ABSTRACT

Cyclic AMP (cAMP) -dependent protein kinase (PKA) is a ubiquitous serine/threonine kinase. PKA plays a key role in the signaling of many G protein-coupled receptors through the consequent production of cAMP. The specificity of PKA actions is achieved by controlling its cellular localization through a family of A-kinase anchoring proteins (AKAPs). AKAPs localize PKA to specific intracellular sites and spatially restrict intracellular signaling events related to various cellular processes, including the regulation of neuroplasticity. A-kinase anchor inhibitor 1 (Akain1) is a novel PKA-binding protein with a unique function in PKA signaling. Akain1 competes with other AKAPs for PKA binding and seems to abrogate its intracellular localization. In particular, Akain1 is preferentially expressed in neural tissues. How Akain1 affects brain function and behavioral characteristics, however, is unclear. To elucidate the function of Akain1, we generated Akain1 deficient mice on the C57BL/6J background using the CRISPR/Cas9 genome editing system and subjected the mice to a comprehensive battery of behavioral tests. Akain1 deficient mice showed some sex different behavioral phenotypes in pain sensitivity, depression-like behavior, and social behavior. As a common phenotype for each sex, Akain1 deficient mice exhibited impaired performance in distinguishing between two similar contexts in the pattern separation test. In addition, Akain1 deficient mice exhibited relative difficulty in reversal learning in the spatial reference tasks. It suggested that Akain1 deficient mice had behavioral inflexibility. These findings suggest that Akain1 has a critical role in pain sensitivity, depression-like behavior, social behavior, behavioral flexibility and discrimination of similar contexts.