The Neuropsychology of Alcoholism

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- Neuropsychologist
- 34 years, Kaiser San Francisco, 1975-2009
  - 10 years working partially in CDRP
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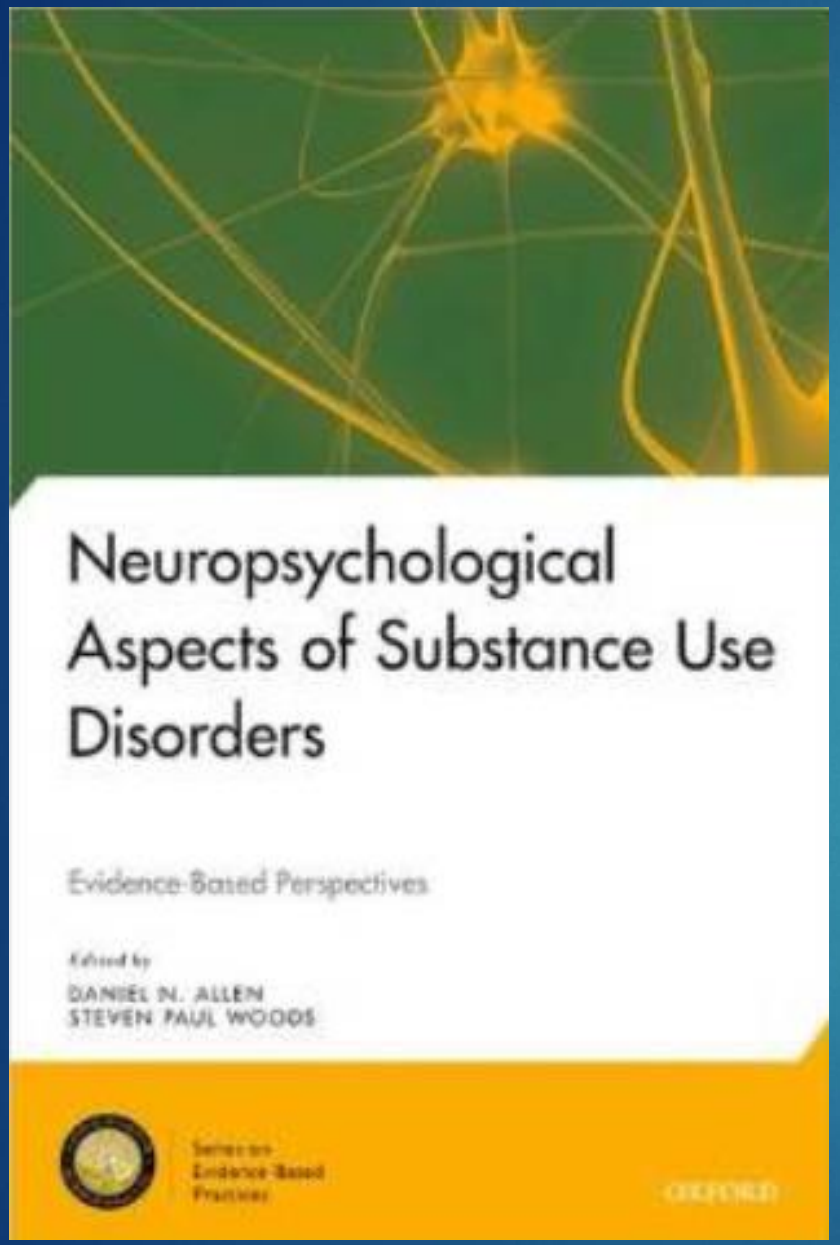


Neuropsychological Aspects of Substance Use Disorders: Evidence-Based Perspectives

by Daniel N. Allen and Steven Paul Woods

Has great individual chapters on specific substances

NOVA PRESENTS
Addiction

Airing Wednesday, October 17 at 9 pm on PBS

Addiction deaths

- In US, 80 K die of excessive drinking; smoking, 400 K deaths

- Iatrogenic addiction: During 2017, there were more than 70,200 overdose **deaths** in the **United States** and 47,600 of those overdose **deaths** involved **opioids**.
- More than 130 people **died** every day from **opioid**-related drug overdoses in 2016 and 2017,

Neuropsychological Perspective

- Substance abuse is not a moral failure.
- Drug and alcohol abuse is a chronic brain disease that causes compulsive substance use, despite harmful consequences
- All behavioral experiences lead to physiological changes in the brain, not just psychological change
- Substance abuse leads to physiological brain changes in cognitive, behavioral, and emotional ability
- You ignore these facts at the risk of failure as a clinician

Most Difficult Psychiatric Patients = NP deficits

- The most difficult psychiatric patients have neuropsychological deficits, including memory and executive deficits:
  - Schizophrenia
  - Bipolar Disorder
  - Borderline Personality Disorder
  - Psychosis
  - Severe Depression
  - OCD
  - Substance Abuse
  - ADHD
- Example: It is the cognitive deficits that predict functional outcome in Schizophrenia, not psychiatric sxs; containment of the latter does not improve the former

Common Neurobiological Substrate for Mental Illness: EF network

- Major 2015 metaanalysis: 193 studies comprising 15,892 individuals across 6 diverse diagnostic groups (schizophrenia, bipolar disorder, depression, addiction, obsessive-compulsive disorder, and anxiety)

- Results: Gray matter loss converged across diagnoses in frontal regions (Anterior cingulate, Insula)

- Lower gray matter in this network was associated with poor executive functioning.

Madeleine Goodkind, et al, 2015

Recommendation: Executive Function Groups

- This study reinforces need for all psych. & CDRP clinics to have a regular Executive Function group for patients.
- Need for teaching behavioral memory techniques, external prosthesis/reminder systems, problem solving strategies.
- All psychologists need to be able to do MoCAs
- Need to do routine MoCAs on more severely impaired psych & CD pts.

Lesson for Post docs on Hospital rounds

- Advise to Post Docs: Do not necessarily believe what pt tells you in the hospital; all older patients want to leave hospital and therefore lie.
- Many language functions well preserved
- Vocabulary continues to increase into old age
- But all other abilities may be impaired; only know if you test for deficits
- All this applies to patients with substance abuse in CD & Psych clinics

Complex Nature of Addiction

- Types of addiction: alcohol, cocaine, heroin, food.
- Are these disorders of reward, with drugs hijacking a natural system that is meant to respond to food, sex and friendship.
- They are also a disorder of learning, where our brains learn negative habits and responses.
- Are they a combination of an environmental stimulus and vulnerable genes?
- Or perhaps are they an inappropriate response to stress, where bad days trigger a relapse to the cigarette, syringe or bottle.

Nature of Addiction

- None of these views are wrong. But none of them are complete, either.
- Addiction is a complex disorder of reward and a disorder of learning.
- It has genetic, epigenetic and environmental influences.
- Addiction is a display of the brain's astounding ability to change — neuroplasticity — and it showcases what we know and don't yet know about how brains adapt to reality. Addiction is example of maladaptive neuroplasticity.

Alcohol

- A central nervous system (CNS) depressant.
- Low doses stimulates neural activity, often increasing social interaction
- Moderate to high doses suppress neural activity

Negative Consequences

- Worldwide, over 3 million people died from alcohol consumption in 2016, equating to 1 in 20 deaths globally. More than 75% of these deaths were among men.

- Causes of death: 28% - injuries; 21% - digestive disorders; 19% due to CV diseases.

- Worldwide, 45% of alcohol is consumed as spirits, followed by beer (34%) then wine (12%).

Neuropathology

- Chronic heavy consumption leads to dose-related neurotoxic CNS damage and a pattern of neuropsychological dysfunction

- There is a pattern of alcohol-specific damage known as the neurotoxicology of essential alcoholism.

- Brain atrophy occurs largely due to white matter atrophy,
  - in Korsakoff's, it results in neuronal loss in PFC, hypothalamus, and cerebellum

D. Gansler & H. Duncanson, 2014

Yoda Says, “With Age and Alcohol, Confused Is the Force”

- Regionally selective volume reductionss are observed most extensively in:
  - the lateral and medial frontal,
  - parietal
  - insular cortices,
  - with additional deficits in temporal and cingulate regions

- Addiction changes in PFC – reduction in Grey Matter = impaired decision making; can recover GM with abstinence

Addictive Drugs in the brain

- All drugs are Trojan horses in the brain
- All addictive chemicals are mimics which look and act like an existing brain neurotransmitter, esp. dopamine (anticipation & reward chemical)
- Increases available amount of dopamine which produces a high; brain responds by reducing dopamine receptors
- Drugs capture reward pathways in the brain which control motivation & compulsion

Brain needs dopamine

- Addiction is a brain disorder, not a problem of will.
- Laura Volkow: addiction leads to reduction in D2 receptors - starving for D; drugs interfere with motivational drive; without D, no motivation
- Food, gambling have same D effect; morbid obese have less D receptors, creating intense craving
- Dopamine deprival causes addtiction; can come back within 14 months of recovery

Dopamine and addiction

- Drugs mimic dopamine
- Brain changes due to drug use; evolutionary brain seeks reward; rat will seek reward stimuli; several 1000 x per hour;
- Dopamine tells brain to pay attention – need more of prior experience; released by endorphins, or external pleasure or excitement;
- Brains are powerless over addiction, slave to it; brain reduces normal dopamine levels in response to drug use
- Drugs can push dopamine 10 x higher; memories of euphoria create cravings; and then to avoid pain of withdrawal in which stress hormones released at catastrophic levels (shakes, anxiety, pain, dysphoria);

Opioids

- Fentanyl (synthetic opiate from China) – 100 x as potent as opioids; 50 x more potent than heroin; 2 grains of salt equivalent will kill you – shuts down breathing; almost no overdoes are admitted to Tx facility

- 80% of Tx centers follow AA; abstinence based approach has failure rate of 80-90% for opioids

- Methadone, only at clinics; Suboxone (buprenorphine) since 2003 – at home, and non-opioid Naltrexone (Vivitrol injection) help with cravings; both cut mortality by 50%; at 1 year, 40-90% are in recovery; can use Tx - learn to be clean/sober

Addiction on Nova

- Overdose is number 1 cause of death for under 50.

- After coal industry shut down, 780 million pain pills in WV & highest overdose rate (7x national ave)– Percocet (oxycontin); iatrogenically induced via doctors; opioid refugees (withdrawal cravings with no medical tx); 70 K deaths per year; prison systems filled with addicts, who give Naloxone on release; increase in hepatitis and HIV

Lower brain volume in in the frontal cortex and insula predispose a person to greater alcohol consumption.

- Historically, alcohol consumption is associated with reduced brain volume and drinking can literally shrink the brain.
- 2019 study: being born with reduced brain volume is a genetically-conferred risk factor for heavier alcohol consumption.
- This does not discount that alcohol abuse may further reduce gray matter volumes, but it does suggest that brain volumes started out lower to begin with/
- Genetically-conferred reductions in gray matter volume in the frontal cortex and insula, which were, in turn, predictive of future alcohol use, including the initiation of drinking in adolescence and future drinking in young adulthood; and greater overall alcohol consumption

Associations between middle/superior frontal gray matter volume and alcohol use are genetically-conferred and predict future use and initiation

- Study based on longitudinal and family data from three independent brain imaging studies – including the comparison of drinking behaviors in twin and non-twin siblings; longitudinal research within children who were never exposed to alcohol at baseline; and gene expression analyses using postmortem brain tissue.
- When compared with siblings with a shared history of low alcohol use, siblings who drank more heavily had lower grey matter volumes. Interestingly, the study found no differences in gray matter volume in brains of same-family siblings where one drank more heavily than the other – both looked like heavy-drinkers. This finding provides additional evidence that lower gray matter volume is a pre-existing vulnerability factor associated with the potential for alcohol use, as opposed to a consequence of alcohol use.
- Genomic risk for alcohol consumption is enriched for genes that are preferentially expressed in the dorsolateral prefrontal cortex relative to other tissues and brain regions. Further, they found that the expression of specific genes in this region are replicably associated with genomic risk for alcohol consumption. These data provide additional convergent evidence that it is biologically plausible that lower grey matter volume in the frontal cortex may be driven by genetic risk for alcohol consumption.

Risk factors for developing AUD (Alcohol Use Disorder)

- Original brain size
- Early adversity
- Genetics (e.g., family history, genotypes): 50% of risk
- Earlier onset of drinking, greater the addiction
- Greater activation of the reward circuit accompanied by blunted executive control systems (reduced PFC)
- Impulsivity, poor affect regulation, and poor executive function
- Antisocial tendencies

Jacobus & Tapert, 2013, *Annual Review of Clinical Psychology, 9,* 703-721.
Lovallo WR, 2013, *International Journal of Psychophysiology, 90,* 8-16.
Peeters M, 2014, *Alcohol and Alcoholism, 49,* 182-186.

Alcohol Benefits in Normals

- 90+ study: longevity correlated with 1 daily drink
- 2009 prospective study (Anstey): light to moderate drinkers compared with nondrinkers in late life have reduced risk of dementia
  - Protective effect on cardiovascular and cerebrovascular health
- Lothian Scottish Study: reverse causality - bright kids (with better brains) grow up to be bright adults (Etoh: social status effect)

Anstey, et al., Am. J. Ger. Psych, 2009

Standard Drink = half ounce of alcohol

Defining the "Standard Drink"

- A standard drink = 14 g ethanol
  - 12 oz of regular beer or cooler (5% alcohol)
  - 5 oz of table wine (12% alcohol)
  - 1.5 oz of hard liquor (40% alcohol, 80 proof)
  - The average person metabolizes about 1 standard drink per hour

Source: National Institute on Alcohol Abuse and Alcoholism. Bethesda, Md: NIAAA; 2004. NIH Publication No. 04-3769.

BAC of .08 = legally impaired

Drinking and Driving

WOMEN

Approximate Blood Alcohol Percentage

Drinks	Body Weight in Pounds									
	90	100	120	140	160	180	200	220	240	
0	.00	.00	.00	.00	.00	.00	.00	.00	.00	**Only Safe Driving Limit**
1	**.05**	**.05**	**.04**	.03	.03	.03	.02	.02	.02	Impairment Begins
2	.10	.09	.08	**.07**	**.06**	**.05**	**.05**	**.04**	**.04**	**Driving Skills Significantly Affected** **Possible Criminal Penalties**
3	.15	.14	.11	.10	.09	.08	**.07**	**.06**	**.06**	
4	.20	.18	.15	.13	.11	.10	.09	.08	.08	
5	.25	.23	.19	.16	.14	.13	.11	.10	.09	
6	.30	.27	.23	.19	.17	.15	.14	.12	.11	Legally Intoxicated Criminal Penalties
7	.35	.32	.27	.23	.20	.18	.16	.14	.13	
8	.40	.36	.30	.26	.23	.20	.18	.17	.15	
9	.45	.41	.34	.29	.26	.23	.20	.19	.17	
10	.51	.45	.38	.32	.28	.25	.23	.21	.19	

One drink is 1.5 oz. of 80 proof liquor, 12 oz. of beer, or 5 oz. of table wine.

