# Improving Treatments for Individuals with Borderline Personality Disorder (BPD) and with Complex Posttraumatic Stress Disorder (CPTSD)

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# Overview

1) What has been achieved in the treatment of BPD?

2) Starting points for improving treatment efficacy
   - Model of BPD / CPTSD

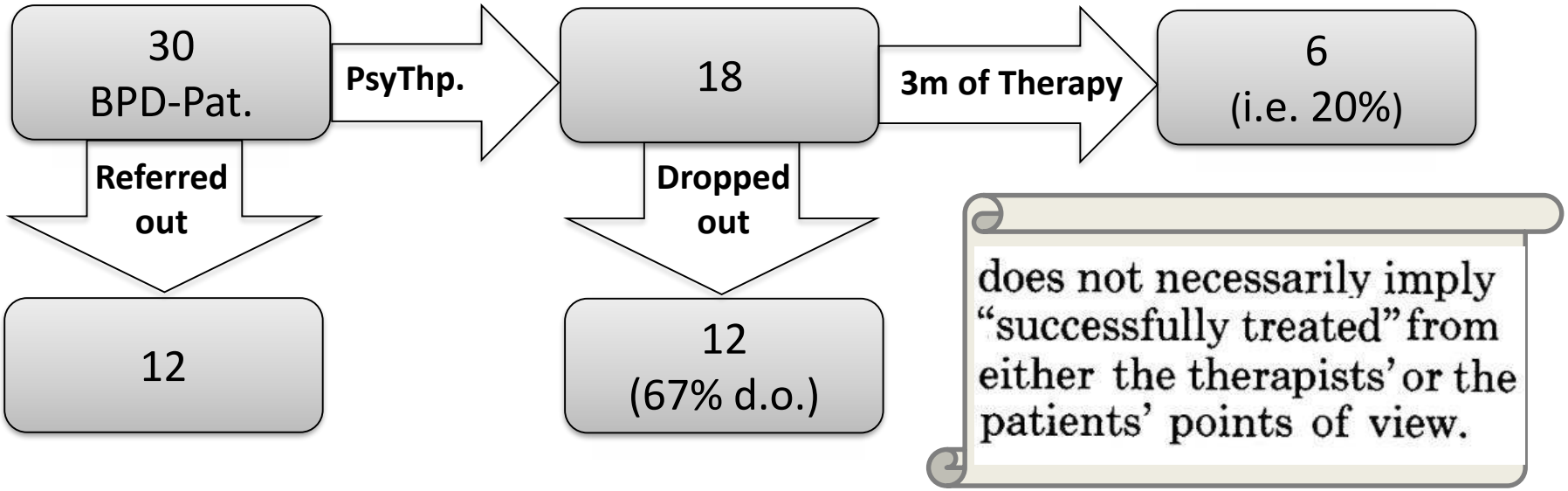
   2.1) Applied basic research: Dissociation
   2.2) Applied basic research: NSSI
   2.3) Neuro-biologically informed approach: Neurofeedback

3) Supporting the patient in building a life worth living
   3.1) patients‘ perspective / feedback
   3.2) positive body image

4) Deficits in current therapies of BPD
   4.1) Excess mortality
   4.2) Somatic comorbidities
   4.3) Psychiatric comorbidities

# Early Treatment Studies for BPD

**E.g., Skodol et al., 1983**

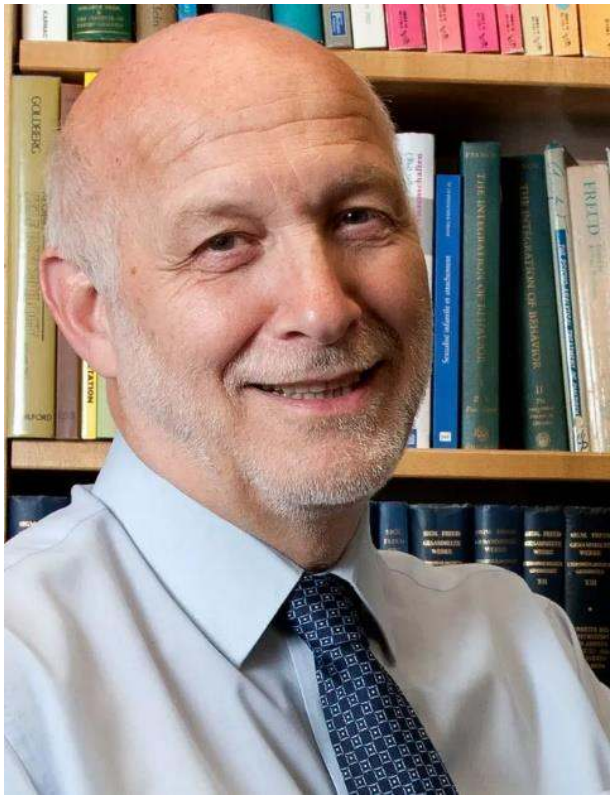



- Very high drop-out rates
- Very low success rates

→ BPD was considered barely treatable, and was (sometimes still is) highly stigmatized

