



Het depressieve brein opnieuw in controle

Over de ontwikkeling van nieuwe neurocognitieve therapieën

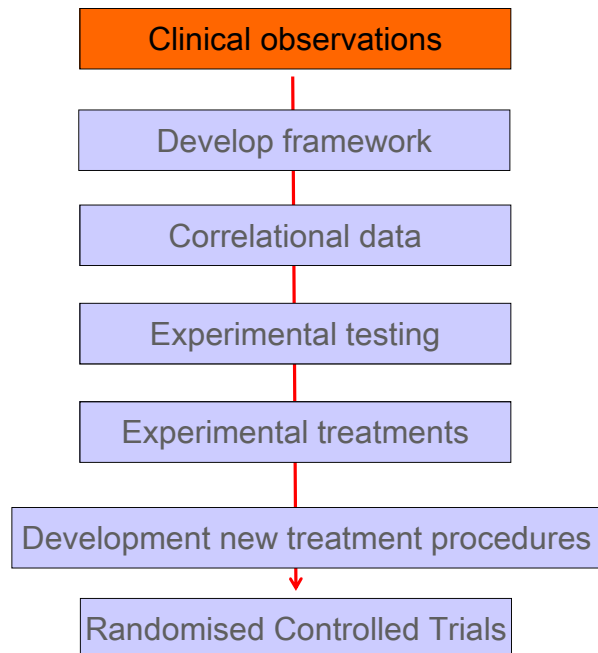
Rudi De Raedt

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Vakgroep Experimenteel-Klinische en Gezondheidspsychologie

Breinwijzer

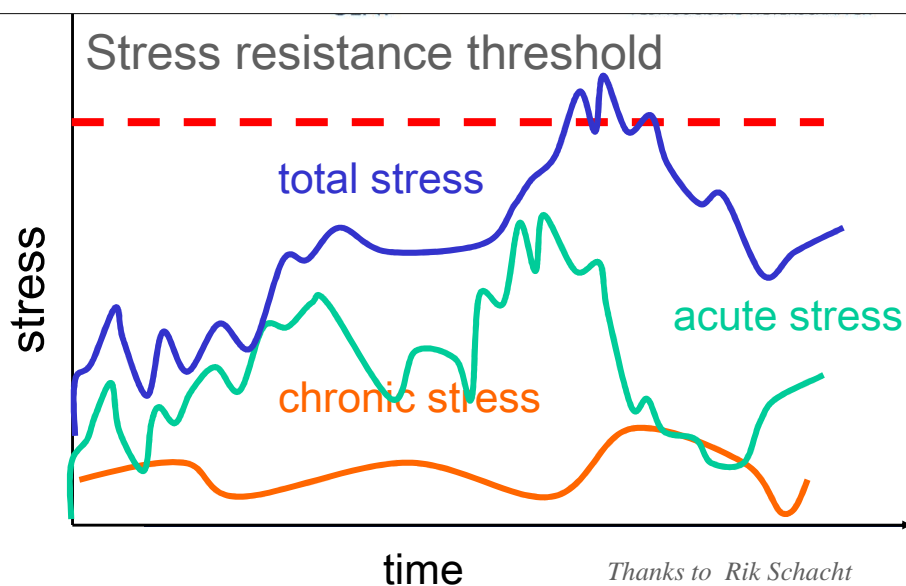
4 December, 2014

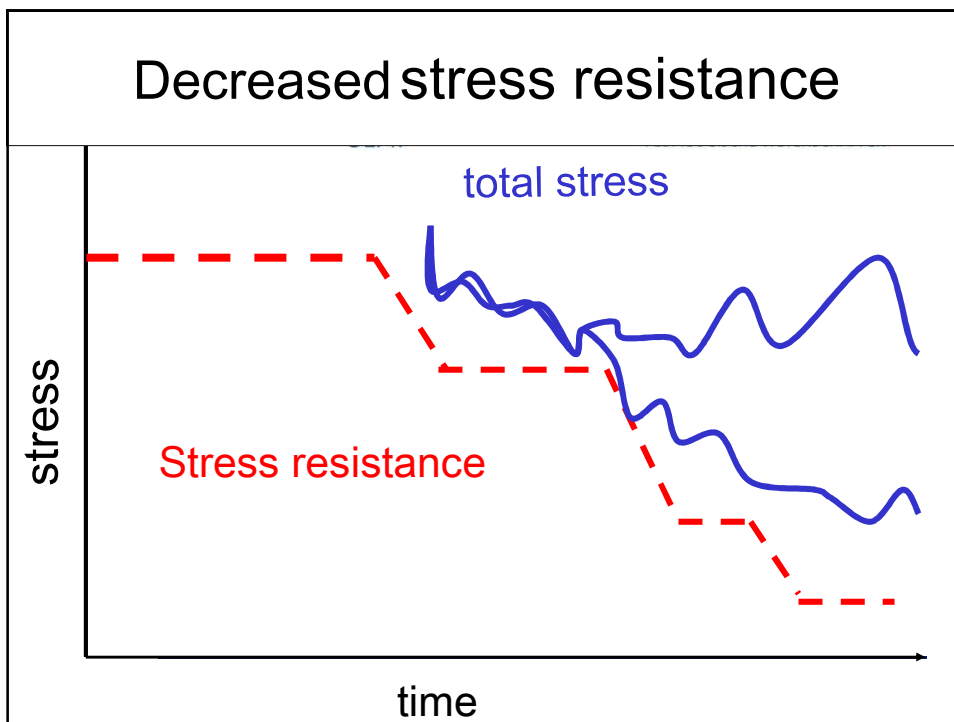
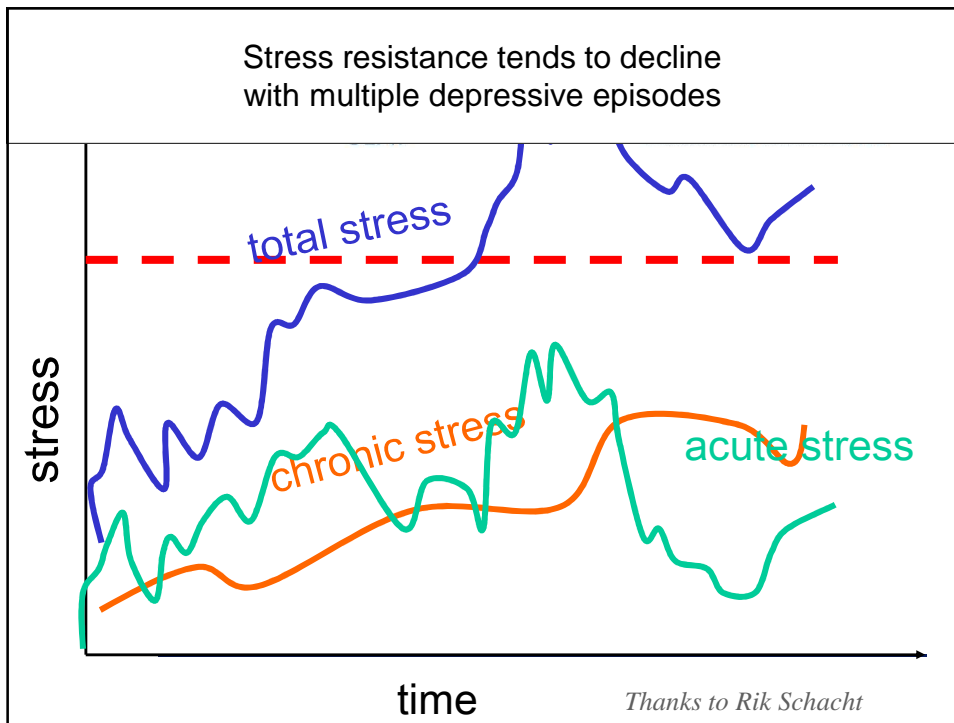


Depressive disorder: the clinical problem

- ✓ Life time prevalence: +/-19% (Kessler et al., 2009)
- ✓ Evidence-based treatment (Cuijpers et al., 2013)
- ✓ However, high relapse rate (Beshai et al., 2011)
- ✓ Number of previous episodes > predictor of recurrence (Kessing, Hansen, Andersen & Angst, 2004)
- ✓ Kindling: successive depressive episodes triggered by progressively milder stressors (Monroe & Harkness, 2005)

