Neurobiological pathways to Addiction

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REVIEW ARTICLE

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Neurobiologic Advances from the Brain Disease Model of Addiction

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Neurobiological pathways to Addiction

- Binge and intoxication
- Withdrawal and negative affect
- Preoccupation and anticipation (or craving)

Path 1: Binge and intoxication

Addictive drugs activate reward regions in the brain by causing sharp increase in the release of dopamine [1]

[1] https://pubmed.ncbi.nlm.nih.gov/12445717/

Path 1: Binge and intoxication

- Repeated experiences of reward become associated with environmental stimuli that precede them (conditioning)

- With repeated exposure to same reward dopamine cells stop firing in response to the reward itself and instead fire in an anticipatory response to conditional stimuli
  - The environmental stimuli (e.g. location, state of mind, people around) that are repeatedly paired with the drug use can then elicit surges of dopamine release that trigger craving for the drug concerned and lead to heavy “binge” use

Path 1: Binge and intoxication

Unlike “natural rewards” (like food or sex)

where dopamine cells stop firing after repeated consumption/ achieve satiation

Addictive drugs circumvent natural satiation and continue to directly increase dopamine levels [2]

https://pubmed.ncbi.nlm.nih.gov/12383779/

Path 2: Withdrawal and negative affect

"Anti-reward" system results in state of severe dysphoria when effects of drug are withdrawn

[3] https://www.nature.com/articles/npp2009109

Path 2: Withdrawal and negative affect

Repeated exposure to dopamine-enhancing effects of most drugs leads to neurological adaptations involving the amygdala (linked to pleasure and fear) [3]

- Increases a person's reactivity to stress
- Develop an emergency of negative emotions *("Profound dysphoria")*
- Fuelled by neurotransmitters involved in stress response such as corticotropin-releasing factor (CRF) being overreactive giving rise to an anti-reward system

[3] https://www.nature.com/articles/npp2009109

Path 3: Preoccupation and anticipation

Impaired signalling in pre-frontal regions weaken an individual's ability to resist strong urges or to follow through on decisions to stop taking the drug

[4] https://pubmed.ncbi.nlm.nih.gov/22011681/

Path 3: Preoccupation and anticipation

- **Changes in function of pre-frontal cortical region implicating and impairing executive processes [4]”**

  - Self-regulation
  - Decision making
  - Flexibility in selection and initiation of action
  - Salience attribution (process by which a particular stimulus selectively grabs one’s attention)
  - Monitoring of error

[4] https://pubmed.ncbi.nlm.nih.gov/22011681/

Biological and social influences

Only a minority of people who use drugs ultimately become addicted

Biological and social influences

- **Susceptibility differs due to variation in individuals' vulnerability**
  - Genetics
  - Environment
  - Development

- **Factors that increase vulnerability**
  - Family history
  - Early exposure to drug use (adolescence a high risk period for substance addiction)
  - High-risk environments (socially stressful environments without familial/social support, easy access to drugs)
  - Mental illness (mood disorders, ADD, psychosis) [5]

Treatment implications (1)

- **Behavioural interventions based on brain disease model involve identifying strategies:**
  - To enhance salience of natural healthy rewards (e.g. social contact, exercise) to compete with direct and acquired motivating properties of drugs
  - To mitigate person's stress reactivity and negative emotional states to assist with self-regulation and managing strong urges
  - To plan ahead in order to avoid situations in one is particularly vulnerable to craving
  - To avoid drug-associated environmental cues to reduce likelihood of conditional craving that may lead to relapse [6]

[6] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6760932/

Treatment implications (2)

- **Opioid use disorder**
  - Opioid agonist therapy
    - One goal of intervention is to control symptoms of withdrawal and cravings thus mitigating the associated risk of emotional dysregulation and dysphoria
  - Opioid antagonists (e.g. naloxone implant)
    - Goal of intervention is to prevent intoxication

- **Alcohol/tobacco**
  - Anti-craving medications (such as naltrexone, acamprosate for alcohol and varenicline/bupropion for tobacco)

References

[1] https://pubmed.ncbi.nlm.nih.gov/12445717/

[2] https://pubmed.ncbi.nlm.nih.gov/12383779/

[3] https://www.nature.com/articles/npp2009109

[4] https://pubmed.ncbi.nlm.nih.gov/22011681/

[5] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3969413/

[6] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6760932/


any
questions?