Behavioral phenotyping of a murine AD-model in a semi-naturalistic environment using RFID tracking

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Neurodegenerative disorders such as Alzheimer's disease (AD), which are characterized by an advancing cognitive decline are increasingly threatening public health. Most animal models of AD consist of transgenic mice that are usually housed singly or in unisexual groups in small barren cages. Such restricted environments, however, prevent the mice from showing a variety of species-specific behavior and consequently may constrain behavioral phenotyping. The aim of this project was to characterize TgCRND8-mice carrying a genetic disposition (human $APP_{Swe+Ind}$) to develop Alzheimer-like pathology and their wild-type conspecifics in a semi-naturalistic environment (SNE). The SNE measured 1.75 by 1.75 by 2.1m (L x W x H) and contained several floors (see Figure 1). The population comprised male and female mice of both genotypes and was allowed to grow to a size of 40 adults. Mice were individually marked using subcutaneously injected RFID transponders as well as a color coding scheme on their tails and ears. In a first step behavioral observations at different ages of the mice were conducted by thoroughly trained experimenters distinguishing up to 55 unique behavioral patterns from various behavioral domains. First results revealed surprisingly little significant differences between genotypes that were true at all ages and for both sexes.

Interestingly the mice established a complex social structure comprising several territories held by dominant males. In a second step direct observations were complemented by RFID-antennas placed at strategically chosen spots within the SNE. The transponder ID is read while a mouse traverses the electromagnetic field which is established by the ring antennas, e.g. when passing through tubes or visiting drinking places. A software that was developed for this setup allowed constant monitoring of several locomotory, activity, and behavioral patterns on a 24h/7d basis. The automated RFID-tracking system was evaluated by direct observation of movement data that correlated highly significantly with the number of antenna contacts. Dominant males patrol their territory borders more frequently than subdominants and thereby triggered significantly more antennae contacts than subdominant animals. This indicates that the RFID-system applied here may indeed facilitate behavioral observations as it allowed the determination of social status by the number of antenna contacts. Both, transgenic and wild-type mice were able to achieve high dominance positions and were able to hold a territory. To test spatial memory performance, a modified Barnes Maze was conducted within the SNE. This test revealed that deficits that are known from TgCRND8 mice

Figure 1. *Semi-naturalistic environment (SNE). RFID marked mice were are automatically tracked when passing a ring-antenna.*

are still present in the SNE. However, marked differences in activity and stereotypic behavior that were observed in TgCRND8 mice in standard cages [1] could not be observed in the SNE. This indicates, that a physically and socially enriched environment can modify the way an individual is able to cope with the disease.

References

1. Ambrée, O., Touma, C., Görtz, N., Keyvani, K., Paulus, W., Palme, R., Sachser, N. (2006). Activity changes and marked stereotypic behavior precede Abeta pathology in TgCRND8 Alzheimer mice. *Neurobiology of Aging*, **27**, 955-964.