

Neurocognitive Functioning in Opiate and Stimulant Users

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Phase I: R21DA18086

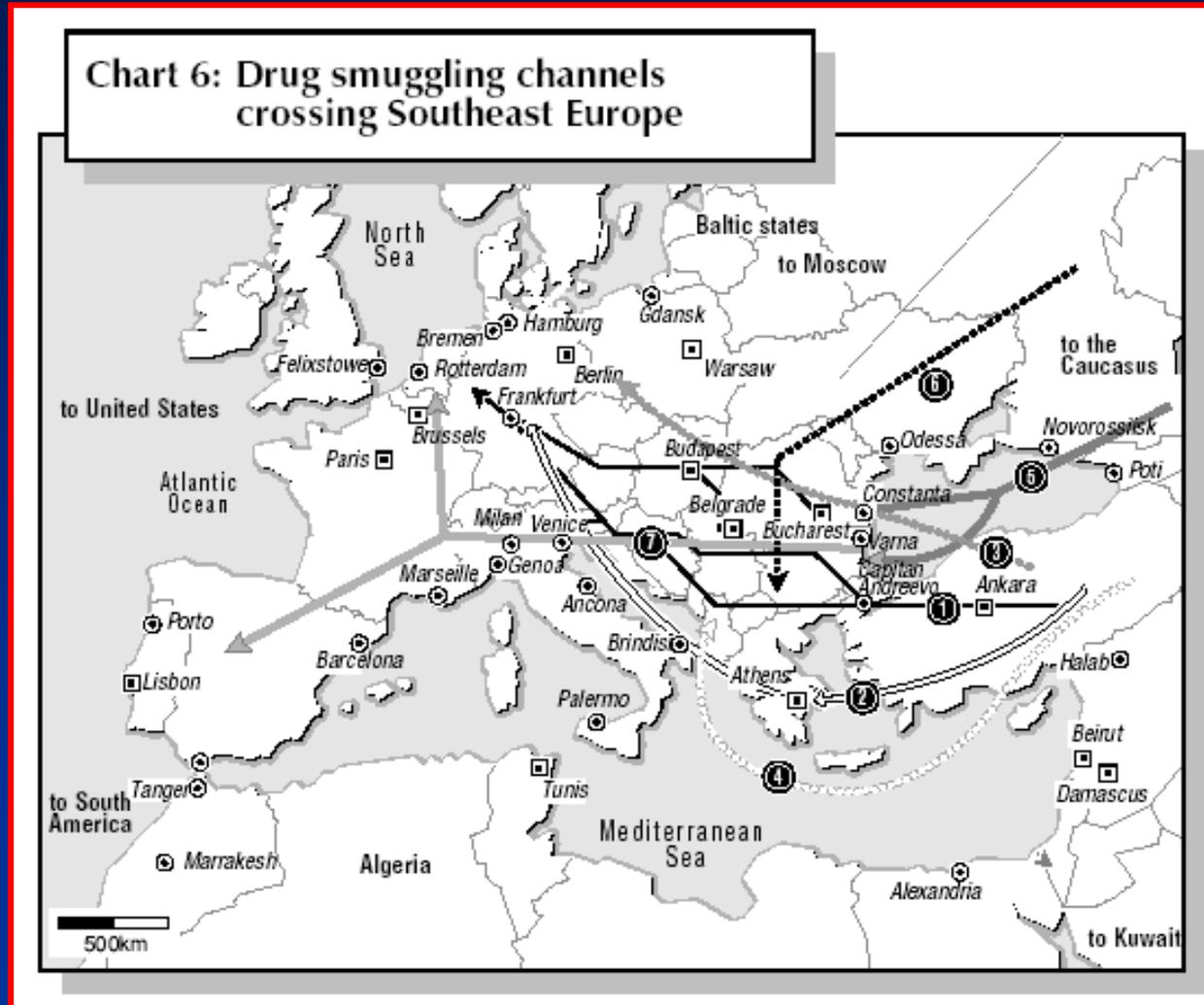
Neuro-Cognitive Sequelae of Opiate Use and Antisocial Behavior

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Why in Bulgaria?