Your body can get rid of 1 drink per hour

Who drinks & how much:

30% don't drink

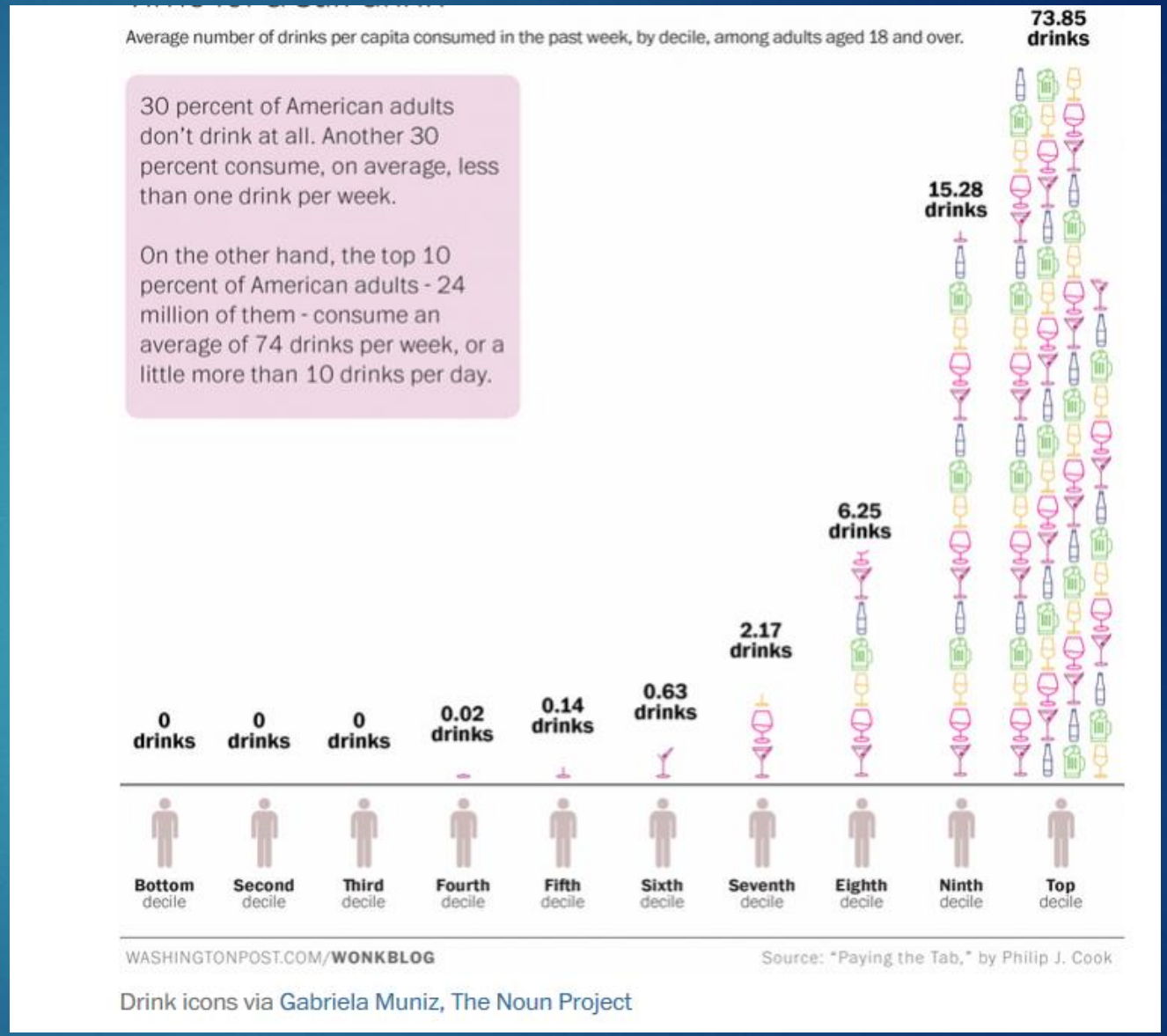
Next 30%: 1 drink per day;

Top 20 %: 2 drinks per day;

Top 10%: 74 alcoholic drinks per week (10 drinks per day) = (70% of the alcohol consumed in any year by everyone)

Median = 3 drinks per week

51% of adults = regular drinkers

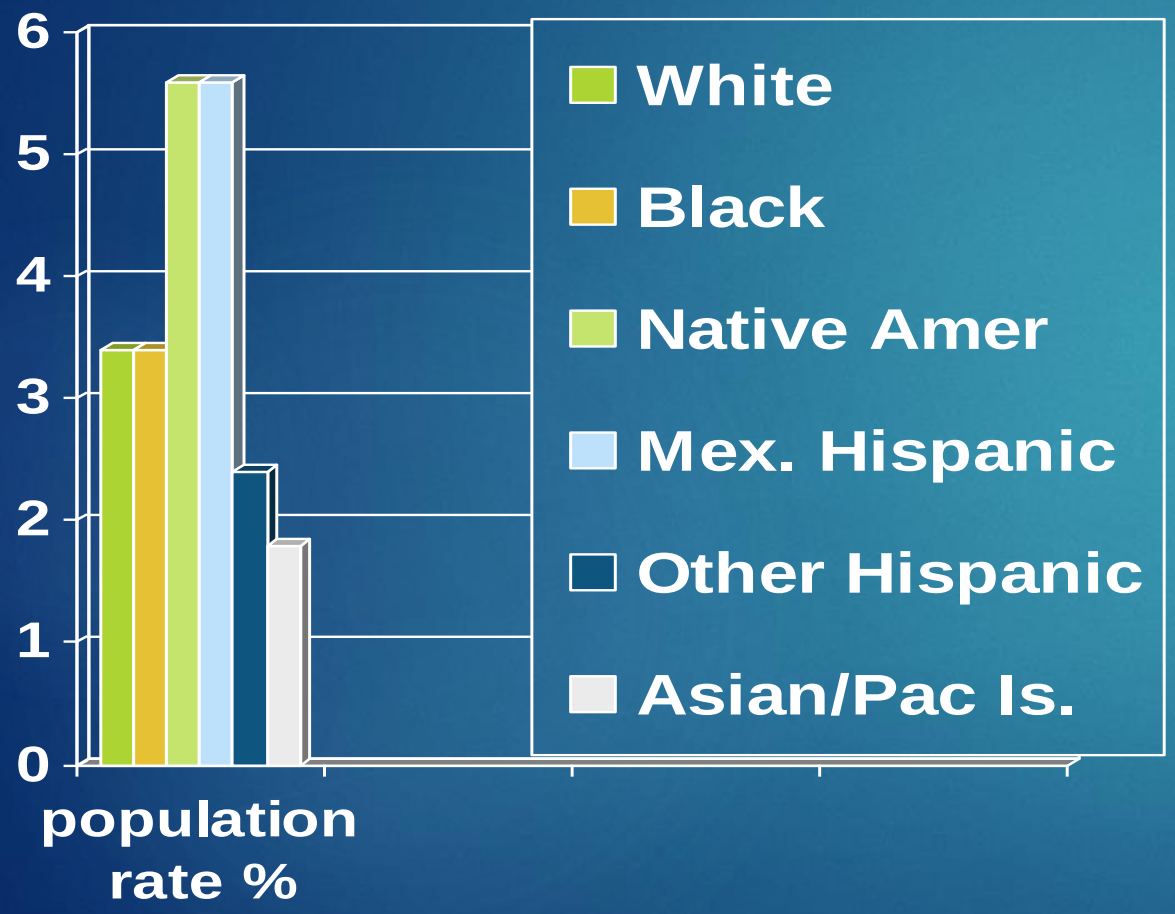


Paying the Tab by P. J. Cook, 2007; (NESARC) data

Ethnicity

- National surveys show variations across ethnicities in drinking, alcohol use disorders, alcohol problems, and treatment use.
- Higher rates of high-risk drinking among ethnic minorities are reported for Native Americans and Hispanics
- Whites and Native Americans have a greater risk for alcohol use disorders relative to other ethnic groups; lowest for Asian-American women.
- However, once alcohol dependence occurs, Blacks and Hispanics experience higher rates than Whites of recurrent or persistent dependence.
- Furthermore, the consequences of drinking appear to be more profound for Native Americans, Hispanics, and Blacks.
- Disparities in alcohol treatment utilization are most apparent for Hispanics.
- Explanations for these differences are complex, likely affected by risky drinking behaviors, immigration experiences, racial/ethnic discrimination, economic and neighborhood disadvantage, and variations in alcohol-metabolizing genes.
- Hispanics and Blacks have greater risk for developing liver disease compared with Whites and Hispanic men have the highest rate of liver cirrhosis mortality

Ethnicity and Alcohol Patterns



- Relative rates of alcohol dependence
- Sample average = 3.5%
- Hispanics and Blacks have a higher risk for developing alcohol-related liver disease than whites

Source: SAMHSA National Household Survey (1991-1993)

Moderate & Binge Drinking

- Moderate drinking is up to 1 drink per day for women and up to 2 drinks per day for men.

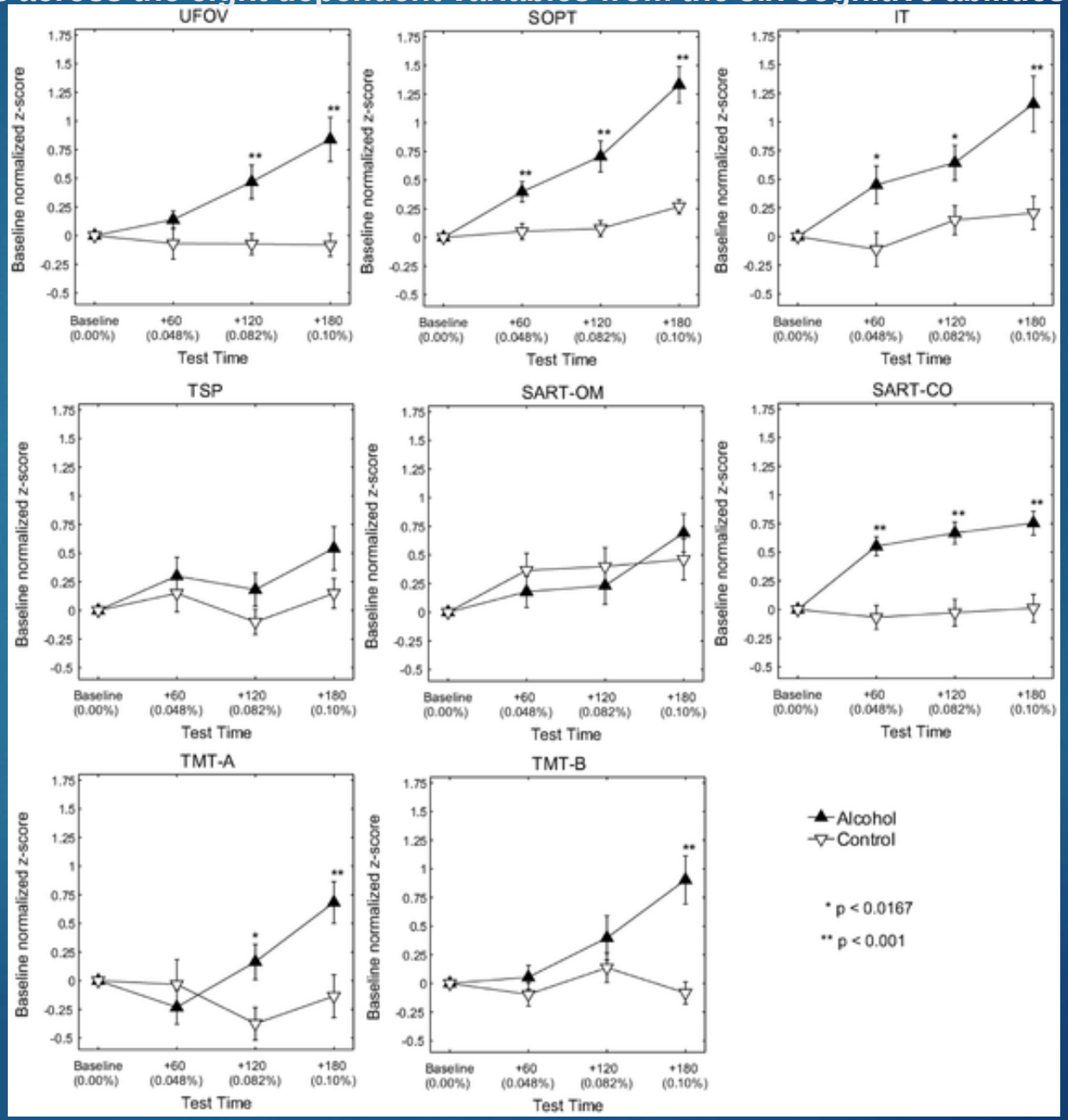
- Binge Drinking: (NIAAA) = blood alcohol concentration (BAC) levels to 0.08 g/dL; 4 drinks for women and 5 drinks for men—in about 2 hours.

- SAMHSA: 5 or more alcoholic drinks on the same occasion on at least 1 day in the past 30 days = alcoholism

http://www.niaaa.nih.gov/alcohol-health/overview-alcohol-consumption/moderate-binge-drinking
http://www.samhsa.gov/capt/tools-learning-resources/binge-drinking-terminology-patterns

Comparison of the mean baseline-normalized performance of the alcohol and control group participants across the eight dependent variables from the six cognitive abilities tests.

As you approach .08 to .10 of alcohol in blood, cognitive NP performance significantly decline



Dry MJ, Burns NR, Nettelbeck T, Farquharson AL, White JM (2012) Dose-Related Effects of Alcohol on Cognitive Functioning. PLOS ONE 7(11): e50977. https://doi.org/10.1371/journal.pone.0050977

Alcohol Use Disorder (AUD)
(Dependence/Abuse)

- Heavy intake – 4 or 5 drinks per day
- Craving
- Social & occupational dysfunction
- Tolerance
- Withdrawal
- Continued use despite negative consequences

Holding your liquor: Low response to alcohol

- Individuals with low response to alcohol can drink much more alcohol before becoming drunk; low response correlates to becoming alcoholic

- Low response implies you will have more alcohol per session of drinking in your brain; greater chance for long term neuronal damage

- Greater chance of low response with family history of alcoholism

Dependence

Three C's...

- Compulsion to Drink
- Loss of Control
- Negative Consequences

Neuropathology

- Alcohol does not bind to a specific brain receptor
- It alters functioning of neuronal membranes & of GABA & Glutamate
- Tolerance to CNS effects occurs whether or not an individual meets full criteria for dependence

DSM-5: Alcohol Use Disorder

- A. Problematic pattern of alcohol use leading to clinically significant impairment or distress; manifested by at least 2 of 11 symptoms within a 12 month period.

Alcohol Use Disorder

- 1. Alcohol is often taken in larger amounts or longer period than intended
- 2. Persistent desire or unsuccessful efforts to cut down or control alcohol use.
- 3. Great deal of time is spent in activities necessary to obtain alcohol, use alcohol, or recover from its effects.
- 4. Craving, or a strong desire or urge to use alcohol.
- 5. Recurrent alcohol use resulting in a failure to fulfill major role obligations at work, school, or home.

Alcohol Use Disorder

- 6. Continued alcohol use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of alcohol.
- 7. Important social, occupational, or recreational activities are given up or reduced because of alcohol use.
- 8. Recurrent alcohol use in situations in which it is physically hazardous.
- 9. Alcohol use is continued despite klg of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by alcohol.

Alcohol Use Disorder

- 10. Tolerance:
  - A. Need for markedly increased amounts of alcohol to achieve intoxication or desired effect.
  - B. Markedly diminished effect with continued use of same amount of alcohol.
- 11. Withdrawal:
  - A. Characteristic withdrawal syndrome for alcohol
  - B. Alcohol (or related substances, such as a benzo) is taken to relieve or avoid withdrawal symptoms

DSM-5: Neurocognitive Disorders

- NCD: The primary clinical deficit is in cognitive function. Only disorders whose core features are cognitive in DSM (not Schiz, bipolar)
- Acquired, not developmental: a decline from previous functioning
- Only DSM-5 diagnoses with known pathologies
- "Dementia" is subsumed under major NCD, but not precluded from use in etiological subtypes in which that term is standard

NCD: Cognitive Domains

- Complex Attention (Sustained, selective divided)
- Executive Function (Planning, decision making, working memory, feedback/error utilization, overriding habits/inhibition, cognitive flexibility
- Learning and memory
- Language (expressive, grammar/syntax, receptive)

NCD: Cognitive Domains 2

- Perceptual-motor (visual, visoconstructional, perceptual-motor, praxis, gnosis)

- Social cognition (recognition of emotions, theory of mind)

DSM-5:
Mild Neurocognitive Disorder

1. Modest Cognitive decline from previous level of performance in 1 or more cognitive domains
    1. Concern of person, informant, or clinician of a mild cognitive decline
    2. Modest cognitive impairment on NP testing
2. Deficits do not interfere with capacity for independence in everyday activities
3. Not in context of delirium
4. Not explained better by another mental disorder

DSM-5: Substance/Medication-Induced Major or Mild Neurocognitive Disorder

- A. Criteria met for major or mild NCD
- B. Neurocognitive impairments do not occur during course of a delirium and persist beyond usual duration of intoxication and acute withdrawal
- C. Involved substance or medication & duration and extent of use are capable of producing neurocognitive impairment.
- D. Temporal course of the neurocognitive deficits is consistent with the timing of substance or medication use & abstinence
- E. Not due to another mental disorder.
- Specify if: Persistent (NCD continues to be significant after extended abstinence)

Substance Abuse: Cognitive Consequences

- Brain damage is a common and potentially severe consequence of long-term, heavy alcohol consumption.
- Even mild-to-moderate drinking can adversely affect cognitive functioning
- Persistent cognitive impairment, with an established pattern of chronic heavy drinking, can contribute to:
  - poor job performance in adult alcoholics,
  - can interfere with learning and academic achievement in adolescents

** Cognitive impairment impedes recovery from alcoholism

Range of Cognitive Impairment

- Mild (subtle) deficit = may or may not evidence impairment in daily life
- Moderate = more likely show some impairment in daily life
- Severe =
  - Wernicke's Encephalopathy (WE) (acute),
  - Korsakoff's Disease,
  - Intermediate-duration neurocognitive disorder associated with alcoholism (chronic)

Alcoholism: NP Impairment

- In Tx, the 90% of alcoholics who are without severe impairment,
  - 50% have no detectable NP deficits with 3 weeks of abstinence
  - other 50% experience mild to moderate NP deficits
- With abstinence:
  - mild to moderate deficits resolve in 70-90% of individuals over a 6 month period
  - persist in the other 10-30%.
- This persistent condition is known as the *intermediate-duration neurocognitive disorder associated with alcoholism* (dx = mild NCD)

D. Gansler & H. Duncanson, 2014

Prevalence of NP Impairment

- 33 – 75% of alcoholics entering treatment display neuropsychological deficits, mostly in the mild to moderate range
  - Executive Functioning (Problem-solving, Abstract thinking, Concept shifting)
  - Learning / Memory (verbal and behavioral)
  - Visualspatial ability
  - Balance & Gait

Eckardt & Martin, 1986; Meek et al., 1989

Substance Abuse: Neuropsychological Deficits

- Substance abuse causes wide range of neuropsychological deficits
- These NP deficits associated with:
  - Treatment process and outcome.
  - Patient ability to learn and have insight.

