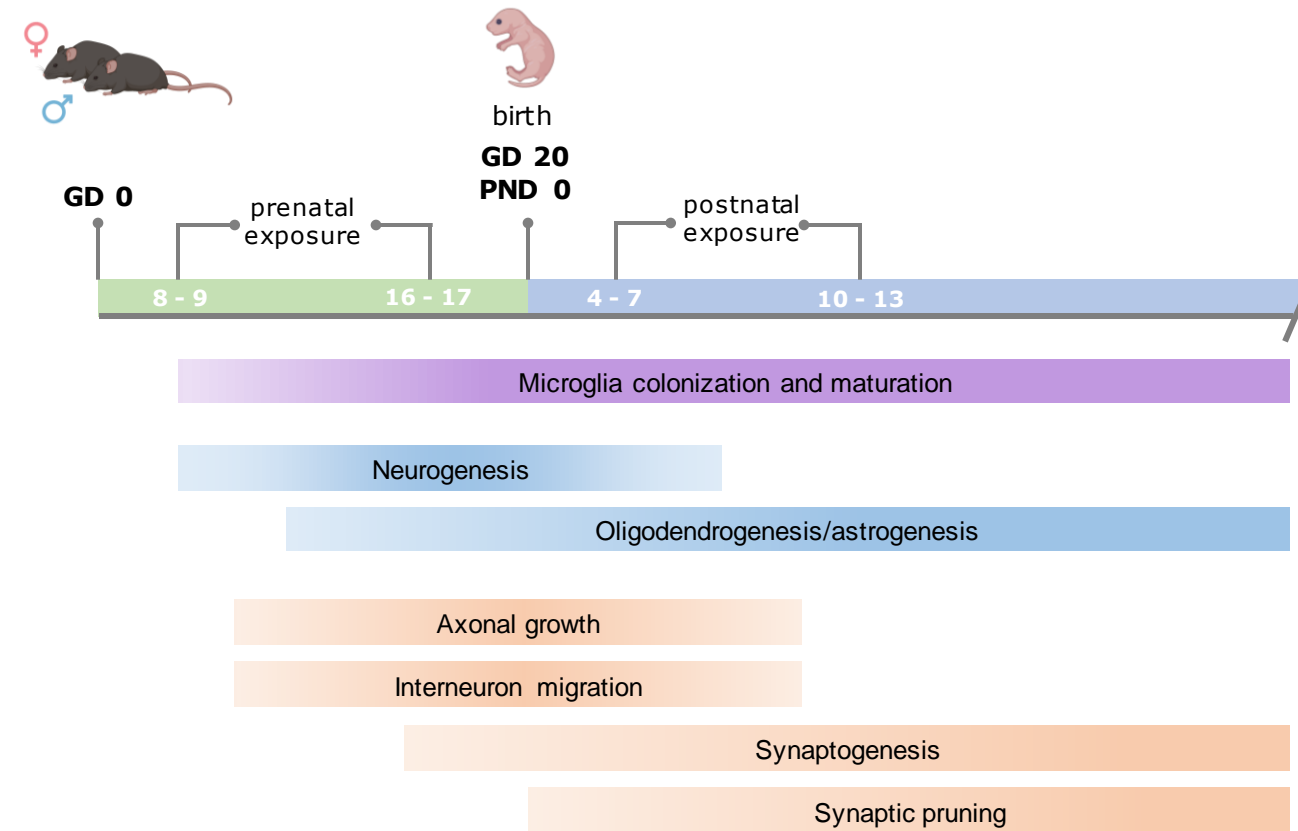
# Experimental timeline



CNPs = carbon nanoparticles

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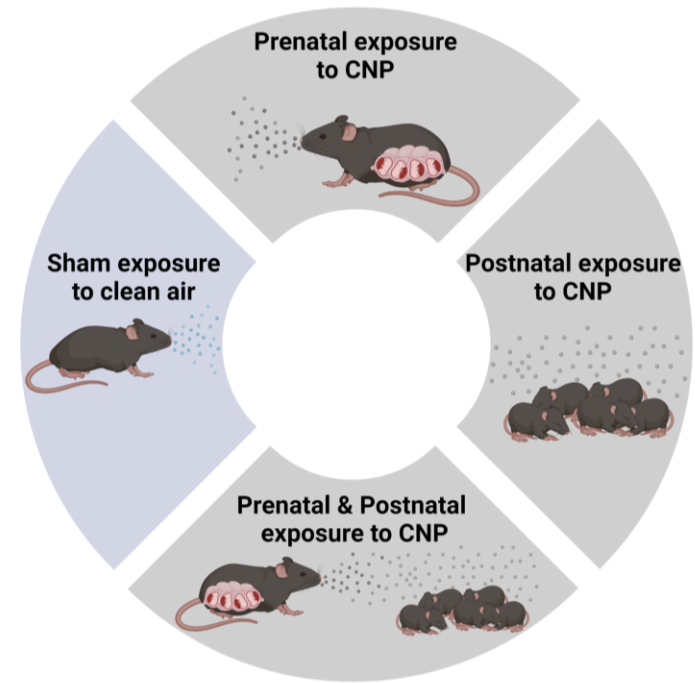
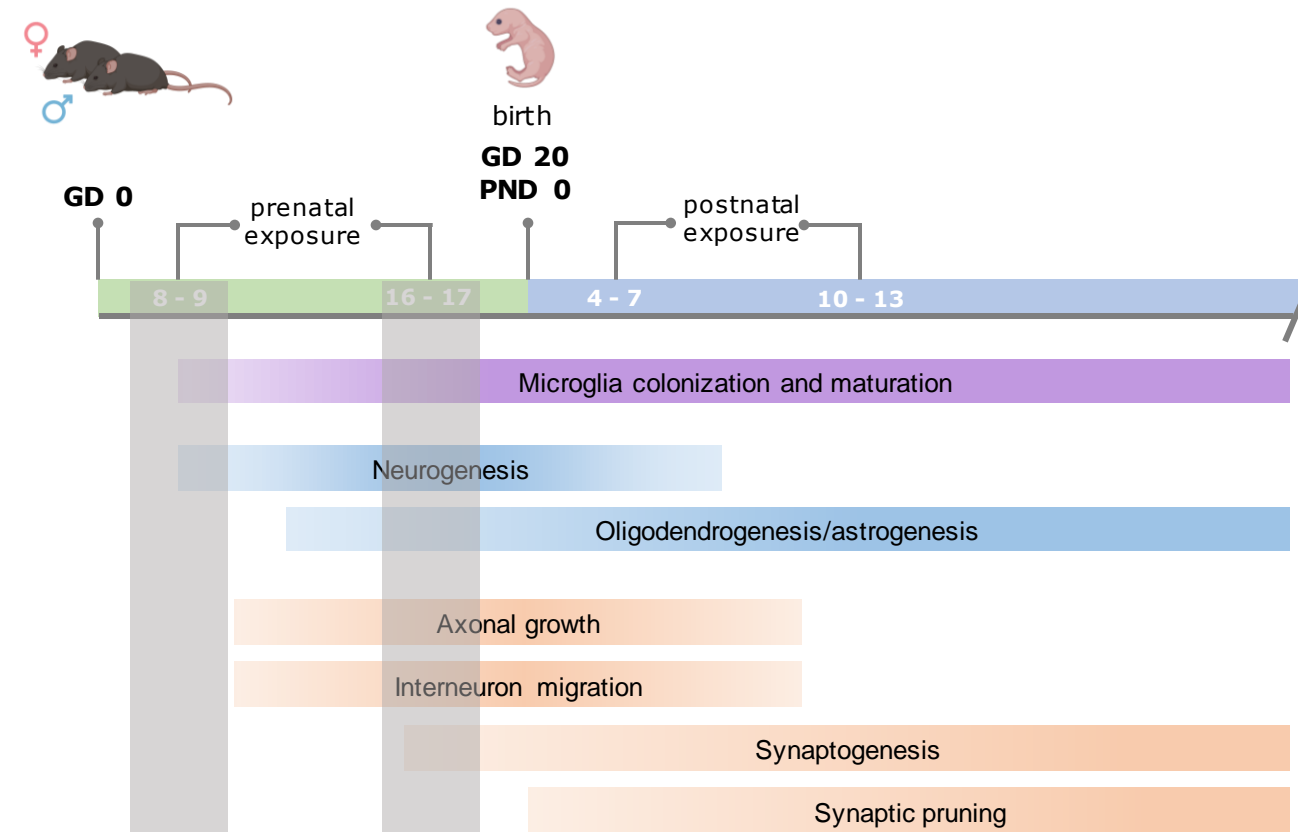
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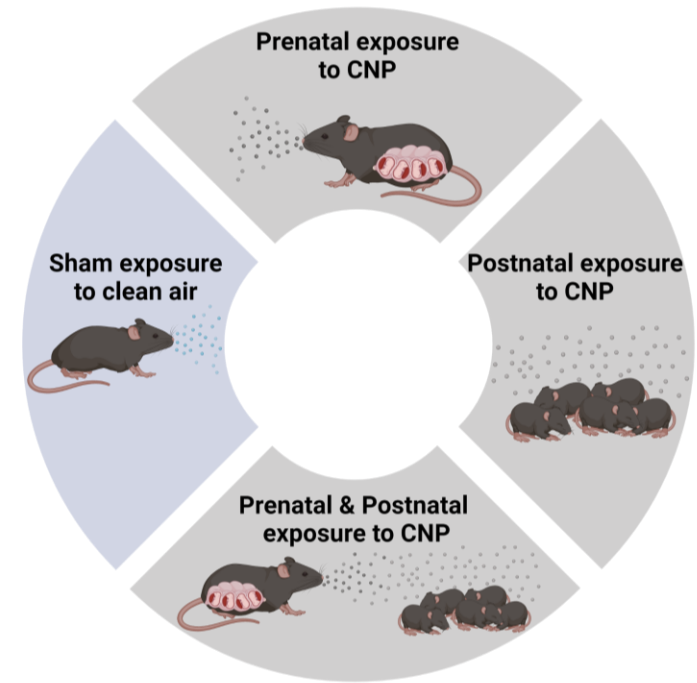
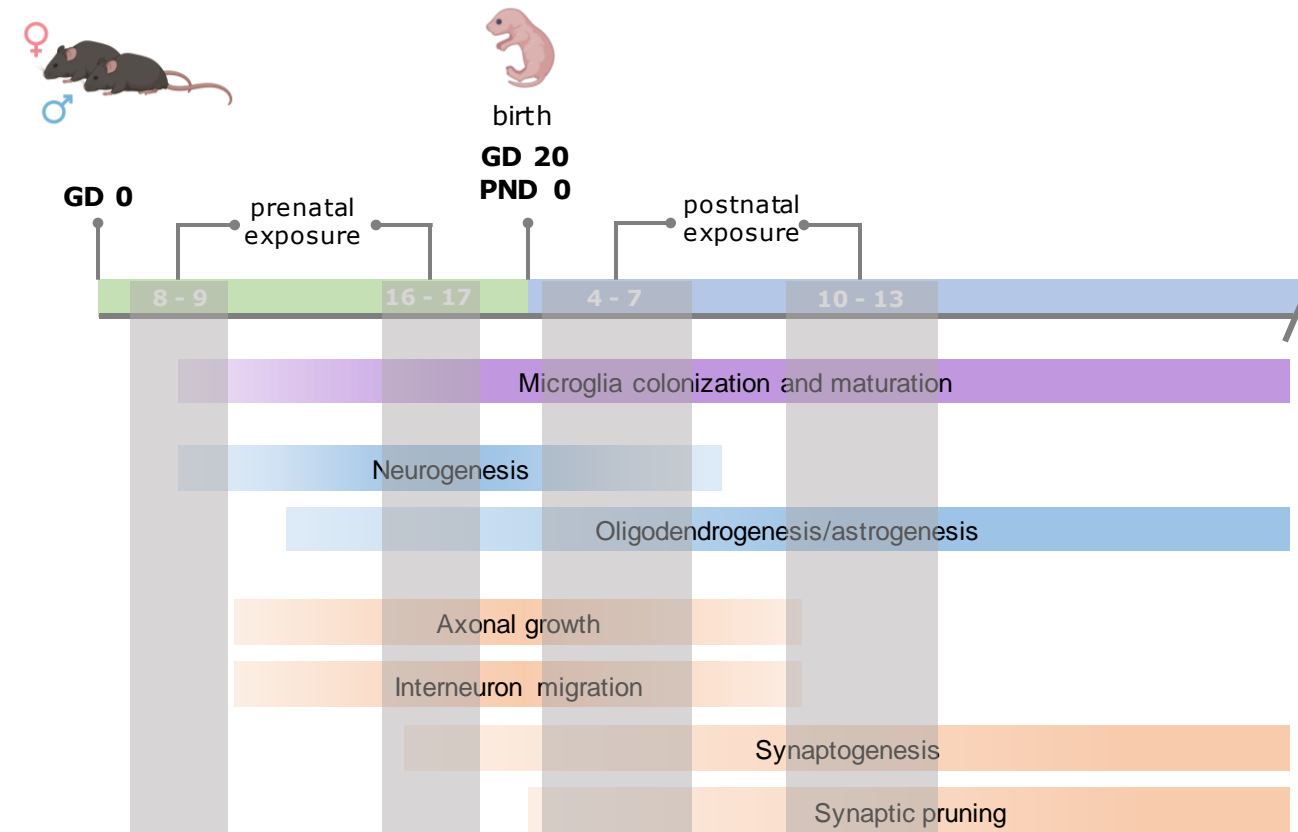


