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THE ROLE OF ADENYLYL CYCLASE 8 IN STRESS RESPONSE

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Adelylyl cyclase 8(AC8) is a brain specific cyclase activated only by calcium. Therefore its activity has been associated with plasticity process underlying learning and memory. AC8 knockout(KO) mice show impaired stress-induced anxiety. Here we try to find whether AC8 is involved in hypothalamus-hypophysis-axis(HPA) regulation and if it influences intracellular signaling of gluccocorticoids in the hippocampus.
First, serum samples were harvest from 8 AC8 KO and 8 wild type(WT) mice at basal, eve, 30 and 120 minutes after stress and at sacrifice with subsequent measuring of corticosterone levels. Second, glucocorticoid receptor(GR), vasopressin(AVP) and corticotrophin releasing hormone(CRH) mRNA expression levels were measured in accumbens nucleus(Acb), periventricular nucleus(PVN), supraoptic nucleus(SON), amygdala and hippocampus. Finally, GR and phosphorilated-GR levels were measured in hippocampus by western blot technique.
There was no difference in corticosterone levels between the two groups, regardless of harvesting time ($p>0.05$). Also, we found no difference between AVP mRNA levels in PVN or SON ($p>0.05$). However, AC8KO mice tend to have lower CRH levels in amygdala and lower GR levels in the hippocampus ($p< 0.05$). More, AC8KO mice have higher phosphorilated-GR levels in hippocampus in comparison with WT ($p=0.01$).
Our data shoes that AC8 does not play a part in HPA regulation. However, it alters the expression levels and phosphorilation patterns of GR in the hippocampus, which can explain the impaired learned anxiety behavior. Since anxiety-impaired stress response is one of few outcomes of AC8 KO phenotype, we imply that this cyclase might represent a potential target for specific antianxiety drugs.

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