What is the Mechanism Behind Benzodiazepine Addiction?

Hypothesis 1:
- Regulation of gene expression, specifically the transcription factors CREB and ΔFosB
- Predictions:
  - Activation of these transcription factors reduce reward-related activity and increased compulsion for rewarding behavior

Hypothesis 2:
- Physiological changes in the GABA subtype receptors, specifically GABAs
- Predictions:
  - Long-term exposure to GABA subtype receptors decreases sensitivity to acute exposure

Hypothesis 3:
- Combination of physiological changes in GABA subtype receptors and regulation of gene expression

Answer

Hypothesis 3
- Combination of physiological changes in GABA subtype receptors and regulation of gene expression

Results

Regulation of Gene Expression via Transcription Factors
- CREB
  - Activation delays within a few days of coming off the drug
  - Mediates a state of reduced reward and reduced emotional activity
- ΔFosB
  - Activation persists up to 2 months
  - Mediates a state of heightened drug sensitivity and increased compulsion for rewarding behavior
- Gene targets of both transcription factors are still unknown in nucleus accumbens

Results

Changes in GABA Subtype Receptors
- Chronic exposure leads to alterations in GABAergic neurotransmission
- Alterations lead to reduced sensitivity of the receptors to acute exposure
- Mechanism leading to alterations is still unknown

Benzodiazepines

Class of drug primarily used for treating anxiety and sleep disorders
General Effects Include:
- Drowsiness
- Confusion
- Impaired coordination
Different types differ in:
- How quickly they work
- How long they last
- Target GABA-benzodiazepine receptor
Questions for the Final

1. What are 2 possible ways that chronic exposure to benzodiazepines leads to addiction?
2. What are the roles of CREB and ΔFosB in benzodiazepine addiction?
3. What is a possible mechanism for alterations to the GABA subtype receptors?