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## Functioning of the endocannabinoid system in stress and anxiety in zebrafish larvae

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### Citation

Luchtenburg, F. J. (2020, October 7). *Functioning of the endocannabinoid system in stress and anxiety in zebrafish larvae*. Retrieved from <https://hdl.handle.net/1887/137310>

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**Issue date:** 2020-10-07

## PROPOSITIONS

Accompanying the PhD thesis

***“Functioning of the endocannabinoid system in stress and anxiety in zebrafish larvae”***

- 1) Behavioral assays in zebrafish larvae are generally suitable for screening of cannabinoid receptor (Cnr) 1 agonists, which show profound effects in these assays (this thesis, Chapter 2 and 3).
- 2) Activation of Cnr1, and not Cnr2, results in anxiolytic effects in zebrafish larvae (this thesis, Chapter 2 and 3).
- 3) Cnr1 activation in the hypothalamus or other brain regions leads to an increase in cortisol production in zebrafish larvae (this thesis, Chapter 4).
- 4) Although zebrafish larvae contain a functional Cnr1, it is not sufficiently activated by endogenous cannabinoids (at least until 5 days post fertilization) to modulate their behavior or the cortisol response (this thesis, Chapter 2, 3 and 4).
- 5) Because zebrafish larvae display a low activity of the endogenous cannabinoid system (at least until 5 days post fertilization), they are an excellent model system for studying the effects of exogenous Cnr agonists (this thesis, Chapter 2, 3 and 4).
- 6) To properly interpret observations on zebrafish embryos and larvae, comparisons should be made with adult zebrafish.
- 7) The medicinal use of cannabis, or its commercial derivatives, should be discouraged, because scientific evidence of their efficacy is still weak (Cohen 2019).
- 8) The technique of synchronous analysis of behavior and brain activity in zebrafish larvae will become an important research tool for studying the link between physiology and behavioral biology (Vanwalleghem 2018).
- 9) The availability of two different endogenous ligands (AEA and 2-AG) for Cnrs allows for the spatial and temporal differentiation of Cnr activation, for example during the stress response (Morena 2016).
- 10) The development of drugs is based on science, but the development of medical care is lagging behind in this respect.
- 11) Gaining knowledge should make a scientist feel smaller, not bigger.

October 7, 2020  
Floris J. Luchtenburg