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Disentangling the relationship between Complex PTSD & "Personality Disorder"

Potential neurobiological consequences of adverse childhood experiences and Borderline Personality Disorder

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Bij ons leer je de wereld kennen

Adverse childhood experiences (ACE)

Stressful / traumatic events before age of 18

- Emotional, physical, sexual abuse; Neglect
- Parental problems (e.g., mental illness, financial difficulties, separation).
- Bullying at school

Psychological Trauma

= Direct or indirect exposure to a deeply distressing or disturbing event

= Emotional response to distressing event(s)

ICD = ... an extremely threatening or horrific event or series of events

Increased risk of revictimization after ACE

(e.g., Cloitre, Cohen, & Scarvalone, 2002; Fereidooni et al., 2023; Gilbert et al., 2009; Walker & Wamser-Nanney, 2022; Widom, 2008)

Potential impact of adverse childhood experiences (ACE)

Odds ratios following ACE

PTSD	5.0 – 7.0
Personality Disorder (PD)	4.7 – 6.4
Affective Disorders	2.1 – 4.0
Diabetes/Obesity	1.5 – 2.0
Ulcerative Colitis	2.3 – 2.6

Cutajar et al. 2010, Green et al. 2010, Kessler et al. 2010, Scott et al. 2010, Spataro et al. 2004, Pérez-Fuentes et al. 2013, Huang et al. 2015, Fuller-Thompson et al. 2015



Psychosocial Consequences

- Emotion dysregulation
- Dissociation
- Chronic depression
- Addiction
- Self-injury
- Aggression

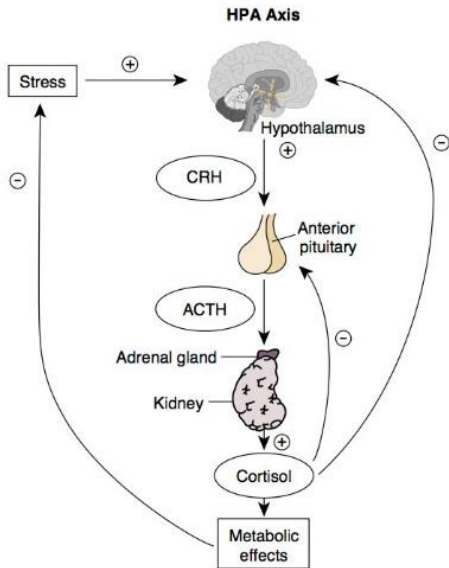
Crowell et al., 2009; Gilbert et al., 2009; Schalinski et al. 2015; Vonderlin et al., 2020

Meta-analysis by Porter and colleagues (2020)

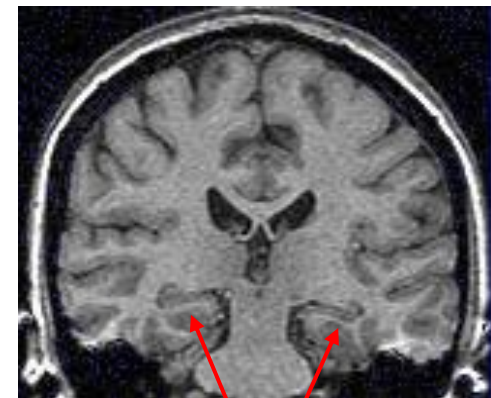
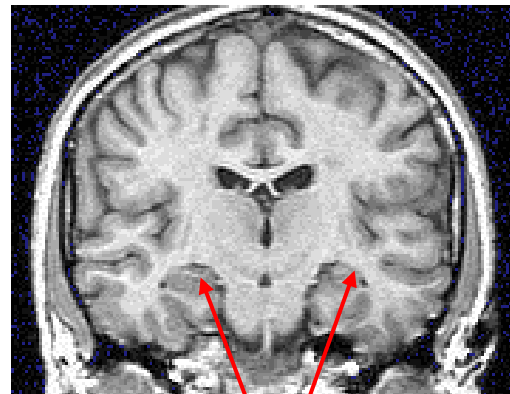
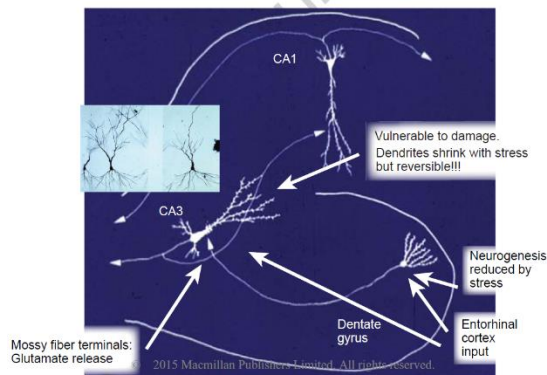
History of emotional, physical, sexual abuse, neglect in Emotional unstable / Borderline PD

- 13.91 times more likely than in non-clinical controls
- 3.15 times more likely than other psychiatric groups (e.g., depression)
- Particularly strong for emotional abuse and neglect

Potential impact of adverse childhood experiences (ACE)



- Early life stress exposure changes neural plasticity and function
- Altered functioning of the hypothalamic pituitary adrenal (HPA) axis and autonomic nervous system
- Altered brain volumes, e.g., in amygdala and hippocampus



Brain networks involved in emotion regulation (Ochsner & Gross, 2008)

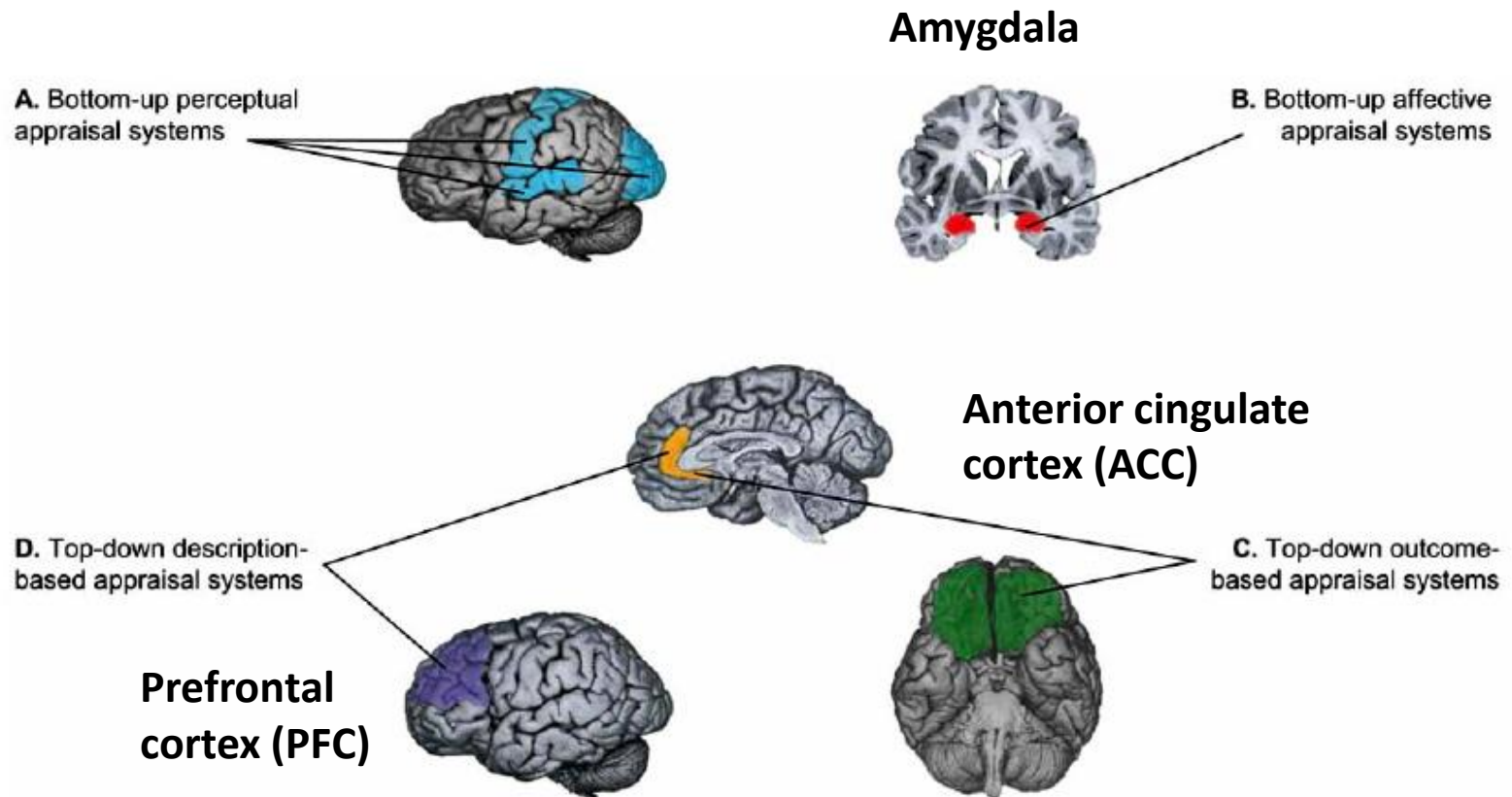
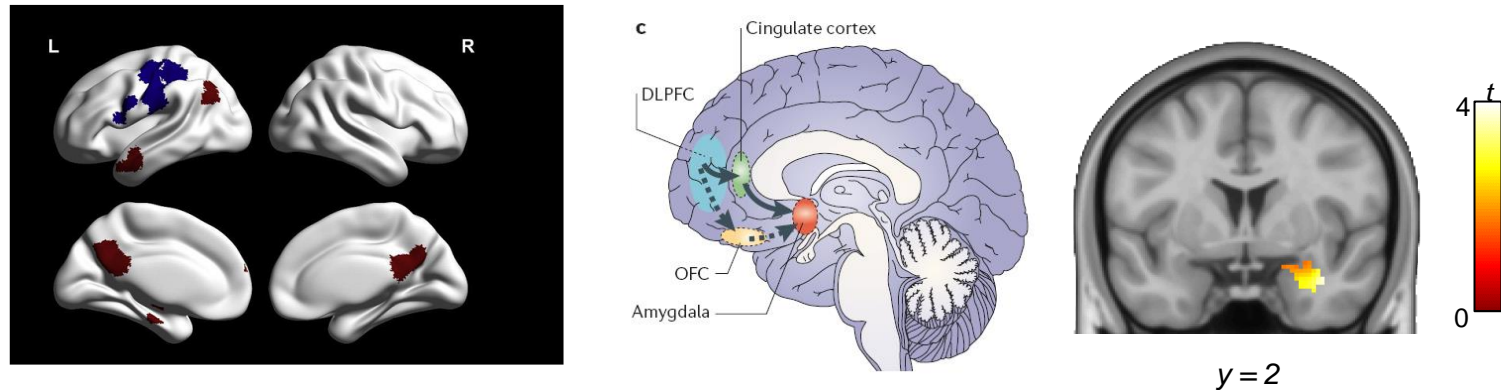


