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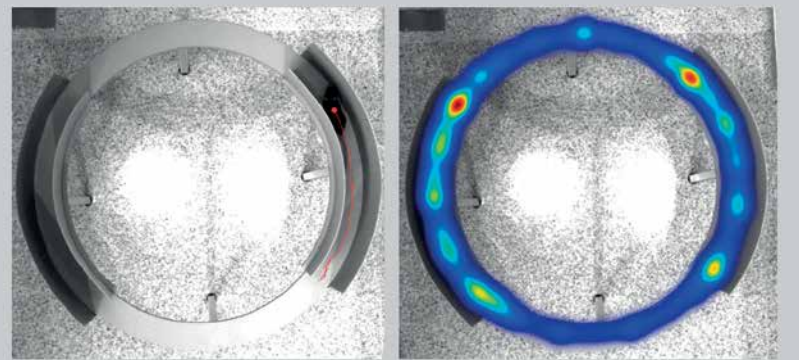

1 *Elevated plus maze test for measuring anxiety using Noldus EthoVision*
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EXPERIMENTAL AUTOIMMUNE ENCEPHALOMYELITIS MODELS FOR MULTIPLE SCLEROSIS

Multiple sclerosis

Multiple sclerosis (MS) is a chronic demyelinating, inflammatory and degenerative neurological disease often occurring in early adulthood. It results in disabling physical symptoms. With progression of the disease, the likelihood increases that comorbid conditions occur (such as cognitive deficits, depression and fatigue).

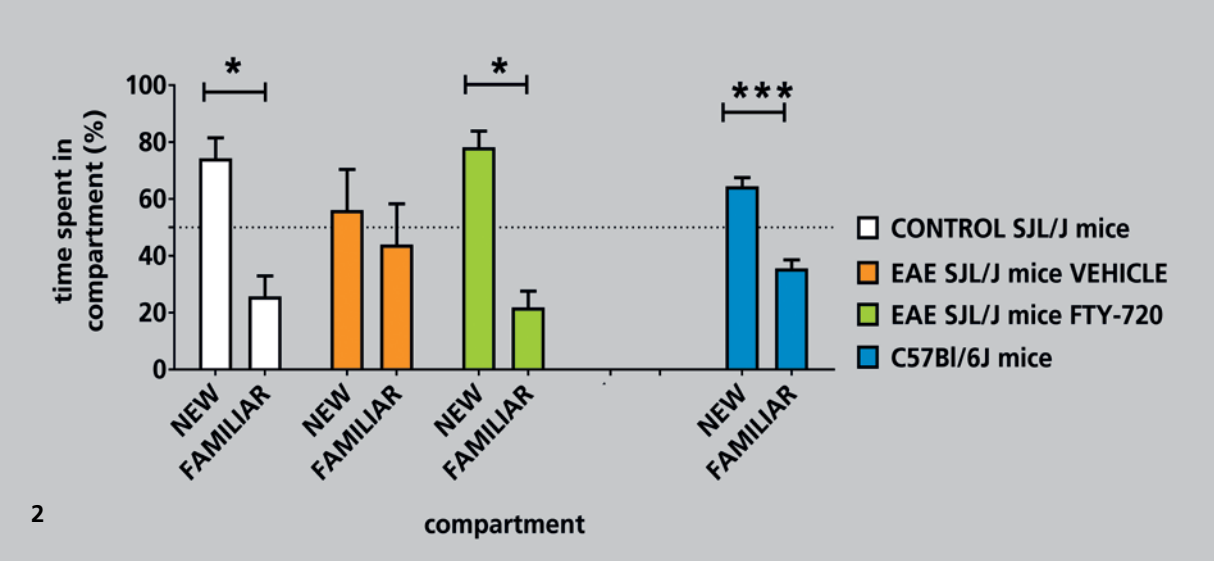
Experimental autoimmune encephalomyelitis

Experimental autoimmune encephalomyelitis (EAE) is a widely-used rodent model for MS, but a single model can hardly capture and adequately incorporate all features of MS. A number of different EAE models are available, resulting in different disease-progression patterns and clinical features. Dependent on the antigen and rodent strain used, the animals develop different disease processes. In addition to studies with drugs and test compounds, we also investigate responses in knockout mice.

Animal models

At Fraunhofer IME Branch for Translational Medicine and Pharmacology, several EAE animal models are available to test compounds.

- Monophasic EAE in Lewis rats (induced by myelin basic protein)
- Protracted-relapsing EAE in Dark Agouti rats (induced by spinal cord homogenate)
- Chronic progressive EAE in C57BL/6 mice (induced by myelin oligodendrocyte protein)
- Relapsing-remitting EAE in SJL mice (induced by proteolipid protein)



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Endpoints/Outcome parameters

It is important to consider which in vivo readouts are relevant for the evaluation of drug effects. We develop animal models for MS and try to mimic the symptoms of MS in animals in order to better predict efficacy of compounds in patients. Our approach is not only to use standard clinical score readouts, but we also offer the possibility to study more subtle and objective readouts that potentially could have a higher translational value.
Clinical signs and ascending paralysis in EAE are commonly assessed on a grading scale. In addition to this, we assess other variables that may be more predictive for the study of disease progression and drug efficacy, also during periods when no clinical scores can be registered, such as the remission interval between two clinical score peaks.

More subtle and objective measurements of balance, motor coordination and muscle strength can be investigated using (semi) automated setups such as rotarod, treadmills and grip strength meter.

MS co-morbid symptoms such as **cognitive impairment, fatigue and mood disturbances** are often untreated and therefore represent potential therapeutic targets. For example, clinical studies have revealed discrete cognitive dysfunction in MS patients already at an early stage of the disease.

About 60% of individuals with MS experience significant cognitive dysfunction.

We offer the opportunity to test effects of compounds on cognitive impairment in EAE animal models using setups such as the Mouse Touch Screen Chambers (Campden Instruments Ltd.).

Selected publications

- Schmitz K, Brunkhorst R, de Bruin N, Mayer CA, Häussler A, Ferreiros N, et al. Dysregulation of lysophosphatidic acids in multiple sclerosis and autoimmune encephalomyelitis. Acta Neuropathol Commun 2017;5:42. doi:10.1186/s40478-017-0446-4.

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- Schmitz K, de Bruin N, Bishay P, Mannich J, Haussler A, Altmann C, et al. R-flurbiprofen attenuates experimental autoimmune encephalomyelitis in mice. EMBO Mol Med 2014;6:1398–422.doi:10.15252/emmm.201404168.

- de Bruin N, Ferreirós N, Schmidt M, Hofmann M, Angioni C, Geisslinger G, et al. Mutual inversion of flurbiprofen enantiomers in various rat and mouse strains. Chirality 2018;35:28–50. doi:10.1002/chir.22826.

- Beyer S, Xie L, Schmidt M, de Bruin N, Ashtikar M, Rüschenbaum S, et al. Optimizing novel implant formulations for the prolonged release of biopharmaceuticals using in vitro and in vivo imaging techniques. J Control Release 2016;235:352–64. doi:10.1016/j.jconrel.2016.06.0135.

2 *Social test (day 26-28) in control versus EAE female SJL mice and the effect of FTY-720: time spent in each compartment in the social recognition test. The EAE vehicle-treated mice show a deficit in social recognition*
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