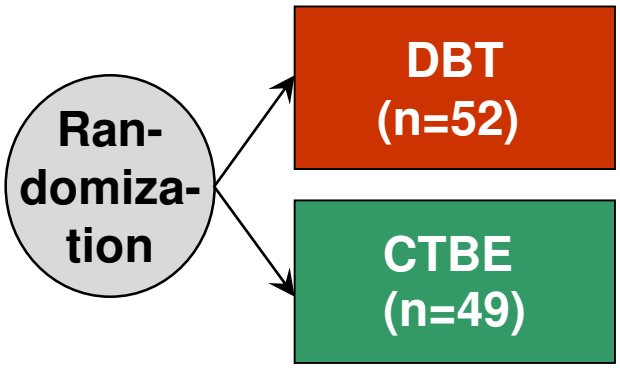
# Disorder-specific Therapies for BPD

## E.g., DBT (by Marsha Linehan), MBT (by Peter Fonagy)

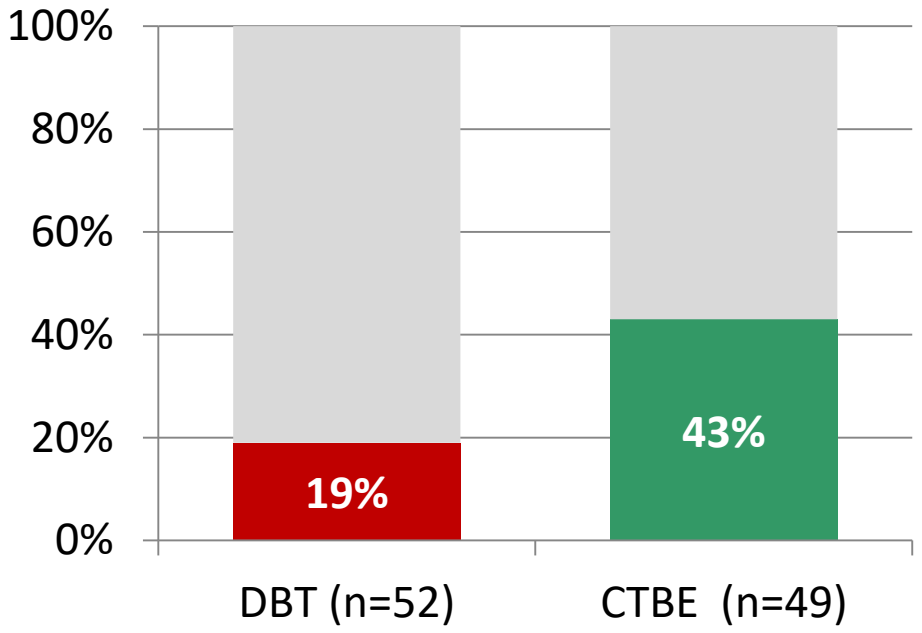


# RCT: DBT vs Community Treatment by Experts

## 1 Year of Outpatient Treatment + 1 Year of follow-up




*Linehan et al 2006*

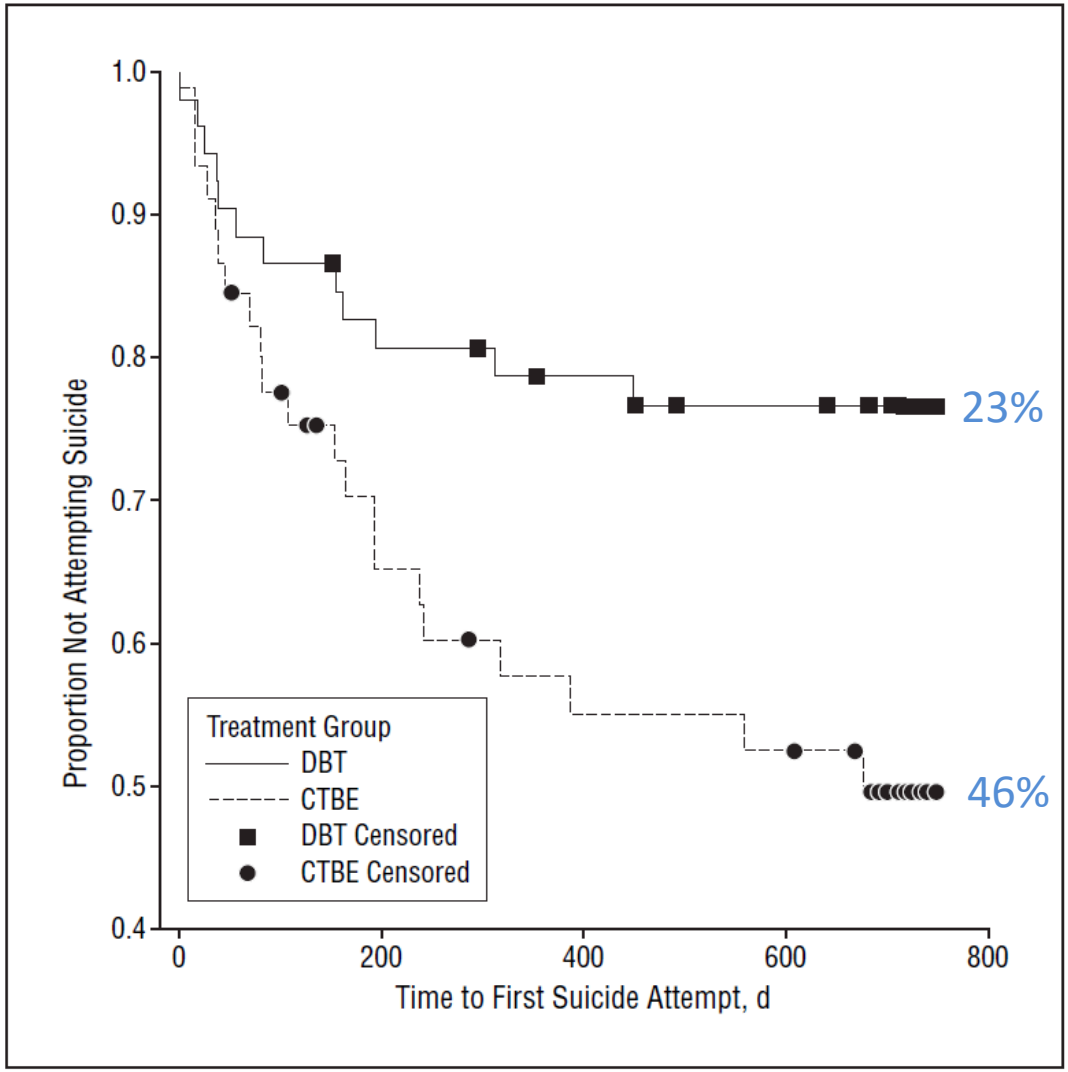



DBT vs CTBE: p=0.005

→ Drop-out rate during 1 year of therapy was sign. lower in the DBT group (and incomparably lower than it was in the early BPD-studies)

# DBT vs Community Treatment by Experts

## Suicide Attempts during 2 years (1 year of treatment + 1 year of follow-up)




Half the rate of suicide attempts in the DBT group (RR=0.5; p=0.005); NNT= 4.2

*Linehan et al 2006*

# Evidence from Single Studies, Meta Analyses and Cochrane Reviews


→ Cochrane Collaboration issues Cochrane Reviews summarizing RCTs on a specific topic.

Cochrane Library

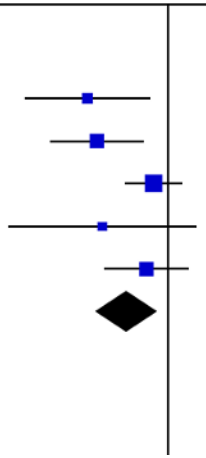
**Psychological therapies for people with borderline personality disorder (Review)**

**Analysis 1.6. Comparison 1: Psychotherapy vs TAU, Outcome 6: Primary: suicide-related outcomes (dichotomous)**

| Study or Subgroup | Psychotherapies Events | Total | TAU Events | Total | Weight | Risk Ratio IV, Random, 95% CI |
|---|---|---|---|---|---|---|
| **1.6.1 End of treatment** | | | | | | |
| Bateman 1999 (1) | 1 | 19 | 12 | 19 | 14.7% | 0.08 [0.01 , 0.58] |
| Bateman 2009 (1) | 2 | 71 | 16 | 63 | 21.4% | 0.11 [0.03 , 0.46] |
| Doering 2010 (2) | 7 | 51 | 11 | 52 | 32.6% | 0.65 [0.27 , 1.54] |
| Philips 2018 (3) | 0 | 24 | 3 | 22 | 7.9% | 0.13 [0.01 , 2.41] |
| Stanley 2017 | 3 | 37 | 6 | 38 | 23.4% | 0.51 [0.14 , 1.90] |
| **Subtotal (95% CI)** | | **202** | | **194** | **100.0%** | **0.27 [0.11 , 0.67]** |
| Total events: | 13 | | 48 | | | |

Heterogeneity: $Tau^2 = 0.45$; $Chi^2 = 7.30$, df = 4 (P = 0.12); $I^2 = 45\%$

Test for overall effect: Z = 2.82 (P = 0.005)



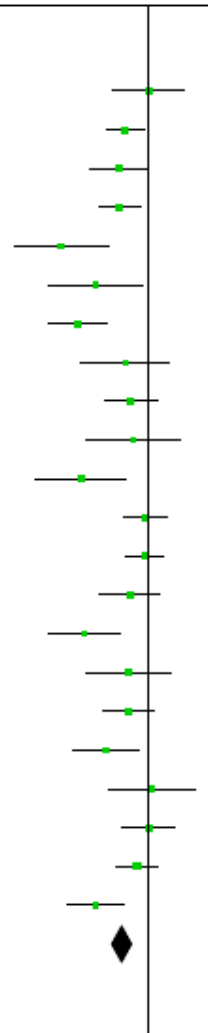

- Clear & strong effect on suicide-attempts (Linehan et al. 2006) is supported by the current Cochrane Review (Storebö et al. 2020)
- When active treatments are compared to treatment as usual (TAU) effects might even be larger than e.g., in Linehan‘s study

## Analysis 1.1. Comparison 1: Psychotherapy vs TAU, Outcome 1: Primary: BPD symptom severity (continuous)

| Study or Subgroup | Psychotherapies Mean | SD | Total | TAU Mean | SD | Total | Weight | Std. Mean Difference IV, Random, 95% CI |
|---|---|---|---|---|---|---|---|---|
| **1.1.1 End of treatment** | | | | | | | | |
| Amianto 2011 (1) | 3.3 | 1 | 16 | 3.3 | 1.1 | 17 | 3.9% | 0.00 [-0.68 , 0.68] |
| Blum 2008 (2) | 9.8 | 8.0623 | 65 | 13.4 | 7.6811 | 59 | 6.5% | -0.45 [-0.81 , -0.10] |
| Bos 2010 (3) | 79.7 | 25.8 | 26 | 95.1 | 29.1 | 26 | 4.8% | -0.55 [-1.11 , 0.00] |
| Doering 2010 (4) | 4.79 | 1.54 | 52 | 5.63 | 1.47 | 52 | 6.2% | -0.55 [-0.95 , -0.16] |
| Farrell 2009 (5) | 18.81 | 9.47 | 16 | 32.75 | 5.9 | 12 | 2.9% | -1.66 [-2.54 , -0.78] |
| Gratz 2006 (6) | 25.83 | 5.72 | 12 | 34.7 | 10.81 | 10 | 2.8% | -1.02 [-1.92 , -0.11] |
| Gratz 2014 (6) | 27.47 | 6.59 | 31 | 35.88 | 5.59 | 30 | 4.8% | -1.36 [-1.92 , -0.80] |
| Gregory 2008b (6) | 33.6 | 12.4 | 10 | 38.4 | 8.62 | 13 | 3.1% | -0.44 [-1.28 , 0.39] |
| Jørgensen 2013 (7) | 2.8 | 2.5 | 42 | 3.6 | 2.1 | 24 | 5.2% | -0.33 [-0.84 , 0.17] |
| Koons 2001a (8) | 3.6 | 1.6 | 10 | 4.2 | 2.3 | 10 | 2.9% | -0.29 [-1.17 , 0.59] |
| Kredlow 2017a (7) | 1.17 | 1.17 | 14 | 4.25 | 3.2 | 12 | 3.0% | -1.28 [-2.14 , -0.42] |
| Laurenssen 2018 (9) | 20.63 | 11.45 | 54 | 21.39 | 10.43 | 41 | 6.1% | -0.07 [-0.47 , 0.34] |
| Leichsenring 2016 (10) | 18.76 | 8.6 | 64 | 19.41 | 9.38 | 58 | 6.5% | -0.07 [-0.43 , 0.28] |
| Leppänen 2016 (11) | 17.54 | 10.14 | 19 | 21.48 | 11.41 | 32 | 4.7% | -0.35 [-0.93 , 0.22] |
| Morton 2012 (12) | 32.76 | 12.47 | 21 | 47.42 | 11 | 20 | 4.0% | -1.22 [-1.89 , -0.55] |
| Philips 2018 (13) | 17 | 9.1 | 13 | 20.7 | 9.1 | 11 | 3.2% | -0.39 [-1.20 , 0.42] |
| Priebe 2012 (14) | 13.1 | 6.9 | 33 | 15.9 | 7.5 | 37 | 5.5% | -0.38 [-0.86 , 0.09] |
| Reneses 2013 (15) | 13 | 7.9 | 18 | 19.1 | 6.9 | 26 | 4.3% | -0.82 [-1.45 , -0.19] |
| Robinson 2016 (16) | 9.64 | 7.41 | 12 | 9.27 | 7.39 | 11 | 3.2% | 0.05 [-0.77 , 0.87] |
| Rossouw 2012b (17) | 2.79 | 0.5385 | 29 | 3.06 | 65.7267 | 30 | 5.2% | -0.01 [-0.52 , 0.50] |
| Schuppert 2012 (18) | 13.29 | 9.53 | 48 | 15.39 | 9 | 49 | 6.1% | -0.22 [-0.62 , 0.17] |
| Soler 2009 (19) | 3.5 | 1.2 | 29 | 4.44 | 0.52 | 30 | 4.9% | -1.01 [-1.55 , -0.47] |
| **Subtotal (95% CI)** | | | **634** | | | **610** | **100.0%** | **-0.52 [-0.70 , -0.33]** |