Fig. (1). Neural architecture of emotion regulation (according to Ochsner & Gross, [18]).

Brain areas implicated in the model: A. somatosensory regions; B. amygdala C. anterior cingulate cortex, orbital prefrontal cortex D. anterior cingulate cortex, dorsal prefrontal cortex. See text for details.

Amygdala hyper-reactivity

- Amygdala reactivity linked to maladaptive stress regulation



Bohus, Stoffers-Winterling, Sharp, Krause-Utz, Schmahl, Lieb. The Lancet (2021);

Schulze, Schulze, Renneberg. Schmahl, Niedtfeld. Biol Psychiatry 2019, p. 226

- In EUPD/BPD: Increased amygdala reactivity (and diminished frontal inhibition), imbalance in cortico-limbic structures (including amygdala, hippocampus, anterior cingulate, orbito-frontal cortex, medial prefrontal cortex)
- Reduced amygdala habituation to aversive stimuli, significantly related to severity of adverse childhood experiences (Bilek et al., 2019)
- Brain activity can change along with psychotherapy (Niedtfeld et al., 2017)

Emotional regulation

“Under-regulation”

→ Strong overwhelming emotions

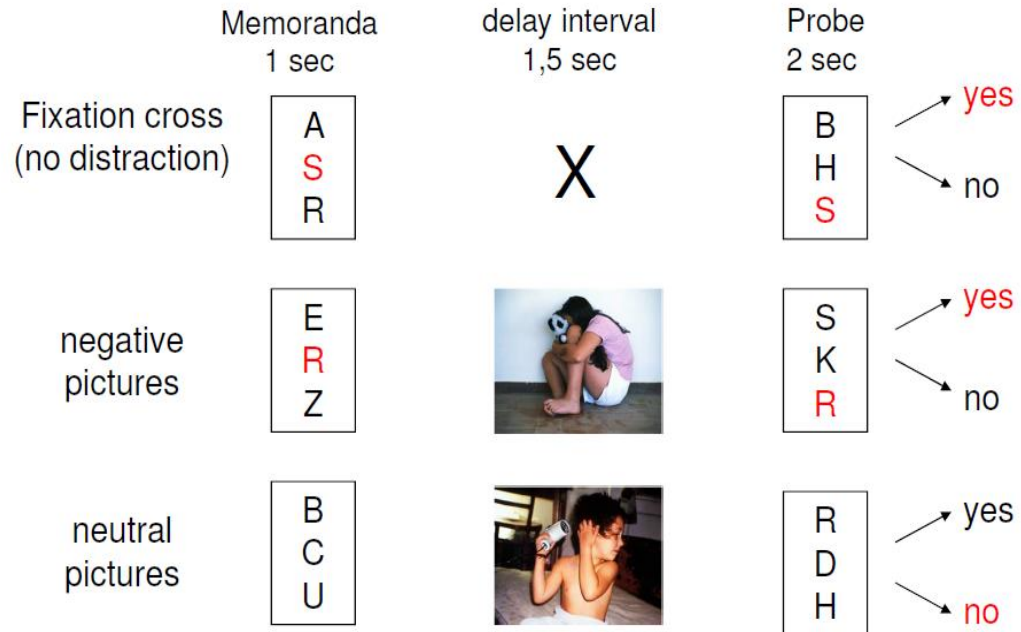
→ Unstable emotions

→ Emotional vulnerability

- **Limited access** to effective emotion regulation strategies
- Use of strategies that increase vulnerability
- Lack of **awareness** and **clarity**
- **Non-acceptance** of emotional responses
- **Impulsivity and difficulties in focusing attention**

Gratz & Roemer (2004); Lanius et al., 2010

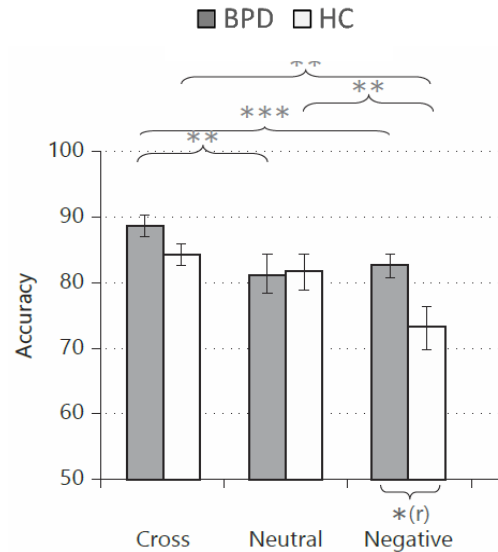
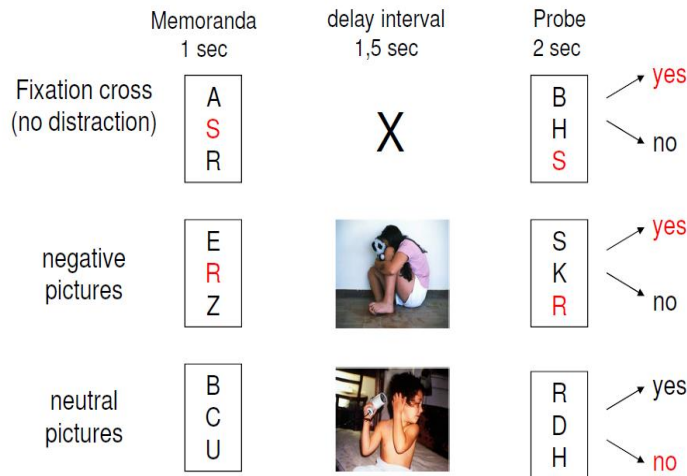
Methods



