Behavioral Characterization of Homozygous BACHD Rats

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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.

Muscle and motor deficits in the Grip Strength and Rota Rod

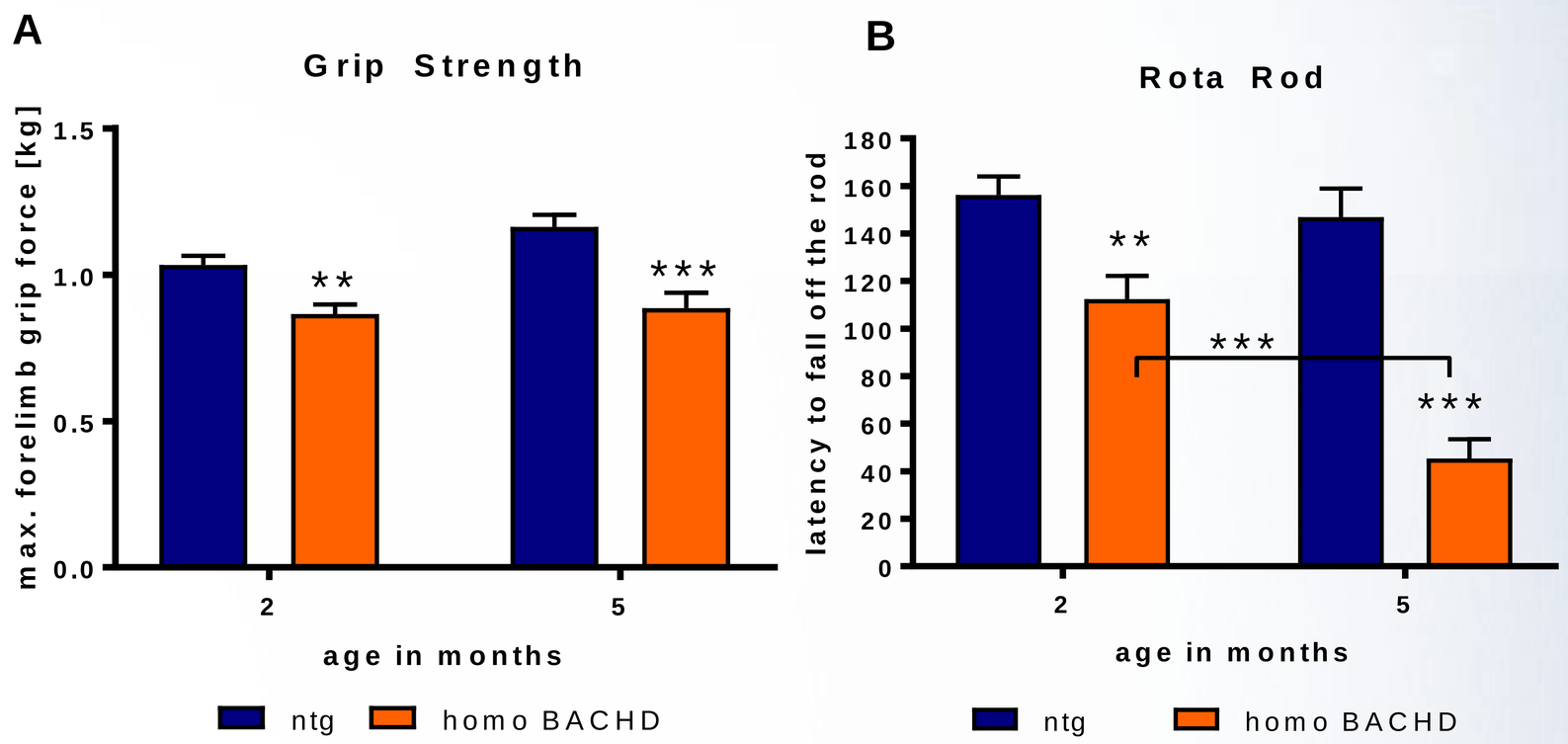

Figure 1: Assesment of muscle and motor perfomance with Grip strength (A) and Rota Rod (B) of homozygous BACHD rats. Forelimb grip strength performance (**A**) and motor coordination expressed as time to fall off the rod in seconds (**B**) of homozygous BACHD and non-transgenic (ntg) rats at the age of 2 and 5 months. Mean ± SEM, Two-way ANOVA followed by Bonferroni's *posthoc* test; **p<0.01; ***p<0.001.

