



UW PACC

Psychiatry and Addictions Case Conference

UW Medicine | Psychiatry and Behavioral Sciences

HOW DO I HELP MY PATIENT WITH METHAMPHETAMINE USE DISORDER?

TY REIDENBAUGH, MD
UW/VA PUGET SOUND ADDICTION
PSYCHIATRY FELLOWSHIP



GENERAL DISCLOSURES

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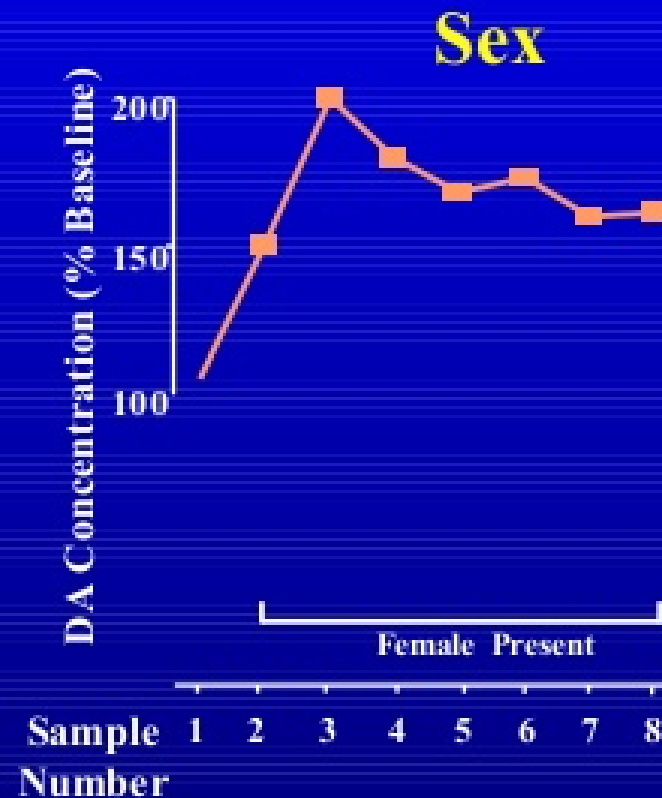
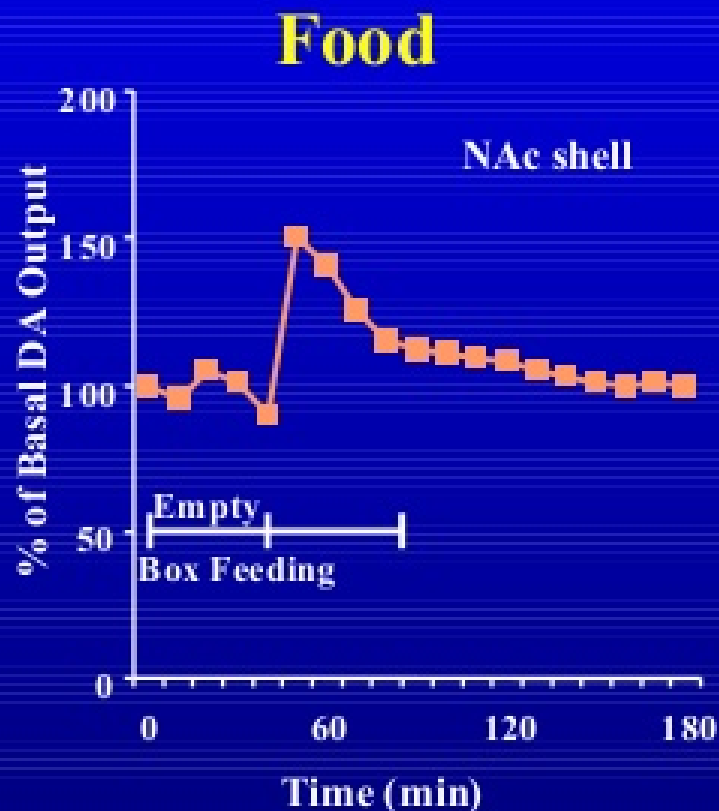
SPEAKER DISCLOSURES

- ✓ Any conflicts of interest?

OBJECTIVES

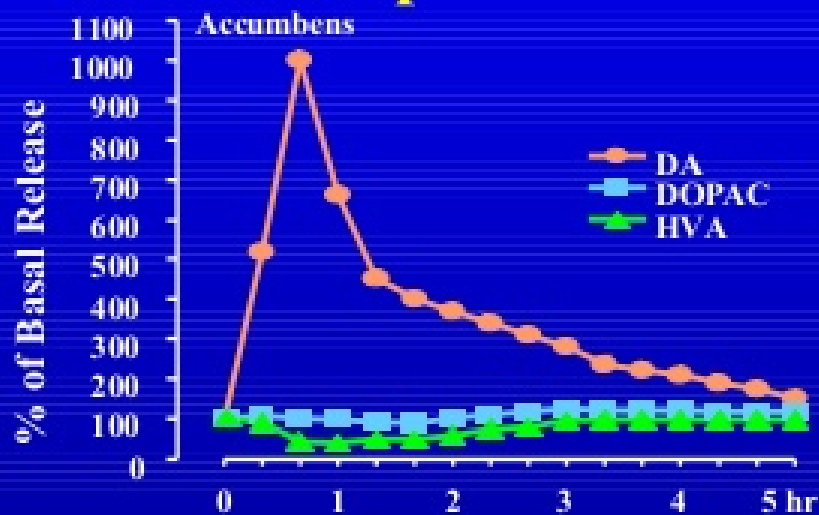
1. Why is it powerful? Why is it bad?
2. Explore pharmacological approaches to tx
3. Look at therapeutic options for treatment
4. Offer suggestions