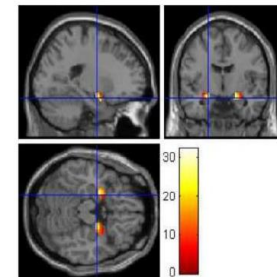
Study 1

Krause-Utz et al., Psych Med., 2012

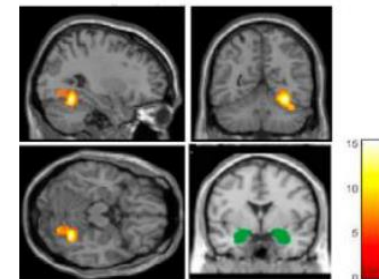
N=22 patients with BPD and ACE vs. N=22 healthy controls



bilateral Amygdala
(p(FDR)<.05)



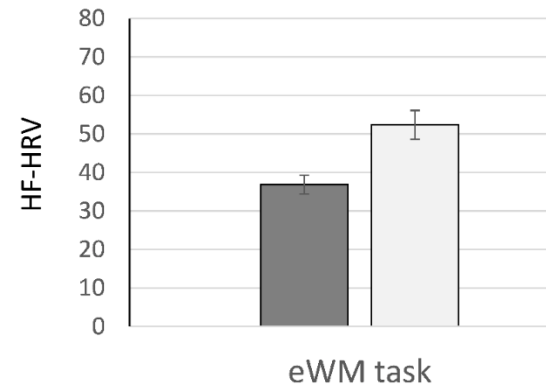
- Increased functional connectivity between amygdala and anterior cingulate
- Increased functional connectivity between amygdala and fusiform gyrus



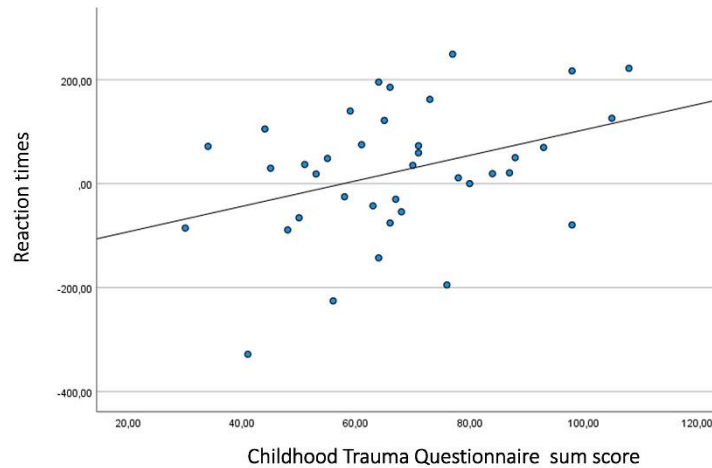
Study 1

Krause-Utz et al., EJPT, 2022;
N= 53 patients with BPD and ACE vs. N=28 healthy controls

Lower heart rate variability
in high-frequency domain
(HF-HRV, 0.15-0.40 Hz)



Severity of adverse childhood experiences predict longer reaction times and reduced HRV



Emotional regulation

“Under-regulation”

“Over-regulation”

- Strong overwhelming emotions
- Unstable emotions
- Emotional vulnerability

- Emotional numbing
- Chronic emptiness

→ **Disconnectedness, dissociation**

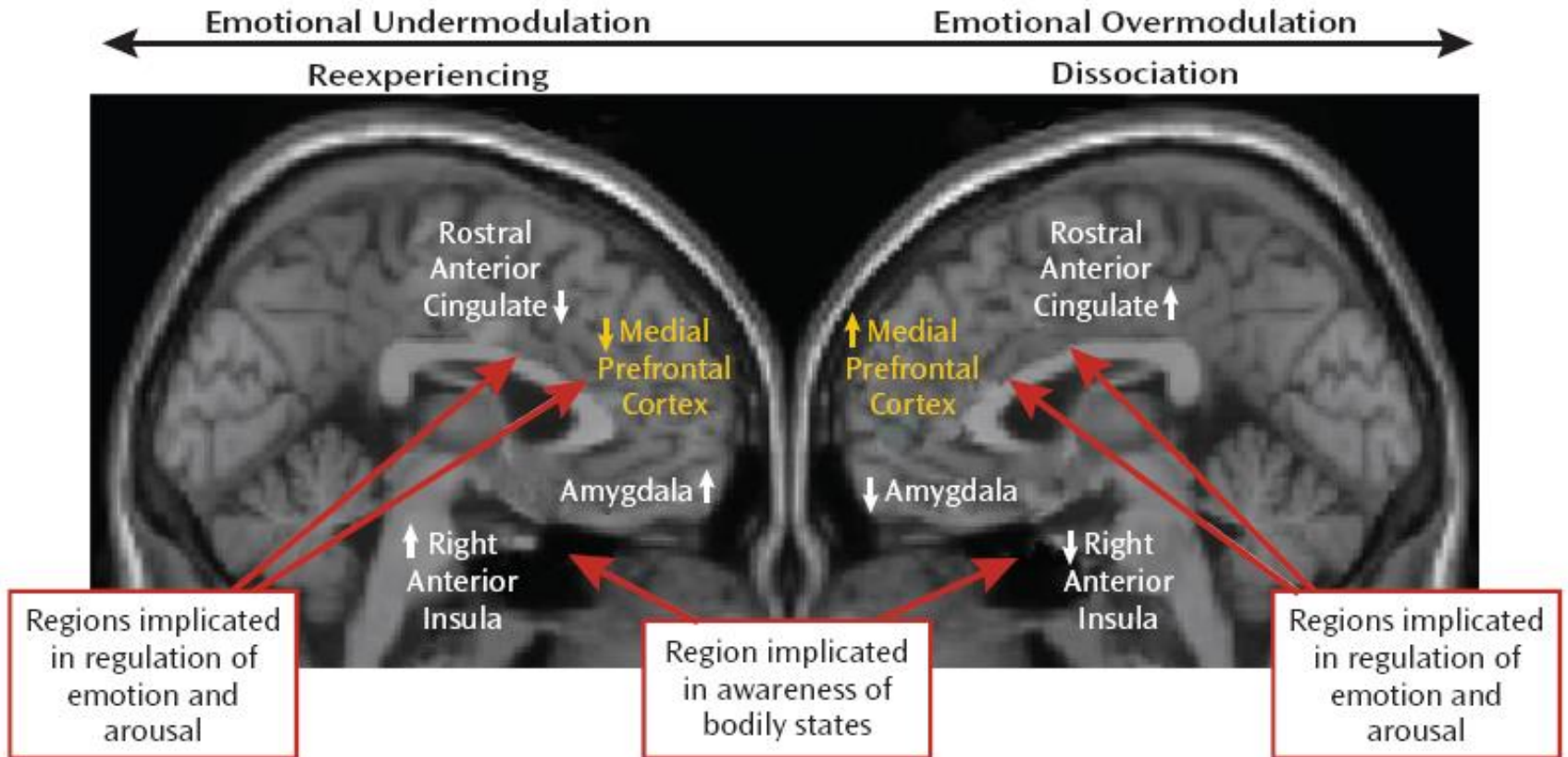
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- **Impulsivity and difficulties in focusing attention**

Gratz & Roemer (2004); Lanius et al., 2010

Emotional under- and overregulation

“Under-regulation”

