Automated Home Cage Assessment of Sca17 Mouse Model

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ABSTRACT

The study of neurodegenerative diseases presents a great challenge in modeling and treatment, requiring that behavior be carefully recorded and analyzed. There is an increase in the use of rodent models used for this purpose, but behavioral tests pose the challenges of being time and resource intensive, as well as demanding specific training and careful planning to ensure relevant results. The use of automated home cages can improve these aspects of behavioral testing. For this reason, we have assessed a SCA17 mouse model with the LabMaster automated home cage system. We report the results for this model as well as the methodology used to improve analysis by automated home cage system.

Author Keywords
Automated home cage, automated behavior assessment, rodent models, SCA17, neurodegenerative disease.

Spinocerebellar ataxia 17 (SCA17) is progressive neurodegenerative disease of autosomal dominant transmission. SCA17 is induced by expansion of the CAG repeats (>42) in the TATA-binding protein (TBP), a transcriptional initiation factor. This leads to atrophy in the cerebellum and Purkinje cell loss, with less pronounced neurodegeneration in other parts of the brain (1,2). The clinical phenotype is heterogeneous, exhibiting ataxia, dementia, dystonia, parkinsonism and dystonia (1,2). Mouse models for SCA17 have been generated and studied using Rotarod, weight and survival. We chose one of these models, SCA17Q-16J, to assess in an automated homecare system with the aim of finding whether we could explore more phenotype parameters in the disease progression.

Large scale behavioral assays of animal models using classical behavioral analysis face limitations due to manpower and training required, time consuming techniques, and costs of breeding and maintaining large amounts of animals. Furthermore, experimenter effect and differing protocols for the number of tests used can give differences when comparing studies. When the same animals are tested several times in a battery of tests, problems of carry-over effects and stress induced by manipulations increase with the number of tests used. On the other hand, when different animals are assigned to different tests, a large number of animals is needed thus increasing the costs. A limitation with using several tests to measure activity is that only one aspect is recorded with each trial, with no concurrent or complex behavior analyzed. Animal models with severe phenotypes pose additional challenge due to the reduced life expectancy and time available for experimentation.

The automated home-cage system LabMaster (developed by TSE system, Bad Homburg, Germany) provides an excellent tool to measure a wide range of behavioral parameters (5). While such automated approach results in concurrent and complex behavioral data, the amount of data produced requires much time to explore and process. A second objective was to find a methodology to reduce the time necessary to explore and interpret the output generated by this system. To process the data, we used the R statistics program for automatic aggregation, grouping, correlation and multivariate analysis that permits a quick screen of behavioral characteristics. The results where also processed with GraphPad Prism for final presentation.

CONCLUSION

We found that the Labmaster automated home cage systems permits a more deep analysis of behavior phenotype for SCA17Q-16J mouse with less time and training requirements than the classical behavior tests published. Also, we were able to produce a methodology and tools that greatly improves the efficiency of analyzing and exploring automated home cage results.

REFERENCES

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