- NP results correlate with:
  - clinician ratings of impairment
  - therapeutic progress,
  - relapse
  - employment status

Importance of Neuropsychological Deficits

- Neuropsychological Deficits interfere with Treatment:
  - Memory limitations
  - Executive Functional Deficits

- Psychogenic vs. Neurogenic Interpretation:

  - Alcoholism and problem denial are intrinsically linked

  - Denial is single biggest obstacle in getting treatment for alcoholism

Deficit blindness (Anosognosia): Need cognitive testing

- Psychological lack of motivation vs. neurological impairment:
- Nature of denial/lack of awareness: Anosognosia
- Alcoholics with significant PFC deficits (based on frontal impairment) will exhibit neurogenic denial of deficits (Anosognosia) – they are deficit blind
- As a clinician, the chance of knowing whether a patient has objective cognitive dysfunction based on their verbal report is probably less than 50%, making cognitive assessment based on only an interview worthless. Need a MoCA!

Prevalence of Frontally Based Impairment

NP testing impairments exhibited by alcoholics on:

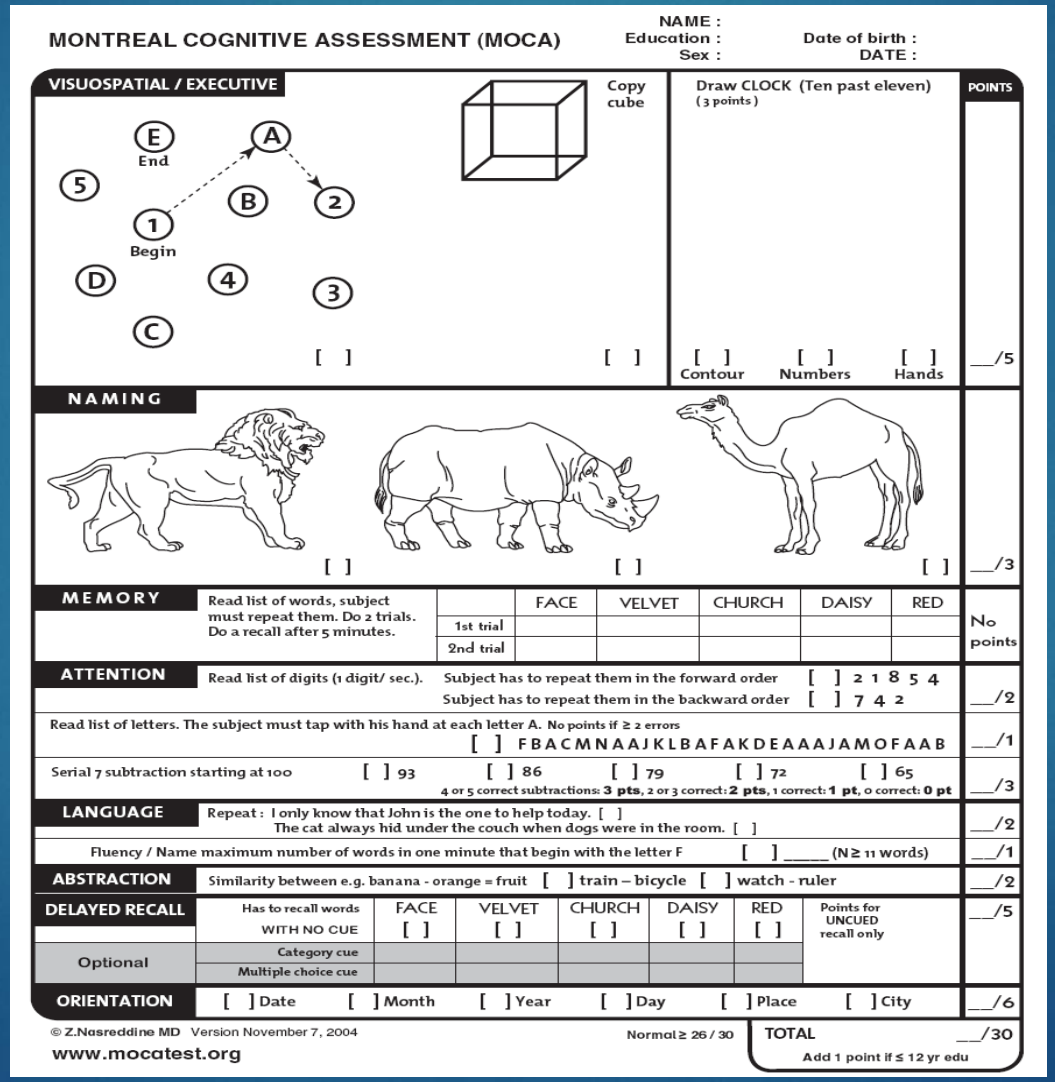
- Category Test= 50%
  - Abstract thinking
- COWAT = 50%
  - Verbal fluency
- Trails-B = 17%
  - Cognitive flexibility
- Stroop = 12%
  - Cognitive response inhibition

Morgenstern & Bates, 1999

Clinical Recommendations 1

- There is no cure for addiction; it is a brain disorder which involves brain atrophy, genetic expression, & long term behavioral memory conditioning; but treatment, medication & AA can lead to long-term sobriety
- Need to do some brief cognitive assessment early
- MoCA: Montreal Cognitive Assessment
- http://www.mocatest.org/
- If significant deficit, may need formal NP testing.

MoCA: Montreal Cognitive Assessment



MONTREAL COGNITIVE ASSESSMENT (MOCA)

NAME :
Education :
Sex :
Date of birth :
DATE :

VISUOSPATIAL / EXECUTIVE — POINTS

Copy cube

Draw CLOCK (Ten past eleven) (3 points)

E End, A, 5, B, 2, 1 Begin, D, 4, 3, C

[ ] [ ]

[ ] Contour [ ] Numbers [ ] Hands

__/5

NAMING

[ ] [ ] [ ]

__/3

MEMORY — Read list of words, subject must repeat them. Do 2 trials. Do a recall after 5 minutes.

	FACE	VELVET	CHURCH	DAISY	RED
1st trial					
2nd trial					

No points

ATTENTION

Read list of digits (1 digit/ sec.). Subject has to repeat them in the forward order [ ] 2 1 8 5 4

Subject has to repeat them in the backward order [ ] 7 4 2

__/2

Read list of letters. The subject must tap with his hand at each letter A. No points if ≥ 2 errors

[ ] F B A C M N A A J K L B A F A K D E A A A J A M O F A A B

__/1

Serial 7 subtraction starting at 100 [ ] 93 [ ] 86 [ ] 79 [ ] 72 [ ] 65

4 or 5 correct subtractions: **3 pts**, 2 or 3 correct: **2 pts**, 1 correct: **1 pt**, 0 correct: **0 pt**

__/3

LANGUAGE

Repeat : I only know that John is the one to help today. [ ]

The cat always hid under the couch when dogs were in the room. [ ]

__/2

Fluency / Name maximum number of words in one minute that begin with the letter F [ ] _____ (N ≥ 11 words)

__/1

ABSTRACTION

Similarity between e.g. banana - orange = fruit [ ] train – bicycle [ ] watch - ruler

__/2

DELAYED RECALL

	Has to recall words WITH NO CUE	FACE	VELVET	CHURCH	DAISY	RED	Points for UNCUED recall only
		[ ]	[ ]	[ ]	[ ]	[ ]	
Optional	Category cue						
	Multiple choice cue						

__/5

ORIENTATION

[ ] Date [ ] Month [ ] Year [ ] Day [ ] Place [ ] City

__/6

 Version November 7, 2004

www.mocatest.org

Normal ≥ 26 / 30

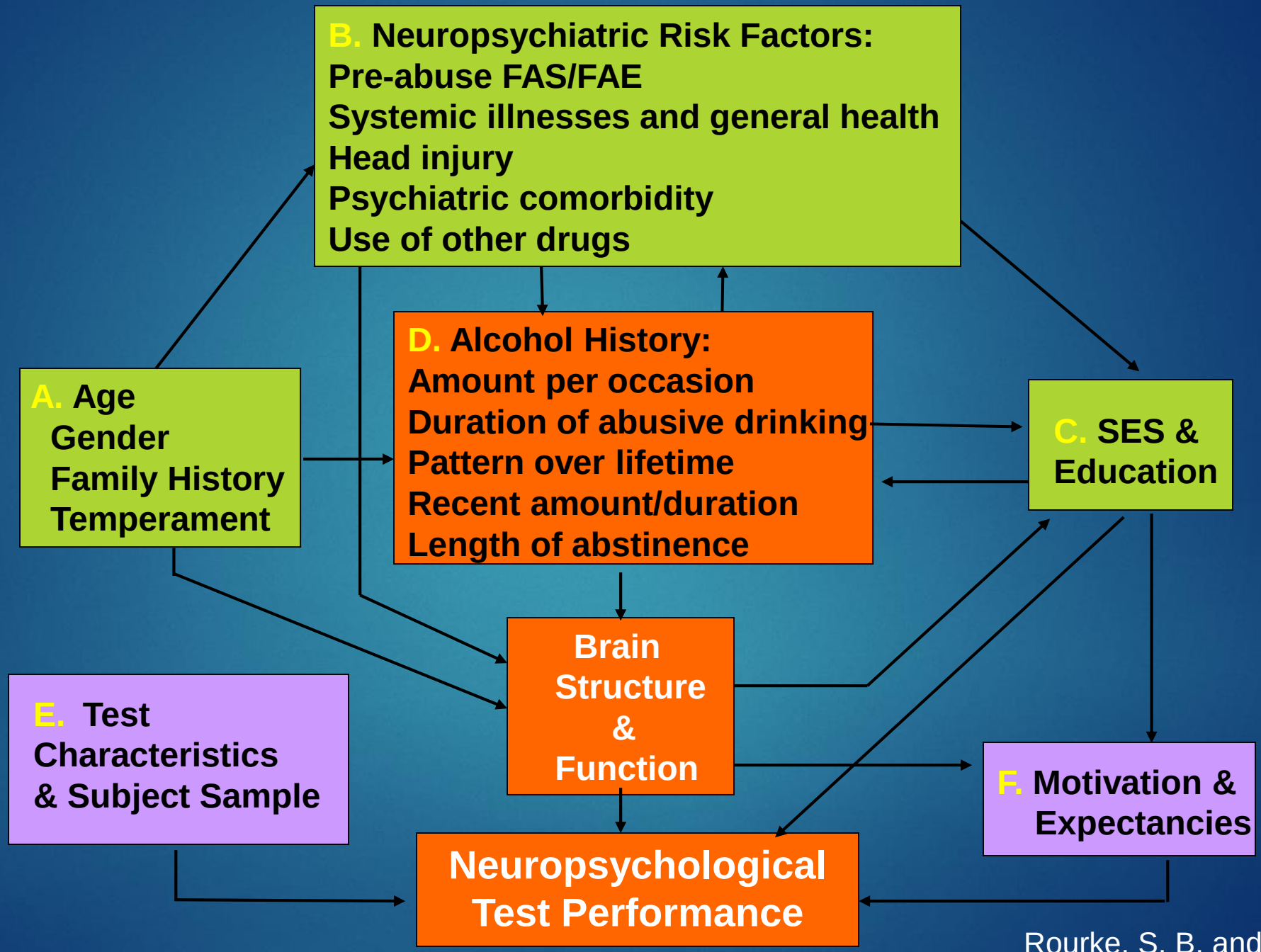
TOTAL __/30

Add 1 point if ≤ 12 yr edu

Neuropsychological Testing Performance

Neuropsychological testing performance outcome in alcoholics is highly multifactorial in nature

Alcohol is not the only cause of deficits.



Rourke, S. B. and Løberg, T, 1996

Neuromedical Risk Factors

- Besides dose-related neurotoxic effects of chronic alcohol consumption, NP deficits due to:
  - Metabolic factors resulting from intoxication and withdrawal syndrome
  - Cerebrovascular disease
  - Hepatic encephalopathy
  - Alcohol-related physical complications (gastritis, esophagitis)
  - Traumatic brain injury (TBI)

Adverse Childhood Experiences Are Common

Household dysfunction:

Substance abuse	27%
Parental sep/divorce	23%
Mental illness	17%
Battered mother	13%
Criminal behavior	6%

Abuse:

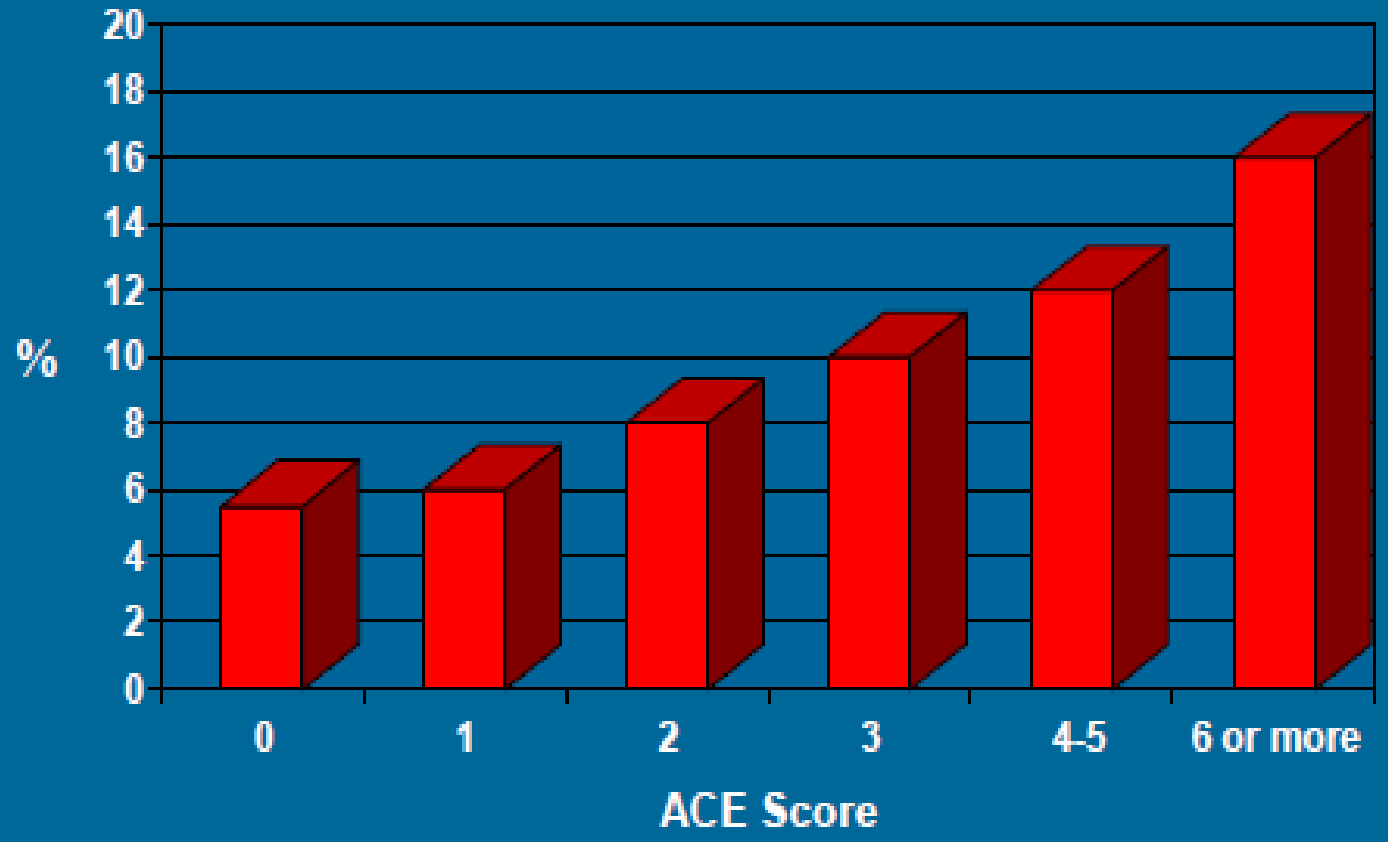
Psychological	11%
Physical	28%
Sexual	21%

Neglect:

