



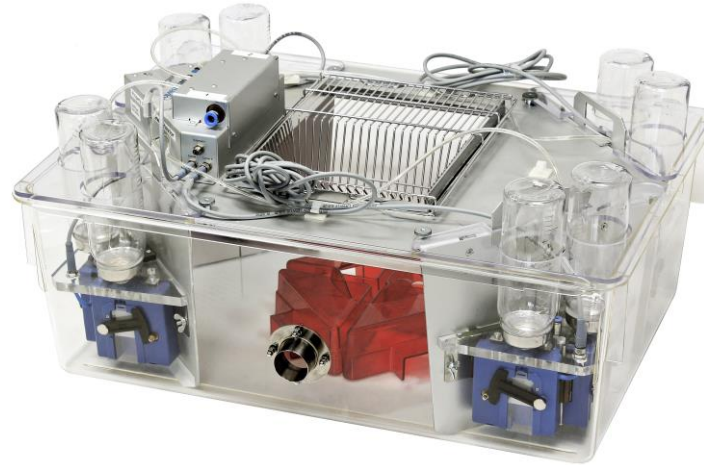
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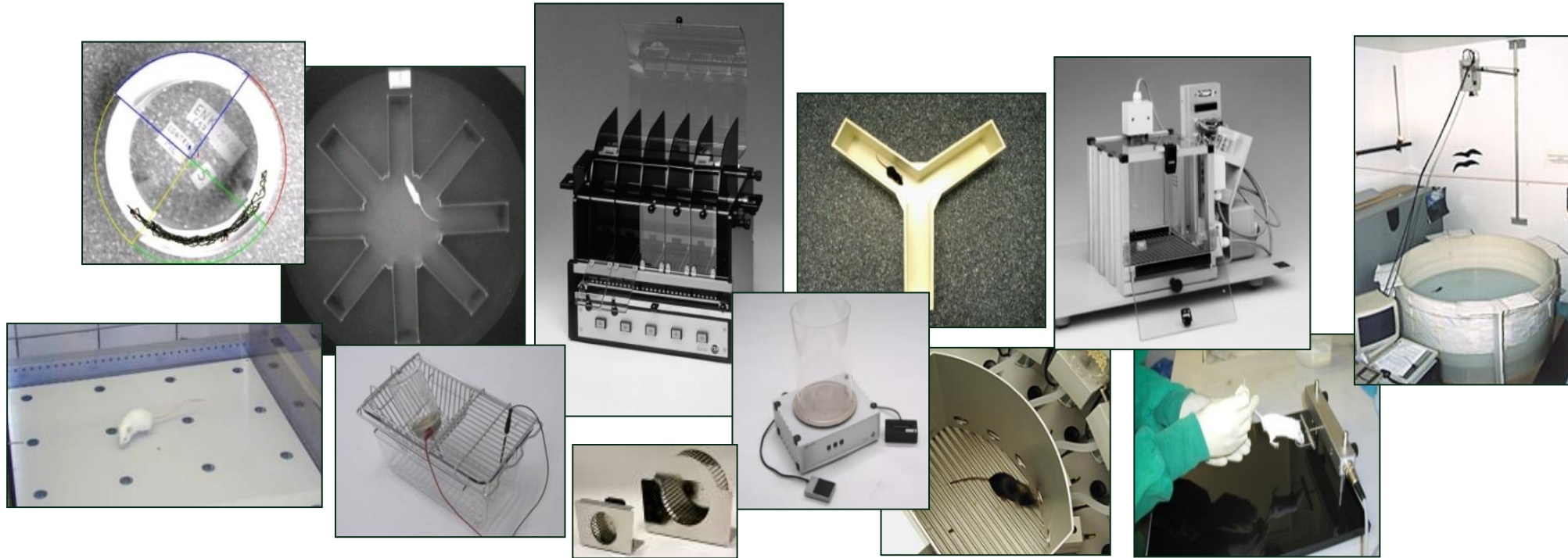


IntelliCage – The Smart Solution for Behavioral and Cognitive Screening of Socially Housed Mice



Dr. Dilip Verma, PhD
Product Manager Behavior II
TSE Systems GmbH

IntelliCage – versus standard behavioral phenotyping



Stand alone systems require lots of resources

(Apparatus, Space, Animals, Time, Personal)

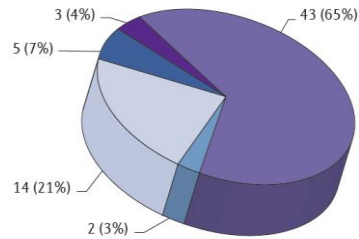
IntelliCage – Limits of some standard phenotyping procedures

Reproducibility

Believe it or not: how much can we rely on published data on potential drug targets?

Florian Prinz, Thomas Schlange and Khusru Asadullah

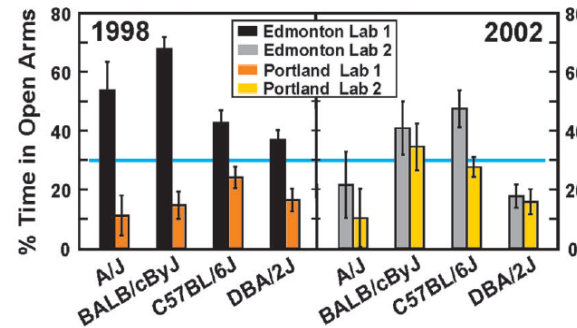
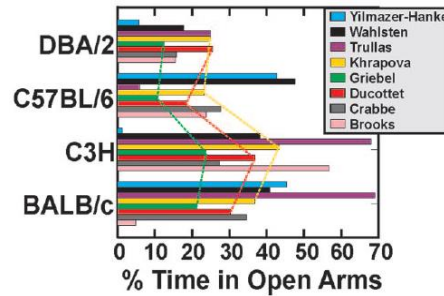
NATURE REVIEWS | DRUG DISCOVERY



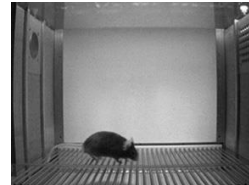
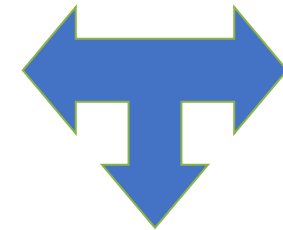
Analysis of the reproducibility of published data in 67 in-house projects.

- Inconsistencies
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Data variability



Translation, ignore social environment



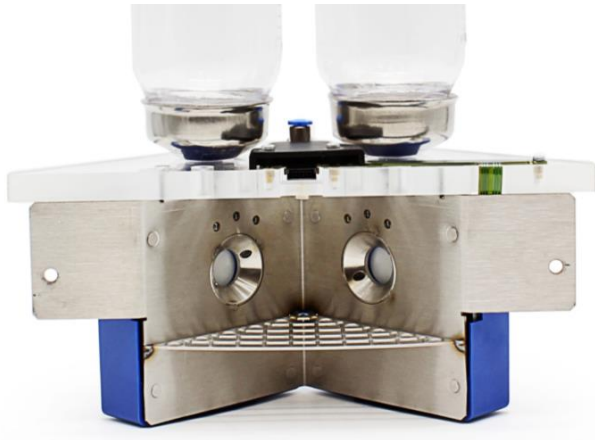
Translational Approach



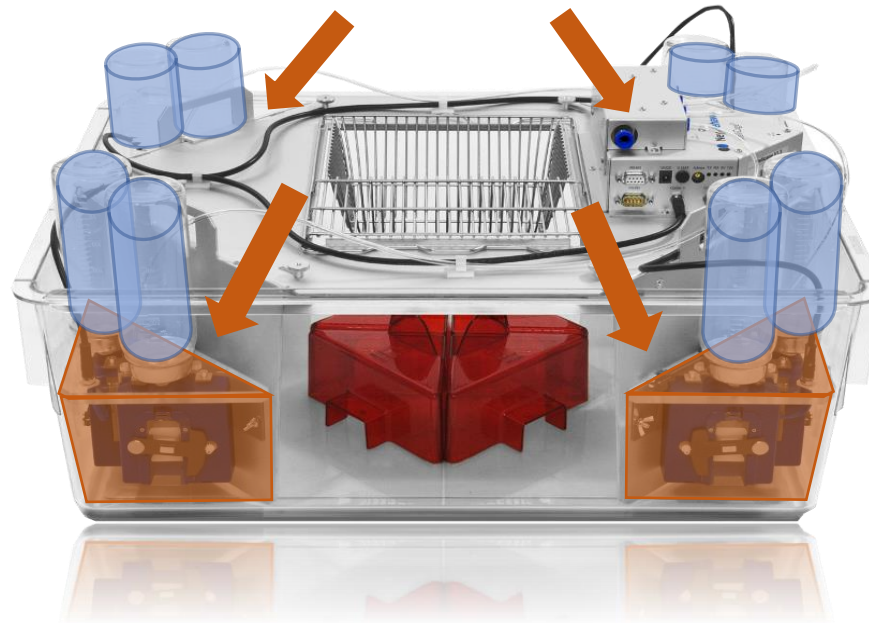
IntelliCage – Hallmarks of intelligent behavioral & cognitive testing

1. **In line with 3R principles** – replace, reduce, refine
2. **Focus on true translational research** – test animals within their social environment
3. **Remove stress, fear and anxiety** – reduce experimenter interference
4. **Remove human bias** – automatize testing to standardize data acquisition & analysis
5. **Allow high-throughput screening** – multiple animals & paradigms within a single system
6. **Experimental flexibility** – multiple freely programmable behavioral & cognitive tasks
7. **Long-term & circadian studies** – continuous testing during light & dark phases for days or even weeks

IntelliCage –Inspiring Design



Mice



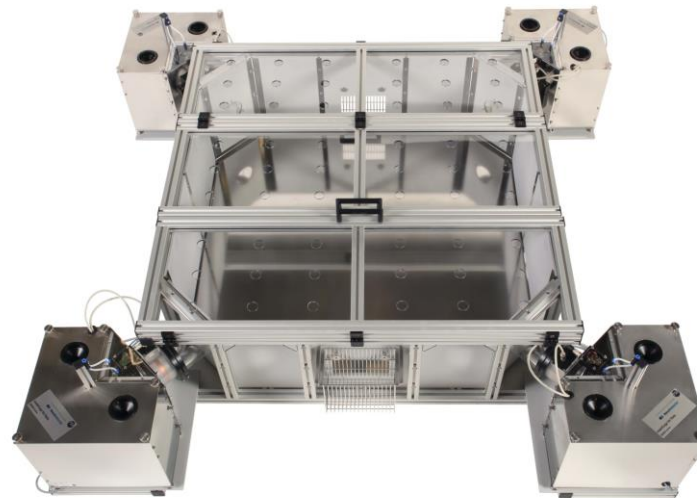
Sensors:

- RFID antenna
- Presence detector
- 2 nosepoke sensors
- 2 lickometers

Actors:

