



CAQ 3

Cabin air quality (CAQ) assessment of long-term effects of contaminants

Results from Animal Study - Mouse Behavioural Tests

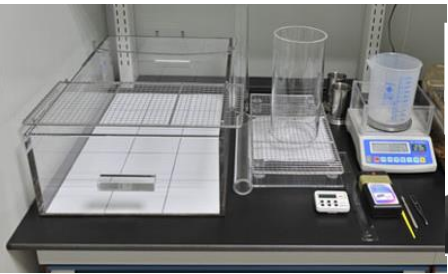
20 February 2024|

Experimental design – part 1



Which functions are tested?

Shirpa



Neurologic alterations;
General health
Autonomous functions
Reflexes
Behavioural aspects
Posture and movement

Grip Strength



Muscle strength

Open Field



Locomotor and
Exploratory activity,
Balance
Anxiety

CatWalk



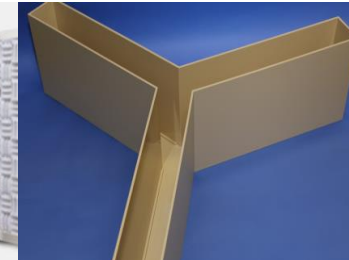
Gait parameters
Coordination
Balance

Prepulse Inhibition



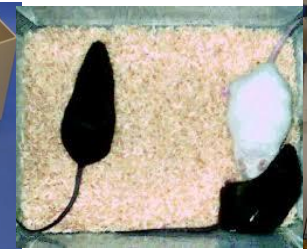
Startle Reflex
Brain function

Y-Maze



Working memory

Social Discrimination



Short-term Memory
Olfaction
Social phobia

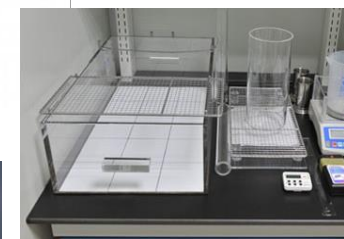
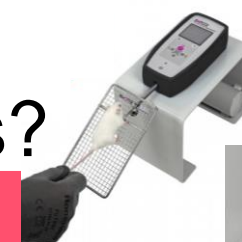
Home cage activity



Activity
Diurnal rhythms

How do the mouse functions relate to human symptoms?

Human symptom	Behavioural Test
Irritation of eyes, nose, throat	Observations during/after exposure
Breathing problems	Observation during exposure, Shirpa
Diarrhea	Shirpa, Cage-side observations
Nausea and vomiting	Observations during/after exposure, body weight (Mice can not vomit)
Fatigue	Home cage activity, Grip Strength, CatWalk, Open Field
Dizziness	Shirpa, CatWalk
Balance/coordination	Shirpa, Open Field, CatWalk
Trembling/ tremor	Shirpa
Loss of consciousness	Observation during exposure and tests
Confusion	Y-Maze
Memory loss	Y-Maze, Social Discrimination
Cognitive impairments	Y-Maze, Social Discrimination
Depression and anxiety	Open Field, Home cage activity, Social discrimination
Brain damage	Brain analysis, Prepulse Inhibition
Toxic encephalopathy	Brain analysis

