

Abstract Information

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Participation :	symposium
Title of the Symposium :	Serotonergic Modulation and Neurochemical Pathways: Implications for Antidepressant Efficacy, Epilepsy, and Neurotoxicity
Category :	Academic/Researcher
Thematic Area :	Neurochemistry
Title :	Brain wide neurochemical analysis of neurotransmitters in response to psychedelic drugs and 5-HT _{2A} receptor antagonist
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Abstract :	<p>The serotonergic receptor subtype 2A (5-HT_{2A}) is an intriguing pharmacological target because it binds classical psychedelics which are 5-HT_{2A} agonists as well as antipsychotic drugs which antagonize 5-HT_{2A} function. The widespread influence of these compounds on the activity of neurotransmitter systems across the brain remains unknown. In mice, we studied the effect of non-selective 5-HT_{2A} agonist TCB-2 (0.3, 3, and 10 mg/kg) alone or in combination with 5-HT_{2A} antagonist MDL100,907 (0.2 mg/kg) with TCB-2 (3 mg/kg) on the tissue level of neurotransmitters [GABA, glutamate, noradrenaline (NA), dopamine (DA), serotonin (5-HT) and their metabolites] 1-h after agonist administration. Post-mortem, tissue content was measured by HPLC in 28 brain regions belonging to various neurobiological networks. Ten minutes before the sacrifice, we placed the animals on a textured floor to promote forced investigatory behaviour after having measured the head twitches from 20 to 50 minutes to determine the efficacy of the treatments. Quantitatively, TCB-2 dose-dependently decreased 5-HT turnover (usually an increase in 5-HT) in all brain regions. It reduced the ratio 3-methoxytyramine/DA in the striatum, and enhanced markers of the DA system in a few cortices (cingulate, somatosensorial) and NA in the cingulate cortex and the ventral hippocampus. Despite the ability of MDL100,907 to prevent TCB-2-induced head twitches in these animals, the decrease in 5-HT turnover induced by TCB-2 was generally insensitive to MDL100,907. However, MDL100,907 blocked TCB-2-induced 5-HT increase in the cingulate and auditory cortices and the ventral hippocampus. It also blocked some DA and NA effects notably in the anterior cingulate cortex. TCB-2 alone or combined with MDL-100,907 did not</p>
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modify amino acid tissue contents. Qualitatively, impressive number of organized correlations assessed by Pearson's correlations was found for all neurotransmitters between brain regions in vehicle-treated animals. TCB-2 dramatically decreased the correlative links. MDL100,907 also reduced the correlative links. The disruptive effect of TCB-2 was partially counteracted by MDL100907 for 5-HT, glutamate, and GABA. Irrespective of its questionable action beyond 5-HT_{2A}R, the data indicate that TCB-2 dramatically alters the activity of 5-HT neurons in the brain and disrupts the correlative links between brain regions for all neurotransmitters.