Neurobiology of Adolescent Substance Use Disorders

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Disclosure

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Learning Objectives

At the conclusion of this presentation participants should be able to:

- Recall the current understanding of the neurobiological basis of substance use disorders; and
- Identify the unique features to the neurobiological basis of substance use disorders in adolescents.
Outline

- Neurobiological of addiction
- Adolescents and neurobiology of addiction
- Clinical implications

Factors Contributing to Vulnerability to Develop a Specific Addiction

- Use of the Drug of Abuse Essential (100%)
- Genetic (25-50%)
  - DNA
  - SNPs
  - other polymorphisms
- Environmental (very high)
  - prenatal
  - postnatal
  - contemporary
  - cues
  - co-morbidity
  - stress-responsivity
  - mRNA levels
  - peptides
  - proteomics
- Drug-Induced Effects (very high)
  - neurochemistry
  - synaptogenesis
  - behaviors

Overall Substance Use Disorder (SUD) Liability

- Selection
- Contagion
- Overall Liability Phenotype


Key Terms

• **Positive reinforcement** - a condition that increases the probability of a response that is associated with the condition (euphoria)
• **Negative reinforcement** - a condition, which when discontinued, increases the probability of a response that is associated with the condition (withdrawal)
• **Classical conditioning (Pavlov)** – Bell (conditioned cue), Food (unconditioned cue) → Salivation (conditioned response)
• **Contingency** - a consistent temporal association between events (e.g., CM)

Key Terms Cont.

• **Incentive** - a stimulus that predicts approach behavior
• **Operant** - a response on which the reinforcer is contingent
• **Action-outcome learning** - action (lever pressing) that is goal directed (obtain drug)
• **Drug taking and drug seeking**
• **Discriminative stimulus** – e.g., drug cues (e.g., drinking buddy, money) that can be the setting for drug use, maintained by drug reinforcement


Limbic Circuit and Addiction

Acute Action of Drugs on Mesolimbic System

Chronic Action of Drugs on Mesolimbic System

Cycle of Addiction

Cue-Reactivity to Cocaine Cues


Why Bother With Adolescents?

- A particularly vulnerable age group due to developmentally normative experimentation, risk taking/impulsivity ¹(Crews et al., 2007)

- Age where almost all substance use begins and progresses to use disorder ²(e.g., Compton et al., 2007)

- Adolescent initiation- may predict greater likelihood of addiction ³(e.g., Hingson et al., 2006), and greater likelihood of brain lesions ⁴(DeBellis et al., 2002)

- Substance use may interfere with normal brain and psychosocial development ⁵(Crews et al., 2007)


Adolescent Alcohol Use Disrupts Cortical Development

Hormans (years) | Rodents (days)
---|---
12 | 20
25+ | 25+

Normal cortical development

Next level cortical excitation in executive functions appears

Critical period of frontal cortical development

Binge drinking disrupts cortical development

Executive Functions

Adolescence

Adult senescence

Adult impulse control, reasoning and planning ability stabilize

Spontaneous recovery

Stable at lower level

Drinking preoccupation and tolerance

Withdrawal, negative affect loss of other activities

Uncoupled drinking addiction

Age

Consequence of Adolescent Onset Drug Use


Greater Nicotine Self-Administration of Nicotine in Adolescent Rats


Greater Sensitivity to Nicotine in Adolescent Rats

Nicotine Self-Administration in Female Rat Offspring After Chronic Prenatal Nicotine Exposure


Adolescent Rats and Alcohol

- Perinatal alcohol exposure leads to greater alcohol ingestion in adolescence and adulthood ¹(Spear and Molina, 2005).
- Adolescent rats less sensitive to some effects of alcohol (e.g., sedation, motor activity) vs. adult rats ²(Spear et al., 2005).
- In humans, insensitivity to alcohol effects in sons of alcoholic fathers predicts alcohol use disorder ³(Schuckit, 1980).


Alcohol Ingestion by Mothers During Lactation Increases Adolescent Alcohol Intake by the Offspring

Conclusion

- Neurobiology of addiction is complex and interacts with genetic, environmental, and substance related factors in manifesting vulnerability to addiction
- Positive reinforcement related neurobiological factors more important in initial substance use
- Negative reinforcement and neuroadaptation more important role in chronic use

Conclusion Cont.

- Adolescent onset linked to worse outcomes
- Challenging to do neurobiological research in adolescents
- Future research should focus on primary and secondary prevention of substance use disorders in adolescents

Thank You

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