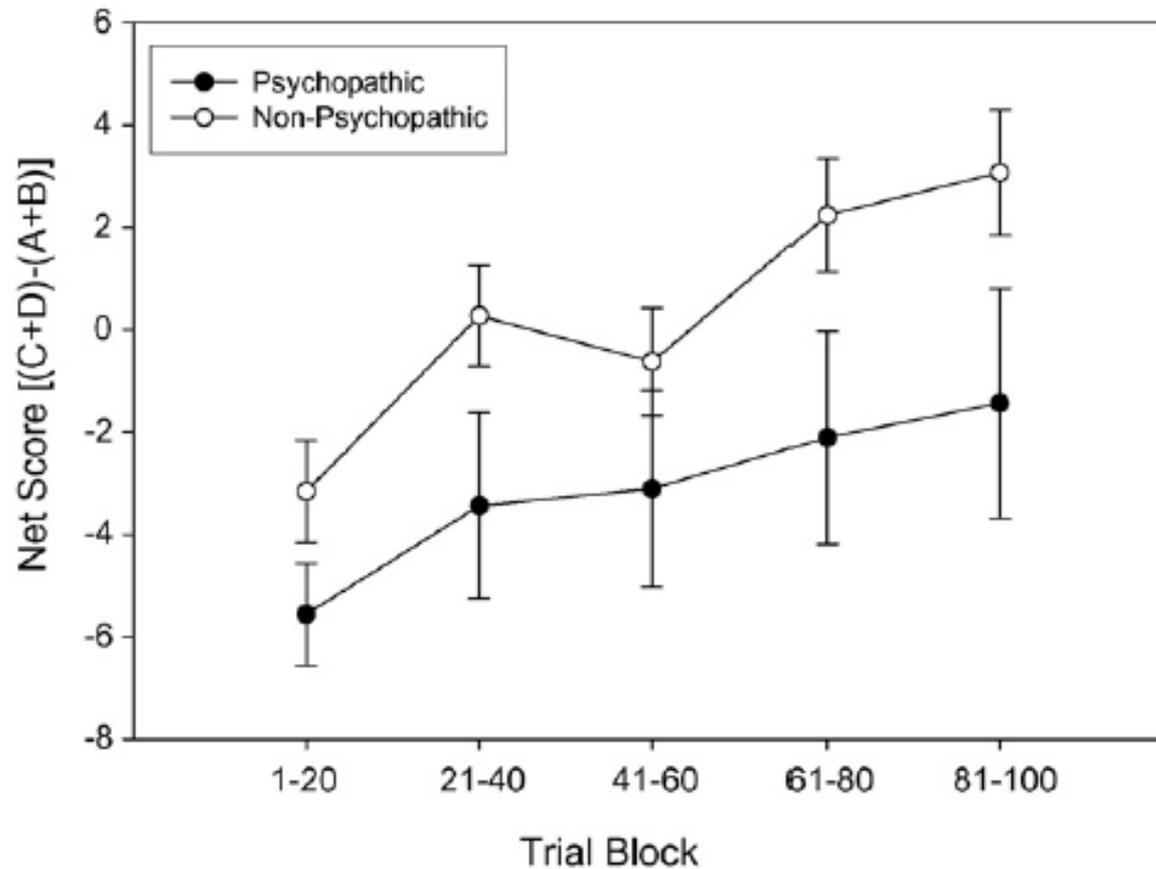
“Pure” monosubstance drug users



Goals

1. Assist Bulgarian scientists in developing research capacity for the study of neurocognitive functioning in relation to drug addiction and antisocial behavior
2. Take advantage of the unique patterns of heroin addiction in Bulgaria to address research questions that cannot be adequately addressed with data collected in USA

Initial Findings





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Short communication

Impaired decision-making in psychopathic heroin addicts

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Psychopathic heroin addicts are not uniformly impaired across neurocognitive domains of impulsivity