Heterogeneity: $Tau^2 = 0.10$; $Chi^2 = 48.68$, df = 21 (P = 0.0006); $I^2 = 57\%$

Test for overall effect: Z = 5.51 (P < 0.00001)

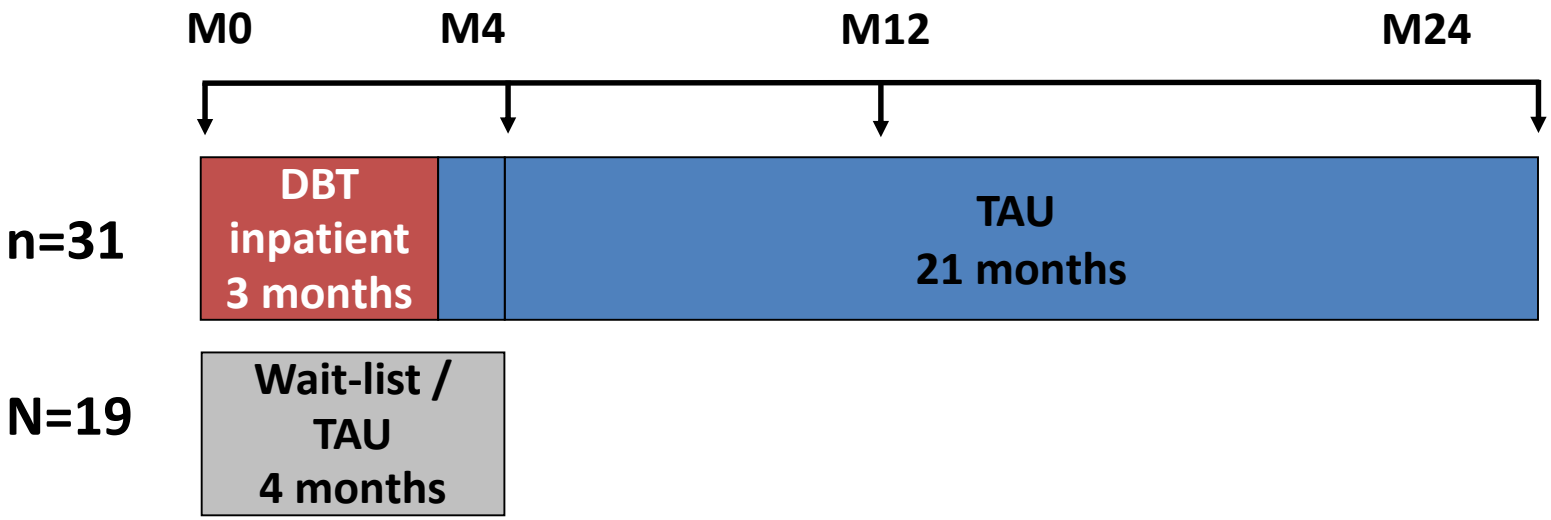


## Individual Treatment Approaches and Authors‘ Conclusion

- “beneficial effects on all primary outcomes in favour of BPD-tailored psychotherapy compared with TAU.”
- “DBT and MBT have the highest numbers of primary trials, with DBT as subject of one-third of all included trials,  followed by MBT.”
- “Subgroup analyses found no evidence of a difference in effect estimates between the different types of therapies (compared to TAU).”

# Do these Effects Persist in the Long Term?

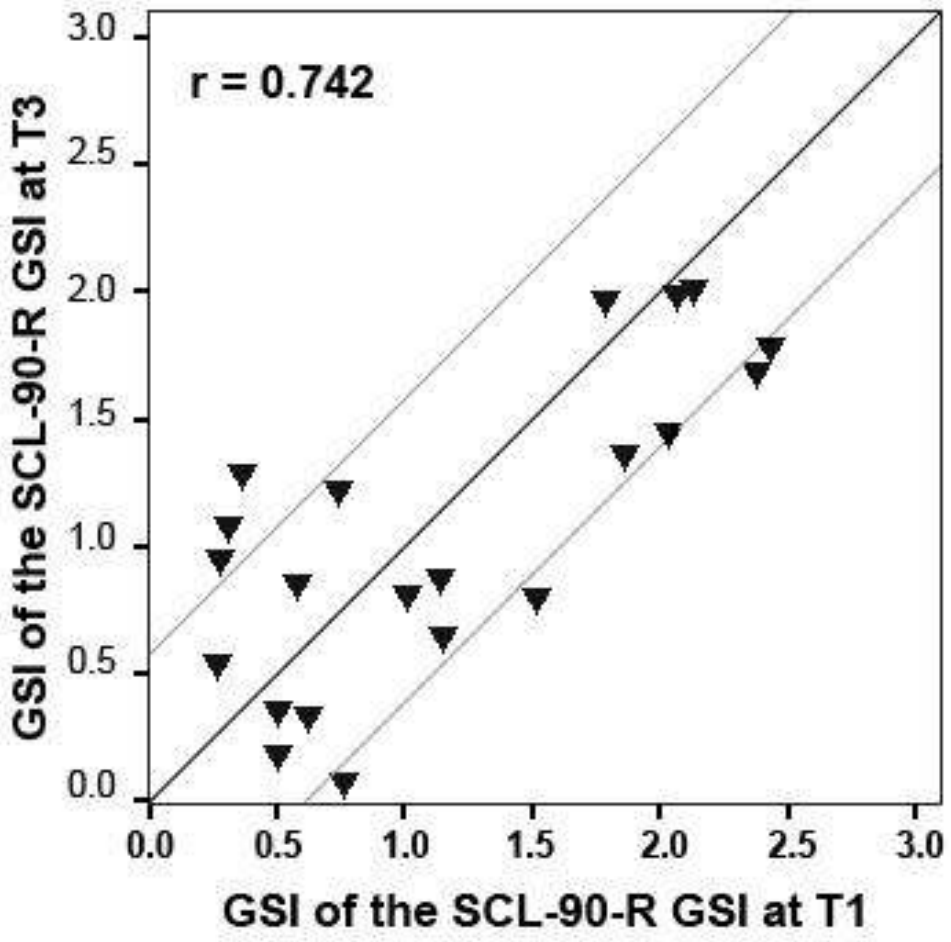
- Still relatively few studies evaluating long term effects of BPD-tailored therapies.
- → follow-up DBT study (n=31 women with BPD)




- Clinically & statistically significant improvements (SCL-90-R, BDI, DES, GAF, NSSI, …) post treatment

*Kleindienst et al 2008*

# Individual Levels of General Psychopathology at Months 1 and 21 after Discharge




⊕ 1) Stable results

2) A patient who responded well to DBT is likely to stay at a good level for at least 2 years.

⊖ A patient who did not fully respond to DBT is likely to stay at a poor level.

*Kleindienst et al 2008*

# What about the Magnitude of these Effects?

→ Meta-Analysis (Efficacy of Psychotherapies in BPD) by Cristea et al., 2017:

| Variable | Stand-alone Design | | |
|---|---|---|---|
| | No. of Trials | Hedges *g* (95% CI)[a] | NNT |
| Posttest | | | |
| Borderline-relevant outcomes[c] | 17 | 0.32 (0.14 to 0.51) | 5.56 |
| Borderline symptoms | 10 | 0.31 (0.04 to 0.57) | 5.75 |
| Self-harm and parasuicidal behavior | 13 | 0.32 (0.09 to 0.54) | 5.56 |
| Suicide | 10 | 0.44 (0.15 to 0.74) | 4.10 |
| Health service use | 13 | 0.40 (0.22 to 0.58) | 4.50 |
| General psychopathology, anxiety, and depression | 13 | 0.32 (0.09 to 0.55) | 5.56 |

[c] Borderline-relevant outcomes include borderline symptoms, self-harm and parasuicidal behavior, and suicide.

- Clinically relevant effects (IMO)
- However, the effects are rather small (IMO)
- With too many pat. not responding or droppng out (ca. 25%)

"DBT may currently be one of the best treatments available, but it is far from being good" *(MML 1996)*

A lot has been achieved → further improvements!

# Summary of Section 1

- Before BPD-tailored psychotherapies have been available outcome in treatment studies was poor with respect to both dropout rates and efficacy.
- **A lot has been achieved** with **specifically tailored treatments**, in particular with **DBT** and also with **MBT**
- However, **dropout rates remain rather high** (around 25%) and **efficacy remains unsatisfactory** (medium between-group effect-sizes at best)

→ **We need to find ways for improving BPD-tailored therapies!**

# Overview

1) What has been achieved in the treatment of BPD?