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# Experimental timeline



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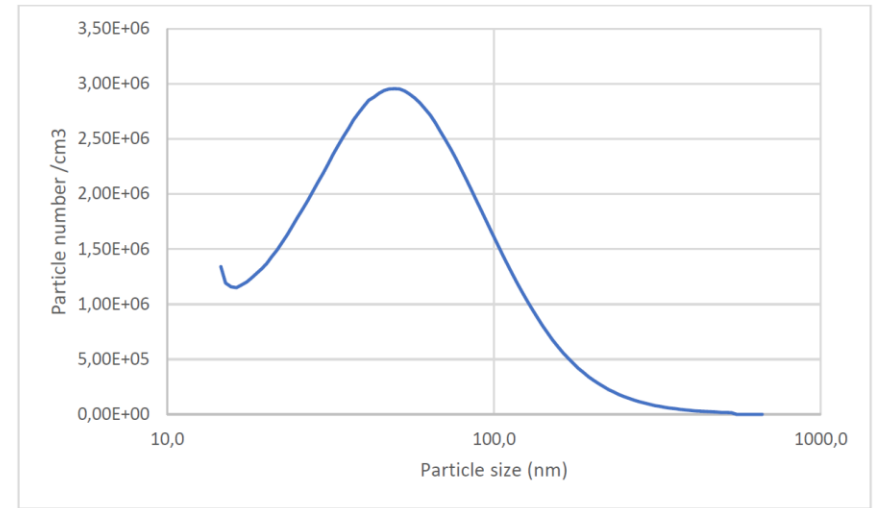
# Exposure to carbon nano particles



Whole-body inhalation units

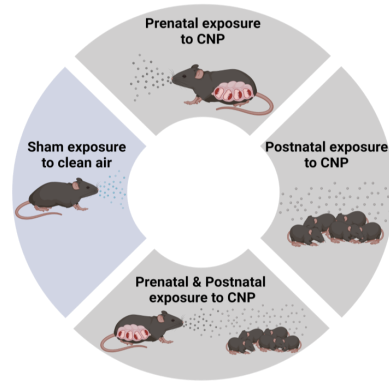


Particle generator

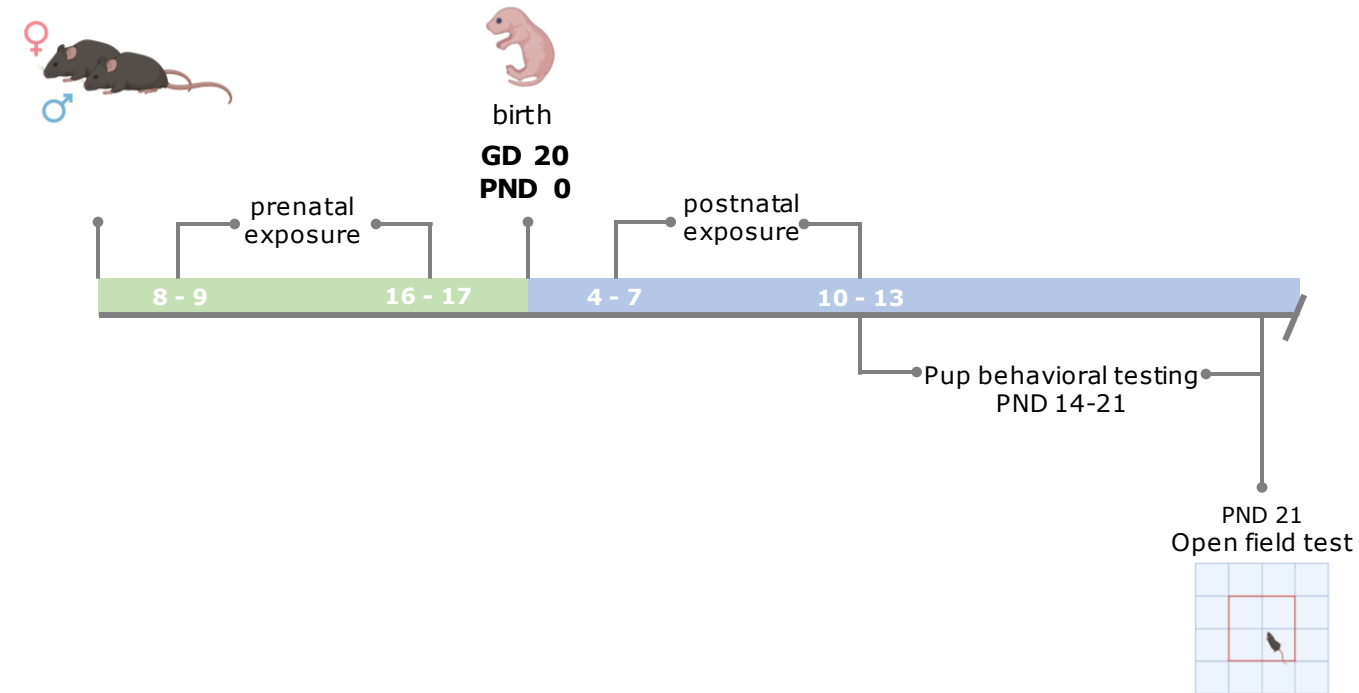


Top view of cage

# Experimental timeline

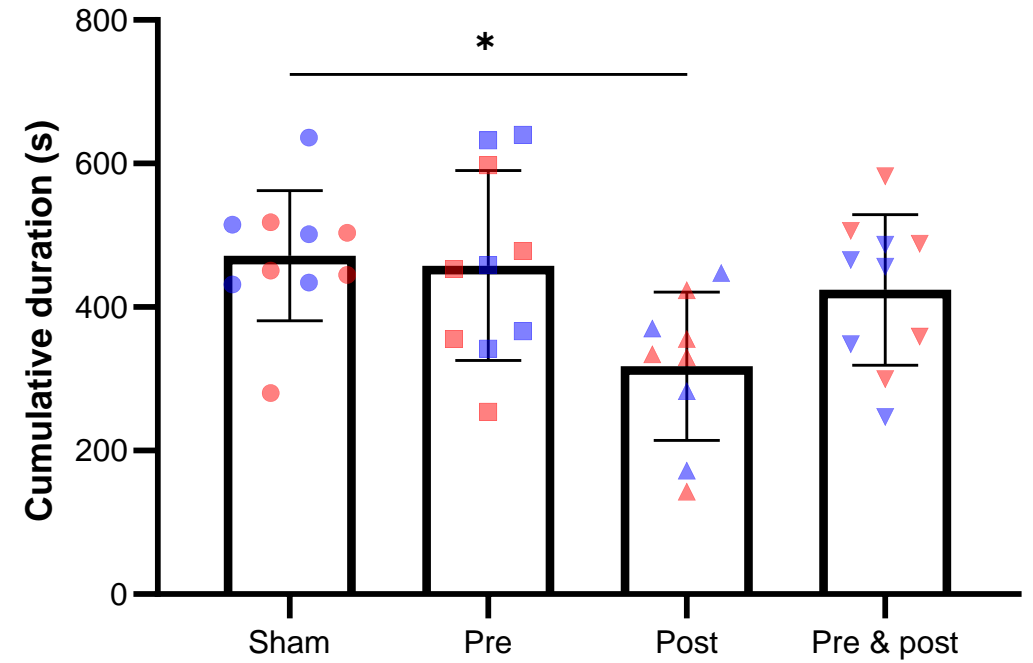
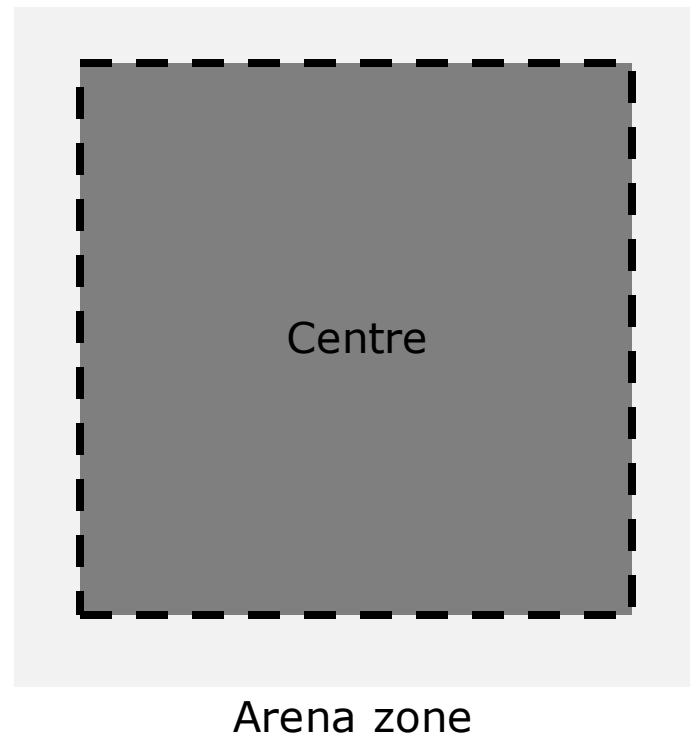


