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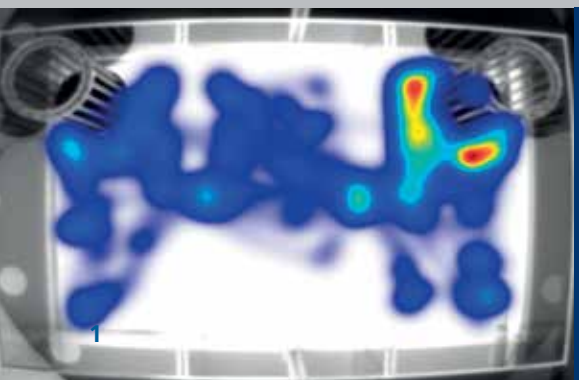
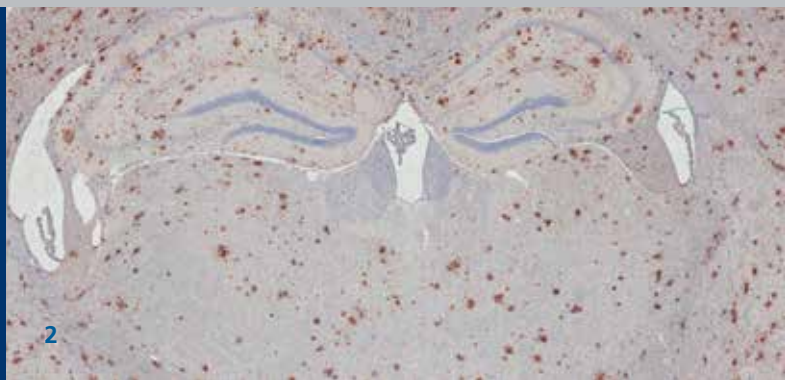




1 *Social Behavior in mice using Noldus EthoVision © Fraunhofer IME / Mike Schmidt.*
2 *Representative photo of mouse brain beta-amyloid staining, in an APP (NL-G-F) knock-in mouse © Fraunhofer IME / Martine Hofmann, Mike Schmidt.*

Fraunhofer Institute for Molecular Biology and Applied Ecology IME

Branch for Translational Medicine and Pharmacology
Theodor-Stern-Kai 7
60596 Frankfurt am Main

Contact:

Dr. Natasja de Bruin
Phone +49 69 8700-25052
natasja.debruin@ime.fraunhofer.de

Dr. Volker Laux
Phone +49 69 8700-25076
volker.laux@ime.fraunhofer.de

www.ime.fraunhofer.de/en/TMP

BEHAVIORAL ANALYSIS IN ANIMAL MODELS FOR THE STUDY OF COMPOUND EFFECTS

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

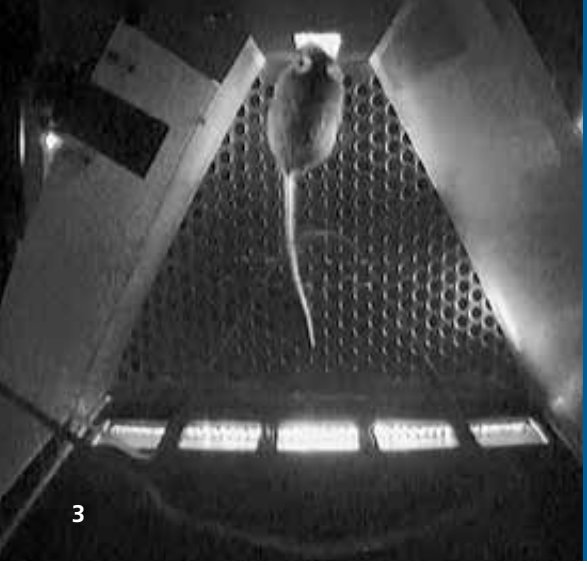
Cognition

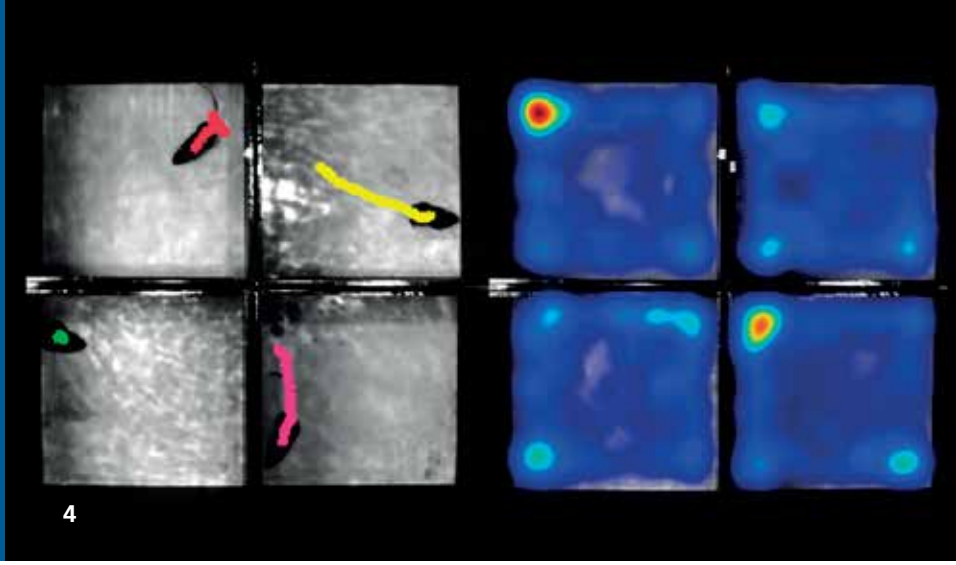
Cognition is a broad concept, defined as mental processes involved in judging, knowing, learning, perceiving, recognizing, remembering, thinking, and understanding that lead to awareness of the world around us. Cognitive deficits occur in many neurological diseases.

Cognition can be measured in animals in a similar fashion to that 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 in Frankfurt we have several tests and 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.)
Different paradigms have been established:

- Two-choice Visual Discrimination and Reversal
- 5-Choice Serial Reaction Time Task (5CSRT)
- Paired-Associate Learning Task (PAL)

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 also 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 anti-anxiety effects of drugs

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

Selected publications

- de Bruin NMWJ, Schmitz K, Schiffmann S, Tafferner N, Schmidt M, Jordan H, Häußler A, Tegeder I, Geisslinger G, Parnham MJ. Multiple rodent models and behavioral measures reveal unexpected responses to FTY720 and DMF in experimental autoimmune encephalomyelitis. Behav Brain Res 2016;300:160–74. doi:10.1016/j.bbr.2015.12.006.

- de Bruin NMWJ, van Loevezijn A, Wicke KM, de Haan M, Venhorst J, Lange JHM, de Groote L, van der Neut MAW, Prickaerts J, Andriambeloson E, Foley AG, van Drimmelen M, van der Wetering M, Kruse CG. The selective 5-HT6 receptor antagonist SLV has putative cognitive- and social interaction enhancing properties in rodent models of cognitive impairment. Neurobiol Learn Mem 2016;133:100–17. doi:10.1016/j.nlm.2016.06.020.

- de Bruin N, Kruse C. 5-HT6 Receptor antagonists: potential efficacy for the treatment of cognitive impairment in schizophrenia. Curr Pharm Des 2015;21:3739–59. doi:10.2174/1381612821666150605112105.

- de Bruin NMWJ, van Drimmelen M, Kops M, van Elk J, Wetering MM de, Schwienbacher I. Effects of risperidone, clozapine and the 5-HT6 antagonist GSK-742457 on PCP-induced deficits in reversal learning in the two-lever operant task in male Sprague Dawley rats. Behav Brain Res 2013;244:15–28. doi:10.1016/j.bbr.2013.01.035.

3 *Mouse touchscreen chamber*
© Fraunhofer IME / Olga Arne.
4 *Locomotor activity in mice using Noldus EthoVision*
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