Endocannabinoid System as Novel Therapeutic Target for Autism Treatment

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The newest dramatic increased prevalence rates of autism and autism spectrum disorders (ASDs) [1] recall the urgent needed for finding a definitive cure, as well as the finding for a specific biomarker for early diagnosis. Recently, several studies highlight a key involvement of endocannabinoid (EC) system in autism pathophysiology [2].

Endocannabinoids are arachidonic acid derived compounds and together with their receptors and the associated enzymes, they the EC system, an intricate network of lipid signalling pathways [3]. The EC “building blocks” are the N-arachidonylethanolamine (anandamide, AEA) and 2-arachidonoyl glycerol (2-AG), that exerts its effects through the G-protein-coupled cannabinoid receptors CB1 and CB2, which, in turn, are negatively coupled to adenylate cyclase enzyme [4].

Beyond autism, EC system is also involved in several other psychiatric disorders (i.e. anxiety, major depression, bipolar disorder and schizophrenia) [2]. This system is also a key regulator of other metabolic and cellular pathways involved in ASDs, such as food intake, energy metabolism, immune system controlling.

Early studies in animal models demonstrated that BTBR mice show an abnormal regulation of dopamine levels functioning with an up-regulated CB2A gene expression [5]. In addition, in the valproic acid induced model of autism, alterations in the brain’s endocannabinoid system have been reported in a newest research [6].

Autism is a human pathology: the possibility of autism activation by EC system has been reviewed [7]. Accordingly, sulfation deficits in acetaminophen (paracetamol) metabolism with the autism population could indirectly increase the endocannabinoids levels, which in turn are able to activate CB1/2 receptors triggering autism. Endocannabinoid-CB2 signalling dysregulation has been reported in monocytes cells extracted from autistic children [2]. More interesting, blood monocyte-derived macrophagic cells from autistic patients also reveal EC system dysregulation, further indicating the involvement of the EC system in autism associated immunological disruptions and pointed to a potential nexus between endocannabinoids, vitamin D and the immune dysregulations observed with autism [8].

Taken together, all these new findings are offering novel perspectives in autism research and indicate that the EC system could represent a novel target option for autism pharmacotherapy. Potential future drugs could target CB2 receptor activation, in order to design new personalized strategies in the pharmacotherapeutical management of autism.

References