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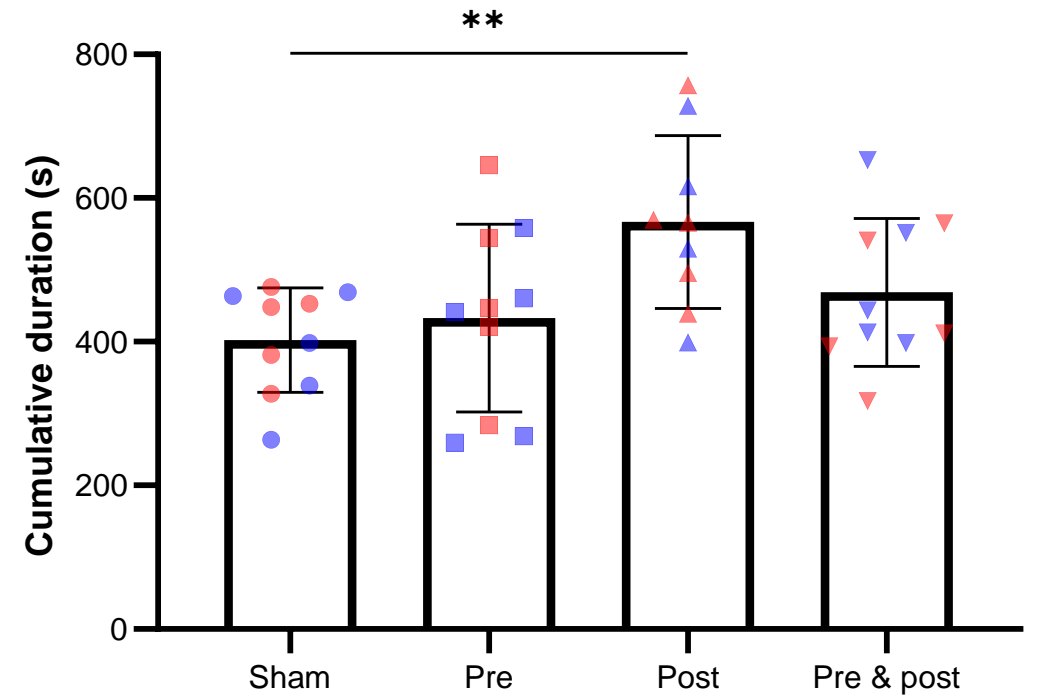
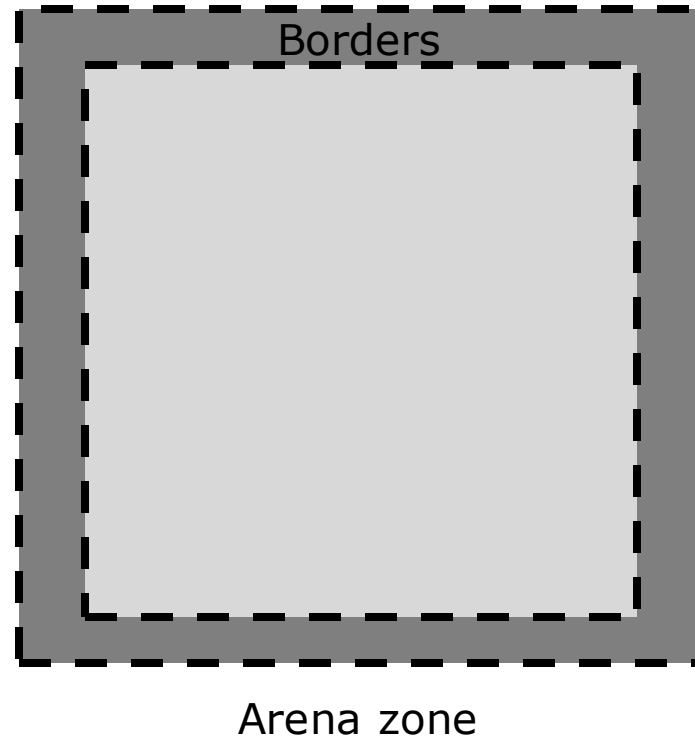
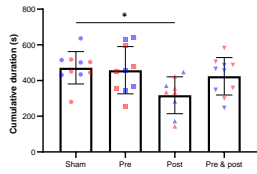
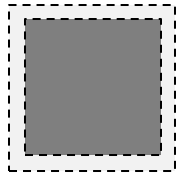
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# Postnatally exposed offspring shows altered behaviour in the open field test



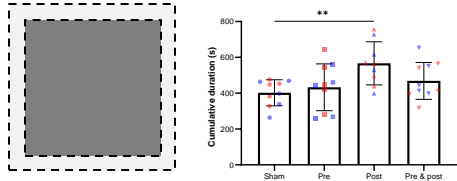
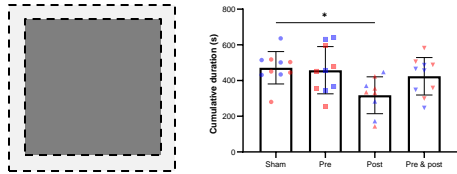
\*One-way ANOVA; ● red symbols = females and ● blue symbols males

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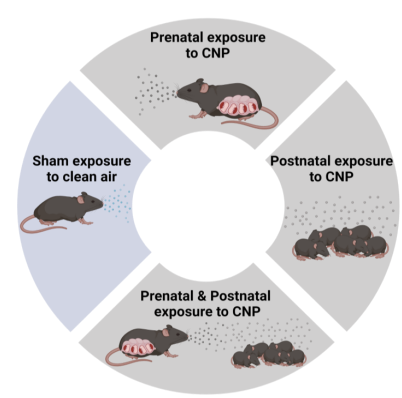


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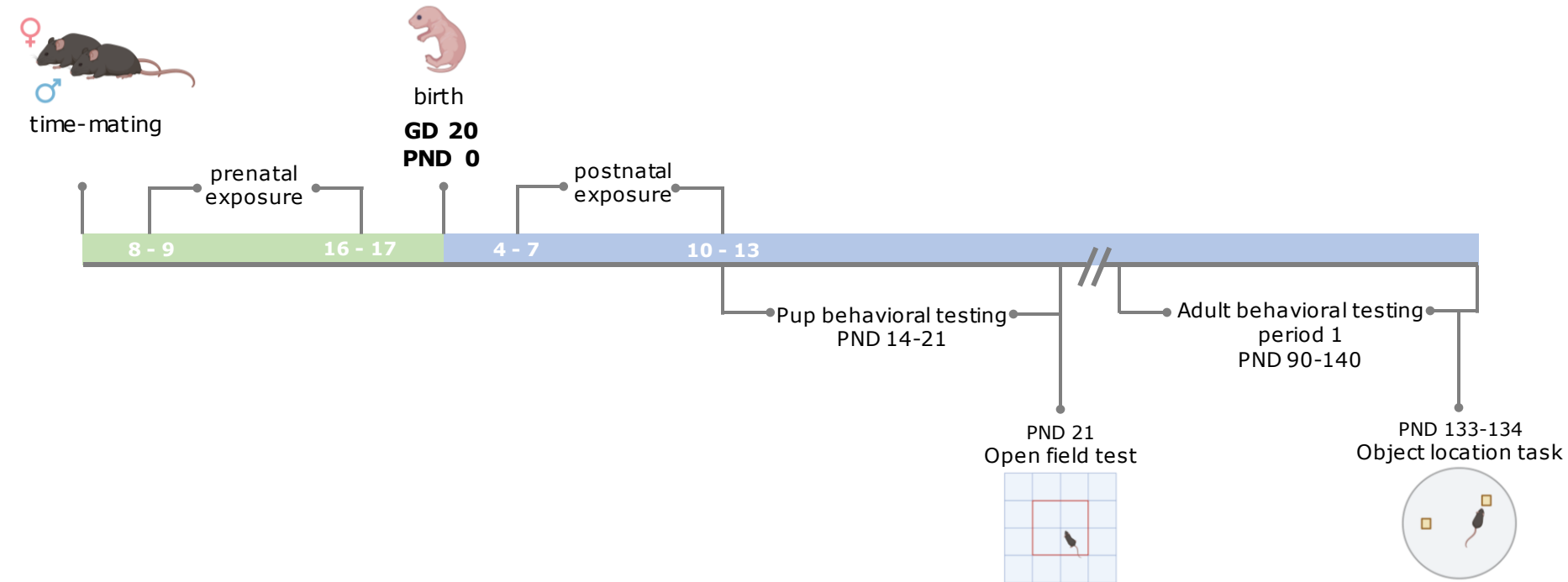
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# Experimental timeline

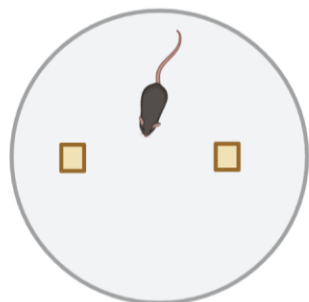


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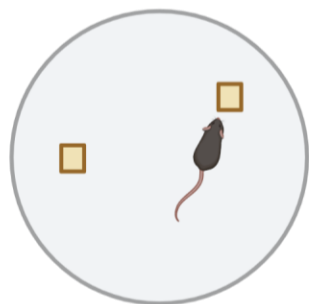


GD = gestational day (mating = day 0), PND = postnatal day (birth = day 0)

# Exposure during early life does not alter cognitive behavior of mature adult mice

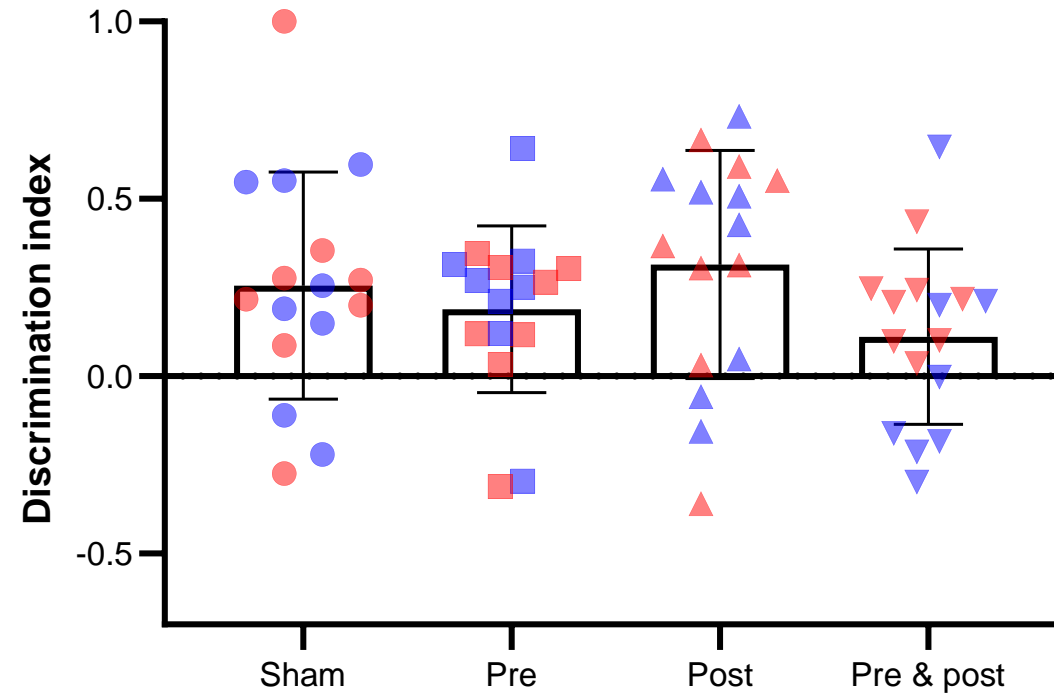
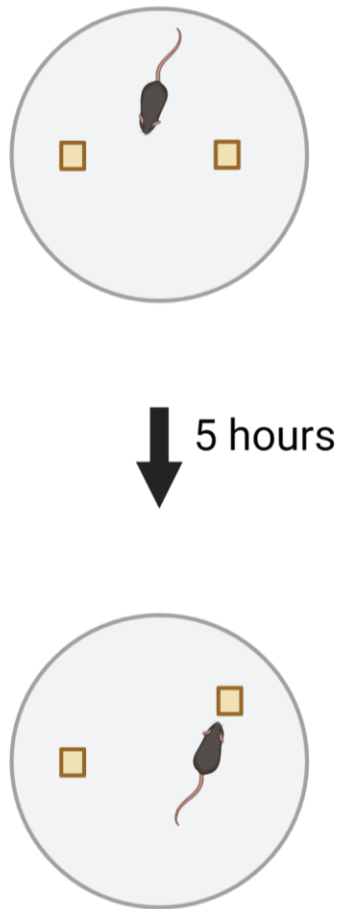


↓ 5 hours

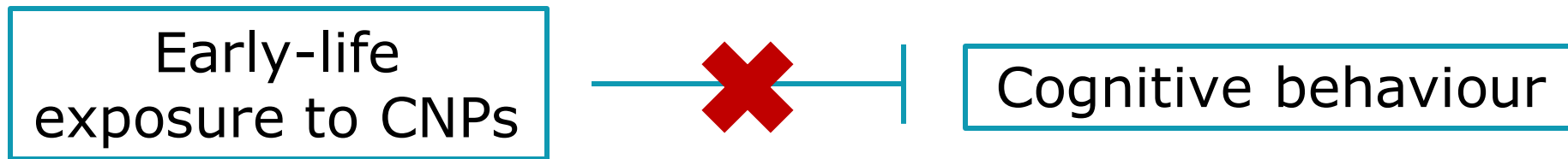




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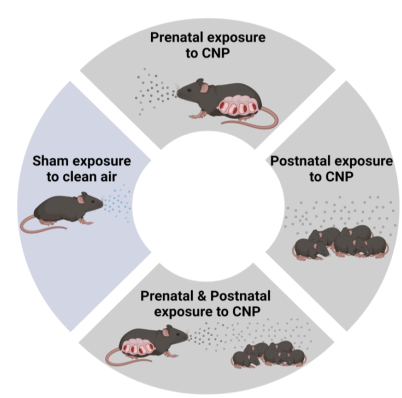


