Behavioral Characterization of Homozygous BACHD Rats
Tina Loeffler1, Stephan Kurat1, Adam Horvath1, Stefanie Flunkert1, Hoa Huu Phuc Nguyen2,3, Robert Wronski1, Birgit Hutter-Paier1
1QPS Austria GmbH, Parking 12, 8074 Grambach, Austria; 2Institute of Medical Genetics and Applied Genomics, University of Tübingen, Tübingen, Germany; 3Department of Human Genetics, Ruhr-University Bochum, Bochum, Germany

BACKGROUND
Behavioral changes in Huntington’s disease (HD) are directly associated with the dysfunction and degeneration of certain brain areas, most prominently striatum and cortex. The sole cause of developing HD is the expansion of an unstable repeat of CAG base triplets in the coding region of the Huntingtin gene, HTT. The BACHD rat overexpresses full length human mutant huntingtin with 97 alternating CAA/CAG repeats and is thus a well suited genetic animal model of HD.

MATERIALS and METHODS
Homozygous BACHD rats at 2 and 5 months of age and age-matched non-transgenic controls were analyzed for behavioral changes. Animals were housed in the AAALAC accredited animal facility of QPS Austria. All animal tests were approved by the local government. To assess cognitive and motor deficits the Barnes maze, Passive avoidance, Grip strength as well as Rota Rod test were used.

RESULTS
Our results show motor deficits analyzed with the grip strength test and Rota Rod in homozygous BACHD rats at the age of two and five months. Additional analyses in the Barnes maze test showed initial learning, memory and relearning deficits at the age of two months, which were further increased at the age of 5 months. Further analysis in the passive avoidance test revealed emotional learning deficits of 2 months old homozygous BACHD rats.

Quantification of polyQ HTT
![Graph showing quantification of polyQ HTT](chart)

Fig. 1: Quantification of polyQ HTT by sandwich immunosorbent assay using the Mesoscale Discovery platform. Whole brain lysate of a 6 months old hemizygous rat and a non-transgenic littermate were used in a dilution series of 1:10, 1:40; 1:160; 1:640 and 1:2560.

SUMMARY and CONCLUSION
In summary homozygous BACHD rats present a very early motor and cognitive phenotype. Cognitive deficits already start at the young age of two months and therefore appear much earlier compared to heterozygous BACHD rats. Although homozygous animals need to be further characterized, our data already suggest that homozygous BACHD rats will be of great importance for future HD research. Testing new compounds that influence HD disease progression could be facilitated, since treatment could be significantly shortened compared to heterozygous BACHD rats.

Contact for more information about the models:
Birgit Hutter-Paier, PhD | Director Neuropharmacology | QPS Austria GmbH | Parking 12 | 8074 Grambach | Austria
birgit.hutter-paier@qps.com | www.qpsneuro.com

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