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**Integrating Multi-Omics Data through Multiplex Networks: A Novel Team Science-based Framework for Understanding the Mechanisms Underpinning Substance Use Disorders and Comorbid Neuropsychological Conditions**

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Understanding the complex interplay of substance use disorders (SUDs) and their comorbid neuropsychological conditions demands not only advanced computational techniques but also a collaborative, interdisciplinary approach to scientific inquiry. Here we present a computational framework using multiplex networks to integrate a vast array of multi-omics data, including genomic, epigenomic, transcriptomic, proteomic, and single-cell datatypes. Central to our methodological innovation is the development of sophisticated algorithms that enable the synthesis of heterogeneous biological datasets into coherent multiplex networks. These networks serve as a platform not just for identifying mechanistic connections between SUDs and neuropsychological comorbidities but also for facilitating team science-based interpretation of complex sets of data. By fostering collaboration among experts in systems biology, omics technologies, neurobiology, and clinical sciences, our approach supports a comprehensive understanding of the results, bridging gaps between computational approaches and biological insights. Our analyses uncover previously uncharted mechanistic underpinnings, providing novel insights into the pathogenesis of SUDs and identifying potential therapeutic targets. Expanding the implications of our findings, we discuss the potential for these strategies to impact therapeutic approaches for treating SUDs. By enabling precise identification of molecular targets and mechanistic networks, our methods pave the way for the identification of new potential therapies for further investigation. As such, these approaches set a precedent for future research initiatives aiming to dissect complex diseases through the lens of multi-omics integration and collaborative team science in the quest for holistic understanding and treatment of SUDs and their neuropsychological comorbidities.