Disclosure

Dr. Grant: Research Grant—Trichotillomania Learning Center, Biohaven and Otsuka Pharmaceuticals.

No medication has been approved for gambling disorder. Therefore, the off-label use of any psychototics, memantine, N-acetylcysteine, and naltrexone for the treatment of gambling disorder will be discussed.
Clinical Features

Repetitive or compulsive engagement in a behavior despite adverse consequences

Diminished control over the problematic behavior

Appetitive urge or craving state prior to engagement in the problematic behavior

Hedonic quality during the performance of the problematic behavior.
Clinical Features (cont’d)

Tolerance

Withdrawal

Impairment in major areas of life functioning

Telescoping

Grant JE, Potenza MN, Weinstein A, Gorelick DA. Introduction to behavioral addictions.

Clinical Features (cont’d)

Executive function deficits are greater in those with gambling disorder than in control subjects, including:

Planning

Cognitive flexibility

Inhibition

Grant JE, Potenza MN, Weinstein A, Gorelick DA. Introduction to behavioral addictions.

Relationship to Substance Use Disorders

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High Rates of Co-Occurrence

Similar Clinical Courses and Clinical Characteristics

Gambling/substances exert effects on brain reward pathways (i.e. ventral striatum) and implicate the dopaminergic and opioid systems

Pro-dopaminergic medication linked with gambling

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Why Treat Gambling Disorder?

Few people with gambling disorder (<10%) receive evidence-based treatments

When untreated, approximately 20-25% of people with gambling disorder report suicide attempts

Gambling disorder associated with spousal and child abuse, lost productivity, ill health, and crime.
Treatment

Cognitive-Behavioral Therapy (CBT)
Length of treatment unknown; brief interventions have shown benefit;
Multiple versions of CBT have shown benefit

Pharmacotherapy
No medication with regulatory approval for gambling disorder
Psychosocial Treatments

Motivational enhancement

Individual and Group Cognitive behavioral therapy
  ◦ social skills, assertiveness, anger management; cognitive restructuring

Imaginal exposure

Brief interventions

12-step programs
Pharmacotherapy:
What Doesn’t Appear to Work?
Antipsychotics

2 double-blind studies of Olanzapine in gambling

Neither showed greater benefit than placebo

Aripiprazole associated with onset of these behaviors
What Appears to Work Somewhat?
Serotonergic Agents

SSRIs and CMI may lead to short-term reductions in gambling, but results are mixed.

Large placebo response that may last for a few months.

No evidence for non-serotonergic antidepressants.
What Appears to Work Quite Well?
Opioid Antagonists

The mu-opioid system:

Underlies urge regulation through the processing of reward and pleasure

Works at least in part via modulation of dopamine neurons in mesolimbic pathway through GABA interneurons.
Naltrexone for Gambling Disorder

METHODS

• n=77 with GD

• Double-blind, placebo-controlled

• 11-weeks

• Dose titration: 25mg/d – 250mg/d

RESULTS

• Significant benefit in CGI-Improvement and Gambling Symptom Rating Scale

Figure 1. Baseline and Terminal Visit Gambling Symptom Rating Scale (Carry Forward Paired t-test)

<table>
<thead>
<tr>
<th>Symptom Severity Measure</th>
<th>Baseline Visit (N=17)</th>
<th>Terminal Visit (N=17)</th>
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<tr>
<td>Urge Strengtha</td>
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<td>Urge Frequencyb</td>
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<td>Thought Frequencyc</td>
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<tr>
<td>Subjective Distressd</td>
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</tbody>
</table>

a 0=None, 2=Mild, 4= Moderate, 6=Severe, 8=Extreme. Significantly different (t=14.28, p<0.05)*.
b 0=None, 1=Once a day, 3=Three times a day, 5= Five times a day, 6=More than five times a day. Significantly different (t=7.29, p<0.05)*.
c 0=None, 1=Once a day, 3=Three times a day, 5= Five times a day, 6=More than five times a day. Significantly different (t=5.25, p<0.05)*.
d 0=None, 2=Mild, 4= Moderate, 6=Severe, 8=Extreme. Significantly different (t=8.66, p<0.05)*.

* Bonferroni corrected
Glutamate Agents
N-Acetyl Cysteine (NAC)

NAC:
An amino acid and antioxidant
Lacks significant side effects
Potentially modulates brain glutamate transmission

Glutamate levels within the nucleus accumbens mediate reward-seeking behavior
Clinical Subtyping

Comorbidity?

Neurocognition?

Genetics?

Imaging?
Open-Label Study of Memantine in Gambling Disorder

RESULTS

- Cognitive flexibility improved from baseline to endpoint

- GD subjects were comparable to healthy controls at study endpoint

  - Pharmacological modulation of the glutamate system may reduce gambling and may do so by improving neurocognitive function related to cognitive flexibility.

<table>
<thead>
<tr>
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<th>Baseline v Endpoint</th>
<th>Baseline v Controls</th>
<th>Endpoint v Controls</th>
</tr>
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<tbody>
<tr>
<td>IDE total errors</td>
<td>T 2.20</td>
<td>P-value 0.037</td>
<td>T 2.09</td>
</tr>
</tbody>
</table>

Grant et al. Psychopharmacology (Berl) 2010 Dec;212(4):603-12
Practical Take-Aways

Gambling disorder is a common, disabling psychiatric disorder

Gambling disorder is commonly misdiagnosed as anxiety or depression or bipolar disorder

CBT and Pharmacotherapy can be helpful for gambling disorder
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