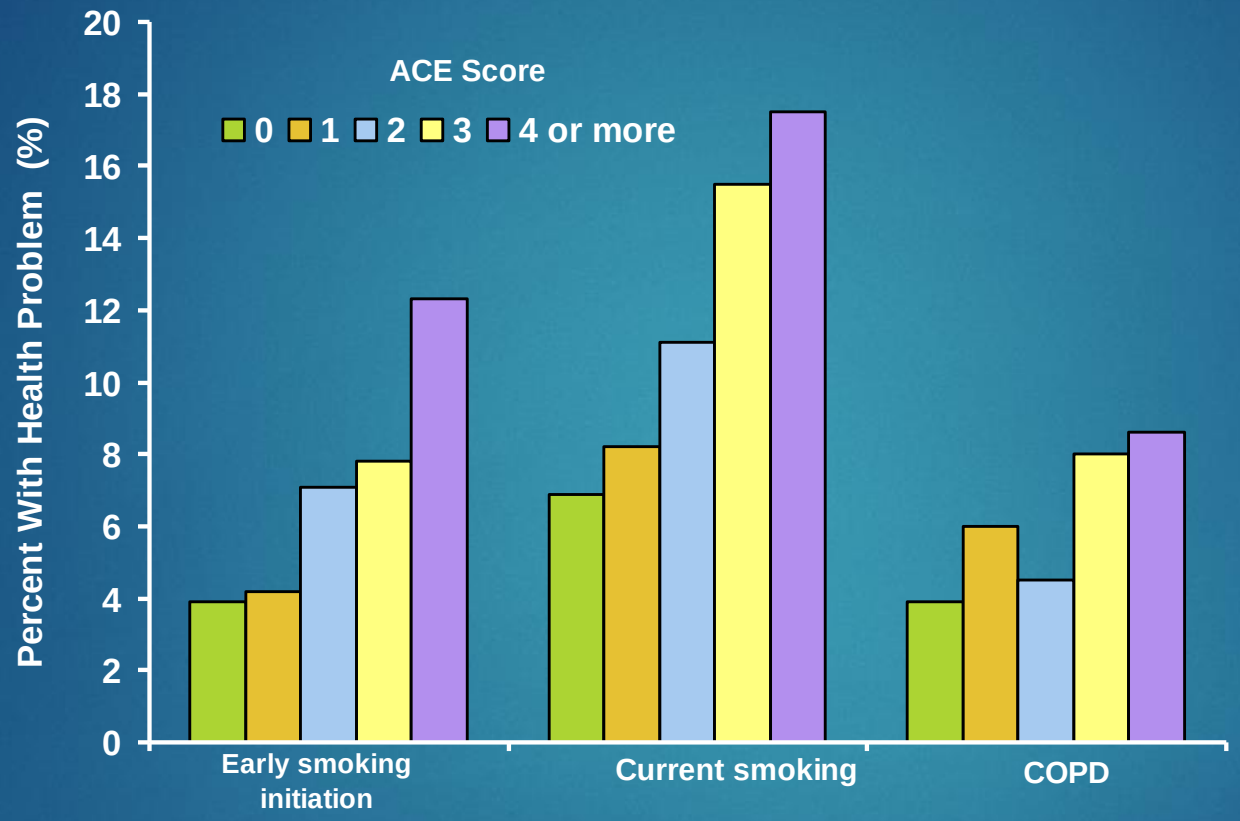
Emotional	15%
Physical	10%

V. Feletti

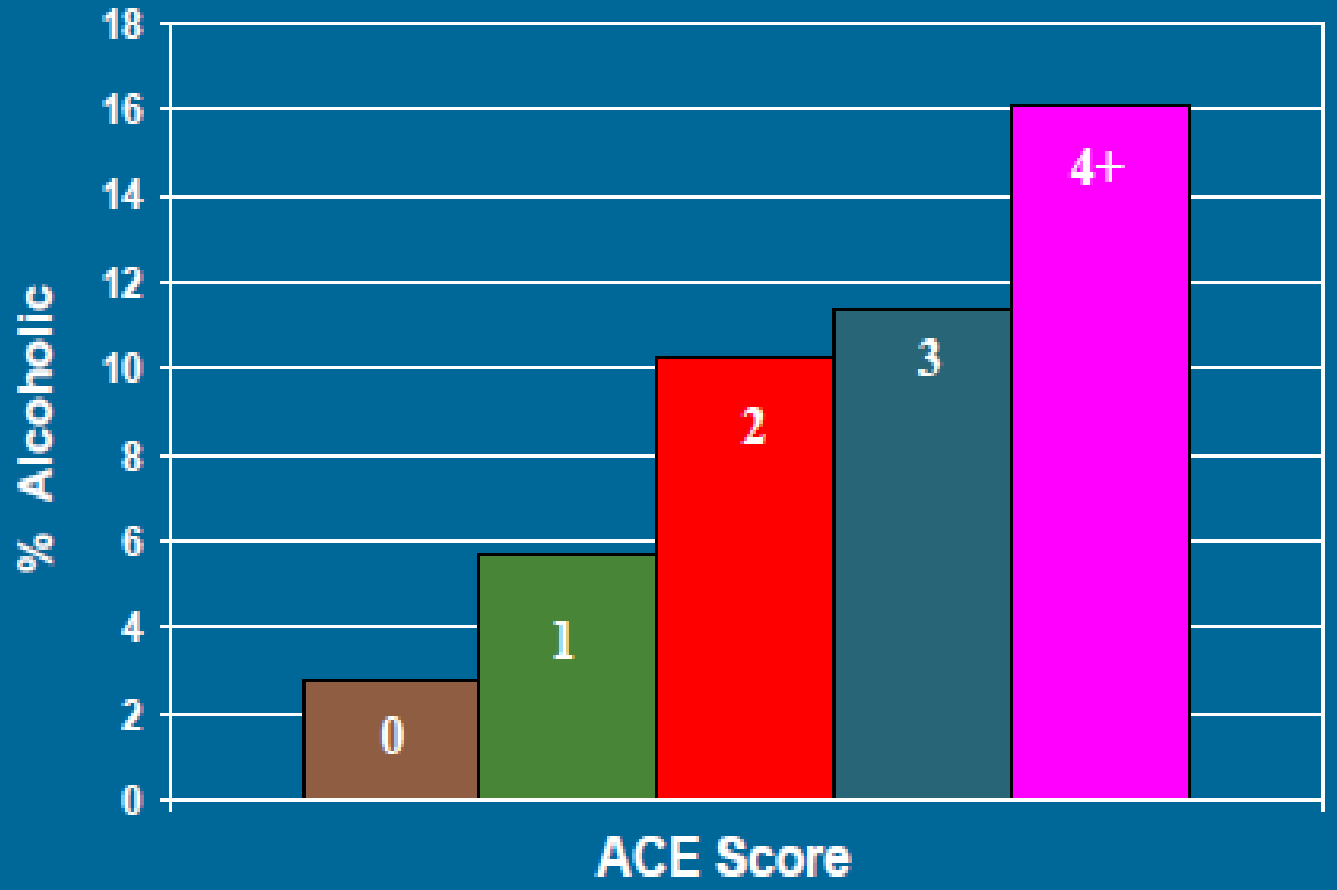
Adverse Childhood Experiences vs. Current Smoking



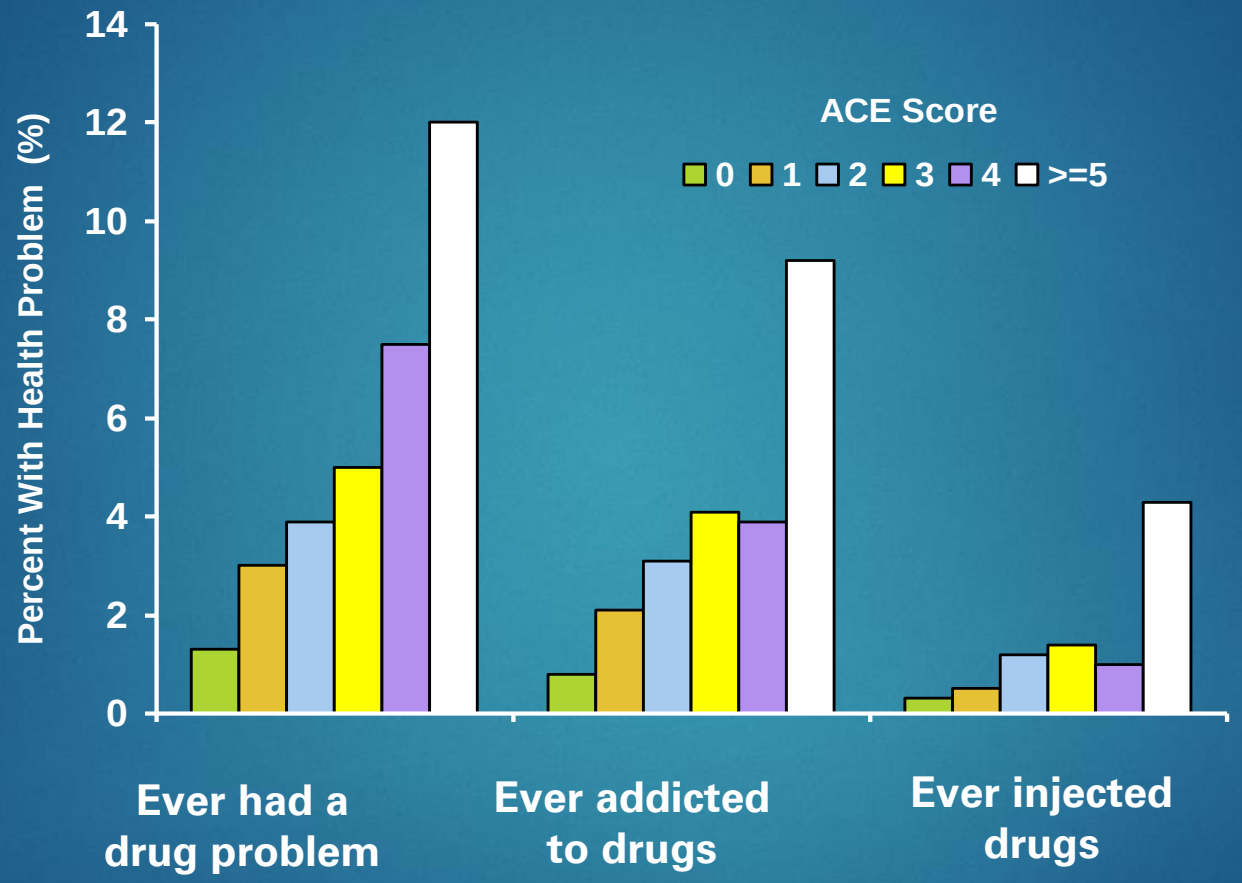
Relationship Between Number of Adverse Childhood Experiences and Smoking Behaviors and Smoking-Related Lung Disease



Childhood Experiences vs. Adult Alcoholism



ACE Score and Drug Abuse



Addiction is related to trauma and poverty:
ACEs – 10 fold increase in addiction; drugs because they cannot stand how they normally feel

Newly Dry Brains:
Neuropsychological Impairment in Abstinent Alcoholics

Bad News: Alcohol is neurotoxic

Good News: Abstinence reverses damage

- Overwhelming evidence:
  - Significant pattern of cognitive deficits in alcoholics/SA: 33-75 % with detectable deficits, long before liver, neurological and medical symptoms;
  - Specific etiology not established

Predictors of NP Impairment

Age: more important than length of drinking history

Family history, genetics

Age of beginning drinking

Years of drinking, esp. 10 years +

Maintenance drinkers worse than binging

Amount of ETOH per session > frequency

Presence of classic sxs (DTs, blackouts, Sz) are unrelated to NP impairment

Years of ETOH, # of drinks not strongly related to NP impairment (.3 to .4 correlation; 20% of variance)

Hawkins, Catalano, & Miller, 1996

ADHD and Chemical Dependency

- Compared with controls, adults with ADHD have a:
  - 3 to 4 fold higher rate of marijuana and cocaine use
  - 3-fold higher rate of alcohol abuse
  - utilize tobacco 40% more

- David Pating, MD, KP CDRP:
  - ADHD Treatment with stimulants reduces SA relapses

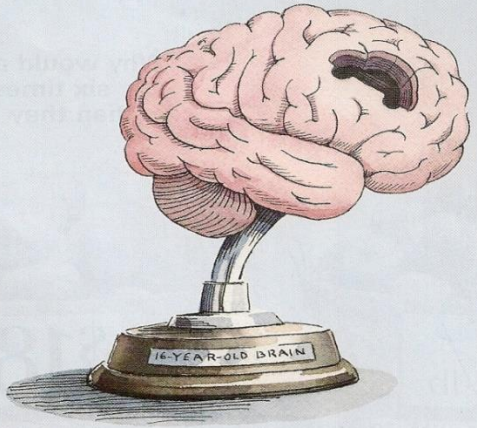
Expectations of Adolescents

"It's sort of unfair to expect (adolescents) to have adult levels of organizational skills or decision making before their brains are finished being built.

-- Jay Giedd, MD, NIH, 2002

Why do most 16-year-olds drive like they're missing a part of their brain?

BECAUSE THEY ARE.



Even bright, mature teenagers sometimes do things that are "stupid."

But when that happens, it's not really their fault. It's because their brain hasn't finished developing. The underdeveloped area is called the dorsal lateral prefrontal cortex. It plays a critical role in decision making, problem solving and understanding future consequences of today's actions. Problem is, it won't be fully mature until they're into their 20s.

It's one reason 16-year-old drivers have crash rates three times higher than 17-year-olds and five times higher than 18-year-olds. Is there a way for teens to get their driving experience more safely — giving their brains time to mature as completely as their bodies? **Allstate thinks so.**

STRENGTHEN GRADUATED DRIVER LICENSING (GDL) LAWS.

GDL laws put limitations on teen driving so kids can gain experience safely. Since North Carolina implemented one of the most comprehensive GDL laws in the country, it has seen a 25% decline in crashes involving 16-year-olds.

HAVE THE DRIVING TALK.

75% of teens surveyed said their parents would be the best influence in getting them to drive more safely. The Allstate Parent-Teen Driving Contract can help start the conversation. **Contact an Allstate Agent to get a free copy or visit Allstate.com/teen for the interactive contract.**

Let's help our teenagers not miss out on tomorrow just because they have something missing today.

It's time to make the world a safer place to drive. That's Allstate's Stand.

Allstate. You're in good hands.

Auto
Home
Life
Retirement

In light of teens' ongoing development and maturation, some states have introduced graduated driver licensing laws to restrict their actions behind the wheel. Courtesy, with permission: The Allstate Corporation

Drug Use starts early and peaks in Adolescence

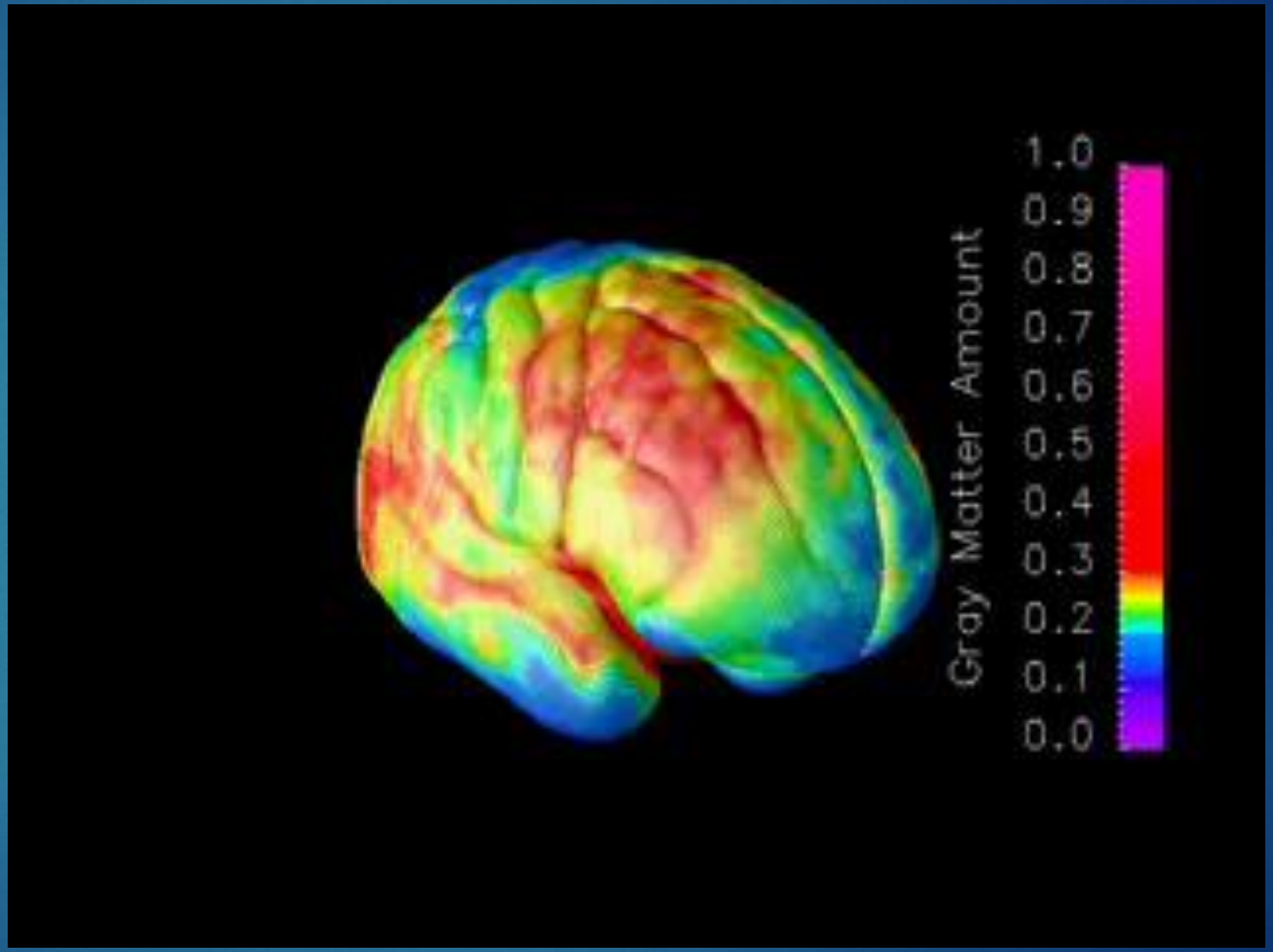
The Adolescent Brain, Steve Hanson, OASAS: http://slideplayer.com/slide/5977856/

