Psychedelic Receptor Dynamics: Unveiling the Molecular Insights of Synthetic LSD for Accelerated Drug Discovery

Fengjun Tian, Chethana Chennuri, Elena Vargas, Julia Bondareva, and Rachel Penton

UNC PSYCHOLOGY & NEUROSCIENCE

Background

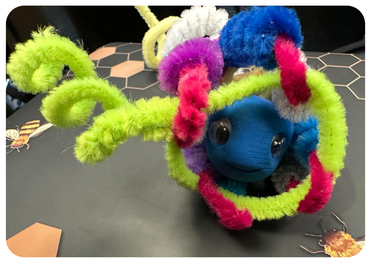
- Serotonin (5-HT) receptors G protein-coupled receptors that exist in various subtypes.
- These receptors display a wide variety of functions that affect brain pathways, specifically those associated with mood disorders (Cao et. al, 2022).
- As the research field expands, scientists are investigating the interactions of synthetic lysergic acid (LSD) at the 5-HT_{2A} receptor as a way to mediate the symptoms of schizophrenia (Cao et al., 2022).
- Due to its similarity to 5-HT_{2A}, we decided to focus on the potential of the 5-HT_{2B} receptor to mediate effects of synthetic LSD via the β-arrestin-1 pathway (Wacker et al., 2018).

Methods & Rationale

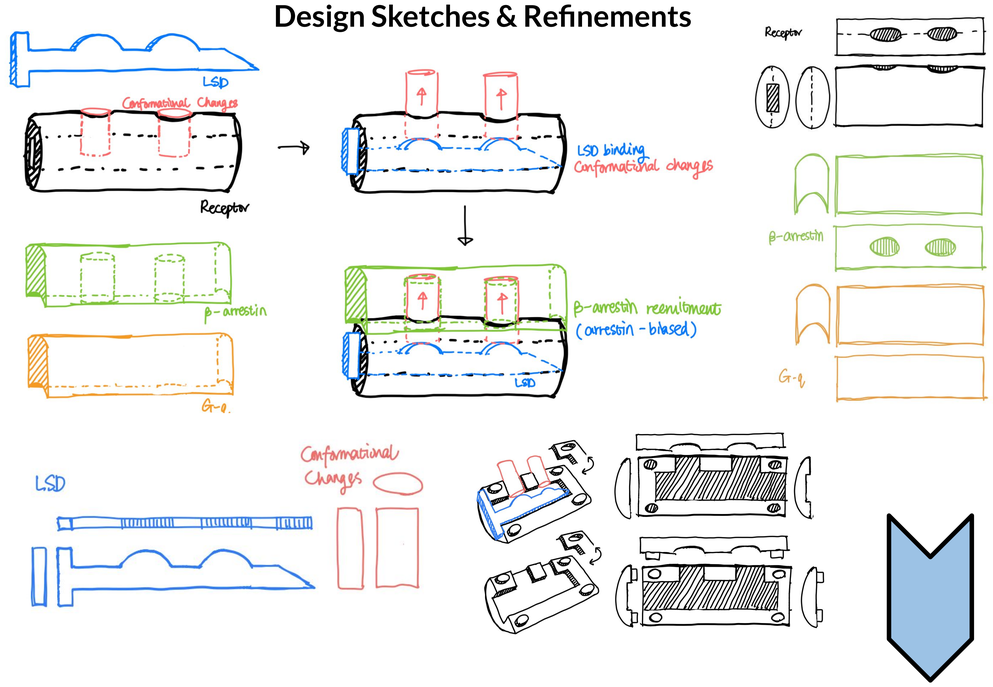
1. Conduct design-related research about the novel mechanism of action of the binding of β-arrestin-1 to 5-HT_{2B} in the presence of synthetic LSD enhances the effects of the drug.
2. Design and 3D print experimental prototypes to refine the model.
3. Explain the functionality by presenting a physically manipulatable, 3D printed model showcasing receptor structure and ligand representation.

Prototyping, Development, & Model Creation

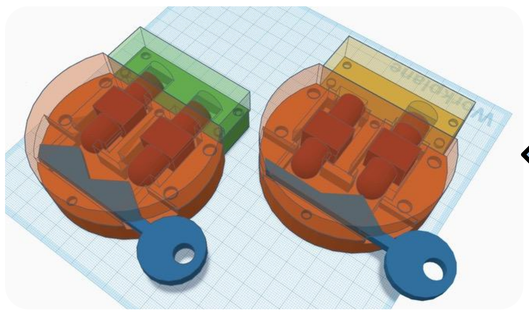
Research & Initial Prototyping



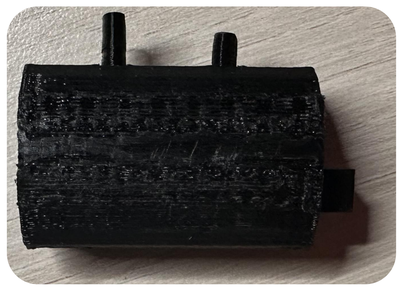
Design Sketches & Refinements

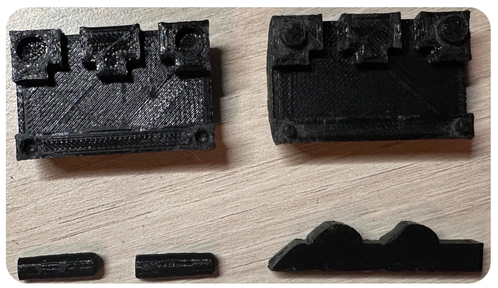


3D Model Refining & Visualization



Initial 3D Prototyping

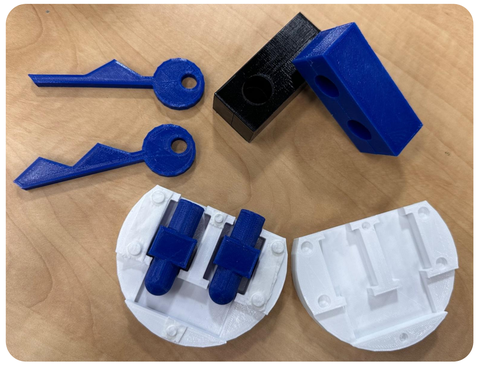


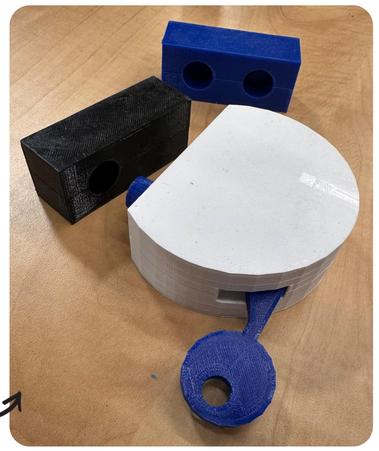


Materials & Equipment

X-ACTO, TINKERCAD, BEAM BE A MAKER, Ultimaker, SUPER GLUE, G2 PREMIUM GEL ROLLER, colorFabb

Final Model & Video





Functioning Model Demonstration!

Discussion

- After many prototypes, the 3D printed model demonstrates the activation of the β-arrestin-1 pathway and increase in difficulty coupling with G_q as LSD changes the conformation of the receptor.
- There were time limitations as well as limited knowledge of 3D print design.

Contributions & References