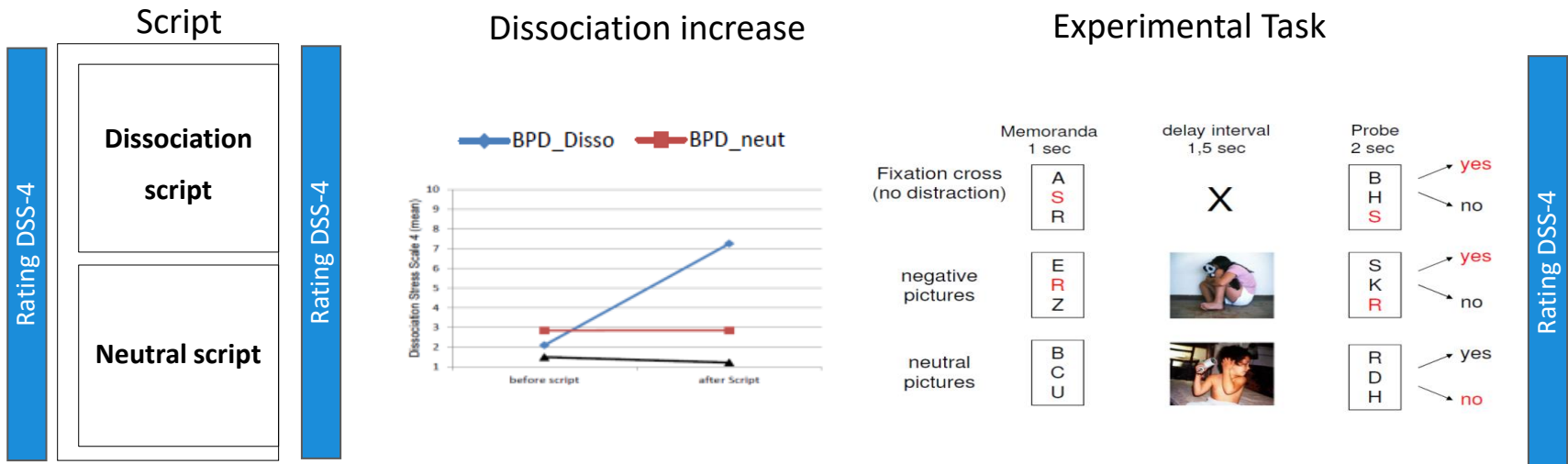
“Over-regulation”



Lanius et al., 2010

Emotional under- and overregulation

Dissociative narratives and script-driven imagery



Functional Magnetic Resonance Imaging (fMRI)

„ [...] We are sitting at the table. I am drifting away and their words do not reach me anymore. As if I was packed up in cotton. I see that they are talking to me but their words just go through me. It is like in slow-motion. Like a movie that does not concern me anymore, a bit frightening actually. This seems to last for an eternity. I am locked inside my body but not really here. [...] “

Most prevalent dissociative experiences

Depersonalization and derealization

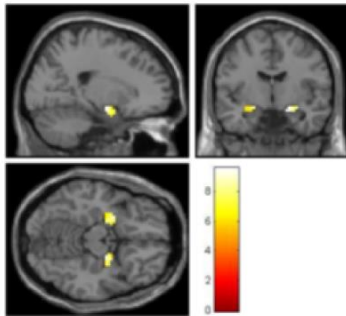
*“like wrapped up in cotton.”; “like a movie that is passing me by”;
“reality starts to feel further away”; “everything is blurred”*

Somatoform dissociation

- Difficulties speaking (*“I cannot speak”; “it is very difficult for me to speak”; “I can't talk anymore”*)
- Loss of bodily control (*“I cannot feel my legs, my body”; “my skin feels numb”; “I can't feel my legs, my body. I feel dizzy.”*).
- Difficulty hearing (*“questions do not reach me, don't realise what we are talking about”*)
- (Self-induced) dissociative absorption (*“I stare on the corridor...”*).

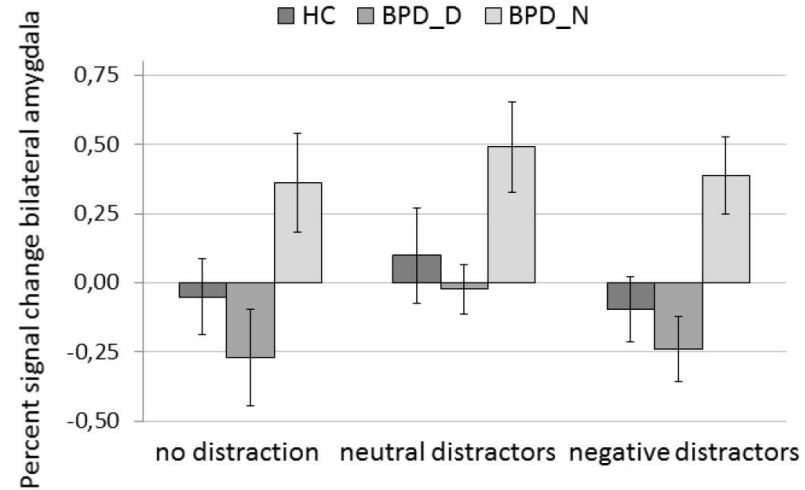
Emotional under- and overregulation

Krause-Utz et al., 2018

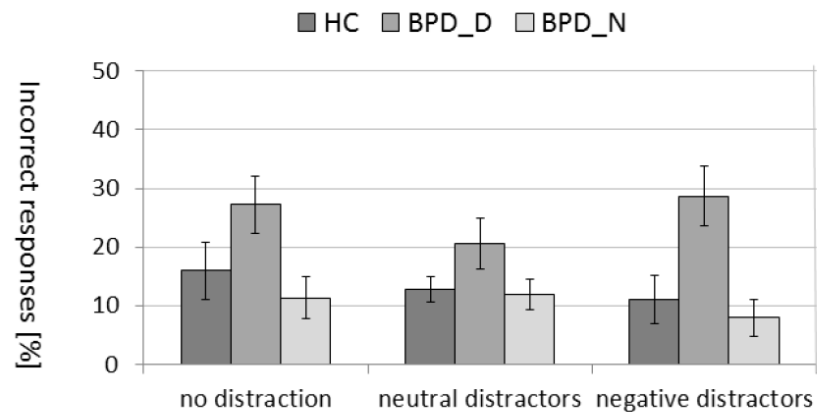


Bilateral amygdala
 [21, -7, -14],
 $F=9.56, Z=5.48$
 [-27, 2, -17]
 $F=8.63, Z=5.14,$
 $p < 0.05$ (FWE corrected)

0



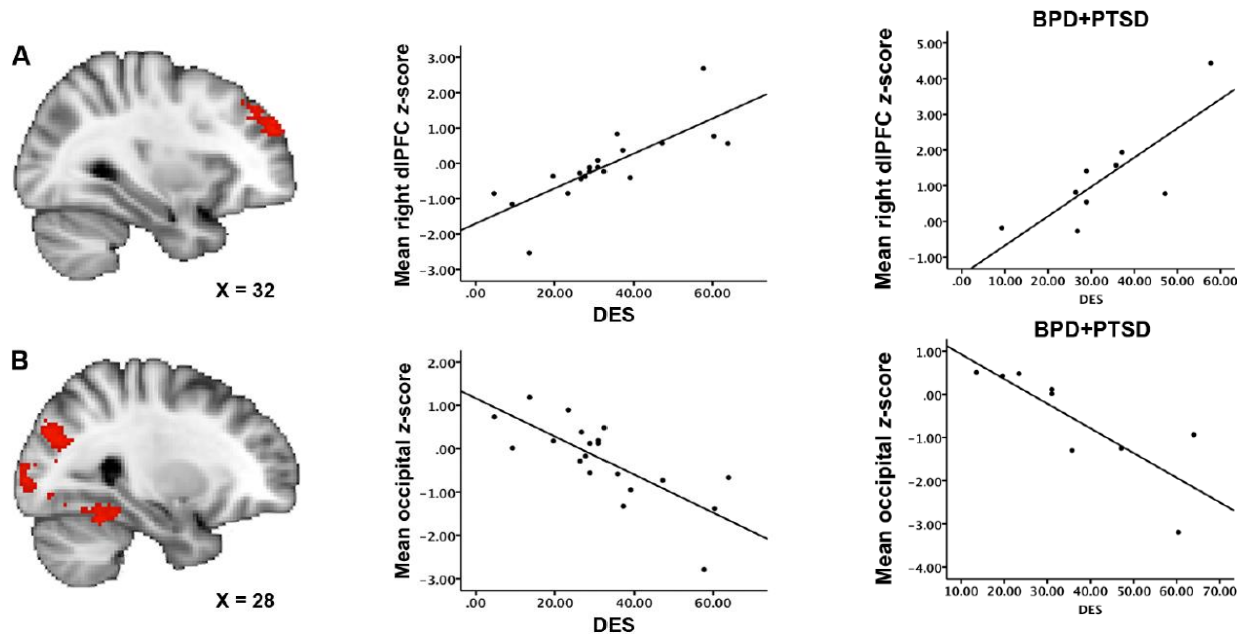
Emotional Working Memory Task



Lower amygdala activity and more incorrect responses during an emotional working memory task in patients with acute dissociation

Empirical evidence in BPD?