The Great Pruning, ages 5 to 21: 50% loss of synaptic connections

Brain maturation:
from back to front

Images of brain
development
in healthy youth:
ages 5 to 21

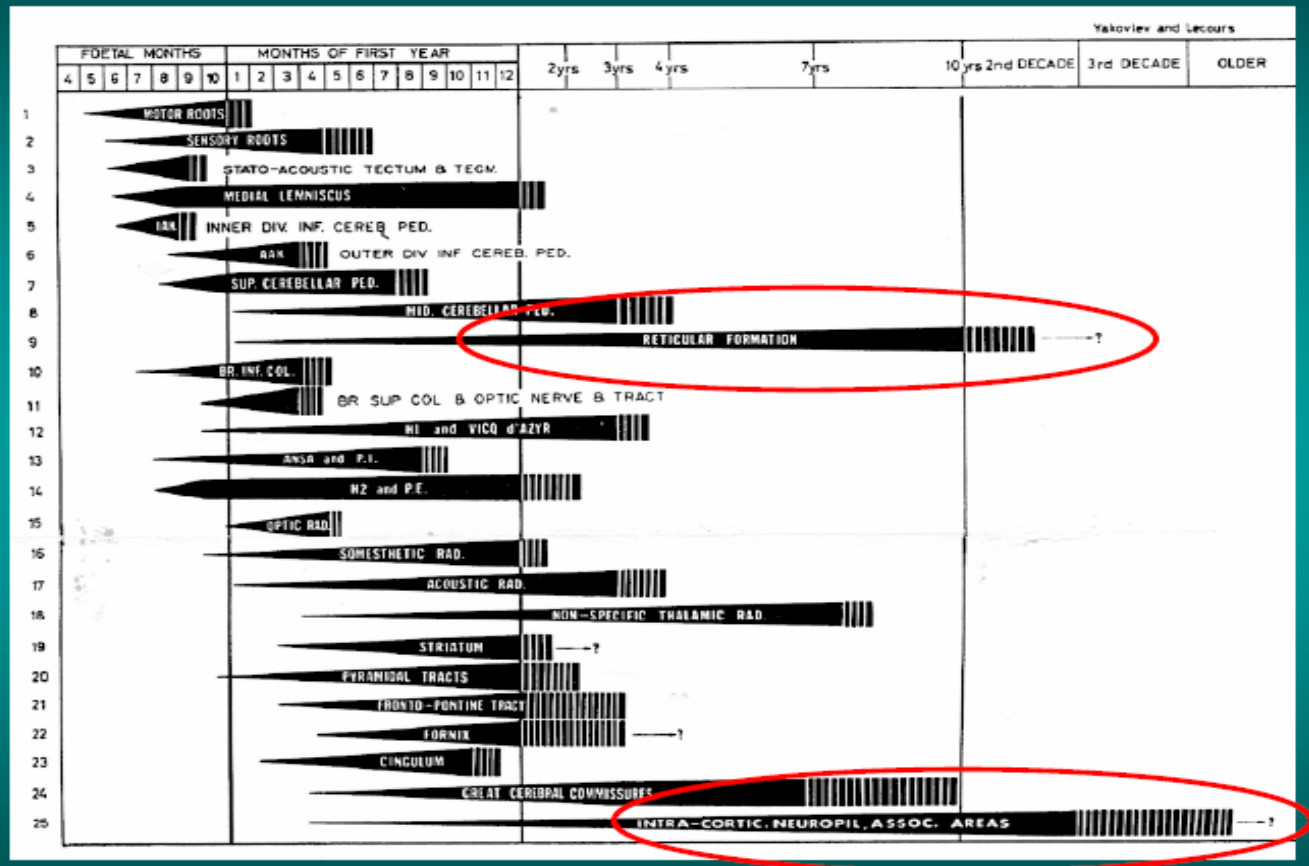
Blue represents
maturation of
brain area



Paul Thompson, PhD, UCLA:
http://www.edinformatics.com/news/teenage_brains.htm

Myelogenetic Cycles: Yakovlev & Lecours 1967

Regional Maturation: Myelogenetic Cycles



Taken from Yakovlev & Lecours, The Myelogenetic Cycles

Adolescence Brain Changes

- More vulnerable to neurotoxic events because brain is in last major developmental period
- While overall brain volume stays same after puberty, there are ongoing synaptic refinement & myelinization results in reduced gray matter and increased white matter volumes by late adolescence.
- Major synaptic pruning (loss of 50% of synaptic connections in the brain)
- Maturation of frontal and limbic regions
- Increase in myelinization (15x faster)
- Dopamine distribution changes (risk taking, reward seeking)

Adolescent Alcohol Exposure Epigenetically Suppresses Amygdala *Arc* Enhancer RNA Expression to Confer Adult Anxiety Susceptibility

- Alcohol exposure early in life has lasting effects on the brain and increases the risk of psychological problems in adulthood. Adolescent binge drinking, even if discontinued, increases the risk for anxiety later in life due to abnormal epigenetic programming. Based on animal study.
- Binge drinking early in life modifies the brain and changes connectivity in the brain, especially in the amygdala
- Epigenetic changes are lasting, and increase susceptibility to psychological issues later in life, even if drinking that took place early in life is stopped.
- Rats with who binged had 40 percent fewer neuronal connections in the amygdala compared with rats that weren’t exposed to alcohol.

Neuroimaging & NP findings in adolescents

- Smaller PFC in teens with AUDs and correlation of smaller volume with greater alcohol consumption
- Hippocampal volume correlate with age at AUD onset (younger age at initiation, smaller volume) and duration (shorter duration, larger volume)
- Both binge drinkers and marijuana users have poorer white matter integrity; binge drinkers show even poorer white matter health in several cortical and subcortical regions.
- Worse NP performance in attention and information processing, memory, visuospatial functioning, language abilities, and executive functioning compared to nondrinking controls.

Jacobus & Tapert, 2013

Deficit Source

ETOH neurotoxicity:

- Mice with 4 m total access to ETOH—50% HC dendritic loss
- Cerebral atrophy most common finding
  - White matter more affected than gray
  - Frontal and parietal regions most affected
- Disrupts hippocampal connections
- Subcortical atrophy
  - Cerebellum
  - Caudate nucleus
  - Limbic system

JCM Brust, 1993

Deficit Source 2

Nutrition: thiamine deficit

Liver disease: hepatic encephalopathy: lower PIQ

Vascular pathology: reduced Cerebral Blood Flow

Traumatic Brain Injury

Age of drinking onset: Cloninger's Type 2 (early onset: symptoms of antisocial personality disorder, more social consequences of drinking and higher sensation-seeking scores, worse prefrontal)

Fetal Alcohol Syndrome

Smoking: COPD

Alcohol and Brain Damage

Alcohol does not kill neurons in adults

Alcohol damages dendrites and white matter, reducing message traffic between neurons and transmission speed.

Damage is mostly reversible, but neuronal structure is changed in the process.

Chronic Heavy Drinking

- On average, NP test performance of heavy drinkers falls with the average to low average range.
- Consumption of 3-4 drinks for 7 days a week are associated with reduced cognitive function.
- Heavy drinkers (26 drinks): performance reductions in word-list generations, VS skills, memory & psychomotor speed

Non-Korsakoff Alcoholism: Mild NCD

- Non-Korsakoff alcoholism (chronic AUD) cognition: deficits in problem solving, abstraction, perceptual motor skills
- Age & maximum quantity & frequency of recent alcohol use predict deficit level; Mild (not Major) NCD
- Younger than 40-45: better recovery & less severe deficits than older

Non-Korsakoff Alcoholism 2

- No correlation between years of alcoholism and severity of NP deficits
- Quantity and frequency of consumption in 6-month period prior to evaluation are best predictors of NP impairment
- Lower extremity motor deficits are correlated with length of drinking
- 2 systems of brain deficit in alcoholism:
  - Cerebellar-pontine-prefrontal (motoric)
  - Prefrontal-parietal corticocortical (cognitive)

Subacute deficits in non-Korsakoff Alcoholism

- Problem-solving/executive functioning, recent memory, VS ability, and perceptual and motor skills deficits

- Executive function often more resistant to recovery of function.
  - Influenced by family hx of alcoholism and is a predisposing vulnerability to alcoholism; due to original PFC GM reduction
  - influenced by psychiatric comorbidity,

- During intermediate duration phase, recovery in any or all functions, but deficits may be long-standing among 10-30% who display them beyond subacute phase.

Individual differences among Non-Korsakoff Alcoholics

- Alcoholics:
  - uncomplicated types vs
  - those with complex neuromedical risks (hepatic, neurological, nutrition, hypoxemia, alcohol withdrawal, psychiatric)

- Minimal Hepatic encephalopathy (MHE) is:
  - most likely manifestation of cirrhosis from alcoholism
  - most likely to complicate the severity and duration of NP presentation (esp. psychomotor slowing, attention & EF, involving fronto-subcortical networks)

Neuroimaging in “uncomplicated” alcoholics

- Gray and white matter volume loss
  - Prefrontal cortex (PFC), most notably the dorsolateral PFC
  - Hippocampus
  - Cerebellum
  - Corpus callosum

- Ventricular enlargement (esp. third ventricle)

- Associated with longer lifetime alcohol use and poorer NP functioning

- Can partially recover with abstinence through regeneration

- Future relapsers had smaller brain volumes than future abstainers in regions of the reward system

Recovery in Non-Korsakoff Alcoholism

- Acute (1-2 weeks), sub-acute (3 weeks to 2 months), and intermediate (2-6 months)

- Recently detoxified: general NP deficits (excluding intact vocabulary) within 1st & 2nd week of detoxification

- In general, if deficits are present in non-Korsakoff alcoholism, the same deficits tend to be present and possibly more serious, in Korsakoff alcoholism

Modal Neuropsychological Findings

Big 4 Major Neuropsychological Deficits in AUD:

Executive Functioning
Explicit Memory, esp. nonverbal
Visual Spatial
Motor Ability

Deficits are mild to severe

Executive Functioning

- EF is distinct from Behavioral Memory (more automatic memory processes that have been overlearned by repetition; & are highly resistant to change).
- EF allows you to respond flexibly to the environment
- EF is essential for successfully navigating nearly all of our daily activities.
- Impairments in EF thus have serious consequences

Coming Up Next:
Example of Behavioral Memory

- Typewriting skills are behavioral memory

Behavioral Memory

Behavioral Memory:
Remembering how to…

Based on behavioral or motoric practice

- Skills, habits
- Playing a musical instrument, Playing sports
- Riding a bicycle, driving a car
- Playing Chess, bridge
- Interpersonal Skills, psychotherapy
- Recovery, Alcoholics Anonymous

Substance abuse and behavioral memory

- All forms of substance abuse are:
  - heavily based on behavioral memory which is highly resistant to change
  - based on nonconscious learning via repetition of behavior

- Recovery is also primarily based on behavioral memory:
  - Making a behavior “second nature” through constant repetition
  - It is not based on insight (which requires functional EF)

Executive Functioning

- EF = Applying knowledge toward real world goal directed behavior

- Executive functioning examples:

  - Self monitoring behavior
  - Anticipate consequence of action
  - Disregard erroneous strategies
  - Inhibit automatic but inappropriate response
  - Comply with treatment
  - Do something when needed (not just know how to do it)

- Prospective Memory: frontally mediated memory of an intention; best predictor of ability to live independently

NP in uncomplicated, recently detoxified Alcoholics

- All cognitive domains except IQ are affected.
- Executive dysfunction may be both a determinant and consequence.
- Most recovery occurs during the first month of abstinence;
- 30-80% have cognitive recovery after 1 month of abstinence
- If deficits persist beyond the first month, recovery may take months or years; 20% will not recover fully.

Neuropsychological Deficits

- Amount of Cognitive Reserve Important (education, complex work, etc.)
- IQ: At risk for lower performance on NART-estimated IQ
- Lower performance on Perceptual Reasoning & Processing Speed on WAIS4
- Attention: complex attention ↓↓
- Working memory: consistently impaired ↓↓

Neuropsychological Deficits 2

- Processing speed ↓↓: one of the most consistently impaired
- Language: normal
- Visuoperceptual & Visuospatial ↓↓: commonly impaired
- EF dysfunction ↓↓↓↓: categorical thinking, set establishment and maintenance, and decision making deficits
  - flexibility, problem solving, cognitive and behavioral inhibition, search strategy
  - Korsakoff: severe EF deficits

Neuropsychological Deficits 3

Sensorimotor functions: ataxia of gait and reduction in manual dexterity are common; fine motor control and grip strength normal;

Sensorimotor: color vision, visual search, response slowing ↓, peripheral neuropathy

Motor Speed: ↓

Neuropsychological Deficits 4

- Memory: common ↓, but not universal; superficial encoding, intrusions, visual memory ↓
  - Recently detoxified: reduced word-list learning & paired associate learning
  - Non-Korsakoff: learning deficits, working memory deficits; subcortical retrieval pattern of memory deficits, with ok retention & recognition
  - Korsakoff: profound cortical deficit in encoding & retrieval of episodic memory
- Procedural/behavioral memory is intact: AA had it right
- Abstinence crucial:

  3 weeks to cognitive recovery in younger alcoholics; longer for older

Summary: Neurocognitive Impairments

Age is significant variable in reversibility of deficits

Continuum: 10% severe; 50-70% some cognitive deficits; 20% normal

- Specific Deficits; Often Subclinical Levels of deficits:
  - Often significantly inferior to community controls
- Not associated with withdrawal processes
- Equivalent impairment for males/females

Cognitive Reserve: what buffers the impact of brain pathology on cognitive function

- Nun's Study Lead to concept of that some people can tolerate brain damage for a longer time without showing intellectual signs of damage.

- Cognitive reserve: difference between amount of brain pathology & actual cognitive function

- CR = more synaptic connections

- CR Benefit: Protective = can have more disease before cognitive decline

Predictors of Cognitive Reserve

- Bigger brain/head circumference
- Higher IQ
- Higher vocabulary level
- Higher education
- Occupational complexity: Work that involves complex thinking and social interaction
- Regular cognitive activity (reading, crossword puzzles)
- Higher literacy
- Social engagement
- Early-age physical activity

Clinical Recommendation 2

- Dissociation of:
  - Semantic Knowledge or ability to describe appropriate behavior (i.e. in therapy) does not equal ability to do it appropriately in real world
- Implications: Don’t depend on verbal insight in Tx
- Neurologically challenged/impaired, not unmotivated
- Do a MoCA!
- Work on behavioral memory enhancement, a la AA.

Memory and Alcohol

State dependent learning / Context dependent memory:

Where is that bottle?

Blackouts = Temporary Amnesia:

BAC level of .2

9 hours to 3 days in length

51% undergraduates = 1x

Alcohol suppresses CA1 in hippocampus: encoding deficit

Acute effects on Memory (subcortical pattern):

Retrieval poorer than Recognition

Retrieval cues aid alcoholics

Alcohol and Neurogenesis

- Moderate alcohol consumption significantly decreases neurogenesis (1400 new stem cells daily) in the adult hippocampus.
- In rats, the number of cells produced in the dentate gyrus of the hippocampus was reduced by nearly 40%.
- Moderate consumption of alcohol for a relatively short period of time can have profound effects on structural plasticity in the adult brain.

Anderson ML et al., 2012

Memory and Alcohol 2

Episodic/factual Memory impaired , esp. visual/nonverbal

Procedural Memory preserved (secret of AA's success)

Poorer semantic encoding strategies (EF):
higher intrusions,
less semantic category usage

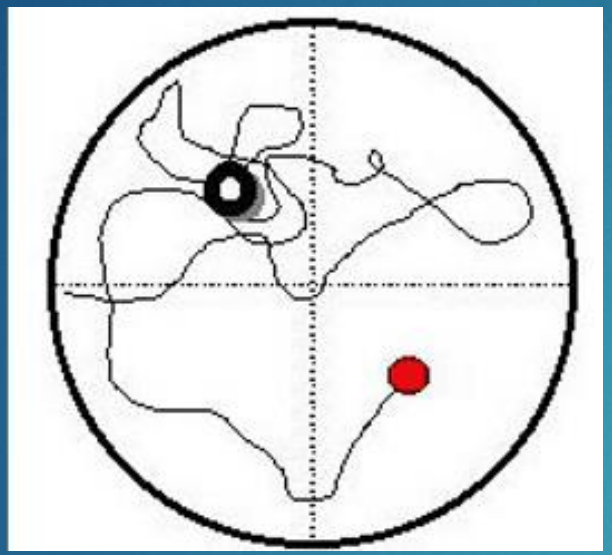
Normal forgetting rates

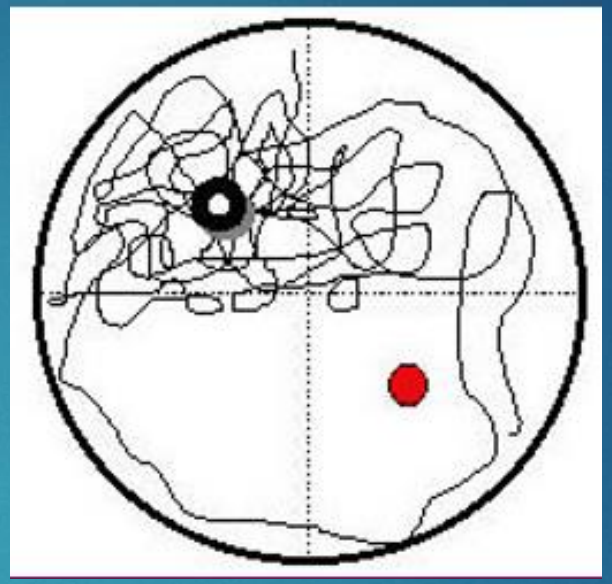
Continuum of memory effects:

social drinkers to alcoholics (retrieval deficit) to Korsakoff (amnesia), esp. nonverbal memory

