

# Persistent Changes in Serotonin Transporter Expression in the Hippocampus and Prefrontal Cortex of Adult Male Mice Following Adolescent Fluoxetine Exposure

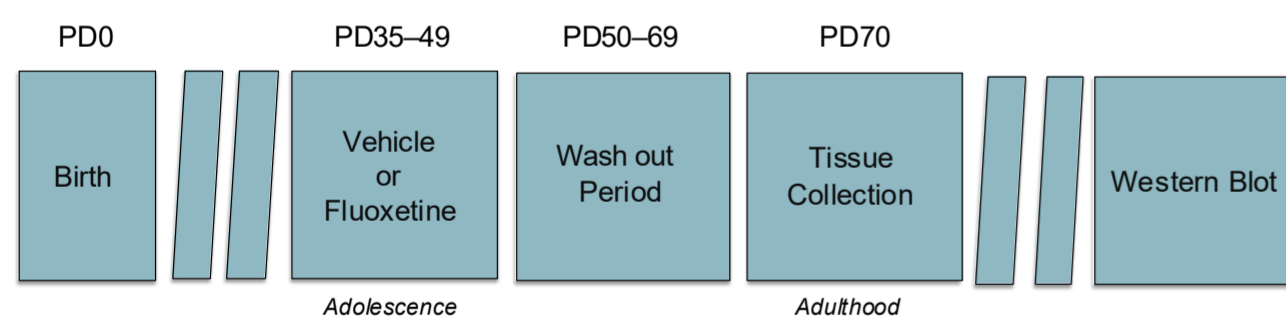
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## ABSTRACT

Prescription rates of the antidepressant fluoxetine, the most dispensed *selective serotonin reuptake inhibitor*, have been rising among the juvenile population. Since adolescence is a critical developmental period in which the brain undergoes neuronal pruning, chronic increases in serotonin levels may lead to long-term neurobiological changes in brain regions responsible for emotional regulation, particularly the hippocampus and prefrontal cortex. Thus, using mice as a model system, we explored how adolescent fluoxetine exposure (AFE) would influence the expression of serotonin transporters (SERT) in the adult hippocampus and prefrontal cortex. To do this, postnatal day (PD)-35 male C57BL/6 mice were administered with fluoxetine (250 mg/l in their drinking water) for 15 consecutive days (PD35-49). Three weeks later, when mice reached adulthood (PD70), bilateral hippocampus and prefrontal cortex tissue were dissected and analyzed for SERT protein expression, using the Western blot technique. We found that, when compared to controls, AFE-mice exhibited increased SERT protein expression in the hippocampus. In contrast, expression of SERTs was decreased in the prefrontal cortex of these mice. Collectively, our data suggest that AFE induces long-term brain region-specific changes in SERT expression. Collectively, this study demonstrates that persistent fluoxetine-induced neurobiological changes are evident in adulthood when exposed to this antidepressant medication during the adolescent stage of development, thus, likely altering emotional behavior in later life.

## METHODS



### Animals

- Male C57BL/6 mice
- Postnatal Day (PD) 35



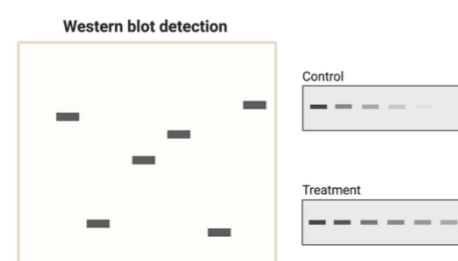
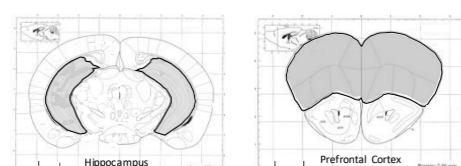
### Pharmacological Treatment

- Fluoxetine (250 mg/L) in water (VEH)
- 15 days (PD35-49)