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Phase II: Varieties of Impulsivity in Opiate and Stimulant Users

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Drug Addiction – Major Public Health Problem in Bulgaria

- Heroin – Balkan Drug Trafficking Route
- Amphetamines – major European producer
- HIV risk behaviors

Objectives

- To understand the role of impulsivity in drug addiction
- Impulsivity is implicated both as antecedent risk factor and as a consequence of drug addiction
- Impulsivity is multidimensional and has different personality, psychiatric, and neurocognitive dimensions

Aims

1. Aim 1 - To determine whether individual differences in trait-like personality and psychiatric dimensions of impulsivity increase vulnerability to neurocognitive deficits in impulsivity
2. Aim 2 - To determine whether some dimensions of impulsivity are common across addictions, whereas others are unique to specific classes of drugs

Participants

| | Heroin | Amphetamine | Controls |
|--------------------|--------|-------------|----------|
| N | 96 | 87 | 105 |
| Age | 29.0 | 23.3 | 24.5 |
| Estimated IQ | 103.4 | 108.4 | 109.3 |
| Years of Education | 12.8 | 12.8 | 13.6 |
| % Female | 20 | 23 | 25 |

Assessment Battery

| Neurocognitive Measures of Impulsivity | Personality Measures of Impulsivity | Psychiatric Measures of Impulsivity | Other Relevant Measures |
|--|---|--|--|
| <u>Impulsive Choice</u> <ul style="list-style-type: none"> Iowa Gambling Task (ABCD & EFGH versions) Cambridge Gambling Task Delayed Reward Discounting Task Balloon Analog Risk Task <u>Impulsive Action</u> <ul style="list-style-type: none"> Immediate Memory Task Stop Signal Task Go/No-go Task | <ul style="list-style-type: none"> Barratt Impulsiveness Scale (BIS-11) Sensation Seeking Scale UPPS Impulsive Behavior Scale Buss-Durkee Hostility Inventory Levenson's Self-Report Psychopathy Scale | <u>Addictions</u> <ul style="list-style-type: none"> Substance Abuse / Dependence (SCID; Addiction Severity Index) Pathological Gambling (Addiction Severity Index) <u>Externalizing Psychopathology</u> <ul style="list-style-type: none"> ADHD (Wender Utah Rating Scale) Conduct Disorder (SCID) Antisocial Personality Disorder (SCID) Psychopathy (Psychopathy Checklist-Screening Version) | <ul style="list-style-type: none"> Alcohol/Drug toxicology screen Opiate/Stimulant Withdrawal Fagerstrom Test for Nicotine Dependence Pedigree (Family History of Substance Use Disorders) IQ Estimation (Raven's) Handedness Beck Depression Inventory-II State-Trait Anxiety Inventory Anxiety Sensitivity Index Risk Assessment Battery HIV Risk Behavior Scale Social Adjustment Scale |

