UC San Diego Health

The Adolescent Brain, Behaviors, & Substance Use

Alexander Wallace, PhD

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Learning Objectives

- Understand how behavior changes throughout adolescence and how those changes are related to the brain
- Gain knowledge on adolescent substance use patterns including frequency of use and how use changes as adolescents get older
- Acquire an understanding of the bidirectional relationship between substance use and behaviors in adolescence

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Questions & Pre-Knowledge Check

- Do you regularly work with adolescents?
- How many adolescents would you estimate use substances?
- What factors lead from substance use experimentation to substance misuse?
- At what age does the brain meet peak maturation?
- What skills develop across adolescence that is different from childhood skill development?

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Outline

- Adolescent Development
- Substance Use
- Substance Use & Brain Behavior Relationships
- Vignettes

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Adolescent Development

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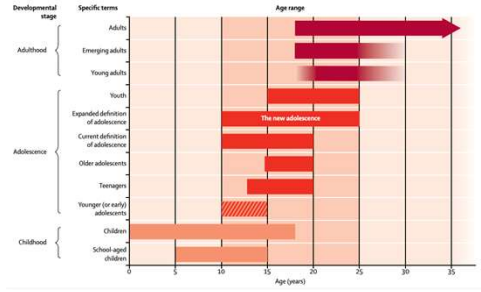
Age of Adolescence



Sawyer et al., 2018

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Age of Adolescence

- Late childhood
  - Ages 9-12 years old
- Adolescence
  - Ages 13-19 years old
- Young Adults/Emerging Adulthood
  - Ages 19-25 years old
  - Sometimes extending up to 29 years old

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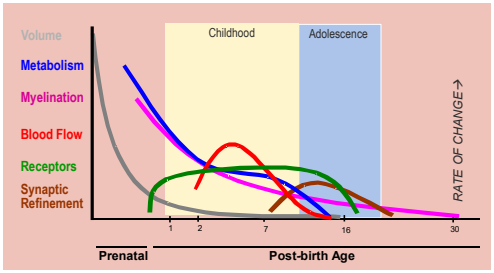
Brain Development



Tapert & Schweinsburg (2005)

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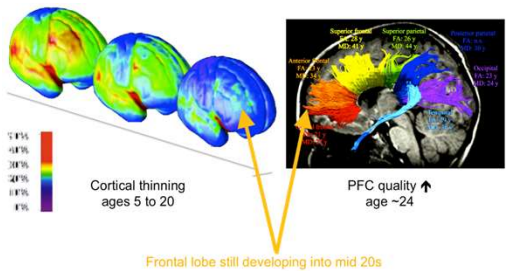
Neurodevelopment



Gogtay et al., 2004 Lebel et al., 2010

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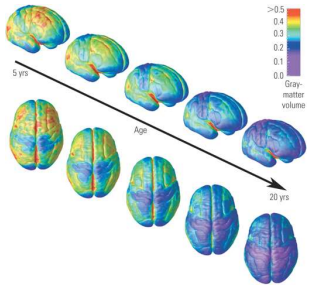
Neurodevelopment



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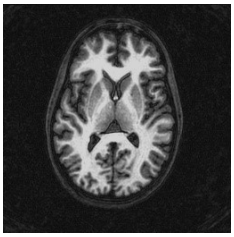
Gray & White Matter



- White matter = tracts of neurons
- Gray matter = 6 layers of neurons, unmyelinated fibers & glia

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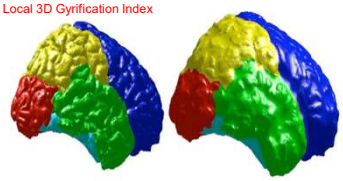
Gyrification

- Dramatic increase in cortical surface area
  - GI= ratio of external brain surface (turqoise line) with outer surface excluding sulci (red line)
  - Prefrontal and temporal/parietal regions have higher GI

Local 3D Gyrification Index



White et al., 2010, Brain & Cognition

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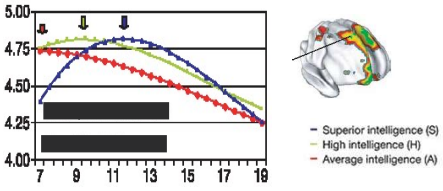
Intelligence & PFC Brain Development

- IQ can be measured as early as 8-9 months, *generally* stable by 13
- More pronounced PFC developmental changes in high IQ children/teens



Superior intelligence (S)
High intelligence (H)
Average intelligence (A)

Shaw et al., 2006; Nature

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Gray Matter Development

-45 children scanned twice. Ages 5-11.

-Cortical thinning in PFC and parietal regions associated with improvements in verbal ability

Sowell et al. 2004

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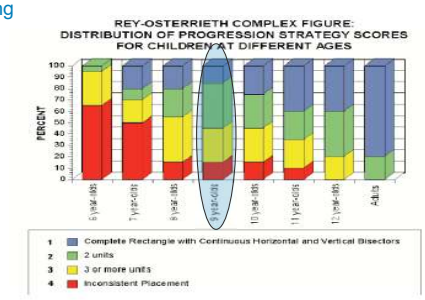
Planning



Akshoomoff, N. and Stiles, J. (1995). Developmental trends in visuospatial analysis and planning: I. Copying a complex figure. *Neuropsychology, 9*, 275-81.