**2) Starting points for improving treatment efficacy**
- **Model of BPD / CPTSD**

**2.1) Applied basic research: Dissociation**
2.2) Applied basic research: NSSI
2.3) Neuro-biologically informed approach: Neurofeedback

3) Supporting the patient in building a life worth living
3.1) patients‘ perspective / feedback
3.2) positive body image

4) Deficits in current therapies of BPD
4.1) Excess mortality
4.2) Somatic comorbidities
4.3) Psychiatric comorbidities

ARTICLE

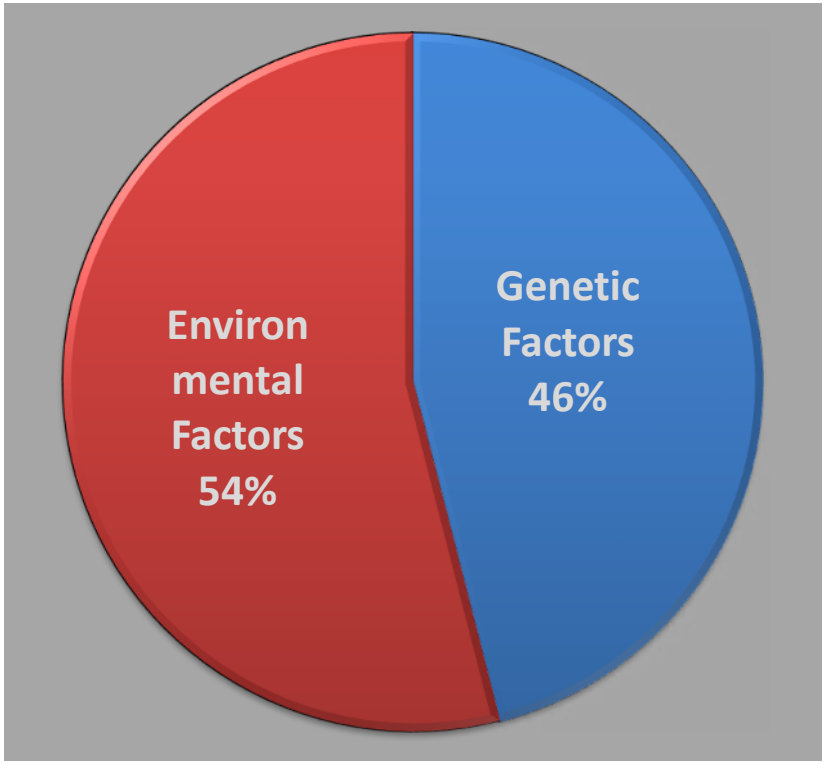
# Familial risk and heritability of diagnosed borderline personality disorder: a register study of the Swedish population

Charlotte Skoglund[1] · Annika Tiger[2] · Christian Rück[1] · Predrag Petrovic[3] · Philip Asherson[4] · Clara Hellner
David Mataix-Cols[1] · Ralf Kuja-Halkola[2]

Register Linkage of
- the National Patient Register (NPR)
- the Multi-Generation Register (MGR)
- the Swedish Twin Registry (STR)
- the Total Population Register
- the Cause of Death Register
- the Medical Birth Register (MBR) (born 1973–1993)

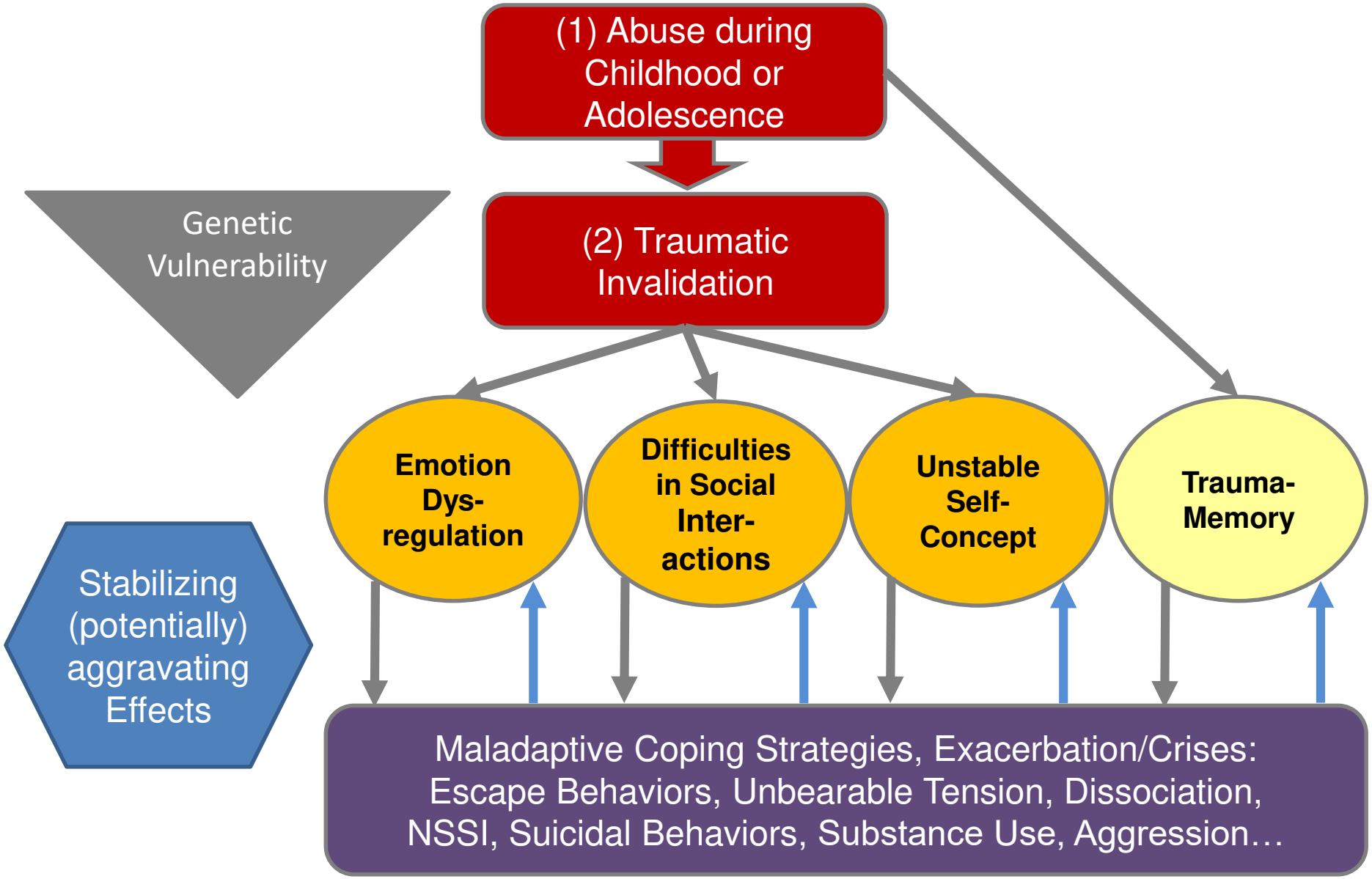
→ 1.85 million individuals incl. 11,665 with a diagnosis of BPD

→ structural equation modelling to estimate heritability of BPD




Skoglund et al. 2021

# Dual Hit Model of BPD



# ICD-11 for Mortality and Morbidity Statistics (Version : 05/2021)

06 Disorders specifically associated with stress

6B40 Post traumatic stress disorder

**6B41 Complex post traumatic stress disorder (CPTSD)**

All diagnostic requirements for PTSD are met.

In addition, Complex PTSD is characterised by severe and persistent

1) problems in affect regulation;

2) beliefs about oneself as diminished, defeated or worthless, accompanied by feelings of shame, guilt or failure related to the traumatic event; and

3) difficulties in sustaining relationships and in feeling close to others. These symptoms cause significant impairment in personal, family, social, educational, occupational or other important areas of functioning.

