Neuroimaging Research on Drug Use and Obesity

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Prepared for:
Center for Translational and Prevention Science

January 22nd, 2018
Neurobiologic Advances from the Brain Disease Model of Addiction

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Neurocircuitry of Addiction

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[Diagrams and images related to neurocircuitry of addiction are shown.]
Dysfunction of reward processing correlates with alcohol craving in detoxified alcoholics

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Received 25 July 2006; revised 7 November 2006; accepted 15 November 2006
Available online 8 February 2007

Preexisting risk factor or consequence of addiction?
Reward-Related Brain Function and Comorbid Substance Use

- Reward deficiency model of addiction (Blum et al., 2000; Volkow et al., 2003)
- Project Team: 85 Ps completed the Adolescent Alcohol and Drug Involvement Scale (AADIS) 1.5 years after baseline fMRI scan
Using fMRI to examine the rewarding brain

**Prefrontal cortical regulation of brainwide circuit dynamics and reward-related behavior**

**INTRODUCTION:** The drive to seek and experience reward is conserved across species and, in mammals, involves interactions between subcortical dopaminergic systems and limbic structures such as the striatum. Impairment of this process, observed across a number of psychiatric conditions, is the clinical symptom of anhedonia (loss of enjoyment). The neural mechanisms underlying anhedonia are unknown but could result from abnormal interactions between cortical and subcortical reward circuits. We sought to test the hypothesis that elevated medial prefrontal cortex (mPFC) excitability (a clinical feature associated with anhedonia) exerts suppressive control over the interactions between two distant subcortical regions: the dopaminergic midbrain and the striatum.

**RATIONALE:** Clinical imaging studies have detected elevated activity in the mPFC in human patients with depression, and treatment is as-

Knutson et al. (2005). *Journal of Neuroscience*

Ferenczi et al. (2017). *Science*
This study fits with the neuroimmune model in that it shows that reduced reward-related brain function prospectively predicts problematic drug use. The idea is that low reward processing causes people search for positive mood inducers in the environment through risky and poor health related behaviors.
Blunted ventral striatal responses to anticipated rewards foreshadow problematic drug use in novelty-seeking adolescents

Decreased VS and VTA during reward anticipation predicts PDU

Increased dlPFC grey matter density predicts PDU
**Ventral Striatal Activation During Reward Anticipation Correlates with Impulsivity in Alcoholics**

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**Background:** Alcohol dependence is often associated with impulsivity, which may be correlated with dysfunction of the brain reward system. We explored whether functional brain activation during anticipation of incentive stimuli is associated with impulsiveness in detoxified alcoholics and healthy control subjects.

**Methods:** Nineteen detoxified male alcoholics and 19 age-matched healthy men participated in a functional magnetic resonance imaging (fMRI) study using a monetary incentive delay (MID) task, in which visual cues predicted that a rapid response to a subsequent target stimulus would either result in monetary gain, avoidance of monetary loss, or no consequence. Impulsivity was assessed with the Barratt Impulsiveness Scale-Version 10 (BIS-10).

**Results:** Detoxified alcoholics showed reduced activation of the ventral striatum during anticipation of monetary gain relative to healthy control subjects. Low activation of the ventral striatum and anterior cingulate during gain anticipation was correlated with high impulsivity only in alcoholics, not in control subjects.

**Conclusions:** This study suggests that reduced ventral striatal recruitment during anticipation of conventional rewards in alcoholics may be related to their increased impulsivity and indicate possibilities for enhanced treatment approaches in alcohol dependence.

**Willing to wait: Elevated reward-processing EEG activity associated with a greater preference for larger-but-delayed rewards**

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How can drug addiction help us understand obesity?

Nora D Volkow & Roy A Wise

To the degree that drugs and food activate common reward circuitry in the brain, drugs offer powerful tools for understanding the neural circuitry that mediates food-motivated habits and how this circuitry may be hijacked to cause appetitive behaviors to go awry.
Neurocognitive Measures

Reward – Brain
- MID
- Primary reward
- Cue reactivity to food/drug cues
- Reinforcement learning paradigms
- Exploitation vs exploration

Reward – Behavior
- CARROT
- EEfRT
- Reinforcement learning
- DDT
- Exploitation vs exploration

Executive control – Brain/Behavior
- Go/No-Go
- N-Back
- Stop task
- Emote Go/No-Go

Threat- Brain/Behavior
- Emotional faces
- IAPS
- Threat of shock
- Fear learning
- Count down to shock
Reward Hyposensitivity Supportive Data
In recent analyses from the Temple dataset, we find similar results to the previous study by Knutson. We find that problematic alcohol use predicts low reward-related brain function over a multi-year follow-up period. Importantly, in very new analyses we also show that low reward-related brain function also predicts problematic alcohol use over a multi-year period.
There is considerable data showing that low reward-related brain function is associated with depression. This is a paper we are writing showing that reduced reward-related brain function prospectively predicts depression onset.
Predicting MDEs: Reward Anticipation

VS Spheres

Caudate Body-Head

These are data from the Temple data set where we show that decreased reward-related brain function in the basal ganglia prospectively predicts depression onset over a multi-year follow-up period. These results are in line with NIN model's perspective of decreased reward brain function being a risk for mental and physical health problems.