Anxiety

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# FG-7142 impacts fear but not anxiety in zebrafish



Anxiety and anxiety disorders are prevalent among humans and most likely underreported. While most studies focus on the anxiolytic effect of drugs, such as diazepam, the effects of pharmacological anxiogenic compounds are understudied. One such compound, β-carboline FG-7142, found in hallucinogenic plants and burned tobacco leaves, is a proconvulsant anxiogenic agent that acts on GABA-A receptors. FG-7142 decreases GABA transmission and increases excitation in the nervous system, which is known to increase arousal, stress and other symptoms related to anxiety disorders.

While the proconvulsant effect of FG-7142 is already well established in humans and rodents, the anxiogenic effect has just started gaining traction. A study in *Scientific Reports* shows that although FG-7142 does not produce an anxiogenic effect in zebrafish, it elicits a dose-dependent fear response.

Using behavioral tests associated with anxiety and fear, the researchers found that increasing FG-7142 doses had no impact on zebrafish behavior in an open-field test, a common tool to study anxiety. On the other hand, when studying the novel object approach test, which measures neophobia towards novel objects, increasing FG-7142 doses increased the effects on zebrafish response, plateauing around the optimal effective dose, from which then the effects decreased, thereby forming a U-shaped response. Zebrafish exposed to FG-7142 in this test exhibited increased immobility and decreased travel within the test tank. Opercular movements, typically influenced by anxiolytic drugs, remained unaffected by FG-7142. When ethanol, an indirect but reliable GABA agonist for zebrafish, was administered in combination with FG-7142, the behavioral patterns were altered when compared to the FG-7142-only group in both the open field and novel object approach tests. This finding suggests that ethanol can block or diminish the effects of the drug.

Overall, while FG-7142 did not elicit anxiogenic profiles in traditional anxiety tests in zebrafish, its ability to induce or alter fear responses shows its potential for studying endogenous fear mechanisms. Further studies, including exploring other classical paradigms such as antipredatory response, are needed to comprehend the drug's broader impact on generalized fear responses in zebrafish and the mechanisms behind such responses.

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**Original reference:** Scatterty, K.R. & Hamilton, T.J. *Sci. Rep.* **14**, 668 (2024)