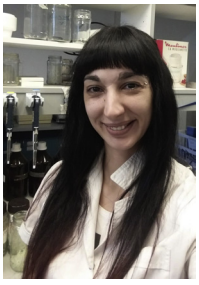
HIGHLIGHTS

- Cocaine disrupts mouse testicular epigenetic homeostasis, increasing DNA methylation in germ cells and sperm.
- Cocaine increased acetylated histone 3 and 4, decreased class I HDAC expression and altered DNMTs and TETs methylation markers.
- Addictive psychostimulants negatively impact male reproductive function and fertility.

RBMO

ARTICLE

Cocaine alters the mouse testicular epigenome with direct impact on histone acetylation and DNA methylation marks



BIOGRAPHY

Candela Gonzalez is a Researcher for the National Research Council in Argentina. Her areas of research cover issues of male infertility and reproduction. This forms part of translational medicine, bridging basic and clinical research and working in conjunction with medical institutions.

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KEY MESSAGE

Cocaine intake in mice disrupts testicular epigenetic homeostasis, increasing global methylated cytosine levels in spermatozoa, and alters global histone acetylation and the expression of DNA methylation markers. These results expand knowledge about the testicular effects of cocaine that negatively impact the reproductive male function.

ABSTRACT

Research question: Recent evidence suggests that cocaine administration in animal models can trigger non-genetic inheritance of addiction traits from father to offspring, affecting development and behaviour. Is chronic cocaine intake involved in alterations of epigenetic homeostasis in the testis?

Design: Epigenetic marks and mediators in testis and isolated germ cells of adult mice treated with cocaine (10 mg/kg) or vehicle (sterile saline solution) were evaluated in an intermittent binge protocol: three intraperitoneal injections, 1 h apart, one day on/off for 13 days, collecting tissue 24 h after the last binge administration (day 14).

Results: It was shown that chronic cocaine intake in mice disrupts testicular epigenetic homeostasis, increasing global methylated cytosine levels in DNA from germ cells and sperm. Cocaine also increased testicular and germ cell acetylated histone 3 and 4 and decreased expression of histone deacetylases HDAC1/2. Immunolocalization studies showed that HDAC1/2 and acetylated histone 3 and 4 proteins localize to meiotic germ cells. Analysis of mRNA expression in isolated germ cells shows decreased levels of Hdac1/2/8, Dnmt3b and Tet1 and increased levels of Dnmt3a gene expression after cocaine treatment.

Conclusions: Cocaine intake is associated with testicular toxicity and significant reproductive function impairment. The results presented here broaden the basic knowledge of the impact of addictive stimulants on testicular pathophysiology, fertility and male reproductive health and imply that altered epigenetic homeostasis by cocaine may have potential consequences on future generations.

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KEYWORDS

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