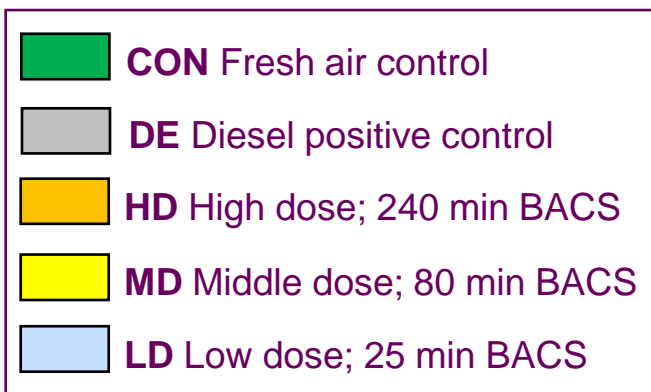


Experimental design – part 2

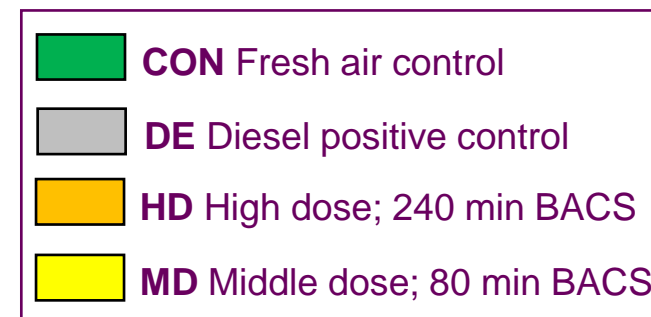


Shirpa
Grip Strength

Grip Strength Shirpa, Open Field, CatWalk, PrePulse Inhibition, Y-Maze, Social
Discrimination



↑
Sacrifice
Sub Acute
(sacrifice within
24h after last
exposure)



↑
Sacrifice
Long Term

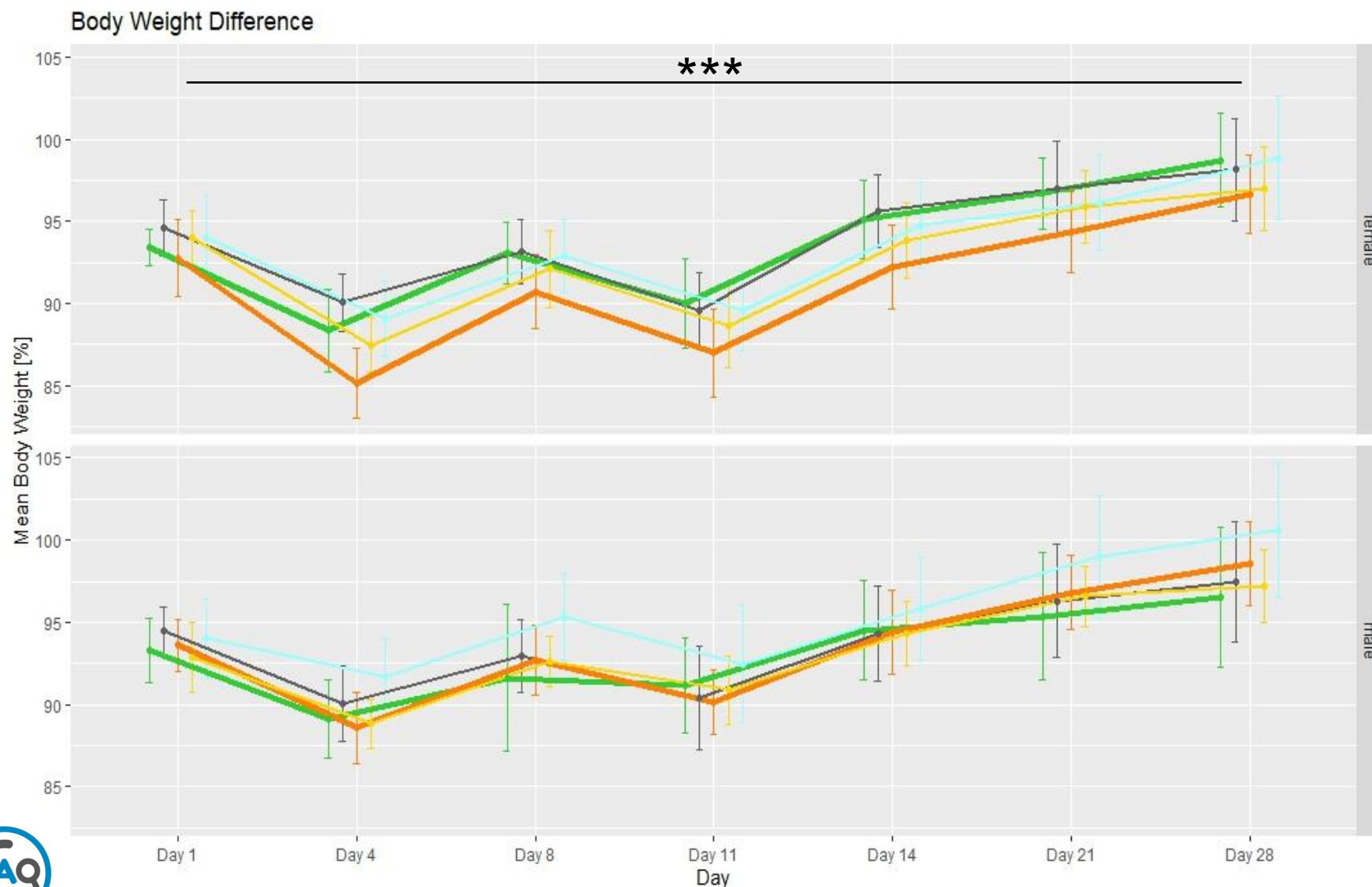
What did we observe?