Clinical observation

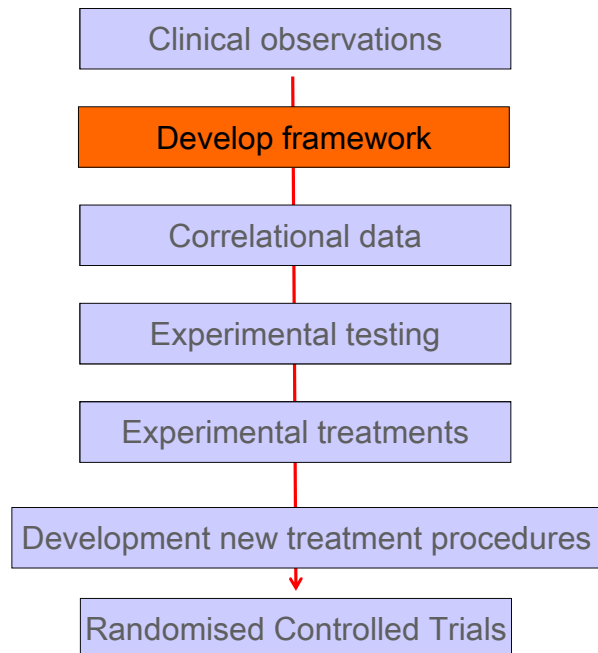


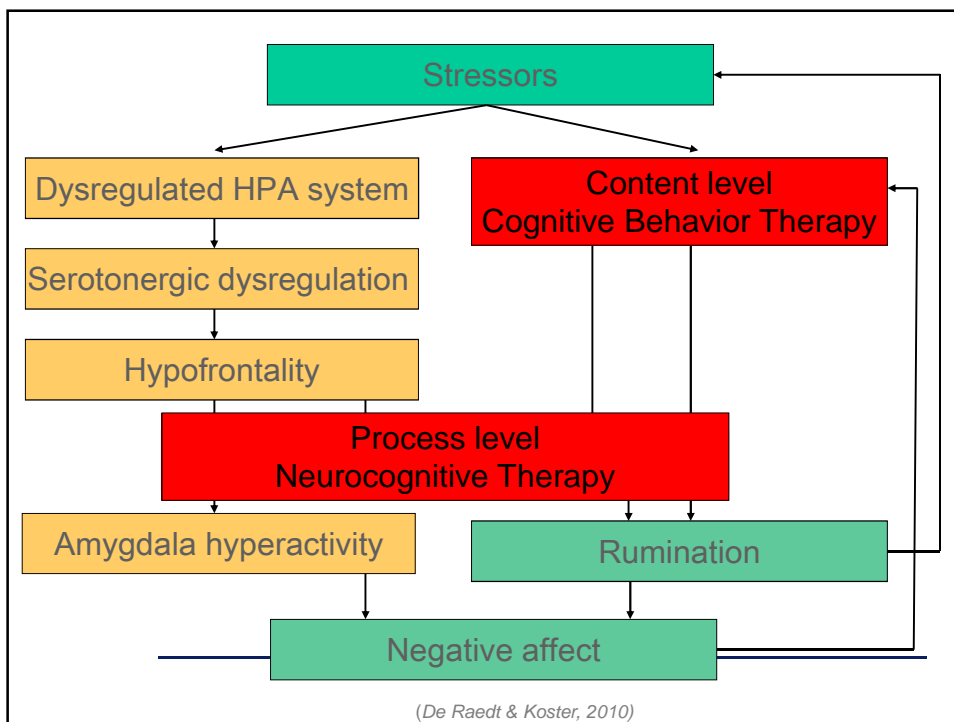
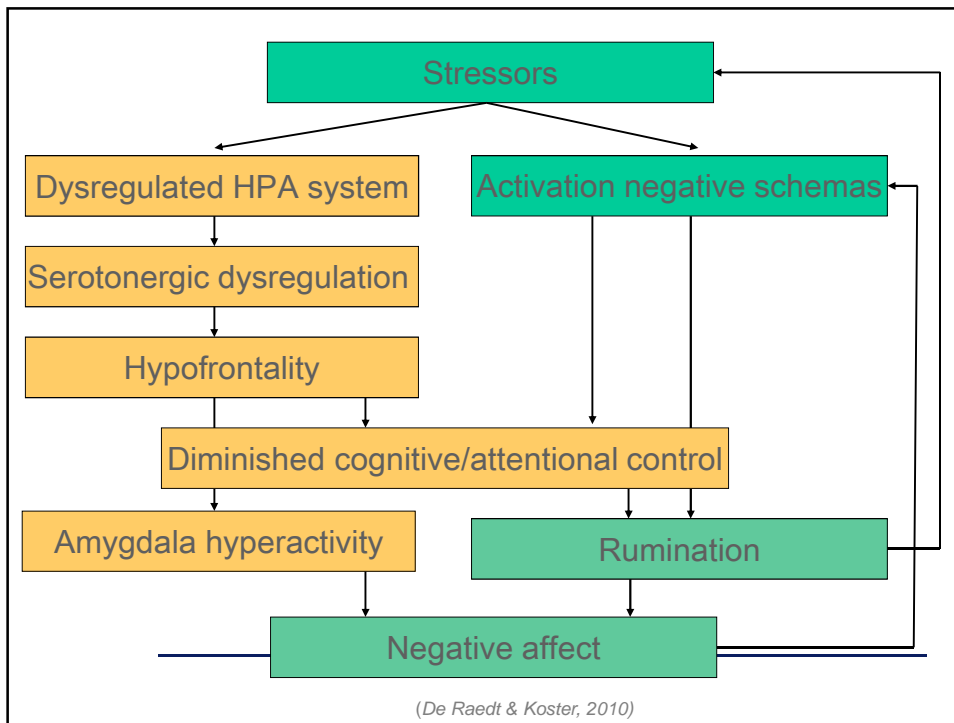




The research line, the challenge

Understanding to stimulate translational research to improve the effectiveness of treatment and relapse prevention interventions





The role of attentional control

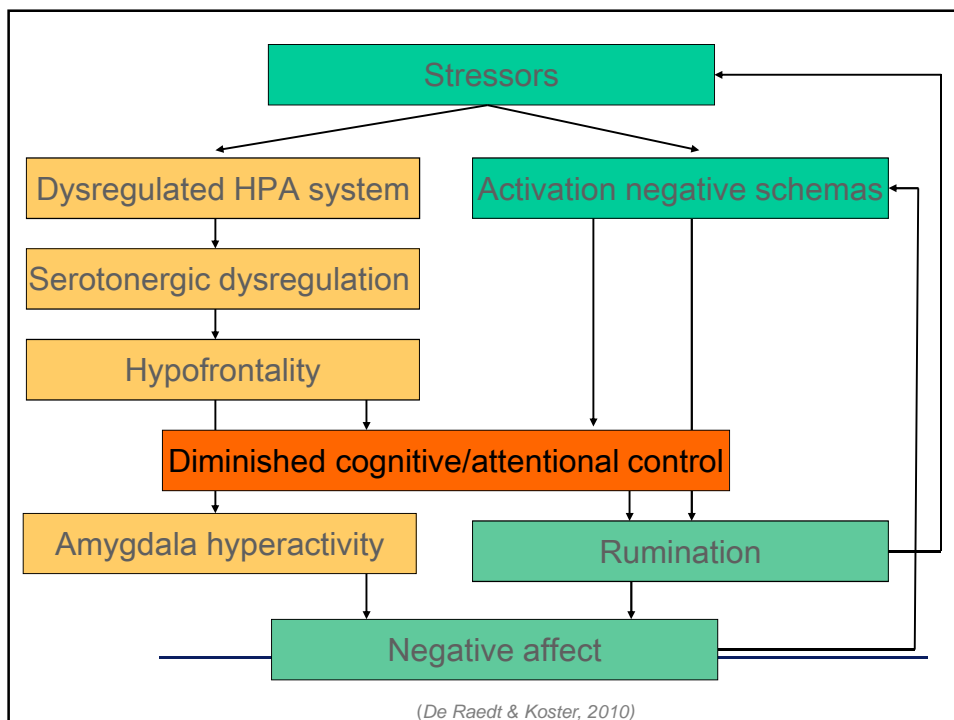
Attention increases «salience» en «influence»
> *increases intensity* (Ingram, 1990)

Discrepancy/conflict > attentional shift

A stressor initiates a «shift» to «evaluate» the situation
(Abramson et al, 2002)

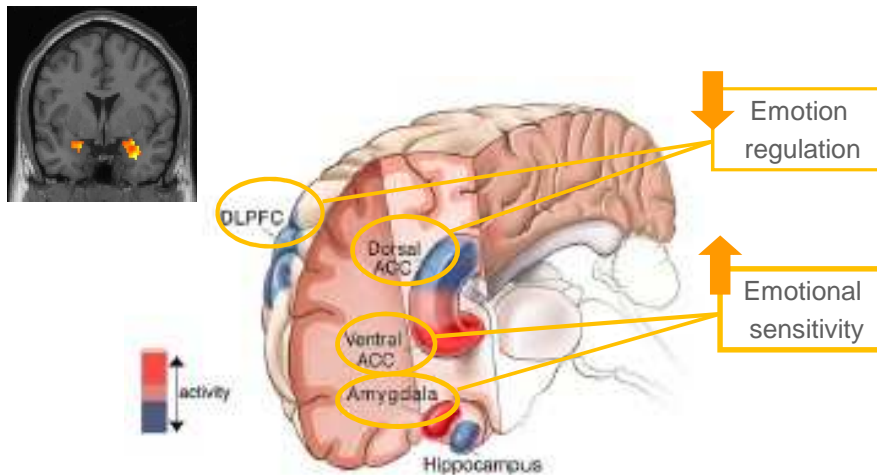
Vulnerable individuals have difficulties with
«disengagement» of this «evaluation»

This perseverative attention focus is «rumination»
(Pyszczynsky & Greenberg, 1987)



