MOUD exacerbates the distinctive metabolic patterns associated with HIV infection and suppressive ART

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Background: Despite effective antiretroviral therapy (ART), people living with HIV (PLWH) exhibit persistent metabolic alterations that may contribute to immune dysregulation and comorbidities. Medications for opioid use disorder (MOUD), including methadone and buprenorphine, act as μ-opioid receptor agonists and may further influence metabolic and immunologic pathways in PLWH.

Methods: We conducted an observational study to characterize metabolic reprogramming associated with ART and assess the additional impact of MOUD exposure. Plasma samples were obtained from 194 participants, including ART-suppressed PLWH (HIV; n=57), ART-suppressed PLWH receiving MOUD (HIV-MOUD; n=31), and healthy controls (CTRL; n=106). The cohort included 43.8% females and 53.1% non-white participants. Untargeted high-throughput metabolomics was performed using flow-injection mass spectrometry detecting 1,331 m/z features. Group comparisons were conducted using Welch's t-tests with Benjamini–Hochberg false discovery rate correction, followed by metabolite set enrichment analysis using MetaboAnalyst.

Results: Compared with CTRL, people in the HIV group exhibited significant disruption of androgen and estrogen metabolism, marked by reduced levels of sulfated steroids, including DHEA-S and androsterone sulfate. In HIV-MOUD participants, MOUD exposure further exacerbated suppression of sulfated steroids and testosterone.

Conclusion: These findings demonstrate that metabolic reprogramming persists in ART-suppressed PLWH and is amplified by MOUD exposure, identifying sulfated steroids as key metabolic signatures with potential implications for immune and systemic health.