Research Article ISSN 2771-9057

Recent Advances in Clinical Trials

# Lower VEGF Plasma Levels in Mothers of Autistic Children- Short Communication

**Russo A.J., PhD[1,2*], Albert Mensah, MD[2] and Judith Bowman, MD[2]**

*[1]Visiting Assistant Professor of Biology, Drew University, Madison, NJ 07940, Research Director.*

*2Mensah Research Institute, Warrenville, Il 60555.*

**[*]Correspondence:**

A.J. Russo, Visiting Assistant Professor of Biology, Drew University, Madison, NJ 07940, Research Director, Mensah Research Institute, Warrenville, Il 60555, Tel: 240-394-0351.

**Received:** 29 Nov 2021; **Accepted:** 24 Dec 2021; **Published:** 30 Dec 2021

**Citation:** Russo A.J., Albert Mensah, Judith Bowman. Lower VEGF Plasma Levels in Mothers of Autistic Children- Short Communication. Recent Adv Clin Trials. 2021; 1(1); 1-3.

## ABSTRACT

*Vascular endothelial growth factor (VEGF), originally described as an endothelial cell-specific mitogen, is produced by many cell types including macrophages and platelets. It plays an important role in the development and function of the central and peripheral nervous system. In this study, we used immune-arrays to measure VEGF in mothers of autistic children and controls. We found that VEGF plasma levels of mothers of autistic children were significantly lower than controls. These results suggest that VEGF may be associated with the etiology of autism and may have a diagnostic role in ASD.*

## Keywords

Children, Vascular endothelial growth factor, Autism.

## Introduction

Autism Spectrum Disorder (ASD) refer to a group of neurodevelopmental disorders characterized primarily by restrictive, repetitive patterns of behaviors, and social communication impairment [1].

The neurotrophins are a family of proteins that have been shown to play an important role in the central and peripheral nervous system, which control many aspects of survival, development, and function of neurons [2].

Vascular endothelial growth factor (VEGF), also known as vascular permeability factor (VPF), was originally described as an endothelial cell-specific mitogen [3]. VEGF is produced by many cell types including tumor cells [4], macrophages [5], platelets [6], keratinocytes [7], and renal mesangial cells [8]. VEGF also plays a role in normal physiological functions such as bone formation [9] and hematopoiesis [10].

VEGF levels in patients with ASD may be lower than that of healthy controls [11].

In this study, we measured VEGF levels in mothers of individuals with autism and neurotypical, age and gender similar controls. We found that VEGF levels were significantly lower in the maternal autistic group.

## Materials and Methods

VEGF plasma levels were measured using immuno-arrays. Plasma from mothers of autistic individuals (n=17; mean age 32.3 years) and controls (n=15 females with no autistic children; mean age 28.2 years) were obtained from the Autism Genetic Resource Exchange (AGRE)**. This study was approved by the IRB of the Health Research Institute

Patient consent was obtained from all patients involved in this study and this study was approved by the IRB of the HRI.

Cellular phosphorylated concentrations were measured using an Immuno-array assay described below.

### Buffy Coat White Blood Cells

All experimental and control cells were obtained from whole blood using centrifugation and were all treated identically then refrigerated (4 C). Plasma and buffy coat samples were frozen at -70C and used for ELISAs and Immunoassay analysis.

### Immuno-array Assays

Immuno-arrays were performed by RayBiotech, Inc, Peachtree Corners, GA. 30092 and described previously [12].

### Statistics

Unpaired t-test and odds ratios with 95% confidence intervals were used for statistical analysis. Correlations were performed using Pearson Moment analysis also with 95% confidence intervals for determining statistical significance.

**We gratefully acknowledge that the Autism Genetic Resource Exchange (AGRE) Consortium and the participating AGRE families provided all autism family serums. The Autism Genetic Resource Exchange is a program of Cure Autism Now and is supported, in part, by grant MH64547 from the National Institute of Mental Health to Daniel H. Geschwind (PI).

## Results

We found that VEGF levels were significantly lower in the plasma of mothers of autistic children (Figure 1).

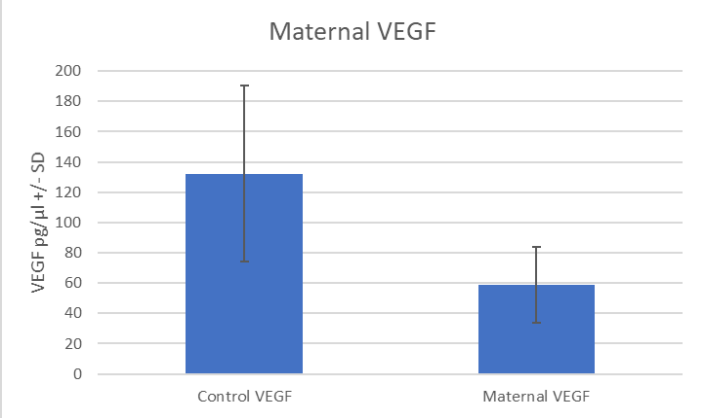


**Figure 1:** VEGF growth factor plasma levels of mothers of autistic children are significantly lower (58 +/- 25 pg/µl) than controls (132 +/- 58 pg/µl) (p=0.014).

