Investigating the Noradrenergic System's Role in Rescuing Lead (Pb)-Induced Stress Behaviors in Zebrafish (*Danio rerio*).

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Despite environmental regulations, lead (Pb) exposure remains a significant public health concern that disproportionately affects vulnerable communities. Early-life exposure disrupts physiological and neurobehavioral development and increases the risk of developing certain anxiety-related disorders throughout the lifespan. The neurobiological mechanisms underlying the development of these stress behavioral alterations and strategies to mitigate them remain poorly understood.

The zebrafish (*Danio rerio*) embryo, a vertebrate model, has gained widespread use in toxicology and neurobehavioral research, providing an ideal platform to address this critical knowledge gap. The noradrenergic (NA) system is conserved in this model, regulating the fight-or-flight response through norepinephrine signaling. Dysregulation of this pathway contributes to anxiety-like behaviors and stress-related disorders. Building on our previous work, we have shown that developmental Pb exposure (75-750 µg/L) induces bimodal stress behavioral phenotypes during Visual Motor Response and Acoustic Motor Response assays, accompanied by dysregulation of NA signaling. This study investigated the mechanisms underlying Pb-induced stress behavioral phenotypes using pharmaceutical modulation of NA receptors. Dechorionated zebrafish embryos were developmentally exposed to Pb (0, 75, or 750 µg/L), then co-exposed to Yohimbine (α_2 receptor antagonist), Phenylephrine (α_1 receptor agonist), or Bopindolol (non-selective β receptor antagonist) for 48h, 16h, or 20min prior to behavioral testing at 5 days post-fertilization. Preliminary findings demonstrate that Yohimbine rescues Pb-induced behavioral abnormalities, suggesting a role for α_2-adrenergic signaling in mediating Pb-induced stress behavioral phenotypes. These findings provide mechanistic insight into the contribution of NA signaling to Pb neurotoxicity and aim to identify potential targets for mitigating Pb-induced stress behavioral deficits.