A large burden of disease; What to do? Therapy, Medication, and/or… Cognitive Training

Reinout W. Wiers
University of Amsterdam
r.wiers@uva.nl

Outline

• Jürgen Rehm – Societal harm of Alcohol
• Psychological Mechanisms: implicit and explicit processes
• What to do? Add cognitive training to the treatment menu
• New directions, challenges

Main problem: when people have resources, they use more alcohol & drugs than is good for them.

Rehm: The harms of alcohol and other drugs

• Alcohol and smoking cause most harm to society
• Trend toward mean: alcohol goes down in EU (but still highest, with many people drinking at conference levels)
• New markets (also for smoking): developing countries

What to do about this burden?

• Society: increase prices, legal age (Room, Babor & Rehm, Lancet 2005)
• Prevention: school-based prevention has small effects, maybe better:
  – general training in self-control at earlier age (cf. Van Lier et al 2009 Drug Alc Dep)
  – Targeted personality-based prevention (Conrod et al, 2006; 2010; 2011)
• Psychology: range of interventions from minimal to therapy, and… cognitive training

No conflict of interest
Funding: N.W.O. (Dutch National Science Foundation), ZonMW (Dutch Medical Science); EU FP7; ERAB Ministry of Justice; NIDA
Dual Process Theories Addictions
(e.g., Bechara, 2005; Wiers & Stacy, 2006; Wiers et al., 2007)

- Addictions as conflict between impulsive/bottom-up processes and reflective/long-term, control processes
- In addictions often relatively strong impulsive processes (and/or weak control)
  > sensitive to current needs (craving, thirst)
  > imbalance stronger as result of addiction

Metaphore: Impulse (horse) and Reflection (horseman)

Addiction: horse who easily runs wild…
Anxiety: fearful horse (both: weak Rider)

Evidence: Many Recent Studies
Relatively automatic processes predict alcohol/drug use in individuals with relatively low executive control (Thush et al. 2008; Grenard et al. 2008; Houven & Wiers, 2009; Friese et al. 2010; Peeters et al. 2012; 2013)

Review:

Treatment suggestion from the simple metaphor:

On taming horses and strengthening riders: Recent developments in research on interventions to improve self-control in health behaviors

Malte Friese, Wilhelm Hofmann, and Reinout W. Wiers

(Model Wiers et al., 2007 Pharm Bioch Behav: update 2014 Oxford Handbook: Substance Use Disorders)
Cognitive Bias Modification

- Main aim is to directly interfere with cognitive process related to maladaptive behavior (the cognitive bias)
- Usually with training variety of task used originally to assess the bias
- Originally developed in anxiety, translated to addiction + new tasks developed (and back-translated)

Attentional Bias, Dot probe test

Alcohol latency trial

Schoenmakers, Wiers et al 2010 DAD

43 alcohol-dependent patients
Randomly assigned to
5 sessions of Attentional re-training or placebo-training

- Generalized effect (untrained pictures)
- Clinical effects (later relapse)

Another Bias: automatic action tendencies to approach alcohol

Irrelevant Feature Version

Format determines action
landscape picture: push  portrait: pull
Pull: approach

push: avoid (withdraw)

Assessment Results
(Wiers, Rinck et al. Genes, Brain, Behav, 2009)

Significant difference
Light vs. Heavy Drinkers
Heavy drinkers Faster to approach alcohol
especially those with risk allele OPRM1
mu-opioid receptor gene, also related to cue-induced craving
van den Wildenberg, Wiers, et al., 2007 ACER

Results: Strong Generalization
Significant generalizations to untrained pictures and to IAT (verbal memory association task):

Retraining: 1st clinical study

214 alcoholics in German clinic (Lindow) in 4 conditions:
- relevant training (push alcohol away)
- irrelevant training (portrait-landscape)
- assessment control (50-50)
- no training

Effect on relapse 1 year later

Adding CBM to CBT results in 13% less relapse a year later
Approach bias modification in alcohol dependence: Do clinical effects replicate and for whom does it work best?

Carrin Eberl, Wolfram Wiers, Steffen Pawelczak, Mike Rinck, Emily Becker, and Johannes Lindenmeyer.

Results: Replication study (Eberl et al., 2013, DCN)

$N = 509$, training / no training

Replication outcome: 9% difference in relapse & mediation & moderation

Replication: Approach bias re-training

$B = 0.570$, $p = 0.041$

$B = -0.372$, $p = 0.048$

$B = 0.400$, $p = 0.014$

$B = -0.374$, $p = 0.009$

Results for 1-year follow-up ($N = 1405$)

Again ~10% less relapse one year later for both types of training (vs. placebo/no training) > CBM for addiction yields a robust clinical effect when combined with CBT

Fresh Data from Lindow (Rinck et al., in prep.)

2 (Approach-bias, real/placebo) x 2 (attentional bias re-training, real/placebo)

Results for 1-year follow-up ($N = 1405$)

Again ~10% less relapse one year later for both types of training (vs. placebo/no training) > CBM for addiction yields a robust clinical effect when combined with CBT

Neural effects of cbm?