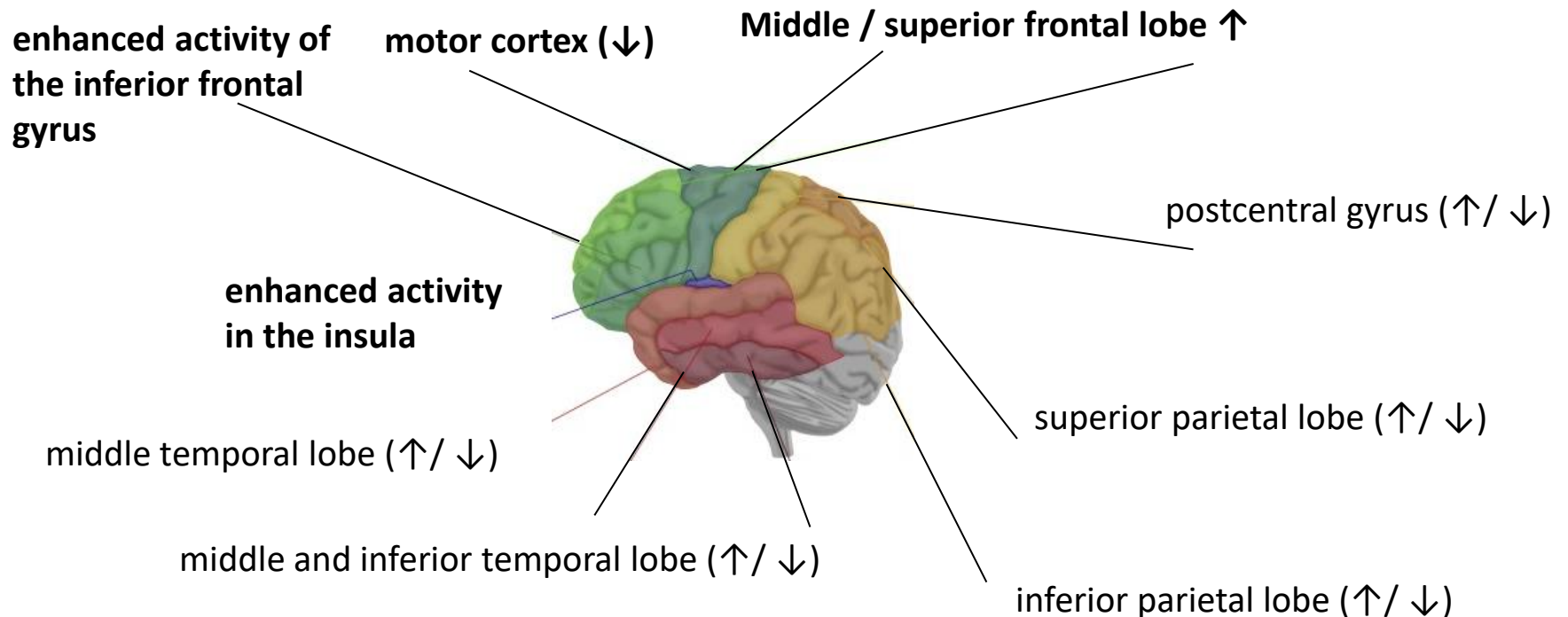
Krause-Utz, Veer, Rombouts, Bohus, Schmahl, & Elzinga, *Psychological Medicine*, 2014



Dissociation predicts amygdala Resting-state functional connectivity in BPD: Increased amygdala functional connectivity with dlPFC (A) and decreased amygdala functional connectivity with occipital lobe (fusiform gyrus) (B)

Brain networks involved in dissociation

Neurobiological findings on dissociation are still very diverse,
cannot always be replicated



Roydeva and Reinders (2020), taken from page 165-166

Summary and discussion



Maskot / Tom Grill / martin-dm/E+ via Getty Images

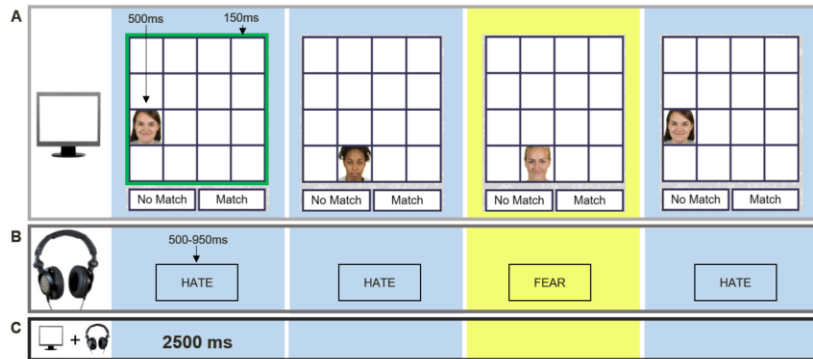
- Hypersensitivity to personally relevant emotional information is linked to deficits in working memory (Kaiser et al., 2016, 2020; Lazarus et al., 2014)
 - Selective attention to stressful (triggering) stimuli can interfere with goal-directed behaviours (Jordan et al., 2013; Koch et al., 2018, Schweizer et al., 2013).
 - Dissociation may dampen emotional reactivity but also interfere with goal-directed behaviour (Ebner-Priemer et al., 2009; Krause-Utz et al., 2018; Winter et al., 2015)
- flexible (and balanced) modulation of emotional attention

Anti-Dissociative Skills

- Psychoeducation and functional analysis (typical triggers and functions)
- Distress tolerance and emotion regulation
- Skills-assisted ambulatory monitoring (app)
- Reducing vulnerabilities (basic self-care: drink, eat, sleep sufficiently)

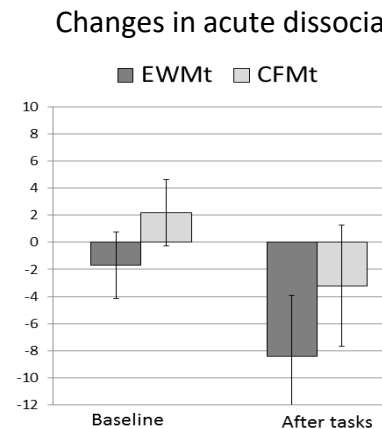
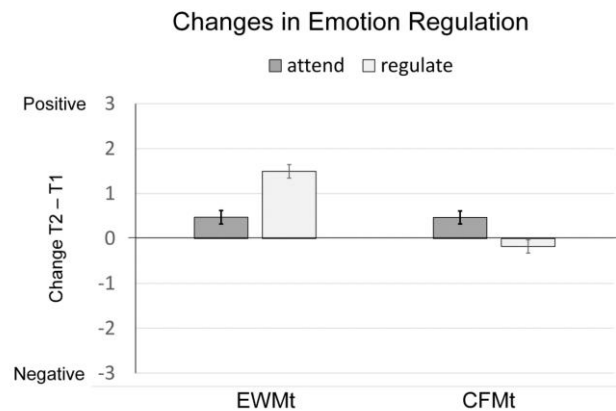


Outlook



Preliminary effectiveness of an eWM training in 50 patients with BPD
 → EWMt : increase of n-back level from Mean: 3.82, SD: ± 0.76 to 5.14 ± 1.08 ($t_{(21)}=6.54, p<.001, d=1.34$).