Memory and Alcohol: Morris Water Maze

Control



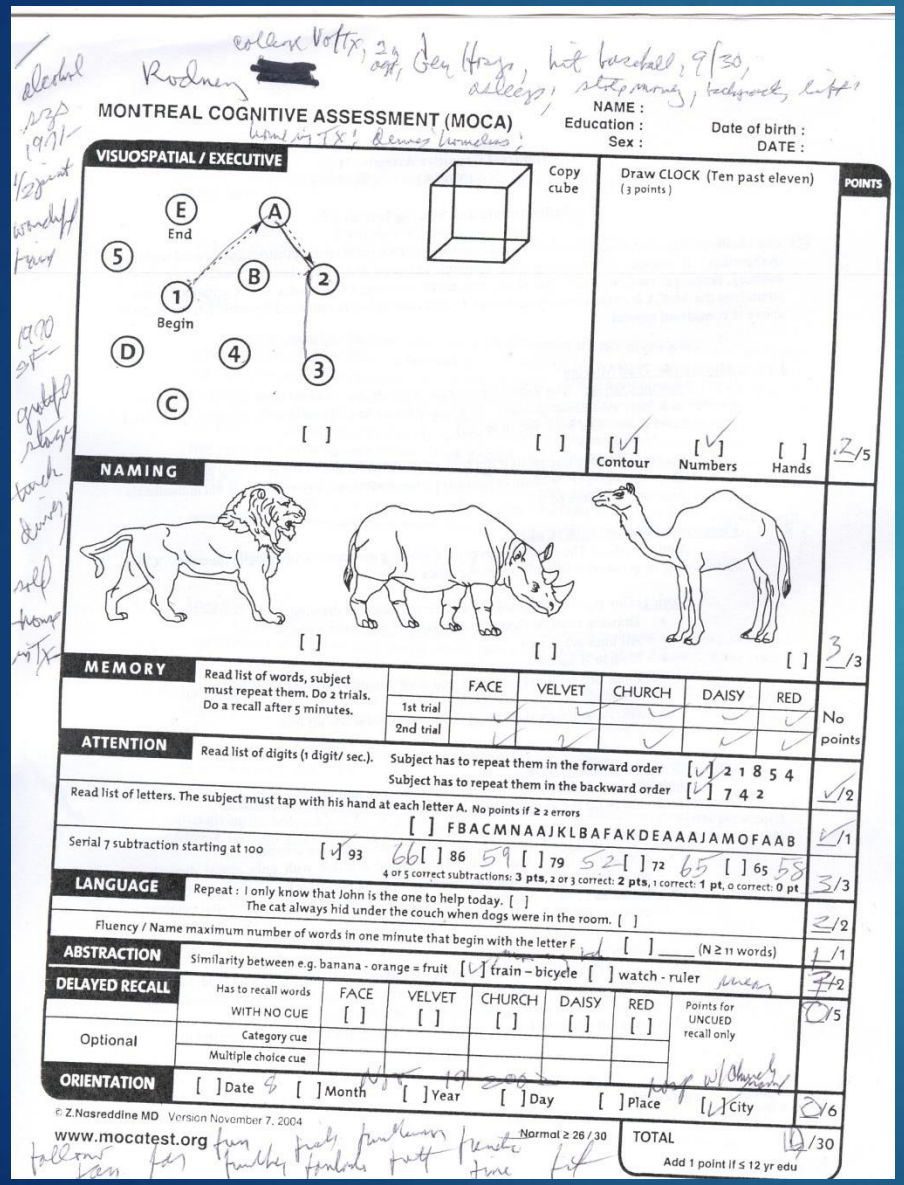


Binger

The black, open circle is the old location and the solid red circle is the new location. Control rats (left) rapidly learn to find the new location. Weeks after treatment when alcohol was no longer present, binge treated rats (right) perseverated on the old location. They never found the new location.

Crews, FT, & Nixon, K, *2008*

RG: 68 yo, homeless alcoholic



MONTREAL COGNITIVE ASSESSMENT (MOCA)

NAME :
Education :
Sex :
Date of birth :
DATE :

VISUOSPATIAL / EXECUTIVE — Copy cube — Draw CLOCK (Ten past eleven) (3 points) — POINTS

NAMING

MEMORY — Read list of words, subject must repeat them. Do 2 trials. Do a recall after 5 minutes.

	FACE	VELVET	CHURCH	DAISY	RED
1st trial					
2nd trial					

No points

ATTENTION — Read list of digits (1 digit/ sec.). Subject has to repeat them in the forward order [ ] 2 1 8 5 4. Subject has to repeat them in the backward order [ ] 7 4 2

Read list of letters. The subject must tap with his hand at each letter A. No points if ≥ 2 errors. [ ] F B A C M N A A J K L B A F A K D E A A A J A M O F A A B

Serial 7 subtraction starting at 100 [ ] 93 [ ] 86 [ ] 79 [ ] 72 [ ] 65. 4 or 5 correct subtractions: 3 pts, 2 or 3 correct: 2 pts, 1 correct: 1 pt, 0 correct: 0 pt

LANGUAGE — Repeat : I only know that John is the one to help today. [ ] The cat always hid under the couch when dogs were in the room. [ ]

Fluency / Name maximum number of words in one minute that begin with the letter F [ ] ____ (N ≥ 11 words)

ABSTRACTION — Similarity between e.g. banana - orange = fruit [ ] train – bicycle [ ] watch - ruler

DELAYED RECALL

	Has to recall words	FACE	VELVET	CHURCH	DAISY	RED
	WITH NO CUE	[ ]	[ ]	[ ]	[ ]	[ ]
Optional	Category cue					
	Multiple choice cue					

Points for UNCUED recall only

ORIENTATION — [ ] Date [ ] Month [ ] Year [ ] Day [ ] Place [ ] City

© Z.Nasreddine MD Version November 7, 2004
www.mocatest.org

Normal ≥ 26 / 30

TOTAL /30

Add 1 point if ≤ 12 yr edu

Hx: hosp. s/p seizure, RH-TBI (concave skull)

Score: 17/30*

Executive↓
Language, Attention ↑
Spontaneous Memory ↓: 0**
Normal Recognition: all 5↑**

Conclusion:
Cognitive Disorder due to alcoholism

Clinical Recommendation 3: Memory

- AA is right: use behavioral memory not insight or talking, esp. in early recovery
- Behavioral repetition/avoidance is target: avoid bars, drinking buddies
- But also external reminder systems to reinforce poor memory
- Download CJV's Executive Skills & Metacognitive Therapy booklet from website

Clinical Recommendation 3: Memory

- Keep it simple: Modify written material to make it concise and to the point.
- Paraphrase concepts, use concrete examples, incorporate visual aids, or otherwise present an idea in more than one way
- If it helps, allow the individual to take notes or at least write down key points for later review and recall.
- External prosthesis: Encourage the use of a calendar or planner; if the treatment program includes a daily schedule, make sure a "pocket version" is kept for easy reference.
- Make sure homework assignments are written down.

Clinical Recommendation 3: Memory

- Do not take for granted that something learned in one situation will generalize to another.
- Procedural memory is sensorimotor specific
- Repeat, review, rehearse; repeat, review, rehearse.

Visualspatial Functions

Simple visualspatial functions intact

Impaired color vision, visual search

Visual-spatial organizational functioning impaired, esp. slowness

Emotional processing impaired:

Emotional cues and facial emotion expression interpretation↓

Clinical Recommendation 4: EF

- US Law vs neuroscience: Knowledge of right & wrong (temporal lobe) can be present along with total inability to inhibit behavior (Orbital frontal)
- US Law: no death penalty or life sentence without parole for adolescents (due to lack of EF); but does not apply to AUD
- Executive Dysfunction is cause of neurogenic lack of awareness & loss of inhibition
- Neurologically based Poor Self Monitoring leads to inability to understand the consequences of one's actions.

Clinical Recommendation 4b: EF

- Caution: when making inferences about motivation based on observed behaviors.
- Non-compliance may not arise from lack of motivation or resistance.
- Unawareness of deficits can be due to executive dysfunction and may not always be due to psychological denial.

Clinical Recommendation 4c: EF

- Inflexibility can lead to perseveration i.e. repeating an inappropriate behavior

- Poor ability to inhibit a response can lead to a broad range of inappropriate behaviors: safety issues; striking out; verbal outbursts; sexual remarks or behaviors; socially Inappropriate comments

Clinical Recommendation 4d: EF

- Let a person know a behavior is inappropriate.
- Do not assume the individual knows and is choosing to do so anyway.
- Provide straightforward feedback about when and where behaviors are appropriate.
- Test prospective memory by having them remember to remind you of something 15 minutes later

Intoxication: Neurological Condition

Intoxication: alcohol is a CNS depressant with neurocognitive deficits:

Slurred Speech

Ataxia

Neuropsychological Deficits (Memory, Executive deficits)

Behavioral disinhibition

Reaction Time↓

No ability to consent

Stages of Neuropsychological Recovery: Acute

Acute deficits: 1 week of abstinence:

Most alcoholics impaired immediately after cessation of drinking

Younger improve over 3-4 weeks to WNL

Older (>40) have slower recovery

Memory and Visual-motor improve markedly

Improvement diminishes or reverses if relapse

Ryan & Butters, 1986

Stages of Neuropsychological Recovery: Short Term

Short term: 2-5 weeks

Younger (<35 age, 5-10 years use) recover to WNL

More chronic history and older age, poorer NP performance:

Executive, perceptual-motor, LT verbal and nonverbal memory (latter worse), visual-spatial deficits

Stages of Neuropsychological Recovery: Long Term

Long Term: 13 months+

Less conclusive evidence for deficits:

- Nonverbal learning and memory, esp. Visual memory↓
- Complex memory, esp. encoding strategy ↓
- Executive functioning ↓

5 years: significant improvement but not as good as controls

Poorer recovery: TMT-B, Digit Symbol

Characteristic Behaviors of detoxified Alcoholics: EF

Executive Functions:

- impaired judgment
- blunted affect
- poor insight
- social withdrawal
- reduced motivation
- distractibility
- cognitive rigidity
- inattention
- perseveration

NP test impairment:

WCST
Categories Test
TMT
Stroop

→ Frontal Lobe Dysfunction

Characteristic Behaviors of Alcoholics: VS

Visual Spatial Dysfunction

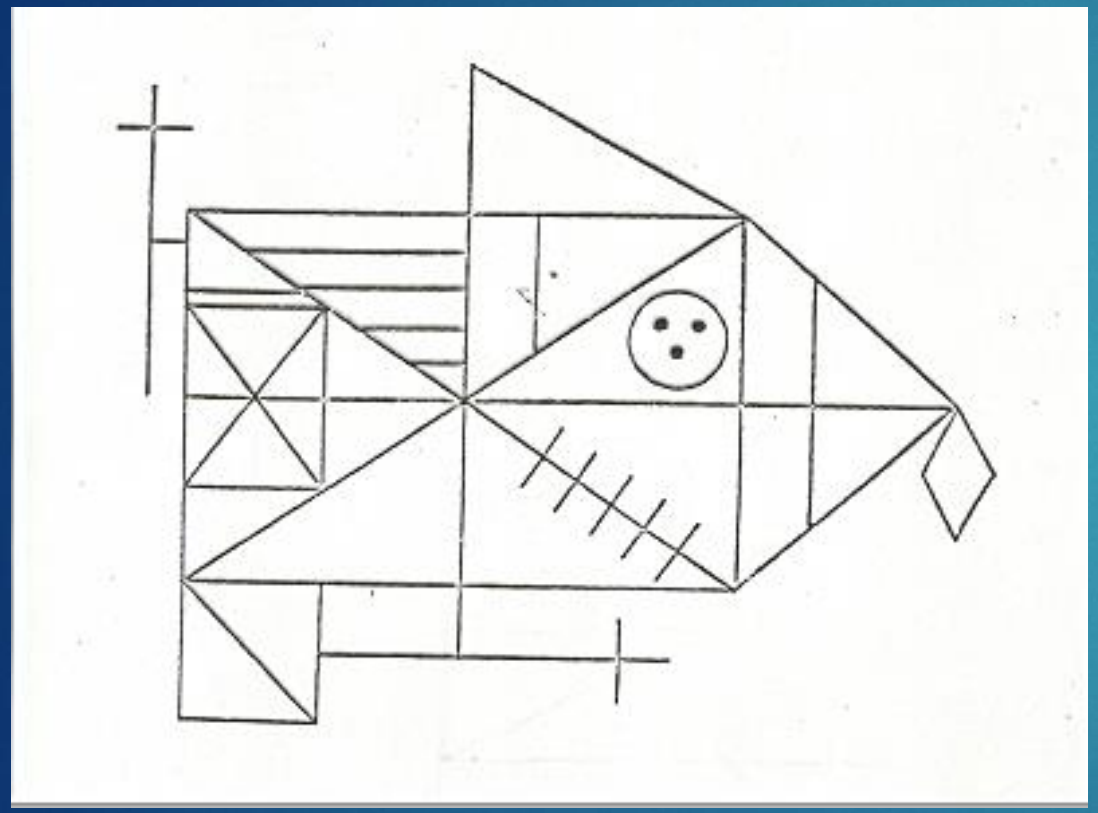
- poor sense of direction
- impaired constructional ability
- impaired spatial placement
- impaired drawing ability

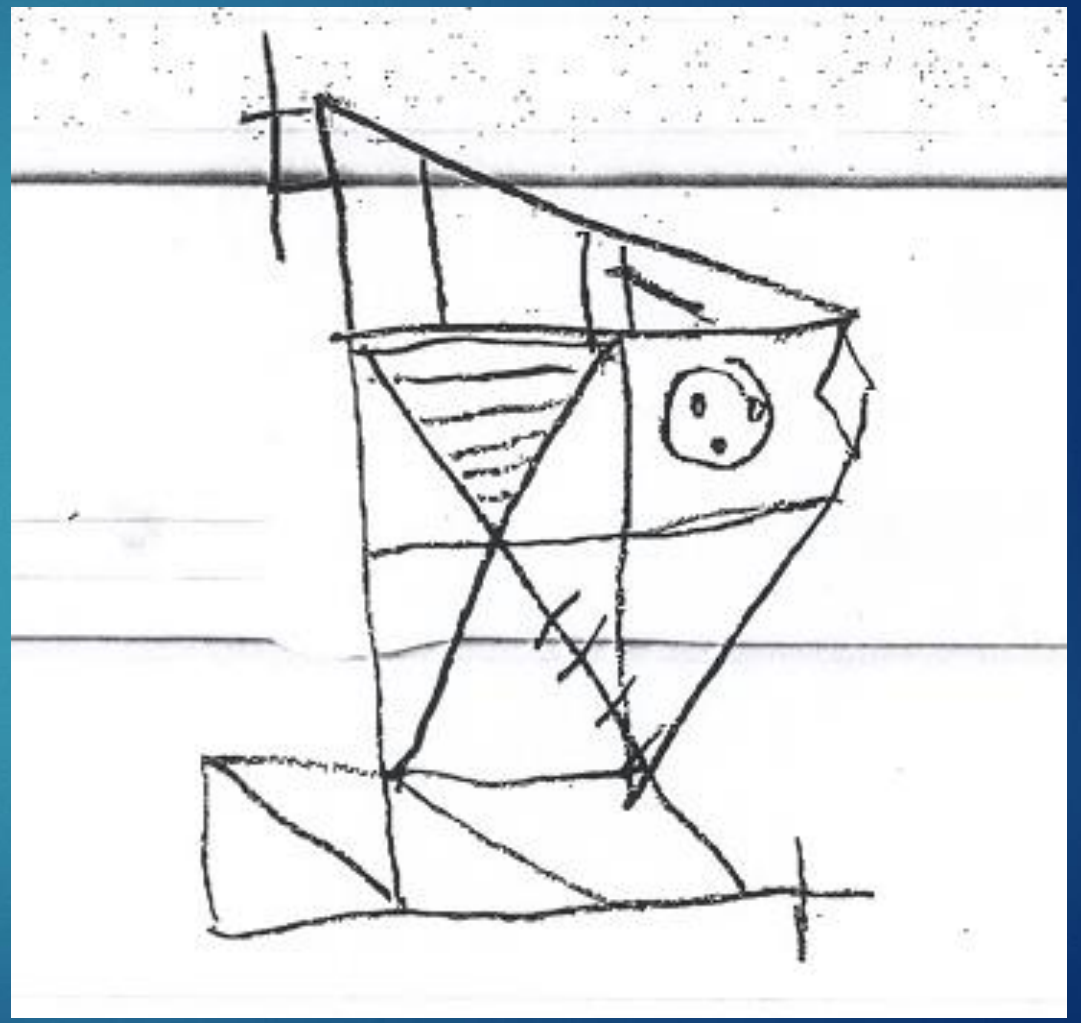
NP test impairment:

Rey Complex Figure
Block Design

→ Parietal Lobe Dysfunction

Visual Impairment on Rey Complex Figure Recall





CJV personal collection

Characteristic Behaviors of Alcoholics: Motor

- **impaired timing**
- **impaired tracking**
- **impaired balance**
- **impaired gait**
- **increased falls**

} Motor Control

→ Cerebellar Dysfunction

Butler E, Druizin M, and Sullivan EV (2005): Chapter 8. Adult adaptations in adulthood: In Rose J and Gamble JG. Human Walking, 3rd edition, pp. 131-147.