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Executive Functioning

- Matching
- Inhibition
- Problem solving
- Set-shifting
- Concept formation
- Abstract reasoning
- Self-monitoring
- Mental Flexibility
- Creativity
- Anticipation
- Goal setting
- Delaying gratification

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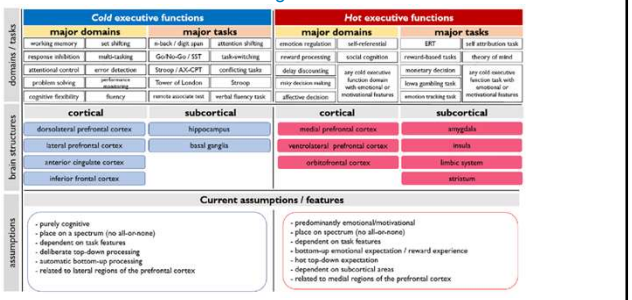
Hot vs Cold Executive Functioning



Salehinejad et al., 2021

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Salehinejad et al., 2021

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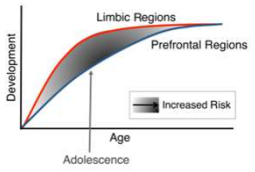
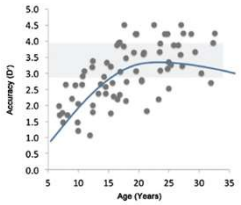
Neurodevelopment & Cognitive Control

Brain Development



Cognitive Control



Casey et al., 2008

Casey & Caudal, 2013

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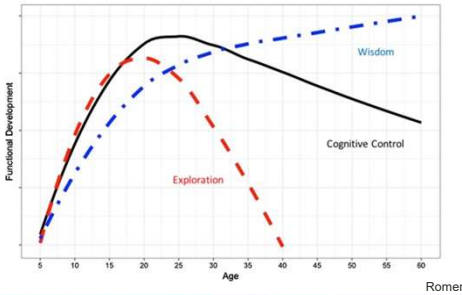
Developmental Risk Taking



Romer et al., 2017

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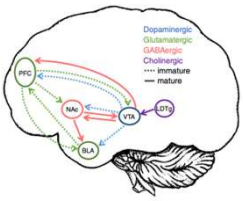
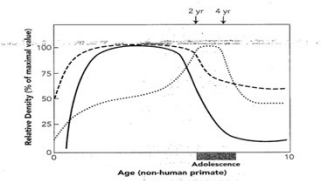
Sensation Seeking





Dotted line= DA receptors; Solid line= inhibitory GABA spines; Dashed line= excitatory glutamate spines

Yuan et al., 2015

Casey et al., 2008

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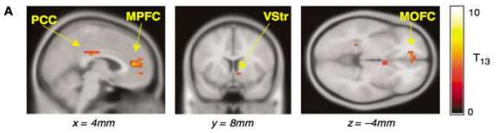
Immediate vs Delayed Rewards

- Immediate rewards: ventral striatum, medial OFC, medial PFC, posterior cingulate cortex and hippocampus more than delayed rewards
  - Limbic and paralimbic cortical projection areas
  - Teens may be MORE influenced by immediate rewards



Casey et al., 2008; McClure et al., 2004

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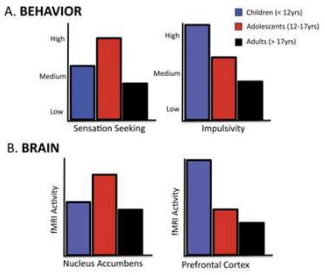
Adolescent Behavior



Casey & Jones, 2010

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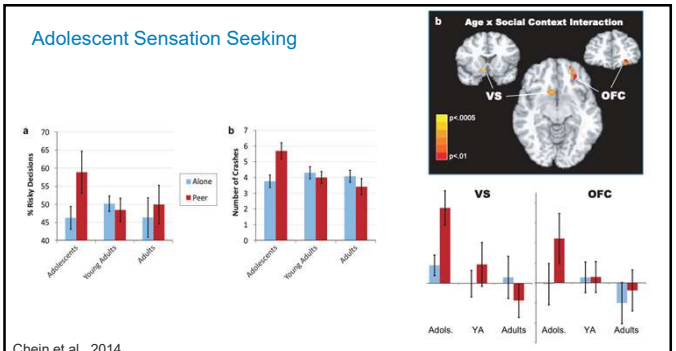
Adolescent Sensation Seeking



Chein et al., 2014

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Substance Use

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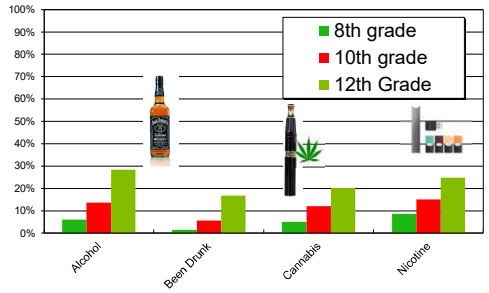
Adolescent Substance Use