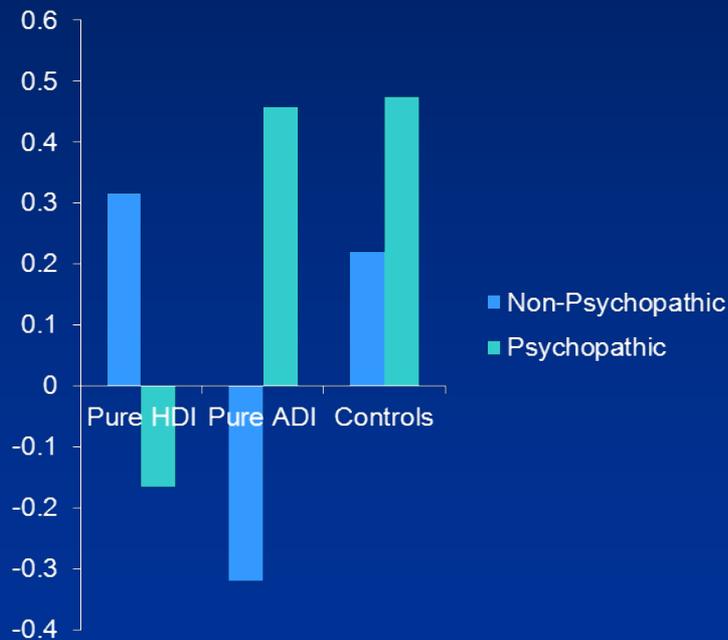
Results

Effects of Trait Impulsivity on Neurocognitive Impulsivity

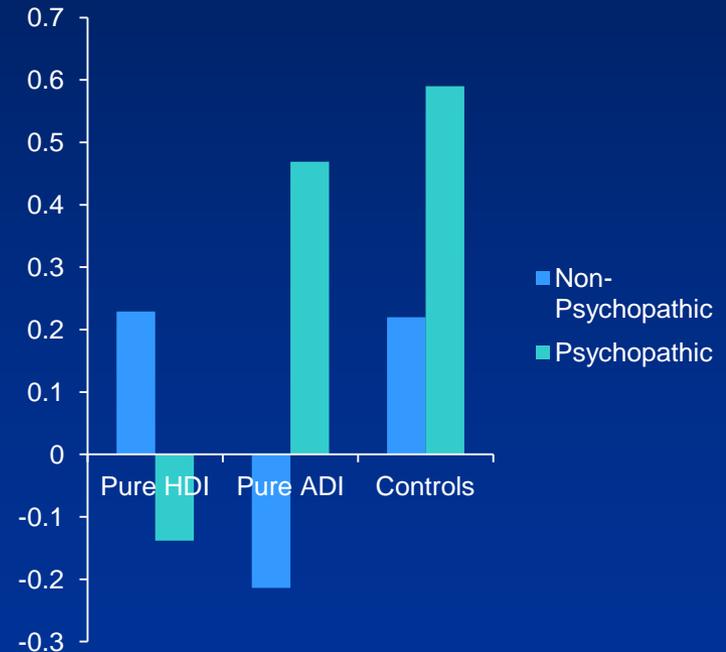
- High trait impulsivity is associated with worse performance on neurocognitive tasks of motor impulsivity / impulsive action in amphetamine users
- High trait impulsivity is associated with better performance on these tasks in heroin users