Gender Differences

Majority of studies: recently detoxified males

Males to Females: 5:1; Men drink 2.5 times more alcohol in lifetime

Women have similar pattern & degree of NP deficits as men

Women metabolize alcohol differently; display NP deficits sooner

Women develop cirrhosis, cardiomyopathy, & peripheral neuropathy sooner

http://www.drugfree.org/join-together/gender-differences-emerge-in-alcohol-use-disorder-treatment/

Gender Differences

- Women have less body water than men of similar body weight, so that women achieve higher concentrations of alcohol in the blood after drinking equivalent amounts of alcohol.

- Women have smaller quantities of the enzyme dehydrogenase that breaks down alcohol in the stomach.

- A woman will absorb about 30% more alcohol into her bloodstream than a man of the same weight who has consumed an equal amount.

- More psychiatric comorbidities

Personality Consequences of Substance Abuse

- SA produces Disinhibition:
  - 48-50% of all assaults,
  - 48-65% of homicides,
  - 34% of drownings,
  - 42% of injuries,
  - 47% of young male car crashes
  - 50% of date rape
  - 16% of child abuse; burglaries, spousal abuse, suicide attempts
- Alcohol involved in 15-25% of suicides and in 55% suicide attempts
- Depression
- Action orientation
- Alexithymia

US Dept Justice: Drug related crime: 1994: http://www.bjs.gov/content/pub/pdf/DRRC.PDF
Vijayakumar, L; Kumar, MS; Vijayakumar, V, *2011.*

Neuroimaging Findings

Recent detoxified: Cerebral atrophy and volume loss, esp. in older

Prefrontal sensitive to effects of aging & ETOH

Prolonged abstinence (6 m) causes White Matter increase, decreased 3rd Ventricle volume

PET studies: NP deficits related to decreased glucose metabolism and hypoperfusion in frontal cortex & subcortical structures

SPECT: reduced rCBF

Connectivity networks: Chronic drinking negatively impacts brain connectivity. A positive association between years of drinking and severity of alcohol problems was mediated by reduced Executive Network connectivity.

Neuroimaging

- Structural MRI:
  - Smaller cortical gray and white matter volumes & larger ventricles
  - Pronounced in frontal, limbic and cerebellar areas
  - Older show greater volume deficits, esp. frontal
  - Hippocampal volume deficits in adolescent and young adults
  - Younger age of onset and longer duration of use correlates with smaller hippocampal volumes
- Functional MRI:
  - Alcoholics use more higher order cognitive processes to do simple tasks
- Diffusion Tensor Imaging:
  - Poor WM integrity, esp. corpus callosum
  - Demyelination

Emotional Perception and Alcoholism

- Alcoholic individuals display abnormalities in their perceptions of facial and linguistic emotional stimuli
  - Impairment in emotional facial-expression recognition
  - Deficits in processing affective cues in speech
  - See more fear and less anger in facial expressions
  - Enhanced fear responses

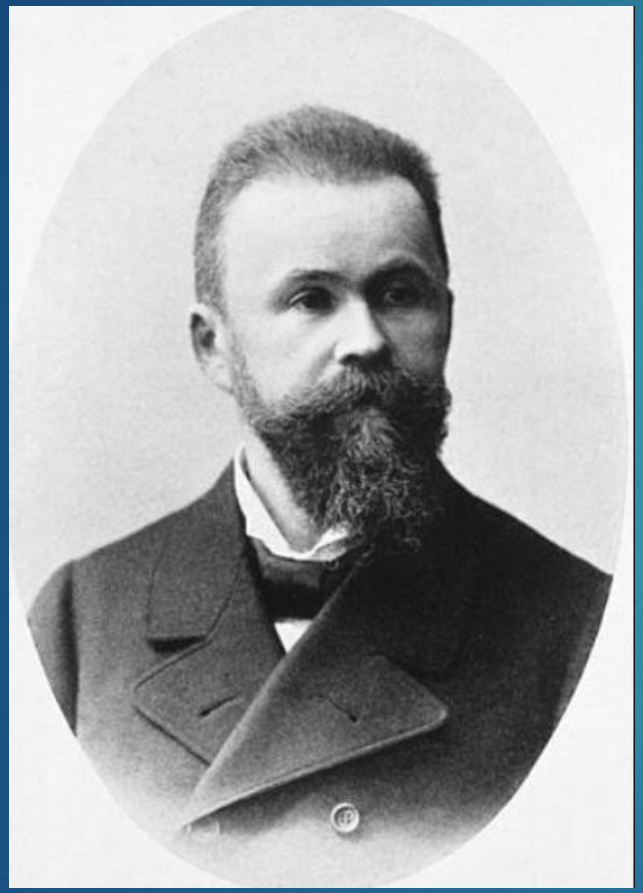
- They perceived the valence of negative facial stimuli to be more neutral as a function of age

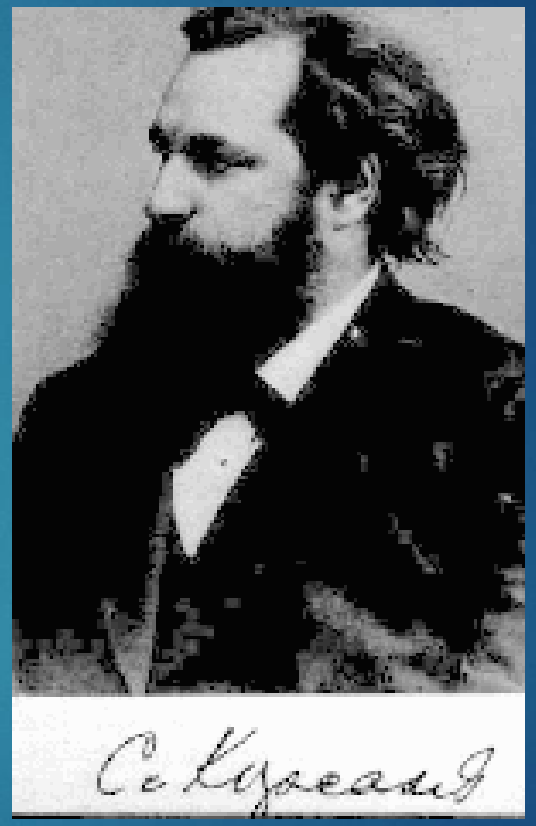
Clark, U, et al., *Neuropsychology*, 2007

Brain in Recovery

- Brain is clearly a dynamic organ
- Structural brain abnormalities can be partially reversible with sustained sobriety, reflecting remyelination & synaptic revoluming:
  - Increase in glucose utilization post 30 days of sobriety
  - Increase in cortical grey volume, even more WM volume, & hippocampal volume with 30 days
  - Neurogenesis increase with sobriety in rats
  - With 5 years sobriety, increased brain volume
  - Increased frontal and limbic areas with recovery

Wernicke-Korsakoff Syndrome





Carl Wernicke, b Poland 1848

Sergei Korsakoff, b Russia 1853

J.F. Lehmann, Muenchen, in public domain

http://home.kpn.nl/b1beukema/vitaminen.html

Wernicke's syndrome

- In 1881, Carl Wernicke described a neurologic syndrome of acute onset characterized by:
  - a global confusional state,
  - ataxia,
  - ophthalmoplegia (eye muscle weakness),
  - nystagmus,
  - polyneuropathy in the arms and legs

- Thiamine (B1) deficiency + heavy drinking

- 10% fatal

Brust, 2000

Korsakoff Syndrome

- In 1887 Korsakoff added the characteristic:
  - problems in new learning (anterograde amnesia)
  - as well as the deficits in remembering past events (retrograde amnesia),
  - and emphasized that these occurred in the *context of clear attention and consciousness*

- Some patients tended to confabulate, sometimes making up stories or events entirely, but more frequently confusing the temporal context of actually experienced events

Wernicke-Korsakoff's Syndrome

Persistent (Korsakoff's):

- Normal IQ
- Severe Anterograde and temporally graded retrograde amnesia imposed over typical neurotoxic alcohol effects:
  - defective encoding;
  - severe retrieval deficit;
  - but can recall stores of sexual content
  - better with recognition;
  - but 2 of 3 recalled 9/11/2001 event

Butters & Stuss, 1989

Wernicke-Korsakoff's Syndrome 4

Executive dysfunction; lack of awareness if frontal; blandness, confabulation

Processing speed impaired

28% slight recovery, 26% permanent syndrome

Korsakoff's Syndrome 1

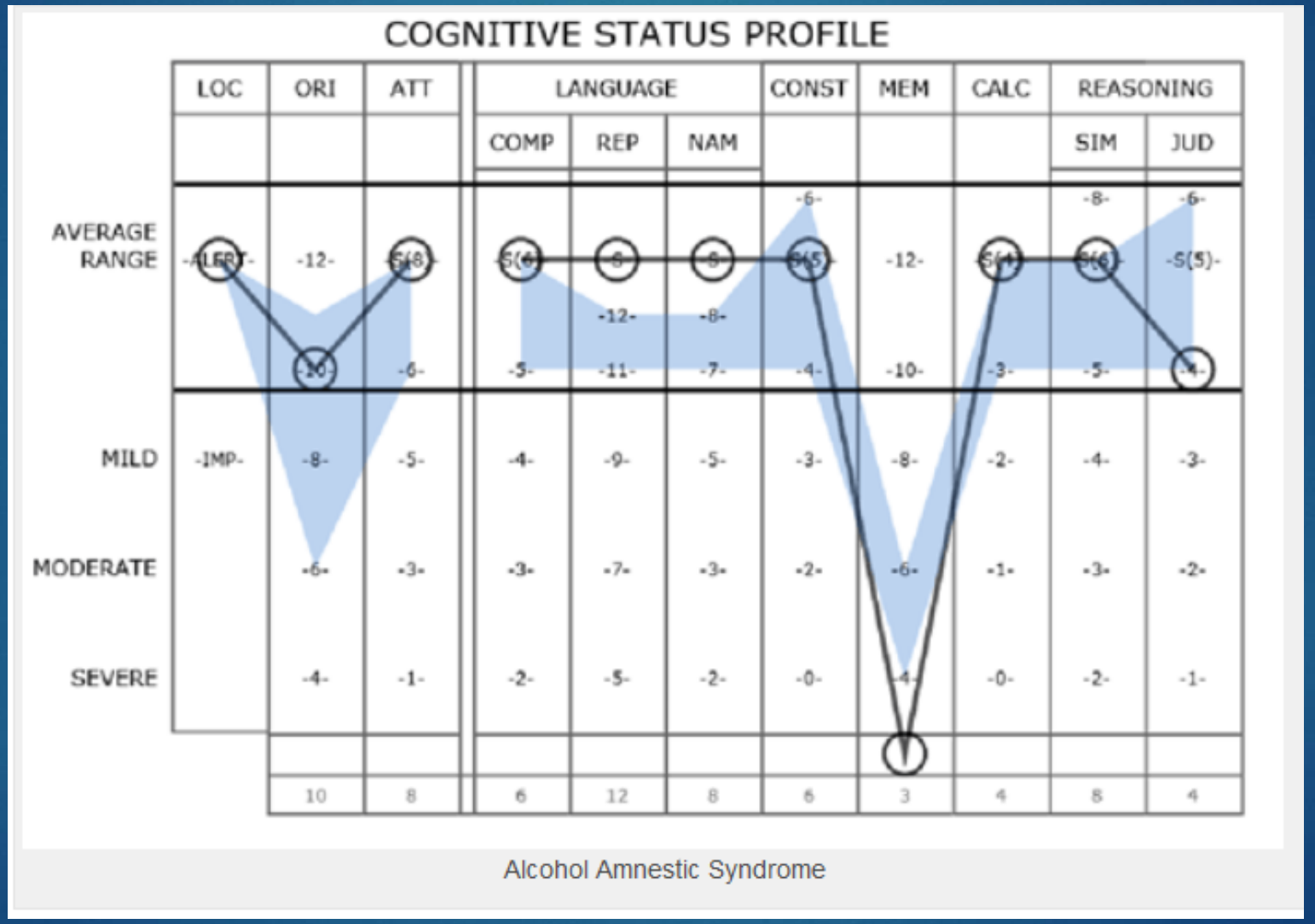
- Dense Amnesia
- Executive Dysfunction (deficits in planning, decision making, and problem solving; poor WCST, TMT)
- Attention Deficit
- Visuospatial and visual-perceptual deficits are also observed on a variety of concept formation tests that require discrimination and classification of complex visual stimuli
- Abnormally long time to identify visually presented material

Kopelman, 1995

Korsakoff's Syndrome 2

- Retrograde amnesia a typical feature, commonly extending back 25 years or more
- Memory for autobiographical information as well as knowledge of public events and facts are affected
- Memories from childhood and early adulthood are remembered better than memories from the recent past. (Kopelman 1989; Fama et al 2004)

COGNISTAT: Korsakoff's



http://novatekmds.com/solutions/cognistat-assessment-system/cas-in-substance-abuse-alcohol-amnestic-syndrome/

Comparing Korsakoff and non-Korsakoff alcoholics

- Sudden Onset in Korsakoff's
- Korsakoff patients are impaired on tests of memory, fluency, cognitive flexibility, and perseveration
- Non-Korsakoff alcoholics may show some milder frontal system deficits as well

Korsakoff's vs. Alcohol induced NCD

- In Korsakoff syndrome patients have a disproportionate disorder of memory

- No distinct neuropathological basis has been established for alcoholic major NCD

-

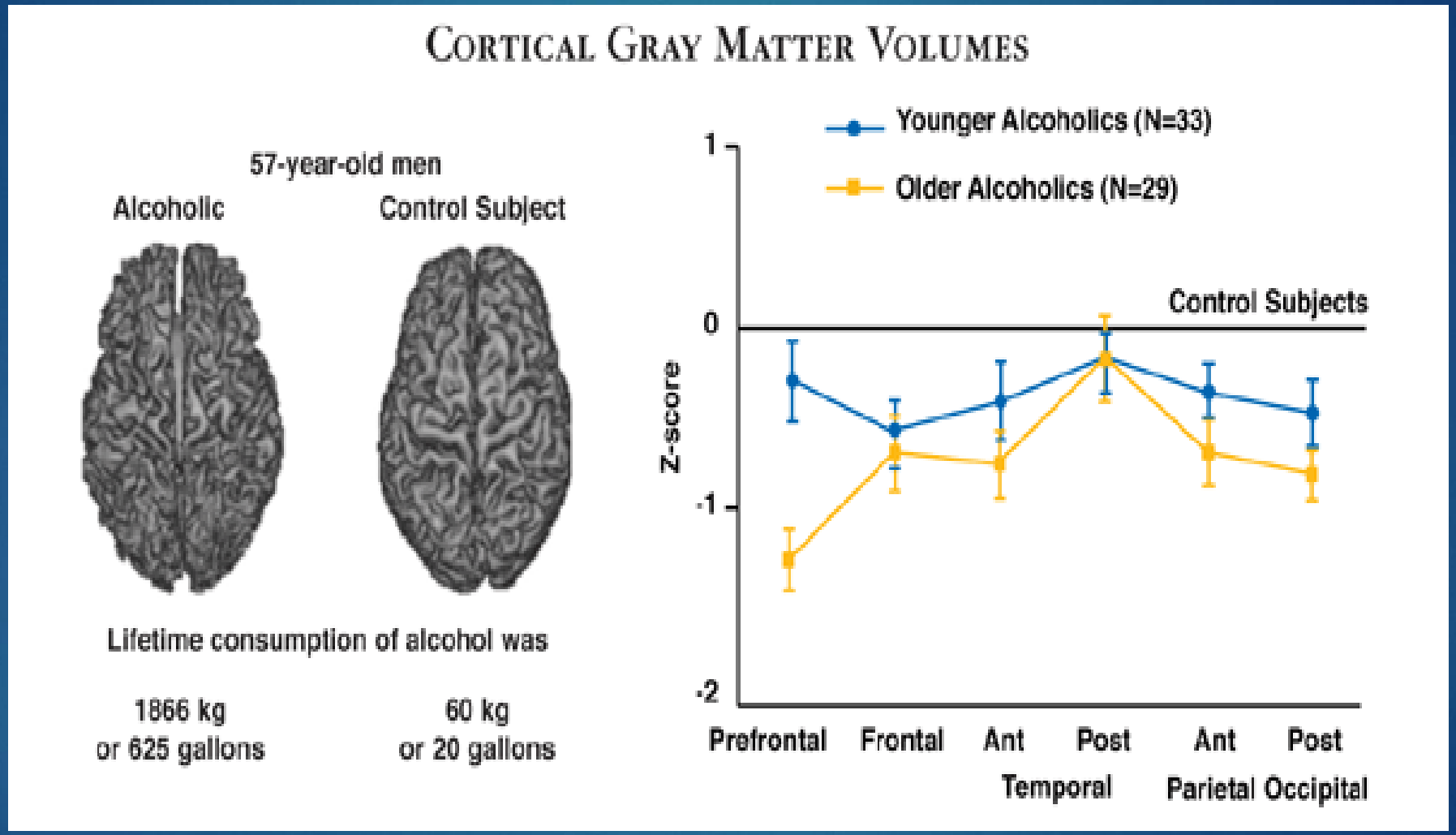
Neuropsychological and Neurological Deficits Associated with Cirrhosis

- NP deficits are independent of other liver disease symptoms (PSE)
- Deficits esp. in spatial, practic, and perceptual-motor: VS, handwriting, VIQ, memory
- Neuropathology: frontal atrophy, cortical hypoperfusion, neuronal necrosis, demyelination
- EEG: triphasic wave pattern
- Issue of some covariance with alcohol effects

TBI and Alcoholism

- Alcohol is present in:
  - 41% of fatal TBI
  - 7% of falls
  - 60% of MVA
  - >70% of MVA comas
  - 1 person injured every 2 min where alcohol present

Alcohol related Atrophy, esp. Prefrontal



Pfefferbaum et al. 1997; http://pubs.niaaa.nih.gov/publications/arh27-2/125-133.htm

Preexisting EF vulnerabilities in nonalcoholic ACAs

- Nonalcoholic adult offspring of alcoholic individuals showed increased impulsiveness and decreased EF, suggesting weakness of 2 distinct neurobehavioral decision systems.

