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Levels of phosphodiesterase 4A and 4B are altered by chronic treatment with psychotropic medications in rat frontal cortex.

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Abstract

Our laboratory has recently demonstrated altered expression of phosphodiesterase (PDE) 4A and 4B in subjects with autism, bipolar disorder, and schizophrenia, suggesting disrupted cAMP signaling in these diagnostic groups. In the current study, we measured expression of PDEs in rat frontal cortex (FC) following chronic treatment with clozapine, fluoxetine, haloperidol, lithium, olanzapine, valproic acid (VPA), or sterile saline for 21 days. Western blotting experiments showed decreased expression of PDE4A subtypes in FC following treatment with clozapine, haloperidol, lithium, and VPA. PDE4B subtypes were similarly reduced in FC following treatment with clozapine, fluoxetine, and lithium. We also measured levels of nine PDE subtypes via qRT-PCR in FC and found significant upregulation of PDE1A and PDE8B following treatment with olanzapine, while treatment with lithium reduced expression of mRNA for PDE8B. Our results demonstrate altered expression of PDE4A and PDE4B in response to a variety of psychotropic medications suggesting potentially new therapeutic avenues for treatment of neuropsychiatric diseases.

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