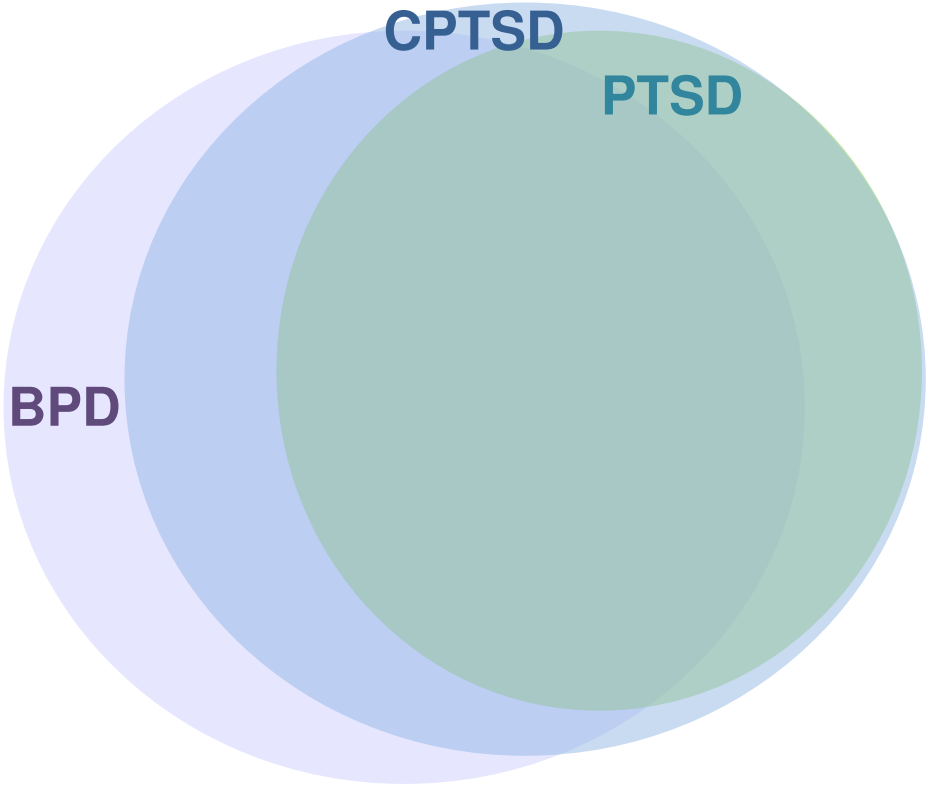
"Complex PTSD […] may develop following […] most commonly prolonged or repetitive events from which escape is difficult or impossible (e.g. torture, slavery, genocide campaigns, prolonged domestic violence, repeated childhood sexual or physical abuse)."

# BPD, PTSD and CPTSD

Differences BPD vs CPTSD:
CPTSD: - includes a full diagnosis of **PTSD** (intrusions, avoidance, hypervigiliance)
*ICD-11*

→ has **to be addressed**!

CPTSD: - possibly rather detached from others
BPD: - possibly more impulsive, angry enmeshment
*Ford & Comtois 2021*




→ BPD and CPTSD are quite similar *(my view)*

Differences PTSD vs CPTSD:
CPTSD: - 3 DSO domains
- more complex
- more severe
than PTSD
*ICD-11*

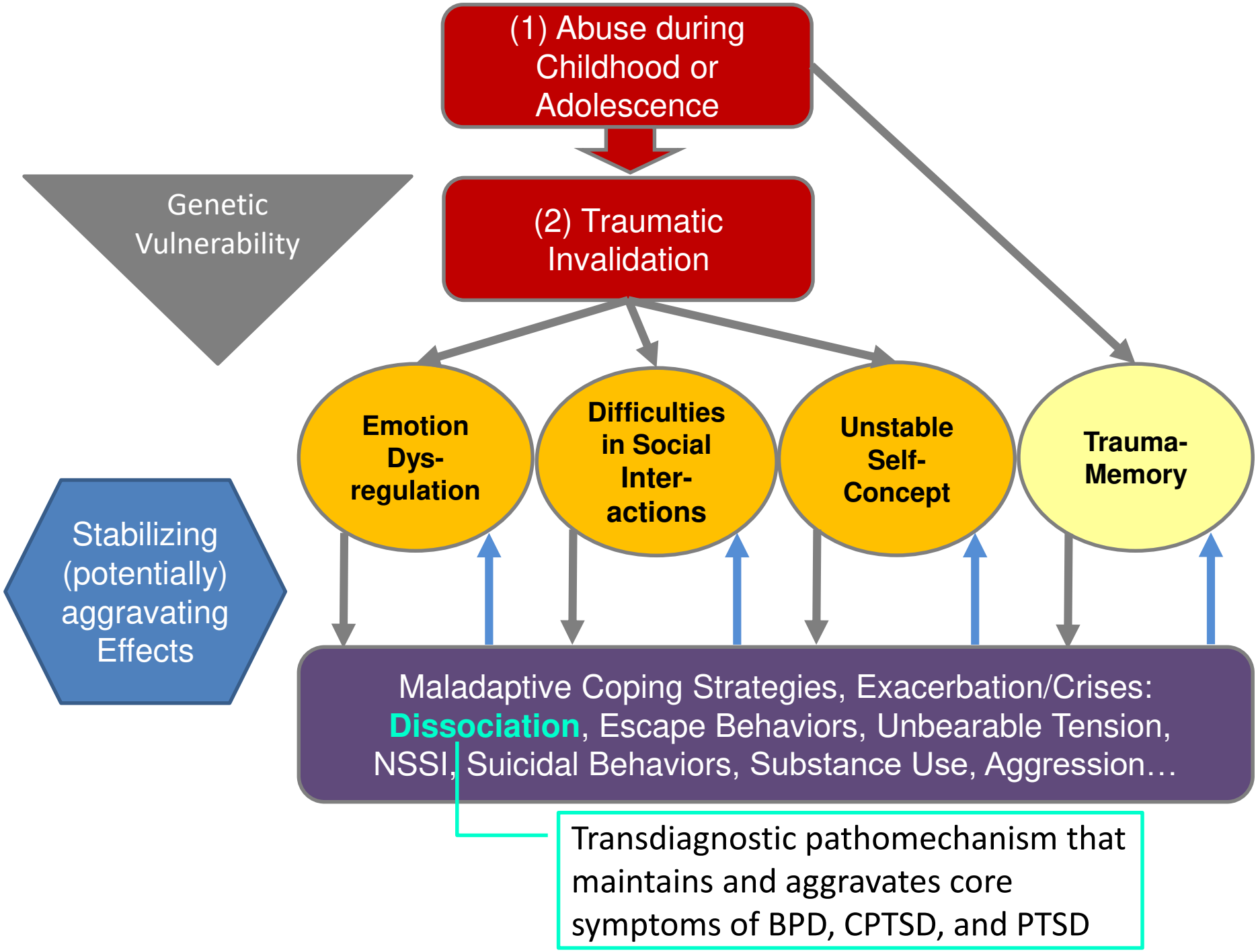
# Dissociation in BPD, PTSD and CPTSD

not listening

- **Dissociation has a variety of manifestations**

  - **Amnesia** *“I don‘t remember how I got here.“*
  - **Depersonalisation** *“I watch myself like a stranger.”*
  - **Analgesia**

  **…**


(1) Abuse during Childhood or Adolescence
Genetic Vulnerability
(2) Traumatic Invalidation
Emotion Dys-regulation
Difficulties in Social Inter-actions
Unstable Self-Concept
Trauma-Memory
Stabilizing (potentially) aggravating Effects
Maladaptive Coping Strategies, Exacerbation/Crises:
Dissociation, Escape Behaviors, Unbearable Tension,
NSSI, Suicidal Behaviors, Substance Use, Aggression…
Transdiagnostic pathomechanism that maintains and aggravates core symptoms of BPD, CPTSD, and PTSD

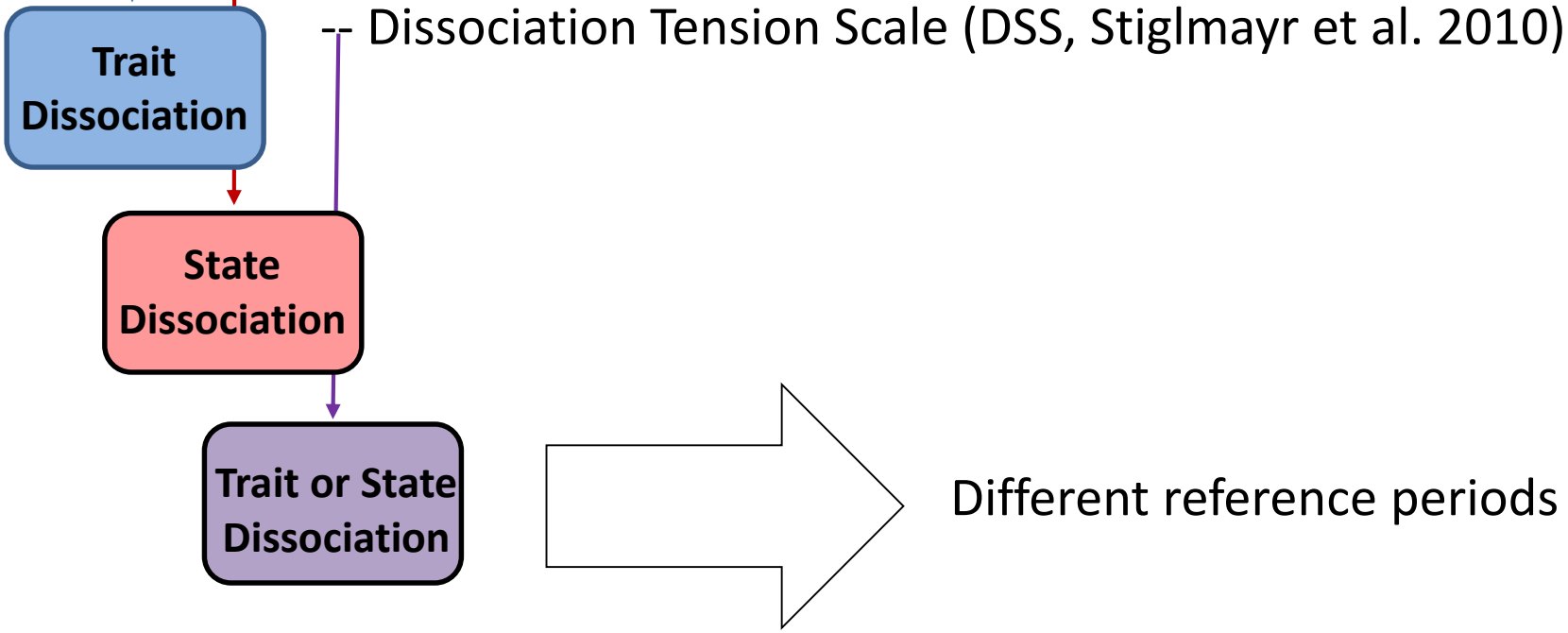
# Assessing Dissociation in BPD, CPTSD, and PTSD