## Discussion

VEGF is a key signaling molecule of the central nervous system, which is involved in neuroprotection, neuronal survival and axonal growth [13]. Plasma VEGF levels were found not to be significantly different between first-episode schizophrenia patients and controls, whereas medicated multiple-episode schizophrenia had higher levels of VEGF than that of control subjects [14]. Meta-analysis reveals heightened blood BDNF, NGF as well as VEGF levels in ASD children [15], and sVEGFR-1 (VEGF receptor-1) is higher in patients with autism [16].

Interestingly, ASD symptom severity was negatively associated with levels of VEGF, in females, but not in males [17].

Our data shows that VEGF levels are significantly lower in mothers of autistic children. These lower levels could be why VEGF levels are subsequently abnormal in autistic children.

This data suggests that VEGF and other neurotrophic factors may have diagnostic as well as therapeutic importance.

## References

1. Li D, Karnath HO, Xu X. Candidate Biomarkers in Children with Autism Spectrum Disorder: A Review of MRI Studies. Neurosci Bull. 2017; 33: 219-237.
2. Skaper SD. Neurotrophic Factors: An Overview. Methods Mol Biol. 2018; 1727: 1-17.
3. Ferrara N, Houck K, Jakeman L, et al. Molecular and biological properties of the vascular endothelial growth factor family of proteins. Endocr Rev. 1992; 13: 18-32.
4. Boocock CA, Charnock-Jones DS, Sharkey AM, et al. Expression of vascular endothelial growth factor and its receptors flt and KDR in ovarian carcinoma. J Natl Cancer Inst. 1995; 87: 506-516.
5. Sunderkotter C, Steinbrink K, Goebeler M, et al. Macrophages and angiogenesis. J Leukoc Biol. 1994; 55: 410-422.
6. Verheul HM, Hoekman K, Luykx-de Bakker S, et al. Platelet: Transporter of vascular endothelial growth factor. Clin Cancer Res. 1997; 3: 2187-2190.
7. Frank S, Hubner G, Breier G, et al. Regulation of vascular endothelial growth factor expression in cultured keratinocytes. Implications for normal and impaired wound healing. J Biol Chem. 1995; 270: 12607-12613.
8. Iijima K, Yoshikawa N, Connolly DT, et al. Human mesangial cells and peripheral blood mononuclear cells produce vascular permeability factor. Kidney Int. 1993; 44: 959-966.
9. Gerber HP, Vu TH, Ryan AM, et al. VEGF couples hypertrophic cartilage remodeling, ossification and angiogenesis during endochondral bone formation. Nat Med. 1999; 5: 623-628.
10. Ferrara N, Carver-Moore K, Chen H, et al. Heterozygous embryonic lethality induced by targeted inactivation of the VEGF gene. Nature. 1998; 380: 439-442.
11. Emanuele E, Orsi P, Barale F, et al. Serum levels of vascular endothelial growth factor and its receptors in patients with severe autism. Clin Biochem. 2010; 43: 317-319.
12. Russo A, Mensah A, Bowman J. Increased Receptor for Advanced Glycation End Products (RAGE) in Children with Autism. EC Pediatrics 9.5 (2020): 31-34.
13. Yasuhara T, Shingo T, Date I. The potential role of vascular endothelial growth factor in the central nervous system. Rev Neurosci. 2004; 15: 293-307.
14. Misiak B, Stramecki F, Stanczykiewicz B, et al. Vascular endothelial growth factor in patients with schizophrenia: a systematic review and meta-analysis. Prog Neuropsychopharmacol Biol Psychiatry. 2018; 86: 24-29.

15. Liu SH, Shi XJ, Fan FC, et al. Peripheral blood neurotrophic factor levels in children with autism spectrum disorder: a meta-analysis. Sci Rep. 2021; 11: 15.
16. Emanuele E, Orsi P, Barale F, et al. Serum levels of vascular endothelial growth factor and its receptors in patients with severe autism. Clin Biochem. 2010; 43: 317-319.
17. Masi A, Breen EJ, Alvares GA, et al. Cytokine levels and associations with symptom severity in male and female children with autism spectrum disorder. Mol Autism. 2017; 8: 63.