Monitoring the Future, 2023

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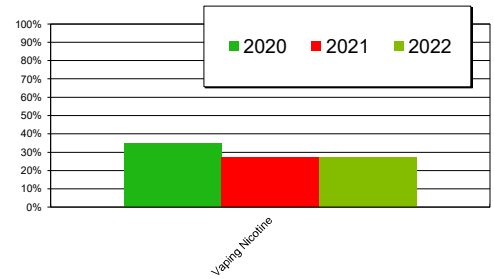
Past Year Nicotine Vaping in 12th Graders



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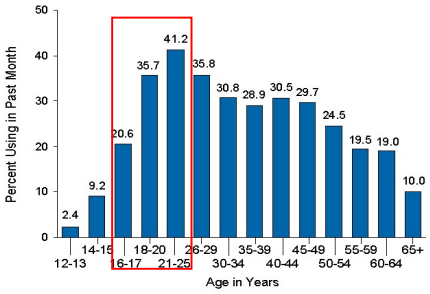
Escalating Substance Use



SAMHSA (2005) NSDUH Series H-27; SMA 05-4061.

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Adolescent Brain Cognitive Development (ABCD) Study

- **11,878 children (including 2,100 twins and 30 triplets) aged 9-10.**
- **Annual assessments (biennial MRI) for ten years.**
- **Data publicly available:**

https://data-archive.nimh.nih.gov/abcd

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Prevalence of Tobacco/Cannabis Use at Baseline

Nicotine

Mean (SD) or %; Range	All (n = 11,857)	Boys (n = 6179)	Girls (n = 5678)
Tried Any Nicotine Product*	0.68 %	0.89 %	0.37 %
Used Cigarette	<0.1 %	0.10 %	<0.1 %
Used ENDS	<0.1 %	0.13 %	<0.1 %
Used Cigar	<0.1 %	<0.1%	<0.1 %
Used Hookah	<0.1 %	<0.1 %	<0.1 %
Used Tobacco Pipe	<0.1 %	<0.1 %	<0.1 %
Used Nicotine Replacement	<0.1 %	<0.1 %	<0.1 %
Used Smokeless Tobacco	0.1 %	0.16 %	<0.1 %

Cannabis

Mean (SD) or %; Range	All (n = 11,857)	Boys (n = 6179)	Girls (n = 5678)
Tried Any Cannabis Product*	0.1 %	0.18 %	<0.1 %
Smoked/Vaped Flower	<0.1 %	<0.1 %	0%
Smoked Blunt	<0.1 %	<0.1 %	0%
Used Edible	<0.1 %	<0.1 %	0%
Smoked/Vaped Concentrate	<0.1 %	<0.1 %	0%
Used Cannabis Tincture	<0.1 %	<0.1 %	0 %
Used Cannabis/Alcohol Drink	<0.1 %	<0.1 %	0 %
Used Synthetic THC	0 %	0 %	0 %

Lisdahl et al., 2021

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Prevalence of Use at Follow-Up

Experimentation

	All	Males	Females	χ^2	*p*-value
Puffed Nicotine					
Y0	0.68%	0.89%	0.46%	7.46	**0.006**
Y1	0.56%	0.82%	0.28%	13.53	**<.001**
Y2	0.97%	1.16%	0.77%	3.71	0.054
Y3	2.78%	2.88%	2.67%	0.18	0.672
Puffed/Tasted Cannabis					
Y0	<0.1%	<0.1%	0%	1.17	0.28
Y1	0.11%	0.15%	<0.1%	1.65	0.199
Y2	0.29%	0.39%	0.18%	3.08	0.079
Y3	0.93%	0.91%	0.95%	0	0.983

Substance Use Initiation

	All	Males	Females	χ^2	*p*-value
Nicotine Use					
Y0	0.59%	0.66%	0.51%	0.09	0.764
Y1	0.39%	0.54%	0.22%	6.58	**0.01**
Y2	0.71%	0.70%	0.73%	0	0.955
Y3	2.08%	2.12%	2.03%	0.03	0.866
Cannabis Use					
Y0	0.13%	0.19%	<0.1%	0	0.983
Y1	0.45%	0.63%	0.26%	7.62	**0.006**
Y2	0.64%	0.84%	0.42%	6.54	**0.011**
Y3	1.10%	1.15%	1.05%	0	0.983

Any Substance Use

	All	Males	Females	χ^2	*p*-value
Nicotine					
Y0	1.12%	1.32%	0.90%	4.47	**0.035**
Y1	0.77%	1.09%	0.41%	16.1	**<.001**
Y2	1.18%	1.32%	1.03%	1.67	0.197
Y3	2.96%	3.09%	2.81%	0.35	0.555
Cannabis					
Y0	0.14%	0.23%	<0.1%	5.06	**0.024**
Y1	0.46%	0.65%	0.26%	8.21	**0.004**
Y2	0.70%	0.94%	0.44%	8.34	**0.004**
Y3	1.15%	1.21%	1.08%	0.13	0.715

Sullivan et al., 2021

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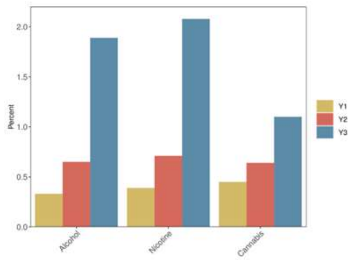
Substance Use Initiation