# Adult re-exposure

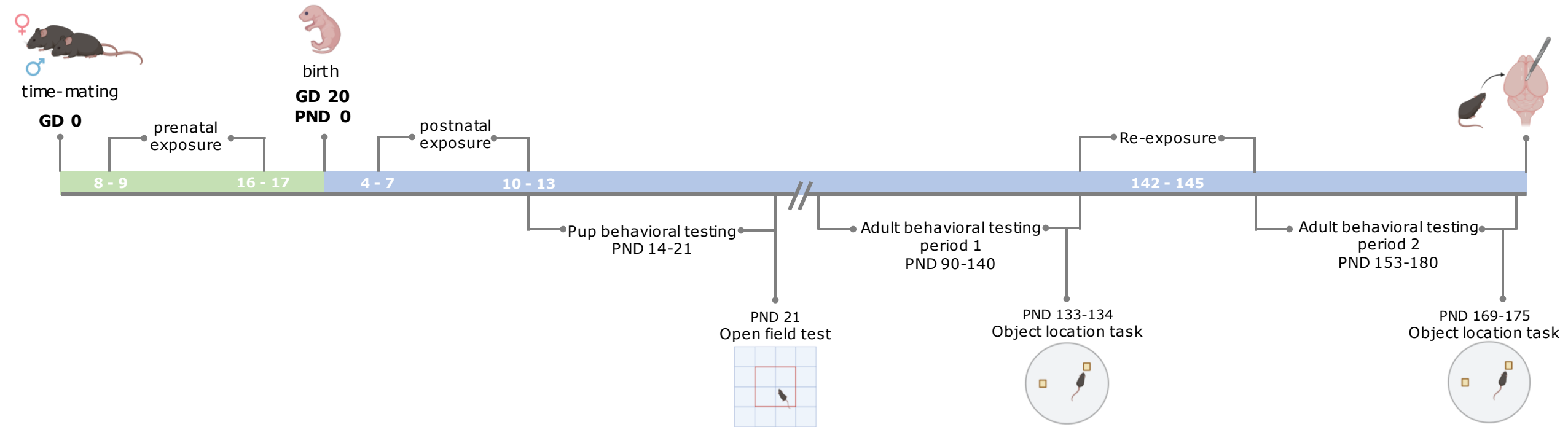


Is there a priming effect of CNP's exposure on cognitive behavior?

# Experimental timeline

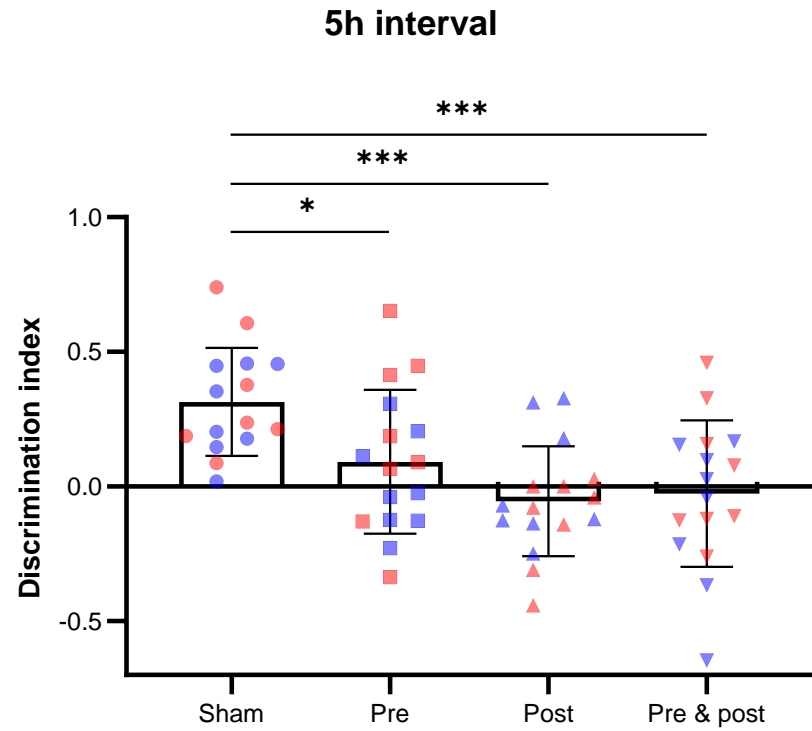


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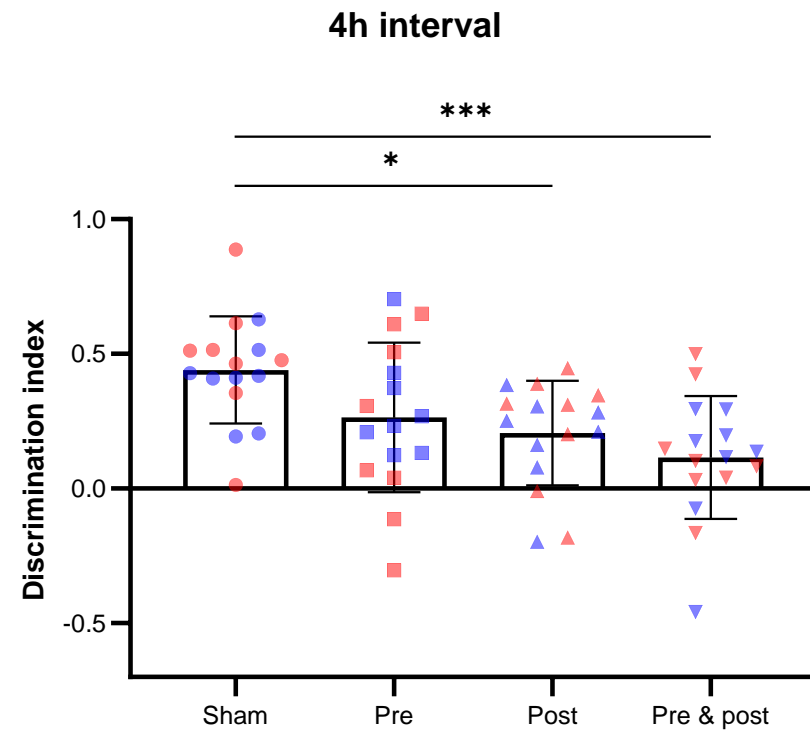
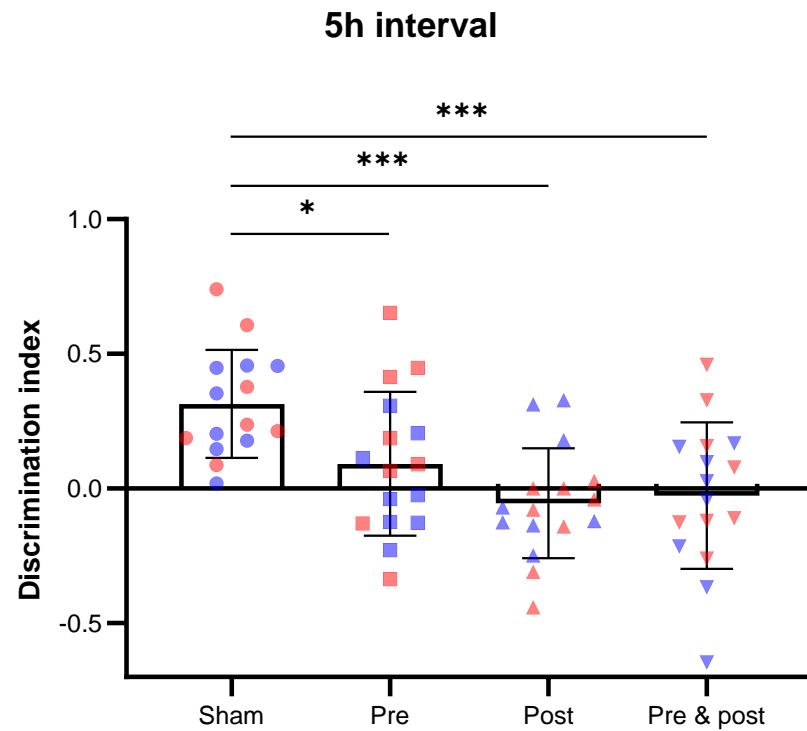
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# Re-exposure to air pollution affects spatial memory of adult mice in the object location task



\*One-way ANOVA; ● red symbols = females and ● blue symbols males

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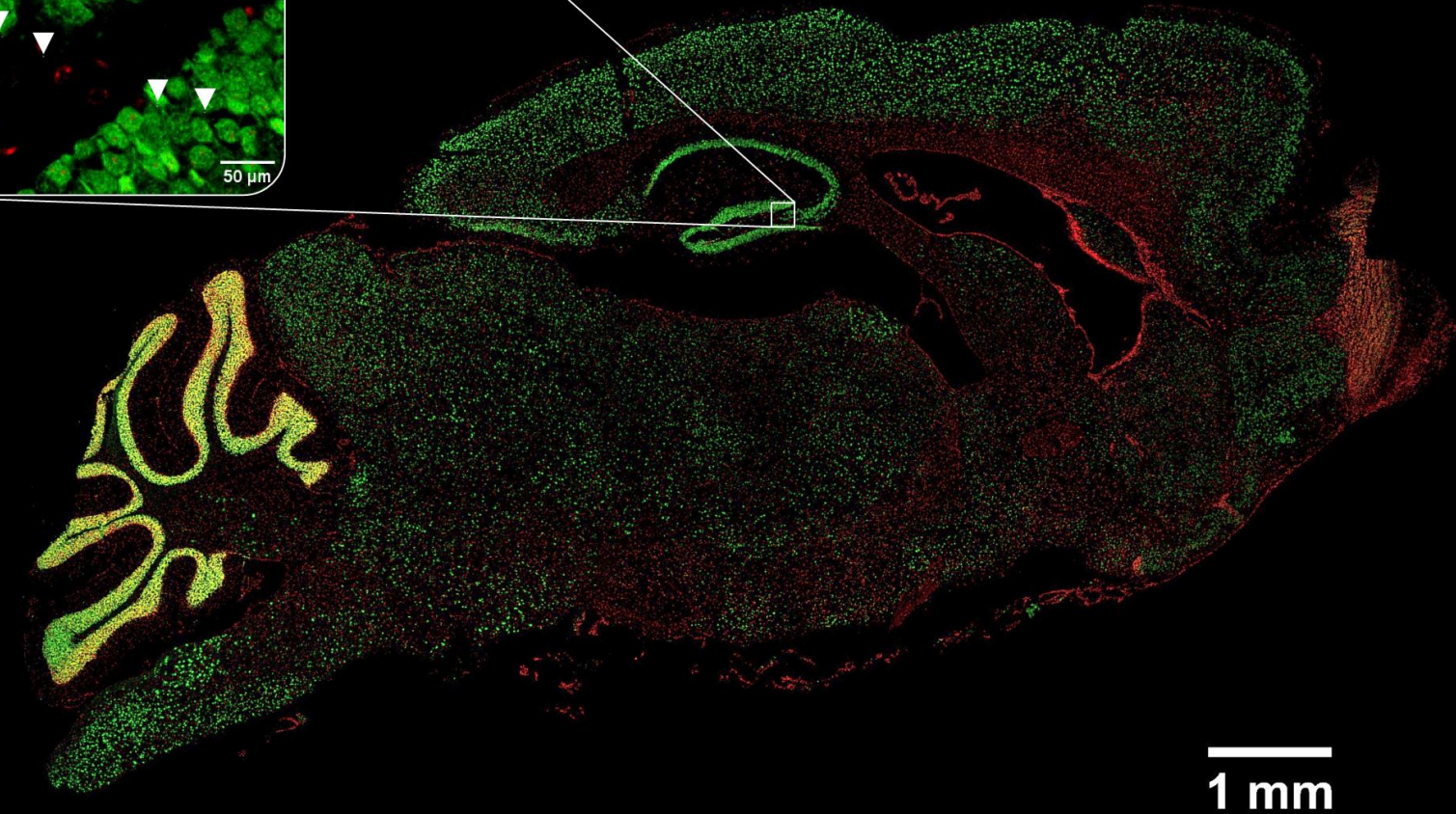
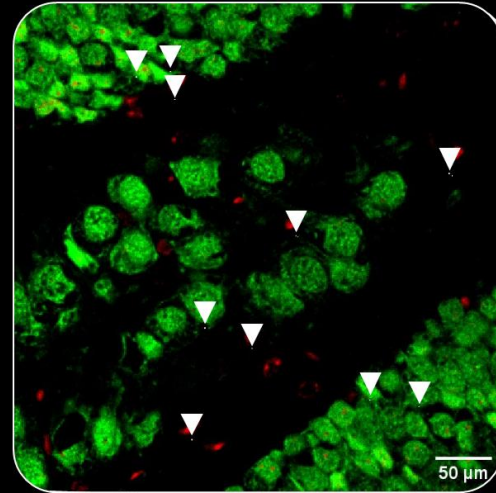