Can be assessed e.g., with the

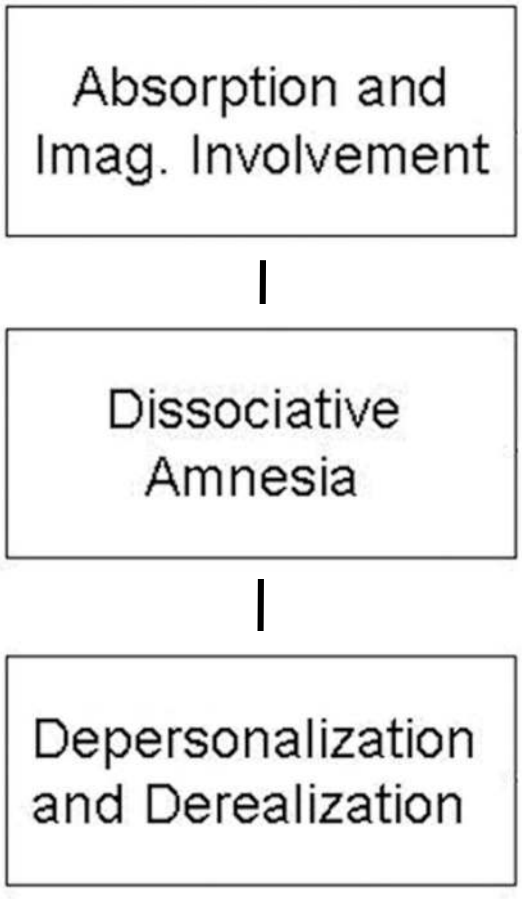
-- Dissociative Experiences Scale (DES, Bernstein & Putnam, 1986)

-- Dissociative Symptoms Scale (DSS, Carlson et al. 2018)

-- Dissociation Tension Scale (DSS, Stiglmayr et al. 2010)



# DES: Subscores and Total Score




**e.g. "Some people find that sometimes they are listening to someone talk and they suddenly realize that they did not hear part or all of what was just said."**

**e.g. "Some people have the experience of finding themselves in a place and having no idea how they got there."**

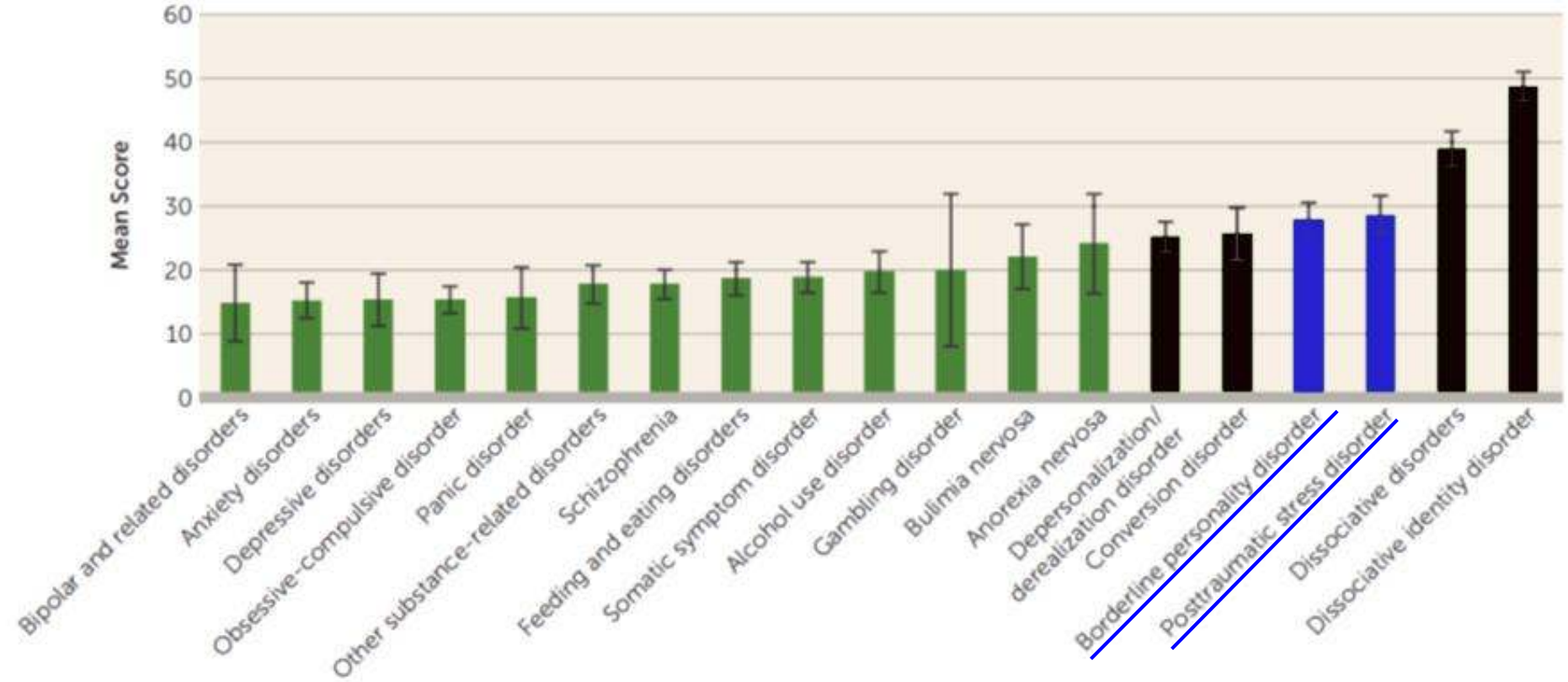
**e.g. "Some people have the experience of looking in a mirror and not recognizing themselves."**

**Total score on a scale from 0 to 100 (=always)**

# Level of Dissociation across Psychiatric Disorders

## Dissociation in Psychiatric Disorders: A Meta-Analysis of Studies Using the Dissociative Experiences Scale

Lisa Lyssenko, Dipl.-Psych., Christian Schmahl, Dr.med., Laura Bockhacker, Dr.med., Ruben Vonderlin, M.Sc., Martin Bohus, Dr.med., Nikolaus Kleindienst, Dr.rer.hum.biol.



# Dissociation in victims of childhood abuse or neglect: a meta-analytic review

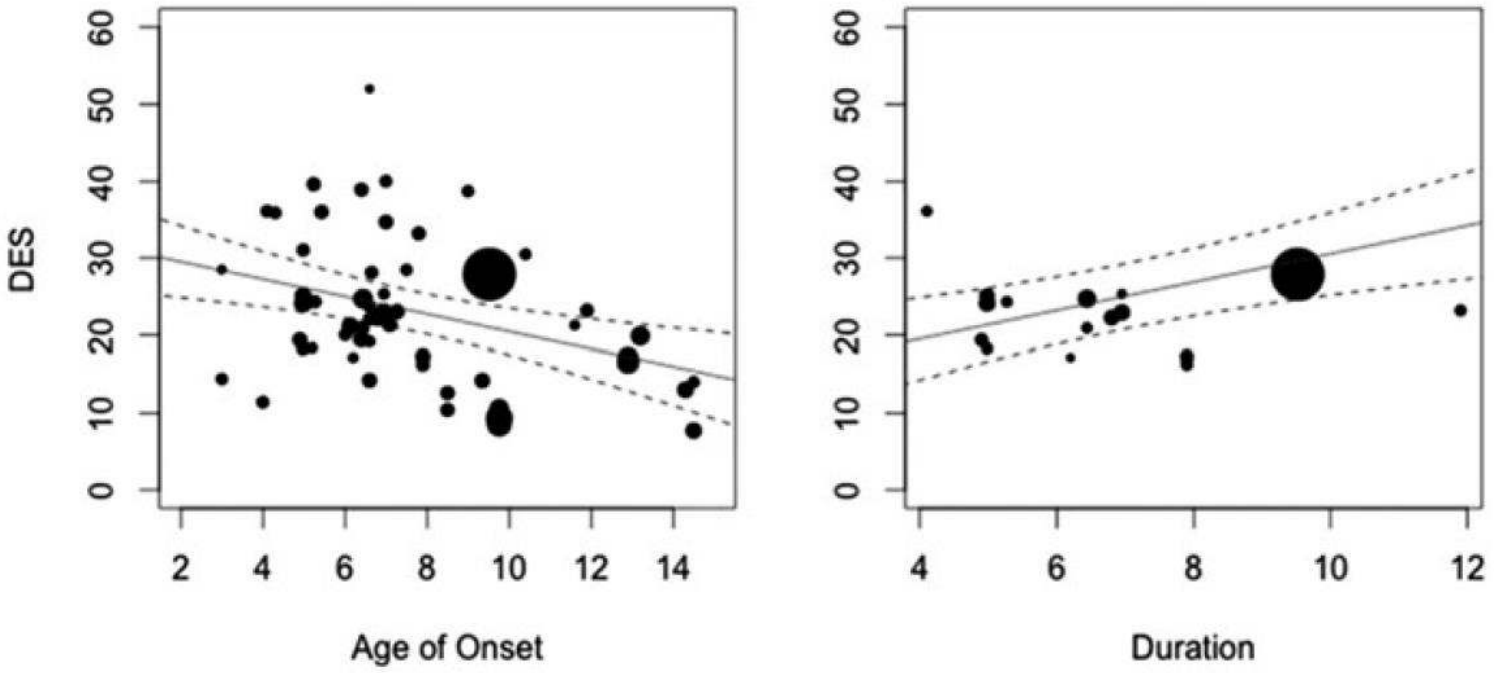
Ruben Vonderlin[1,2,*], Nikolaus Kleindienst[1,*], Georg W. Alpers[2], Martin Bohus[1,3]
Lisa Lyssenko[1,*] and Christian Schmahl[4,5,*]

Meta-regression to investigate whether the level of dissociation (DES) is related to characteristics of CA.