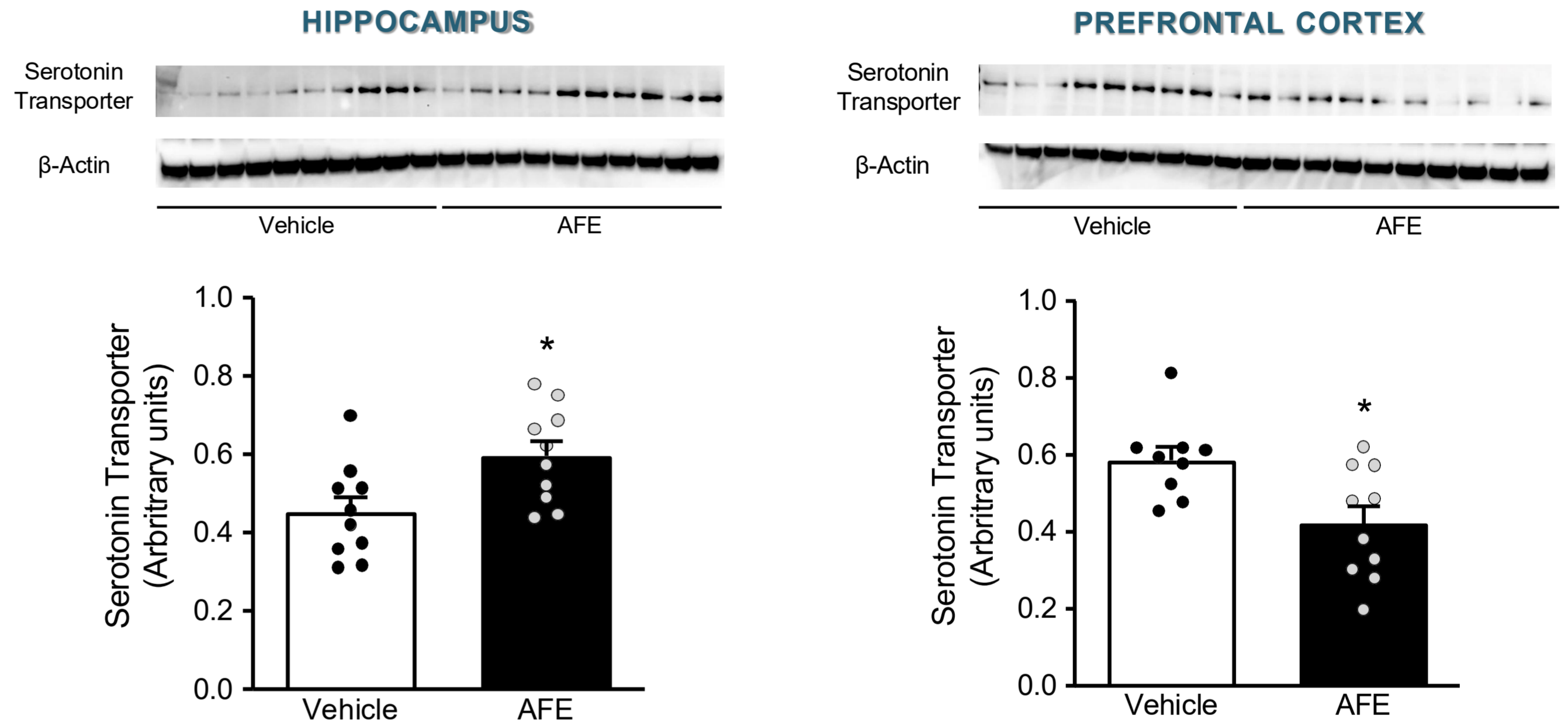


### Western Blotting

- Hippocampus and Prefrontal Cortex
- Serotonin Transporter (SERT)



## SEROTONIN TRANSPORTER EXPRESSION



**Figure 1.** Adolescent fluoxetine exposure (AFE) increases serotonin transporter expression in the hippocampus of adult male mice. Fluoxetine exposure during the juvenile period of development (postnatal day 35-49) increased hippocampal serotonin transporter protein expression when mice reached 70 days of age (adulthood), when compared to vehicle-treated controls (n= 10 per group). Western immunoblot of hippocampus samples, with  $\beta$ -Actin as a loading control, were performed under identical protocols. \* $p < 0.05$ . Data are presented as mean + SEM.

**Figure 2.** Adolescent fluoxetine exposure (AFE) decreases serotonin transporter expression in the prefrontal cortex of adult male mice. Fluoxetine exposure during the juvenile period of development (postnatal day 35-49) decreased prefrontal cortex serotonin transporter protein expression when mice reached 70 days of age (adulthood), when compared to vehicle-treated controls (n= 10 per group). Western immunoblot of hippocampus samples, with  $\beta$ -Actin as a loading control, were performed under identical protocols. \* $p < 0.05$ . Data are presented as mean + SEM.

## CONCLUSION

- Our findings in male mice demonstrate that adolescent fluoxetine exposure (AFE) increases serotonin transporter (SERT) expression in the adult hippocampus, while simultaneously decreasing it in the prefrontal cortex.
- Region-specific alterations in SERT expression following AFE highlight the need for continued evaluation of juvenile antidepressant use, as short-term symptom relief may come at the cost of long-term neurobiological and behavioral maladaptations in adulthood.

## ACKNOWLEDGEMENTS

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