Sullivan et al., 2021

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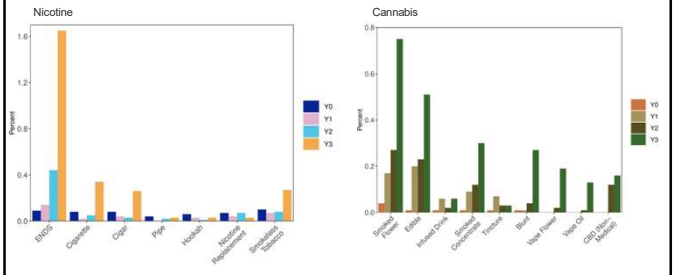
Routes of Administration



Sullivan et al., 2021

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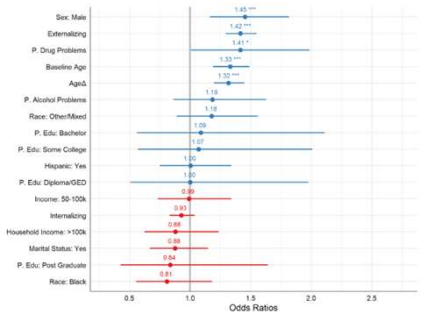
Who is Using?

SU Initiation



Sullivan et al., 2021

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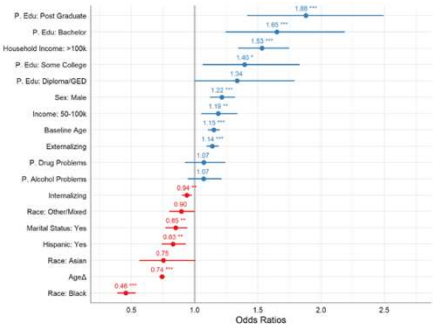
Who is Using?

Any Use



Sullivan et al., 2021

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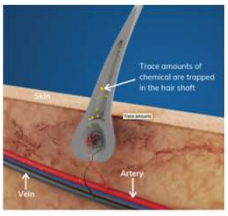
Hair Toxicology

- **Benefits:**
  - 3 month SU window (~1 cm hair = 1 month)
  - Non-invasive
  - Gives specific drug analytes
- **Cons:**
  - Can't collect from all (e.g., short hair)
  - Expensive to assay
  - Teasing out environmental contamination requires lab to wash sample



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Hair Toxicology

- 7% of low-risk randomly selected participants were positive for 1-2 drugs: cannabis, alcohol, nicotine, and cocaine
- Additional hair samples (for low and high risk) screened positive but were unable to be confirmed due to insufficient quantity of hair
  - Not included in these numbers

	% of Sample Tested
Cannabinoids	6.1%
THCCOOH-only	2.0%
Alcohol	1.9%
Amphetamines (non-Rx)	1.9%
Cocaine	1.7%
Nicotine	0.9%
Opiates	<1%
Fentanyl	<1%
Benzodiazepines	--
PCP	--
Any Positive Result	10.4%

Wade et al., 2021

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Hair Toxicology

Any SU	- Hair	+ Hair
- Self	82%	9%
+ Self	7%	2%

Alcohol	- Hair	+ Hair
- Self	95%	2%
+ Self	3%	<1%

Cannabis	- Hair	+ Hair
- Self	92%	5%
+ Self	2%	<1%

Cocaine	- Hair	+ Hair
- Self	98%	2%
+ Self	0%	0%

Wade et al., 2021

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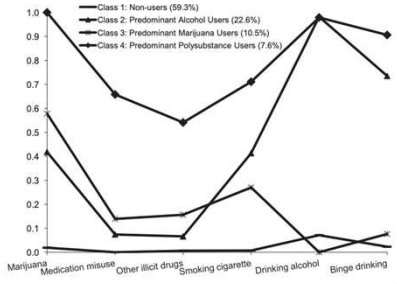
Polysubstance Use



Conway et al., 2013

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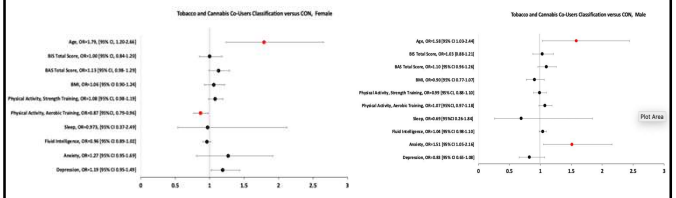
Predictors of Polysubstance Use



Wallace et al., Under Review

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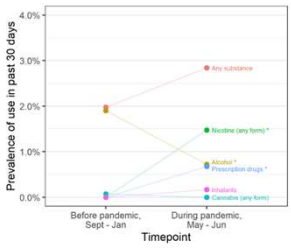
COVID-19 Pandemic



- Alcohol Decreased
- Nicotine and Prescription Drugs increased
- Other forms of Substance use remained stable

