

Question/Biological Problem: Can ecliptic pHluorin be used to better understand if potential vesicle release issues are a potential cause for anxiety?

Anxiety disorders are prevalent in today's society, affecting approximately 18.1% of the adult population in the United States [1]. Given that causes can stem from genetic factors, brain chemistry, and life events; there are many different brain chemistries that could occur in each case making them difficult to treat. Based on previous research, there is a neurotransmitter imbalance that causes anxiety. There is believed to be reduced activity of GABA, which may be caused by an imbalance of endogenous inhibitors, stimulators of the GABA receptor, or both. Additionally, there may be imbalances in norepinephrine and 5-HT responses [2]. Ecliptic pHluorins target vesicular release by sensing pH changes. This is done by using green fluorescent protein (GFP) that is sensitive to pH [3]. Previously, adenosine receptors have been tracked in hippocampal neurons in relation to schizophrenia with some success using ecliptic pHluorin [4]. This could be applied in other regions of the brain in order to determine the relation of GABA receptors, norepinephrine, and 5-HT receptors.

AIM: Use ecliptic pHluorin in order to assist in imaging of vesicle release onto GABA, norepinephrine, and 5-HT receptors in order to determine if hypothesized causes of anxiety are correct and aid in selection of treatment for anxiety.

Research Model and Plan:

- Create mouse models with neurotransmitter imbalances including: GABA, norepinephrine, and 5-HT. Separate models will be made for each individual transmitter plus a combined model.
- Use ecliptic pHluorin in order to observe vesicle release for each mouse in comparison to control mice. This will prove efficacy of the method.
- Compile data and compare in order to confirm efficacy of ecliptic pHluorin with GABA, norepinephrine, and 5-HT receptor.
- Use ecliptic pHluorin in humans with diagnosed anxiety disorders to visualize vesicle release in comparison to subjects with normal brain chemistry. Note differences in brain chemistry and use this to provide treatment input and possibly develop new treatments.

References

- [1] "Facts & Statistics," Anxiety & Depression Association of America, [Online]. Available: <https://adaa.org/understanding-anxiety/facts-statistics>. [Accessed 27 09 2021].
- [2] E. o. D. A. W. D. i. Neurotransmission, Merck Manuals Professional Version, [Online]. Available: <https://www.merckmanuals.com/professional/multimedia/table/v1031995>. [Accessed 27 9 2021].