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Re-exposure to air pollution affects spatial memory of adult mice in the object location task



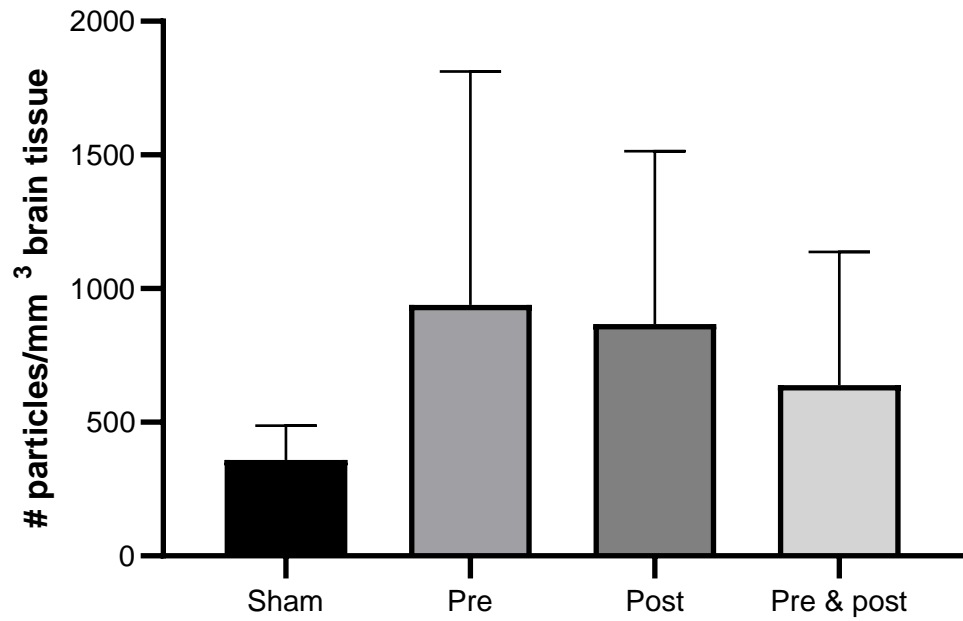
Carbon particles can be observed  
in the hippocampal region of  
exposed mouse brains



Neuronal cells are stained with neuronal  
nuclear maker (NeuN, green) and a nuclear  
stain (red)

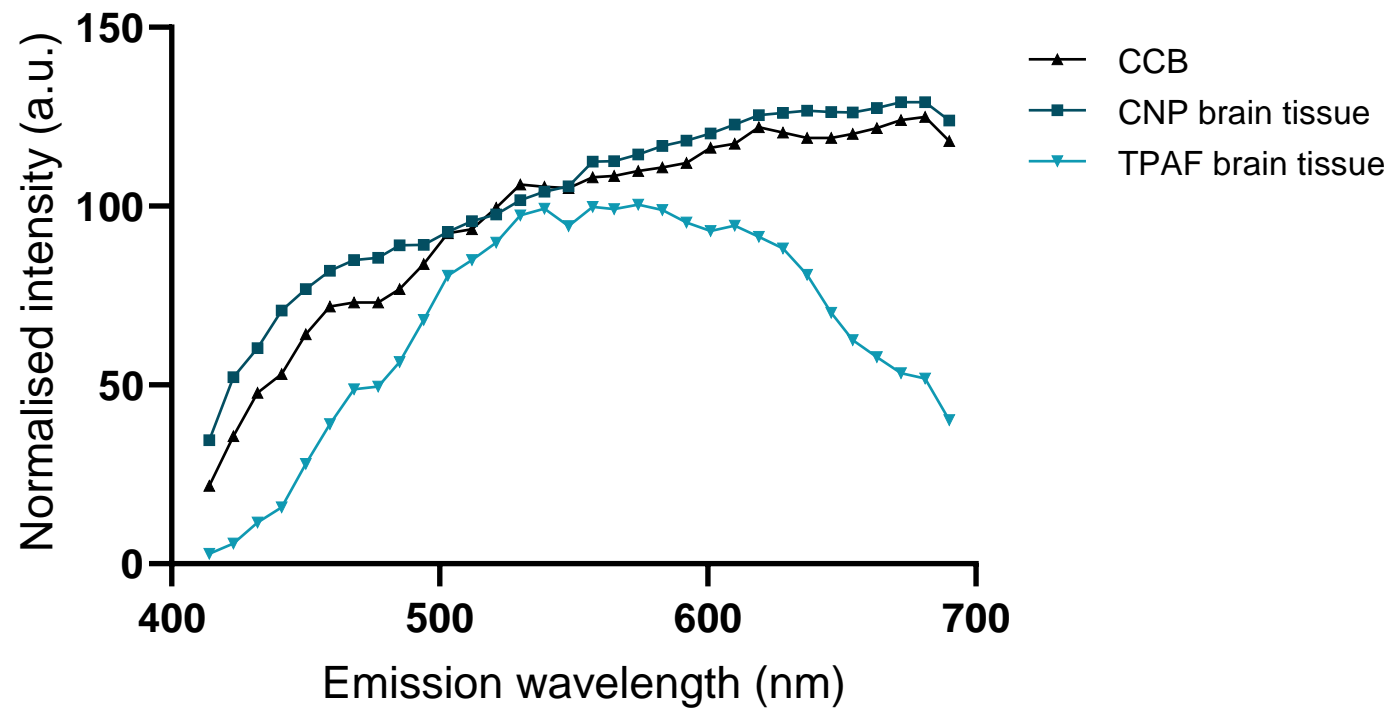
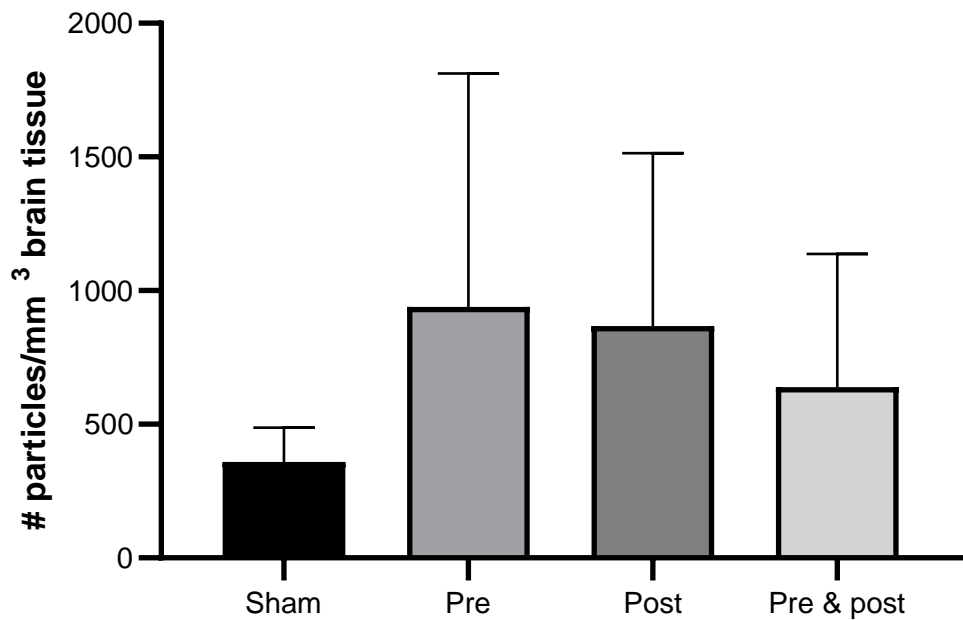


# Particle transfer into the brain

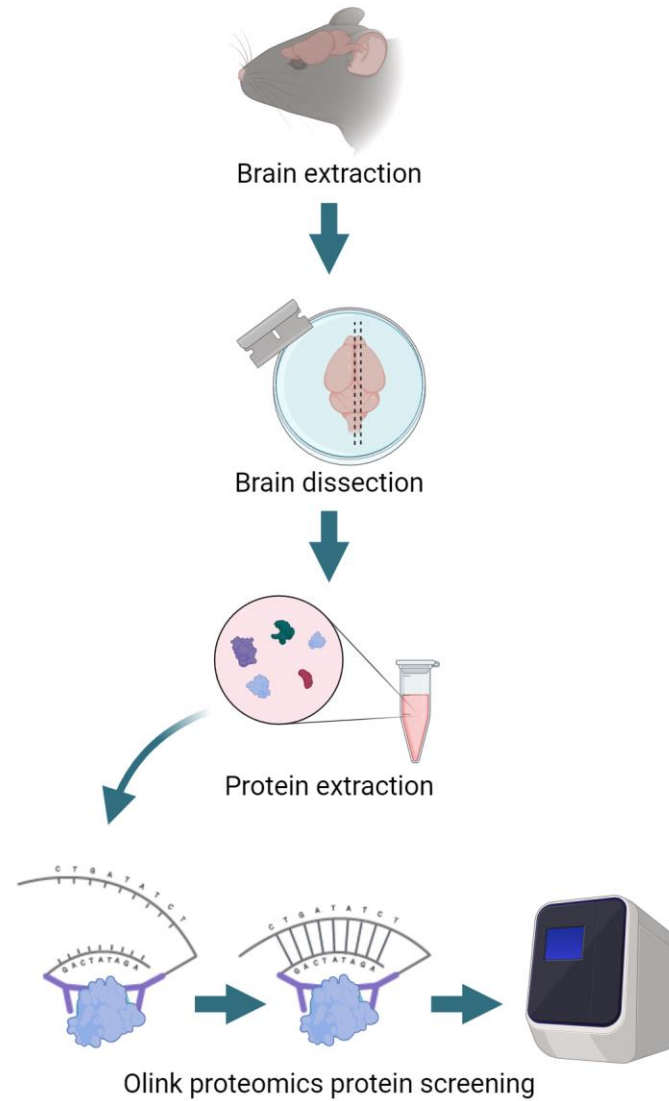


CNPs = carbon nanoparticles, CCB = conductive carbon black, and TPAF = background signals