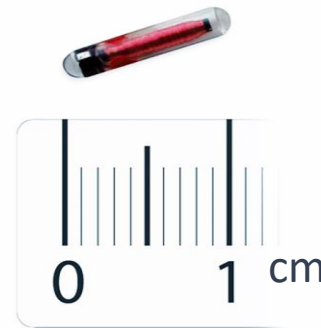
- 2 motorized doors
- 2 rows of 3 stimulus LEDs
- Air-puff valve

Rats



- Spacious central compartment with food grid and shelter
- 4 fully automated **operant conditioning corners**
- Innovative technology for behavioral screening & cognitive assessment

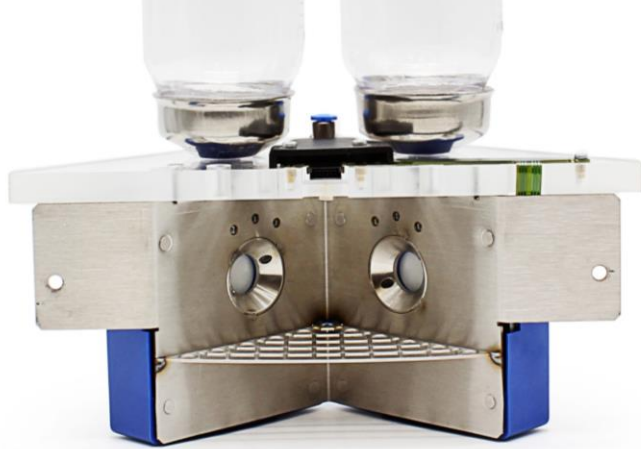
IntelliCage – Animal Identification



- Latest RFID transponder technology
- Transponder injected subcutaneously
- RFID antennas in operant corners identify visiting animals

12 & 7 mm RFID transponder were tested and are available according to user's requirements

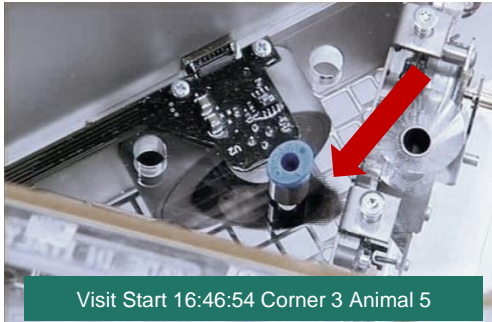
IntelliCage – Smart Function



Measurements

Sensors

- Presence detectors & RFID antennas register START / END of a corner visit
- Light beams register START / END of a nose poke event
- Lickometers register the number and duration of licks

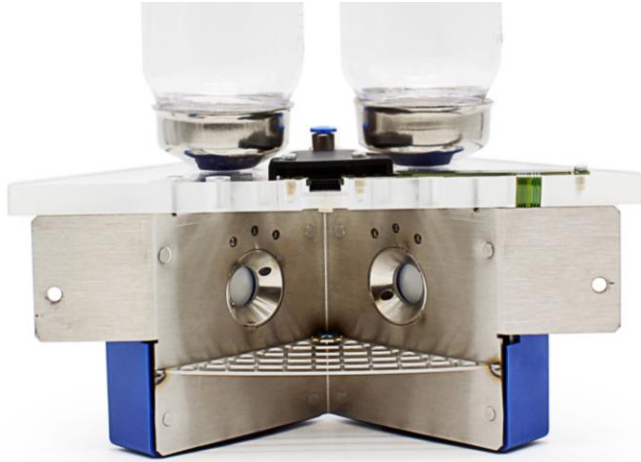


Corner Visit

Nose Poke

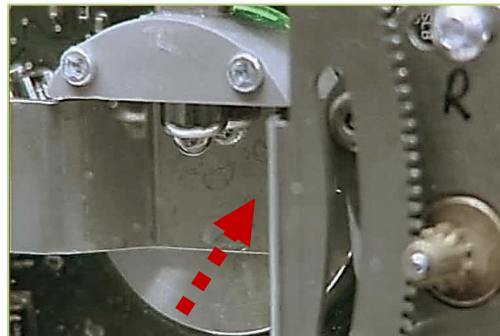
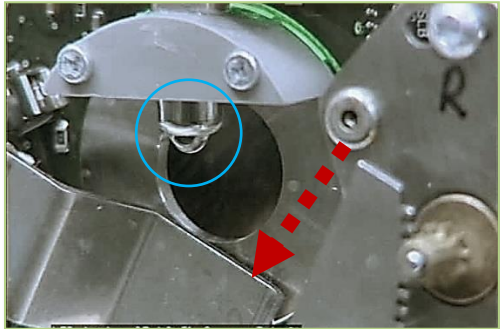
Licks

IntelliCage – Smart Function



Actors

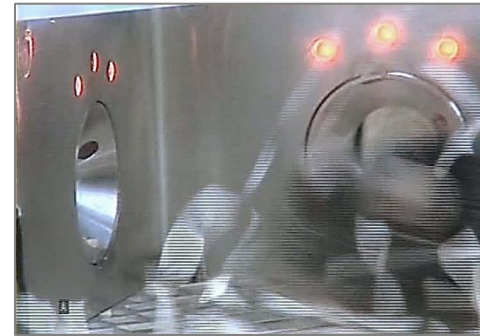
- Motorized doors provide access to water bottles as reward for learning tasks
- Multicolor LEDs serve as conditioned stimuli
- Air puffs act as aversive stimuli during learning tasks



Motorized Door



Stimulus LEDs



Air Puff

IntelliCage – Unique Flexibility

Free programming of many behavioral and cognitive tasks

Spontaneous Behavior

- Free Adaptation
- Nosepoke Adaptation

Operant Conditioning

- Continued Stimulus (LED Scheme)
- Fixed Ratio
- Progressive Ratio
- Impulsivity & Differential Reinforcement of Low Responding (DRL)

Spatial and Temporal

- Place Learning
- Avoidance Learning
- Reversal Learning
- Alternation
- Serial Reversal
- Patrolling
- Coverage
- Drinking Sessions/ Temporal Learning

Social and Others

- Competition/Hierarchy Analysis
- Differential Synchronization

Memory

- Impulsivity & Delay Discounting
- Attentional Shift
- Neophobia
- Conditioned Aversion

Discrimination Learning & Preferences

- Light Discrimination (LED Scheme)
- Taste Aversion
- Compound Cue

Programmable components

- 2 bottles per corner
- Corner and side within each corner
- Number of nose poke
- Stimulus light
- Delays
- Air-puff
- Doors

Applications

Behavioral Phenotyping

Automated high-throughput behavioral phenotyping in a social group. With highly standardized phenotyping procedures, the IntelliCage covers multiple behavioral and cognitive domains and allows the comparison of multiple animal models of any disease or single/multiple gene knockouts.

True longitudinal studies

Animals either stay in the IntelliCage for a prolonged period or re-visit the system several times during their lifespan. Both approaches allow the detection of age-dependent signs or disease symptoms (e.g. Huntington's disease, Alzheimer's disease, aging research)

Mechanistic studies

Brain lesion studies for testing the involvement of specific structures in different behavioral domains, leading to a better general understanding of behavior and underlying brain functions.

Pharmacological studies

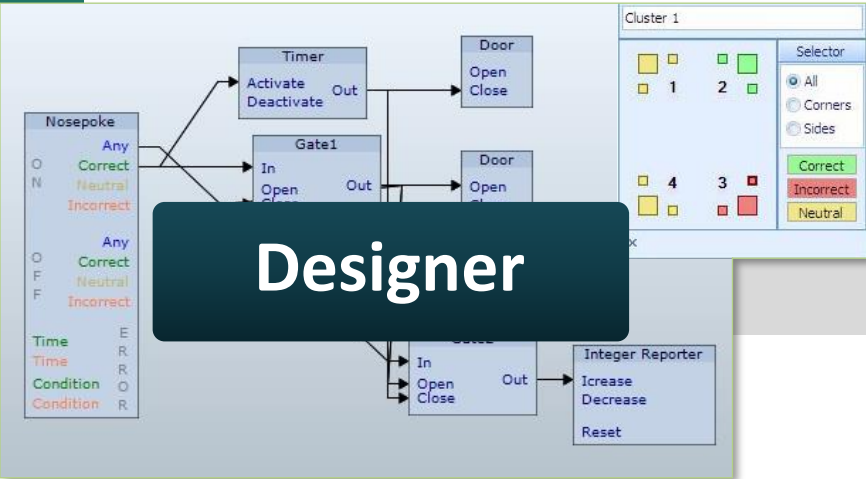
Drugs can be administered orally in the drinking water or via osmotic mini-pumps while the animals are undergoing behavioral or cognitive testing. Highly standardized conditions and protocols allow comparisons of data of different sexes, age groups, or genetic backgrounds.

Wireless telemetry studies

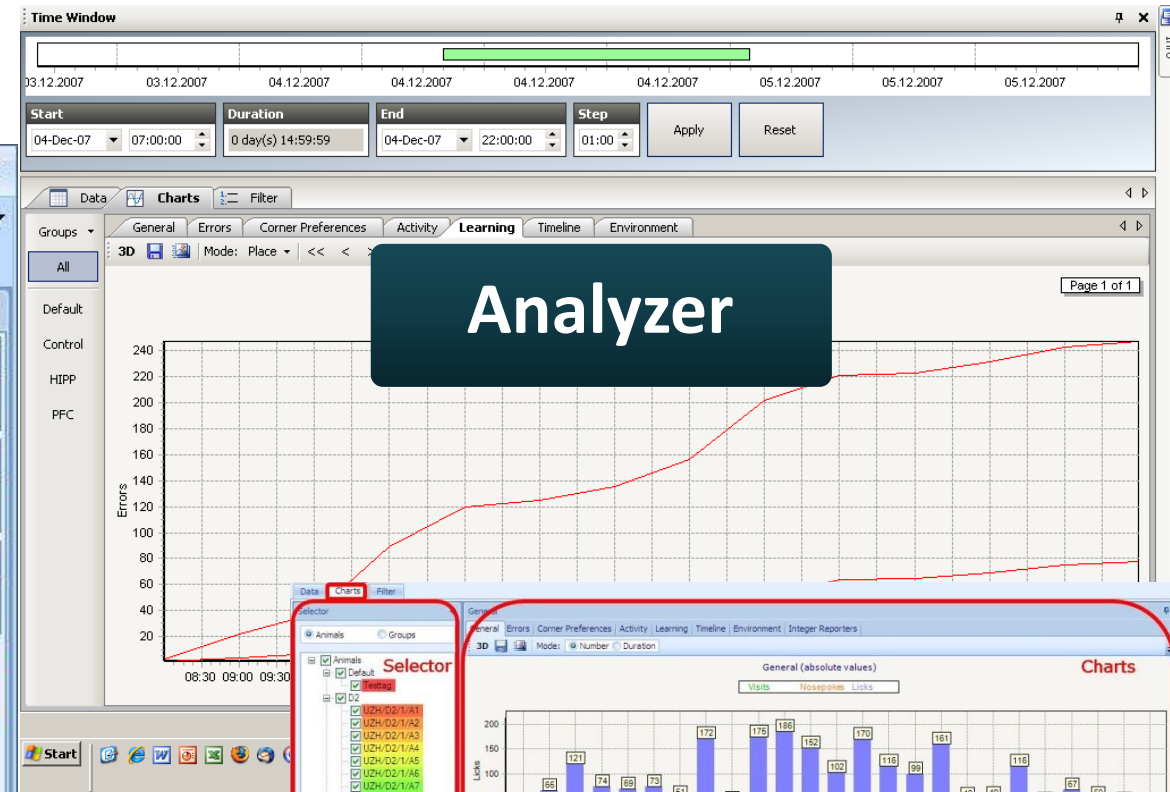
The ability to combine the automated behavioral phenotyping of the IntelliCage with our wireless telemetry system Stellar for simultaneous EEG, ECG, Blood Pressure, and Activity measurements.

