
HOUSING CONDITIONS MODULATE THE COGNITIVE PERFORMANCE IN TRANSGENIC MICE OVEREXPRESSING THE SCHIZOPHRENIA SUSCEPTIBILITY GENE TCF4

M. BrzŹzka¹, D. Badowska², P. Falkai¹, M. Rossner¹

¹Psychiatry, Ludwig-Maximilians-University, MŹnchen, Germany ; ²Neurogenetics, Max-Planck-Institute of Experimental Medicine, GŹttingen, Germany

INTRODUCTION: The basic helix-loop-helix (bHLH) transcription factor TCF4 was confirmed in the combined analysis of several large genome-wide association studies (GWAS) as one of the most significant schizophrenia (SZ) susceptibility genes. *TCF4* influences verbal learning and memory in humans and modulates sensorimotor gating in SZ patients. We showed recently that transgenic mice overexpressing Tcf4 in forebrain (Tcf4tg) display profound deficits in fear memory and sensorimotor gating.

METHODS: We investigated the influence of different environmental conditions on the behavior and cognitive performance of Tcf4tg mice by exposing 4 weeks old animals for 4 weeks to single cage housing (SH) or to group housing in enriched environment (EE). In SH, animals were housed under poor conditions without any enrichment. In contrast, EE cages contained two separate compartments: the first with one-way entrance and one-way exit for drinking/feeding, and the second compartment with tubes and a running wheel enabling physical exercise. Animals underwent a profound analysis addressing basic behavior and cognitive performance.

RESULTS: We demonstrated that SH (isolation stress) increases whereas housing in EE (combination of social support with physical exercise) rescues the cognitive impairment of Tcf4tg mice. We provided evidence that the manifestation of the phenotype of Tcf4tg mice depends strongly on environmental factors. This substantiates the importance of G×E interactions in the manifestation of schizophrenic phenotypes.

CONCLUSIONS: The observed phenotype of Tcf4tg mice may resemble the situation in patients where symptoms can be elicited by the 'second hit' (social stress) and can be ameliorated by social support or physiotherapy.