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OC.12- EPIGENETIC LANDSCAPE OF D-AMINO ACIDS SYSTEM GENES DURING DEVELOPMENT AND IN SCHIZOPHRENIA

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D-aspartate and D-serine modulate NMDA receptor-dependent transmission. Herein, we aimed to describe an epigenetic landscape of the genes modulating D-amino acids system evaluating the impact of their expression on D-amino acids levels during development, and in a neuropathological condition like schizophrenia. It is acknowledged that in the mammalian brain, D-aspartate content decreases after birth, as a result of the postnatal expression of the catabolizing enzyme D-aspartate oxidase (DDO). On the other hand, D-serine displays a region-specific occurrence during ontogenesis, under the regulation of the biosynthetic enzyme, serine racemase, and the catabolizing enzyme, D-amino acid oxidase (DAAO). Our studies in the mouse brain revealed that postnatal Ddo gene expression is paralleled by progressive demethylation within its putative promoter. In this regard, we revealed that embryonic cortical neurons treated with the DNA-demethylating agent, azacitidine, showed non-physiological increased Ddo mRNA levels. Then we analyzed DNA methylation state and mRNA expression of the genes regulating D-aspartate and D-serine levels at different stages of mouse development, from birth to adulthood, and in different brain regions, like the hippocampus, cortex and cerebellum. Our analysis revealed decreased Ddo gene methylation and specular increased mRNA levels in the hippocampus and cerebellum. Moreover, demethylation of Daao gene is associated with increased transcription in the cerebellum during development. Finally, we translated our studies to post-mortem brain regions of patients with schizophrenia. Epiallele classes and configuration analyses provided distinct area-specific patterns suggesting the occurrence of an orchestrated distribution of epialleles in diverse cell populations.