Natural Rewards Elevate Dopamine Levels

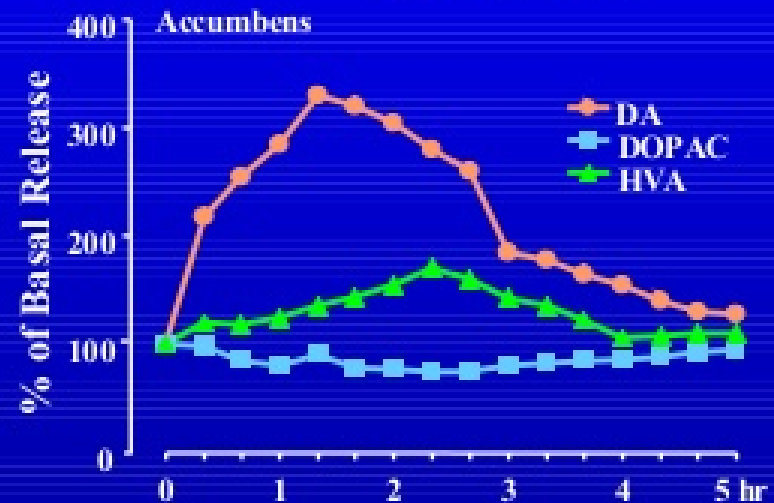


Effects of Drugs on Dopamine Release

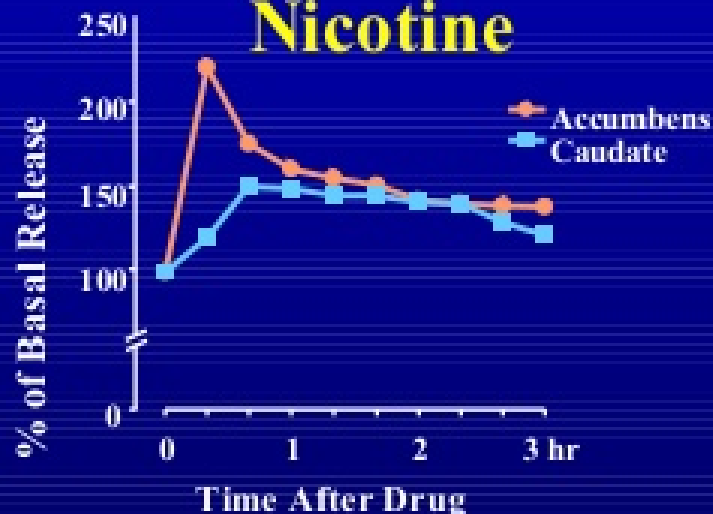
Amphetamine



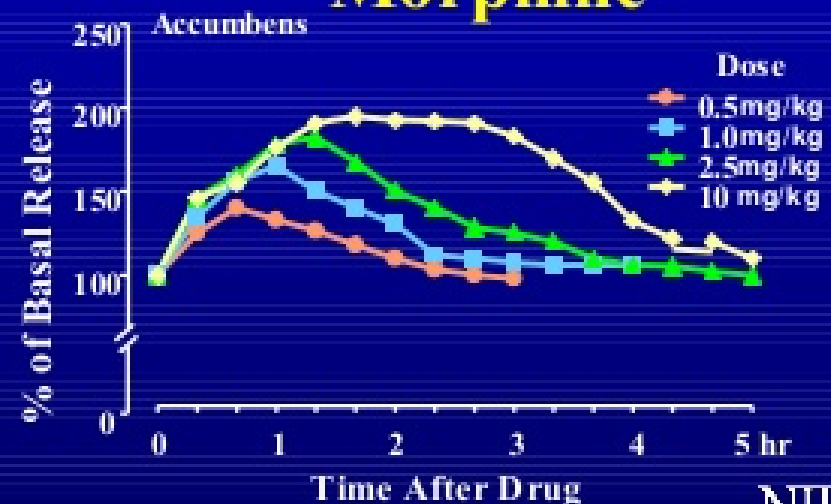
Cocaine



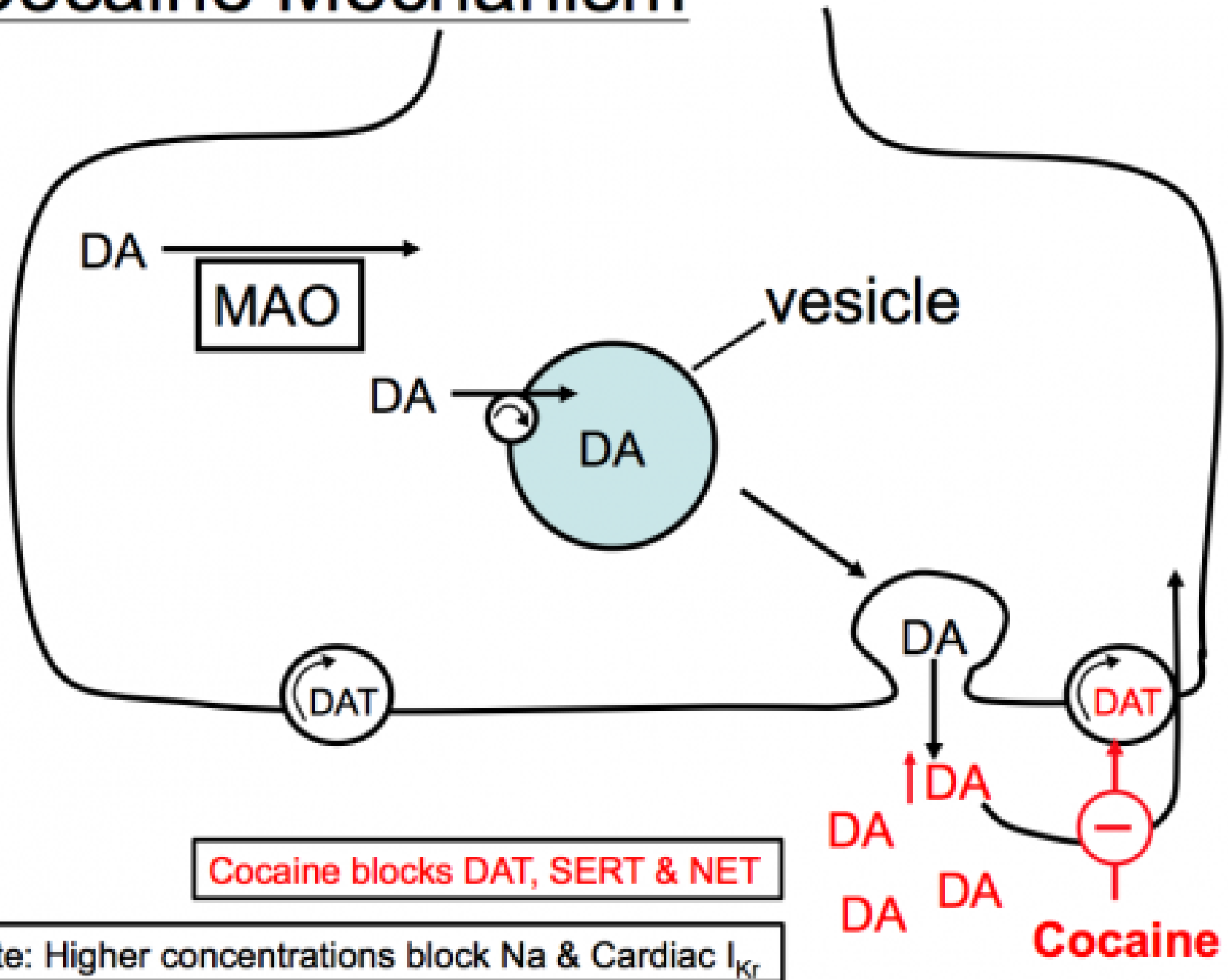
Nicotine



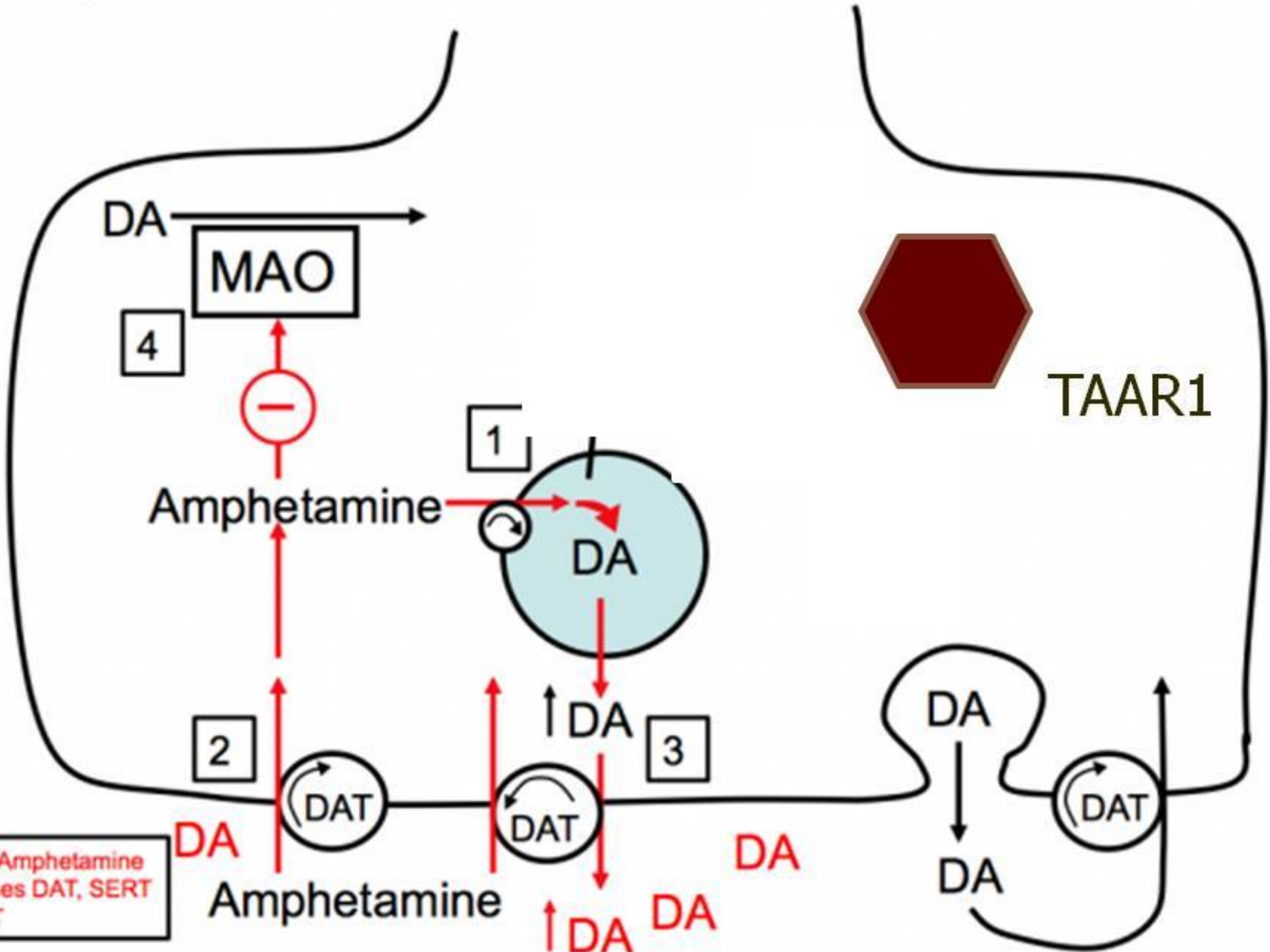
Morphine



Cocaine Mechanism



Amphetamine Mechanism



Note: Amphetamine reverses DAT, SERT & NET

MORBIDITY

- MA use is 22.5-fold higher in MSM; is an independent risk factor for HIV/STD; HIV incidence is 40-fold ↑ Colfax et al., 2011
