Leaving Epigenetic Scars Cannabis Smoking Changes your DNA

A group of researchers determined whether decades of regular cannabis smoking create distinct, reversible deoxyribonucleic acid (DNA) methylation marks in mid-life adults.

Study

The Dunedin Multidisciplinary Health and Development Study followed 1,037 infants born in New Zealand (NZ) in 1972-1973. At the age of 45, 818 participants (94% of survivors) provided peripheral blood samples. Only non-Māori participants were included in DNA methylation analyses.

Laboratory staff extracted DNA from buffy-coat leukocytes, performed sodium-bisulfite conversion, and quantified genome-wide methylation on the Illumina Infinium HumanMethylationEPIC 850,000-probe BeadChip. Exposure was defined in two ways.

First, case-control analyses contrasted long-term cannabis users, persistent weekly or more frequent cannabis smoking, or cannabis dependence at multiple assessments (n = 73), with lifelong cannabis- and tobacco-free controls (n = 182) and with long-term daily tobacco smokers (n = 56). Second, dose-response models regressed methylation at 246 literature-derived cannabis CpG sites on a six-level persistence index summarizing regular cannabis use across six waves (ages 18-45).

Sequential covariate adjustment included sex, array principal components, white-blood-cell composition, childhood socioeconomic status (SES), low childhood self-control, family history of substance dependence, and persistent alcohol, tobacco, and other illicit drug use. Accurate regression managed outliers, and Bonferroni correction controlled multiple testing.

Parallel models used an analogous tobacco-dependence index. Gene-expression correlations were examined in a subset with paired transcriptomic data at age 38. Ethical approval and written informed consent were obtained, and data access was managed in accordance with study policy.

Findings

Long-term cannabis smoking produced a selective epigenetic signature. Among 246 candidate CpG sites, 35 differed between long-term users and never-users, with 17 surviving Bonferroni correction. Dose-response analyses showed that greater persistence of regular cannabis use predicted differential methylation at 52 markers; this shrank to 17 after multiple-test correction and to nine after full covariate adjustment. The nine (cg05575921, cg21566642, cg03636183,

cg21161138, cg01940273, cg02978227, cg17739917, cg05086879, cg23079012) were uniformly hypomethylated and included the classic smoking-related AHRR site cg05575921.

Comparative analyses showed substantial overlap with tobacco effects. Long-term tobacco smokers exhibited hypomethylation at the same nine loci, and the overall DNA profiles of the two groups differed only slightly; only three CpG sites reached stringent significance in head-to-head testing. This convergence suggests that inhaled combustion products, rather than delta-9-tetrahydrocannabinol (THC), drive many cannabis-related changes.

Biological relevance emerged when methylation was paired with transcriptomics. In 38-year-old participants, hypomethylation at six of the nine loci was correlated with higher expression of AHRR, Pyrimidinergic Receptor P2Y6 (P2RY6), Leucine-Rich Repeat Neuronal 3 (LRRN3), G Protein-Coupled Receptor 15 (GPR15), and Desmocollin 2 (DSC2). These genes regulate xenobiotic metabolism, immune signaling, vascular function, and cell adhesion, representing pathways plausibly linking heavy smoking to cardiopulmonary disease.

Quitting mattered, as cannabis quitters showed intermediate methylation levels between long-term users and never-users, and each additional persistence-free year nudged methylation toward control values. Tobacco quitters exhibited a nearly identical recovery pattern, reinforcing the central role of smoke exposure and its reversibility.

Hypomethylation at cg05575921 averaged 0.3 standard deviations in persistent weekly+ cannabis users, which is about half that seen in persistent tobacco smokers, consistent with lighter cannabis consumption. The nine-site panel explained a modest proportion (approximately four percent) of variance in lifetime cannabis exposure, a secondary finding relative to the primary epigenetic signature results. Sensitivity checks using alternative modeling strategies produced parallel results. Associations persisted after adjusting for leukocyte composition, underscoring biological specificity.

Taken together, the data indicate that even persistent weekly+, long-term cannabis smoking imprints a traceable, partially reversible, and modest record in peripheral blood, offering a potential biomarker for exposure surveillance and cessation counseling. However, the utility of such a biomarker is still under investigation.

Conclusion

To summarize, long-term cannabis use leaves a small but consistent epigenetic footprint in midlife. Nine hypomethylated CpG sites, also altered by tobacco, track cumulative exposure, correlate with genes controlling detoxification, immunity, and vascular tone, and drift back toward normal after quitting. Findings point to smoke inhalation, rather than THC alone, as the primary driver and indicate that cessation can restore the epigenome.

Although the clinical repercussions remain uncertain, blood methylation signals could aid public health surveillance as legalization expands.

The study was conducted in a single New Zealand birth cohort, using blood-based methylation data, and focused on smoked cannabis; generalizability to other populations and cannabis use modalities (such as vaping or edibles) remains to be determined.

Further research is needed to test causality, explore heavier or non-smoked cannabis patterns, and link these changes to concrete health outcomes in diverse global populations.

Source:

https://www.news-medical.net/news/20250630/Cannabis-smoking-changes-your-DNA-leaving-epigenetic-scars.aspx