Pathological Gambling: Neurobiological research and its relevance for treatment and relapse prevention:
Recent research and future questions

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Psychobiological:

- Neuroimaging in Pathological gambling: predictors of the course of addictive disorders (2007-2011; Goudriaan)
- Effect of rimonabant and modafinil on impulsivity and craving in alcohol and cocaine addiction: neuroimaging (2008-2012; Schmaal, Goudriaan)
- Craving in alcohol addiction (2000-2006; Ooteman)
- Neurocognitive functions in pathological gamblers (2001-2005; Goudriaan)
  - Neuroimaging in PG (de Ruiter)
- Neurotoxicity of ecstasy (1999-2008; Reneman, de Wim, Schilt)

Benchmarking (Oudejans)

Are scratchcards addictive verslavend? (1999-2004; de Fuentes)

Effectiveness of treatments

Center for Addiction Research (CVO Utrecht):
Epidemiology of PG in the Netherlands (de Bruin, 2004)
Overview presentation

Recent research in PG
- Neurocognition, neuroimaging
- Relevance research for treatment and relapse prevention

Windows on future research
- Topics
- Opportunities for collaboration
Why would you study pathological gambling as an addictive disorder, in neurobiological research?

- Similarities in neurocognitive and neurotransmitter abnormalities in PG and substance dependence
- But: lots of methodological problems in current research
- What are the implications of neurobiological markers?
Memory (hippocampus)
Conditioned response (amygdala)

Reward circuits (ventral tegmental area, nucleus accumbens)

Reward sensitivity
Loss sensitivity

Stress system (Koob and LeMoal)

Stress reactivity

Attentional bias
(cingulate gyrus, prefrontal cortex, orbitofrontal cortex)

Reward circuits (anterior cingulate, prefrontal cortex)

Cognitive Flexibility

Top-down control (prefrontal cortex)
Research goals

- What neurocognitive and psychophysiological functions related to reward and punishment processing are diminished in pathological gambling?
- Does pathological gambling resemble a substance dependent group more (Alcohol), or does it resemble an impulse control group more (Gilles de la Tourette’s disorder)?
- Study in a PG group matched for age, gender, IQ, without comorbid substance dependence or major other psychopathology
Neurocognitive functions in pathological gambling: a comparison with alcohol dependence, Tourette syndrome and normal controls

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Which EFs are abnormal in PG (n=50; abstinent)?

- Five domains tested:
  1) Inhibition
  2) Cognitive Flexibility
  3) Working Memory
  4) Planning
  5) Decision making
  6) Control tasks
Goudriaan, Oosterlaan, de Beurs, van den Brink (2006), *Addiction.*
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Brain functions in problem gamblers, compared to nicotine dependence and normal controls: an fMRI study (AIAR: 2003-2006)

Response Perseveration and Ventral Prefrontal Sensitivity to Reward and Punishment in Male Problem Gamblers and Smokers

Neuropsychopharmacology (2008), 1–12
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Michiel B de Ruiter\textsuperscript{a,1,2,3}, Dick J Veltman\textsuperscript{1,3}, Anna E Goudriaan\textsuperscript{1}, Jaap Oosterlaan\textsuperscript{2}, Zsuzsika Sjoerds\textsuperscript{2,3} and Wim van den Brink\textsuperscript{1}

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- Reward and loss sensitivity
- Cognitive flexibility
- Cue reactivity
- Response inhibition

- Reward circuits
  (ventral tegmental area, nucleus accumbens)
- Reward circuits
  (anterior cingulate, prefrontal cortex)
- Stress system
  (Koob and LeMoal)
- Memory
  (hippocampus)
- Conditioned response
  (amygdala)
- Reward circuits
  (cingulate gyrus, prefrontal cortex, orbitofrontal cortex)
- Top-down control
  (prefrontal cortex)

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Functional MRI: sensitive for changes in oxygen levels in blood, in active brain areas.
Reversal learning in gamblers and smokers

- Probabilistic reversal learning task
Wins

Losses

Controls

Smokers

Gamblers

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Conclusions

- Gamblers and nicotine dependent persons are similar with regard to
  - Punishment or loss sensitivity (VLPFC)
  - Insensitivity for wins is specific for problem gamblers

- These disturbances may sensitize a person for
  - Developing addictive behaviors
    - prospective research needed
  - Are related to the course of the disorder
    - longitudinal research needed
Predictors of relapse:
- duration of disorder (26%),
- reward sensitivity (Iowa Gambling Task; Card Playing Task)
- inhibition (Stop Signal Task; Stroop) (24%)
- 76% classification accuracy
- neurocognitive measures are better predictors than self-report measures
Can neurocognition and brain functions predict relapse?

Neural Activation Patterns of Methamphetamine-Dependent Subjects During Decision Making Predict Relapse

Martin P. Paulus, MD; Susan F. Tapert, PhD; Marc A. Schuckit, MD

Arch Gen Psychiatry. 2005;62:761-768

Cue-Induced Brain Activity Changes and Relapse in Cocaine-Dependent Patients

Thomas R Kosten, Barbara Ellen Scanlan, Karen A Tucker, Alison Oliveto, Cherekma Prince, Rajita Sinha, Marc N Potenza, Pawel Skudlarski and Bruce E Wexler

Neuropsychopharmacology (2006) 31, 644–650

The role of self-reported impulsivity and reward sensitivity versus neurocognitive measures of disinhibition and decision-making in the prediction of relapse in pathological gamblers

A. E. Goudriaan, J. Oosterlaan, E. De Beurs and W. Van Den Brink

Risk-Taking on Tests Sensitive to Ventromedial Prefrontal Cortex Dysfunction Predicts Early Relapse in Alcohol Dependency: A Pilot Study

Neurobiological vulnerability: practical consequences

- Relapse
- Treatment effects (Marsha Bates et al.)
  - Pharmacological possibilities?
  - Prevention?
  - Training?
Future research: Interventions to improve neurobiological vulnerability

- Psychopharmacological
  - Agents to improve impulsivity? (modafinil?)
  - Agents to improve craving/cue reactivity?

- Improving brain functioning
  - EEG Biofeedback
    - Effects of an EEG biofeedback protocol on a mixed substance abusing population. Scott et al., Am J Drug Alcohol Abuse. 2005
  - Diminishing cue reactivity/attentional bias
    - Attentional retraining
    - Exposure therapy + (combi neuroimaging research)
Starting projects at AIAR

- Changing impulsivity in alcohol and cocaine dependence: modafinil and rimonabant
  - Longitudinal study: in treatment
  - fMRI study: pharmacological effect
  - Follow-up: relapse

- Lianne Schmaal, Dick Veltman, Wim van den Brink, Anneke Goudriaan
Proposal

Type I: Late onset, high anxiety/depression, stress related drinking

Type II: Early onset, high Antisocial traits, high reward sensitive

Slots: Late onset, high anxiety/depression, stress related gokken

Cards: Early onset, high Antisocial traits, high reward sensitive

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Why research collaboration?

- Combining research questions, that are not possible when doing small scale studies
- Studying subtypes of PG, that differ between countries, or that are similar (E.g. slot machine gamblers versus card gamblers)
- Interaction between neurobiological factors and environmental factors (e.g. proximity of casinos)
Conclusions

- In the treatment of addiction more attention should be paid to the improvement of neurocognitive functions, and the reduction of impulsivity.

- In addition to cognitive behavioral and pharmacological interventions, neurofeedback and other neurophysiological and neurocognitive treatments should be studied more intensively.
Thank you for your attention:

??????? Time for questions ????

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