IntelliGent Software

Designer



Analyzer



Controller

The IntelliCage Controller interface shows a grid of cages (Cage 1 to Cage 4) and four corners (CORNER 1 to CORNER 4). Each corner has controls for Air, Presence, and Nosepoke/Lick. A 'Start' button is highlighted with a red box. The interface includes a menu (File, Controller, Settings, Tools, Help), a console, and various control options like 'Open Door', 'Close Door', 'Temperature', and 'Illumination'.



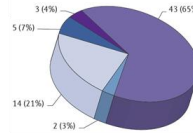
IntelliCage – Limits of some standard phenotyping procedures

Reproducibility

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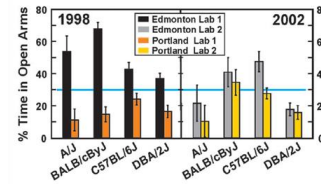
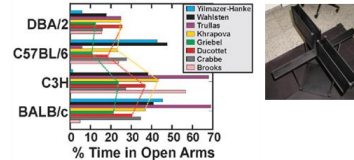
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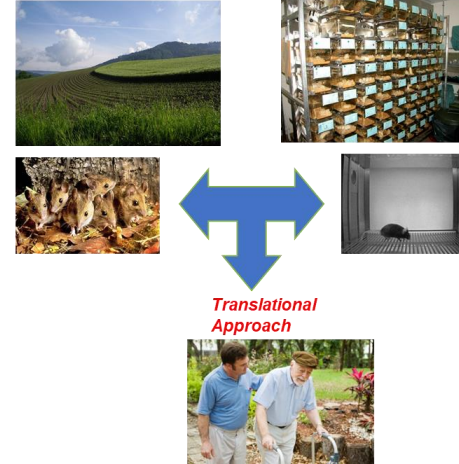
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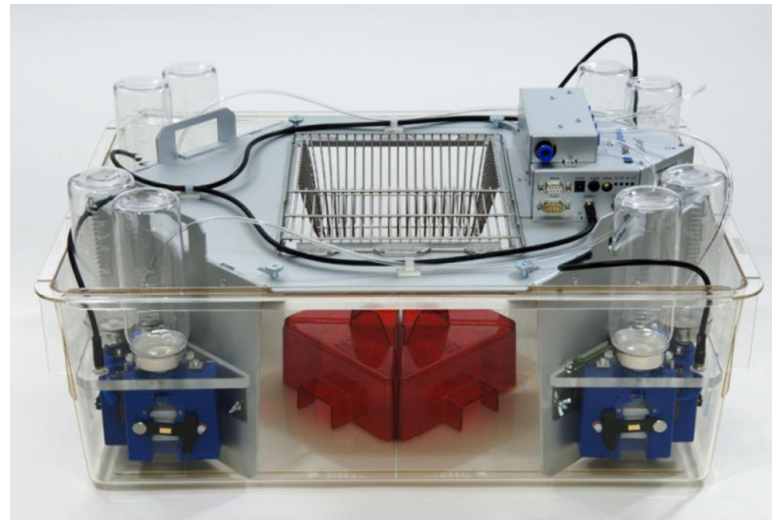
Data variability



Translation, ignore social environment

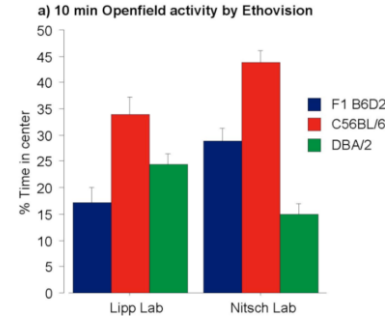


Fully automated individual behavioral testing in a social group can help

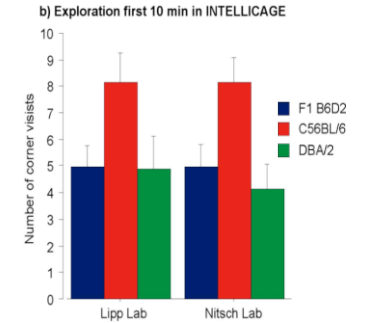
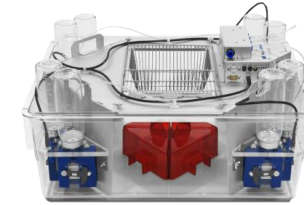


Data variability

Locomotor and exploratory activity in the open field test



Locomotor and exploratory activity in the INTELLICAGE



Data reproducibility

REPLICABILITY

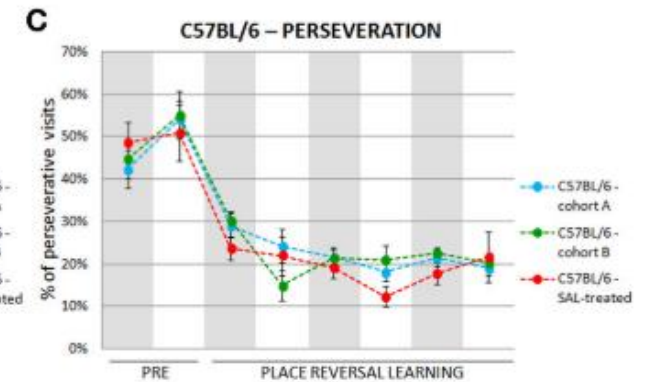
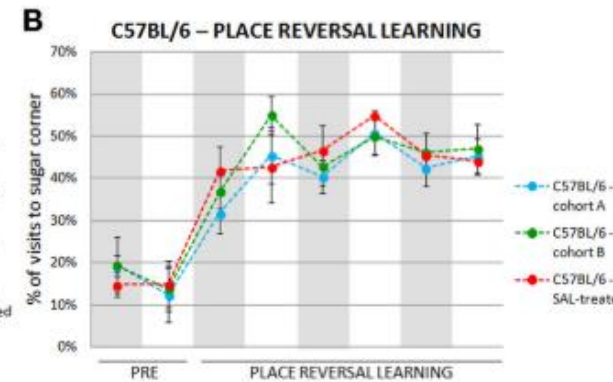
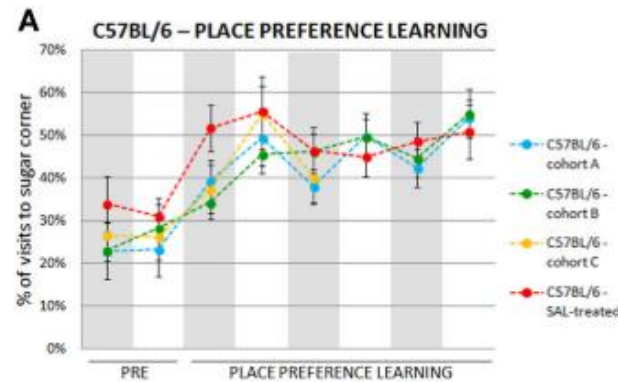
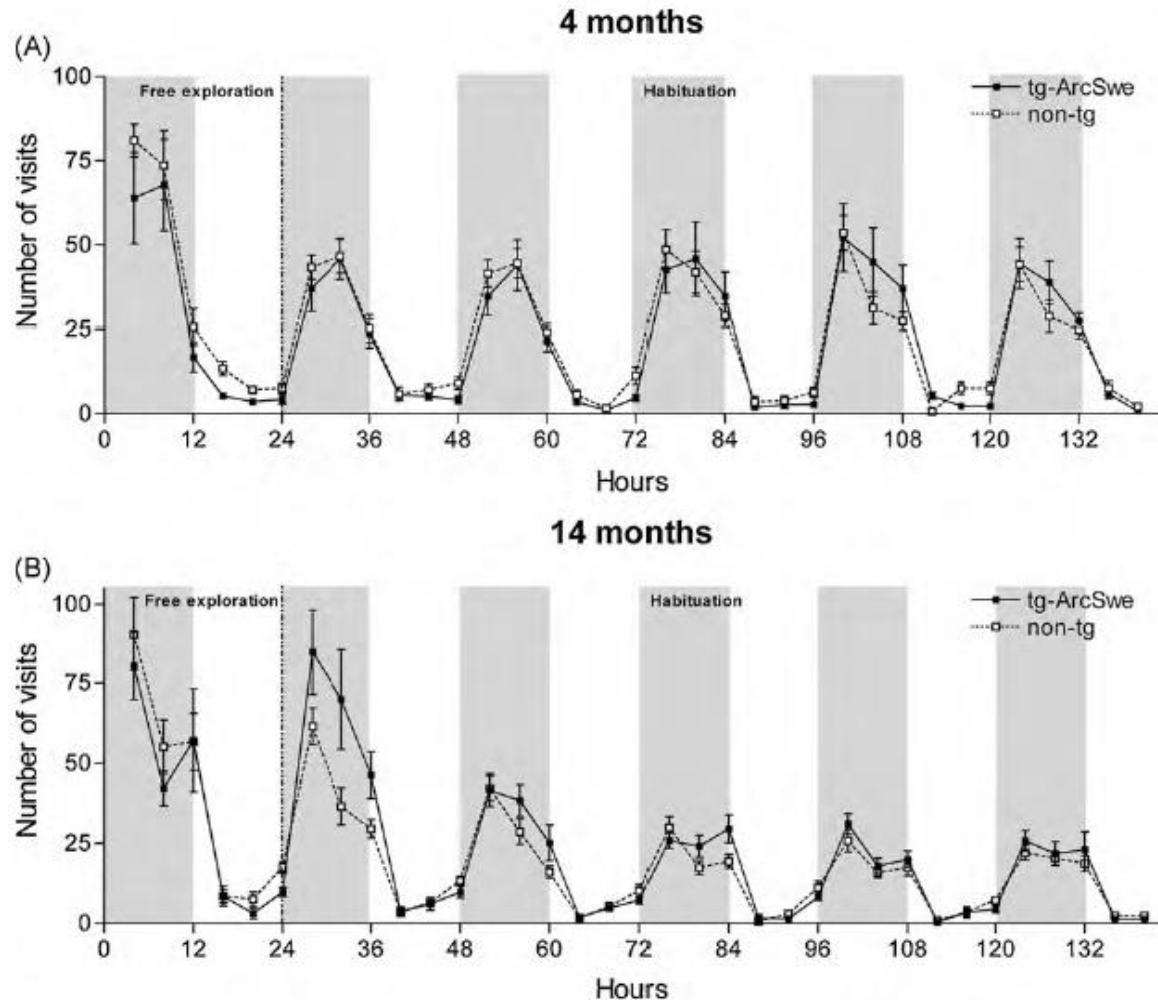


FIGURE 3 | Self-designed automated behavioral tests are highly replicable. The results of place preference learning (A) in four cohorts ($n = 41$), reversal learning (B) and perseveration (C) in three cohorts ($n = 30$) of C57BL/6 mice. Dots represent the actual data, while dashed lines serve to guide the eye.

