ABSTRACT

ALTERED INFLAMMATORY RESPONSES ASSOCIATED TO NEUROGENESIS OF INDUCED PLURIPOTENT STEM CELLS DERIVED FROM AUTISTIC PATIENTS

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Introduction: Autism Spectrum Disorders (ASD) are characterized by impairment in social interactions, communication deficits, and restricted repetitive interests and behaviors. The biological basis of ASD is complex and largely unknown, however mechanisms leading to alterations in synaptic transmission and immune system functioning in ASD have been addressed from numerous perspectives, including genetic, environmental and neuroimmune. Objectives: Evaluate the expression of cytokines and neurotrophins during neurodevelopment as well as its role in the synapses in an in vitro model of autism. Materials and methods: In this work, we used as a model human iPS cells derived from keratinocytes from autistic patient and healthy controls to compare cytokines and neurotrophins levels during neurodevelopment. Results: Our data revealed increasing of the number of neurons in the autistic when compared with controls groups. Furthermore, it has been suggested that in autism, formation of neuronal connections, or elimination of inappropriate synapses, happen an atypical manner. A change in the levels of mGluR5 and vGlut2 in neurons derived from iPS cells with autism when compared to controls was observed in our data, suggesting an imbalance of glutamatergic signaling. Our data revealed that although there is a tendency to increase in cytokines and neurotrophins in young and mature neurons derived from iPS cells from autistic patients, this increase was only significant after stimulation with IL1β, demonstrating the important role of environmental factors in the development of the disorder. We also verified synaptic loss associated with an exaggerated response of autistic neurons in response to IL1β compared with controls. Conclusions: This study revealed important aspects of the dynamic relationship between altered immune response, synaptic loss, and regulation of neurotrophins in neurons derived from ASD iPS cells.

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