- Proportion of total CHF patients having MA-associated cardiomyopathy is increasing. Function as assessed by New York Heart Association Functional classification is directly correlated to MA use. Sliman, et al., 2015
- MA-induced psychosis occurs in 15-23% of individuals with recreational use but may be up to 60% in dependent users in treatment settings. Arunogiri, et al., 2000
- Periodontal disease (bruxism, dental caries, xerostomia)

PHASES OF SUBSTANCE ABUSE THAT ARE TARGETS OF PHARMACOTHERAPY

- Intoxication/overdose
- Withdrawal/detoxification
- Abstinence initiation/use reduction
- Relapse prevention
- Sequelae of SUD (psychosis, agitation, etc.)
- Sequelae of Treatment/iatrogenic

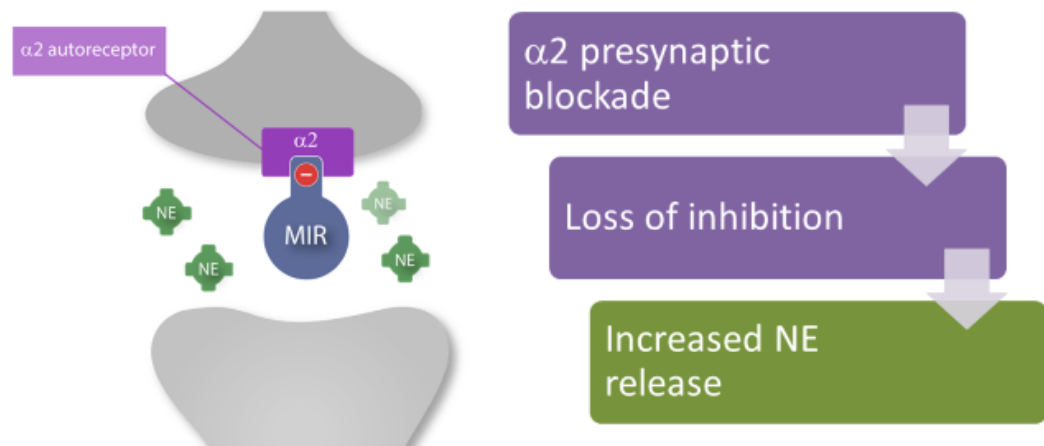
MEDICATIONS LACKING EFFICACY FOR METHAMPHETAMINE DEPENDENCE

- Desipramine (Shoptaw et al., 1994)
- Imipramine (Galloway et al., 1996)
- Fluoxetine (Batki et al., 2000)
- Sertraline (Shoptaw et al., 2006)
- Gabapentin (Shoptaw et al., 2006)
- Baclofen (Shoptaw et al., 2006)
 - (Baclofen showed possible effect in adherent subjects)
- Aripiprazole (Tiihonen et al., 2007)
 - (Amphetamine/methamphetamine)

MIRTAZAPINE

- MOA and theory: mixed monoamine agonist/antagonist that facilitates release of NE, 5HT, (DA?) to address depressed levels of these NTs in drug users to attenuate cravings, drug seeking and withdrawal