→ Is the level of Dissociation affected by

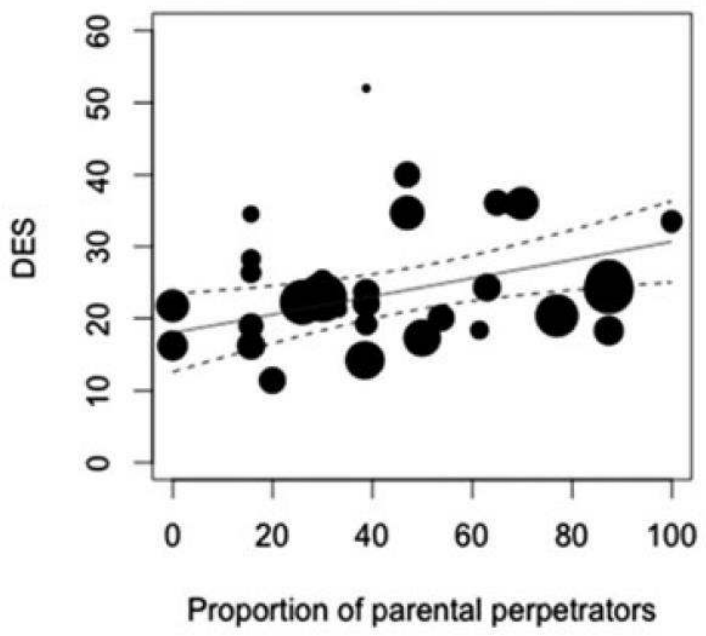
- Age of onset
- Duration
- Multiple trauma (CSA + CPA)
- Perpetration through primary caregivers (parents)
- …

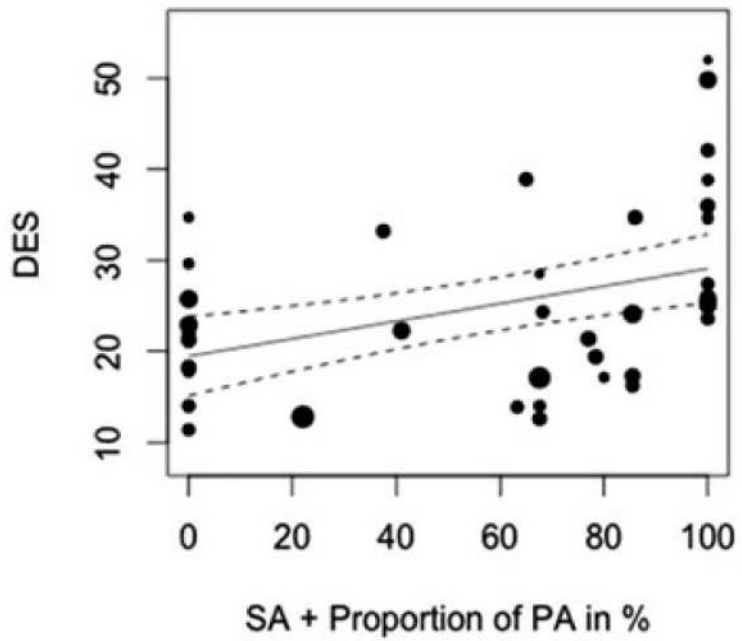
# Dissociation related to Trauma Onset and Duration




→ Highest levels of dissociation in individuals who experienced **early and long lasting childhood abuse**

# Dissociation related to Trauma Characteristics




The highest levels of dissociation were observed in those with **CSA**

- in particular when the parents were involved in the abuse
- and when CSA was accompained by CPA

# Potentially Negative Effects of Dissociation

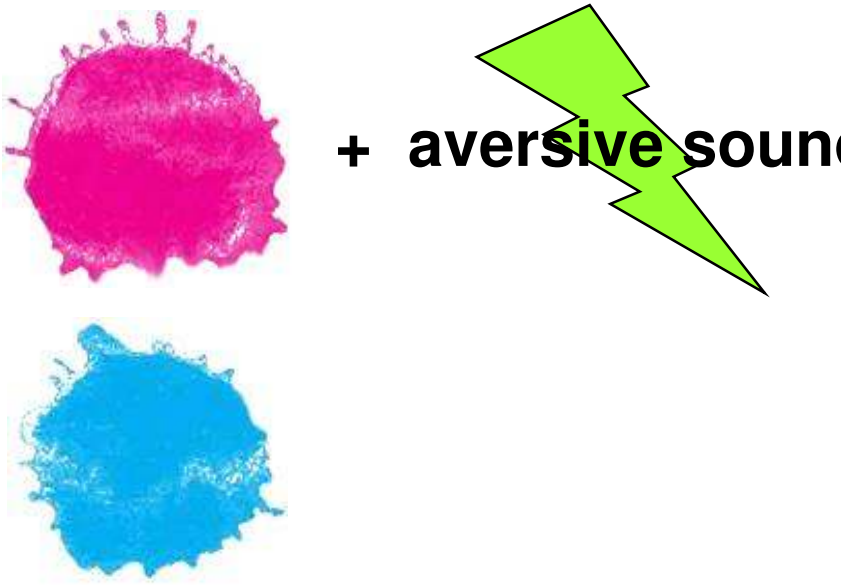
- Might aggravate other aspects of BPD
  - detrimental to coherent sense of self and for goal directed behaviors
  - engender dysfunctional behaviors such as NSSI
  → hereby complicating psychotherapeutic treatments

- Might prevent treatments from being full effective
  → highly controversial topic

# Emotional learning during dissociative states in borderline personality disorder

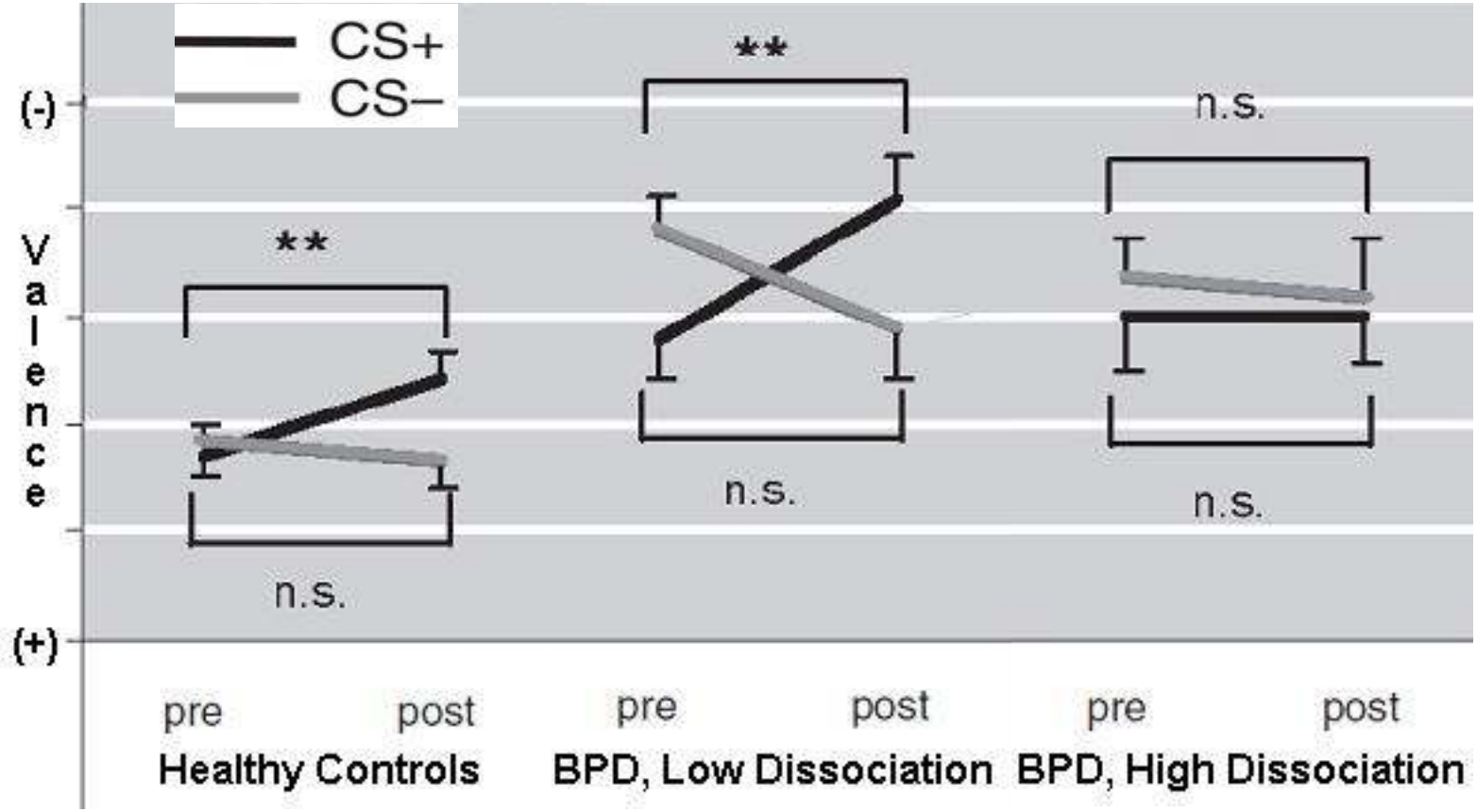
Ulrich W. Ebner-Priemer, PhD; Jana Mauchnik, PhD; Nikolaus Kleindienst, PhD; Christian Schmahl, MD; Martin Peper, PhD, MD; M. Zachary Rosenthal, PhD; Herta Flor, PhD; Martin Bohus, MD

