

Behavioral analysis including motor, emotional and cognitive dimensions in animal models and in the study of compound effects

Species: rats and mice

Fields of application: Neurodegeneration

The development of animal models for pain and neurodegenerative diseases using both genetic and substance-based approaches is important to the field, as it improves the knowledge on the pathophysiological mechanisms of disease and provides experimental tools for testing novel therapies. In these models, it is also very relevant to characterize behavioral features such as motor abilities, emotional changes and cognitive performance, since often these are changed in animal models for pain and neurodegenerative diseases. Thus these results can provide information on benefits or side effects of compounds.

Cognition is a broad concept, defined as mental processes involved in judging, knowing, learning, perceiving, recognizing, remembering, thinking, and understanding that lead to the awareness of the world around us. Cognitive deficits occur in many neurological diseases. Cognition can be measured in animals in a similar fashion as in humans which offers the opportunity to investigate cognitive deficits in animal models mimicking aspects of neurological diseases.

Also, other behavioral assessments are important, for example measurements of motor capabilities and gait, anxiety, mood, arousal, social behavior and motivation.

Endpoints/Outcome parameters: Co-morbid symptoms such as cognitive impairment, fatigue and mood disturbances are often untreated and therefore represent potential therapeutic targets. Our aim is the identification of cognitive and behavioral deficits in various disease models and subsequently the *in vivo* testing of drugs for their ability to normalize cognitive and behavioral deficits in various disease models.

Readout parameters

At Fraunhofer IME-TMP we have several tests/tasks available for the measurement of cognition:

- social recognition
- Barnes maze: spatial memory task that requires subjects to learn the position of a hole that can be used to escape the brightly lit, open surface of the maze
- Mouse Touch Screen Chambers (Campden Instruments Ltd.):
 - ✓ Two-choice Visual Discrimination and Reversal
 - ✓ 5-Choice Serial Reaction Time Task - 5CSRT
 - ✓ 5-Choice Continuous Performance Test - 5C-CPT
 - ✓ Paired-Associate Learning Task - PAL
 - ✓ Location Discrimination - LD
- Intellicage: a novel approach for studying cognitive behavior of mice without handling by the experimenter.

More subtle and objective measurements of balance, motor coordination and muscle strength can be investigated using (semi) automated setups, such as:

- rotarod
- threadmill
- open field
- grip strength meter

For measurement of behaviors including the emotional dimension, we are able to assess:

- social interaction
- elevated zero maze: a paradigm to evaluate antianxiety effects of drugs

We apply video tracking technology (Noldus) which is very useful in many different behavioral tests.

Optogenetics: Optogenetics is a technology that allows targeted, fast control of precisely defined events in biological systems as complex as freely moving mammals. We are currently exploring opportunities to use optogenetic techniques and behavioral readouts in freely moving mice. Optogenetics can be used in a number of ways. For example, specific optogenetic stimulation of neurons in brain areas with a known function can be used instead of drugs or electrode stimulation, thereby activating or inhibiting processes. By assessing the effect of this stimulation on animal behavior, one can gain insight into neuronal functioning.

Quality management and validation:

References:

de Bruin NMWJ, Schmitz K, Schiffmann S, et al. (2016) Multiple rodent models and behavioral measures reveal unexpected responses to FTY720 and DMF in experimental autoimmune encephalomyelitis. *Behav Brain Res* 300:160–174. doi: 10.1016/j.bbr.2015.12.006

Schmitz K, de Bruin N, Bishay P, et al. (2014) R-flurbiprofen attenuates experimental autoimmune encephalomyelitis in mice. *EMBO Mol Med* 6:1398–1422. doi: 10.15252/emmm.201404168

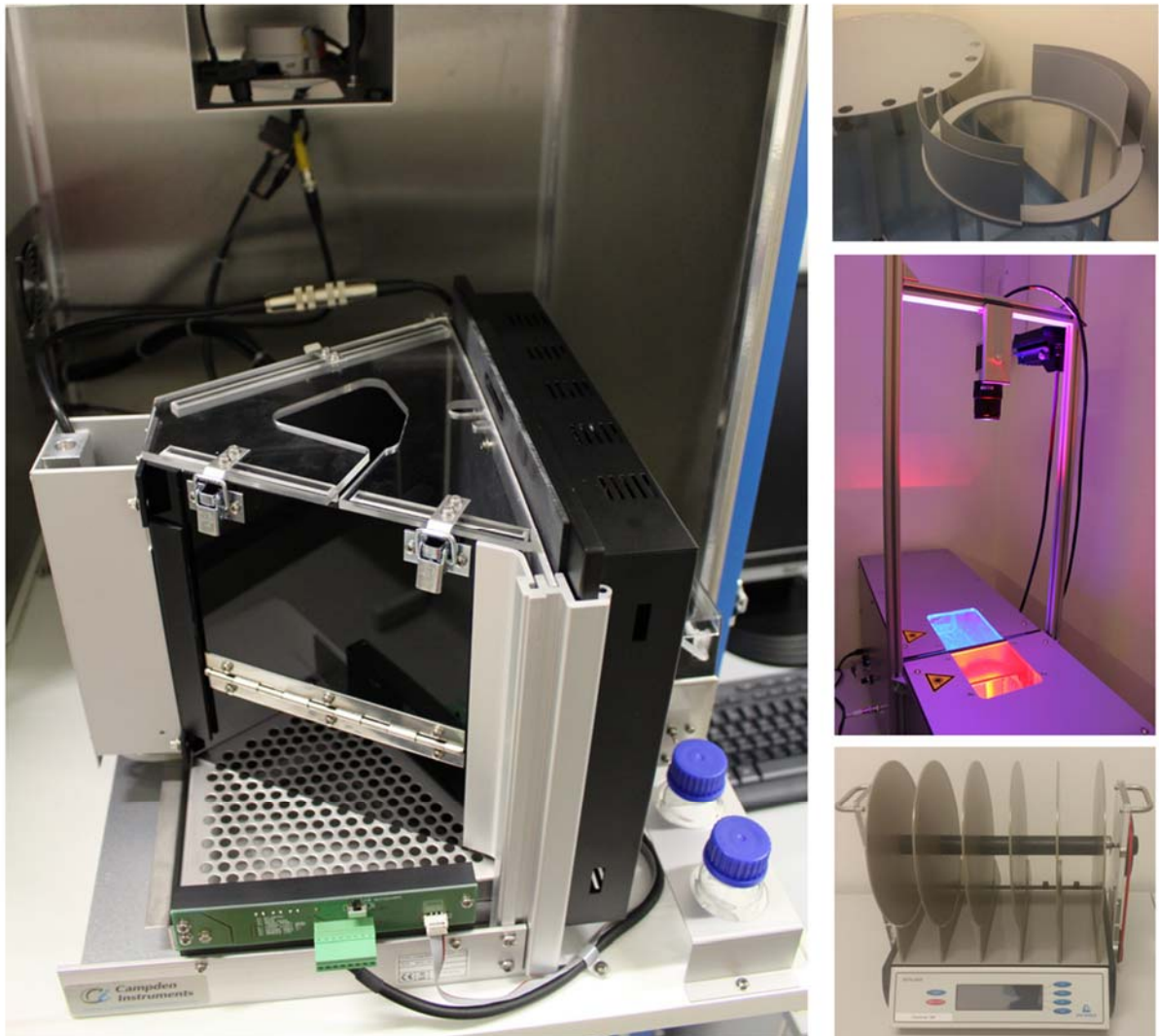


Figure: Examples of behavioral and cognition setups at Fraunhofer IME-TMP

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