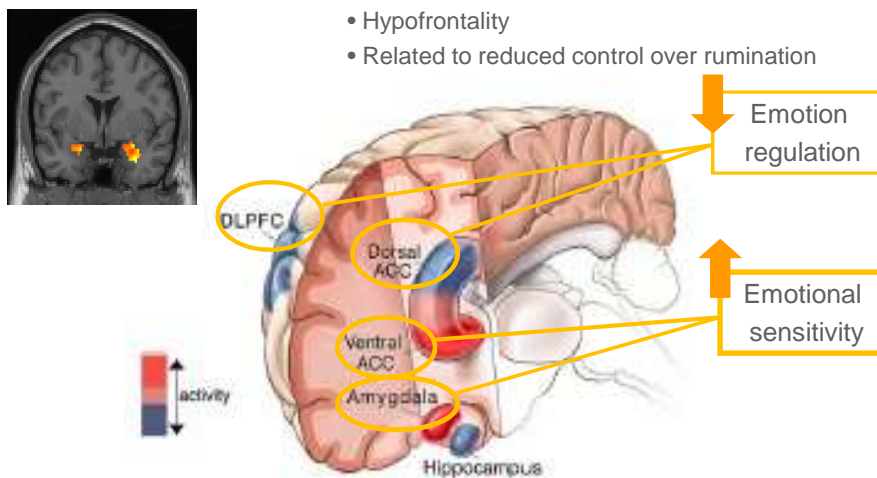
The depressed brain

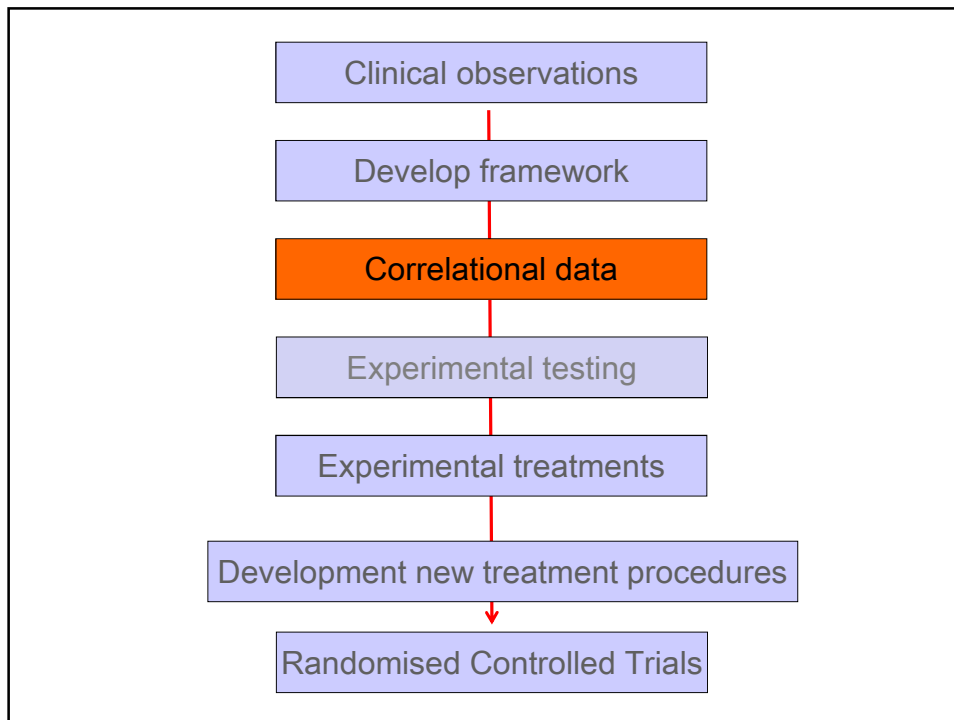
- Assymmetric prefrontal activity pattern
- Hyperactive amygdala



The depressed brain

- Assymmetric prefrontal activity pattern
- Hyperactive amygdala
- Hypofrontality
- Related to reduced control over rumination





Diminished cognitive control > episodes

- ✓ ERPs during cognitive control task
- ✓ Cognitive control, indexed by ACC related amplitude, decreases with number of prior depressive episodes ($r=.51$; $p < .01$)

(Vanderhasselt & De Raedt, 2009)

Two processes of decreased control

✓ Over external information

Depression > difficulties to disengage from negative information

(For overview: De Raedt & Koster, 2010)

✓ Over internal processing

Rumination > shifting and inhibition impairments when negative information is held in working memory

(For overview: Koster, ... De Raedt, 2011)

Prefrontal Control > Disengagement > Rumination

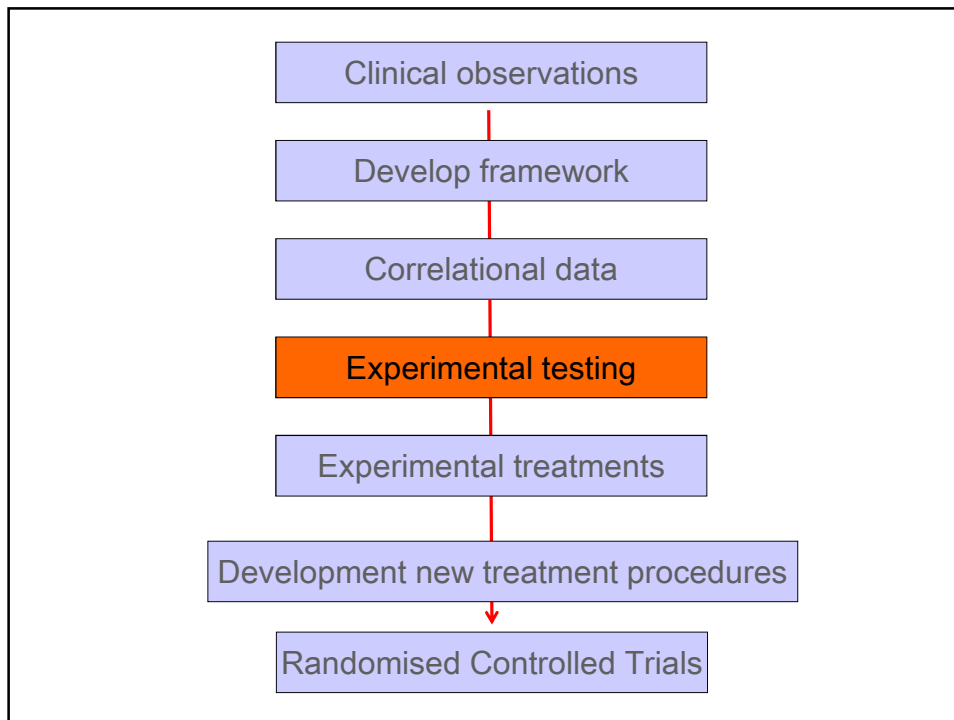
Ruminators > more dACC activity during inhibition of negative in favour of positive stimuli

(Vanderhasselt, ... De Raedt, 2013; Vanderhasselt, Kuehn & De Raedt, 2013)

And

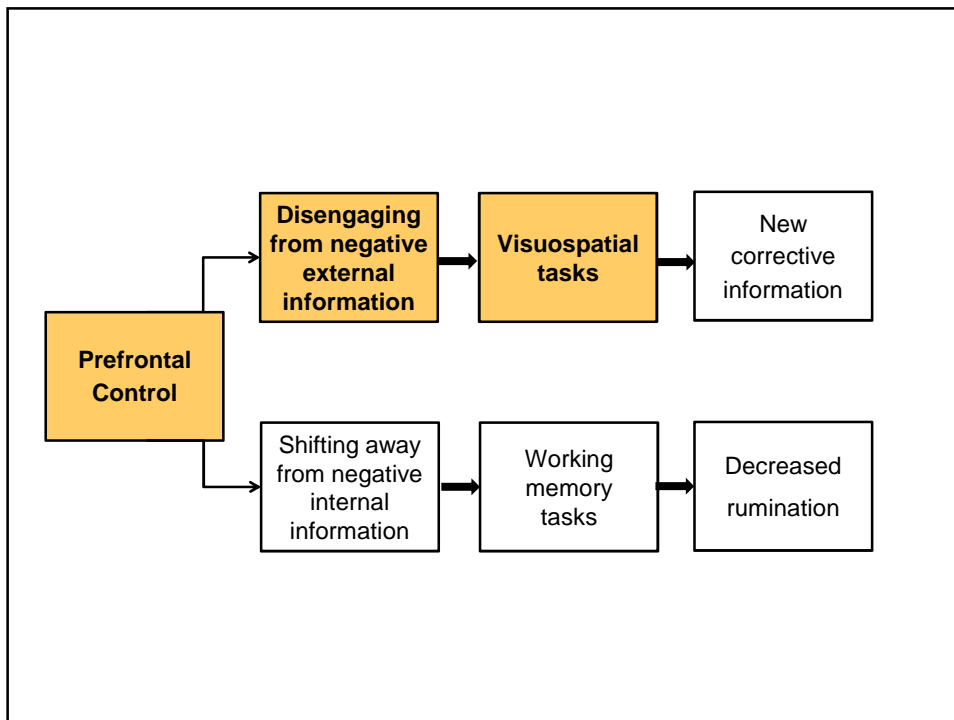
Reappraisers > more dACC / DLPFC activity during inhibition of negative info

(Vanderhasselt, Baeken, Van Schuerbeek, Luypaert & De Raedt, 2013)



Depression: causal hypothesis Diminished cognitive control

- ✓ The failure of dorsal brain (dACC/DLPFC) areas related to cognitive control to regulate ventral emotion producing systems
(Phillips et al., 2003, 2008)
- ✓ Necessary for cognitive restructuring in CBT: reappraisal *(De Raedt, 2006)*



Experimental psychopathology approach:
induce frontal asymmetry in healthy individuals

Effects HF-rTMS over right DLPFC
on disengagement from angry faces during fMRI



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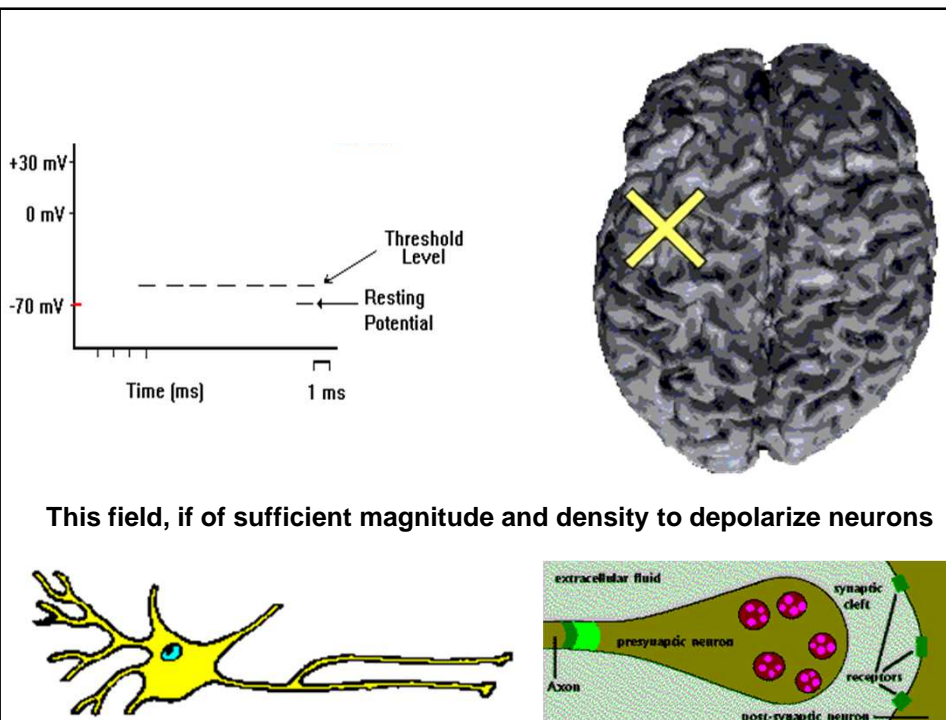
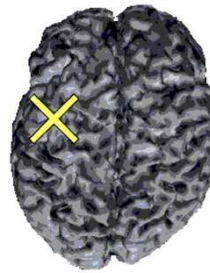