Krause-Utz, Walther, Schweizer, Lis, Hampshire, Schmahl, & Bohus. 2020



Changes in eWM (performance speed after emotional distraction) predicted changes in ER ($B=-0.007, SE=.003, t=2.22, p=.034, CI: [-0.014, -0.001]$)

Thank you

All participants of our studies



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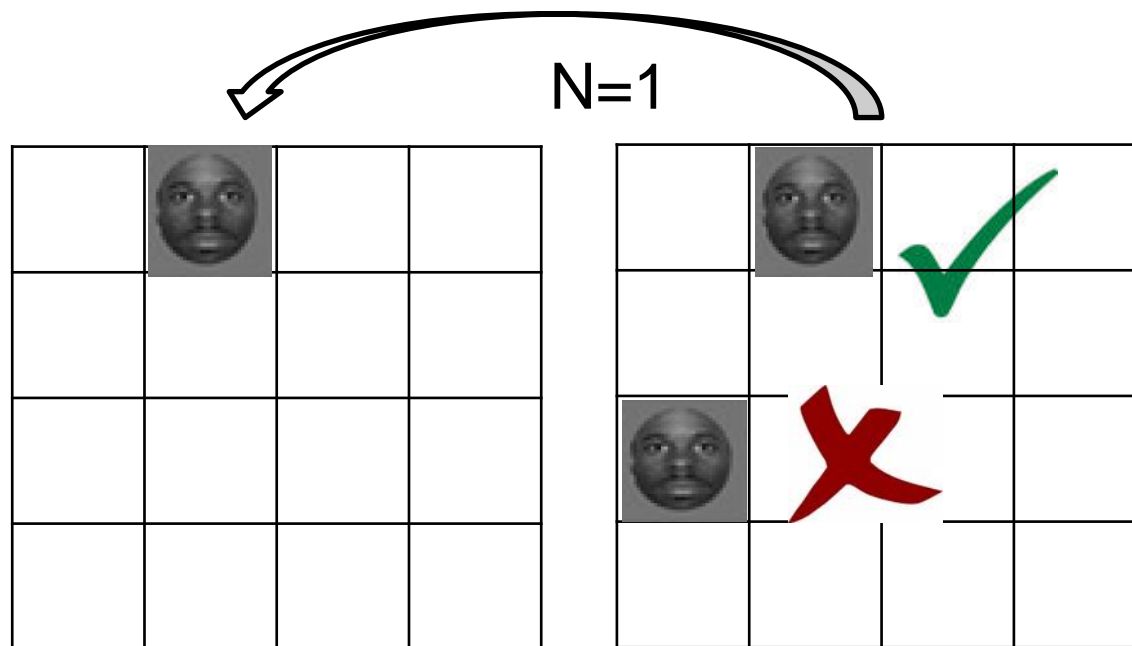
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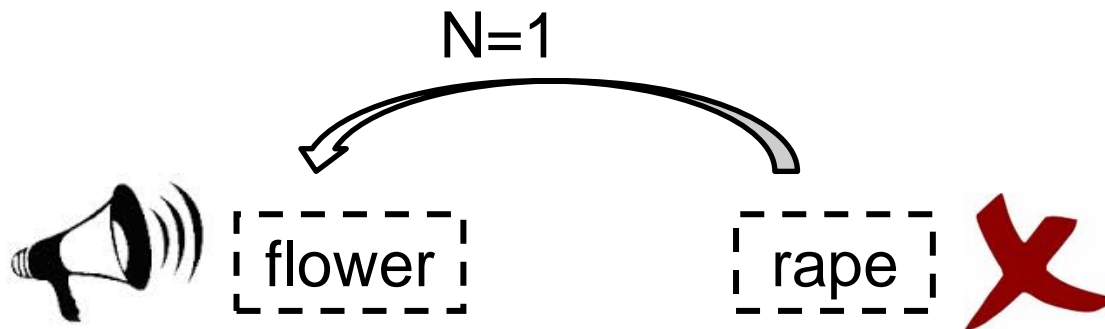
Background

Emotional Working Memory Training

Visual: day 1, 3, 5
Auditory: day 2, 4, 6
Dual: day 7 onwards



Susanne Schweizer

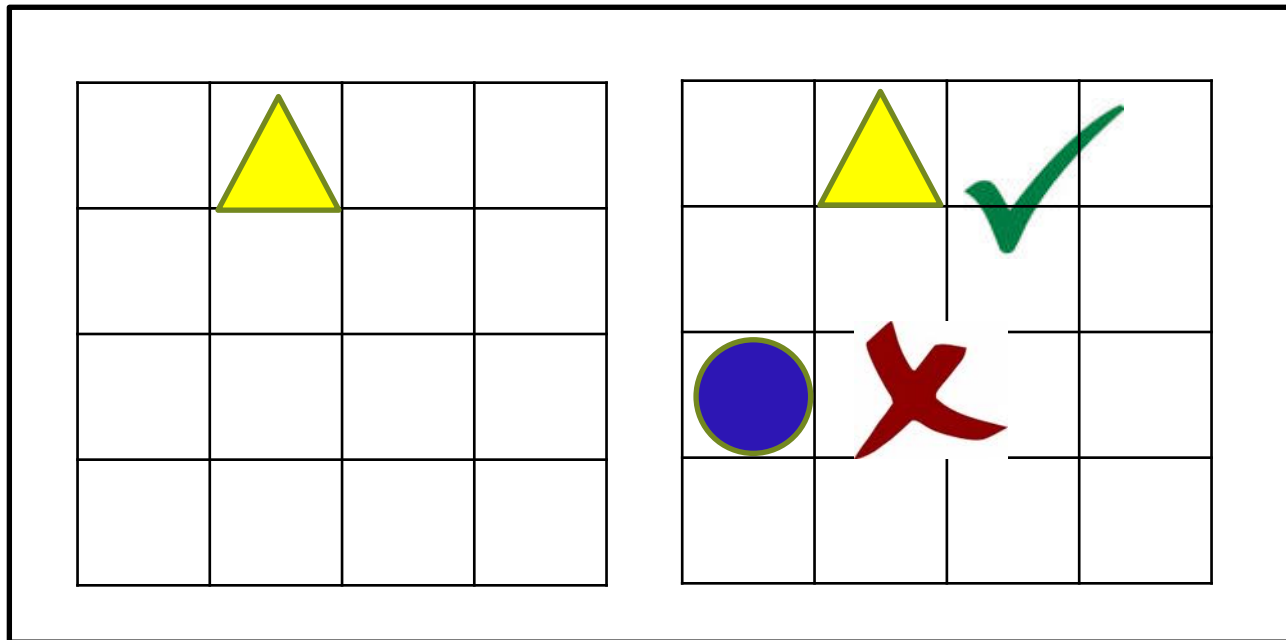


Background

Emotional Working Memory Training

Schweizer, Grahn, Hampshire, Mobbs, & Dalgleish. *J Neurosc*, 2013

Placebo training



Cognitive feature match task (non-emotional stimuli)

Difficulty ↑ Start with N=1, increasing difficulty (adaptive to performance)

Methods

Adapted Emotional Working Memory Training

Krause-Utz, Walther, Schweizer, Lis, Hampshire, Elzinga, Schmahl, & Bohus. 2020

Proof-of principle study – Randomized Controlled Trial in 50 women with BPD

- Daily training between 20–30 min, with increasing difficulty
- Opportunity to stop the training session after 10 minutes
- Training manuals
- Regular weekly contact
- Individual evaluation of acceptance / motivation

fernzuhalten.

