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ACCEPTED MANUSCRIPT

Evidence for a long-term protection of wheel-running exercise against cocaine psychomotor sensitization in adolescent but not in adult mice

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Highlights

- Continuous exercise attenuates cocaine sensitization in both adolescent and adult
- Exercise during youth can mitigate later in life cocaine sensitization
- Exercise during adulthood does not impact later in life cocaine sensitization

Abstract

Rodents housed with a running wheel can exhibit attenuated cocaine seeking and cocaine-induced psychomotor activation. However, the longevity of such a protection and the influence of the developmental stage during which exercise is displayed received little attention. Here, females and males C57BL/6J mice, aged 28 (adolescents) or 77 (adults) days were housed with (n=56) or without (n=28) a running wheel. After 3 weeks in these conditions, half of the exercised mice were deprived of their wheel (n=28) whereas the other half and the sedentary mice were kept in their respective environments. After 3 additional weeks, mice were tested for initiation of psychomotor sensitization to 9 once-daily intraperitoneal injections of 8 mg/kg cocaine (following 2 drug-free sessions). The expression of sensitization was assessed on a single session 30 days after the last cocaine injection. Continuously exercised mice (wheel throughout experimentation) were less responsive to the initiation and the expression of cocaine effects, regardless of the gender and the developmental period during which exercise was introduced. A 3-week regimen of wheel-running exercise during adolescence (from 28 to 50 days of age) attenuated in later life the initiation and the expression of sensitization in

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