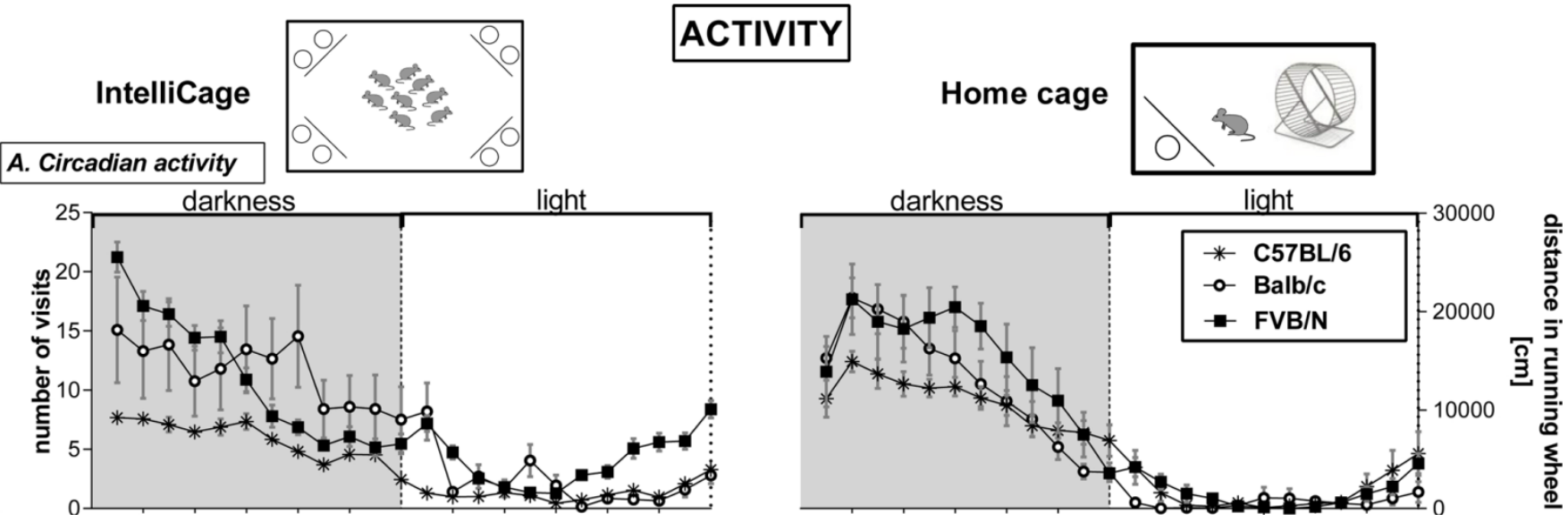
IntelliCage – Long-term Experimentation



- Behavior and performance analysis over days or weeks
- Clear circadian patterns of naturally behaving animals

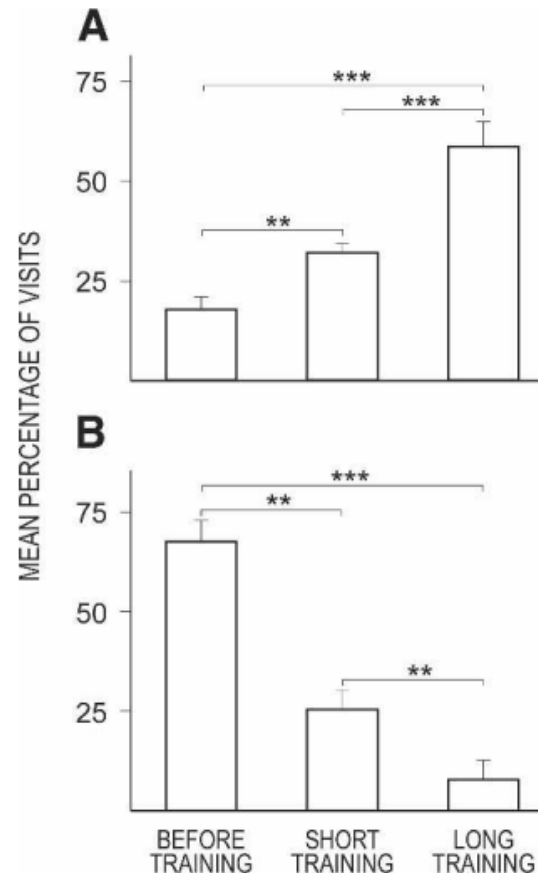
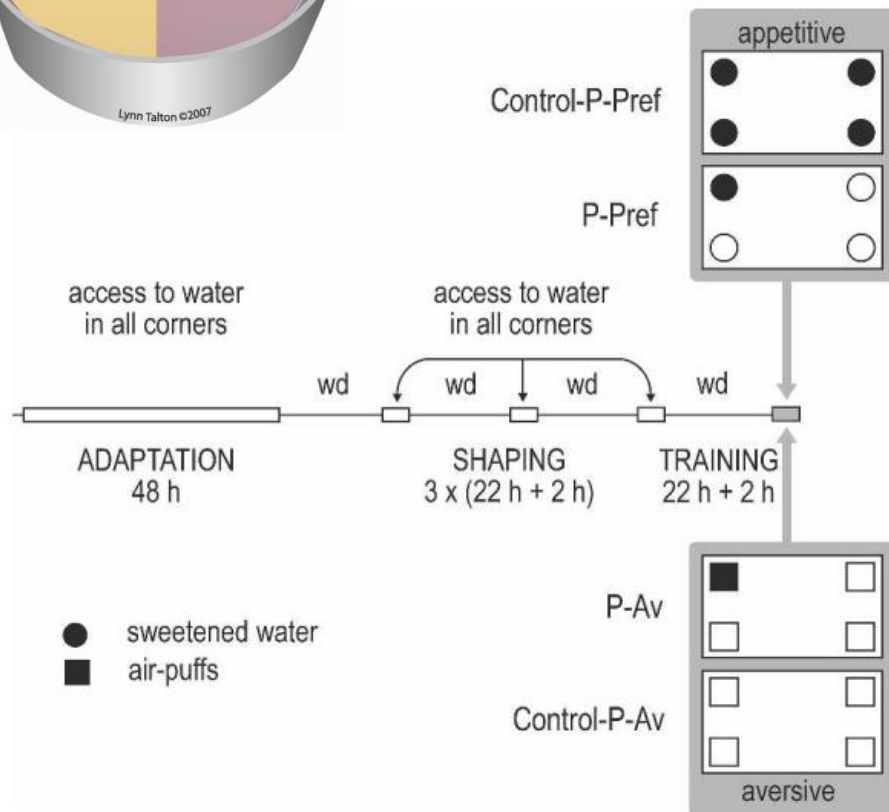
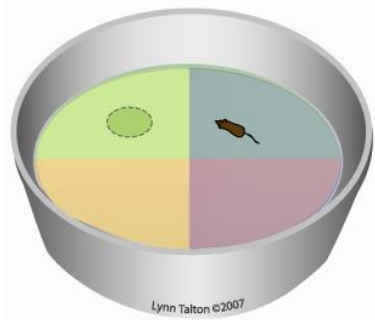
- **Habituation**
- **Circadian pattern**
- **Age dependent decline in activity**

IntelliCage – Comparable with standard home cage



- Changes in circadian activity in the IntelliCage are comparable to activity in standard home cages with a running wheel
- Clear circadian patterns of naturally behaving animals

IntelliCage – Automated Experimentation



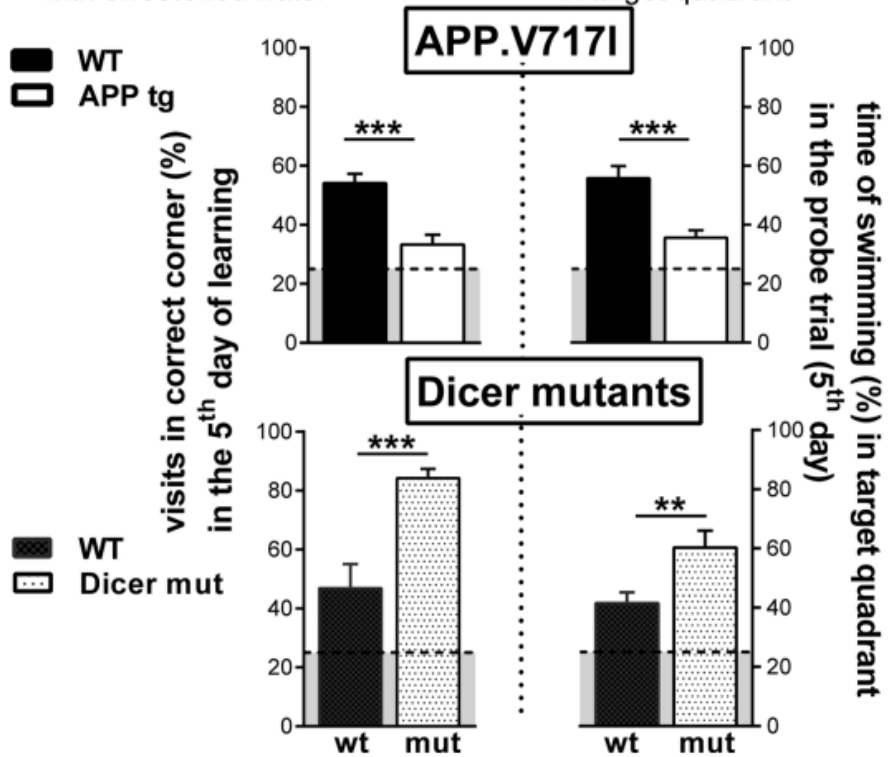
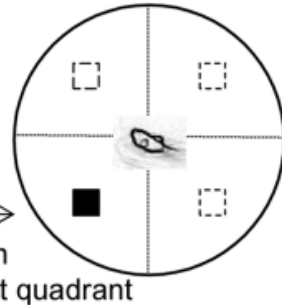
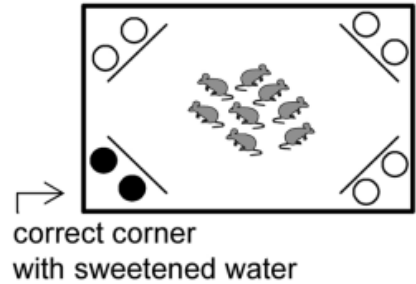
- Automated replacement of **time-consuming** behavioral paradigms, such as the Morris water maze
- Spatial learning and memory

