Abstract

Objective: HYBID (Hyaluronan Binding Protein Involved in HA Depolymerization, KIAA1199) is a hyaluronan (HA) binding protein, which involves in depolymerization of HA. It is reported that HYBID mRNA is expressed in the lung, heart, skin and brain in murine and human. However, the role of HYBID in the brain remains unclear. In this study, we have made HYBID KO mice and evaluated its function in the central nervous system.

Methods: To investigate the role of HYBID in brain, behavioral tests were performed by using HYBID KO mice. In situ hybridization was performed to investigate the localization of HYBID mRNA in mouse brain.

Results: HYBID mRNA was expressed in the brain, especially hippocampus and cerebellum in wild-type mice, but not KO. HYBID KO mice showed decreased memory ability in a novel object recognition test. The expression of Hyal1 and Hyal2 mRNAs was not changed in the HYBID KO mouse brain. These results suggest that HYBID plays a key role in memory function in the brain.

Conclusion: HYBID may be involved in brain function, such as memory and learning.

Policy of Full Disclosure: None.

PT681

The protective role of erythropoietin on the cognitive power deficit of the brain and histological changes in the hippocampus of diabetic mice.

Amer Al Ansari, Ebrahim Rajab, Manal Othman, Muhammad AlNaisar, Ahmed Almubarak

Arabian Gulf University, College of Medicine and Medical Sciences, Manama, Bahrain

Abstract

Long-term diabetes is associated with accelerated ageing of the brain as evidenced by impairment of cognitive function and motor performance as well as degenerative changes in the hippocampus. A neuroprotective role for erythropoietin (EPO) has been reported in some CNS injuries like stroke and spinal cord injury. The aim of this study was to examine the effects of erythropoietin on the induced cognitive deficits in STZ-induced diabetes mellitus. Twelve male BALB/c mice aged 5–7 weeks (20-25g) were administered streptozotocin i.p. (STZ; Sigma-Aldrich) 55mg/kg/day for 5 days. Diabetic mice were randomly assigned to either control (i.e. sodium citrate buffer i.p.) (n=6), or EPO treatment (Sigma-Aldrich) 5U/g/day (dissolved in sodium citrate buffer; i.p.) (n=6), three times per week beginning six weeks after the induction of diabetes. An additional group of six mice served as normal controls. Water maze performance by measuring the latency to reach the platform was significantly higher in the Diabetic group (42.5 ± 5.4 s, ANOVA p< 0.05) After water maze testing, the mice were decapitated and the brains removed and processed for light microscopic evaluation of dentate region of the hippocampus. In the diabetic mice, there were degenerative changes in the dentate region of the hippocampus, in the form of cell loss and shrinkage and darkening of the nuclei of other cells compared to normal mice. In contrast, there was improvement in the neurogenesis and also in the nuclear shape of the cells of the dentate region in EPO-treated diabetic mice. Conclusion: Diabetes resulted in deterioration in the cognitive power of the brain and histological degenerative changes in the dentate region of the hippocampus. These changes were ameliorated by the administration of EPO which may be useful in the treatment of diabetic neuropathy.

PT682

A novel mutation associated autism in Neuroligin1

Moe Nakanishi, Takashi Arai, Maju Bucar, Xiao Ji, Xiaoxi Liu, Jun Nomura, Eiki Takahashi, Toru Takumi

RIKEN Brain Science Institute, Japan, University of Pennsylvania, USA

Abstract

Neuroligins (Nlgs) are postsynaptic adherent molecules consisting of five family members (Nlgn1, 2, 3, 4X and 4Y). A number of genetic studies showed that the mutations of Nlgn2, 3 and 4 have been associated with neuropsychiatric disorders including autism spectrum disorder (ASD). However, only few genetic and functional analyses have been reported in Nlgn1.

In this study, we introduced whole-exome sequencing technique to find mutations in ASD siblings and identified a novel mutation predicted as damaging by in silico analysis. To uncover its functional significance, we performed comprehensive analyses both in vitro and in vivo.

We introduced this Nlgn1 mutation into the mouse primary hippocampal neurons. The Nlgn1 mutation altered not only subcellular localization from cytoplasm to endoplasmic reticulum (ER) but also dendritic spine induction.

To address how this mutation affects behavioral phenotypes, we generated knock-in mice with Nlgn1 mutation by direct injection of CRISPR/Cas9 RNA with guide RNA. In a series of behavioral tests, we found several autistic traits, such as impaired social communication, in addition to hippocampal dependent spatial memory deficit. Furthermore, our biochemical studies revealed that Nlgn1 protein was significantly decreased in the forebrain of mutant mice (both whole lysate and synaptosomal fraction). These results suggest that this novel Nlgn1 mutation is involved in ASD traits in a haploinsufficient manner and reinforce the significant association between mutations in Nlgs and neuropsychiatric disorders.

PT683

Effects of acute administration of moderate and high caffeine doses on the spatial memory and motor coordination in mice.

Sayed Almosawi, Sadig Mahdi, Hasan Baksh, AbdulrAhman Qareeballa, Faisal Falamarzi, Bano Alsahel, Malik Alraabaani, Ali Aljalban, Amer Kamal

Arabian Gulf University, College of Medicine and Medical Sciences, Manama, Bahrain

Abstract

Caffeine is the most wildly consumed psycho-stimulant substances known to man. Caffeine has important effects on alertness. While moderate caffeine use is “generally recognized as safe” but heavy caffeine consumption has been associated with serious adverse health effects. The aim of this study was to evaluate the effects of moderate (0.1 gm/L) and high (1 gm/L) doses of caffeine administered mixed with drinking water on the learning and memory and motor coordination in mice. BLC57 mice were divided into 3 groups: control group (n=8 males, no caffeine), moderate dose group (n=8 males) and high dose group (n=8, males) were tested for spatial memory by the Morris-water