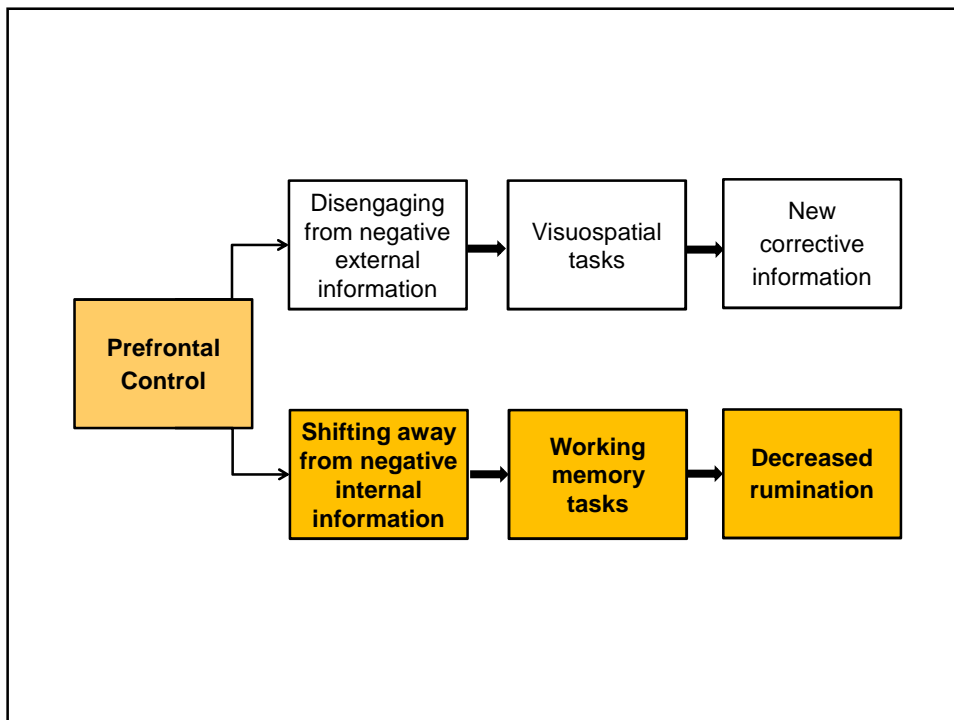
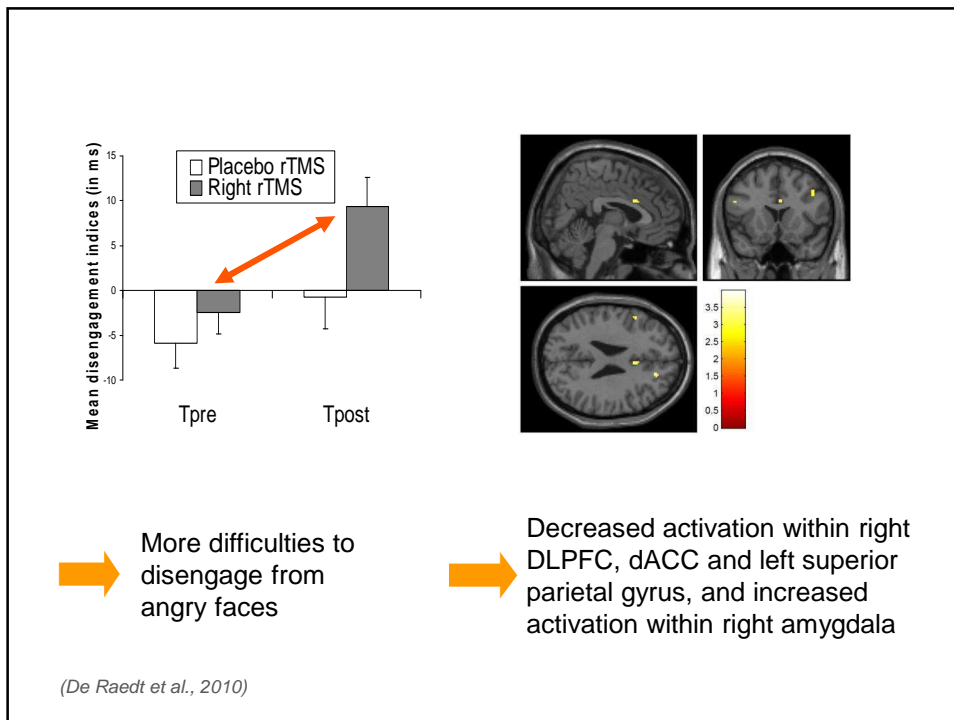
repetitive Transcranial Magnetic Stimulation (rTMS):



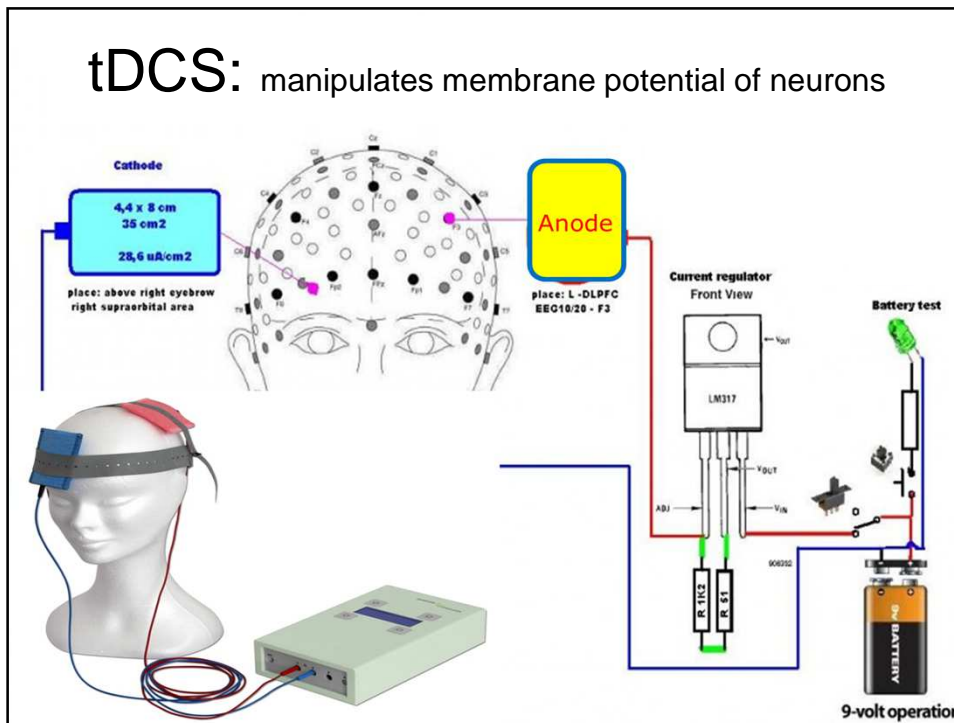
Dorsolateral Prefrontal Cortex (BA 46/9)

