Increased RSK2 in Children with Autism

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Abstract

The RSK kinases are actuated by the MAPK pathway. RSK2 has many functions such as cell survival and cell division control. In this study, we used immune-array technology to measure the concentration of RSK2 in a group of individuals with autism and a group of neurotypical controls. RSK2 concentration was significantly higher in the autism group compared to the controls. Since RSK may be associated with insulin signaling and glucose metabolism, and related to insulin resistance, this report suggests a role for dysfunctional glucose metabolism in the etiology of autism.

Keywords: RSK2; Children with Autism

Introduction

RSK2 is associated with cell persistence through programmed cell death proteins such as BAD and GSK3β; chromosome formation by activation of factors such as p53, cell cycle alteration, cell conversion and immune control by altering cytokines function [13].

The RSK kinases are activated by the MAPK pathway [1,2]. RSK is structured as two kinases interspaced by a linker region [3,4] and is activated through ERK first phosphorylation [5]. The biological role of RSK is diverse. It is associated with regulation of development, cell motility, survival and growth through its ability to modulate the mTORC1 pathway [5-11].

Insulin may also activate RSK independently of the mTOR pathway. It may alter glucose metabolism by interfering with insulin signaling in muscle and the liver [12].

In this study, we used immune-array technology to measure the concentration of RSK2 in a group of individuals with autism and a group of neurotypical controls.

Materials and Methods

Subjects

RSK2 (phosphorylated) was measured in white blood cells of 26 autistic children and 12 neurotypical controls (age and gender similar).
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Individuals with autism, diagnosed by the Autism Diagnostic Interview-Revised - ADI-R and met the DSM-IV criteria (n = 26; 20 male; mean age 10.7 years), and controls (n = 12; 10 male; mean age 9.8 years) were attained from volunteer patients from the Health Research Institute (HRI).

This study was approved by the IRB of the HRI and patient consent was obtained from all volunteers.

RSK2 concentrations were measured using Immuno-array technology.

Buffy coat white blood cells

All experimental and control cells were isolated using centrifugation and then refrigerated (4°C). Plasma and buffy coat samples were frozen at -7°C before use.

Immuno-array assays

Immuno-arrays were completed by Ray Biotech, Inc, Peachtree Corners, GA. 30092 [14].

Statistics

Statistical analysis was done using T-tests with 95% confidence and Pearson Moment for correlations.

Results

Immuno-arrays were used to establish the concentration of RSK2 in autistic children (N = 26) and 12 age and gender similar neurotypical controls (N = 12).

RSK2 concentration was significantly higher in the autism group (6224 +/- 1698 pg/µl), compared to the concentration in the neurotypical controls (2605 +/- 2777 pg/µl) (p = 0.003) (Figure 1).

Discussion

In a previous study we found that GSK3A levels were significantly higher in autistic individuals [14]. We also found that GSK3A and MKK3 levels correlated significantly with one another in individuals with autism and they both had a significant correlation with p38. In contrast, Insulin or P38 levels were not different in the autistic group. This suggests that excess GSK3A and MKK3 is where the dysfunction lies [15].

Conclusion

RSK has been shown to influence insulin resistance and therefore may be a partner in regulation of glucose metabolism [16]. The data presented here demonstrates increased RSK2 in an autistic group and suggests a role for abnormal glucose transport in the etiology of autism.

The Health Research Institute is a clinical center and research institute, specializing neuro-behavioral disorders, including autism.

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Figure 1: RSK2 is significantly higher in the autistic group (6224 +/- 1698 pg/µl) than in the control group (2605 +/- 2777 pg/µl) (p = 0.003).

Bibliography


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