

## **Laboratory mouse lines derived from outdoor natural selection tested in IntelliCages: reduced initial novel object exploration and prolonged place avoidance**

Knapska E (1), Wolfer DP (2,3), Perepelkina OV (4), Poletaeva II (4), Lipp HP (2,5)

(1) Nencki Institute of Experimental Biology, Dept. of Neurophysiology, Warsaw, Poland

(2) Institute of Anatomy, University of Zurich, Switzerland

(3) Institute for Human Movement Sciences and Sport, ETH Zurich, Switzerland

(4) Laboratory of Genetics and Physiology of Behavior, Moscow State University, Russian Federation

(5) School of Laboratory Medicine, Kwazulu-Natal University, Durban, South Africa

A natural selection experiment in Russian outdoor pens resulted in mouse lines (MF1 and MF2) differing significantly from randomly mated control mice in the laboratory (MFC), in showing reduced intra/infrapyramidal mossy fiber projections in the hippocampus (IIP-MF). The lines were further bred in Moscow and, after embryo transfer, in Zurich. Standard tests conducted in Moscow with mice from the 15th generation revealed reduced activity of the MF1 and MF2 versus MFC mice in a small openfield, and reduced approaching to a novel object in a small open field in Zurich (18th) generation. MF1, MF2 and MFC mice from the 26th generation were tested in IntelliCage to verify persistence of reduced curiosity and temporal changes in behavior after exposure (i) to a novel object in a corner of IntelliCage, and (ii) for place avoidance after delivering air puffs in corners specific for subgroups of mice. MFC mice spent significantly more time in a corner with a novel object during 7 min than both MF1 and MF2 mice. However, after 24 h both MF1 and MF2 mice had spent significantly more time in that corner. Conversely, visits in a corner delivering air puffs showed a strong and persistent decline in the MF1 and MF2 versus the MFC mice.

These data indicate that natural selection altered, together with the IIP-MF distribution, the behavioral phenotype already after the sixth outdoor generation, resulting in persistent behavioral changes reflecting the environmental pressure of a habitat favoring a fearful phenotype associated with retarded novel object exploration..