Neurobiology and Treatment of Alcohol Dependence

Nebraska MAT Training

September 29, 2011
Prior treatment episodes for persons starting treatment for alcohol dependence, 2009

SAMHSA (2009) Treatment Episodes Data Set.
FRONTAL LOBE
Consciousness
Reasoning
Planning
Goals
Values
Sense of Self
Amygdala
Ventral Tegmental Area (VTA)
FRONTAL LOBE
Consciousness
Reasoning
Planning
Goals
Values
Sense of Self
Acute Stress Response
Increased pulse
Hyperventilation
Sweating
Nausea
Vomiting
Myth # 1

• When a person doesn’t work the program, they don’t “want” to get well.

Reality

• When a person’s motivational system is profoundly impaired by addiction, their higher order “wants” and voluntary behavior are overridden by the survival drive to use.
I NEED TO USE !!!!!!!!!!

Host of rationalizations

CRAVING
I NEED TO USE !!!!!!!!!!!!

Host of rationalizations

CRAVING

FRONTAL LOBE
Consciousness
Reasoning
Planning
Goals
Values
Sense of Self
Four Neurotransmitters affected by chronic alcohol use

GABA – γ-aminobutryic acid
Glutamate
Endorphins (opioids)
Seratonin
Non-addictive medications that aid in treatment of alcohol dependence

**FDA-approved for alcohol dependence**

- Acamprosate (Campral®)
- Naltrexone oral and depot (Vivitrol®)
- Disulfiram (Antabuse®)

**Depression and Anxiety**

- SSRI’s and SNRI’s
GABA and Glutamate
Downregulation of GABA receptors
The brain’s neurons become insensitive to GABA
Upregulation of Glutamate receptors
The brain’s neurons become hypersensitive to glutamate.
Some symptoms of alcohol withdrawal

- Anxiety and Nervousness
- Irritability
- Jumpiness or shakiness
- Tremors
- Rapid heart rate
- Sweating
- Seizures
Acamprosate (Campral®)

Helps to stabilize the glutamate / GABA imbalance by subtly inhibiting glutamate activity
Abstinent at 60 days

Acamprosate: 67%
Placebo: 50%
Abstinent at 48 weeks

Acamprosate: 45%
Placebo: 25%
Abstinent at 96 weeks

22% who don’t need to go to treatment again after 2 years

Acamprosate: 39%
Placebo: 17%

who don't need to go to treatment again after 2 years

Abstinent at 96 weeks
Acamprosate

A non-addictive medication
that costs about
$4.50 / day
and is covered by most
Insurance companies
Endorphins (opioids)

Alcohol use causes a rush of our endogenous opioids (endorphins), resulting in:

- Analgesic effects
- A dopamine “high”
- Behavioral reinforcement
Genetic differences

Persons *with* family history of alcoholism

- Lower baseline levels of β-endorphins
- Greater release of β-endorphins after exposure to alcohol

Naltrexone

- Blocks the endorphin rush and the consequent dopamine “high”
- Reduces cravings caused by euphoric recall
**NALTREXONE** causes an observable reduction of activity in the midbrain when an alcohol dependent subject is presented visual cues.

Hugh Myrick; Raymond F. Anton; Xingbao Li; Scott Henderson; Patrick K. Randall; Konstantin Voronin. *Effect of Naltrexone and Ondansetron on Alcohol Cue-Induced Activation of the Ventral Striatum in Alcohol-Dependent People.* Arch Gen Psychiatry. 2008;65(4):466-475.
**NALTREXONE** reduces clients’ subjective craving for alcohol making it easier to stop drinking.

**Fig 1.**—Mean (± SEM) craving scores for the naltrexone hydrochloride-closed circles) and placebo-treated (open circles) groups across the 12 weeks of the study.

By reducing cravings, **NALTREXONE** contributes significantly to relapse prevention efforts.

Alcohol relapse: cumulative abstinence duration (CAD) by Treatment Group.

FEENEY G F X et al. Alcohol and Alcoholism 2006;41:321-327

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Disulfiram

By blocking the breakdown of acetaldehyde, alcohol disulfiram causes the symptoms of a “hangover,” including:

- Increased heart rate
- Shortness of breath
- Nausea and vomiting
- Throbbing headache
SICKNESS
Grams of ethanol per week

- Baseline
- Weeks 1-12
- Weeks 13-52

Acamprosate
Naltrexone
Disulfiram
A word on Antidepressants

- Antidepressants have been shown to both to reduce hyperactive stress response in the hypothalmus-pituitary-adrenal axis and to have dopinergic effects in the meso-limbic-cortical reward pathway.

- These are the same pathways effected by drugs of abuse. Addictive drugs have an *immediate* effect on the Stress Axis and Reward Pathway while antidepressants have a *gradual* “mood stabilizing” effect.
Dopamine

STRESS - HPA

REWARD - MLC

Corticotrophin releasing hormone (CRF)
Medication Compliance

• For persons with addiction, the transition from drugs with immediate intense rewards to medications that gradually improve their well-being is consistent with the entire transition from short-term addictive thinking to long-term sober thinking

**Counselors play a crucial role in helping clients transition from addictive drug use to compliance with non-addictive medications**
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