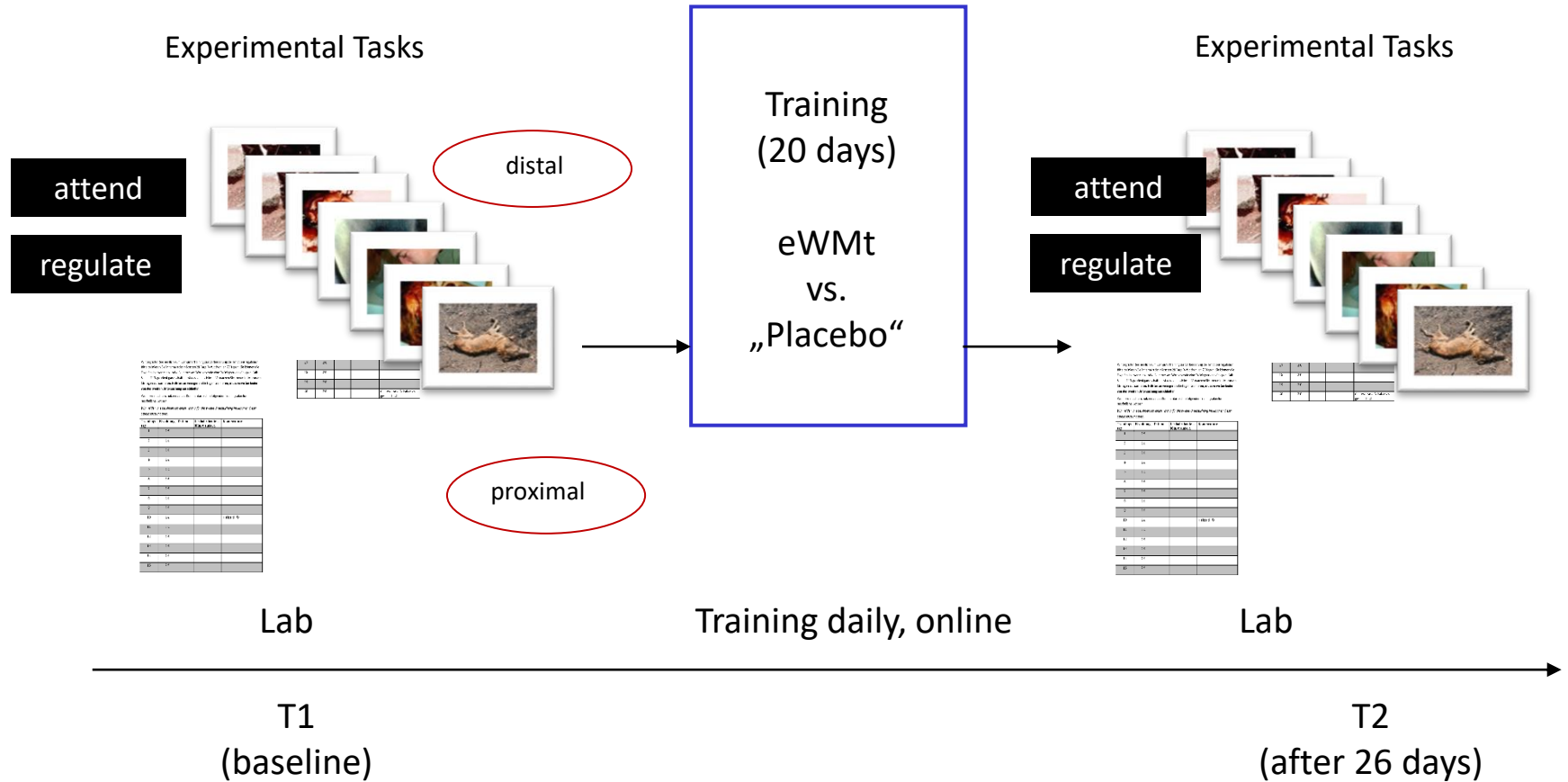
Dieses Training wurde entwickelt um die mentale Kontrolle zu üben, die Sie befähigt, auszuwählen, welche Information Sie im Kopf behalten und welche nicht.

Bei Teilnehmern ohne eine Borderline-Störung konnte gezeigt werden, dass dieses Training darüber hinaus die Emotionsregulation verbessert hat. Wir möchten nun herausfinden, ob dieses Training auch Menschen mit einer Borderline-Störung helfen kann.



Methods

Emotional Working Memory Training



Results

Emotional Working Memory Training

Trainings effects

Both groups significantly improved their performance

→ EWMt : increase of n-back level from Mean: 3.82, SD: ± 0.76 to 5.14 ± 1.08
($t_{(21)}=6.54, p<.0001, d=1.34$).

→ CFMt: From 1556.11 ± 1200.59 to 4218.21 ± 2951.99 on the last training day
($t_{(18)}=3.47, p=.003, d=1.18$).

→ Similar training duration in sec. ($t_{(48)}=0.53, p=.601$).

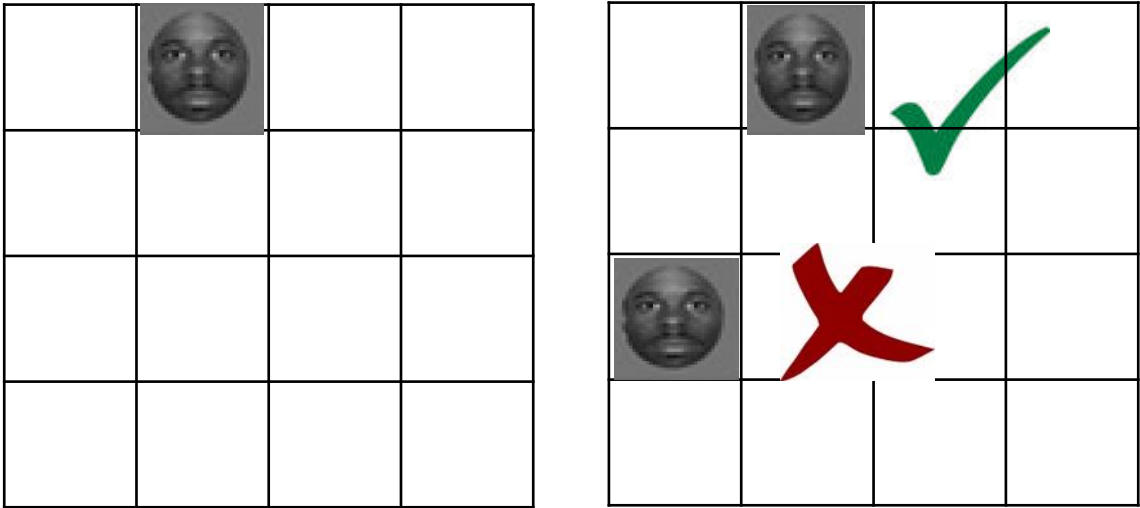
→ Positive correlation with training duration in eWMt ($r=.431, p=.016$), but not in CFMt
($r=.263, p=.262$).

