Gambling Disorder: A Disease for Multiple Contexts

Kirk Moberg, MD, PhD
Medical Director, Illinois Institute for Addiction Recovery
Clinical Professor, Depts. Of Internal Medicine and Psychiatry & Behavioral Medicine
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Disclosures

• Dr. Moberg has nothing to disclose.
Objectives

• Discuss the relevant neurobiology
• Comparisons and contrasts between substance use disorders and process addictions with a focus on gambling
• Expansion of what is known regarding gambling into other process addictions including treatment
What do we know?

• We know less about process addictions than chemical addictions.
• We know more about gambling than the other process addictions.
• Dopamine, a chemical that plays a role in chemical addictions, also plays a role in gambling disorder. There is evidence for involvement of other neurotransmitters as well.
• The mesolimbic and mesocortical systems are involved in both chemical and gambling disorders.
• Parkinson’s disease patients provide an interesting model to study some process addictions.
THE REWARD SYSTEM: THE CORE
Similarities

• Early age of onset
• Chronic relapsing patterns
• Many resolve on their own
• Tension or arousal before
• Relief during ("high")

Grant et al., 2010
Is gambling disorder a dopamine deficiency disorder?

- Low dopamine levels may be baseline
- Low dopamine levels may be the result

- ...and the results are equivocal in gambling

Probst & Eimeren, 2013
Salience attribution

• Stronger activation of reward system following cues
  – Drugs
  – Unclear with gambling

Probst & Eimeren, 2013
Adding another dopamine circuit

VTA to NA: reward pathway
SN to dorsal striatum: coordination of motor function
Dopamine and glutamate interactions
Miller et al., 2013
Relevant areas of the brain

• Reward and reinforcement
  – Ventral tegmental nucleus
  – Ventral pallidum
  – Nucleus accumbens
• Memory
  – Hippocampus
  – Amygdala
• Executive function
  – Pre-frontal cortex
• Coordination of movement and behavior
  – Substantia nigra
  – Dorsal striatum
Executive functions

• Differentiate among conflicting thoughts
  – Good vs. bad
  – Better vs. best
  – Same vs. different
  – Future consequences of current activities
  – Differentiate between conflicting thoughts
  – Working toward a defined goal
  – Expectation based on actions
  – Behavioral inhibition
  – Social “control”
Neuroanatomical hypothesis
Cilia 2010 and 2011

• Is gambling disorder a neural disconnectivity disorder?
• 3 populations
  – Parkinson’s disease + gambling (group 1)
  – Parkinson’s disease w/o gambling (group 2)
  – Normal controls (group 3)
• Single Photon Emission Computed Tomography (SPECT)
• Normal connection between anterior cingulate cortex and striatum
  – Anterior cingulate cortex—error detection (visualized by increasing activity)—losing
  – Striatum—shifts behavior in the context in increasing errors—stopping
• Shifting strategy abnormal in group 1
• Conclusion: behaviors don’t change despite errors
Cingulate: error detection
Striatum: coordination of motivation with behavior
Implicated neurotransmitters

• Norepinephrine—arousal and excitement
• Serotonin—impulse control
• Dopamine—rewarding and reinforcing aspects
• Opioids—pleasures and urges
• Cortisol—stress responsivenes
• Glutamate—cognitive functioning and flexibility

Potenza, 2013
Where does dopamine fit in?

• Reward deficiency hypothesis
  – Vulnerable individuals have low D2 receptor density and have a need for strong reinforcers.
  – Blum et al., 1996.
• Sensitization theory (salience attribution)
  – Vulnerable individuals are sensitized to triggers and cues after repeated use.
    • Robinson & Berridge, 2008.
• Impaired response inhibition and salience attribution
  – Low D2 receptor density creates vulnerability and is maintained by salience attribution.
    • Goldstein & Volkow, 2002.

Reuter et al., 2005; Grant et al., 2006; Grant et al., 2010; van Holst et al., 2010, Karim & Chaudhri, 2012; Probst & Elmeren, 2012; Joutsa et al., 2012; Grant et al., 2013; Potenza et al., 2013; Potenza, 2013
Another dopamine observation

• Dopamine agonists and antagonists have been linked to gambling behaviors.

