The Role of VMAT in the Development and Expression of Amphetamine-Induced Behavioral Sensitization

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Background

- **Addiction** to stimulant drugs is a socioeconomic problem:
  - Individual: physical, psychological & loss of work productivity
  - Society: biomedical & financial burden

- ***Sensitization:*** a major factor in craving and relapse to drug abuse
  - In response to repeated exposure to AMPH, there is an increase in:
    1) behavioral responses
    2) overflow of dopamine (DA) from brain mesotelencephalic systems

- **Altered DA Pathways:**
  - Motivational/reward neural circuitry (Robinson and Berridge, 2000)
  - Motor circuitry
  - Cognitive circuitry

- **AMPH modulation of DA transmission**

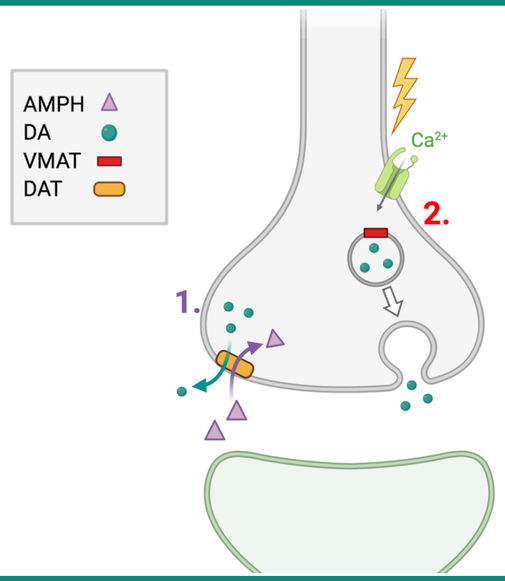
  1. **Acute Pharmacodynamics of AMPH**
     - AMPH Reverses DAT Function (Reuptake)

       ⇨ *DA Overflow*

  2. **Long-term ⇨ Conditioned Response**
     - In the Presence of Drug-related Cues (discriminant cues, sDr)

       ⇨ *Exocytosis*

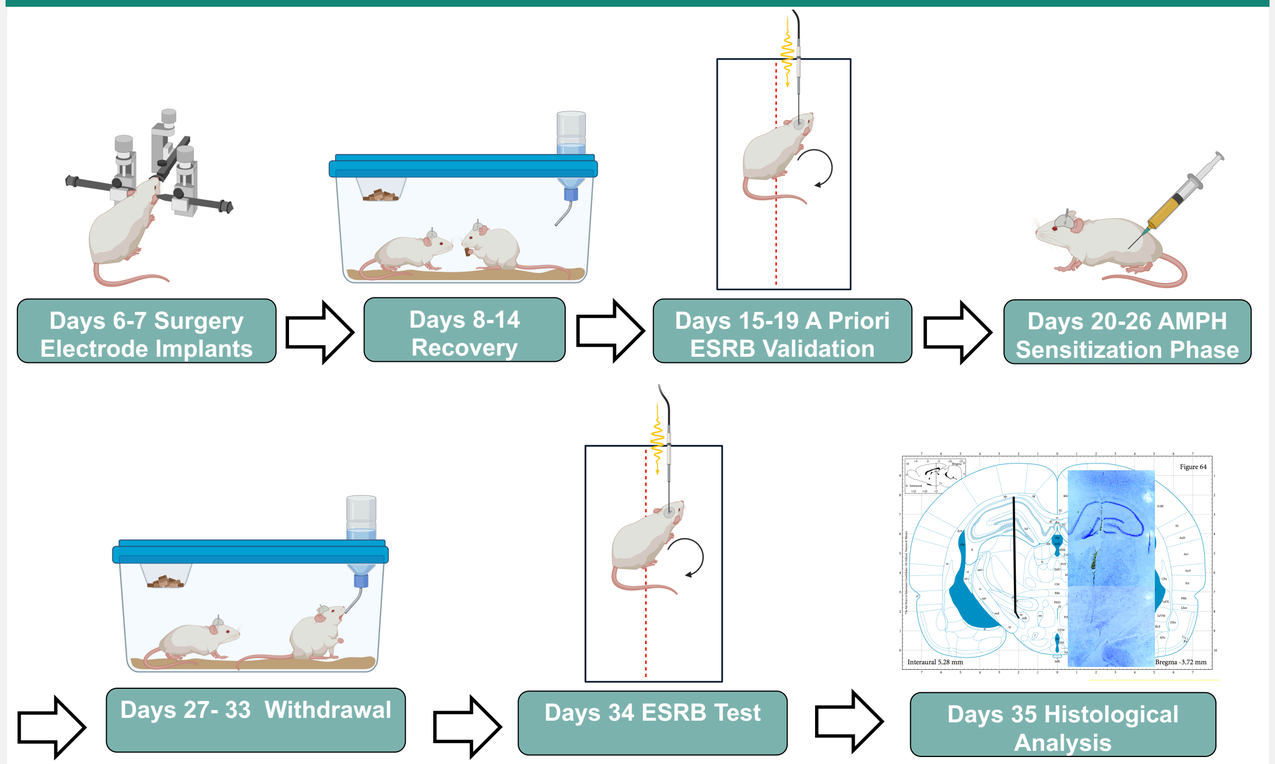
Hypothesis



- **Hypothesis: A Redistribution of Intracellular DA**
  Does sensitization alter exocytosis of DA at the transporter for cytoplasmic DA into vesicles?

- **We predict:**
  - ESRB will be sensitized in rats with a history of amphetamine (AMPH) treatment
  - Blocking access of AMPH to VMAT, by pretreating with the VMAT blocker tetrabenazine (TBZ) during a sensitizing phase, will attenuate sensitization of ESRB

Methods



Predicted Results

	Group	Pretreatment	Sensitization Treatment	Expression of Sensitization
1)	CONTROL	SALINE (SAL)	SAL	
2)	TBZ CONTROL	TBZ	SAL	
3)	SENSITIZED	SAL	AMPH	↑
4)	EXPERIMENTAL	TBZ	AMPH	✗

- SAL+AMPH group will show enhanced ESRB compared to their baseline rates (recorded before they ever receive AMPH)
- TBZ pretreatment followed by AMPH (TBZ+AMPH Group) will prevent the expression of sensitization
- This experiment is ongoing because the COVID virus has stopped our progress.

Future Directions

- If our predicted results are true, we will have a model to identify pharmacotherapeutic targets for the treatment of substance use disorder.

References

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