Pelham III et al., 2021

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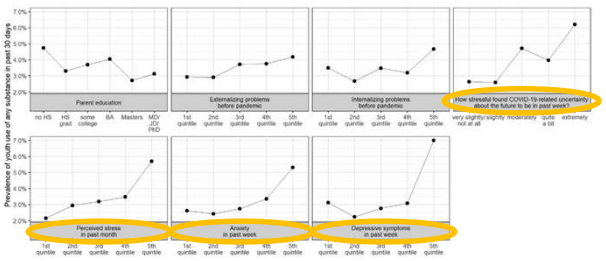
COVID-19 Pandemic



Pelham III et al., 2021

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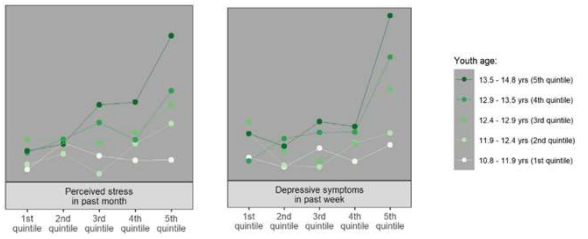
COVID-19 Pandemic



Pelham III et al., 2021

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Harmful Drinking

- Recommended Alcohol Amounts
  - Men: 2 Drinks or less a day
  - Women: 1 Drink or less a day
- Heavy Drinking
  - Men
    - More than 4 drinks on any day
    - More than 14 drinks per week
  - Women
    - More than 3 drinks on any day
    - More than 7 drinks per week

NIAAA, 2023

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Small Group Discussions

1) How do these rates compare to what you would expect/see in your own clinical practice?

2) Are there any findings that are surprising to you?

3) What substances are you currently hearing teenagers talking about?

4) How do you think this use related to adolescent brain development?

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Substance Use Brain Changes

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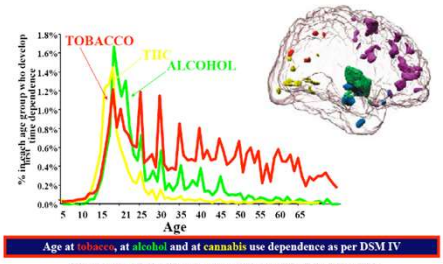
Adolescence & Substance Use



Age at tobacco, at alcohol and at cannabis use dependence as per DSM IV

NIAAA National Epidemiologic Survey on Alcohol and Related Conditions, 2003.

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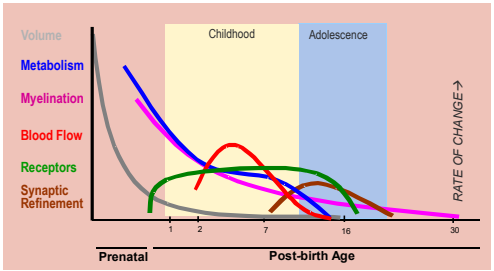
Brain Development & Substance Use



Tapert & Schweinsburg (2005)

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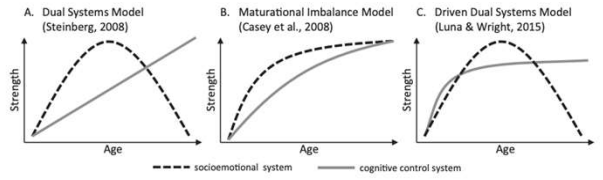
Dual Process Theory



Shulman et al., 2015

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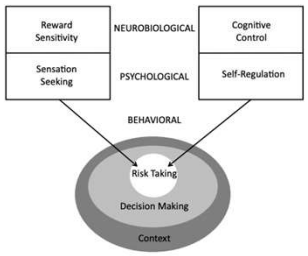
Dual Process Theory



Shulman et al., 2015

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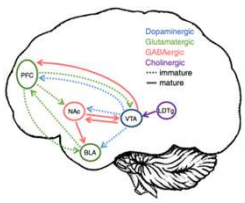
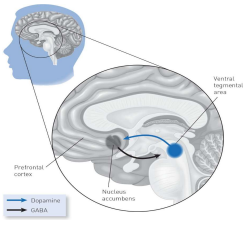
Substance Use and Rewards



Yuan et al., 2015



NIAAA, 2004

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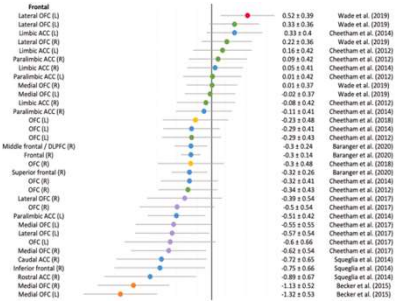
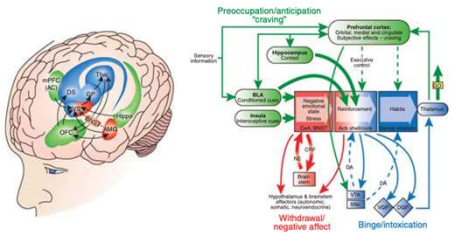
Premorbid Brain Markers



Lee et al., 2021

52

Neurocircuitry of Addiction



Koob & Volkow, 2010

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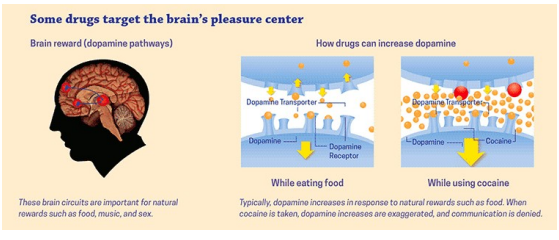
Drugs of Abuse