Potenza, 2013
Dopamine dysregulation syndrome
Normal motor function

• Dopamine cell bodies in substantia nigra
  – Project to:
    • Dorsal striatum

• Result: control of fine motor movements

Fenu et al., 2009
Dopamine dysregulation syndrome
Impaired motor function

- Dopamine deficient cell bodies in substantia nigra
  - Project to:
    - Dorsal striatum

- Result: poor control of fine motor movements
Dopamine dysregulation syndrome
Normal reward function

• Dopamine cell bodies in Ventral Tegmental Nucleus
  – Project to:
    • Ventral striatum (Nucleus accumbens)
    • Pre-frontal cortex

• Result: Reinforcement of behaviors (affective and impulsive)
Dopamine dysregulation syndrome
Impaired reward function

• Dopamine deficient cell bodies in Ventral Tegmental Nucleus
  – Project to:
    • Ventral striatum (Nucleus accumbens)
    • Pre-frontal cortex

• Result: Impulsive behaviors (ADHD like?)

• NB: Loss of dopamine in VTA not as bad as SN
Post dopamine replacement therapy

• Increased motor system function
  – Relief of motor symptoms of PD
• Increased reward system function leading to decreased impulse control (ICD)
• Addictive behaviors with respect to the DRT
Parkinson’s model

- Dopamine cell bodies
  - Substantia nigra
  - Dorsal caudate-putamen
    - Motor systems impaired
  - Ventral tegmental area (receive glutamate)
    - Nucleus accumbens (receive glutamate)
    - Pre-frontal cortex (send glutamate to VTA and NA)
    - Ventral caudate-putamen
      - Reward circuitry mildly impaired

Fenu et al., 2009
Anti-Parkinsonian Medications

- Dopamine replacement therapy—all D receptors
  - levodopa
- Monoamine oxidase inhibitors—inhibit metabolism
  - Selegiline
- Dopamine agonists—D2/D3
  - Bromocriptine
    - Parlodel®
  - Amantadine*
    - Symmetrel®
  - Ropinirole
    - Requip®
  - Pramipexole
    - Mirapex®

* Indirect: increases release and inhibits re-uptake of dopamine
Anti-Parkinsonian Medications

- Gambling
- Hypersexuality
- Spending
- Binge Eating
- Skin picking
- Pathological internet use
- Punding

Fenu et al., 2009
Treatment

• Cognitive Behavioral Therapy
• Motivational Interviewing
• 12 step
• Financial Planning
• Self restriction from casinos—video gaming, internet gaming
• Medication Assisted Treatment
Medication Assisted Treatment (Grant et al., 2010)

- Opioid antagonists
  - Nalmefene—Grant et al., 2006; Grant et al., 2010
  - Naltrexone—Kim et al., 2001; Grant et al., 2008; Grant et al., 2008
- Selective serotonin reuptake inhibitors
  - Paroxetine—Kim et al., 2002
  - Fluvoxamine—Hollander et al., 2000; Blanco et al., 2002
  - Sertraline—Saiz-Ruiz et al., 2005
  - Escitalopram—Grant & Potenza, 2006; Black et al., 2007
- N-Acetyl Cysteine—Grant et al., 2007
- Carbamazepine—Black et al., 2008
- Lithium—Hollander et al., 2005
Amantadine is a complex medication...or a drug looking for an indication

- Anti-viral (influenza)
- Dopaminergic (Parkinson’s, cocaine withdrawal)
- NMDA receptor antagonist (Alzheimer’s, gambling)

Hubsher et al., 2012
A suggested algorithm

- If urges or cravings to gamble are present
  - Trial of opioid antagonist
  - If co-occurring SUD trial of opioid antagonist
  - If depression/anxiety playing a major role trial of SSRI
  - If mania/hypomania playing a major role trial of Li

- Always consider CBT

Grant and Kim, 2006
Other process addictions

• Hypersexuality
  – Opioid antagonists—naltrexone (Bostwick & Bucci, 2008)

• Kleptomania
  – Opioid antagonists—naltrexone (Grant & Kim, 2002)

• Shopping/spending
  – SSRIs—citalopram (Koran et al., 2002)

• Hoarding
  – SSRIs—paroxetine (Saxena et al., 2006)

• Binge eating
  – SSRIs—sertraline (McElroy et al., 2000); citalopram (McElroy et al., 2003)

• Internet gaming
  – SSRIs—escitalopram (Dell’Osso et al., 2008)

• Trichotillomania
  – Opioid antagonists—naltrexone (Carrion, 1995)
Summary and major themes

• Medication Assisted Treatment for chemical addictions was not initially evidence based but has been transformed.
• The neurobiology of chemical addiction is well understood and the knowledge base continues to grow.
• The neurobiology of process addictions is not as well understood but the knowledge base continues to grow.
• There is considerable overlap of treatment approaches between the chemical and process addictions.
• Gambling disorder is an excellent model to study process addictions.
• Opioid antagonists and SSRIs are major classes of medications that show promise in the treatment of process addictions.