The recovery process for substance use disorders: psychobiological correlates of psychosocial interventions

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Psychosocial interventions for recovery are able to induce stable changes in the brain function and possibly to revert brain dysfunction.
Denial
Moralism
Ignorance

Good boy

Bad boy
Subst. Abuse

Attitudes, practices, and preparedness to care for patients with substance use disorder: Results from a survey of general internists.
Wakeman, 2016

22% felt prepared to screen SUD
7% to discuss behavioural treatments
9% to discuss medication treatments

31% felt that SUD is different from other chronic diseases because using substances is a choice

12% of hospitalists believe that someone who uses drugs is committing a crime and deserves punishment
genetic factors, environmental, social factors contribute to the determination of a person’s unique susceptibility to using drugs initially, sustaining drug use, undergoing the progressive changes in the brain that characterize addiction.

Volkow et al., 2016

Drug dependence, a complex multifactorial health disorder (UN General Assembly, 2016)
Individual vulnerability underlying drug initiation and alcohol abuse

- Early childhood wellbeing, care social inclusion
- Parent child secure attachment
- Gene variants, positive temperament
- Pregnancy: mother wellbeing
- Parent child insecure attachment
- Gene variants, problematic temperament
- Pregnancy: mother stress

- Early childhood adversity, stress neglect abuse trauma social exclusion
- Lack of bonding to family and school
- Drug availability peer pressure
- No drug availability Low peer pressure

- Bonding to family and school
- No mental health disorders/SUD
- Early onset mental health disorders/SUD
- Drug availability peer pressure
- No drug availability Low peer pressure

- Parent child secure attachment
- Gene variants, positive temperament
- Pregnancy: mother wellbeing
- Parent child insecure attachment
- Gene variants, problematic temperament
- Pregnancy: mother stress
Vulnerability factors for substance use disorders

- Prenatal stress
- Early chronic stress: neglect – abuse, weak attachment
- Lack of school connectedness
- Parents substance use
- Exposure to drugs in early teens
- Continuous substance use
- Disrupted dopamine system
- Glucocorticoids HPA axis dysfunction
- Compulsive behaviour

Substances available for non medical purposes
Genetic and epigenetic regulatory events underlie the changes throughout the reward circuitry in humans.

Motivational system highjacked by drugs.

Conditioned compulsive behavior established.

Methylation - Acetylation
Psychiatry J.
Epigenetic and Neural Circuitry Landscape of Psychotherapeutic Interventions.
Miller, 2017.

How corrective environmental factors may promote epigenetic change and reconfigure neural templates, allowing for symptomatic improvement.

Psychotherapy is one such factor.
SCI REP.

DNA methylation signatures of chronic alcohol dependence in purified CD3+ T-cells of patients undergoing alcohol treatment.
Brückmann et al., 2017

The mean global DNA methylation was significantly lower in patients prior to treatment compared to controls, but reverted back to levels similar to controls after treatment.
Brückmann et al., 2017
Psychother Psychosom.

**Review of psychodynamic psychotherapy neuroimaging studies.**
Abbass et al., 2014

**normalization of synaptic or metabolic activity**

in
- limbic
- midbrain
- prefrontal regions

in association with **improved clinical outcomes**.

Psychotherapy has demonstrable effects on brain function in diverse clinical populations.
Treatment intervention

1) Emotions regulation
Alexithymia in Young Adults With Substance Use Disorders: Critical Issues About Specificity and Treatment Predictivity.
Parolin et al., 2018
Dysregulated responses to emotions among abstinent heroin users:
Correlation with childhood neglect and addiction severity

Childhood neglect
Altered response to emotions
HPA axis dysfunction
Addiction Severity

Gerra et al., 2013
- expression of emotions

- regulation of emotions

particularly difficult for people with Substance Use Disorders

trigger factor maintaining the substance use

target for treatment
PTSD Symptom Severity and Emotion Regulation Strategy Use During Trauma Cue Exposure Among Patients With Substance Use Disorders: Associations With Negative Affect, Craving, and Cortisol Reactivity. Tull et al., 2018

PTSD symptom severity:
- adaptive (e.g., distraction)
- maladaptive (e.g., suppression) regulation strategies.

cortisol reactivity

negative affect

target for treatment
Responders to psychotherapy showing higher gene expression at post-treatment than non-responders.