Human symptom	Behavioural Test	Diesel control (240min/day* 20days 1.5 mg/m ³)*	High Dose (240min/day* 20days 15mg/m ³)*	Medium Dose (80min/day* 20days 15mg/m ³)*
Irritation of eyes, nose, throat	Observations during/after exposure	No effects	No effects	No effects
Breathing problems	Observation during exposure, Shirpa	No effects	No effects	No effects
Diarrhea	Shirpa, Cage-side observations	No effects	No effects	No effects
Nausea and vomiting	<u>Body weight</u> (Mice can not vomit)	No effects	Subtle effects in ♀	No effects



Body weight changes during exposure [%]

Body weight
Small effect in females
HD



Females: ANOVA RM: Group effect: CON vs HD

Days post exposure day 1 (Day 28 = Exposure day 18)



What did we observe?

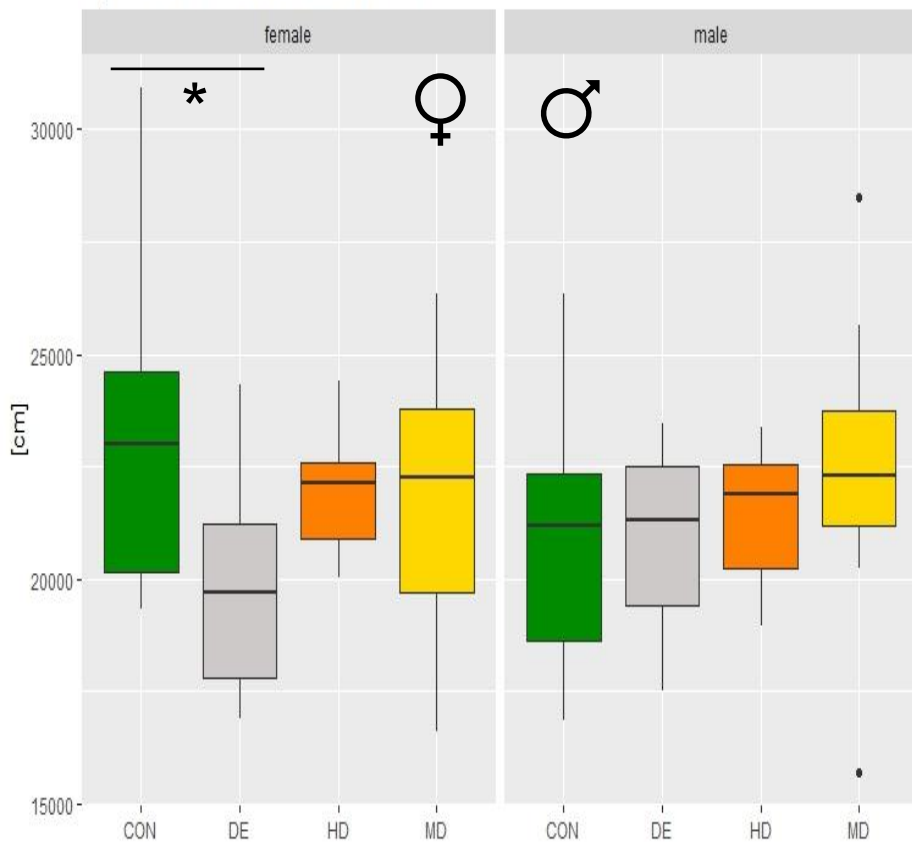
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Fatigue	Home cage activity, Grip Strength, CatWalk, <u>Open Field</u>	Effects in ♀	No effects	No effects
Dizziness	Shirpa, <u>CatWalk</u>	No effects	Very subtle effects in ♀	No effects
Balance/coordination	Shirpa, Open Field, <u>CatWalk</u>	No effects	Very subtle effects in ♀	No effects
Trembling/ tremor	Shirpa	No effects	No effects	No effects