Mirtazapine blocks α_2 presynaptic autoreceptors



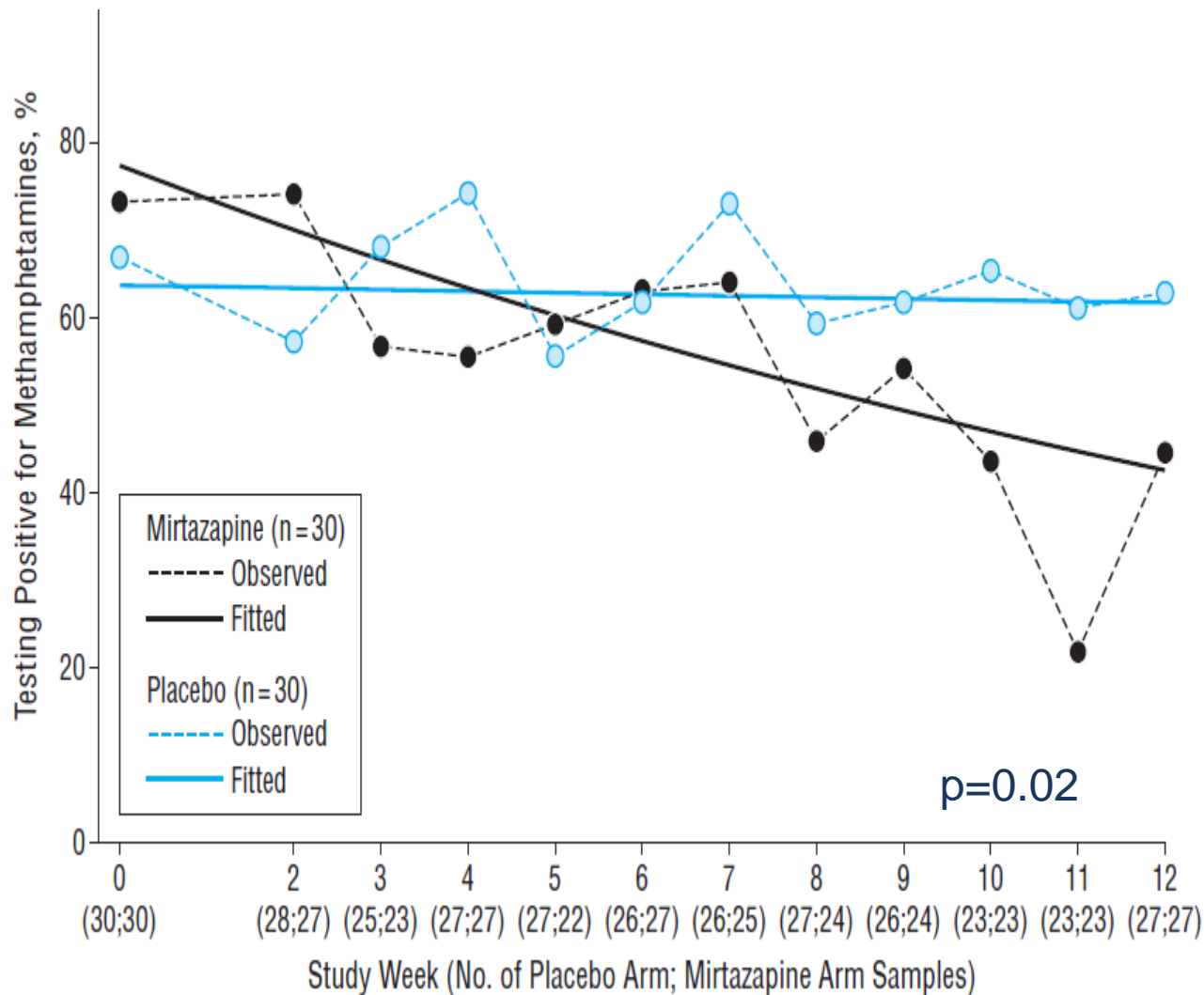
MIRTAZAPINE

Methamphetamine dependent, tx seeking MSM (n=60)

- Mirtazapine (30 mg) group had a 40% ↓ in +UDS (73% to 44%) vs PLC 6% ↓ (67% to 63%)
- NNT to achieve neg weekly UDS = 3
- No significant difference observed in depression scales
- Results occur in the context of low/moderate adherence (M 48.5%, PLC 48.7%)
- Frequency/severity of METH use not assessed
- Weekly UDS

Colfax, et al., 2011

Mirtazapine for Methamphetamine Dependence in MSM



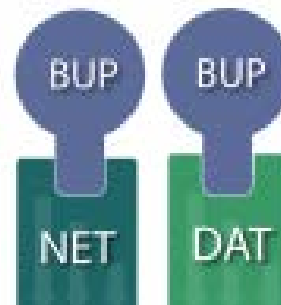
Colfax et al., 2011

Mirtazapine 15 mg qhs x 7 d, then 30 mg qhs
Counseling given weekly

BUPROPION

- MOA and theory: DA/NE re-uptake inhibitor
 - Blocks access of MA to DAT
 - \uparrow VMAT-2 activity \rightarrow \downarrow cytoplasmic availability of DA for reverse transport on DAT
 - Been shown to \downarrow MA self-admin (rats/non-human primates)
- 2 RCTs found some efficacy in subgroup with less than daily use

Mechanism of Action



- Reuptake inhibition of:
 - Norepinephrine transporter (NET)
 - Dopamine transporter (DAT)
- MOA may involve the presynaptic release of NE and DA.

BUPROPION

MA dependent participants with < daily use (n=43)

- 12w, RCT, DB, PC 12 week study of bupropion SR 150 mg BID v placebo.
 - MA on 29 or fewer of the past 30 days
 - UDS 3x/wk
 - Primary outcome measure: abstinence at wk 12
- No effect: 29% v 14%, $p=0.087$
- Plasma [bupropion] were correlated with better retention and more MA –UDS, 54 v 18%, $p=0.018$
- Med adherence by plasma levels was low (32%)

Heinzerling, et al., Addiction, 2014

NALTREXONE

- MOA and theory: Mu-opioid blocker. Opioid receptors modulate mesolimbic dopamine neurons
 - Chronic admin of cocaine → ↑ mu-R binding in areas relevant to reward (NA, amygdala)
 - PET reveals ↑ mu-R binding in limbic areas of chronic cocaine users a/w self-reported cravings

