Psychological intervention with working memory training increases basal ganglia volume:

A VBM study of inpatient treatment for methamphetamine use

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Outline

• Background

• Methods

• Main findings

• Conclusions

• Future directions
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Background
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- The notion underlying the *addiction* concept is that substance use or behavior that was *impulsively* acted upon for pleasurable recreation becomes *compulsively* driven.

- *Substance related and addictive disorders (DSM-5) – mild – moderate – severe*

- *Impulsivity* versus *compulsivity*, what’s the difference?
  
  - *Impulsivity*: Little ‘thinking’ involved, knee-jerk, automatic, non-consciously derived, e.g. binge-eating, drug taking, aggression. A natural tendency.

  - *Compulsivity*: ‘Thinking’ is consumed by desire to obtain a substance or engage in a behaviour, cannot think of anything else, obsessions, ruminations, cognitive bias. A maladaptive tendency.
According to the South African Community Epidemiology Network on Drug Use (SACENDU), impulsive, compulsive and attention deficits contribute to rising relapse rates for addiction in South Africa.

This is problematic for a low-to-middle income (LMIC) country.

Curative measures in South African populations are costly, particularly in terms of providing clinical interventions that attempt to reduce relapse.

Preventative measures, such as strengthening cognitive resilience in children and adolescents, may be an encouraging avenue to pursue for a LMIC.
Background

- Skinner’s operant/instrumental conditioning (ventral striatum/nucleus accumbens) and learning

- Pavlov’s classical conditioning (dorsal striatum) and habit formation

Everitt, 2014 – EJN: 40, 2163-2182
Brain regions involved in addiction

A. Brain reward pathways

- Prefrontal cortex (PFC)
- Cingulate gyrus (CG)
- Striatum
- Substantia nigra
- Nucleus accumbens (NAc)
- Ventral tegmental area

B. Non-addicted brain

- Control & Self-regulation (PFC, CG)
- Salience (NAc) → Drive (OFC) → NOT Go
- Memory (Am, Hip)

C. Addicted brain

- Control & Self-regulation (PFC, CG)
- Salience (NAc) → Drive (OFC) → Go
- Memory (Am, Hip)
The striatum problem of addiction

BRAIN RECOVERY WITH PROLONGED ABSTINENCE

Healthy Person

METH Abuser 1 month abstinence

METH Abuser 14 months abstinence
A reminder of the location of the striatum
A reminder of the fronto-striatal network

- Functions:
  - Reward (motivation)
  - Pleasure, euphoria
  - Motor function (fine tuning)
  - Compulsion
  - Perseveration

- Dopamine Pathways:
  - Frontal cortex
  - Nucleus accumbens
  - VTA
  - Hippocampus
  - Raphe nucleus
The dorsolateral prefrontal cortex (DLPFC)

MRI Scans of Healthy Children and Teens Over Time

The DLPFC in ANOREXIA NERVOSA

Restraint and BMI predicts 57% of variance in the DLPFC volume in anorexia.

AGE RELATED REDUCTION IN THE RIGHT DLPFC IN HEALTHY WOMEN BETWEEN 18yrs – 50yrs

NO AGE RELATED REDUCTION IN ANOREXIA WOMEN OF SIMILAR AGE…. WHAT IS SAVING THEIR VOLUME?

HIGHER RESTRAINT SCORE = LARGER DLPFC VOLUME.

Restraint and BMI predicts 57% of variance in the DLPFC volume in anorexia

Brooks et al. BMC Psychiatry (2011)
The DLPFC in obesity

Elderly obese (n=59) Elderly Lean (n=97)

Brooks et al., 2013 (Int J Obesity)
Impulse control spectrum

ADDICTION??

Brooks et al., 2012, BMC Psychiatry
The DLPFC in ADDICTION

Loughead et al., 2015. Neuropsychopharm
The DLPFC is linked to WORKING MEMORY

Baddeley & Hitch, 1974
Working memory and addiction

• Capacity to keep in mind lots of cognitive strategies/predictions about the environment

• Over-sampling the environment versus “jumping to conclusions”
Brain and working memory training

- No studies in humans have yet demonstrated volumetric changes following working memory training in addiction, however...

- Animal studies of WM training support the hypothesis that frontostriatal circuitry changes coincide with learning and memory. For e.g....