IntelliCage – Automated Experimentation

SPATIAL LEARNING

IntelliCage
visits in correct corner (%)

Morris water maze
time (%) in target quadrant



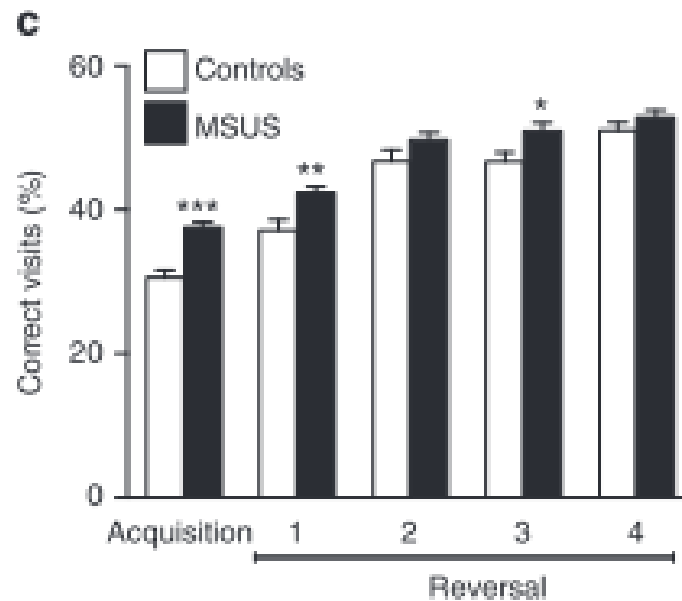
Decreased cognitive ability

Increased cognitive ability

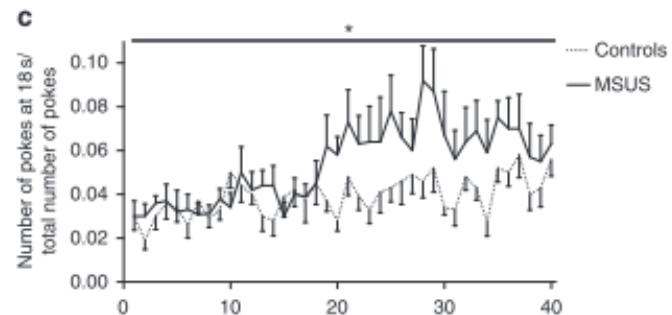
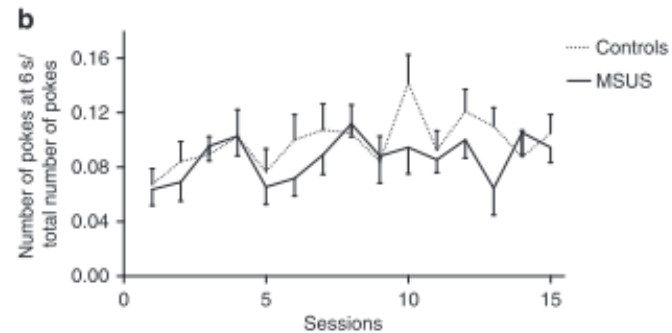
- Spatial Learning tests in the IntelliCage and Morris water maze detect parallel changes in mutant mice

IntelliCage – Automated Experimentation

Behavioral sequencing task

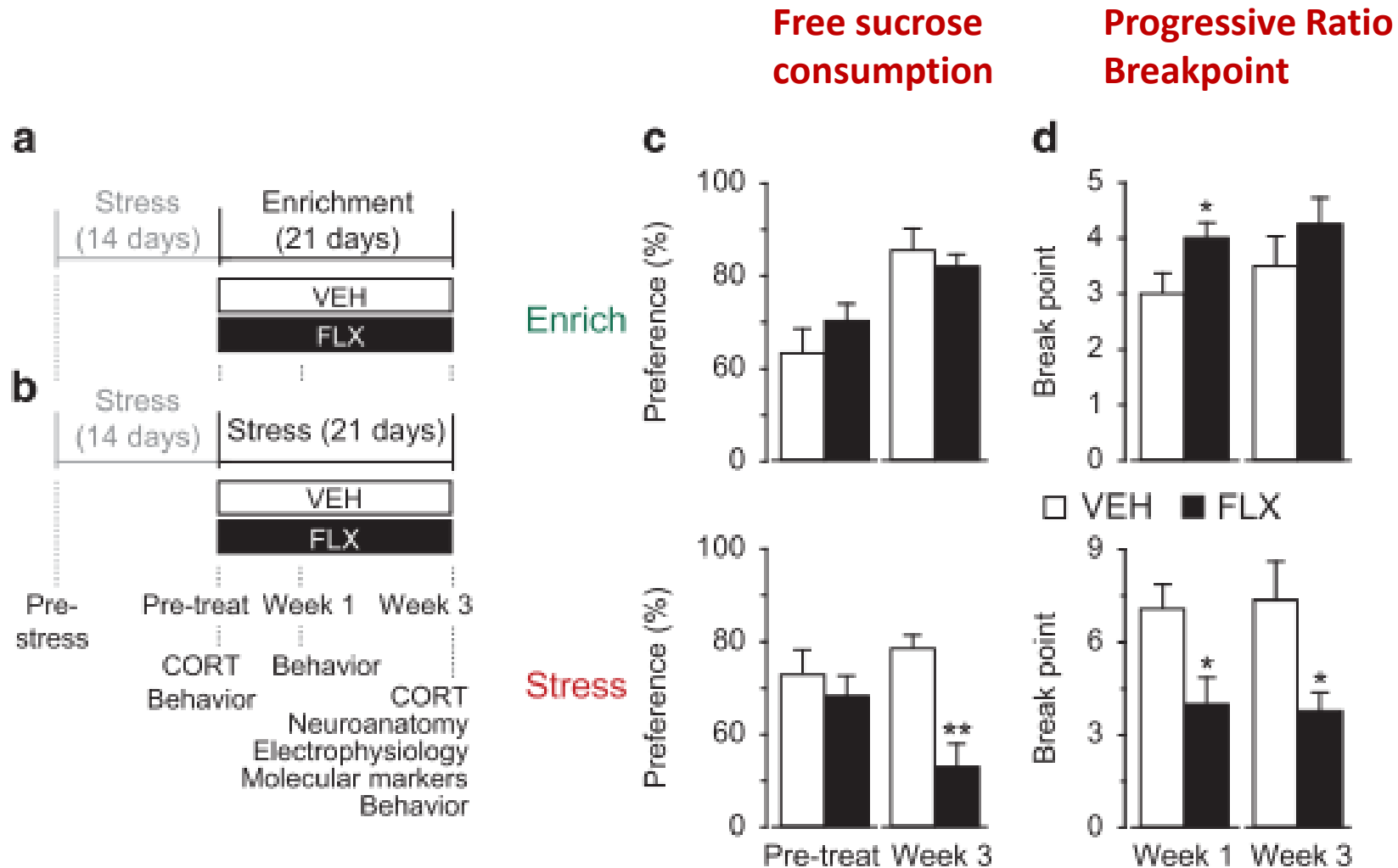


DRL (differential reinforcement of lower rates)



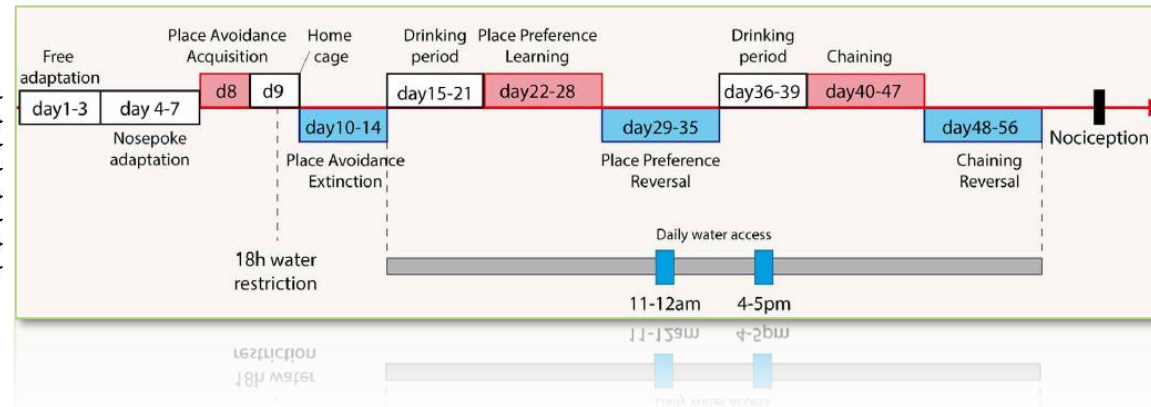
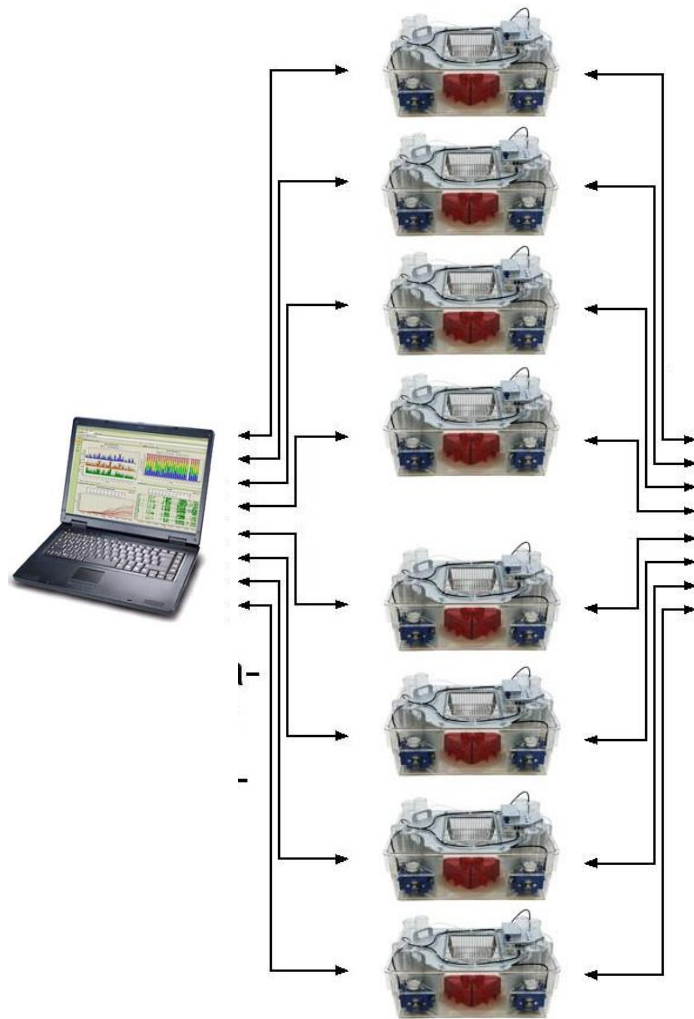
- Automated replacement of **complex** and **time-consuming** operant behavioral paradigms, usually performed in the skinner box over weeks