Jayaram-Linstrom, Am J Psych, 2008

NALTREXONE

80 treatment seeking amphetamine dependent pts

- RCT, DB, PC, 12 wk trial of Ntx (50 mg) v PLC
 - Inclusion criteria: used >12 days in the past 12 wks BUT have two weeks –UDS prior to study
 - 2x/wk UDS; and plasma levels to confirm adherence
 - Primary outcome measure: total number of –UDS
 - 47.5% and 45% of enrollees had adult ADHD

Jayaram-Linstrom, Am J Psych, 2008

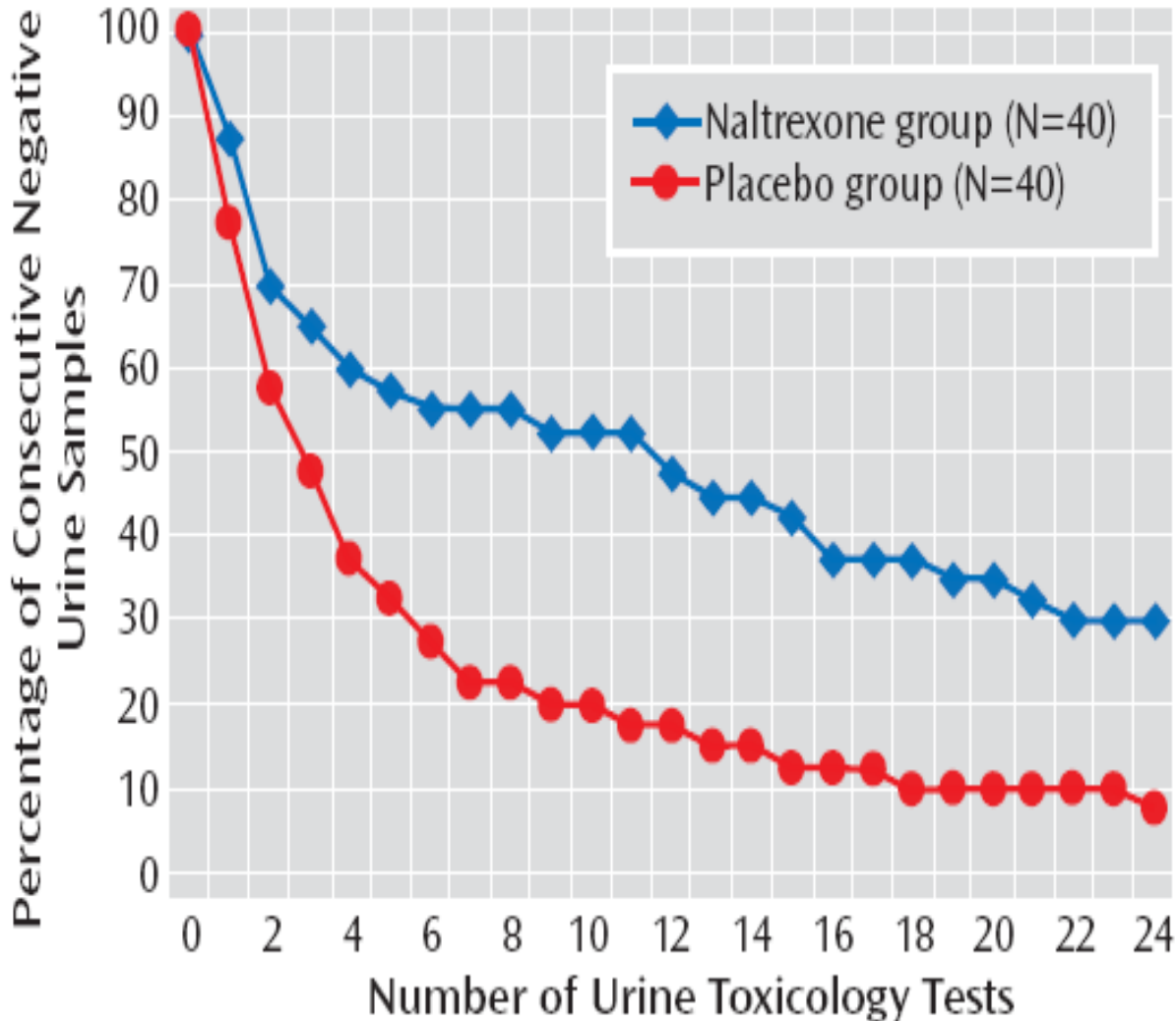
NALTREXONE

- Avg percentage of –UDS, 79.7% v 64.1%,
p=0.05
- Avg –UDS until relapse 15.5 v 8.2
- Reduction in cravings by self-report was evident from week 4 onward for Ntx group
- No difference among pts with ADHD

Jayaram-Linstrom, Am J Psych, 2008

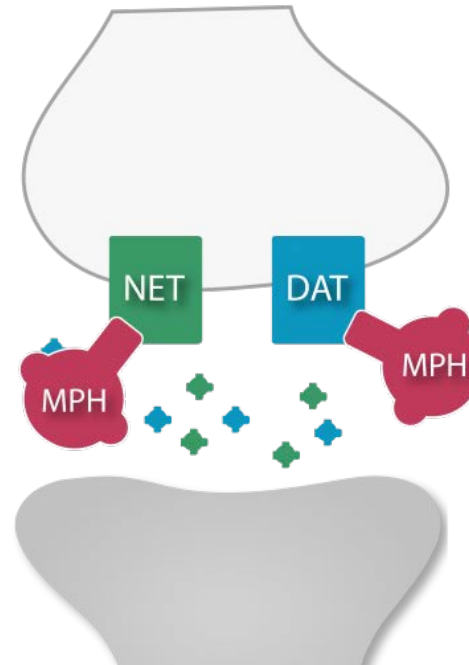
NALTREXONE FOR AMPHETAMINE DEPENDENCE

JAYARAM-LINDSTRÖM ET AL., 2008



REPLACEMENT THERAPY

- Methylphenidate MOA and theory: Blocks the dopamine and NE transporter
- Elevate basal levels of dopamine