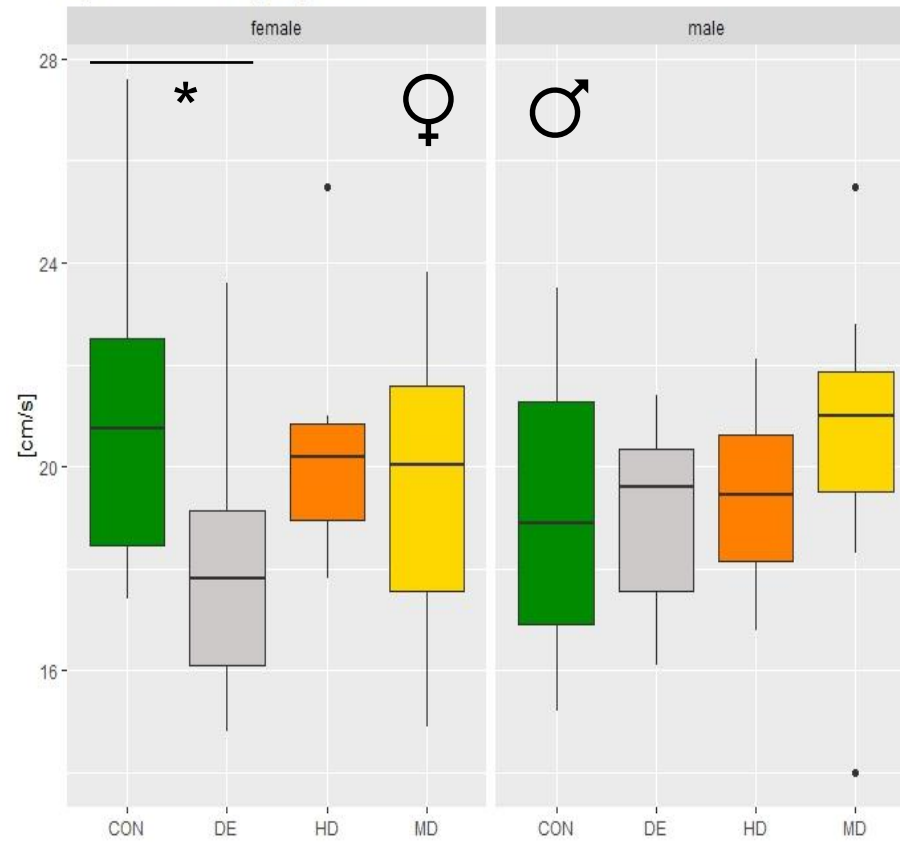
Behavioural Tests- Open Field

Open Field:
Effects in female DE

Open Field Total Distance traveled



Open Field Average Speed



CON
DE
HD
MD

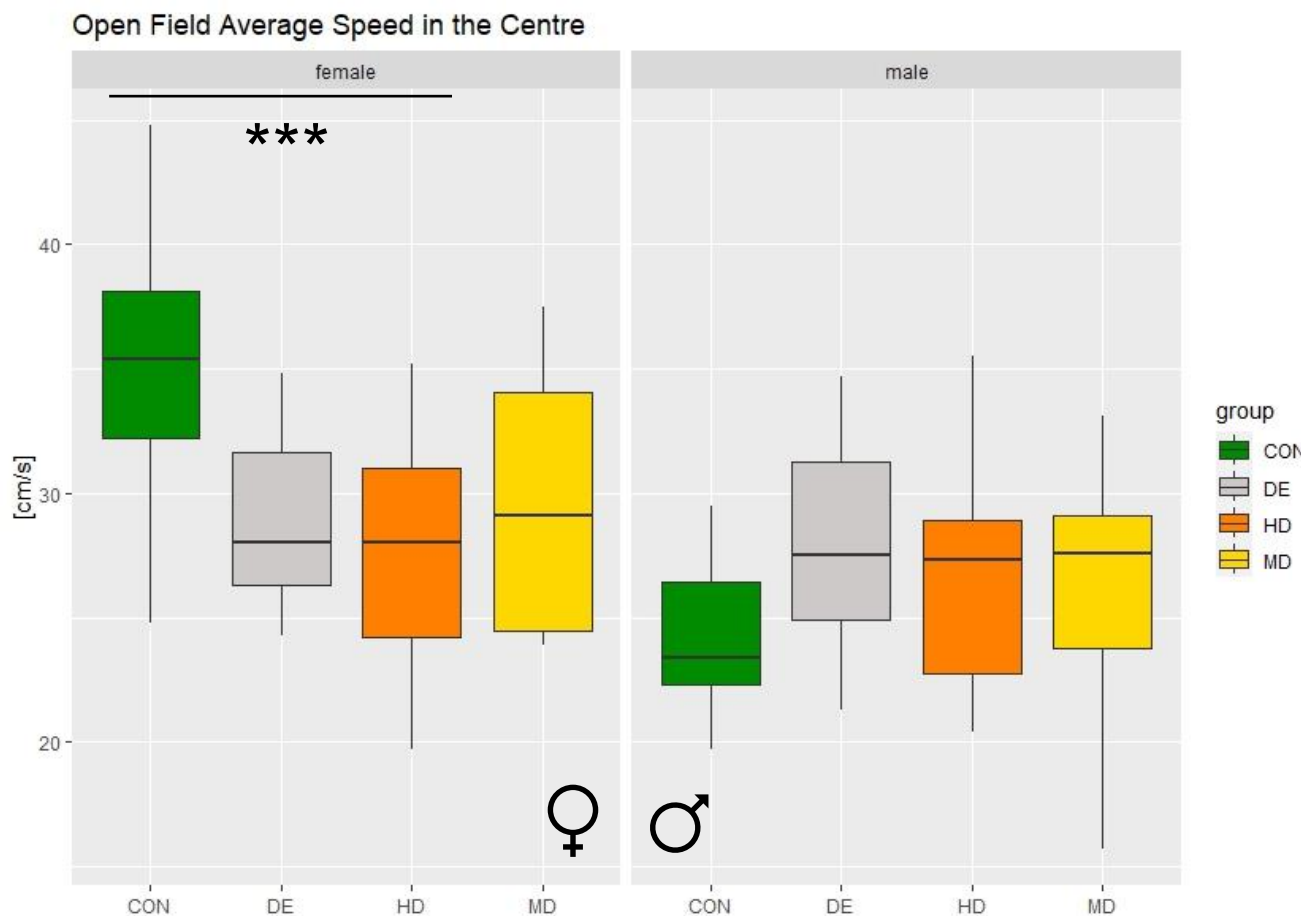
Open Field:
Female DE show reduced activity in the OF



HELMHOLTZ MUNICH

12-13 days post exposure

Behavioural Tests- Open Field



Female HD and DE show reduced speed in the centre of the arena

sex*group interaction $p = 0.009$;
Females $p = 0.009$ (CON vs HD/DE),
males n.s.

Open Field:

Very subtle effect in females HD and DE



Open Field:

No hints for increased anxiety, altered locomotion and exploration

HELMHOLTZ MUNICH

12-13 days post exposure

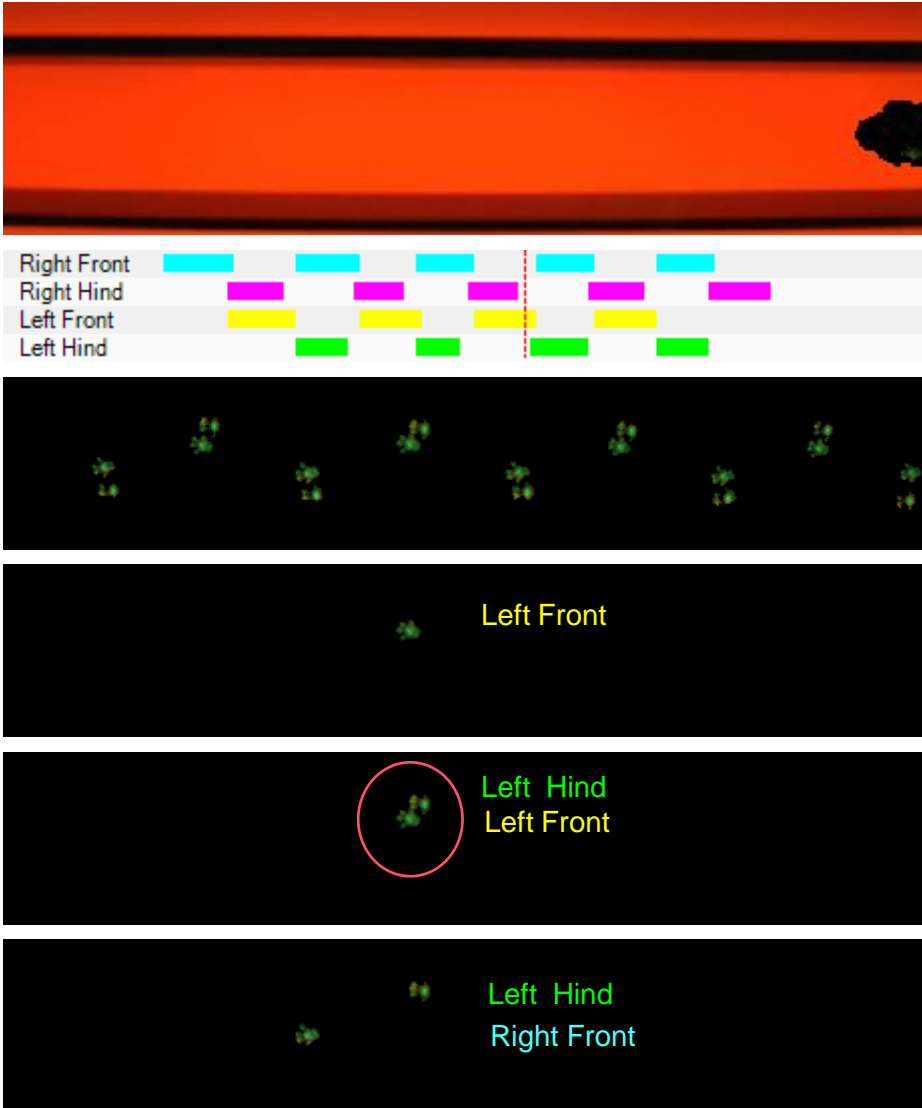


Gait analysis on the „CatWalk“

Lateral Support-
Both paws of one side are on the floor



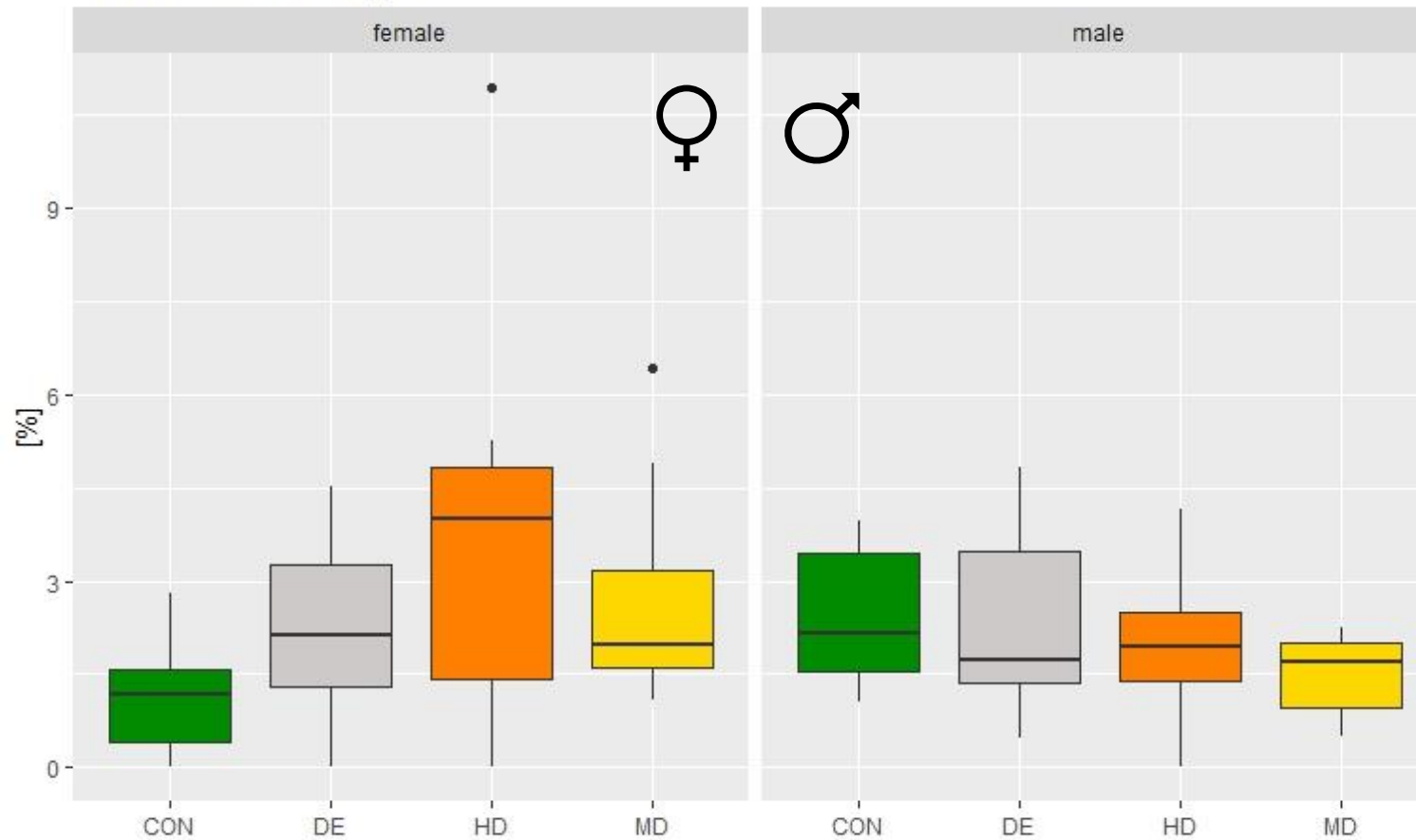
Control



High Dose

Behavioural Tests- CatWalk

CatWalk Lateral support



Female HD show a small increase in lateral support

Females: group effect: $p=0.037$ (CON vs HD),
males n.s.

CatWalk:

Very subtle effects in
females HD



CatWalk:

Slight changes towards
stabilizing gait



HELMHOLTZ MUNICH

13-21 days post exposure

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Memory loss	Y-Maze, Social Discrimination	No effects	No effects	No effects
Cognitive impairments	Y-Maze, Social Discrimination	No effects	No effects	No effects
Depression / anxiety	Open Field, Home cage activity, Social discrimination	No effects	No effects	No effects
Brain damage	Brain analysis, Prepulse Inhibition	<i>In analysis</i>	<i>In analysis</i>	<i>In analysis</i>
Toxic encephalopathy	Brain analysis	<i>In analysis</i>	<i>In analysis</i>	<i>In analysis</i>



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* DE: actual concentration based on gravimetrics; HD and MD: nominal concentration, based on the amount of oil-injected

Summary



Diesel



High dose



Medium dose

240min/day for 20 days

1.5 mg/m³ (actual concentration)

240min/day for 20 days

15 mg/m³ (nominal concentration)

80min/day for 20 days

15 mg/m³ (nominal concentration)

Effects

- Reduced activity in the Open Field

Subtle effects

- Stronger body weight loss at start of exposure
- Slightly more unstable gait

No effects

➔ We have no indication that exposure to oil-related fumes has a major impact on mouse behaviour.

Thank you for your attention!



InstPharmToxBw



 Thank you!