Convergence of 5-MeO-DMT molecular signature to Pioglitazone and plasticity effects

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5-MeO-DMT, a naturally occurring psychedelic compound, acts as a potent agonist of serotonin receptors, particularly the 5-HT2A receptor, which plays a crucial role in mood regulation, cognition, and perception. This compound has garnered significant attention for its ability to rapidly alleviate symptoms of depression and anxiety, particularly in naturalistic settings where its effects have been observed outside of traditional clinical environments. While its primary mechanism of action involves serotonin receptor activation, the full spectrum of 5-MeO-DMT's effects on the brain remains largely unexplored.

To investigate the broader actions of 5-MeO-DMT, we adopted a bioinformatics approach. Specifically, we analyzed a proteomics dataset derived from human brain organoids treated with 5-MeO-DMT, utilizing the gene set enrichment analysis web server Enrichr. This platform allowed us to cross-reference the proteomic changes induced by 5-MeO-DMT with a comprehensive databank of drug-regulated genes. Remarkably, the proteins altered by 5-MeO-DMT treatment showed significant overlap with datasets associated with the thiazolidinedione drugs Rosiglitazone and Pioglitazone, both of which have been investigated for their potential use in mitigating cognitive decline and treating Alzheimer\'s disease.

The proteins regulated by 5-MeO-DMT were found to be involved in pathways critical for neuroplasticity, immunomodulation, and metabolism, suggesting that 5-MeO-DMT may exert effects beyond serotonin receptor activation. To further explore the role of 5-MeO-DMT in neural plasticity, we conducted an in vitro assay using human neurospheres, which serve as a model for studying neurite outgrowth. Treatment with 5-MeO-DMT led to a marked increase in neurite outgrowth compared to untreated controls, indicating that this compound may promote structural changes in neurons that underlie its therapeutic effects.

These findings highlight the potential of 5-MeO-DMT not only as an antidepressant but also as a modulator of brain plasticity, which could have far-reaching implications for the treatment of neurodegenerative diseases such as Alzheimer\'s. By promoting neural growth and modulating pathways involved in immune response and metabolism, 5-MeO-DMT might offer a novel therapeutic approach that addresses both the symptomatic and underlying causes of these conditions.

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