Effects of Psychopathy on Neurocognitive Impulsivity

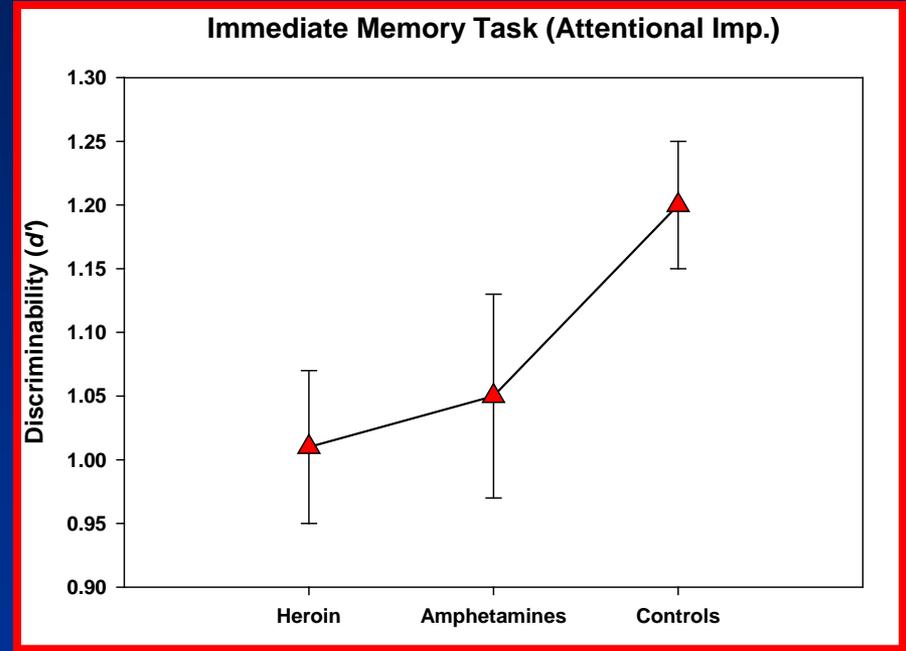
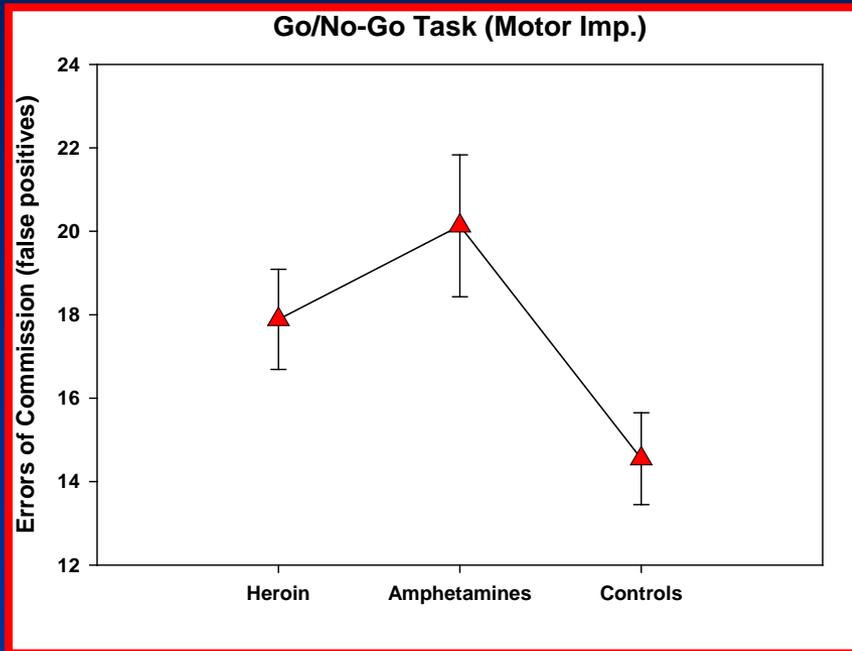
Cambridge Gambling Task Overall Proportion Bet



