STIMULANT USE AND PSYCHIATRIC COMORBIDITY

NUŠA ŠEGREC nusa.segrec@psih-klinika.si
ANDREJ KASTELIC
andrej.kastelic@psih-klinika.si

Center for Treatment of Drug Addiction
University Psychiatric Clinic Ljubljana, Slovenia
- high rate of concurrent psychiatric disorders among stimulant users

- a sample of 298 cocaine abusers seeking inpatient treatment

- 55.7% met current and 73.5% met lifetime criteria for a psychiatric disorder other than a substance use disorder

- major depression, minor bipolar conditions (e.g., hypomania, cyclothymic personality), anxiety disorders, antisocial and borderline personality, and history of childhood attention deficit disorder, PTSD

- \( \frac{1}{2} \) cocaine users have lifetime diagnoses of depression; 20-25% cyclic mood disorders

- higher prevalence among stimulants users than in general population
- **affective disorders**, **alcoholism** and **paranoia** usually follow the onset of stimulant use

- **anxiety disorders**, **antisocial personality**, **phobias** and **attention deficit disorder** typically precede stimulant use

- panic attacks correlate with cocaine use – risk of this problem may increase because of sensitisation to cocaine
comorbid psychiatric disorders versus stimulant-related disorders

- acute and chronic stimulant intoxication: phobias, OCD, panic disorder, GAD
- withdrawal from stimulants: major depression
- stimulant-induced psychosis: schizophrenia
demographic, clinical and historical correlates of substance abuse in patients with co-existing mental disorders

A. **Demographic correlates**

- gender (men)
- age (younger individuals)
- education (lower levels of educational attainment; the relationship tends to be stronger for drugs than alcohol)
- marital status (unmarried)
- cannabis = alcohol rural/urban environment; cocaine more in urban setting

B. Clinical correlates

- antisocial personality disorder, conduct disorder in younger patients

- adherence to treatment: irregular use of prescribed medications + substance use are associated with more relapses and hospitalizations

C. Historical correlates

- **social functioning before the onset of the disease**: most patients with dual diagnosis have better social functioning before the onset of disease compared to those without substance use disorder (they have greater exposure to substance use through their greater peer contacts)

- **substance use disorder in family**: risk factor for development of dual diagnosis

- **trauma and PTSD**: correlates with substance use

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# Neurotransmitters

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Withdrawal from chronic stimulant use leads to decreased synaptic availability of dopamine (DA) and serotonin (5-HT). This dual deficit contributes to withdrawal symptoms, drug craving, and relapse. DA dysfunction underlies anhedonia and psychomotor disturbances, whereas 5-HT dysfunction causes depressed mood, obsessive thoughts, and lack of impulse control. Protracted withdrawal phenomena are postulated to contribute significantly to relapse.
Individuals who experience more intense highs from cocaine tend to suffer more severe withdrawal symptoms. Quitting cocaine may be more difficult for them, because it involves greater sacrifice of pleasure and more physical and mental distress. (Adapted from Sofuoglu et al., 2003, with permission from Elsevier.)
withdrawal symptoms

- “crash” (dysphoria, anxiety, agitation → craving → fatigue, increasing depression, anhedonia, decreased mental and physical energy, intense desire for sleep, insomnia - replaces drug craving → hypersomnolence, intense hunger (a few days)

- “protracted withdrawal” - symptoms opposite stimulans intoxication: 90-120 days after discontinuation of substance use (mild dysphoria, difficulty concentrating, anhedonia, lack of energy, short-term memory disturbance, irritability); suicidality!

- prolonged in MA users

- significant changes in brain functioning lasting more than 6 months
The misuse of psychostimulant drugs: methamphetamine/amphetamines and crack/cocaine – is associated with the co-occurrence of depressive symptoms. Characterization of the type and time course of depressive symptoms in relation to stimulant use may inform the development of more target treatments for stimulant use disorders.

Studies suggest that dysphoria, irritability, and somatic/vegetative symptoms are common within the context of a stimulant use episode and during short-term abstinence. These symptoms tend to resolve to subclinical levels over more extended periods of abstinence. Other depressive symptoms, such as anhedonia (i.e., inability to experience pleasure) and amotivation (i.e., reduced drive to perform activities), however, may persist over longer periods of remission. In addition, there is some evidence to suggest that anhedonia and amotivation may actually predate stimulant use.
stimulant-induced psychoses

- increased use of cocaine by patients with severe mental illness over the past decade
- after short-lived euphoria person experiences anxiety, depression, irritability, extreme fatigue and paranoia; tactile hallucinations of insects crawling underneath the skin – known as formication
- cocaine-induced paranoia is well known in regular cocaine users (which use it on heavy basis)
- more prevalent among amphetamine and MA users than cocaine users (shorter half-life)

Ellinwood EH, King G, Lee TH. Chronic amphetamine use and abuse. Neuropsychopharmacology 2000
- **Acute** administration of very large doses of central stimulants (laboratory-induced)

- **Chronic** repeated intoxication: hallucinations (up to 80%) – auditory visual, paranoid ideation, fears of persecution, hyperactivity, panic

- Japan: epidemic of injected amphetamine use in the past, psychosis appeared to be prolonged and chronic (also laboratory induced psychoses with amphetamines)

- Psychotic symptoms occur in approximately 40% of patients who are dependent on amphetamines, particularly in those receiving high-dose
stimulant - induced psychoses

