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The apple never falls far: paternal exposure to morphine has deleterious consequences on male progeny

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The ripple effects of drug abuse extend far beyond the addicts to harshly impact families and social networks. Environmental insults, such as exposure to drugs of abuse, can affect the neurodevelopment of future generations via epigenetic reprogramming of the germline. Epigenetic inheritance refers to traits transmitted from parents to progeny via mechanisms independent of changes in the DNA sequence. According to recent reports, the fathers of 5 million children are afflicted by substance abuse, which underscores the need for further studies. To address this question, we have developed a multigenerational animal model of paternal opioid exposure. Male rats self-administered morphine for 60 days (the duration of spermatogenesis) and controls received saline. Sires were mated with drug-naïve females to produce first generation progeny. We hypothesized that paternal morphine exposure would confer higher addiction-like behaviors in the next generation. We found that male, but not female offspring of morphine-exposed sires show increased morphine self-administration and that the reinforcing efficacy of morphine was higher in morphine-sired males compared to saline-sired controls. This phenotype appeared to be reward specific, in that sucrose and cocaine self-administration were unaffected by paternal opioid exposure. Ongoing studies are aimed at defining epigenetic remodeling events in the germline of drug-exposed sires and in the brain of their offspring that are functionally relevant to behavioral abnormalities in this multigenerational model of drug taking. These findings have laid the groundwork for identifying areas of vulnerability in the children of drug-abusing fathers as well as potential biomarkers related to addiction susceptibility.