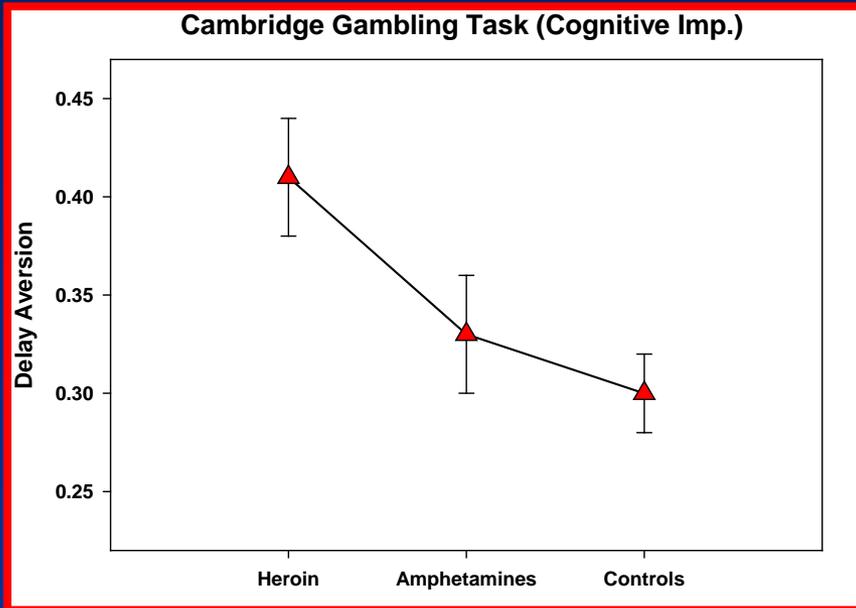
Cambridge Gambling Task Risk Taking



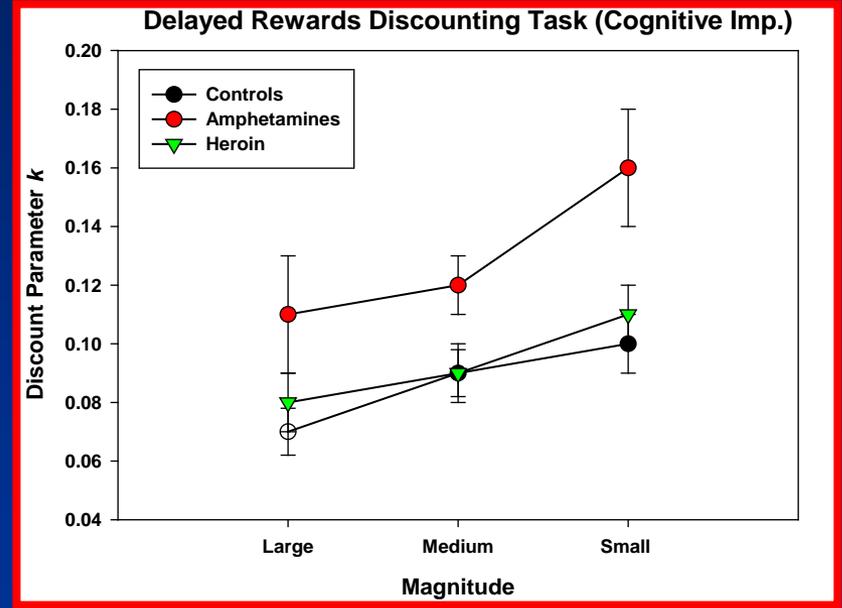
Common Effects across Addictions



Unique Effects of Opiates and Stimulants



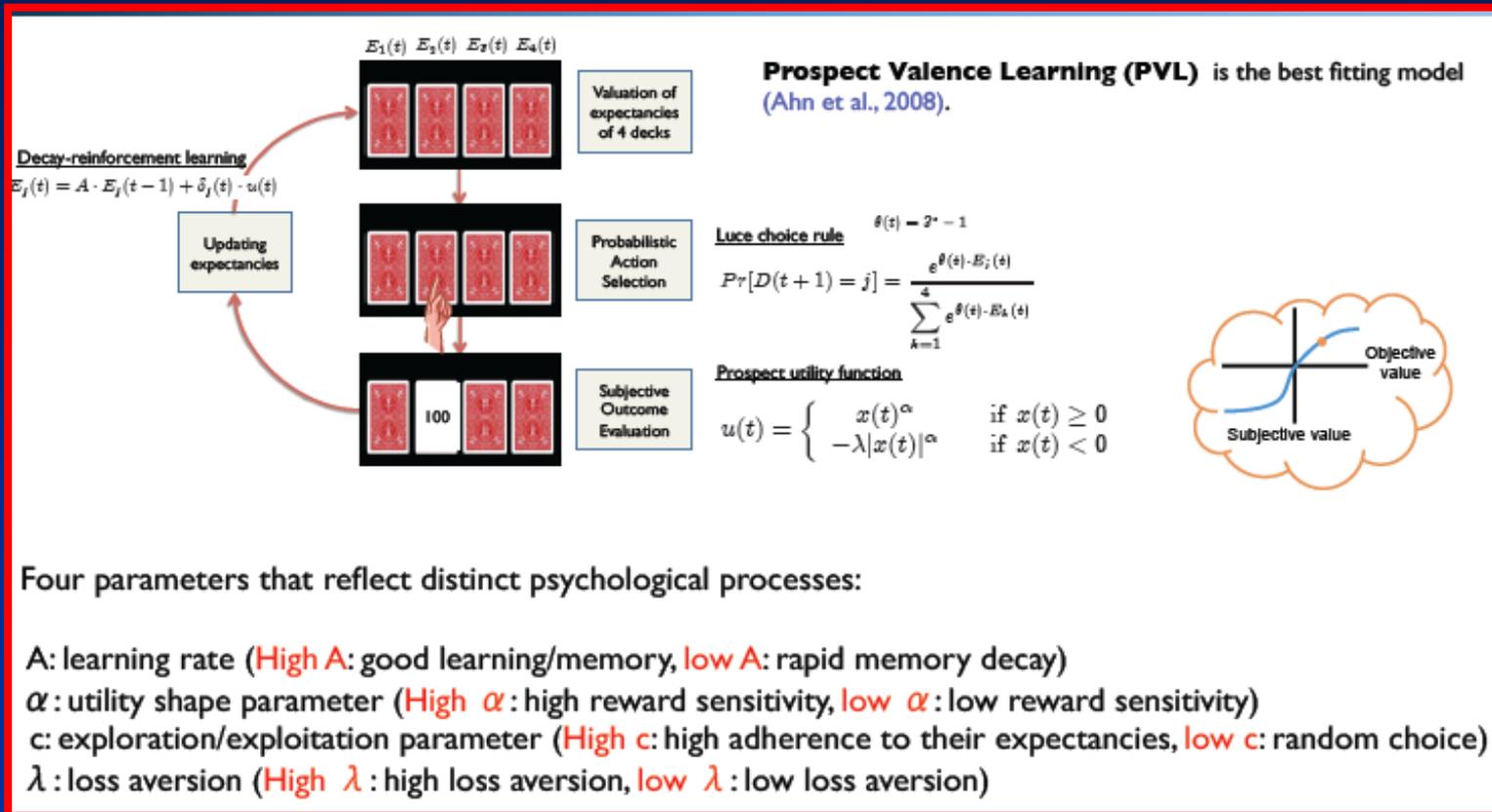
Heroin



Amphetamines

New Directions for Future Research

