



### **Neural and Physiological Phenotypes in Zebrafish Models of Stress**

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**Objective:** To validate the experimental utility of zebrafish (*Danio rerio*) in stress research, and explore the correlation between physiological and neural/behavioral stress responses.

**Methods:** Behavioral data in the novel tank test translates zebrafish stress/anxiety into quantifiable endpoints (latency to enter the top half of the tank, number of entries, time spent exploring the top half of the tank, fear-like erratic movements and freezing bouts). As a corresponding physiological measure of stress, whole-body cortisol levels were assessed using ELISA.

**Results:** Chronic administration of the SSRI antidepressant fluoxetine [2 weeks] reduces anxiety behavior and lowers whole-body cortisol levels. To induce an anxiogenic response, zebrafish were subjected to a model of benzodiazepine withdrawal syndrome. After chronic administration of the benzodiazepine diazepam, drug treatment was halted for 3 days before novel tank testing and subsequent cortisol assessment. While behavioral data signified a strong anxiety-like phenotype, cortisol levels also tended to rise in these fish.

**Conclusions:** Our experiments substantiate zebrafish as dependable and consistent subjects in anxiety research, as well as in studies focusing on drug dependency and withdrawal. Based on the strong correlation of behavioral data and cortisol analysis, zebrafish prove to be an excellent model organism for experimental stress research.