NIDA, 2020

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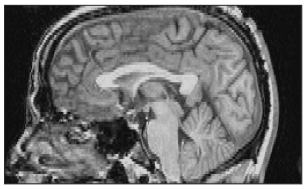
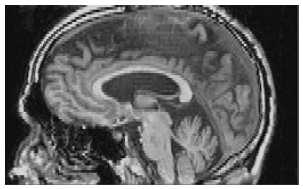
Adult Substance Use Brain Changes



Healthy Control



Alcoholism

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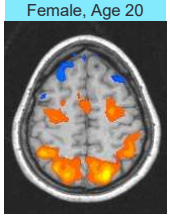
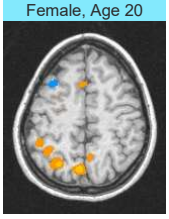
Brain Activation in Young Women

Light Drinker
Female, Age 20



Alcohol-dependent
Female, Age 20



Activation

Under-activation

Tapert et al., 2001

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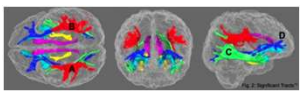
Nicotine and White Matter Integrity

Analyses (p)				
	FA		MD	
	All Nicotine	ENDS-Only	All Nicotine	ENDS- Only
Left Superior Longitudinal Fasciculus (lSLF)	.128	.5477	.0695*	.4043
Right Superior Longitudinal Fasciculus (rSLF)	.1243	.5272	.0209**	.1456
Left Inferior Longitudinal Fasciculus (lILF)	.2557	.302	.4257	.4488
Right Inferior Longitudinal Fasciculus (rILF)	.0338**	.0574*	.0626*	.1864
Left Inferior Fronto-Occipital Fasciculus (lIFOF)	.2093	.5813	.2793	.593
Right Inferior Fronto-Occipital Fasciculus (rIFOF)	.0669*	.1842	.3028	.593
Corpus Callosum (CC)	.341	.419	.5218	.5827
(**) p significant at p<.05 (*) p significant at p<.1				



Wirtz, Sullivan, & Lisdahl, In Prep

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Changes to Behavior

- Continued substance use lead to longstanding cognitive changes
  - Learning & memory
  - Cognitive flexibility
  - Abstract reasoning
  - Visuospatial skills
  - Motor skills (balance, speed)

(Brandt et al., 1983; Butters et al., 1980; Goldman et al., 1983; Parsons, 1998; Rosenbloom et al., 2004; Rourke & Grant, 1999; Sullivan et al., 2002)

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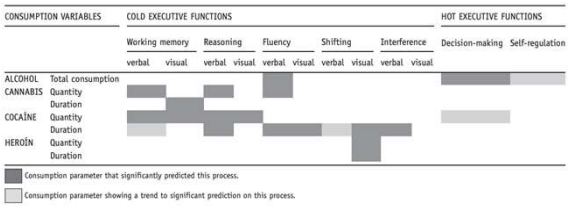
Substance Use & Behavior



Fernandez-Serrano et al., 2010

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Adolescent Substance Use & Behavior

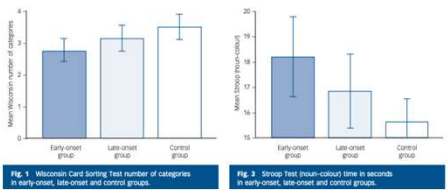

Fig. 1 Wisconsin Card Sorting Test number of categories in early-onset, late-onset and control groups.

Fig. 3 Stroop Test (noun-colour) time in seconds in early-onset, late-onset and control groups.

Fontes et al., 2018

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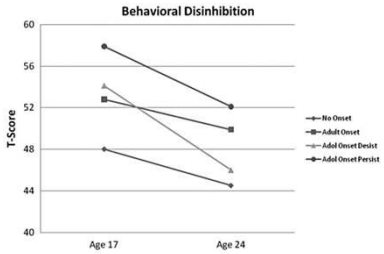
Trajectories of Disinhibition



Hicks et al., 2011

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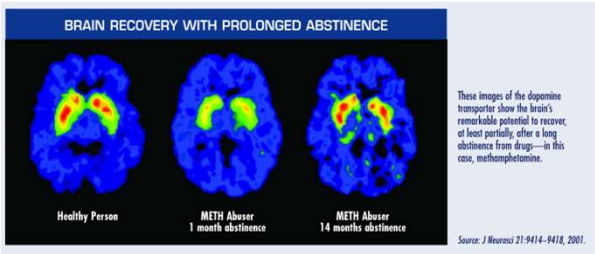
Substance Use Abstinence



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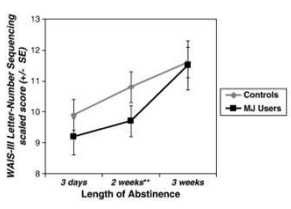
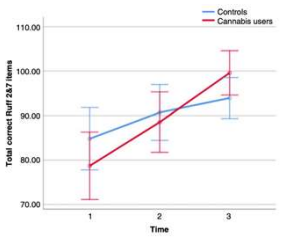
Abstinence & Cognition



