Ruprecht-Karls-Universität Heidelberg
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Dissertations-Kurzfassung

The role of scavenger receptors Stabilin-1 and Stabilin-2 in psychiatric diseases

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Objective: Recently, STAB1 and STAB2 were identified as candidate genes associated with psychiatric diseases. The aim of this project was to conduct a behavioral analysis with transgenic mice having a global deletion of either scavenger receptor gene Stab1 (Stab1-KO) or Stab2 (Stab2-KO) to screen for phenotypic alterations associated with major psychiatric diseases.
Method: Stab1-KO, Stab2-KO and wild type control mice were tested within a total of 23 behavioral experiments assessing five major phenotypic categories: locomotor activity and motor behavior, basal behavior, anxiety- and depression related behavior, specific psychiatric endophenotypes and cognitive functions.
Results: Stab1-KO mice exhibited anti-manic-like phenotypes including decreased locomotor activity, increased PPI, attenuated amphetamine-induced locomotor activity and less interest in female urine. In addition also elevated anxiety- and depression-related behaviors and anhedonia were observed in Stab1-KO mice which represent symptoms found in bipolar depression. Similar to Stab1-KO mice, Stab2-KO mice exhibited decreased locomotor activity, increased PPI and an attenuated amphetamine-induced hyperlocomotion. However, Stab2-KO mice exhibited behavioral alterations of negative and cognitive symptoms of schizophrenia including decreased preference for social novelty, decreased sucrose preference (anhedonia), decreased motivation to press a lever for sweetened food pellets and impaired spatial short-term memory.
Conclusion: Elimination of Stabilin1 production will not lead to mood stabilization but will lead to the induction of bipolar depression. Investigating which one of the ligands of scavenger receptor Stabilin1 is necessary to balance and to maintain healthy mood might help to understand the molucular phathology of bipolar disorder. Elimination of Stabilin2 production might protect an organism from developing positive symptoms but with the disadvantage that negative and cognitive symptoms are elicited. Understanding the molecular mechanism of mood regulation, in which Stabilin2 is involved, might lead to the development of new medication with a profile of side effect better tolerated by the patients.