IntelliCage – Anhedonia Core Symptom Depression



- Assessment of Anhedonia **without social isolation**
- Social Isolation a method to induce a depressive like phenotype

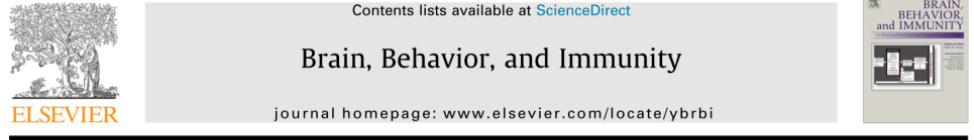
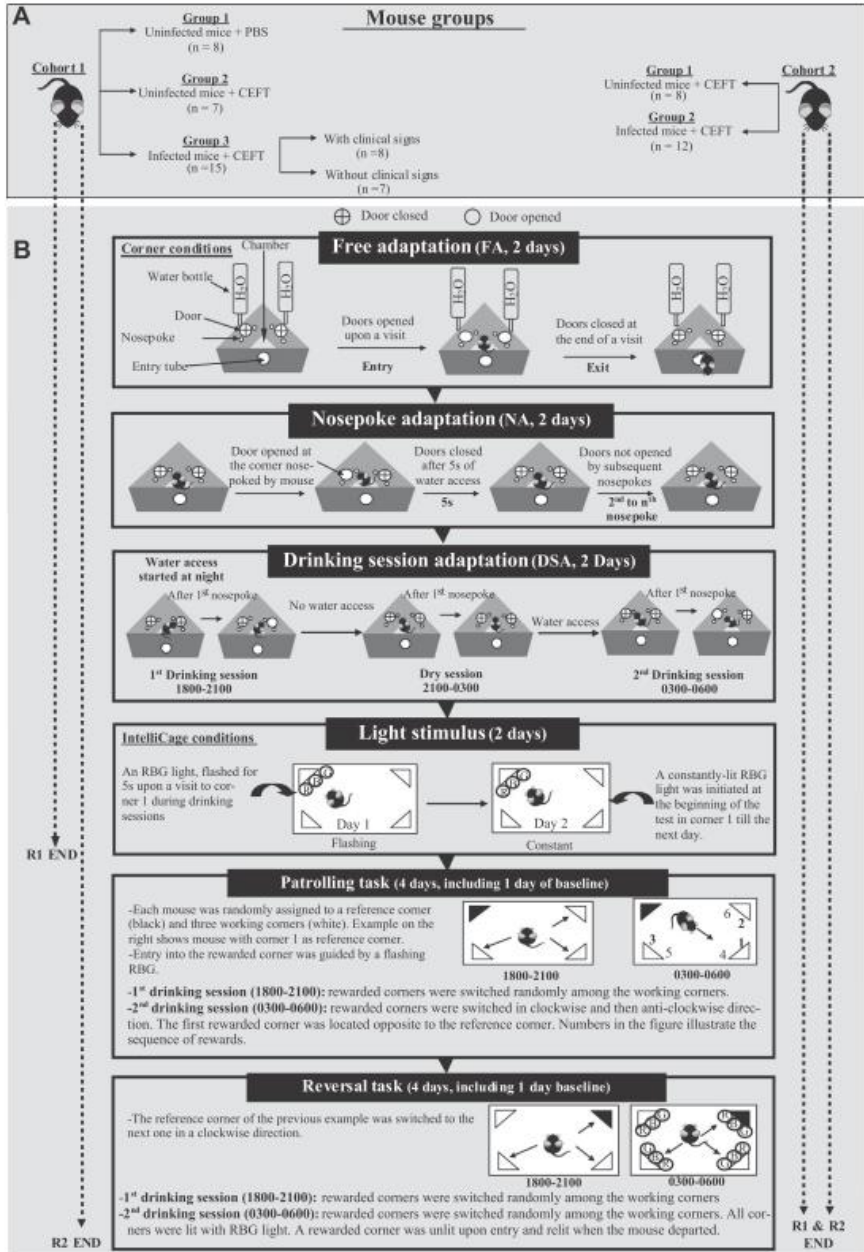
IntelliCage – High Throughput



Up to 128 mice simultaneously!
Test batteries with multiple tasks run non-stop!

- Up to 8 IntelliCages operate in parallel
- Up to 16 mice per IntelliCage
- An unlimited number of freely programmable cognitive tasks
- Data acquisition around the clock

IntelliCage – Automated Test battery –high throughput



A novel automated test battery reveals enduring behavioural alterations and cognitive impairments in survivors of murine pneumococcal meningitis

L.K. Too^a, H.J. Ball^a, I.S. McGregor^b, N.H. Hunt^{a,*}



A novel automated behavioral test battery assessing cognitive rigidity in two genetic mouse models of autism

Alicja Puścian¹, Szymon Łęski¹, Tomasz Górkiewicz¹, Ksenia Meyza¹, Hans-Peter Lipp^{2,3} and Ewelina Knapska^{1*}



Learning and memory with neuropathic pain: impact of old age and progranulin deficiency

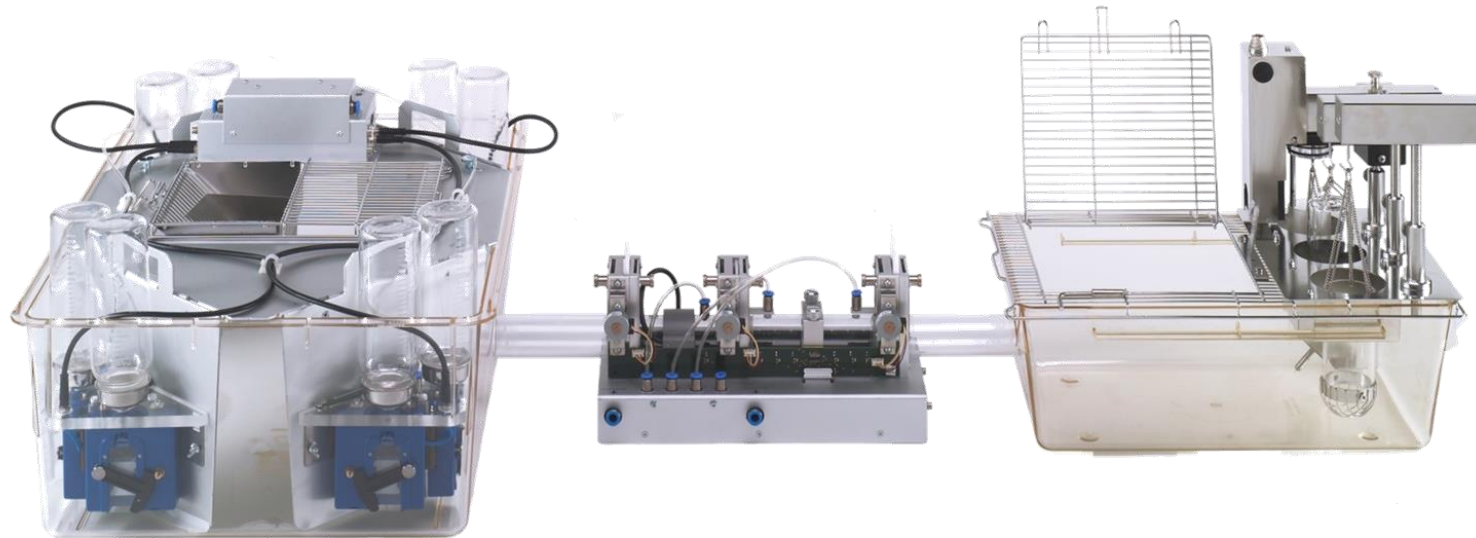
Boris Albuquerque¹, Annett Häussler¹, Elisabetta Vannoni², David P. Wolfer^{2,3} and Irmgard Tegeder^{1*}

- Sequences of different experiments to test different cognitive function without interruption

Advantages and Benefits of the IntelliCage

- New generation behavior & cognition test system
- Results identical to time consuming standard methods
- Animals in social groups, high translational value and animal welfare
- Fully automated, high standardization, efficiency and accuracy
- Long-term High-throughput screening with great experimental flexibility
- IntelliCage reduces lab space, animals and costs