Electromagnetic induction of an electric field in the brain

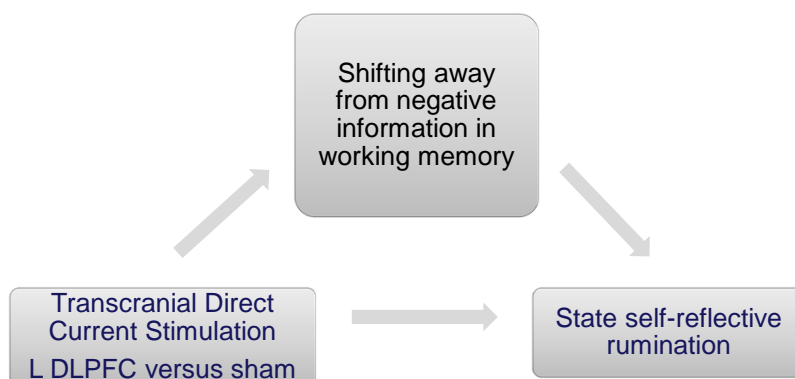


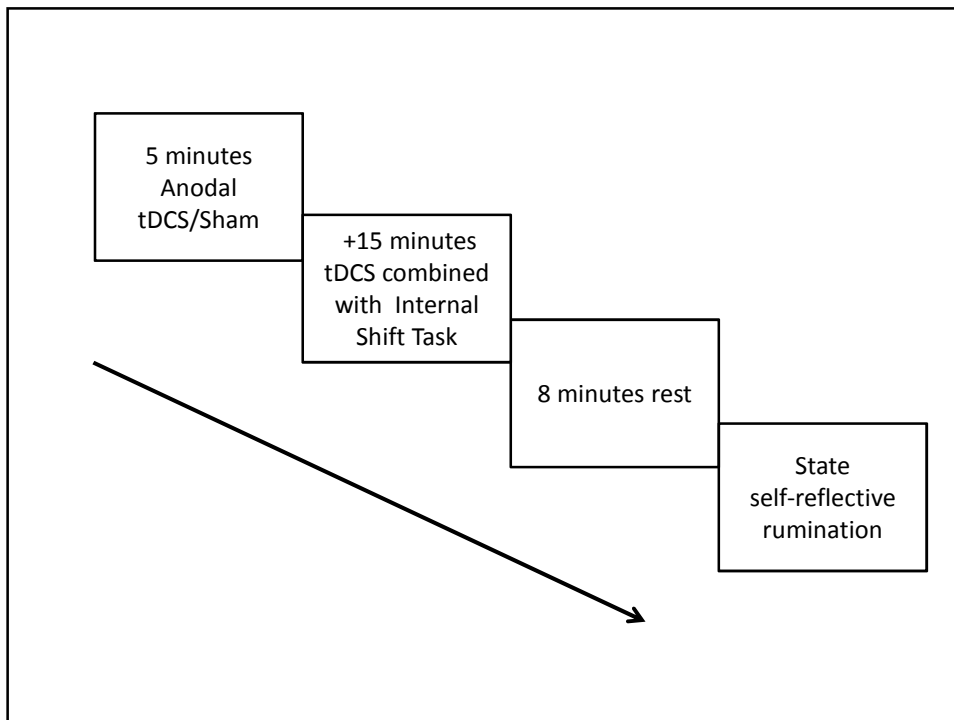


tDCS: manipulates membrane potential of neurons



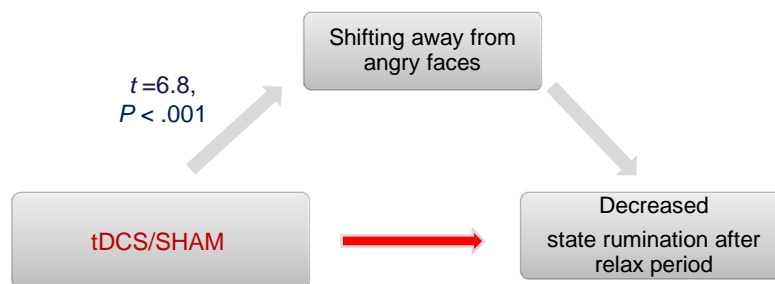
Hypothesis





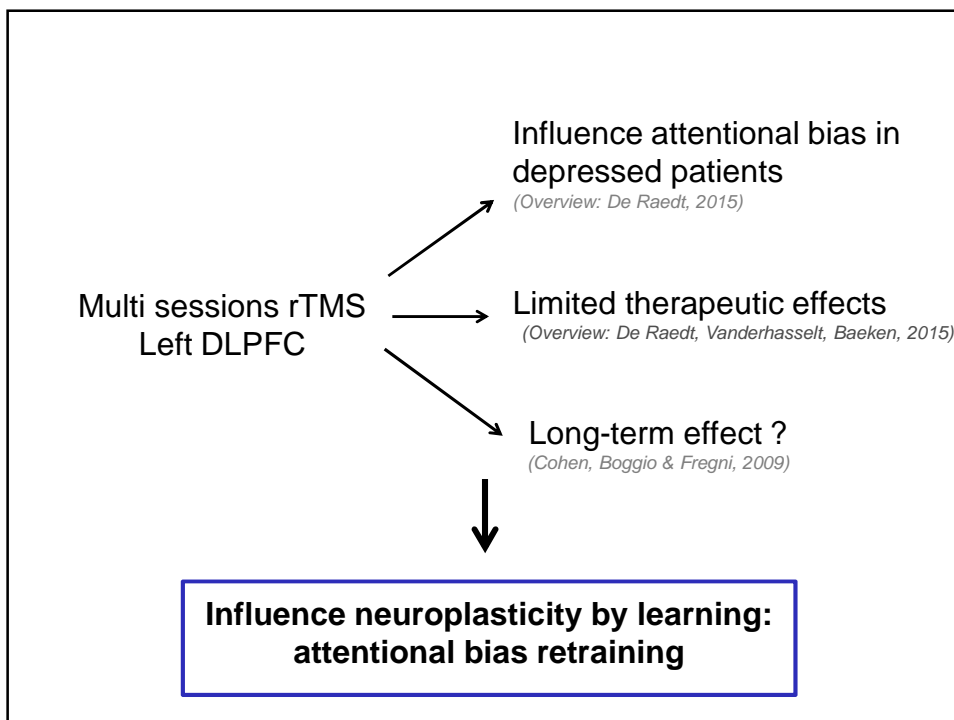
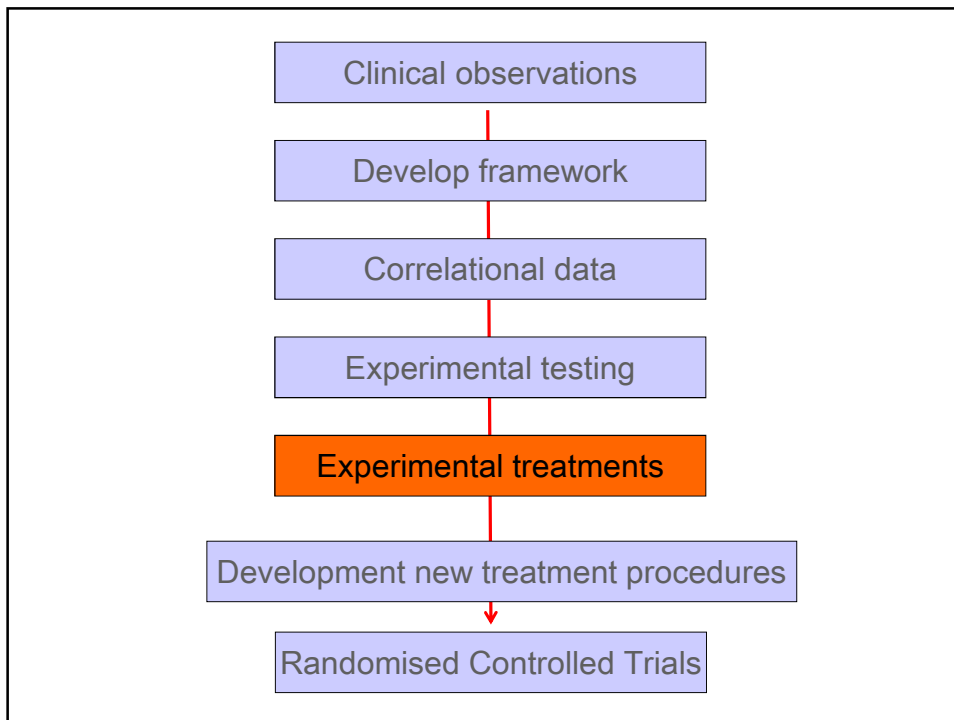
Results

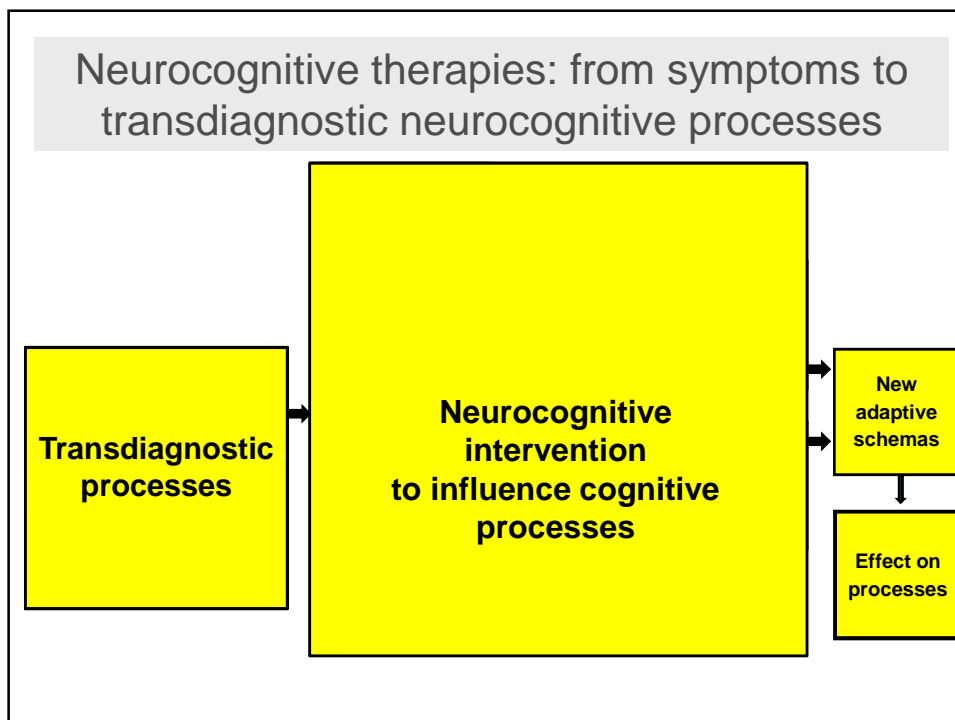
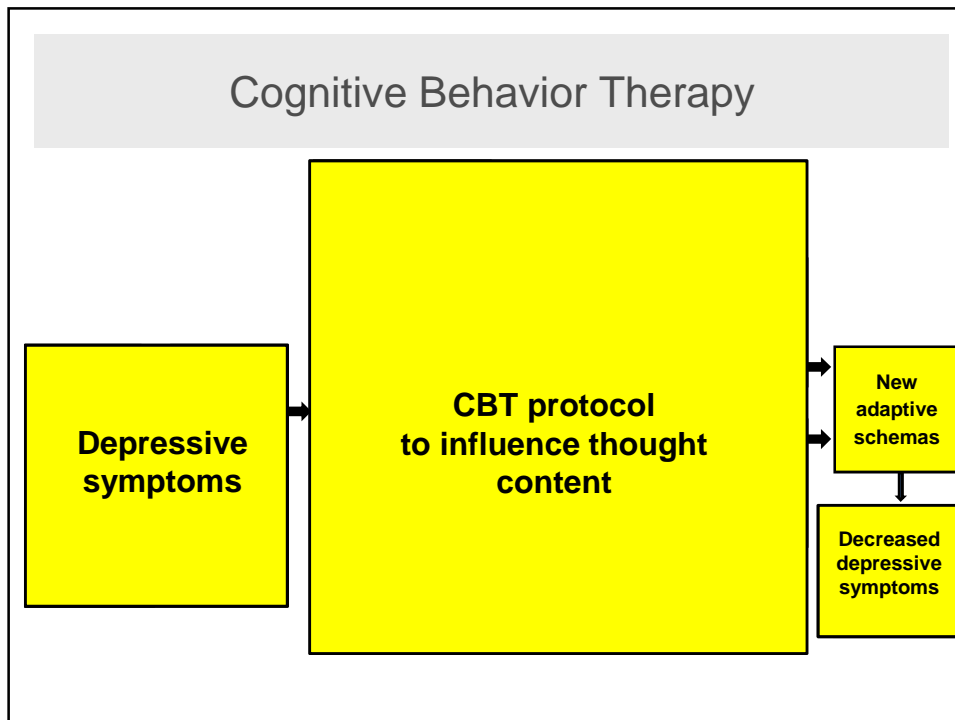
Mediation analysis: only significant angry>neutral shift!