- Volume increase in the medial striatum in mice is implicated in spatial WM training (Pooters et al., 2015)
Brain and working memory training

• Epigenetic effects in the dorsal and medial striatum in mice after WM training (Cassanelli et al., 2015).

• Methylation sequences in prefrontal cortex neurons of mice are shown to be susceptible to WM training effects (Jakovcevski et al., 2015)

• Cerebellar volume is associated with plasticity-related volume increases during motor WM learning in mice (Yamazaki et al., 2015)
Brain and working memory training

• The nature of volumetric changes following a course of psychological intervention for methamphetamine use is not yet known

• Given that standard treatment (e.g. CBT, DBT) is still linked to high relapse rate post treatment....

• It is useful to compare volumetric brain changes after standard treatment AND working memory training that may boost treatment effects
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25 healthy control males baseline measures
- MRI scan
- Questionnaires
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41 males being treated at the inpatient centre over 8 weeks for methamphetamine use disorder
- MRI scan
- Questionnaires

17 male patients received treatment as usual
24 male patients received treatment as usual AND 4 weeks cognitive training
- 20 x ½ hour sessions of progressively difficult N-back task
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**Research Design**

- **Treatment as usual with DBT**
  - Psycho-education
  - Re-feeding

- **Cognitive training App**
  - Over 4 weeks, 30 minutes daily

**Questionnaires**
- Impulsivity
- Self-control
- Mood
- Anxiety
- Depression
- Self-regulation

**N=25**

**N=17**

**N=24**
Average characteristics of methamphetamine user

• Male
• Age 22 years
• Matriculation level education
• Mixed-race
• Methamphetamine as primary substance
• Nicotine/dagga/mandrax smoker
• No HIV
• No psychoses
• Abstinent for 2 weeks in clinic (after admission)
Clinical and research setting

Cape Universities Brain Imaging Centre (CUBIC), UCT Dept. of Psychiatry (below) Head of Dept. Prof. Dan Stein (right)

Maitland Treatment Centre (above) – led by Kamal Kamaloodien (right)

Prof Dan Stein

Kamal Kamaloodien
Curb Your Addiction (C-Ya)
N-back (working memory) task
Curb Your Addiction (C-Ya)
N-back (working memory) task
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C-Ya training in adults with methamphetamine addiction

LEARNING HAPPENED!!
Neuropsychological data after C-Ya training

- Barratt Impulsivity Total Score
- Self Regulation Questionnaire Total Score
- HADS Depression Score
- % Mood score

Brooks et al., Under Review
Principal Component Analyses

Brooks et al., Under Review
ANCOVA Volumetric Results

- Bilateral Cerebellum
- Bilateral Dorsal Striatum
- Medial Prefrontal Cortex

Brooks et al., 2016
NeuroImage: Clinical
Positive correlation with higher working memory accuracy in scanner (both groups)

- Medial Prefrontal Cortex

Brooks et al., 2016
NeuroImage: Clinical
Larger volume at baseline compared to both follow-up groups (risk for motor impulsivity?)

- Bilateral Cerebellum

Brooks et al., 2016
NeuroImage: Clinical
More pronounced larger basal ganglia volume with cognitive training compared to treatment as usual.
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**Conclusions**

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<thead>
<tr>
<th>Treatment as Usual</th>
<th>Working Memory Training</th>
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<tbody>
<tr>
<td></td>
<td>Lowers self-reported impulsivity</td>
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<tr>
<td></td>
<td>Increases self-reported self-regulation</td>
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<td></td>
<td>Lowers self-reported depression</td>
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<td></td>
<td>Increases self-reported mood</td>
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<td>Larger bilateral cerebellum volume at baseline may indicate risk for continued impulsivity</td>
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<td>Larger medial prefrontal cortex volume may indicate good treatment outcome</td>
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<td>Larger left dorsal striatal volume</td>
<td>More pronounced bilateral striatal volume</td>
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Future directions

- Methylation studies – how does working memory training alter genetic expression in fronto-striatal circuitry in humans with addictive and other impulsive/compulsive disorders?

- Can working memory training enhance impulse control in children prone to ADHD and exposed to substance use?

- Can the Curb Your Addiction App be used by people who find it difficult to attend regular treatment in Cape Town, to improve relapse rates?
THANKS!!

https://www.drsamanthabrooks.com/curb-your-addiction