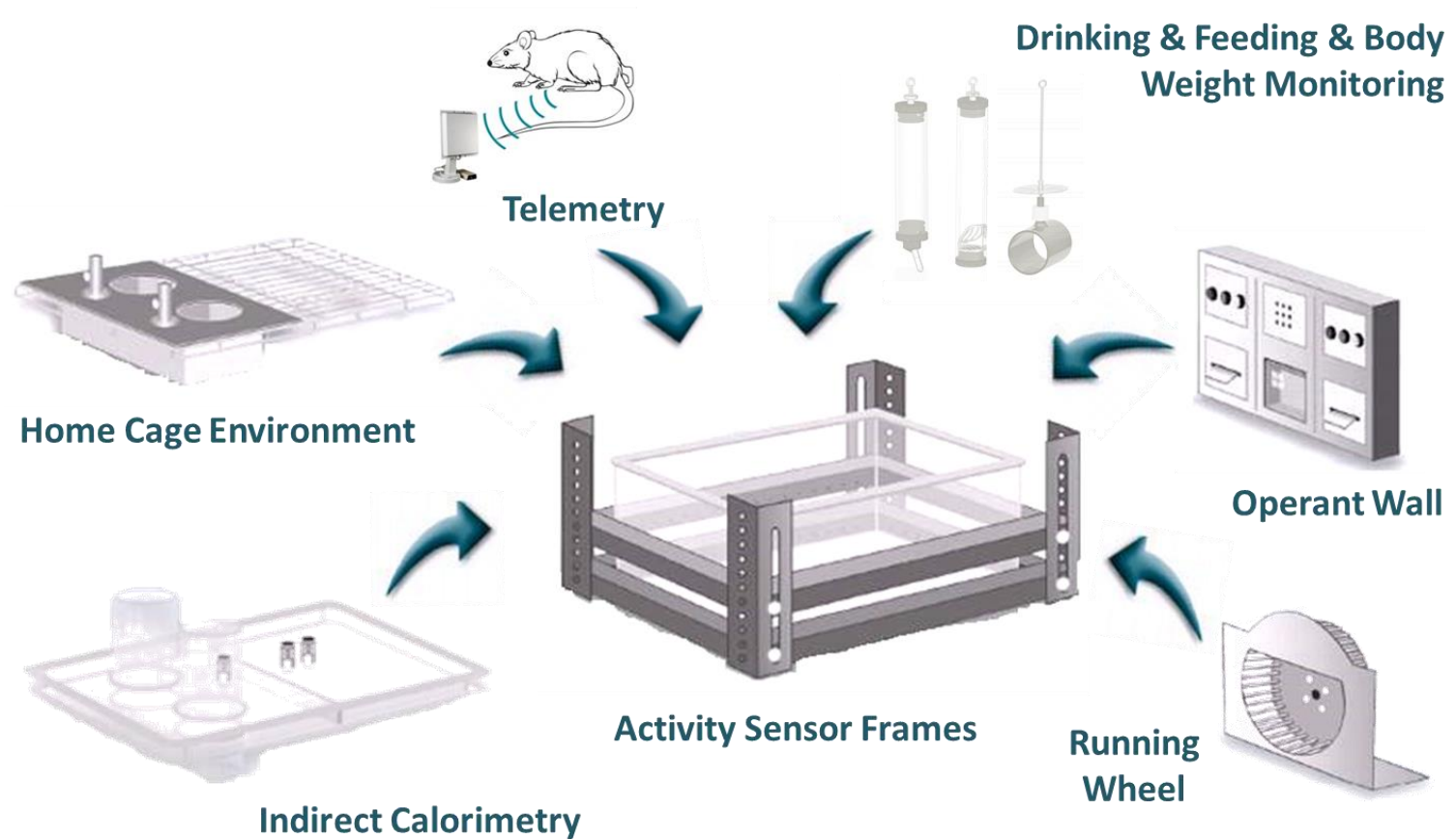
IntelliCage – Add-Ons



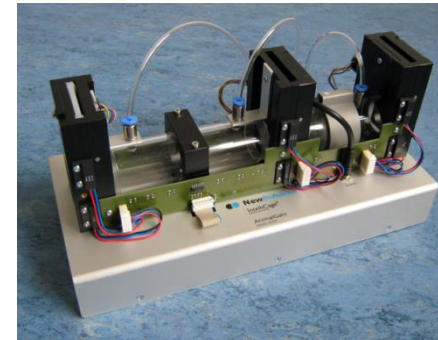
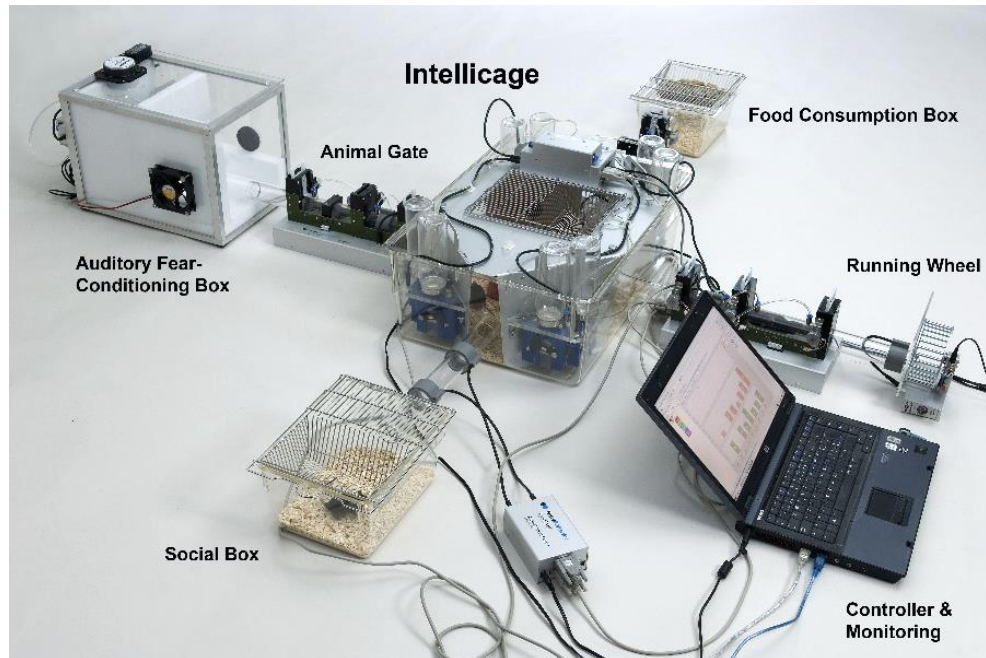
AnimalGates → selective passage of individual animals to

- PhenoMaster
- SocialBox
- AudioBox
- TraffiCage

PhenoMaster



PhenoWorld Mice



AnimalGate

...allows selective passage of individual animals to further compartments



A novel automated behavioral test battery assessing cognitive rigidity in two genetic mouse models of autism

Alicja Puścian¹, Szymon Łęski¹, Tomasz Górkiewicz¹, Ksenia Meyza¹, Hans-Peter Lipp^{2,3} and Ewelina Knapska^{1*}

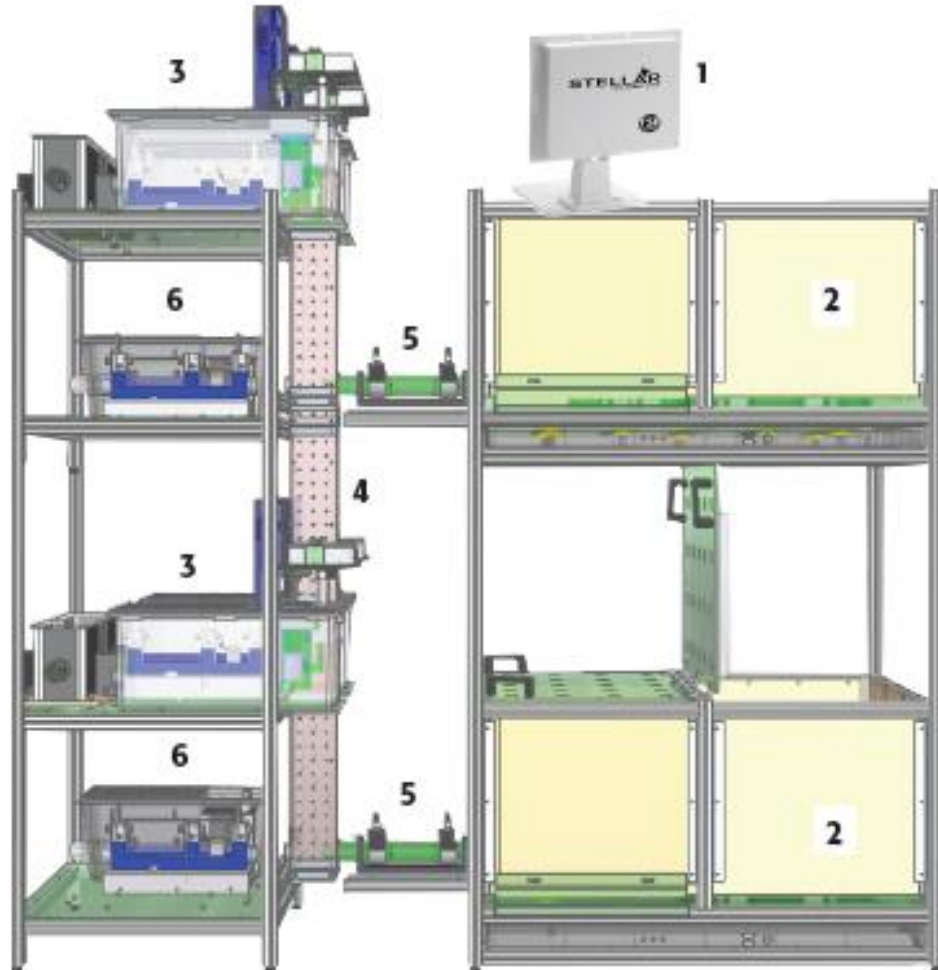
¹ Department of Neurophysiology, Nencki Institute of Experimental Biology, Warsaw, Poland

² Division of Functional Neuroanatomy, Institute of Anatomy, University of Zurich, Zurich, Switzerland

³ Department of Physiology, School of Laboratory Medicine, Kwazulu-Natal University, Durban, South Africa

Thanks for your attention

Dilip.Verma@tse-systems.com



PhenoTower - Paris

1. Stellar Telemetry
2. Social Main Arenas
3. Choice Arenas
4. Stairway
5. AnimalGates/SocialTubes
6. Operant Conditioning Arenas