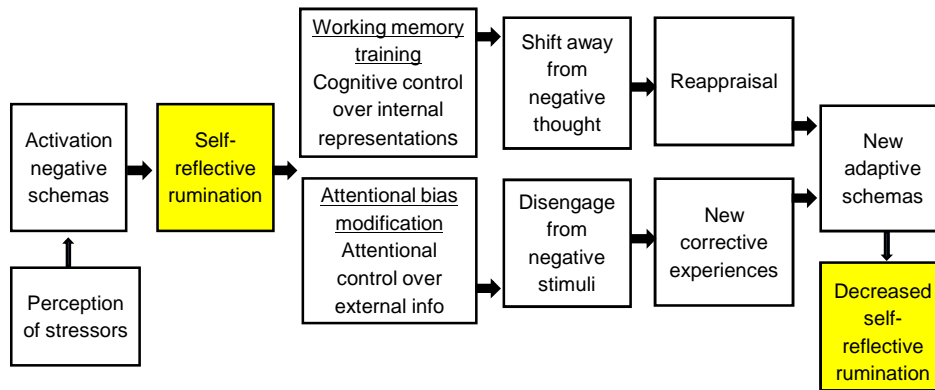
Mediation effect: $\beta=0.363$, $t=2.133$, $p=.041$

(Vanderhasselt, Brunoni, Loeys, Boggi, & De Raedt, 2013)



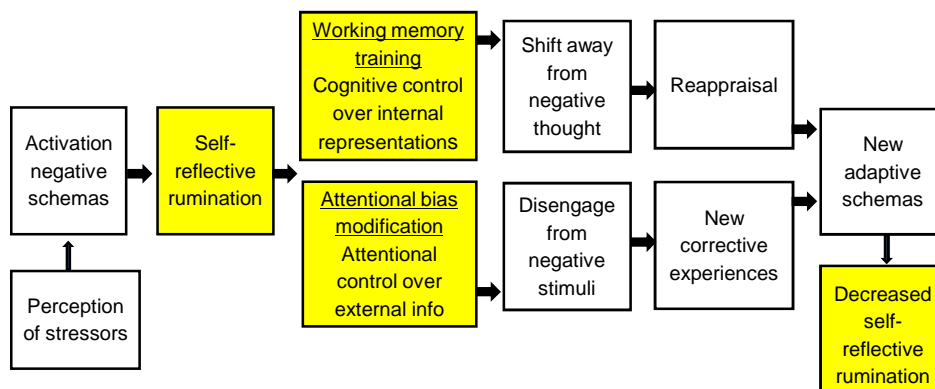


Neurocognitive therapies: from symptoms to transdiagnostic neurocognitive processes



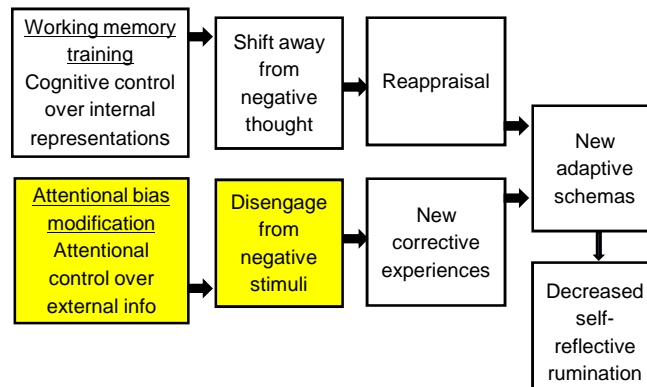
De Raedt, R. (2015). A neurocognitive approach to major depressive disorder: combining biological and cognitive interventions. In J. Mohlman, A.S. Weissman & T. Deckersbach (Eds.), *From symptom to synapse: a neurocognitive perspective on clinical psychology*. New York: Routledge.

Neurocognitive therapies: from processes to mechanisms



De Raedt, R. (2015). A neurocognitive approach to major depressive disorder: combining biological and cognitive interventions. In J. Mohlman, A.S. Weissman & T. Deckersbach (Eds.), *From symptom to synapse: a neurocognitive perspective on clinical psychology*. New York: Routledge.

Neurocognitive therapies



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Causal assumption

Information processing impairments are a causal factor in the origin and/or maintenance decreased stress resilience and depression



NEUROCOGNITIVE THERAPIES
INCREASING
COGNITIVE/ATTENTIONAL CONTROL
AS COGNITIVE REVALIDATION





Cognitive Bias Modification: MacLeod et al., 2002

Would attentional bias retraining work in depression?

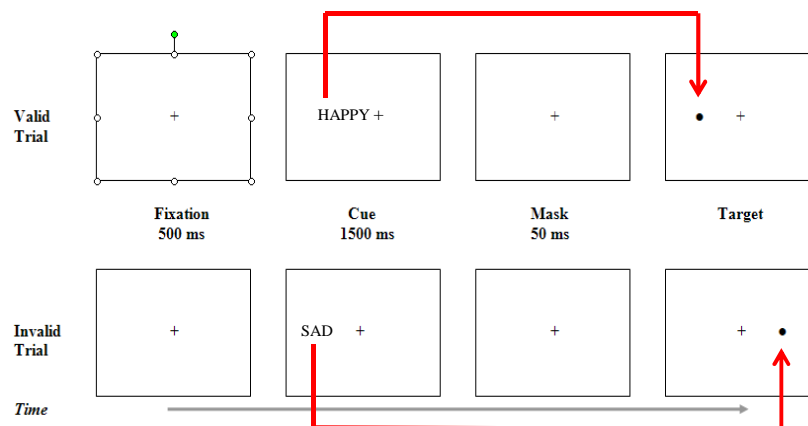
Effects of training are related to changes
DLPFC activity *(Browning et al., 2012)*

CBM improves stress reactivity in healthy
adults *(Baert, Casier & De Raedt, 2012)*

Training attention towards positive: 90% valid trials

Training attention away from negative: 90% invalid trials

10 days, 2000 trials, 200 trials or 10 min/day





Results

- Participants moderate symptoms: **Decrease** depressive symptoms
- Participants severe symptoms: **Increase** depressive symptoms
- Depressed patients: **No effects** of the training on top of TAU

DEPRESSED PARTICIPANTS ARE NOT ABLE TO DEPLOY THEIR ATTENTIONAL RESOURCES DURING TRAINING

(Baert, De Raedt, Schacht & Koster , 2010)



Other studies

Works in mild depressed undergraduates

(Wells & Beevers, 2010)

Does not work in dysphoric individuals

(Kruijt, Putman & Van der Does , 2013)

Works in remitted depressed

(Browning et al., 2012)

Conclusion:

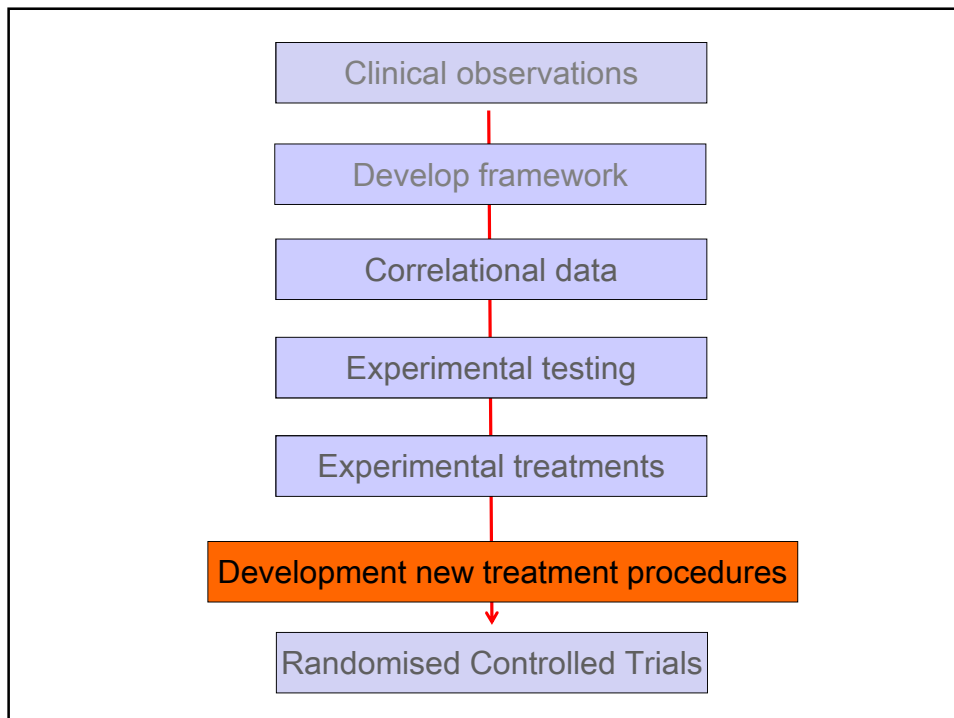
Therapeutic effects of CBM decreases with severity of depression

(Baert, De Raedt, Schacht, & Koster, 2010)

Depressed patients not able to activate DLPFC during cognitive control training?