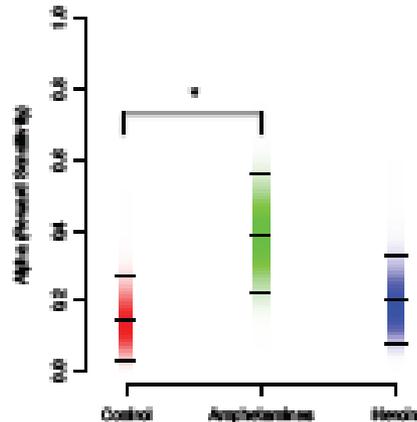
Computational Modeling of Decision-Making



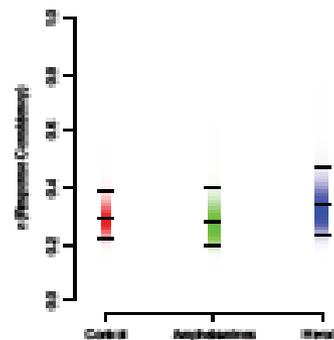
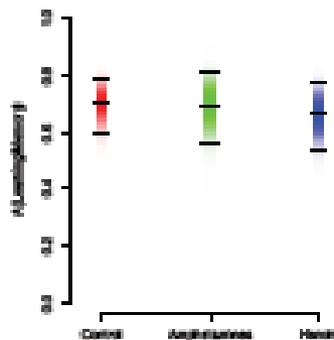
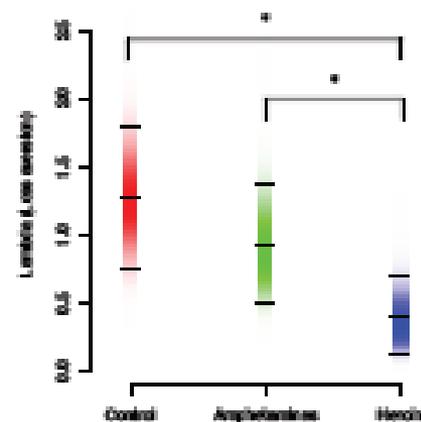
Computational Modeling Results

Distinct mechanisms underlying the performance deficits of the amphetamine and heroin users.

