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Strain Differences in Susceptibility to Opioid Side Effects In Female Mice

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Previous genetic research has primarily concentrated on analgesic and addiction profiles of opioids, but studies of side effects is lacking. Susceptibility to side effects may be important for determining individuals' risk of addiction. The aim of this study was to compare morphine induced urine retention, blood oxygen saturation, constipation, and activity in female mice of A/J and C57BL/6J inbred strains. Seven-week-old female mice (n=15/strain) were subcutaneously injected with either saline or morphine doses of 15 or 40 mg/kg body weight twice daily for two days with each injection one hour apart. Activity Time was measured for 5 minutes one half hour after the second injection. A Void Spot Assay (VSA) was used to measure urine retention Immediately after the second injection. Fecal droppings during VSA were counted and weighed. One hour after the second morphine injection on Day 2 of the protocol blood was collected from the facial vein to measure blood oxygen saturation using an iStat cartridge (Abbot Laboratories). On both days of the protocol, the saline injected control mice of both strains produced fecal droppings while mice injected with morphine did not produce any droppings (indicative of constipation). C57BL/6J strain mice exhibited significantly less morphine-induced reduction in oxygen saturation and urine retention and a substantial increase in activity time compared to A/J strain mice. These data support the importance of genetic variation in sensitivity to opioid-related side effects.