

GBR12909 INDUCES MANIA-LIKE BEHAVIOR AND COGNITIVE IMPAIRMENTS IN ADULT ZEBRAFISH

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INTRODUCTION: Dopamine is an important neurotransmitter mostly involved with reward processing, motivation, and motor control. Dopamine plays an important role in cognition and behavior and its levels are regulated by dopamine transporter (DAT). GBR12909 is a dopamine-uptake inhibitor that binds to DAT, increasing extracellular dopamine levels. Dopaminergic overstimulation is known to elicit neurotoxic effects in the brain, which are associated with cognitive deficits and mania-related responses. The zebrafish (*Danio rerio*) has evolutionarily conserved dopaminergic pathways, making this species suitable for modeling human neuropsychiatric conditions. The behavioral sensitivity to neuroactive compounds makes zebrafish a relevant model organism in behavioral toxicology. **OBJETIVE:** This study aimed to evaluate mania-like and cognitive changes in zebrafish following GBR12909 exposure. **METHODOLOGY:** Adult zebrafish were weighed, isolated, and injected intraperitoneally with saline (control) or GBR12909 (15 mg/kg). After 30 minutes, four behavioral tests were performed: open field test (OFT) for anxiety-like behaviors and locomotor activity; light-dark for anxiety-related behaviors; Y-maze test to assess cognitive flexibility and working memory; and the shallow water test (SWT) for despair-like responses. **RESULTS AND CONCLUSION:** In the OFT, GBR fish had more immobile episodes and spent more time in the homebase section, while light-dark test results showed reduced transitions and time spent in the lit area, suggesting increased anxiety. In the Y-Maze, zebrafish exhibited more turns in total, more repetitive turns, and fewer alternations. Notably, GBR-treated fish showed reduced distance traveled, average velocity, and turn angle, along with increased immobility and latency to mobility in the

SWT. Therefore, GBR12909 induced behavioral alterations in zebrafish consistent with mania, anxiety, cognitive impairment, and depressive-like symptoms. Our novel findings highlight the neurobehavioral consequences of dopaminergic overstimulation and reinforce the suitability of zebrafish as a powerful model system in behavioral toxicology and neuropsychiatric research.

Dopaminergic system; Behavioral toxicology; Mood disorders.

