Disclosures

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- Consultant to Gambling and Legal Entities on Issues Related to Impulse Control Disorders
“Youth” of Imaging

- Brain Imaging is a Relatively New Field
  - fMRI Introduced in 1990s
  - Data Acquisition Techniques and Analytic Approaches Continue to Evolve and Improve
- Newer Analytic Approaches May Permit Improved Insight into the Pathophysiology of Gambling Disorder and Other Addictions
GLM Versus ICA

- Most fMRI Manuscripts Published to Date Examine BOLD Signal Using a General Linear Model

- Independent Component Analysis (ICA) is a Data-Driven Computational Technique to Identify Independent Sources that Comprise a Measurement or Signal and Can Be Applied to fMRI to Identify Functionally Integrated Activations (or Functional Networks)

- ICA is Consistent with Fundamental Brain Properties: Balanced Inhibition/Excitation, Concurrent Co-Localized Activation and Deactivation, and Functional Heterogeneity (Xu et al, 2013a, 2015a, 2015b)

- Compared to GLM, ICA Implicates More Brain Regions During Tasks (Including Regions Cancelling Each Other in GLM-Based Analyses) (Xu et al, 2013b, 2014, in press)

EASG, Sept 15, 2016
Brain Function During Quitting Versus Chasing Losses And Quitting in PG and CD

HC (n=23)
Campbell-Meiklejohn et al, 2008

PG, CD, HC (n=72)
Worhunsky et al in preparation
Decision-Making and Loss Processing

**GLM**

**Medial frontal**
- Decision-making: Quit > Chase
- Loss before: Quit > Chase

**Amygdala-striatal**
- Decision-making to: Chase and Quit
- Loss before decision to: Chase and Quit

**ICA**

Worhunsky et al in preparation

EASG, Sept 15, 2016
White Matter and PG

- White Matter Connections Are Important to the Operation of Brain Networks


- While Prior Studies Have Used TBSS to Assess FA and MD, None Examined Crossing Fiber Integrity or Compared PG with A Substance Addiction

- FA and MD Measures Might Be Suboptimal in Regions of Crossing Fibers (Behrens et al, 2007), and Estimating Primary (PVE1) and Secondary (PVE2) Fiber Orientations May Be More Informative in These Areas
Differences in Secondary Crossing Fibers in Addictions

Regions Implicated Include Corticostriatal and Parieto-Occipital Tracts Previously Implicated in Reward Processing and Addiction

Yip et al, in press, Biol Psychiatry CNNI
Secondary Crossing Fiber Findings Not Attributable to AUDs

Yip et al, in press, *Biol Psychiatry* CNNI
Transdiagnostic Vs Categorical

- Two Current Potentially Competing Theories as Seen in DSM-5 and RDoC Discussions
- Diagnostic Categories Be Heterogeneous; Some Transdiagnostic and Biological Factors May Link More Closely and Thus Be More Amenable to Interventions
- Preliminary Data Suggest Each Approach Has Utility
  - COMT Variation Linked to Cognitive Function and Tolcapone Treatment for Gambling D/O (Grant et al, 2013)
  - DBH Variation Linked to Subjective and Neural Emotional Responses Across Groups (Yang et al, 2016)
  - Cortical Volume Differences Specific to Cocaine-Use Disorder and Subcortical Volumes Linked to Impulsivity Across Disordered (Gambling, Cocaine) and Healthy Populations (Yip et al, Submitted)

EASG, Sept 15, 2016
Gray Matter Volume in PG and CD

A. Main effects of diagnostic group

B. Associations with impulsivity

Yip et al, submitted
Conclusions & Future Directions

• Significant Progress Has Been Made in Understanding Neurobiological Aspects of Pathological Gambling / Gambling Disorder and Other Addictions

• Data Acquisition and Analytic Approaches Continue to Evolve and Improve

• Applying These Advances May Generate Better Understandings That May be Translated into Improved Prevention and Treatment Strategies
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