Methylphenidate MOA

- DAT inhibition
- NET inhibition

REPLACEMENT THERAPY

- MPH-SR (54 mg) v Abilify (15 mg) v placebo
 - Fewer amphetamine positive UDS
 - 67.3% v 90.7% v 82% Tiihonen, et al, Am J Psych, 2007

MPH-SR v placebo with behavioral support and CM

- Greater reduction in MA use from baseline 6.56 v 3.82, $p=0.05$
- High MA (>10 days) users reported fewer using days (6.35 v 11.25, $p=0.049$)
- No difference among groups exhibiting 3+ consecutive neg UDS
- Cravings as measured by CQ-Now were greater at 10 ($p=0.03$) and 14 weeks ($p=0.007$) for PLA grp

Ling, et al., Addiction, 2014

REPLACEMENT THERAPY

- High co-occurrence of SUD and ADHD
- A narrow dose range of MPH is a common denominator in ADHD/SUD studies
- Long term drug use may down regulate dopamine systems →
 - increased tolerance
 - Require higher doses to reduce ADHD symptoms than in stimulant naïve patients

REPLACEMENT THERAPY

- RCT, DB, PC trial of 54 Swedish inmates with ADHD and chronic, IV amphetamine (N=54).
- Hypothesis: tx of ADHD → ↓ drug use
- Primary outcome measure: neg UDAS

Konstenius, et al., *Addiction*, 2004

REPLACEMENT THERAPY

- MPH group showed greater improvement in all domains of ADHD
- MPH vs placebo
 - Pan neg UDAS: 23% v 16%, $p=0.047$
 - Amphetamine neg UDS: 23% v 14%, $p=0.019$
 - Other drugs 44% v 29%, $p=0.032$
 - Retention: 51 days vs 18 days $p=0.001$

Stabilization dose: 17 (63%), 180 mg; 3 (11%), 144 mg; 2 (7%) 96 mg.

Konstenius, et al., *Addiction*, 2004

CONTINGENCY MANAGEMENT

162 tx seeking gay, bisexual men randomized into CBT, CM, CM+CBT, or GCBT

- VBRT: \$2.50 for neg UDS, ↑ for serial –UDS
 - No significant diff in methamphetamine –UDS
 - Retention: 9, 12, 13 and 11 weeks respectively
 - Weeks of serial abstinence: 2, 5, 7 and 3.5 weeks

Shoptaw, et al., Alcohol Dep, 2005

MATRIX TREATMENT MODEL

(RAWSON ET AL., 2004)

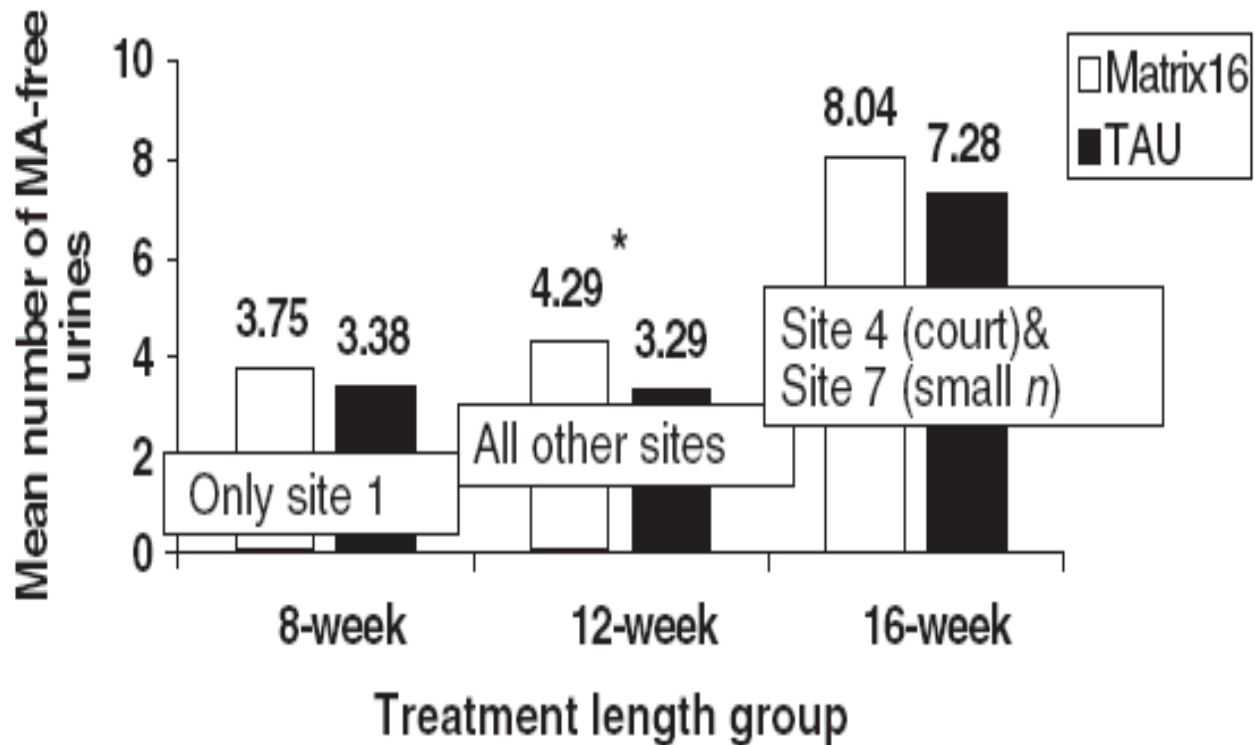
- 16 weeks
- 36 CBT Group Sessions
- 12 Family Education Sessions
- 4 Social Support Group Sessions
- 4 Individual Counseling Sessions
- Weekly Urine/Breath Testing
- Encouragement to attend 12-Step