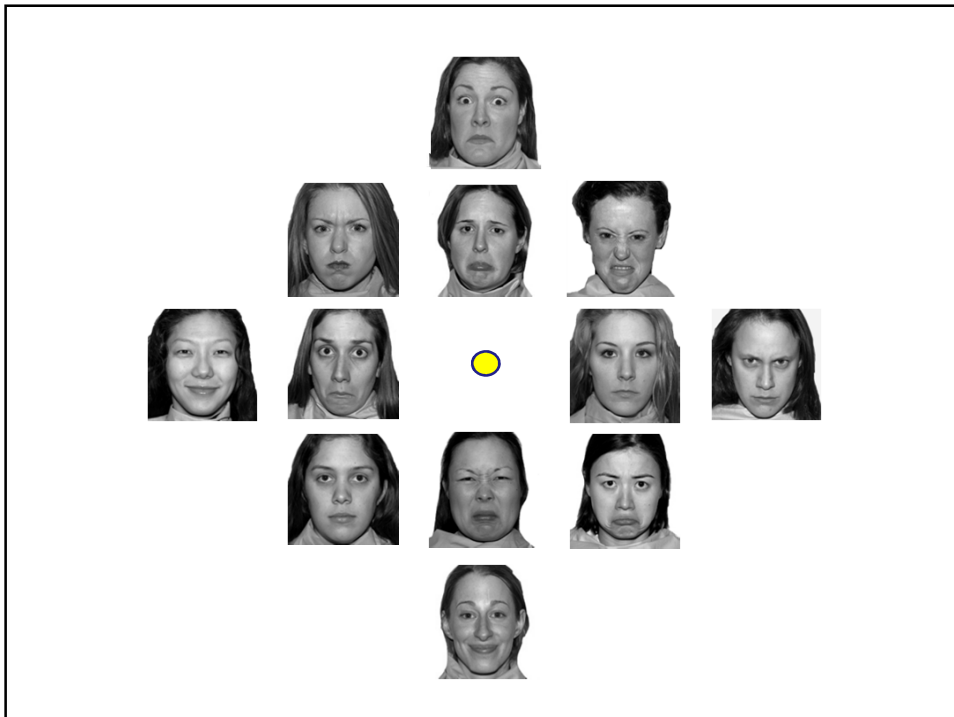
(De Raedt, Vanderhasselt, Baeken, in press)

- 1) Development of more potent strategies
- 2) Combining training with DLPFC stimulation?

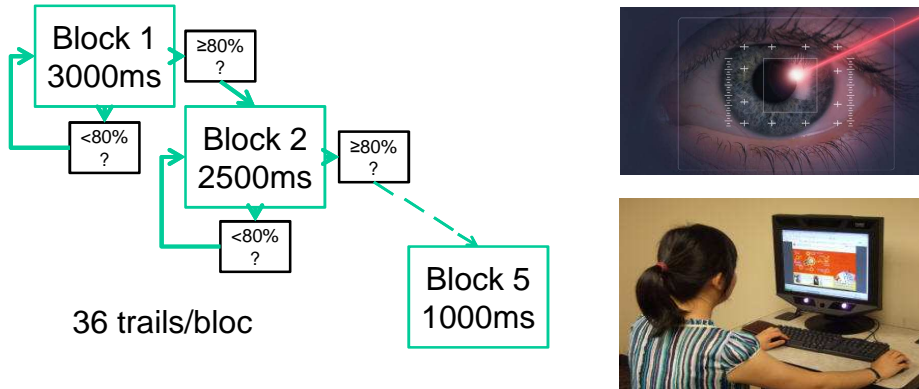


Development of more potent strategies

- ✓ Active training with reinforcement
- ✓ Gradual increase speed
- ✓ Training real behaviour: eye movements
- ✓ Ecological validity
 - > Many stimuli different emotions
 - > Away from negative towards positive in one trial



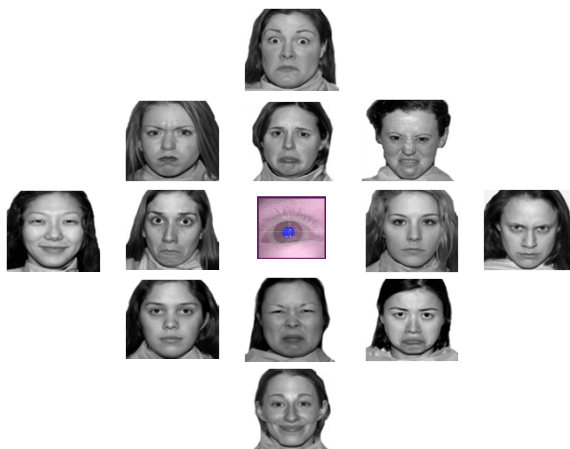
Interactive operant conditioning of eye-movements



Dependent variable: reaction negative feedback > faces

Pupil dilation: task engagement (DLPFC) predicts effect of happy training (not neutral training) on mood during negative feedback

(Price, Greven, Siegle, Koster, & De Raedt, under review)



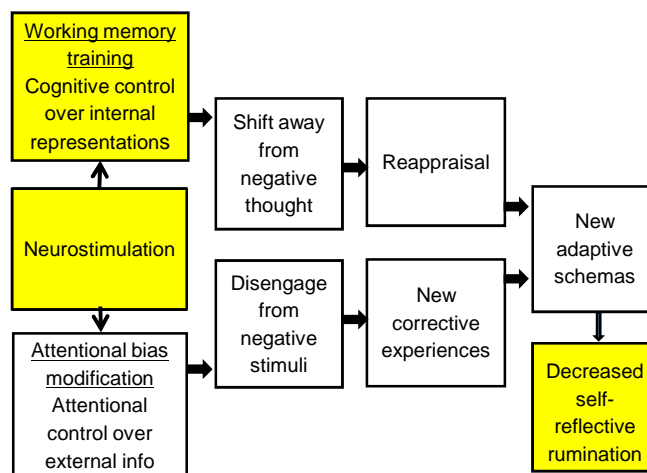
- ✓ DLPFC related task engagement predicts positive effect of training
- ✓ Depressed patients not able to deploy attentional resources during training

(Baert, De Raedt, Schacht & Koster, 2010)



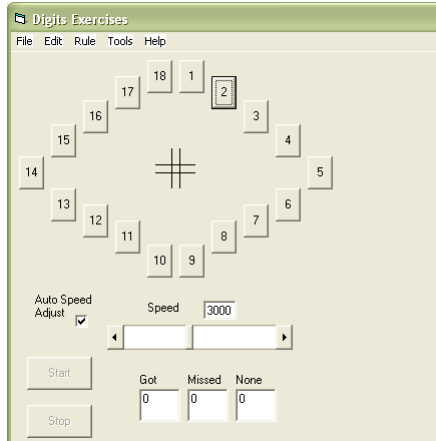
Combining DLPFC stimulation with Cognitive Control Training

Neurocognitive therapies: Combining techniques



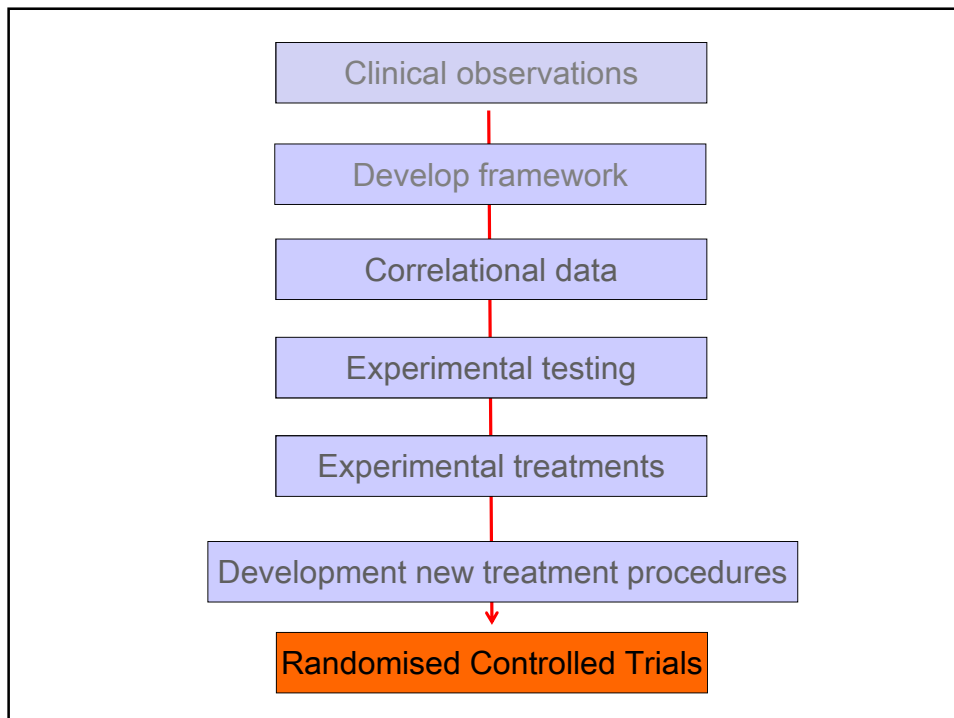
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Paced Auditory Serial Addition Task: Working memory training