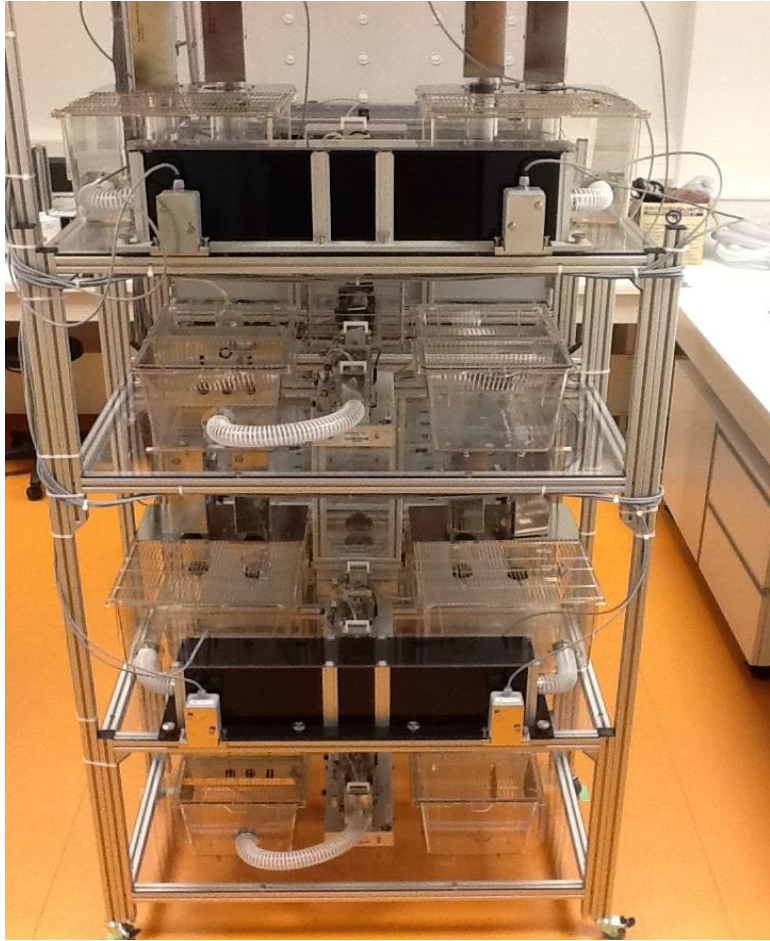


ARTICLE

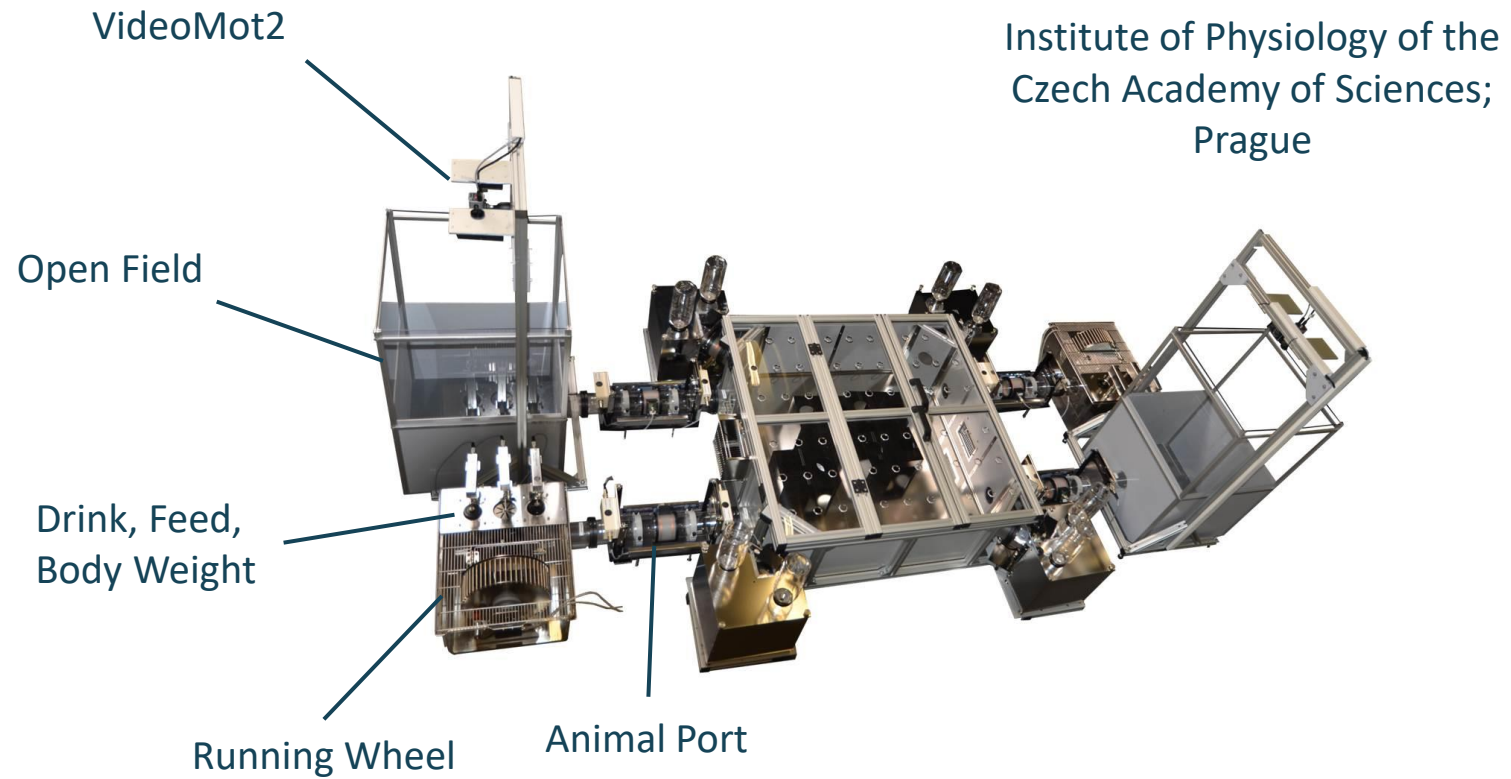
DOI: [10.1038/s41467-018-05526-5](https://doi.org/10.1038/s41467-018-05526-5) OPEN

Social interactions impact on the dopaminergic system and drive individuality

N. Torquet¹, F. Marti¹, C. Campart¹, S. Tolu¹, C. Nguyen¹, V. Oberto¹, M. Benallaoua¹, J. Naudé¹, S. Didienné¹, N. Debray^{2,3}, S. Jezequel^{3,4}, L. Le Gouestre^{3,4}, B. Hanneke¹, J. Mariani^{2,3}, A. Mourot¹ & P. Faure¹



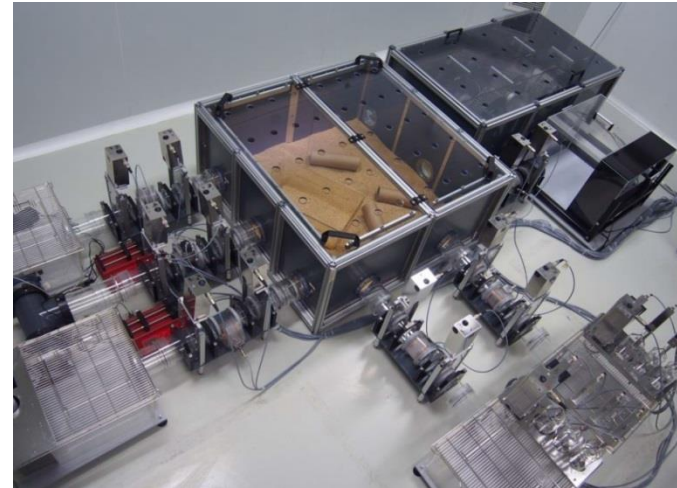
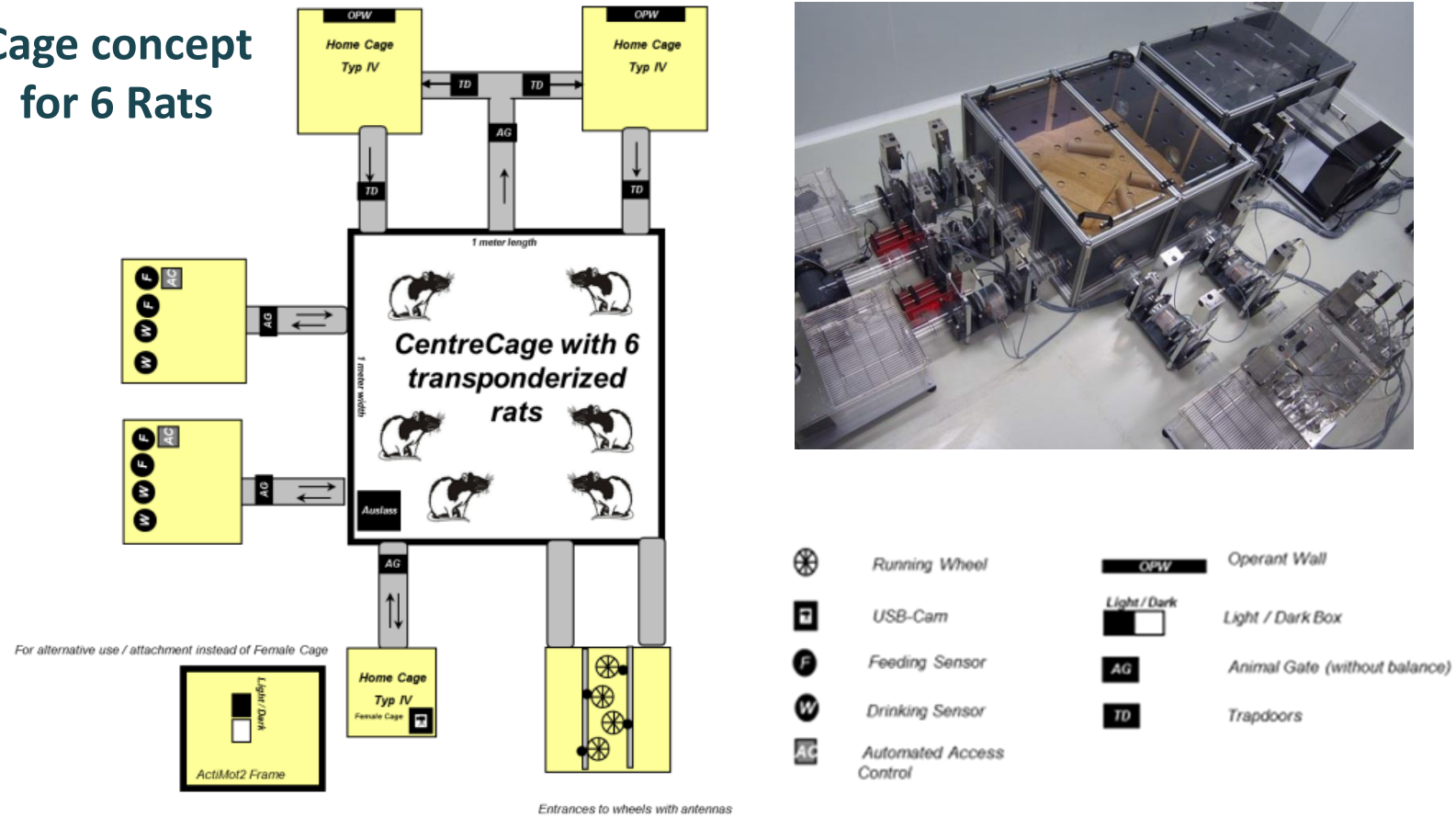
PhenoWorld Rats



Institute of Physiology of the
Czech Academy of Sciences;
Prague

PhenoWorld Rats

Cage concept for 6 Rats

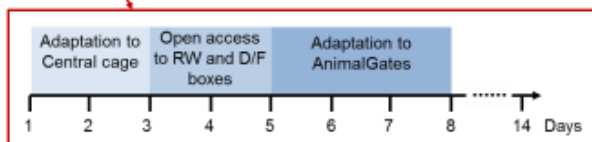
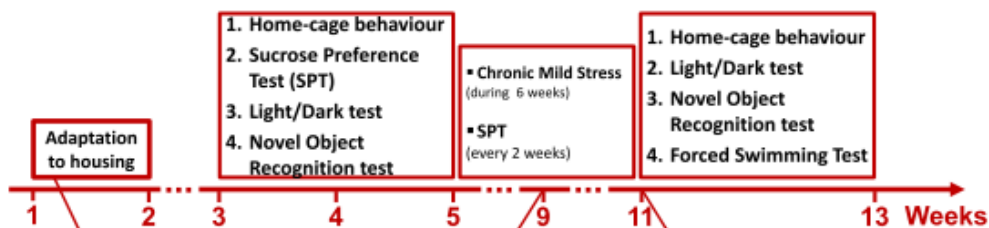


ORIGINAL ARTICLE

PhenoWorld: a new paradigm to screen rodent behavior

M Castelhana-Carlos^{1,2}, PS Costa^{1,2}, H Russig³ and N Sousa^{1,2}

Methods



LEGEND

- **Groups:**
PhW – 6 animals in PhenoWorld
Std(6) – 6 animals in standard cage
Std(2) – 6 animals in pair-housed
- **+ CMS** – indicates the animals were submitted to Chronic Mild Stress.
- **+ Flx** – indicates the animals were submitted to Fluoxetine treatment.

