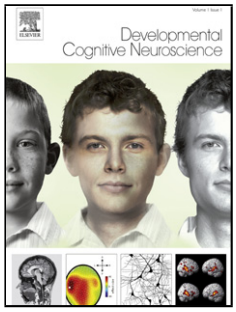

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Cognitive performance of juvenile monkeys after chronic fluoxetine treatment

Running title: Fluoxetine & cognition in juvenile monkeys

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Abstract

Potential long term effects on brain development are a concern when drugs are used to treat depression and anxiety in childhood. In this study**,** male juvenile rhesus monkeys (three-four years of age) were dosed with fluoxetine or vehicle (N=16/group) for two years. Histomorphometric examination of cortical dendritic spines conducted after euthanasia at one year postdosing (N=8/group) suggested a trend toward greater dendritic spine synapse density in prefrontal cortex of the fluoxetine-treated monkeys. During dosing, subjects were trained for automated cognitive testing, and evaluated with a test of sustained attention. After dosing was discontinued, sustained attention, recognition memory and cognitive flexibility were evaluated. Sustained attention was affected by fluoxetine, both during and after dosing, as indexed by omission errors. Response accuracy was not affected by fluoxetine in post-dosing recognition memory and cognitive flexibility test, but formerly fluoxetine-treated monkeys compared to vehicle controls had more missed trial initiations and choices during testing. Drug treatment also interacted with genetic and environmental variables: MAOA genotype (high- and low transcription