Cannabis Messes with Your 'Genes' in Ways You Don't Realise: Abstinence is Best Policy Practice.

Dalgarno Institute Research Report

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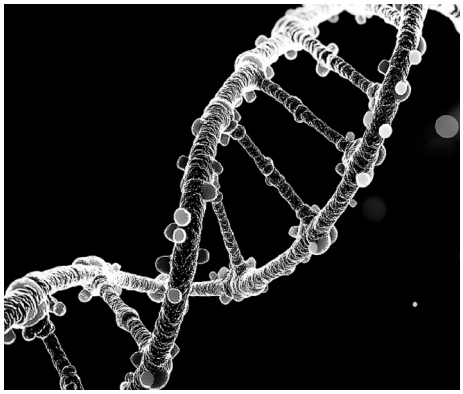
Marijuana's primary psychoactive compound, Δ9-tetrahydrocannabinol (THC), drives persistent epigenetic changes that undermine neuroplasticity and reward system integrity, with cannabidiol (CBD) offering limited mitigation upon repeated exposure. These modifications, observed across preclinical and human studies, heighten risks for addiction, cognitive impairment, and intergenerational effects, particularly in vulnerable populations like adolescents.

EPIGENETICS FUNDAMENTALS



Epigenetics refers to modifications like DNA methylation, histone acetylation (e.g., H3K9/14ac), trimethylation (e.g., H3K9me3), and non-coding RNAs that alter gene expression without DNA sequence changes. These regulate mesolimbic dopamine pathways critical for reward, motivation, and plasticity, but cannabinoids disrupt them. THC binds CB1 receptors, triggering maladaptive neuroadaptations that persist post-exposure.

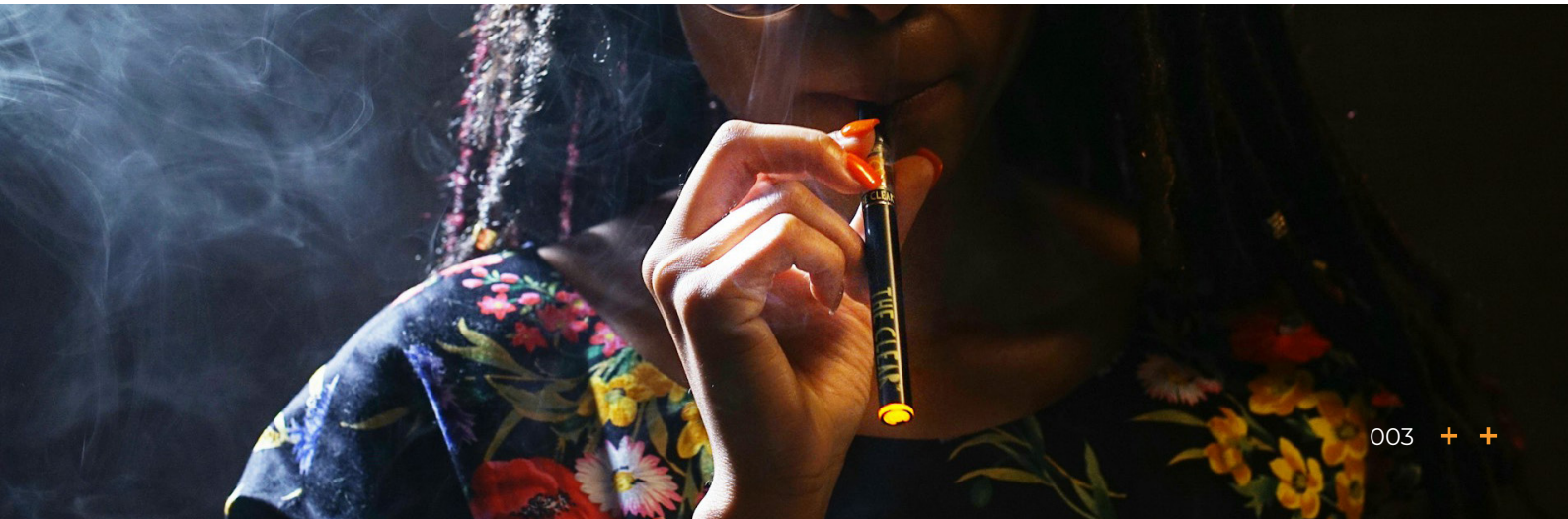
CBD-THC INTERACTIONS AND INDUCED EPIGENETIC ALTERATIONS

THC: Acute THC suppresses locomotion, but repeated dosing (e.g., 10 mg/kg in mice) induces rebound hyperactivity tied to elevated H3K9/14ac in the ventral tegmental area (VTA) and ΔFosB accumulation in the nucleus accumbens (NAc), promoting addiction-like states. These markers indicate enduring chromatin remodelling, impairing sensorimotor gating (prepulse inhibition deficits) and reward homeostasis. Human parallels include THC-linked DNA hypomethylation in blood and brain regions, accelerating epigenetic clocks and cognitive decline.

Interactions with CBD: While CBD can acutely modulate some THC effects, repeated co-dosing at ratios like 1:1 or 5:1 fails to prevent epigenetic shifts or behavioural tolerance. Epigenetic studies note CBD's role in broader pharmacogenomic responses, but THC-driven changes dominate in mesolimbic regions. This implies limited protective potential against marijuana's epigenetic risks in therapeutic contexts.

BROADER NEGATIVE IMPLICATIONS

Developmental THC exposure causes persistent DNA methylation changes and histone trimethylation (e.g., H3K9me3) at genes like Drd2 and Penk, reducing dopamine receptor expression and altering striatal function into adulthood. In sperm, THC alters methylation at hundreds of CpG sites, raising intergenerational risks for neurodevelopmental disorders. Lifetime use accelerates epigenetic ageing, linking to cognitive deficits, psychosis susceptibility, and addiction vulnerability.



THE LONG TERM AND OFTEN IRREVERSIBLE GENERATIONAL HARMS

Developmental and Intergenerational Risks: Prenatal THC exposure induces lasting striatal hypomethylation at Drd2/Penk loci, reducing dopamine signalling and fostering adult behavioural deficits. Sperm epigenome studies reveal THC-associated differential methylation at 100+ sites, potentially transmitting neurodevelopmental vulnerabilities across generations. Adolescent use exacerbates these via heightened mesolimbic plasticity windows.

Health and Societal Ramifications: Epigenetic acceleration from chronic use correlates with psychosis, anxiety persistence, and metabolic dysregulation via immune gene alterations. Reversibility is partial; abstinence diminishes some sperm marks but not brain imprints. High-potency strains amplify DNA damage risks, per recent reports.

RECOMMENDATIONS FOR PRACTICE

These epigenetic disruptions underscore marijuana's potential for long-term harm, especially in adolescents and during gestation, where reversibility is limited even after abstinence. Personalisation via pharmacogenomics (e.g., CYP2C9 variants) is proposed, but negative outcomes like altered immune and metabolic gene expression persist. Public health strategies should prioritise prevention given the evidence of non-reversible brain imprints.

Integrate PGx testing (e.g., CYP2C9 for THC dosing) with epigenetic biomarkers in clinical decision systems for medical marijuana. Monitor DDIs, titrate low, and prioritise abstinence in youth/gestation amid limited CBD protection. Again, policy should emphasise prevention, given non-reversible neural legacies.

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References:

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