Psychotherapy constitutes a form of “environmental regulation” that may alter epigenetic state.
Treatment intervention

2) Attachment
Addiction as an attachment disorder. Unterrainer et al., 2017

Substance Use Disorders as a possible expression of an attachment disorder

Disorganized
Insecure
Anxious

Silent epidemic
A general link between substance Use Disorders and insecure attachment.

Fearful avoidant attachment -------------- Heroin use disorder

Fostering attachment security might improve treatment outcome

Epigenetic modification of the oxytocin and glucocorticoid receptor genes is linked to attachment avoidance in young adults.

Ein-Dor et al., 2018
An insecure attachment style was more common among the SUD outpatients compared to non-clinical groups.

Patients with a fearful attachment style scored higher on psychological distress than patients with a secure attachment style.

Significantly more patients had a secure attachment style at treatment end.

The psychological treatment of patients with SUD contributed significantly to changes from insecure to secure attachment style.
Increased attachment security is related to early therapy drop-out in substance use disorders. Fuchshuber et al., 2018

A negative predictive value of increased attachment security for Treatment Adherence in Substance Use Disorders inpatients
Front Psychol.

**Parenting quality in drug-addicted mothers in a therapeutic mother-child community: the contribution of attachment and personality assessment.**

De Palo et al., 2014

prevalence of insecure attachment representations (90%),

dangerous / not protective experiences in infancy: neglect and rejection

insightful indications both for **treatment planning** and intervention on parenting functions
Maternal support in early childhood predicts larger hippocampal volumes at school age. Luby et al., 2012

Maternal support has been shown to promote specific gene expression and neurogenesis.
Treatment intervention

3) Connectedness, compassion and love
Addict Res Theory.

Clinical theory in therapeutic communities (TCs) for substance abuse treatment: the importance of peer interactions in bringing about change.

TC residents react more pro-socially to behavioural intervention by peers than by staff.
The neurobiological link between compassion and love.
Esch and Stefano, 2011

Love and compassion exert pleasant feelings and rewarding effects

- brain's limbic motivation
- reward circuit activation
- self-regulation of emotions
- approach behaviors
- pair bonding
- social contact in general

Love, attachment and compassion can be highly effective in stress reduction, survival and overall health
BMJ Open.
Enhancing Social Interaction in Depression (SIDE study): protocol of a randomised controlled trial on the effects of a Cognitively Based Compassion Training (CBCT) for couples. Aguilar-Raab et al., 2018

- reduction of depressive symptoms ↓
- attention towards the partners face ↑
- relationship quality and empathy ↑

stress-related biomarkers:

- cortisol ↓
- α-amylase ↓
- interleukin (IL)-1β/IL-6 ↓
- heart rate ↓
- methylation of oxytocin-receptor-genes ↑
- methylation of serotonin-transporter-genes ↑
The relationship between sense of community belonging and self-rated mental health among Canadians with mental or substance use disorders. 
Pali et al., 2018

Self-rated mental health was reported as follows:
poor or fair (38.1%)
good (33.7%)
very good or excellent (28.2%)

Those reporting very strong compared to very weak community belonging had an increased odds of better mental health.

Findings indicate the importance of social and community-based interventions to effectively engage and retain individuals in services for the prevention and treatment of mental and substance use disorders.
Cytokine variations and mood disorders: influence of social stressors and social support.
Audet et al., 2014
- greater social connectedness
- perceived social support
- optimism
- preference for adaptive coping responses

a broader profile of psychosocial resilience that reduces risk of adverse physical health outcomes.

Cortisol ↓
Inter-leukine ↓
Heart rate ↓
Psychological status ↑
Treatment intervention

4) Physical Exercise
SUD: "imbalance" between frontal/regulatory and cortical-subcortical circuits, leading to impulsive and reward-driven behaviours.

Exercise stimulates dopaminergic systems that, in turn, enhance general plasticity, learning, and memory.

Exercise may help to reinforce the underdeveloped connections between reward and regulatory processes

rationale for the utilization of exercise, particularly "assisted" exercise
After 8 weeks, participants in the exercise group displayed a significant increase in striatal D2/D3 receptor availability, whereas those in the education group did not.

