

Automated longitudinal testing offers a cost-effective, high-throughput way to monitor various slowly developing behavioral changes in rats or mice, as seen in depression or neurodegenerative diseases (Alzheimer, Huntington) or Parkinson. The animal is observed continuously in an instrumented home cage environment (PhenoTyper®), fully automated and without any human interference. This avoids the confounding effects of novelty, stress, transportation and handling.

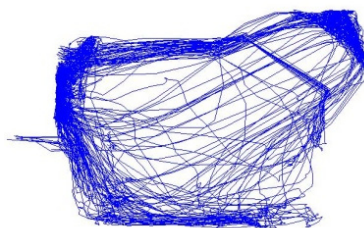
## Example study: Mice model for Parkinson's disease<sup>1</sup>

Mutations in a few genes including  $\alpha$ -synuclein have been associated with Parkinson's disease. Since these mutations result in a nigrostriatal dopaminergic degeneration, transgenic animal models have been developed to investigate the role of  $\alpha$ -synuclein and other genes involved in the pathogenesis of Parkinson. During this study, double transgenic mice as an animal model for Parkinson's disease (obtained via a collaboration with the University of Tuebingen) have been studied in the PhenoTyper for several weeks. Usually the first behavioral deficits in these mice are detected at the age of 48 weeks. Now using a fully automated observation technique we have seen differences already at the age of 20 weeks. The mutants showed a clear reduction in distance moved as can be seen qualitatively from track plots covering 1 hour of observation. In addition, the histogram represents the quantitative data and it refers to the global spontaneous activity during 1 week.

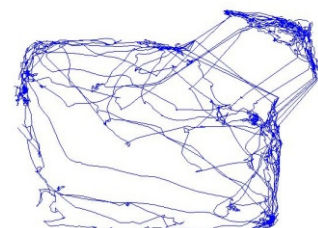
Top view PhenoTyper home cage system



Wild type



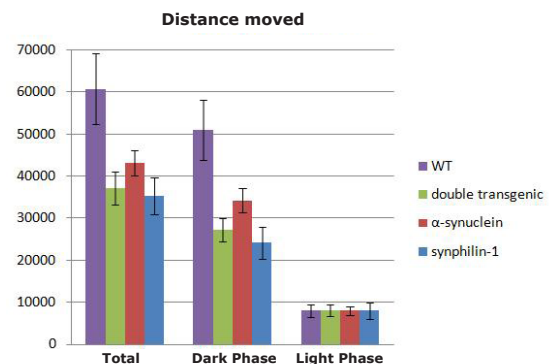
Mutant (double transgenic)



On the left the home cage system in which the mice were housed. On the right using track plots a comparison between the activity of a wild type mouse and a mutant shows a clear difference.

## Conclusion and future approach

Distance moved in the dark phase (thus the active phase for the mice) was significantly diminished for all mutants. There was no difference between the single and double knock outs. There is outstanding evidence that these transgenic animal models of Parkinson show motor impairments reflecting in an easily detectable reduced activity level using an automated recording technique.



The daily distance moved during an entire week is a good parameter to estimate the spontaneous activity level of the animals. The difference between the wild type and the transgenic mice is particularly evident during the active phase of the mice while there is no difference during the resting period (light phase).

By using an integrated approach it is also possible to monitor the cognitive deficits of the animals by implementing several tests into the PhenoTyper looking for early behavioral signs of Parkinson's disease. An early detection of symptoms related to Parkinson is fundamental for the development of neuroprotective strategies that will slow or stop the progression of the disease.

<sup>1</sup> This is a study in the context of the NEUROMODEL project, a Marie Curie Initial Training Network funded by the EU 7<sup>th</sup> Framework Programme.

