Beroendemekanismer- ett beroende som andra?

Neuroendokrina responser till spel om pengar

Anna Söderpalm Gordh
Dopamine and the Reward System

• Studies in animal models have demonstrated that mesocorticolimbic dopamine pathways are involved in the brain’s reward system and that the nucleus accumbens in the ventral striatum is a critical region for mediating the rewarding effects of drugs.

• Virtually all drugs of abuse, including alcohol, have an impact on dopaminergic activity within this brain region.

• Studies in humans have shown that mesolimbic dopamine release is correlated with the positive subjective effects of the drug.
Dopaminfrisättningen korrelerar till önskan om mer drog

Amphetamine-Induced Increases in Extracellular Dopamine, Drug Wanting, and Novelty Seeking: A PET/[^11]C]Raclopride Study in Healthy Men

Marco Leyton, Isabelle Boileau, Chawki Benkelfat, Mirko Diksic, Glen Baker, and Alain Dagher
Cortisol and Dopamin

- Glucocorticoids and stress interact with the dopamine reward system in ways that may increase vulnerability for developing addiction. For example, preclinically adrenalectomy (which prevents cortisol production), decreases drug self-administration. Re-introduction of glucocorticoids at levels similar to those induced by stress reverses this effect.

- The magnitude of stress-induced cortisol release significantly correlates with mesolimbic dopamine release in the ventral striatum.

- Glucocorticoids themselves also are believed to have reinforcing properties in rats as they seem to modulate self-administration of alcohol and increase brain sensitivity to other addictive drugs (e.g., stimulants and opioids) in the animals. Thus, increased levels of cortisol may have reinforcing effects, acting on the brain to perpetuate behaviors (e.g., alcohol consumption) that maintain high cortisol levels.

- The interactions of the stress response and the rewarding effects of drugs also have been investigated in humans. Imaging studies using PET found that higher cortisol levels in response to amphetamine administration or to a psychosocial stressor were positively associated with amphetamine-induced dopamine release in the ventral striatum. Furthermore, subjects with a high cortisol response to these stimuli reported more positive subjective drug effects after amphetamine administration than did subjects with a low cortisol response. These studies provide evidence that cortisol may play a role in drug reinforcement through its interactions with the dopaminergic reward pathway, which may, in turn, influence vulnerability for and maintenance of alcohol and other drug use.
Vad händer med puls och kortisolet när vi spelar på en black-jack maskin?
In regular gamblers, casino gambling increases heart rate and salivary cortisol.
In regular gamblers and problem gamblers, casino gambling increases heart rate and salivary cortisol.

Meyer et al., 2004
Hur ser baseline cortisolnivåerna ut hos spelmissbrukare?
In general, pathological gamblers do not show increased basal levels of ACTH and cortisol in comparison to healthy controls.
Könsskillnader?
Male gamblers have significantly greater salivary cortisol before and after betting on a horse race, than do female gamblers.
Sex differences in response to the TSST

Kirschbaum et al., 1999
Gambling pathology is associated with dampened cortisol response among men and women

Paris et al., 2010
Dopamin och spelmissbruk
Chatecolamine responses to casino gambling in problem gamblers

Meyer et al., 2004
The catecholamines have also been found to play an important role in pathological gambling, just as in drug addiction

Table 1. Mean±S.D. concentrations of mono- amines and metabolites (nmol/l) in the CSF of ten pathological gamblers and seven controls

<table>
<thead>
<tr>
<th></th>
<th>Gamblers</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>DA</td>
<td>22.1±6.3*</td>
<td>34.3±7.8</td>
</tr>
<tr>
<td>DOPAC</td>
<td>117.0±19.6*</td>
<td>77.1±11.3</td>
</tr>
<tr>
<td>HVA</td>
<td>477.1±63.1*</td>
<td>297.6±60.0</td>
</tr>
<tr>
<td>DOPAC/DA</td>
<td>5.7±2.0*</td>
<td>2.4±0.7</td>
</tr>
<tr>
<td>HVA/DA</td>
<td>23.0±6.8*</td>
<td>8.9±2.1</td>
</tr>
<tr>
<td>NA</td>
<td>128.8±30.0*</td>
<td>85.7±19.4</td>
</tr>
<tr>
<td>MHPG</td>
<td>55.4±12.6*</td>
<td>37.0±8.9</td>
</tr>
<tr>
<td>MHPG/NA</td>
<td>0.5±0.2</td>
<td>0.5±0.2</td>
</tr>
<tr>
<td>5-HT</td>
<td>4.8±1.2</td>
<td>5.3±1.1</td>
</tr>
<tr>
<td>5-HIAA</td>
<td>309.0±41.8</td>
<td>326.7±50.8</td>
</tr>
<tr>
<td>5-HIAA/5-HT</td>
<td>69.2±24.4</td>
<td>65.3±22.6</td>
</tr>
</tbody>
</table>
Amphetamine Primes Motivation to Gamble

Zack & Poulos, 2004
Vilka gener är inblandade?
Diagram showing which of the 31 genes were included in the regression equation, the \( r^2 \) or fraction of the variance of pathological gambling attributed to each gene, and significance level of each gene.
This diagram shows the total $r^2$ for genes of each of the five gene groups. This value is highest for the dopamine genes, next highest for the serotonin and norepinephrine genes, lower for the other genes and lowest for the GABA genes.
Våra studier

- Study 1: We hypothesize that pathological gamblers show alterations in reward acutely in relation to a gambling situation.

- Study 2: We hypothesize that individuals (with no gambling addiction) who are High Cortisol Responders (HCR) to stress will show an altered reward activity to gambling, with respect both to objective and subjective measures.

- We hypothesize that HCR subjects will gamble for a longer time period compared to LCR in a laboratory gamble model.
The laboratory environment:

- a sofa with pillows
- chairs
- a table
- lamps
- magazines
- boardgames
- a TV
- bookshelf
- a rug
- curtains in window
Alcohol challenges:

Acute doses

Consumption
Subjective mood test:

- Biphasic Alcohol Effect Scale (BAES)
- Addiction Research Center Inventory (ARCI)
- Visual Analogue Scale (VAS)
- Profile Of Mood Scale (POMS)
- Drug Effects Questionnaire (DEVQ)
Objective measures:

Blood pressure
Alcometer
Voice
Film
Motor activity
Studie 1
High versus Low cortisol responders
”High cortisol responders” till stress äter mer än ”low cortisol responders”

Adam and Epel, 2007