Effects of Cognitive Bias Modification Training on Neural Alcohol Cue Reactivity in Alcohol Dependence

Method: In a within-subjects, randomised design, 52 alcohol-dependent patients received training to neutralise or avoid alcohol cues. The task was conducted in a fMRI scanner while they were asked to watch a film about alcohol cues and CO2 of soft and hard drinks, while their brain was scanned in fMRI. The training consisted of different training conditions: control, avoidance training and neutralisation. In the control condition, participants watched a film without training. In the avoidance training condition, participants were instructed to avoid any alcohol cues and CO2 of soft and hard drinks, while in the neutralisation condition, participants were instructed to neutralise their reactions to alcohol cues and CO2 of soft and hard drinks. The training sessions were conducted in a fMRI scanner and were separated by a 24-hour period.

Results: Avoidance training, alcohol cue-cue avoidance training or no training was scanned in the amygdala bilaterally, as well as in the right fusiform gyrus, although only in the real training group. No significant changes in amygdala activity were observed in the placebo group. No changes were observed in the control condition.

Amygdala Cue Reactivity change:

(Alcohol>Soft drink) CBM > Placebo

$p < .05$, FWE SVC

C.E. Wiers et al (2015)
Or direct brain stimulation?

**t-DCS (transient Direct Current Stimulation)**

- Weak current between two electrodes.
- Increases excitability of underlying cortex

Add direct brain stimulation?

- **tDCS**
- Effect > increased working memory (Fregni et al., Gladwin et al, 2012)
- Less craving! (Baggio, Fregni, Den Uyl et al., 2015)
- Current studies: can it improve training outcomes in alcoholism?

**Computerized training: online only?**

- Website ([www.impliciet.eu](http://www.impliciet.eu)): self-help or add-on to psychotherapy
- Now in Dutch
- But set up for Translation & Adaptation (e.g., Italian Project, Boffo Et al, 2015)
- ALICE-RAP
- FP7 EU Project
- Now also gambling

**New Developments/Challenges:**

1. Online Only?
   - **Alcohol**: Wiers et al., 2015 Add Behavs. Main effect of time (training / placebo conditions all reduce drinking) > no quit attempt
   - **Smoking**: Elfeddali, ... Wiers, in press Health Psychology
   - Online recruitment (e.g., links on smoking info sites)
   - Participants (18+, Wanting to quit smoking)
     - Heavy smokers after training double chance of having remained abstinent half a year later

2. New developments
   - Training on smartphones/tablets
     - Note that angle is smaller, so important to establish that bias can be changed. Two initial studies showed this is possible:
       - Anxiety: Enock, Hofmann & McNally (2014)
       - Smoking: Kerst & Waters (2014)
     - Both found changes in attentional bias on mobile device, but no change in behavior.
     - What was missing?
     - CBT/MI! (long-term goals)
3. New developments

> new opportunities: combine with unique features of smartphone: might “know” when you need training better than you!

Conclusions

- Both bottom-up incentive reactions and top-down regulatory control important in addiction
- Their interaction can be affected by cognitive training paradigms
- So far mostly effective as add-on to regular therapy, not as replacement
- But: regular therapy can be given over the computer (as effective as face-to-face, see Riper et al., 2014 for meta-analysis).

Take home message:

There is more in the menu of treatment than “talk therapy” and medication:

Varieties of Cognitive Training

Psychotherapy

Cognitive Behavior Therapy (CBT): very good, many and most recommendable in our lab,

Motivational Interviewing

Popular, also in combination with CRT. Roughly equally effective. $12

You are not a bad person

The famous motto says. If you are a high risk and in trouble, it’s not your fault, try to say. Many years of research...?

Good old pharmacotherapy

Effective, but there’s nothing better than doing a good cuda... $14

Medication

Disulfiram.

Makes you sick when you drink. But doesn’t reduce craving. Can be dangerous for that reason. $15

Naltrexone.

Reduces craving in some. Genetic screening advised. $18

Acamprosate.

Helps some patients, more in Europe than in US. $21

“Today’s special” Baclofen.

Still off-label, but promising results and off patent! Try a high dose and tweaked formulation. $31

Modafinil.

Very good if you’re an impulsive decision maker. $14

Cognitive Training

Attention Training.

Effective in many (but not all) studies in anxiety. Promising results in addiction. Give it a try. $15

Action Tendancy Training.

Developed in the house and found effective in multiple studies. $18

Training of Working Memory.

Not the easiest choice, but might have a general effect. Helps problem drinkers with strong alcohol associations. $17

Selective inhibition training.

First positive results with alcohol and eating. First clinical studies running now. $21

Interpretation-bias training.

Successful in anxiety, first studies in addiction now. $14

Mindfulness Meditation.

Seems to help with many problems. We don’t know how exactly yet. But trust us, it’s OK. $15

Running. Not only good when depressed, attentional bias for cigarettes also reduces. $16

Training of self-discipline (good behavior) in primary school. Kids drink and smoke at later age! $21

Different Training

Psychotherapy

Good idea to first build motivation to change, focus on long-term perspective, $8

Training.

Choose your favorite training. $14

Medication

Still not fully satisfied? Maybe medication or neurostimulation may help. $5

Different Training
Andere training. Mindfulness Meditatie. We weten nog niet precies hoe het werkt, maar het lijkt te werken bij veel problemen.

Hardlopen. Niet alleen lekker bij depressie, de aandachtbias voor sigaretten wordt ook minder!

Zelfdiscipline trainen op de lagere school. Kinderen leren niet alleen meer, ze gaan ook later roken en drinken.

Gerichte persoonlijkheid gebaseerde preventie op de middelbare school.