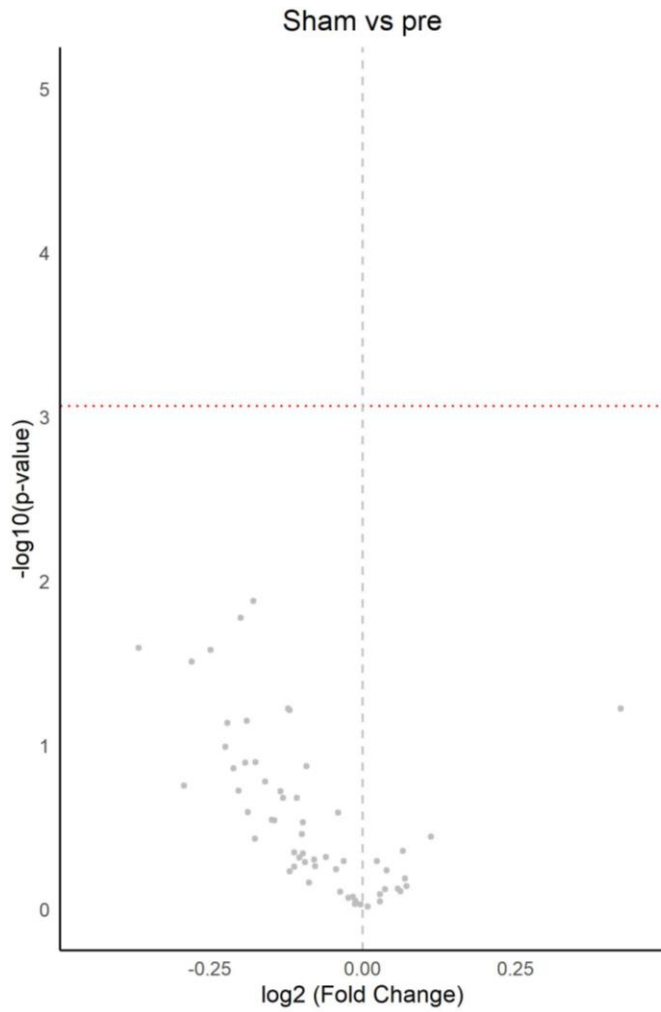
# Particle transfer into the brain



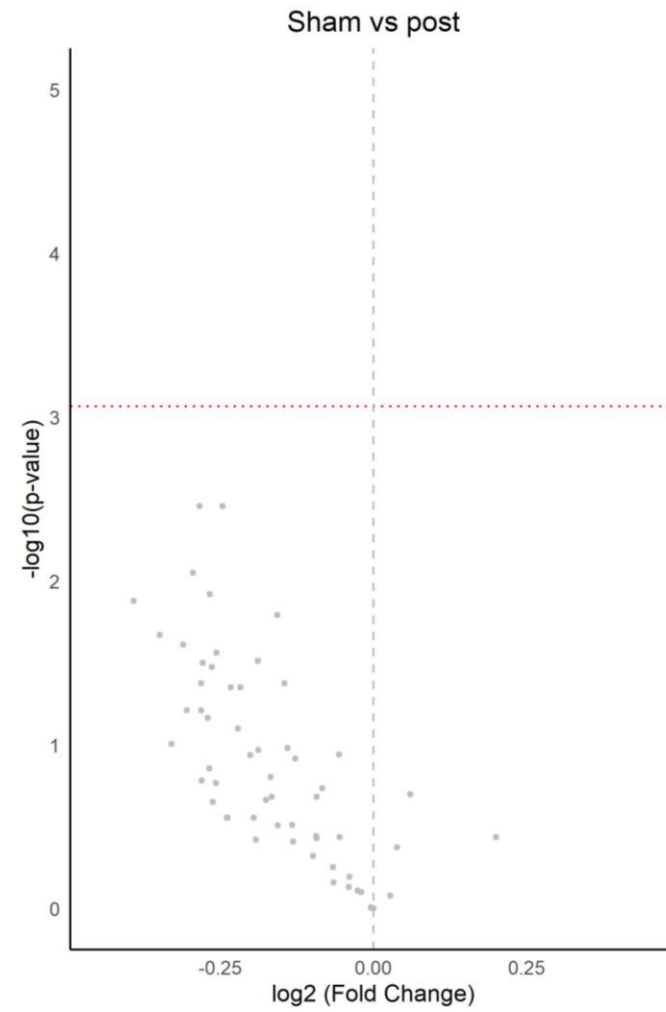
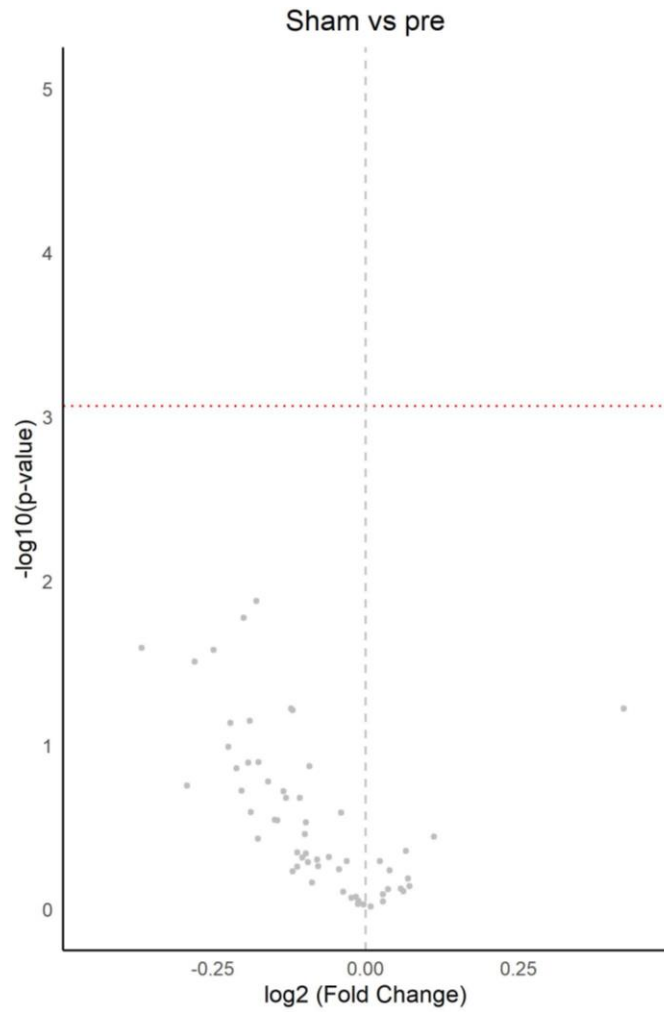
# Proteomic profiling of exposed mice brain



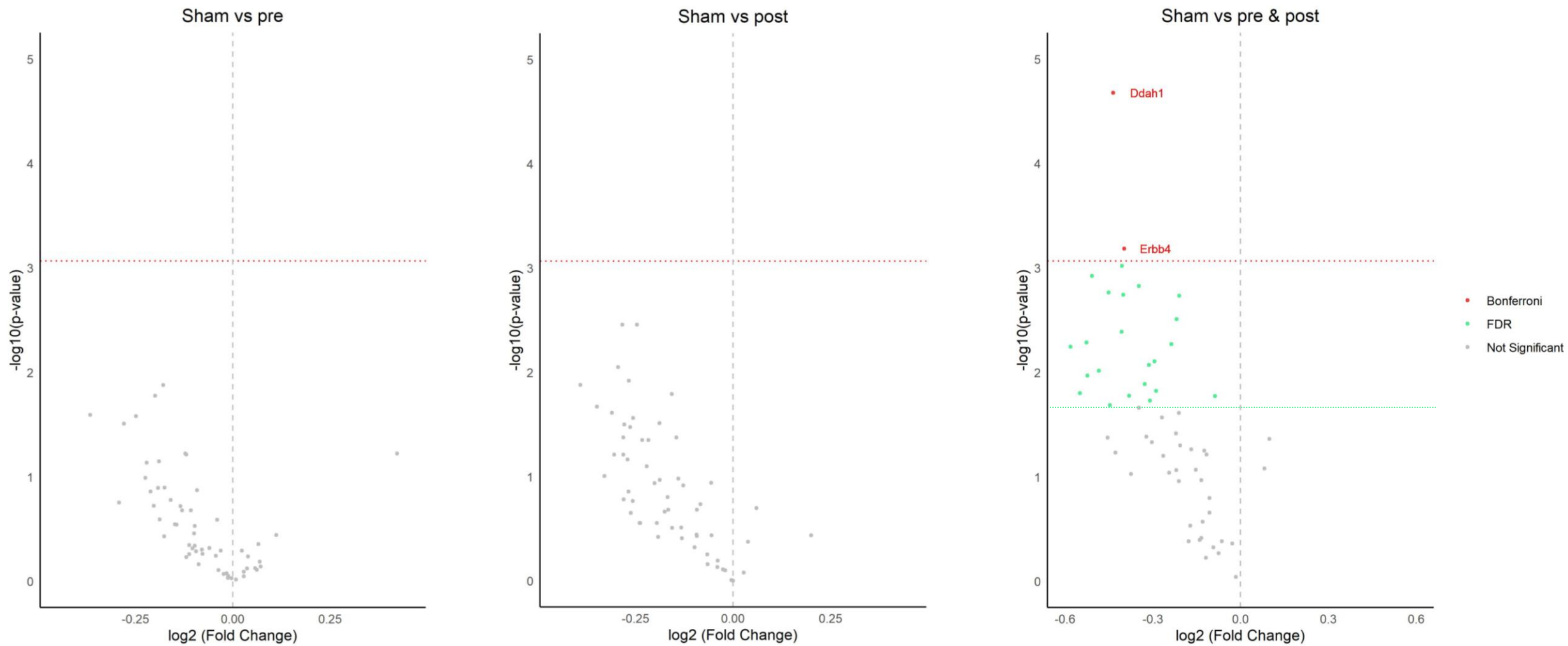
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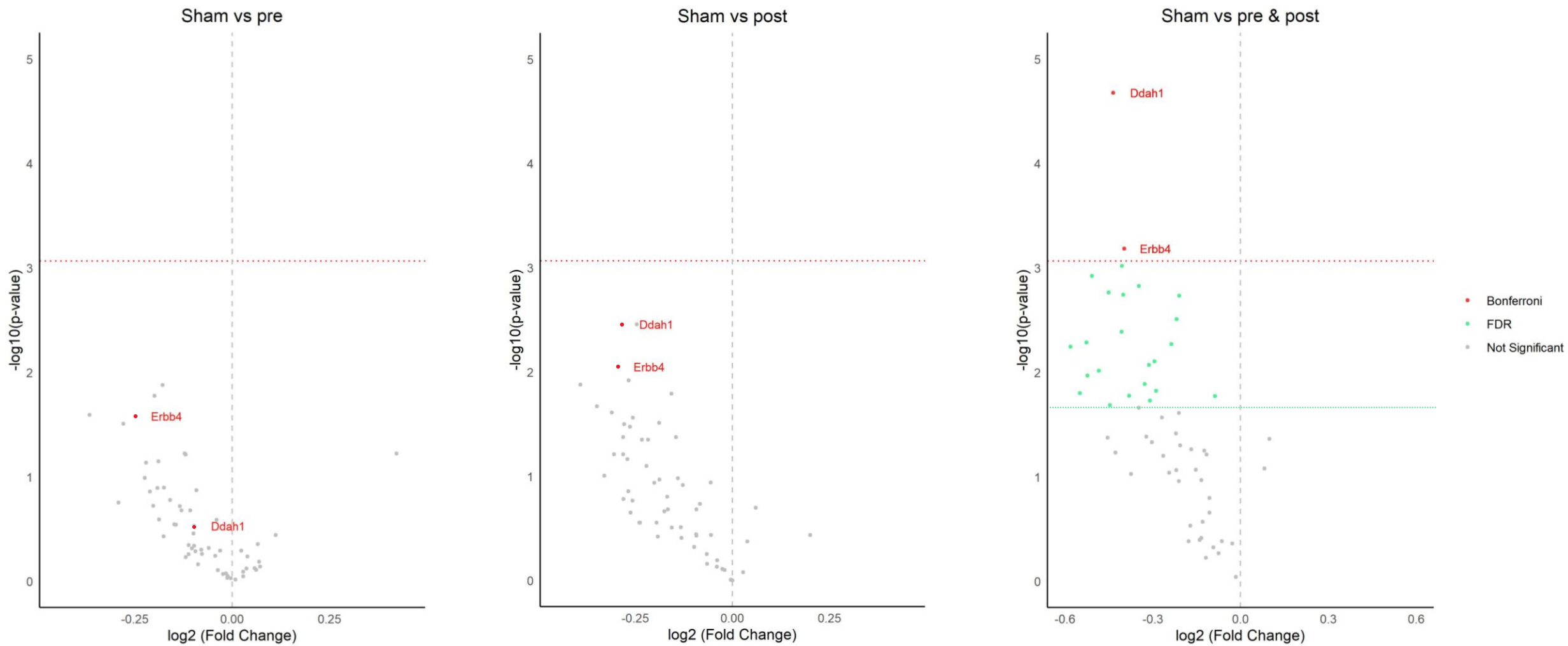
# Proteomic profiling of exposed mice brain



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## CONCLUSION

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Higher levels of CNPs in the brains of pre- and postnatally exposed mice were related to **increased anxiety-like behaviour and impaired spatial memory** in exposed offspring.