Background

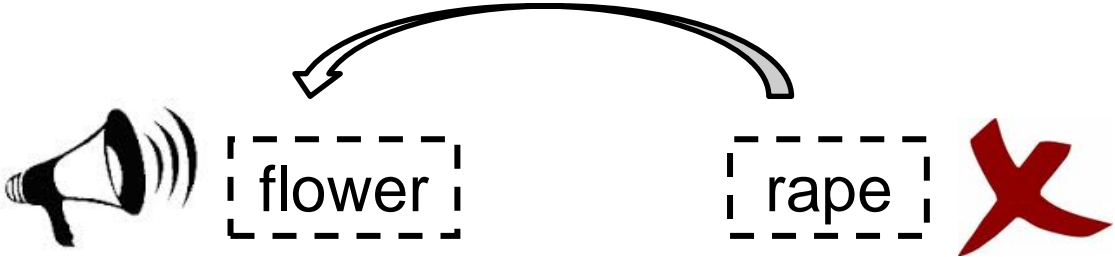
Emotional Working Memory Training



Visual: day 1, 3, 5
Auditory: day 2, 4, 6
Dual: day 7 onwards



N=1



Susanne Schweizer

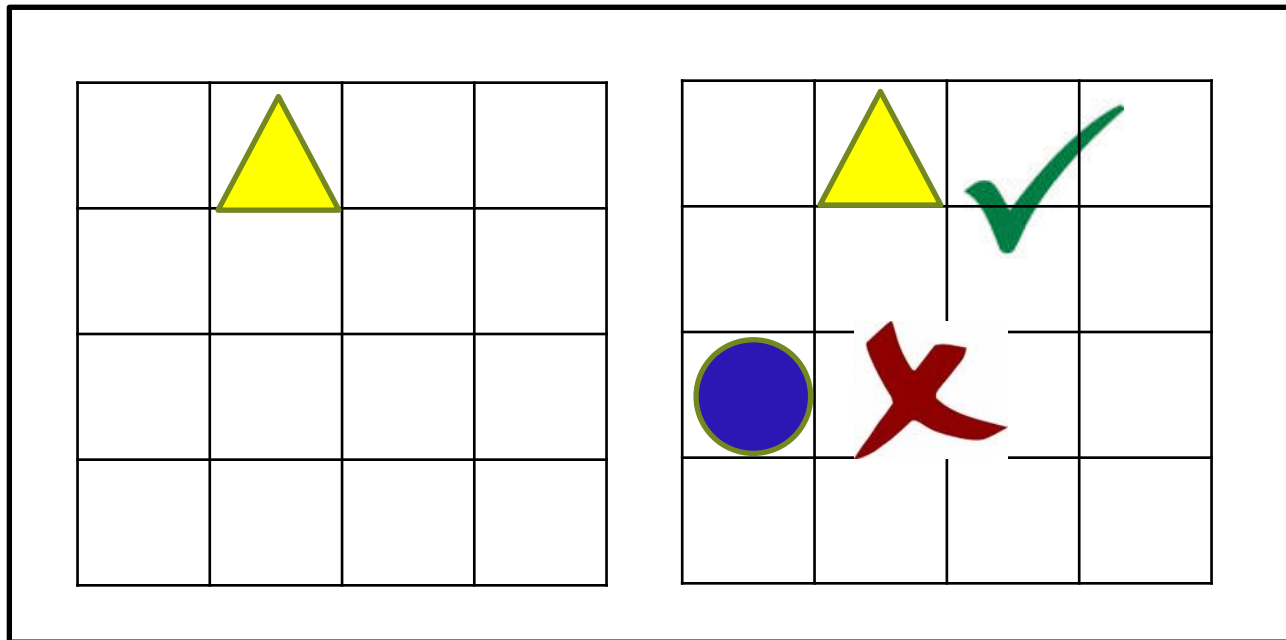


Background

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Schweizer, Grahn, Hampshire, Mobbs, & Dalgleish. *J Neurosc*, 2013

Placebo training



Cognitive feature match task (non-emotional stimuli)

Difficulty ↑ Start with N=1, increasing difficulty (adaptive to performance)

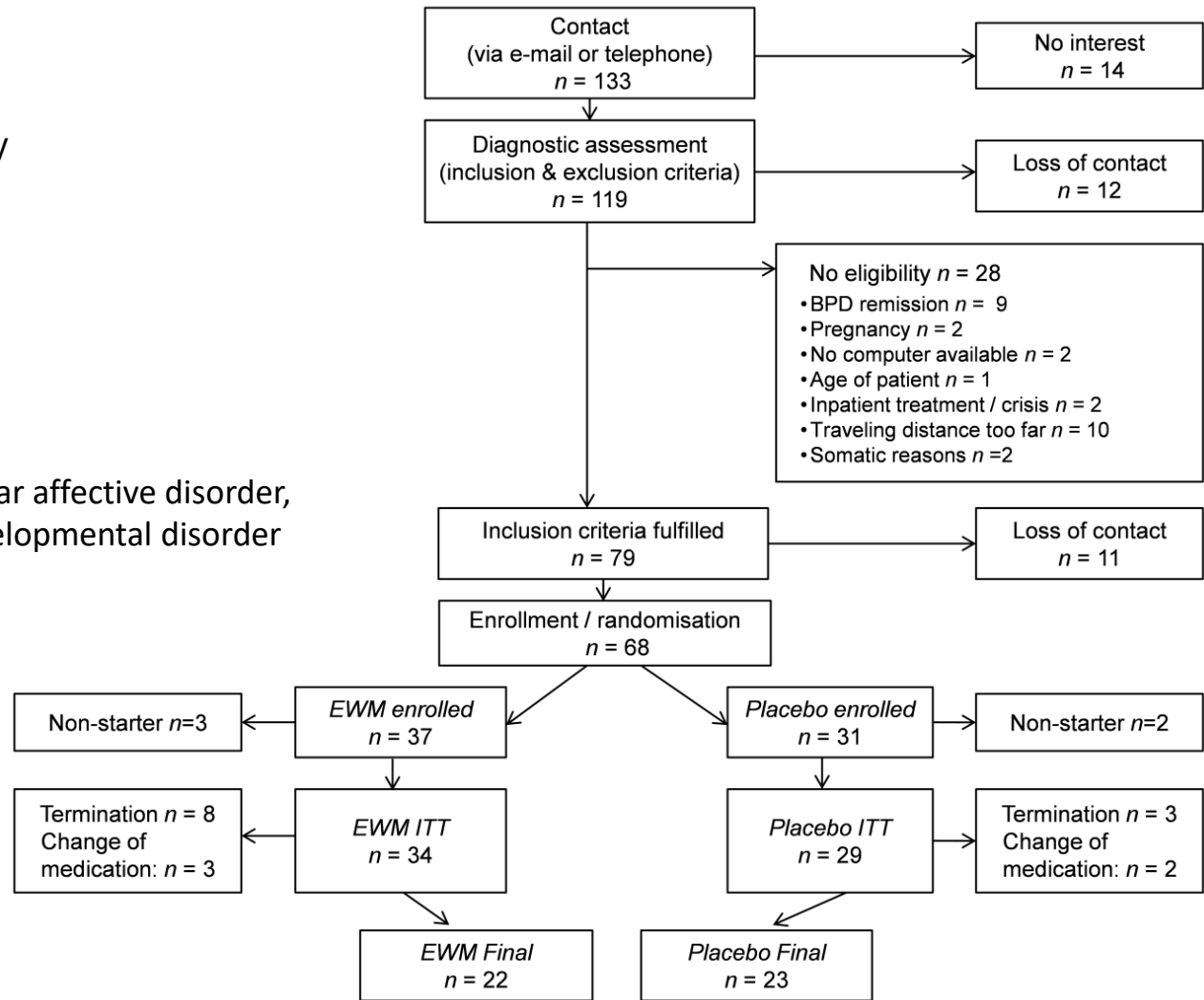
Inclusion:

- Female
- BPD according to DSM-IV
- 18 – 50 years

Exclusion:

- Inpatient treatment
- Severe somatic illness
- Change in medication
- Substance dependence
- Psychotic disorder, bipolar affective disorder, mental retardation, developmental disorder
- Suicidal crisis

Power analysis: $n=46$
(15% β -error, 0.80)



Sample

	EWM	CFM	Group statistics (<i>t</i> and X^2)
Age	30.70 ± 9.40	34.09 ± 10.33	$t_{(41)}=1.12, p=.270$
Intelligence	29.55 ± 10.33	31.14 ± 3.17	$t_{(41)}= 1.62, p=.114$
Years of education			
9 years	<i>n</i> =3 (15%)	<i>n</i> =2 (9%)	
10 years	<i>n</i> =9 (45%)	<i>n</i> =7 (32%)	$X^2=1.89, p=.389$
12 years	<i>n</i> =8 (40%)	<i>n</i> =13 (59%)	
Antidepressants	<i>n</i> =7 (35%)	<i>n</i> =7 (32%)	$X^2=0.10, p=.750$
Antipsychotics	<i>n</i> =1 (5%)	<i>n</i> =3 (14%)	$X^2=0.82, p=.365$
DERS Total	123.13 ± 19.93	129.50 ± 17.88	$t_{(41)}=1.11, p=.276$
ERQ Cognitive Reappraisal	3.41 ± 1.19	3.82 ± 1.00	$t_{(41)}= 1.22, p=.228$
ERQ Suppression	3.64 ± 1.34	4.17 ± 1.51	$t_{(41)}=1.22, p=.238$
STAI	44.17 ± 9.06	52.89 ± 8.82	$t_{(41)}=3.00, p=.005$
BDI-II Total	24.90 ± 12.38	31.26 ± 10.03	$t_{(41)}=18.6, p=.070$
BSL-23 Total	1.58 ± 0.84	2.07 ± 0.64	$t_{(41)}= 2.16, p=.037$
DES Total	19.77 ± 8.24	29.93 ± 11.98	$t_{(41)}=3.19, p=.003$

Note: This table shows means ± standard deviation or frequencies (*n*) with percentages (%). BDI-II=Beck Depression Inventory II; BSL-23=Borderline Symptom-Liste-23; DERS=Difficulties in Emotion Regulation Scale; DES=Dissociative Experiences Scale; ERQ=Emotion Regulation Questionnaire; STAI=State-Trait- Anxiety Inventory.

- Recruited at outpatient unit of the Central Institute of Mental Health, Mannheim, Germany
- Drop-out rates did not differ significantly from completer (all $p>.05$)