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Anxiety-like behavior and other consequences of early life stress
in mice with increased protein kinase A activity

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Short title: PKA activity and stress

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Highlights

- Loss of one Prkar1a allele is associated with an anxiety-like phenotype in adult mice.
- Developmental differences in anxiety behavior were found for WT and Prkar1a⁺⁻ mice.
- Prkar1a⁺⁻ adolescent mice demonstrated higher exploratory and novelty seeking behavior.
- Loss of one Prkar1a allele is associated with vulnerability to stress in adolescence.

Abstract

Anxiety disorders are associated with abnormalities in fear-learning and bias to threat; early life experiences are influential to the development of an anxiety-like phenotype in adulthood. We recently reported that adult mice (Prkar1a⁺⁻) with haploinsufficiency for the main regulatory subunit of the protein kinase A (PKA) exhibit an anxiety-like phenotype associated with increased PKA activity in the amygdala. PKA is the main effector of cyclic adenosine mono-phosphate signaling, a key pathway involved in the regulation of fear learning. Since anxiety has developmental and genetic components, we sought to examine the interaction of a genetic defect associated with anxiety phenotype and early life experiences. We investigated the effects of neonatal maternal separation or tactile stimulation on measures of behavior typical to adolescence as well as developmental changes in the behavioral phenotype between adolescent and adult wild-type (WT) and
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