Hanson et al., 2010



Wallace et al., 2020

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Adolescent Vulnerability

- Teens have more limbic activity and immature PFC
- Exposure to drugs sensitizes the reward circuitry, and they are already prone to over-react to rewards and under-react to punishment
- Teen onset is associated with increased risk for dependence
- Teen use is associated with greater decrements in neurocognition
- There is hope with abstinence

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Substance Use Screening

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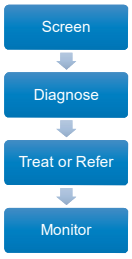
Assessment

- All patients in psychological/medical settings need to be evaluated for alcohol/substance use
- Quantity and frequency used must be assessed
  - How much is in a drink??
- Many screening tools for alcohol related problems are available



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Do's & Dont's to Enhance Accuracy

- **DO**
  - Be open/ non-judgmental
  - Use open ended questions's
  - Be specific: beer, wine, mixed drinks, LIST the drugs
  - Ask how often
  - Ask how much
  - Ask how long
  - Ask about specific problems due to use
  - Corroborate the data
- **DON'T**
  - Confront
  - Use Yes/No
  - Use jargon
  - Ask about 'alcohol'
  - Accept 'social, occasional, or rarely'
  - Accept 'no' to 'drugs'

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"On the fly" screening

- So, you said you drink/use 5 times a week, about 10 drinks/occasion? (increase 20%)
- How many times would you have had a DUI in your life, if you were caught?
- Who complains about your drinking/drug use?
- Have you found you've been drinking/using more but enjoying it less?
- What prescriptions, or OTCs, have you taken that seem to be more needed than useful?

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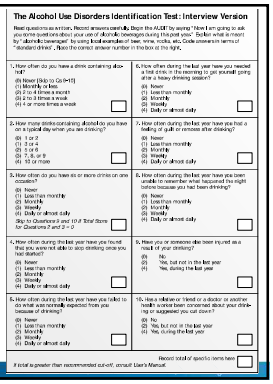
Alcohol Use Disorders Identification Test (AUDIT)

- Format:
  - Oral Administration or Self-Report
  - 10 items
- Cost: Free!
- Time: ~2 minutes
- Scoring:
  - Scores for each question range from 0-4
  - Cut off 8 for harmful drinking

Babor, Higgins-Biddle, Saunders, Monteiro, 1989



The Alcohol Use Disorders Identification Test: Interview Version

Read questions as written. Record answers carefully. Begin the AUDIT by saying "Now I am going to ask you some questions about your use of alcoholic beverages during this past year." Explain what is meant by "alcoholic beverages" by using local examples of beer, wine, vodka, etc. Code answers in terms of "standard drinks". Place the correct answer number in the box at the right.

1. How often do you have a drink containing alcohol?
(0) Never (Skip to Qs 9-10)
(1) Monthly or less
(2) 2 to 4 times a month
(3) 2 to 3 times a week
(4) 4 or more times a week

2. How many drinks containing alcohol do you have on a typical day when you are drinking?
(0) 1 or 2
(1) 3 or 4
(2) 5 or 6
(3) 7 to 9
(4) 10 or more

3. How often do you have six or more drinks on one occasion?
(0) Never
(1) Less than monthly
(2) Monthly
(3) Weekly
(4) Daily or almost daily
Skip to Questions 9 and 10 if Total Score for Questions 2 and 3 = 0

4. How often during the last year have you found that you were not able to stop drinking once you had started?
(0) Never
(1) Less than monthly
(2) Monthly
(3) Weekly
(4) Daily or almost daily

5. How often during the last year have you failed to do what was normally expected from you because of drinking?
(0) Never
(1) Less than monthly
(2) Monthly
(3) Weekly
(4) Daily or almost daily

6. How often during the last year have you needed a first drink in the morning to get yourself going after a heavy drinking session?
(0) Never
(1) Less than monthly
(2) Monthly
(3) Weekly
(4) Daily or almost daily

7. How often during the last year have you had a feeling of guilt or remorse after drinking?
(0) Never
(1) Less than monthly
(2) Monthly
(3) Weekly
(4) Daily or almost daily

8. How often during the last year have you been unable to remember what happened the night before because you had been drinking?
(0) Never
(1) Less than monthly
(2) Monthly
(3) Weekly
(4) Daily or almost daily

9. Have you or someone else been injured as a result of your drinking?
(0) No
(2) Yes, but not in the last year
(4) Yes, during the last year

10. Has a relative or friend or a doctor or another health worker been concerned about your drinking or suggested you cut down?
(0) No
(2) Yes, but not in the last year
(4) Yes, during the last year

Record total of specific items here

If total is greater than recommended cut-off, consult User's Manual.