Structured exercise training can ameliorate striatal D2/D3 receptor deficits in methamphetamine users.
Physical Exercise and Job Skills
Treatment intervention

5) Cognitive/ executive function training
Impact of general cognition and executive function deficits on addiction treatment outcomes: Systematic review and discussion of neurocognitive pathways.
Domínguez-Salas et al., 2016

- General cognition → Treatment adherence
- Limited cognitive-executive resources → Less ability to benefit from talk therapies

Cognitive training
School completion

Cognitive training interventions that improve task-switching performance may be beneficial in promoting effective emotion regulation and improved SUD treatment outcomes.
Task-Switching Performance Improvements After Tai Chi Chuan Training Are Associated With Greater Prefrontal Activation in Older Adults.
Wu et al. 2018

Role of Pre-Frontal Cortex in recovery
significant gains in memory for knowledge-related events

selective decrease in hippocampal activation for successful memory formation

knowledge facilitates binding in the hippocampus
by enhancing its communication with the association cortices

Studying in the recovery process
Treatment intervention

6) Dealing with co-occurring mental health disorders
Depression and anxiety are prevalent in methamphetamine users.

Short-term abstinence improves depression and quality of life but does not improve anxiety in methamphetamine users.

*Addressing depression and anxiety is important to achieve better results*
Cognitive Behavioural Therapy (CBT) to treat panic disorder: responders were shown to have increased methylation of the MAO-A gene (reaching levels similar to controls), while non-responders showed demethylation.

Miller, 2017
Int J Neuropsychopharmacol. 
**Plasticity of Functional MAOA Gene Methylation in Acrophobia.** 
Schiele et al., 2018

Psychotherapy increased MAO methylations and reduce anxiety
Increased *BDNF* methylation in saliva of patients with borderline personality disorder
Thomas et al., 2018

*BDNF* methylation in saliva of Borderline Personality Disorder patients significantly decreased after a 12-week psychotherapeutic intervention.
19.4% of the patients screened positive for concurrent adult ADHD
Lower education attainment rate
Lower employment rate
More co-occurring mental health disorders
Higher smokers rate
Homovanillic acid (HVA) plasma levels inversely correlate with attention deficit-hyperactivity and childhood neglect measures in addicted patients. Gerra et al., 2007
Treatment intervention

7) Activate reward/motivation
J Addict Med.
Possible evidence for re-regulation of HPA axis and brain reward systems over time in treatment in prescription opioid-dependent patients.
Bunce et al., 2015

- dorsolateral prefrontal cortex activation by natural reward cues
- day-time cortisol levels

correlated with the number of days since last drug use (time in supervised residential treatment)

re-regulation of dysregulated hypothalamic-pituitary-adrenal axis and brain reward systems over the drug-free period in residential treatment
Increased frequency of social interaction is associated with enjoyment enhancement and reward system activation. Kawamichi et al., 2016

the high-frequency condition produced stronger activation in the ventral striatum, which is part of the reward system, and the pre-cuneus, representing positive self-image, which might be translated to social reward.
Med Hypotheses.
Do dopaminergic gene polymorphisms affect mesolimbic reward activation of music listening response?
Therapeutic impact on Reward Deficiency Syndrome (RDS).
Blum et al., 2010

it is reasonable to assume that music is a strong indirect D2 agonist by virtue of Dopamine neuronal release in the NAc and may have important therapeutic applicability in Reward Deficiency Syndrome (RDS)
Int J Psychophysiol.

**Neuroendocrine responses of healthy volunteers to 'techno-music': relationships with personality traits and emotional state.**

Gerra et al., 1998

Beta-endorphine
ACTH
Norepinephrine
Growth Hormone
Cortisol

Changes in emotional state and NE, beta-EP and GH responses to techno-music correlated positively with the **novelty-seeking** temperament score

Behaviour-modification method of providing reinforcement in exchange for objective evidence of a desired behaviour.

Negative urines → Job skills → [Image of money]
Treatment intervention

8) Spirituality
- having personal beliefs
- fostering feelings of hope
- building a new sense of identity
- gaining ownership over one's life,
- finding support in spirituality
Yoga
Meditation
Acupuncture
Mindfulness
Religious/spiritual practices

cortisol
epinephrine
norepinephrine
inflammatory processes
cytokines
J Reward Defic Syndr.
NIDA-Drug Addiction Treatment Outcome Study (DATOS)
Relapse as a Function of Spirituality/Religiosity.
Schoenthaler et al., 2015

Stronger spiritual/religious beliefs and practices are directly associated with remission from abused drugs

- Emotions regulation
- Interacting with peers in a social environment
- Perceiving secure and organized attachment
- Belonging to the group/community
- Exercising regularly
- Training cognitive/executive function
- Appreciating natural rewards
- Experiencing compassion and love
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