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## STRENGTHS AND LIMITATIONS

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- Complete neurobehavioural assessment from birth to adulthood in mice
- Focused on the ultra fine fraction of air pollution

### LIMITATIONS

- Presence of background exposures may dilute the effects of the observed findings

## CONCLUSION

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Higher levels of CNPs in the brains of pre- and postnatally exposed mice were related to **increased anxiety-like behaviour and impaired spatial memory** in exposed offspring.

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### LIMITATIONS

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## FUTURE

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- Investigate potential underlying pathways
- Validation within our ENVIRONAGE birth cohort study to confirm our findings





IUF

LEIBNIZ RESEARCH  
INSTITUTE FOR  
ENVIRONMENTAL  
MEDICINE

## Collaborators

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Prof. Hannelore Bové  
Prof. Marcel Ameloot  
Prof. Tim S. Nawrot  
Prof. Tim Vanmierlo  
Prof. Flemming R. Cassee  
Prof. Michelle Plusquin



Rijksinstituut voor Volksgezondheid  
en Milieu  
*Ministerie van Volksgezondheid,  
Welzijn en Sport*

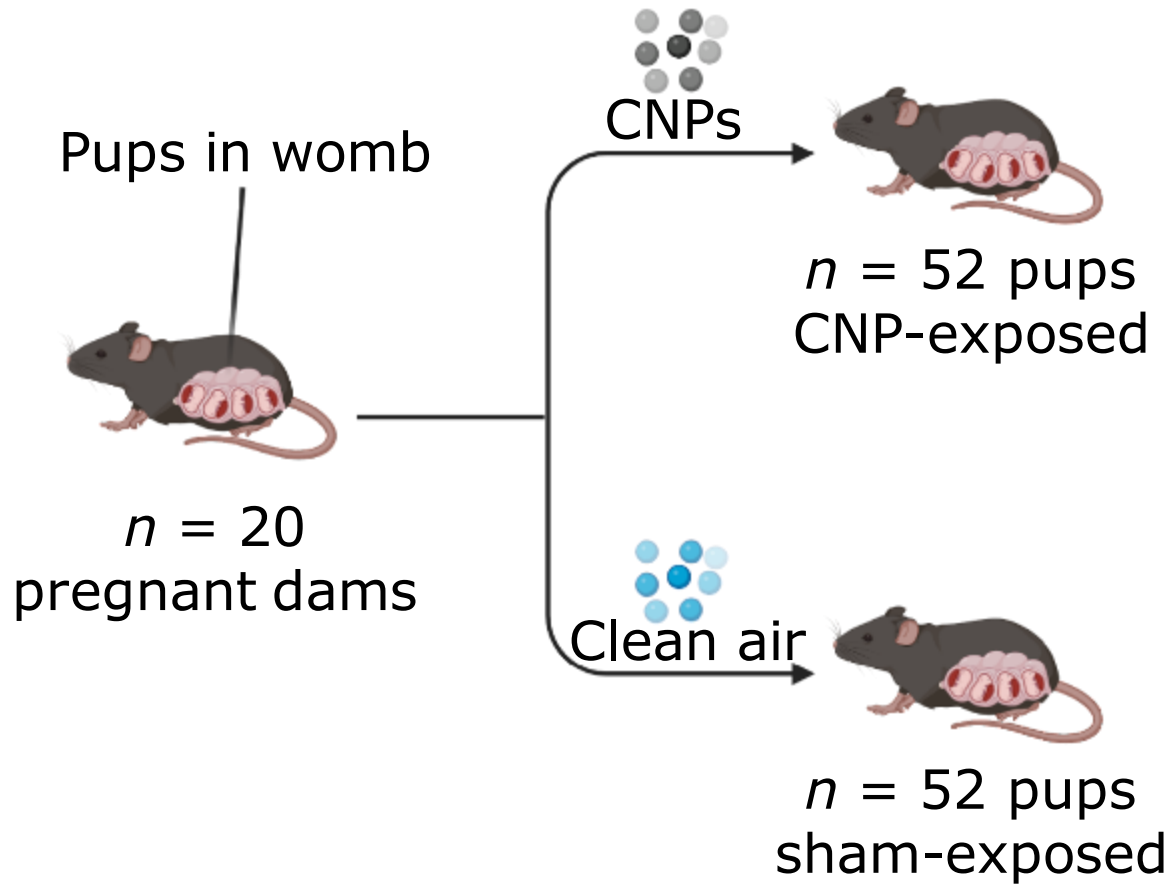
**CMK**  
CENTRUM  
VOOR MILIEUKUNDE



**UHASSELT**

# Experimental groups

**GD 8, 9, 16, 17**

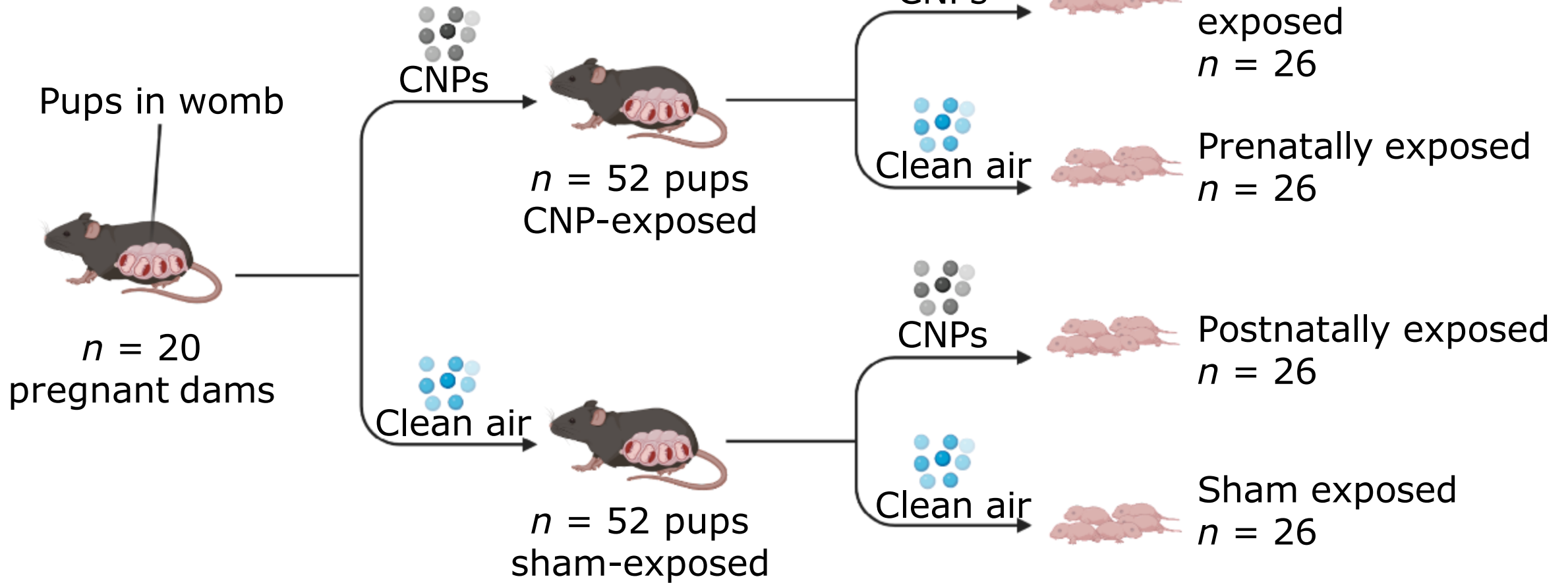


CNPs = carbon nanoparticles  
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# Experimental groups