- stimulant-induced psychoses are very likely to clear within several days to about a month of abstinence
- cocaine –induced psychosis resolves more quickly (1-3 days) than MA – induced psychosis (up to 2-3 weeks)
- only 1-15% of patients maintain some psychotic symptoms after month; they mostly disappear in a few days or one month
- if hallucinations and/or delusions without insight continue after a month to 6 weeks of abstinence, the symptoms may well represent an independent psychotic disorder that requires long-term antipsychotic medication
stimulant-induced psychoses

- large enough dose of stimulant drug can produce brief psychotic reaction (usually only hours in length)

- more pronounced in patients who already have active symptoms of psychosis with pre-existing psychotic symptoms and is seemingly unaffected by antipsychotic medication

- patients with schizophrenia (taking antipsychotic therapy) are not necessarily protected against deterioration of psychotic illness in this case

- long term use of stimulants can lead to so called „sensitisation“ and development of chronic psychosis – long term treatment with low doses of antipsychotics is useful in those cases
stimulant-induced psychoses

- cocaine when taken with alcohol forms a metabolite cacaethylenne, which has significantly long half-life and is more potent than cocaine

- greater risk of violence and unsafe sexual behaviour

- withdrawal from crack cocaine can be followed by intense craving and withdrawal symptoms

other stimulant (amphetamine) induced psychopatologies  

- confusional states
- emotional lability syndromes (might have characteristics of manic episode)
- bizzare sexual behaviour
- destructive outbursts
- unmotivated assaults (fugue-like responses)

Ellinwood EH, King G, Lee TH. Chronic amphetamine use and abuse. Neuropsychopharmacology 2000
patients with drug induced psychotic disorder

- significantly later age of onset of psychosis
- greater conjugal ties
- greater antisocial personality disorder comorbidity
- more frequent homelessness
- poorer family support
- more subjects had a parent with a substance abuse problem
- more severe forms of substance use disorders
- characterized by long periods of substance use, multiple drugs
- severe psychosocial problems
- greater dependence
- visual hallucinations are more frequent

➢ subjects with primary psychosis had more severe psychiatric symptoms associated with less insight, a finding that is not limited to positive symptoms but also includes negative symptoms and general psychopathology

➢ certain types of auditory hallucinations (i.e. two or more voices conversing with one another or voices maintaining a running commentary on the person's thoughts or behaviour) have been considered to be particularly characteristic for schizophrenia

➢ people who abuse cocaine and become paranoid maintain their abstract thinking and basic clear thinking; they have delusions that are poorly developed and of a non-bizarre nature

...pharmacotherapy of stimulant addiction

- **atomoxetine**: (NET inhibitor-treatment of ADHD): attenuate some subjective effects ("good effects")
- **alpha2-adrenergic agonists**: clonidine, *lofexidine*, guanfacine; attenuate stress-induced reinstatement of cocaine seeking
Cocaine causes euphoria and reinforcement by raising dopamine levels in the mesocortical reward system. One potential way to counterbalance this effect is to elevate mesocortical levels of gamma-aminobutyric acid (GABA), a neurotransmitter that pushes dopamine levels downward by inhibiting the activity of dopaminergic (dopamine-releasing) neurons (gamma-Vinyl GABA, topiramate, tiagabine).

TA-CD Vaccine works by stimulating the production of cocaine-specific antibodies that bind to cocaine molecules and prevent them from crossing the blood–brain barrier (blunting the drug’s euphoric and reinforcing effects). Two doses of TA-CD were tested in cocaine-dependent patients in a 12-week outpatient treatment program. Preliminary outcome data suggested that the vaccine reduced the euphoric effects of cocaine; the higher dose was associated with more cocaine abstinence compared with the lower dose (Martell et al., 2005).

pharmacotherapy of stimulant addiction

- **Bupropion**’s efficacy rests upon its ability to support positive mood by inhibiting the reuptake of dopamine into cells, leaving more of the neurotransmitter circulating in the mesolimbic system; the same mechanism may be helpful in easing the negative mood symptoms of methamphetamine withdrawal.
- Studies have shown bupropion to be ineffective in treating cocaine dependence, but it may have promise for methamphetamine dependence.
- Atypical antipsychotics, especially aripiprazole, may have a role in reducing craving (cocaine in comorbid schizophrenia and MA-induced psychosis)

Center for Treatment of Drug Addiction, University Psychiatric Clinic Ljubljana, Slovenia

- Outpatient clinic
- Detoxification unit
- Day center
- Intensive treatment unit
- Adolescent program
- Crisis intervention
- Training, research, coordination

- Center of excellence
outpatient program for patients with dual diagnosis
center for treatment of drug addiction,
university psychiatric clinic ljubljana, slovenia

- for patients with comorbidity of substance use and other mental disorder
- integrative treatment program (integrating psychiatric and substance abuse services/approaches)
- outpatient program – daily hospital
- primarily substance-abuse treatment setting
design

- group therapy program
- low intensity program
- inclusion criteria: comorbidity of substance use disorder and mental illness, some degree of motivation (desire)
- exclusion criteria: acute relapse of mental disorder (for example: psychotic illness – which requires hospitalisation)
- psychoterapy group: co-lead by a psychiatrist and psychologist
- psychoeducational group
- supportive and educational therapy model
- up to 10 patients
  - each group: 60 min
- reduce use of drugs (abstinence)
- reduce rates of relapses and hospitalisations (comorbid mental disorder)
- better adherence to and response to medication
- reduce suicide risk
- support to family members
- reduce aggression, violence, criminal behavior, victimisation
- reduce homelessness
- reduce risky behavior and infectious illnesses
- reduce accidents due to acute effects of drugs
- indirectly reduce morbidity and mortality