Related to DLPFC
activation

*Siegle, Ghinassi, & Thase, 2007,
Cognitive Therapy and Research*



Randomized double blind trial Neurostimulation & working memory training

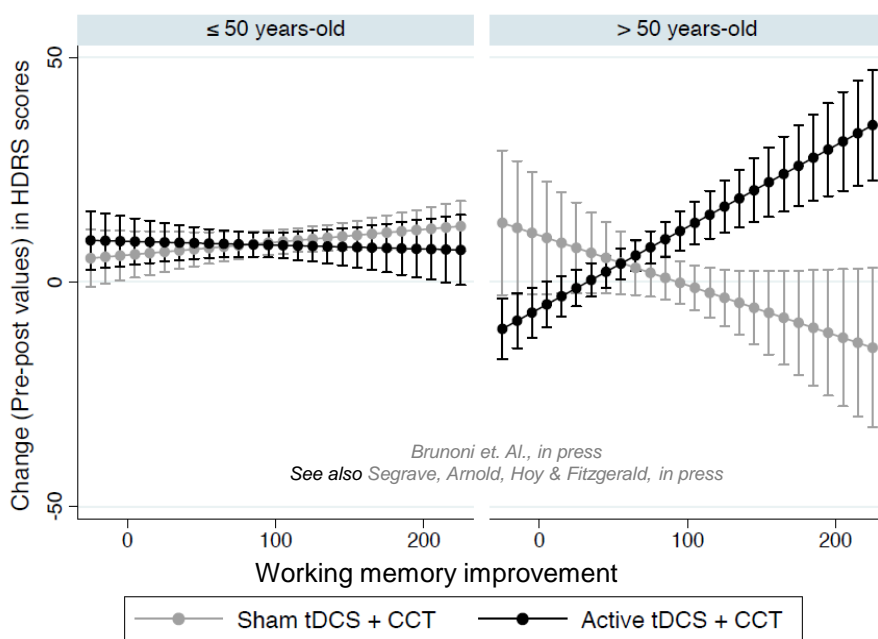
A sample of
depressed
patients

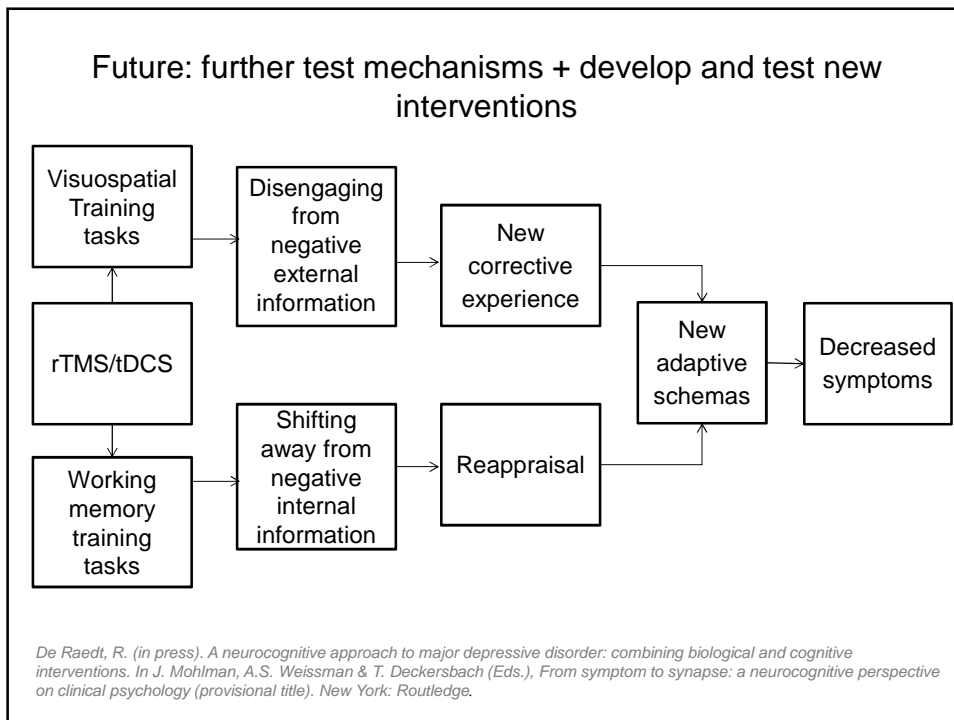
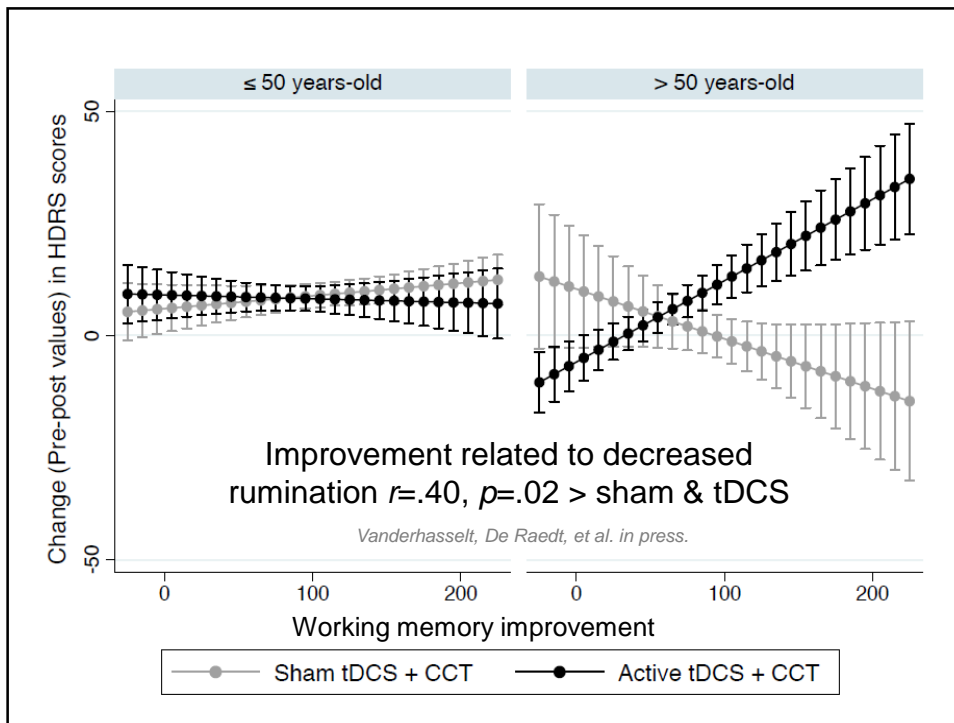
Pre measures

Post measurements

Two weeks of training: 10 sessions

- 40 patients, randomization in 2 groups:
- Sham (placebo) tDCS + CCT
 - Active tDCS + CCT
- Two weeks, 5 sessions / week, 15 minutes per session





IMPACT

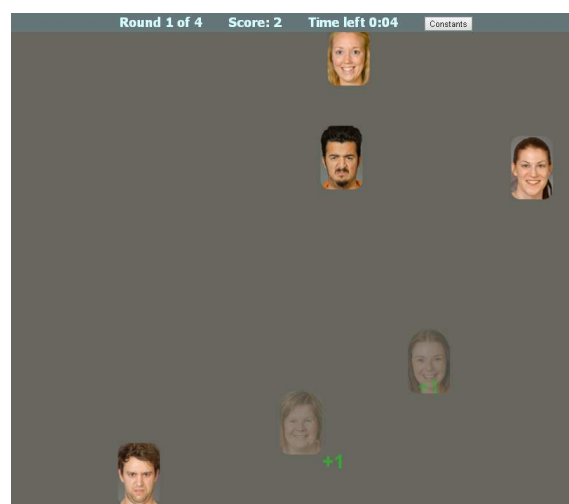


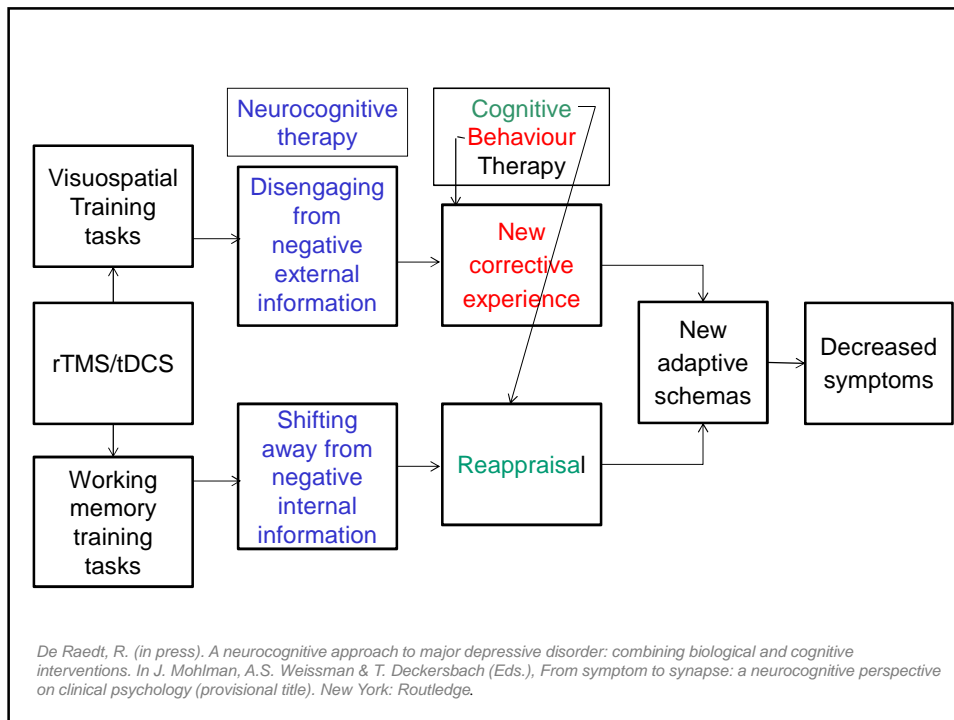
Intrinsically-Motivating Playable Attentional Control Training

IMPACT Collaborators:

Harvard University: Phil Ennock, Richard McNally, Donald Robinaugh,
Ghent University: Rudi De Raedt, Ernst Koster,

Impact game







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Concerted Research Action
Special Research Fund



Fonds Wetenschappelijk Onderzoek
Research Foundation – Flanders



Fund
Willy Gepst



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NEUROSCIENCE

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- Joke Heylen

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