



## **TITLE: The effects of postnatal erythropoietin and nano-erythropoietin on behavioral alterations by mediating K-Cl co-transporter 2 in the valproic acid-induced rat model of autism**

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### **ABSTRACT**

In this study, based on the excitatory/ inhibitory imbalance theory of autism, the time window of GABA switch, the role of K-Cl co-transporter 2 (KCC2) in adjustment GABA switch, and brain permeability to erythropoietin (EPO), the effects of postnatal -EPO and nano- erythropoietin (NEPO) have been evaluated in the valproic acid (VPA) rat model of autism. VPA were administered for animal modeling of autism at gestational day (GD) 12.5 (600mg/kg). Male offsprings were injected with EPO and NEPO in a clinically proper postnatal dosing regimen on postnatal days (PND) 1-5, and autistic-like behaviors were tested at the end of the first month. Then animals were sacrificed, and neuron morphology and KCC2 expression were examined by Nissl staining and Western blot. According to our findings, high-dose NEPO improved autism-associated phenotypes. Neuroprotective effects of EPO and NEPO have been shown in the hippocampus. Postnatal NEPO treatment reversed KCC2 expression abnormalities induced by prenatal VPA. Our results might support the role of KCC2 in ASD and the excitatory/ inhibitory imbalance hypothesis. We suggested Nano-erythropoietin and other KCC2 interventions as a new approach to the early treatment and prevention of autism.

### **BIOGRAPHY**

Sara Haratizadeh has completed his PHD in 2023 from Kerman University of medical sciences, Iran. Recently, she started working as an assistant professor at Mashhad University of Medical Sciences, Iran. She has 13 publications that have been cited 107 times, and her publication h-index is 5. She has various experiences in autism and spinal cord injury animal models.



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