CALIFORNIA STATE SCIENCE FAIR
2012 PROJECT SUMMARY

Name(s)
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Project Number
S1204

Project Title
ERK-Related Synaptic Deficits in a Mouse Model of Autism: Potential Therapeutic Solutions to an Epidemic

Abstract

Objectives/Goals
To interrogate whether ERK-related protein defects specific to synapses of the hippocampus are consistent across multiple mouse models of autism.

Methods/Materials
Hippocampal homogenates were made from subfield dissections of the bilateral hippocampi, while synaptoneurosomes were made from forebrains. Bands of Western blot analyses were visualized using ECL+ chemiluminescence (Amersham), quantified using ImageJ (NIH), and normalized to sample content. To make whole brain sections, brains were fast frozen and cryostat sectioned on the coronal plane at 20 micrometers. To conduct dual-labeled immunohistochemistry, primary and secondary antibodies were used and tissue was cover-slipped with VectaShield containing DAPI (#H-1200, Vector Labs). For hippocampal slice experiments and fast frozen brain sections, 3 to 4 tissue sections through each slice were used to acquire image z-stacks (0.2 micrometer steps). Images were processed for iterative deconvolution and automated in-house software was used to construct three-dimensional (3D) montages.

The experiment used Western blot analyses and dual-labeled immunohistochemistry to independently interrogate the protein levels of ERK, p-ERK, and p-CREB in both the total CA1 hippocampus and in only the CA1 hippocampus synapses of both C57/BL6 wild-type (WT) and BTBR T+tf/J mice.

Results
While synaptic levels of total ERK were shown to be normal in the BTBR hippocampus, synaptic p-ERK and p-CREB levels were both demonstrated to be significantly below wild-type levels.

Conclusions/Discussion
ERK-related protein defects specific to hippocampal synapses were shown to be consistent across multiple unrelated mouse models of autism and thus can potentially be used as a biomarker for diagnosing autism. In addition, these defects were shown to be synapse-specific, allowing for more focused future research. Lastly, BDNF defects can be tested for in the future and have been shown to be a potential drug target for curing autism.

Summary Statement
I discovered that ERK-related protein defects were synapse-specific and that these defects can potentially be used both as a biomarker for diagnosing autism and as a drug target for curing autism.

Help Received
I want to thank Dr. Christine Gall and graduate student Ronald Seese for their invaluable guidance and editing of my project. I also want to thank my parents and my science teachers, Mr. Knight and Ms. Bunch, for their continued support of my science education.