**GD 8, 9, 16, 17**

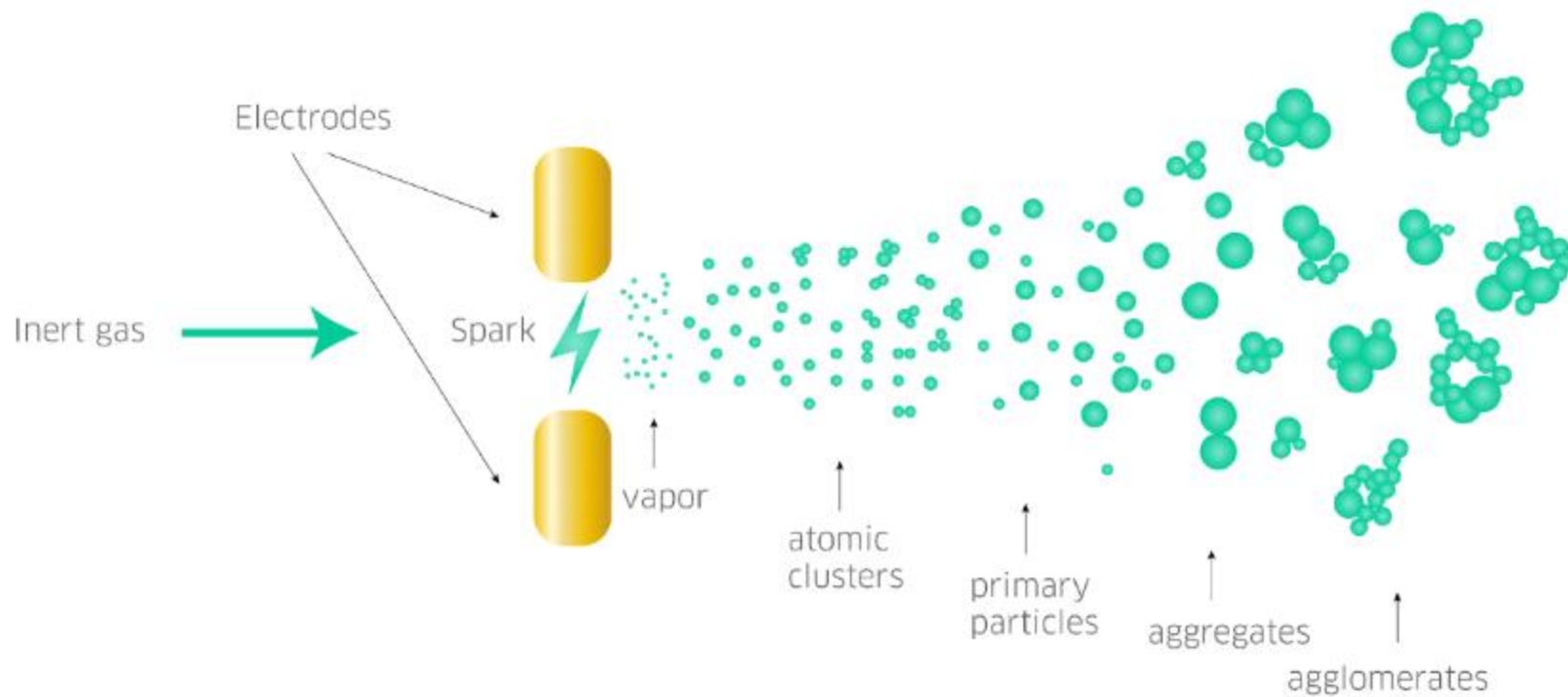
**PND 4-7; 10-13**



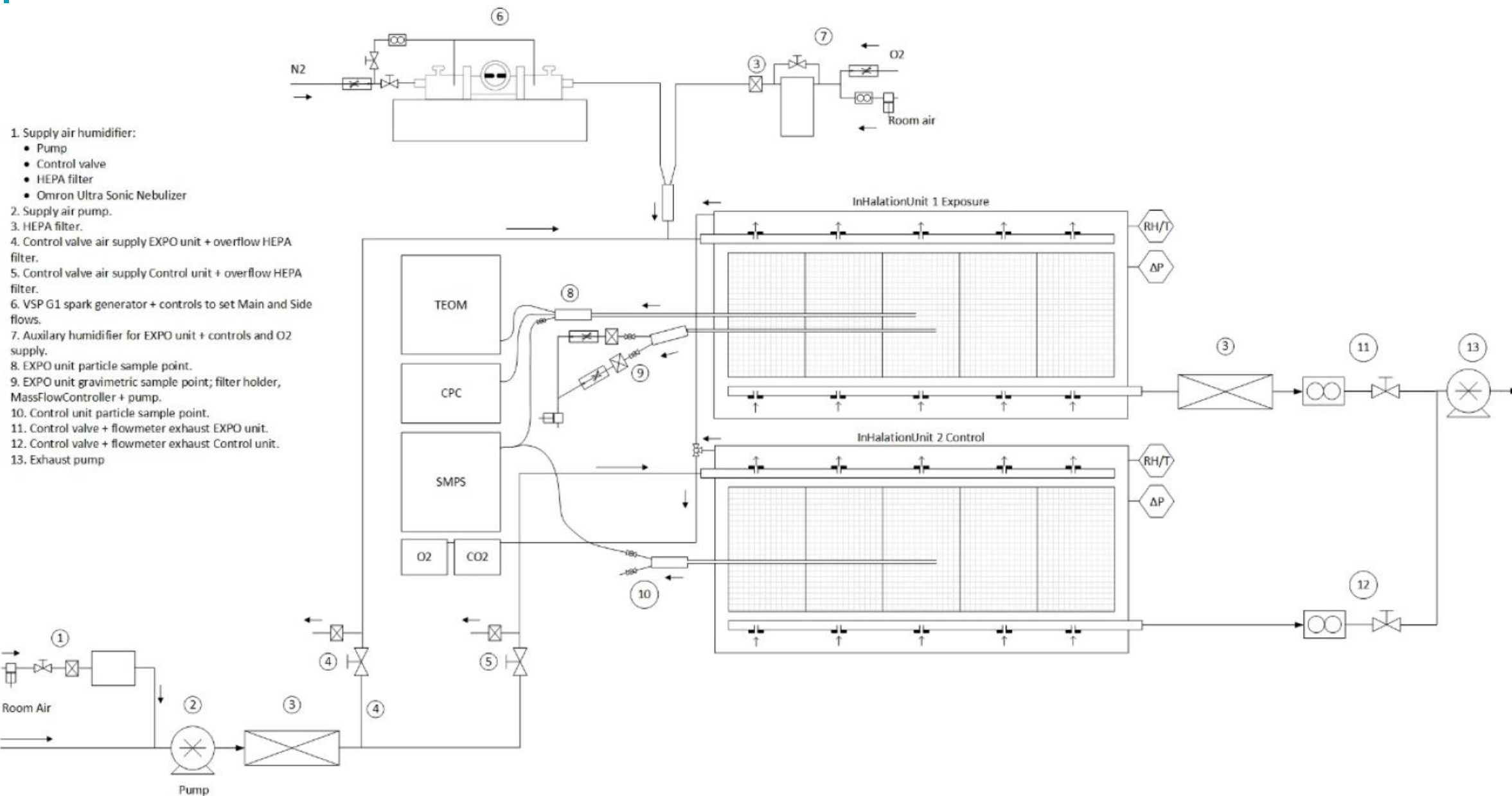
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# CNP generation



# Whole-body exposure setup



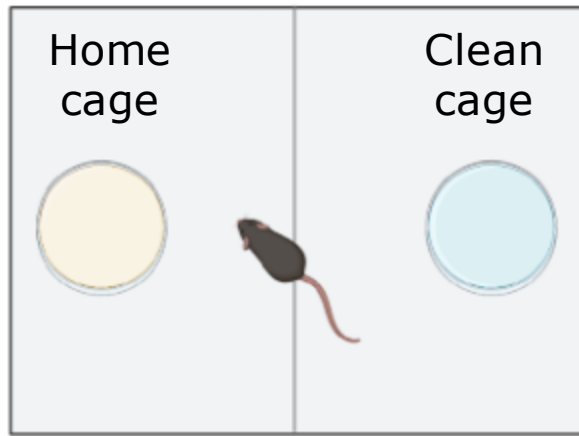
## Exposure characterization and monitoring

- Particle number  
(condensation particle counter)
- Real time mass measurement  
(tapered element oscillating microbalance)
- Size distribution of particles  
(scanning mobility particle sizer)
- Gravimetric mass concentration  
(measured by weighing filters)

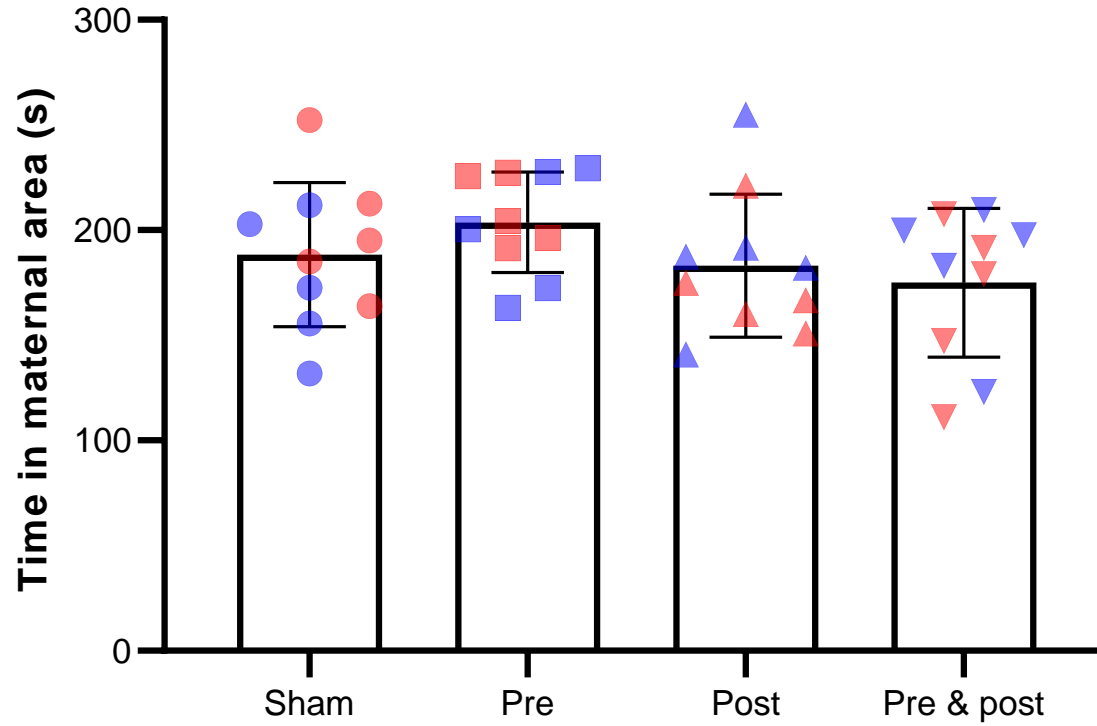




# Olfactory function

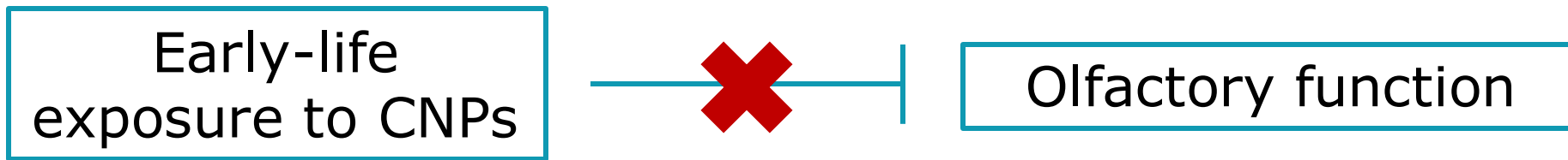


Arena zones

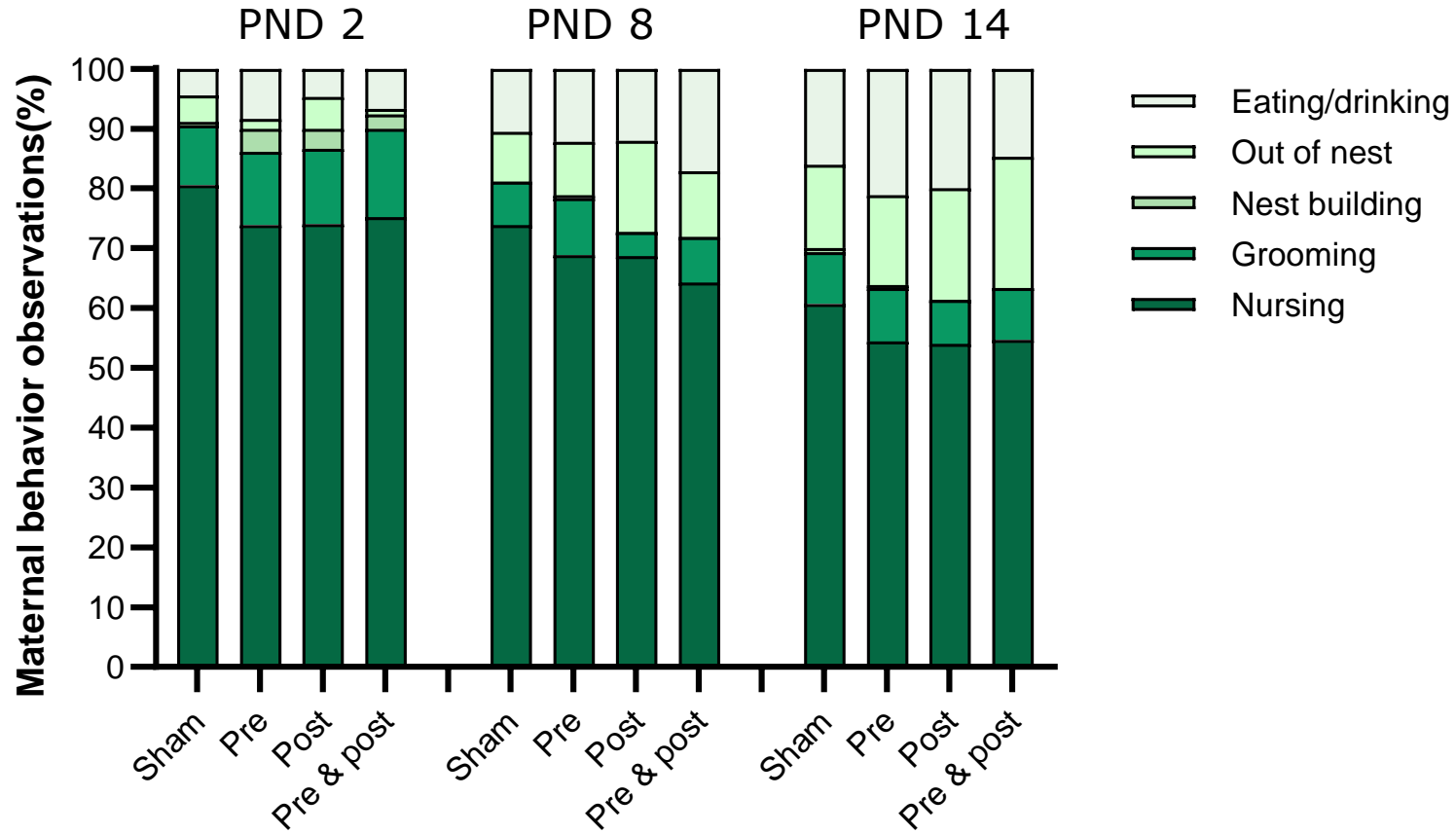


\*One-way ANOVA ( $\alpha = 0.05$ ); test was carried out for 5 min on postnatal day 19

# Olfactory function



# Maternal behavior



\*One-way ANOVA ( $\alpha = 0.05$ ); test was carried out for 1h

## Maternal behavior