MATRIX COMPARED TO TREATMENT AS USUAL

(RAWSON ET AL., 2004)

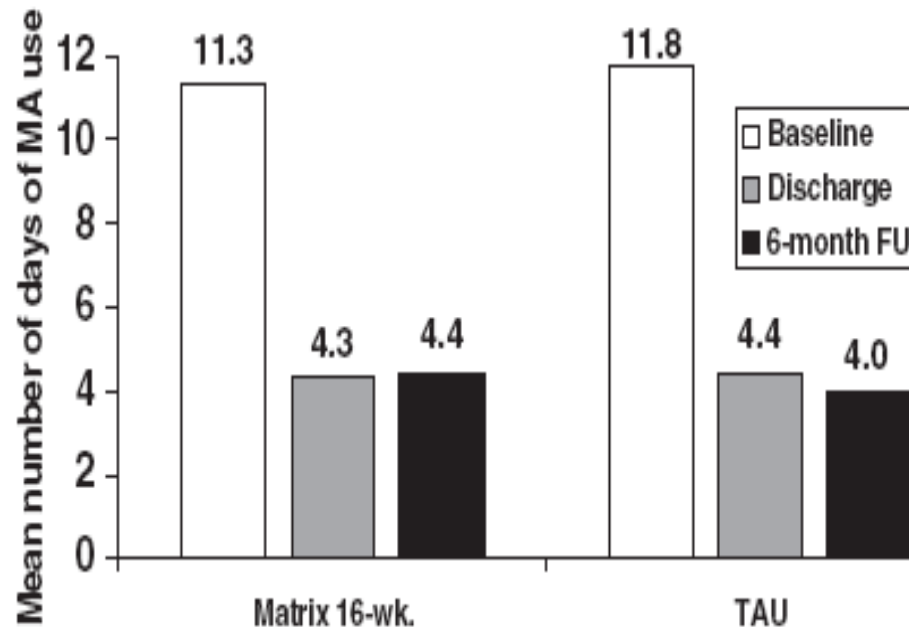
- 8 sites
- 978 MA dependent participants
- Random assignment to Matrix or TAU

Matrix Compared to Treatment as Usual



Rawson et al., 2004

Matrix Compared to Treatment as Usual



- 66% UAs neg at D/C for Matrix
- 69% UAs neg at D/C for TAU
- 69% UAs neg at F/U for Both

RESIDENTIAL TREATMENT (MATES)

- Large reductions in MA use at 3 months with reduced benefit thereafter
- Most significant improvement at 1 year was found in those remaining abstinent (~20%)
 - Longer duration in treatment
 - Receiving individual counseling sessions
 - Rapport with treatment providers
 - Low income
 - IV user yielded a lower probability of abstinence

APPLICATIONS

- Mirtazapine for pts with elements with depression/anxiety, insomnia and who are concerned with sexual SE
- Bupropion for pts with less than daily use of METH, depression, SAD, nicotine abuse and who are concerned with sexual SE
- Naltrexone for pts who also struggle with alcohol and opiates
- Assess for ADHD and treat
- High frequency MA users may be candidates for replacement therapies

HARM REDUCTION

[HTTPS://DEPTS.WASHINGTON.EDU/HARRTLAB/RESOURCES/](https://depts.washington.edu/harrtlab/resources/)



Safer-use Strategies: Uppers/Stimulants

Stimulants are “uppers” and include cocaine, crack, meth, MDMA (Molly) and bath salts as well as prescribed drugs like Ritalin and Adderall. Here are some tips to help you stay safer and healthier no matter how you choose to change your use. By making some changes in your use, you can reduce your substance-related harm. You are worth it!

Ways to stay healthier when you use

Prepare for safer sex

- **Why?** Stimulant use can lower your inhibitions and turn up your sex drive.
- **How?** It's a good idea to think ahead and carry condoms, dams, lube and gloves with you. These barriers can prevent unwanted pregnancy and sexually transmitted infections like HIV and hepatitis C.

Test your drugs

- **Why?** You can find out if your drugs are cut with other drugs (like fentanyl) or fillers (like levamisole) that could harm you.
- **How?** Talk to providers about getting a urine drug testing kit and testing liquids before you shoot them. For pills and powders, check out <https://dancesafe.org> for testing kits.

Try to eat

- **Why?** Stimulants can drain your body and dull your appetite. Food and water replenish these important nutrients to help you stay healthy.
- **How?** Try to eat nutritious foods before using, pack healthy snacks and water on the go, and avoid using over a long time. Let your body rest for at least a day after using.

Take care of your mouth

- **Why?** Some stimulants cause mouth dryness, sores, cracks, and teeth clenching.
- **How?** Drink water to keep yourself hydrated, and chew gum to keep your mouth moist and your teeth from grinding. Brushing your teeth can help control increased bacteria due to dry mouth. Use chapstick to prevent lip and mouth cracking.