Cognitive and emotional deficits in the Barnes Maze and Passive Avoidance Test

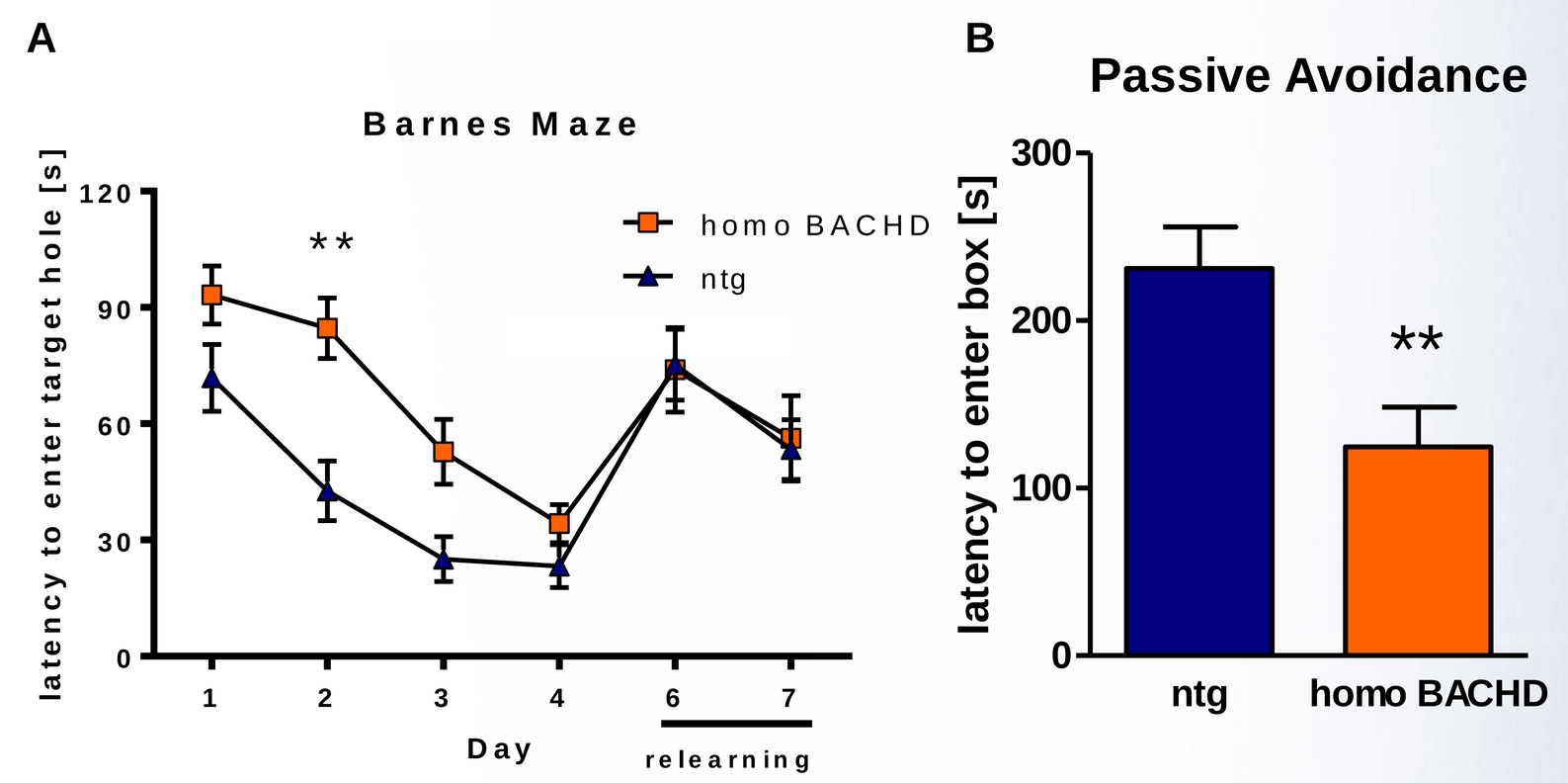

Figure 2: Barnes maze and Passive avoidance test of homozygous BACHD rats. A: Latency to enter the target hole during learning and relearning in seconds of 5 months old homozygous BACHD rats; Two way ANOVA followed by Bonferroni's *posthoc* test. **B**: Latency to enter the dark chamber on day 2 of the Passive avoidance test of 2 months old homozygous BACHD rats. Mean + SEM; Mann Whitney U-test; **p<0.01.

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.

We look forward to support your research

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