POSTER

THERAPEUTIC POTENTIAL OF NEUROTROPHINS IN AUTISM SPECTRUM DISORDER

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Autism spectrum disorder (ASD) is a neurodevelopmental condition defined by social deficits and repetitive behaviors. Its multifactorial etiology disrupts pathways essential for neural maturation. Neurotrophins (NT), vital for synaptic plasticity, are increasingly implicated in ASD, with signaling aberrations causing atypical connectivity and disrupted excitatory-to-inhibitory (E/I) balance [1]. This study investigated the therapeutic potential of intranasal NT administration in BTBR T+Itpr3tf/J (BTBR) mice, a preclinical model of ASD. Following a two-week daily treatment regimen in both male and female cohorts, behavioral tests were conducted to target core ASD-associated domains. Neurochemical profiles were quantified via high-performance liquid chromatography (HPLC), while spatial transcriptomics mapped region-specific gene expression shifts. Concurrently, human induced pluripotent stem cells (hiPSCs) were successfully reprogrammed from peripheral blood mononuclear cells (PBMCs) of ASD patients and subsequently validated for genomic integrity. Cerebral organoids derived from these lines are under development to explore NT-mediated cellular dynamics. In vivo results demonstrated that NT supplementation attenuated repetitive behaviors and improved social interactions in the BTBR cohort, revealing pronounced sex-dimorphic responsiveness. Molecular analyses indicated a shift toward E/I ratio normalization, corroborating the behavioral outcomes. Finally, the validated patient-derived hiPSC lines provided a robust platform for organoid research. Notably, after 20 days of culture, ASD-derived organoids exhibited a "small brain" phenotype, displaying a significantly reduced size relative to controls.

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References

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