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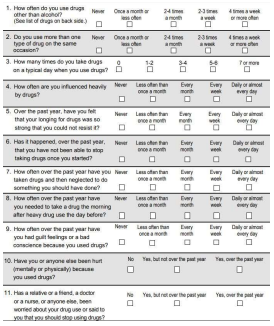
Drug Use Disorders Identification Test (DUDIT)

- Format:
  - Self-Report
  - 11 items
- Cost: Free!
- Time: ~2 minutes
- Scoring:
  - Scores for each question range from 0-4
  - Male: 6 or higher
  - Women 2 or higher



1. How often do you use drugs other than alcohol? (See list of drugs on back side.)	Never ☐	Once a month or less often ☐	2-4 times a month ☐	2-3 times a week ☐	4 times a week or more often ☐	
2. Do you use more than one type of drug on the same occasion?	Never ☐	Once a month or less often ☐	2-4 times a month ☐	2-3 times a week ☐	4 times a week or more often ☐	
3. How many times do you take drugs on a typical day when you use drugs?	0 ☐	1-2 ☐	3-4 ☐	5-6 ☐	7 or more ☐	
4. How often are you influenced heavily by drugs?	Never ☐	Less often than once a month ☐	Every month ☐	Every week ☐	Daily or almost every day ☐	
5. Over the past year, have you felt that your longing for drugs was so strong that you could not resist it?	Never ☐	Less often than once a month ☐	Every month ☐	Every week ☐	Daily or almost every day ☐	
6. Has it happened, over the past year, that you have not been able to stop taking drugs once you started?	Never ☐	Less often than once a month ☐	Every month ☐	Every week ☐	Daily or almost every day ☐	
7. How often over the past year have you taken drugs and then neglected to do something you should have done?	Never ☐	Less often than once a month ☐	Every month ☐	Every week ☐	Daily or almost every day ☐	
8. How often over the past year have you needed to take a drug the morning after heavy drug use the day before?	Never ☐	Less often than once a month ☐	Every month ☐	Every week ☐	Daily or almost every day ☐	
9. How often over the past year have you had guilt feelings or a bad conscience because you used drugs?	Never ☐	Less often than once a month ☐	Every month ☐	Every week ☐	Daily or almost every day ☐	
10. Have you or anyone else been hurt (mentally or physically) because you used drugs?		No ☐	Yes, but not over the past year ☐		Yes, over the past year ☐	
11. Has a relative or a friend, a doctor or a nurse, or anyone else, been worried about your drug use or said to you that you should stop using drugs?		No ☐	Yes, but not over the past year ☐		Yes, over the past year ☐	

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Timeline Followback (TLFB)

- Format:
  - Interview
  - Self-Report
- Cost: Free
- Time:
  - 90 days = 15 minutes
  - 360 days = 30 minutes
- Scoring:
  - Computer: Self-scored
  - Quantitative estimates of use

Sobel & Sobel, 1992

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CRAFFT

- Very fast screening questions for youth <21 (yes/no, use alcohol, MJ or other drugs to get high- if yes, then ask below)

- **C** - Have you ever ridden in a CAR driven by someone (including yourself) who was "high" or had been using alcohol or drugs?
- **R** - Do you ever use alcohol or drugs to RELAX, feel better about yourself, or fit in?
- **A** - Do you ever use alcohol/drugs while you are by yourself, ALONE?
- **F** - Do you ever FORGET things you did while using alcohol or drugs?
- **F** - Do your family or FRIENDS ever tell you that you should cut down on your drinking or drug use?
- **T** - Have you gotten into TROUBLE while you were using alcohol or drugs?

https://crafft.org/

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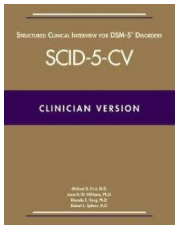
Structured Clinical Interview for the DSM-V (SCID-5)

- Format:
  - Structure interview
- Cost: $144
  - Discounted rate for APA: $115
- Time:
  - Whole: 45-120 minutes



First, Williams, Karg, & Spitzer, 2016

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Small Group Discussions

1) How often do you screen for substance use when talking with adolescents?

2) Do you have any concerns talking about substances with teenagers?

3) What barriers exist that prevent you from discussing substance use with teenagers?

4) Do you think you'll use any of these screening tools in the future?

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Resources

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Resources

- National Institute on Alcohol Abuse and Alcoholism (NIAAA; niaaa.nih.gov)
  - Rethinking Drinking
    - https://rethinkingdrinking.niaaa.nih.gov/
  - Helping Patients with Alcohol Related Problems
    - https://www.niaaa.nih.gov/health-professionals-communities/core-resource-on-alcohol
- National Institute on Drug Abuse (NIDA; nida.nih.gov)
  - Screening Tools and Prevention
    - https://nida.nih.gov/nidamed-medical-health-professionals/screening-tools-prevention
  - Health Professional Education
    - https://nida.nih.gov/nidamed-medical-health-professionals/health-professions-education

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Vignette

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Vignette #1

A 19 year old female comes in for a referral for Attention Deficit-Hyperactivity Disorder (ADHD). During the visit, she reports that she uses cannabis about once a month and drinks about two bottles of wine a week, usually going through a bottle in one sitting.

What concerns, if any, would you have about her substance use? What feedback would you give her about her use?

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Vignette #2

A 16 year old male reports that he currently vapes nicotine everyday with occasional alcohol use on the weekends. This youth reports that he would like to cut down on his nicotine use but does not know how.

What recommendations/resources would you give to this youth? What considerations around the teenagers potential executive functioning skills would you make in providing recommendations?

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Questions

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