Department of Neurobiology, Care Sciences and Society

Automated behavioral phenotyping of inbred mouse strains and mouse models of Alzheimer disease

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av

Alina Codiţă

Huvudhandledare:
Professor Abdul H Mohammed
Karolinska Institutet
Institutionen för NVS
KI-ADRC

Bihandledare:
Professor Bengt Winblad
Karolinska Institutet
Institutionen för NVS
KI-ADRC

Associate Professor Eirikur Benedikz
University of Southern Denmark
Institute of Molecular Medicine

Fakultetsopponent:
Profesor Richard Paylor
Baylor College of Medicine, Texas, USA
Depts of Molecular and Human Genetics
and Neuroscience

Betygsnämnd:
Professor, MD Klas Blomgren
Göteborg Universitet
Institutionen för Neurovetenskap

Associate Professor Rochellys Diaz Heijtz
Karolinska Institutet
Institutionen för Neurovetenskap

Dr. Johan Sandin
AstraZeneca, R&D Södertälje
Section of Neurology

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ABSTRACT

Behavioral characterization of mouse models for human diseases requires robust phenotyping methods. Widely used behavioral methods yield inconsistent results across laboratories, in spite of standardization efforts.

This thesis evaluated an automated device - *the IntelliCage* - which enables behavioral testing of group-housed mice. In a multi-center study, inter-laboratory consistency of behavioral measurements in IntelliCage was evaluated [study I]. Three strains of mice: C57BL/6NCrl (B6), DBA/2NCrl (D2) and (C57BL/6 x DBA/2) F1/NCrl (C6D2F1) were tested simultaneously in four laboratories. No statistically significant interaction effect of *Laboratory* x *Strain* was obtained, indicating that strains were consistently ranked across laboratories. Significant *Laboratory* effects were obtained for several *Activity* and *Learning* variables due to uncontrolled local factors. During the adaptation phases B6 mice made more visits to IntelliCage corners than D2 mice. B6 mice discriminated best following place learning and D2 were best at re-learning the task.

Using the same study design we evaluated the effect of additional components (add-ons) availability on IntelliCage measures [study II]. In the enriched condition (IntelliMaze) access to additional space was made through the "SocialBox" and "AnimalGate" add-on devices. The unconditioned activity during adaptation dark phases was reduced in the presence of add-ons. During the place conditioning paradigms, the number of trials needed to reach the learning criterion was lower in the presence of add-ons. The strain ranks for activity measures were consistent with the results of study I.

In study III, a double transgenic Amyloid precursor protein (*APP*) model of Alzheiemer disease, (the tg-ArcSwe) was tested longitudinally in the IntelliCage. A deficit in extinguishing place preference for a previously rewarded corner at 4 months was shown. At 14 months the tg-APPArcSwe mice were impaired in a passive avoidance test in the IntelliCage. Measures of passive avoidance behavior were found to moderately and inversely correlate with the level of Calbindin-28k immunoreactivity in the polymorphic layer of the dentate gyrus.

Finally, the effects of IntelliCage exposure as well as relationships between variables obtained during IntelliCage testing and classical behavioral tests were assessed [study IV]. We found that only a limited amount of variance in the conventional tests could be accounted for by IntelliCage variables.