- EF weaknesses may qualify as a suitable endophenotype (genetically based behavior pattern) candidate for alcoholic disease.

Drink a little Alcohol?

- Drinking one drink per day correlates with positive health outcomes; drinking more increases heart disease
- Alcohol consumption, particularly of wine, is associated with higher incomes and education levels, which in turn are associated with lower rates of smoking, lower rates of mental illness and better access to health care.
- Heavy drinking increases the risk for death by 31% to 54%.
- Latest 2014 British Study: 2.5 drinks per day produces memory impairment 10 years later

Alcohol & Dementia

- Cohort studies have varied in terms of the types of alcohol and thresholds of consumption assessed and have typically used self-reported consumption.
- Nonetheless, a J-shaped relationship has been fairly consistently reported between alcohol consumption and dementia risk, with low to moderate consumption associated with better outcomes than heavy consumption or non-consumption.
- Alcohol use disorders are probably associated with poor diet and lifestyle, smoking, cardiovascular comorbidity, lower adherence to medical treatments, depression, and potentially social isolation, all of which predict dementia.

Heavy drinking & dementia risks

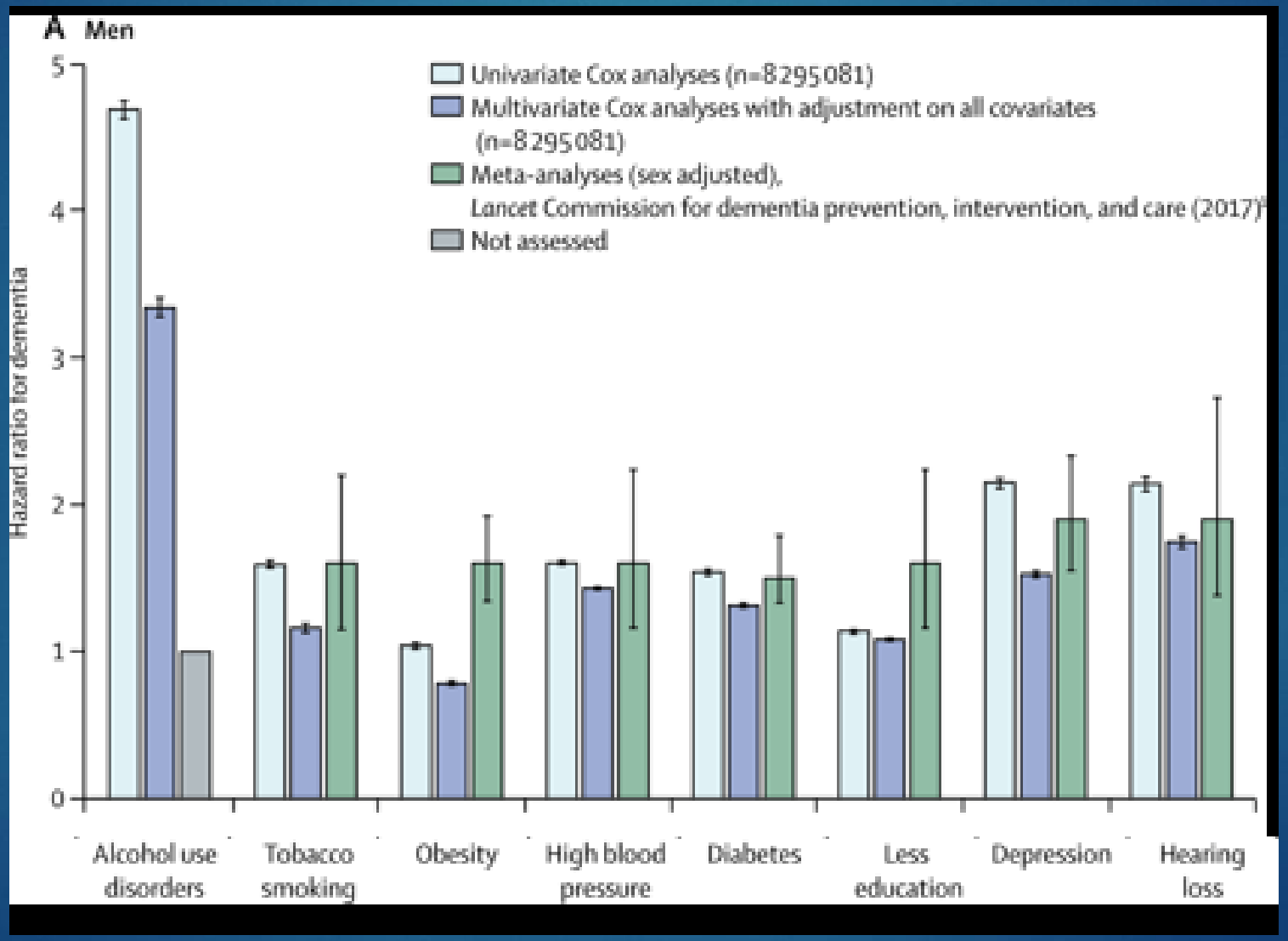
- Heavy drinking seems detrimentally related to dementia risk, whatever the dementia type.
- First, ethanol and its metabolite acetaldehyde have a direct neurotoxic effect, leading to permanent structural and functional brain damage.
- Second, heavy drinking is associated with thiamine deficiency, leading to Wernicke–Korsakoff syndrome.
- Third, heavy drinking is a risk factor for other conditions that can also damage the brain, such as epilepsy, head injury, and hepatic encephalopathy in patients with cirrhotic liver disease.
- Fourth, heavy drinking is indirectly associated with vascular dementia because of the associations of heavy drinking with vascular risk factors such as high blood pressure, hemorrhagic stroke, atrial fibrillation, and heart failure.
- Finally, heavy drinking is associated with tobacco smoking, depression, and low educational attainment, which are possible risk factors for dementia

Heavy Drinking 'Strongest' Modifiable Risk Factor for Dementia

- Heavy alcohol consumption is a major risk factor for all types of dementia, but particularly early-onset dementia.
- 2018: n = all hospital admissions in France; 31 million people over a 6-year period; 80% of the 65+ French population; 1 M with dementia; 945 K with AUD
- Strong association between a history of alcohol problems and dementia; esp. in early-onset dementia, with 57% of the 57K dementia pts under the age of 65 years having a history of alcohol use disorders (66% of men and 37% of women); hazard ratio was 3+; Alcohol use disorders were more frequently recorded in vascular dementia, esp. HTN.
- Risk for dementia was three times greater if the patient had a history of alcohol use disorders (prob. 5+ drinks/day)
- Results suggest that heavy drinking is the strongest potentially modifiable risk factor for dementia that we have ever seen

Michaël Schwarzinger,, et al., 2018

Potentially modifiable risk factors for dementia, n = 11M



Current best theory: Two-systems compromise model

- Best fits current data

- Posits alcohol neurotoxic compromise of
  - Cerebellar-pontine-prefrontal (motoric)
  - Prefrontal-parietal cortico-cortical system (cognitive)
  - producing motor and cognitive compromise, respectively

- It is based on a pattern of compromise of executive function, visuospatial abilities, and ataxia of gait, along with relative sparing of declarative memory and upper limb speed and strength

Recovery and White Matter

- Reversal of atrophy: abstinence followed by reversal of sulcal and ventricular enlargement
- Increased cortical grey matter after 2-4 weeks of sobriety
- Increase in white matter volume related to decrease in 3rd ventricular size, 2-7 months

Recovery of Deficits

With longer sobriety, there is significant improvement in brain structure and function.

De-atrophication: dendritic & white matter regrowth

3 weeks as typical recovery

Drinking pre and post age 40

Neuropsychological deficits improve over 4 to 5 years

Neuropsychology of Alcoholism - Parsons et al. 1987

Recovery 2: Reversal of Atrophy

- Cognitive functions and motor coordination improve within 3 or 4 weeks of abstinence; cerebral atrophy reverses after the first few months of sobriety.
- Structural pathology often disappears with long-term abstinence.
- Frontal lobe blood flow continues to increase with abstinence, returning to approximately normal levels within 4 years.

Neuropsychology of Alcoholism - Parsons et al. 1987

Recovery 3: Executive Functioning is slowest to recover

- Skills that require novel, complex, and rapid information processing take longest to recover.
- New verbal learning is among the first to recover.
- Visual-spatial abilities, abstraction, problem solving, and short-term memory, are the slowest to recover.
- May be persistent impairment in these domains, particularly among older alcoholics [over 40]

Neuropsychology of Alcoholism - Parsons et al. 1987

Chronic substance abuse effects on NP evaluation

Domain	IQ/Achv	Atten	PSpeed	Lang	Vspatial	Mem	EF	SensMot
Cannabis	-	-	-	-	-	-	-	-
Amphetamine	?	+++	+++	-	?	+++	+++	?
Barbiturates	?	+++	?	-	+++	+++	+++	+++
Benzos	+++	+++	+++	-	+++	+++	+++	+++
Opiates	-	-	-	-	-	+++	+++	-
Hallucinogens	?	?	?	?	?	?	?	?
Ecstasy	?	+++	?	?	?	+++	?	?
Cocaine	-	+++	?	-	?	+++	+++	?
?=unk								

C. J. Vella based on D. Gansler & H. Duncanson, 2014

MJ and greater Neuropsychological deficits

- Increasing evidence that adolescent cannabis use onset results in greater neurocognitive deficits compared with adult onset, especially very early onset

- Regular exposure to exogenous cannabinoids may disrupt healthy neurodevelopment, especially in the PFC and parietal cortices, which underlie higher-order cognitive functioning. This early initiation during the sensitive period of adolescence may place individuals at risk

- Weekly cannabis use before age 18 has been linked with deficits in neuropsychological tasks.

MJ and Cognitive deficits

- Evidence is building to suggest that regular cannabis use during the teenage or emerging adult years (typically ages 15–25 years) is associated with cognitive deficits.

- Two longitudinal studies that followed adolescents with substance use disorders over 8 years found that increased cannabis use during the follow-up period significantly predicted poorer attention and verbal memory.

- Early-onset cannabis users exhibit poorer cognitive performance than late-onset users or control subjects

Cannabis / Marijuana/ THC

- Intoxication: widespread Cognitive ↓
- Acute Deficits (24 hours):
  - Attention, Executive, immediate recall, RT, time underestimation
- Long Term Deficits, Chronic Use:
  - subtle working memory↓, Digit Symbol ↓, EF ↓,
  - amotivational syndrome?
- Dependence: Memory, sustained attention, EF, RT ↓

Schwartz, 1991; I. Grant, 1978

Acute Effects of MJ

- Produces sedation, mood elevation & occasionally hallucinations.
- There is no dispute that cannabis produces cognitive impairment during acute intoxication; effects can be shown using driving or flight simulators; esp. memory & learning
- Primary immediate cognitive effect: adverse effects on learning & memory, etc.
- Primary adverse effect of acute marijuana use is diminished psychomotor performance: marijuana has been found to play a significant role in car accidents with 33 percent of drivers arrested at the scene of the accident being positive for marijuana

Earlier Age of onset: more EF deficits

- Newer neuroimaging research: subtle, long-term effects of cannabis on cognition and brain functioning

- Starting between 14–22 years old and stopped by age 22: significantly more cognitive problems at age 27 than their non-using peers

- Users who began smoking before the age of 17 had significant impairments in measures of executive functioning, including abstract reasoning, verbal fluency, and verbal learning and memory

Bolla et al., 2005; Solowij et al., 1995; 2002; Grant et al., 2003; Brook et al., 2008; Pope et al., 2003

MJ and EF: Acute effects

- Acute Effects of MJ on EF (0 to 6 hours after use):
- Disruptions in
  - Attention/concentration ↓↓ in light users
  - Sustained attention ↓↓
  - Learning and memory functions ↓↓
  - information processing speed ↓↓
  - planning and decision making ↓↓
  - inhibition ↓↓
  - working memory ↓↓ ↓↓

Rebecca D. Crean, et al., 2011

MJ and EF: long term effects

- Long-term effects of MJ on EF (3 weeks or longer since last use):
  - Normal attention or concentration (28 days to 1 y)
  - Impaired decision-making and risk-taking
  - Impulsivity & inhibition: Normal Stroop, Impaired WCST - intact set shifting and maintenance but impairment in concept formation, planning and sequencing
  - Normal Working Memory
  - Impaired Verbal Fluency in onset pre-17

Rebecca D. Crean, et al., 2011

A Neuropsychological Perspective on Treatment Tactics 1

Neurologically challenged/Impaired, not unmotivated

Wait 2-3 weeks for cognitive assessment

Neurogenic lack of awareness: Anosognosia - impaired insight into deficits

Don’t depend on insight: insight therapy inappropriate early on, not phase appropriate

Neuropsychological Function and Treatment Process / Outcome

- Clinicians' misattributions of patients' behaviors
  - Verbal skills (previously learned information) remain relatively preserved, so patients appear unimpaired
  - Clinicians fail to identify cognitive impairment in at least 40% of patients

- Neuropsychological dysfunction may result in more rule violations in treatment and higher drop out rates

- Low motivation and minimization and denial are likely due to cognitive deficits

(Fals-Stewart et al., 1994)

A Neuropsychological Perspective on Treatment Tactics 2

- Think external prosthetics for neurological vs. psychological Tx
- Need different treatment approaches for cognitively impaired clients: different levels of care depending on level of cognitive impairment
- Need for Mental Status screening, i.e. MoCA

Clinical Implications of NP perspective

- Patient – Treatment Matching:
  - Pre-treatment neuropsychological assessment
    - Target skills to individual patient's neuropsych profile
  - Reduction in number of skills taught in CBT
    - Behavioral possibly better than cognitive focus
  - Extensive repetition

NP Rehabilitation

- Cognitively impaired patients might benefit from TBI cognitive rehabilitation research in addition to traditional alcohol treatment;
  - A la TBI, schizophrenia, cog rehab (i.e. Elizabeth Twamley, UC San Diego)

- Employ errorless learning strategies for simple verbal information (http://www.projectlearnet.org/tutorials/errorless_learning.html)

- Encourage elaborative processing (http://adaptivereading.pbworks.com/w/page/3949397/FrontPage)

- Provide clear rules for actions and structure tasks/routines

A Neuropsychological Perspective on Treatment Tactics 3

- Encourage Physical Exercise: neurogenesis & EF enhancement
- Replace use of executive function with procedural memory/prospective memory tactics
  - Airline Pilot research: Flip procedure books
  - Implementation Intentions (50%↑):
    - "When situation ***x*** arises, I will perform response ***y***"
  - Steps: the how, the when and the where of doing any goal

A Neuropsychological Perspective on Treatment Tactics 4

- Emphasize Procedural/behavioral memory:
  - AA had it right – walk the walk
  - Behavioral strategies:
    - behavioral repetition
    - concrete instructions
    - sponsor model
    - avoid triggers
- Use of reminder strategies
  - Calendars, dayminders
  - Google calendar (text message reminders)

Debate over using medications to curb addiction

- Use of medications to blunt cravings & withdrawal effects
- Is taking drugs to quit drugs real recovery? Substituting one opioid for another? 49% of 3000 residential opiod TX programs do not offer medications
- AA vs JourneyPure Program ($15 K/month): 70,000 overdose deaths in 2017
- Abstinence based vs M.A.T. = medication assisted treatment

Addicts need medication, not just abstinence

- Addiction is not treated as a disease; stigmatization and criminalization do not work
- With overdose victims, target is revival, not Tx - Naloxone/Narcan = extent of intervention; puts them into acute withdrawal = need medical treatment (a human rights issue)
- Mass General is one of few that offers drugs to lower cravings; 75-80% return for Tx
- Infants born in withdrawn are slowly reduced on methadone; every 25 minutes baby born addicted to opioids; can cost $1M per infant; many become wards of state

Addicts need medication, not just abstinence

- Stop disease by stabilizing the disease
- Vancouver Canada: 1st legal clinic to use drugs under medical supervision; Insite – supervised injection sites; provide medication & treatment; harm reduction model; overdose and HIV have declined 35%; injection sites are illegal in USA; the most expensive housing are ER rooms and jail cells
- Fentanyl found in 88% of illegal drugs
- Every dollar spent on harm reduction reduces medical care by $7; loss of 500 billion dollars per year

Evidence-Based Practices Resources:

- NIH:
  - http://pubs.niaaa.nih.gov/publications/AA70/AA70.htm
- SA and MH Services Admin:
  - http://www.nrepp.samhsa.gov/
- National Institute on Alcohol Abuse:
  - http://www.niaaa.nih.gov/guide
  - http://www.niaaa.nih.gov/alcohol-health/overview-alcohol-consumption/alcohol-facts-and-statistics
- National Institute on Drug Abuse
  - https://www.drugabuse.gov/publications/principles-drug-addiction-treatment-research-based-guide-third-edition/acknowledgments
- Univ. of Washington Alcohol & Drug Abuse Institute:
  - www.pscyhologicaltreatments.org

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