Reward sensitivity (Amphetamine > HC)



Loss Aversion (Heroin < HC, Amphetamine)



Similar learning/memory and exploration/exploitation across groups.

Heroin Drought in Europe 2010-2012

- Current Methadone Abusers n=26
- Compared with stable MMT patients (target n=30)
- In collaboration with “Initiative for Health Foundation” in Sofia

Neurogenetics

- DNA from 199 consenting participants (61 heroin, 61 amphetamines, 77 controls) collected, extracted and stored at the Molecular Medicine Center, Medical University, Sofia.
- 45 SNPs genotyped on 88 participants
- R01DA018823 “Neurogenetic Mechanisms of Opioid Dependence in a Bulgarian Roma Isolate” (under review)
- Co-PI with Alexandre Todorov (Washington University, St. Louis)

Focus on the Roma Population

- Genetic isolate with high specific vulnerability to heroin addiction
- Heroin – 1st drug used in 60% of cases, 53% report never having used another illicit drug other than heroin more than 5 times
- Particularly high risk group: 4.8% HIV+ (vs. 0.4% of non-Roma)
- In collaboration with Foundation Roma in Plovdiv and Diverse and Equal Foundation in Sofia
- Preparing targeted school-based drug and alcohol abuse prevention interventions for adolescents

Research Capacity-Building

- Translation and piloting of psychiatric instruments, self-report questionnaires, experimental neurocognitive paradigms, and clinical neuropsychological measures
- Cross-cultural adaptations of assessment instruments:
 - Psychopathy Checklist: Screening Version (Wilson et al., Submitted)
 - Barratt Impulsiveness Scale – 11 (Turan et al., in preparation)
- Student training and involvement in research
 - New Bulgarian University (2 graduate students)
 - Medical University Sofia (1 MD/PhD student, 2 graduate students)
 - Sofia University (1 graduate students)

Research Capacity-Building

- Publications in Bulgarian journals:
 - Bozgunov et al. (2011), *Clinical and Consulting Psychology*
 - Vassileva et al. (in press), *Bulgarian Journal of Psychology*
- 3 additional publications, 4 under review
- Conference presentations in Bulgaria:
 - 6th National Congress of the Bulgarian Psychological Association Sofia, (2011)
 - Keynote Address “Addiction as a brain disease” (Vassileva)
 - Symposium “The role of impulsivity in drug addiction and comorbid disorders” (Vasilev, Bozgunov, Naslednikova, Raynov, Vassileva)
 - Poster “Validation of the Bulgarian version of the Barratt Impulsiveness Scale -11” (Turan, Milanova, Vasilev, Vassileva)
 - Summer Research Forum at Varna Free University “Czernorisetz Hrabar” (Bozgunov, 2012; Vasilev, 2012)
 - Research conference at St. Cyril and Methodius University, Veliko Tarnovo (Bozgunov, 2012)
 - New Bulgarian University, Dept. of Cognitive Science (Naslednikova, 2012)
- 8 presentations in USA and 2 in Europe

Research Capacity-Building

- Development of additional international research collaborations
 - Molecular Medicine Center, Medical University, Sofia (Dr. Radka Kaneva)
 - Dept. of Psychiatry, Alexandrovska University Hospital, Sofia (Prof. Vihra Milanova)
 - Washington University, St. Louis, MO (Dr. Alexandre Todorov)
 - Indiana University, Bloomington, IN (Dr. Jerome Busemeyer)
 - King's College London (Dr. Patricia Conrod)

Challenges

- Post-communist / authoritarian style of leadership
- Unreasonably high financial expectations
- No traditions in local collaboration
- Stigma against drug addiction
- Brain drain
- Financial crisis
- Currency exchange rates

Collaborators

USA

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Vladimir Velinov, MD
Dorita Krasteva, MD

Thank You!

