Substance Use Disorder
(the clinical talk)

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Disclosure Statement

- Book Royalties
- Consulting – MicroTransponder Inc.
Treatment Topics
(cognitive enhancement and extinction)

- What works?
- Where are there problems?
- What can we do about them?
- How are we failing with the new ideas?
- Next steps
Drug Abuse is Bad

- Individual
  - Loss of other goals, pleasures, activities
  - Loss of relationships
  - Loss of income, home, role
  - Loss of health
  - Loss of life
- Family
- Society
Percentage of Crime Victimizations Attributable to Drug Abuse

Data from the Office of National Drug Control Policy
Treatment Strategies

- Detoxification
- Self-help (e.g., Alcoholics Anonymous)
- Pharmacotherapy
  - Agonist therapies
  - Antagonist therapies
  - Other pharmacotherapy
- Counseling-based treatments (e.g., Individual Drug Counseling; 12-Step Facilitation)
- Cognitive-Behavioral Therapies
CBT

- Contingency Management
  - Community Reinforcement
  - Behavioral Couples Therapy
- Broader CBT “package” treatments
- Relapse Prevention (Marlatt & Gordon, 2005)
Not Only Effective for SU Outcomes

- Drug treatment reduces likelihood of HIV infection by 6 fold in injecting drug users
  - Treatment is less expensive than not treating or incarceration (1 yr methadone maintenance = $4,700 vs. $18,400 for imprisonment)
  - Every $1 invested in treatment yields up to $7 in reduced crime-related costs
  - Savings can exceed costs by 12:1 when health care costs are included
  - Reduced recidivism
Psychosocial Treatment for Substance Dependence
Meta-Analysis (39 comparisons)

Dutra et al., et al. 2008
Psychosocial Treatment for Substance Dependence
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Trying to Improve Outcomes

- Use exposure to weaken the association between drug-use cues and craving
- And the association between craving and drug use
- A strategy for increasing resilience (less pushed around by cues)
Exposure in SUDs

- External and internal cues for use (conditioned stimuli)
- Based on functional analysis
CRAVING

Substance use
Interoceptive Cues

- **Somatic cues**
  - Often substance of choice withdrawal symptoms

- **Emotional Cues**
  - Anxiety
  - Frustration/anger
  - Sadness/loneliness
  - Shame/guilt
  - Boredom
But Exposure Procedures Give Only Modest Gains

Why?
But Exposure Procedures Give Only Modest Gains

- Learning is poor
  - Attention, arousal, memory...salience of learning
  - In our study of fear conditioning, SUD patients had trouble learning the contingency (Basden et al., unpublished)

- Extinction is context dependent
Can Exposure Be Improved with Memory Enhancers

- D-cycloserine success in the Anxiety Disorders
Current Pharmacotherapy

Exposure

ADM

BZ

Extinction
Novel Pharmacotherapy

Exposure → Learning → Extinction

DCS

enhance
A Very Different Solution: Enhancing Extinction Learning with Pharmacotherapy

- Rather than anxiolysis, use pharmacotherapy to enhance the effects of exposure – putative memory enhancers

- The N-methyl-D-aspartate (NMDA) receptor within the amygdala is important in extinction

- D-cycloserine can enhance extinction learning
  - DCS enhancement is resilient to reinstatement
  - May help generalization to other relevant CSs

(Davis, 2002, Biological Psychiatry, Vol 52)
(Ressler et al., 2004; Arch Gen Psychiatry, 1136-1144.)
(Richardson et al., 2004 Learning and Memory, 510-516)
NMDA Antagonist into Amygdala Blocks Development of Extinction

Increasing FEAR

startle amplitude

Vehicle

AP5

Pre Post Pre Post

60 lights without shocks

60 lights without shocks

Falls, Miserendino, Davis, J Neurosci, 1992
D-Cycloserine Given Systemically Enhances Extinction in Rats


*Pre-extinction test
Post-extinction test
Post Extinction DCS

Ledgerwood et al. (2003) Behav Neurosci 117: 341-349
DCS group maintained significantly greater improvement at 3 month follow-up

Ressler et al., Arch Gen Psychiatry 2004, 1136-1144.
Exposure + DCS for Social Anxiety Disorder

**SPAI Scores**

- **Pre-Test Post-Test 1-mo FU**

**SPAI -total Scores**

- 60
- 80
- 100
- 120
- 140

**Placebo (N = 13)**

**D-cycloserine (N = 10)**

Hofmann et al., 2006,
Archives Gen Psychiatry , 298-304
Main effect of time (p = .001)
Logical Memory Scores Across the Weeks of Testing (N = 33)

Otto et al., in press, *Psychother Psychosom*
Application to Substance Use Treatment

- Despite success in animal studies...
- And ... initial success
  - Positive smoking study (Santa Ana et al., 2009)
- Lots of Failure...
  - Alcohol (Hofmann et al., 2011; Kamboj, Massey-Chase et al., 2011; Watson et al., 2011)
  - Smoking (Kamboj, Joye et al., 2011)
  - Cocaine (Price et al., 2012)
Why?

- Poor contingency
  - Use of drug during the post-session period?
- Context Effects
  - Failure to allow use in clinic
  - No blockade for use out-of-clinic
- Amygdala dependency
Context?

Fear Conditioning:
*Cues signal danger*

Fear Cue → Danger
With Exposure:

*Cues take on ambiguous meanings*

Fear Cue

- Probably safe
- Danger
- Sorta Cool
The Meaning of Cues is Linked to Context

Context 1

Fear

cue

Context 2

Probably safe

Sorta Cool

The Meaning of Cues is Linked to Context

Street

Drug Cue → Drug Response

Clinic

Alternative Focus

Drug Response → Nothing

Options

- Use broader cues, where exposure might be cleaner
  - DCS for emotional exposure
- Do cue exposure in a relapse prevention phase
  - When there is low likelihood of use
- Use other agents and methods
  - Yohimbine
  - Exercise
  - Targeted Cognitive Activity (CCT)