- N=33 patients with BPD (unmedicated), n=35 HC participants
- Were asked to rate the valence of inkblots




*Ebner-Priemer et al. 2009*

# Learning vs Dissociation




**Time x Type x Dissociation: $F_{1,65}$=8.4, p=0.005 (for Valence)**

**… dto. for skin conductance**

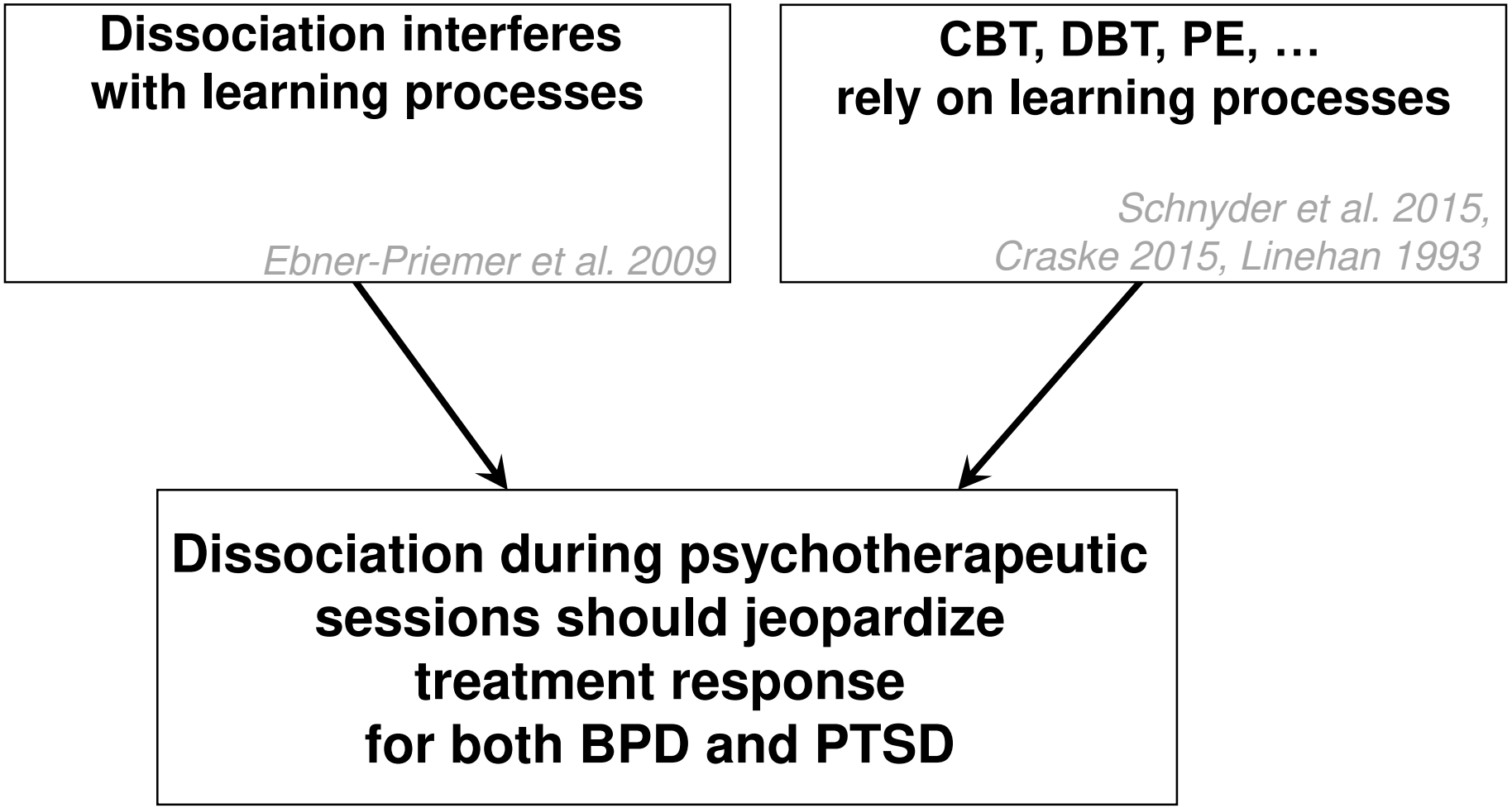
# Emotional learning during dissociative states in borderline personality disorder

Ulrich W. Ebner-Priemer, PhD; Jana Mauchnik, PhD; Nikolaus Kleindienst, PhD; Christian Schmahl, MD; Martin Peper, PhD, MD; M. Zachary Rosenthal, PhD; Herta Flor, PhD; Martin Bohus, MD

**Conclusion:** … learning processes seem to be inhibited during state dissociative experience.

*Ebner-Priemer et al. 2009*

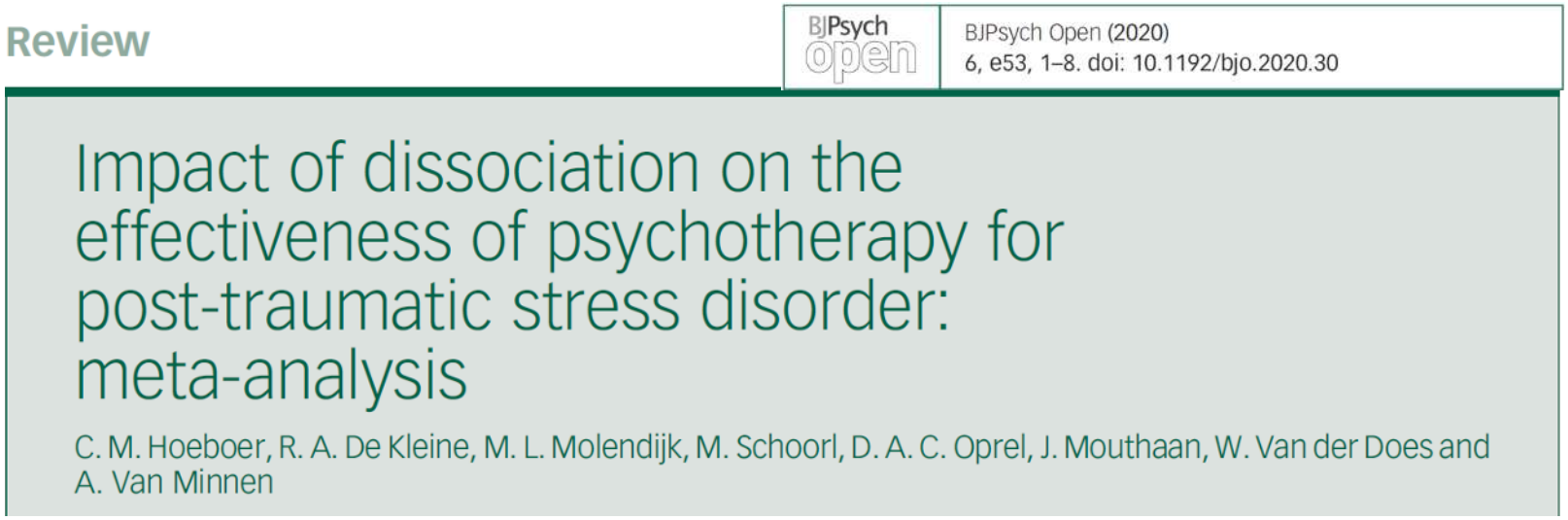
# Clinical Application, Rational



# Rationale ≠ Evidence

## → Literature on Dissociation (Baseline) as a Predictor for Treatment Outcome

- BPD: very few studies, no clear results
- PTSD: >20 studies summarized in a recent meta-analysis



Review

BJPsych open

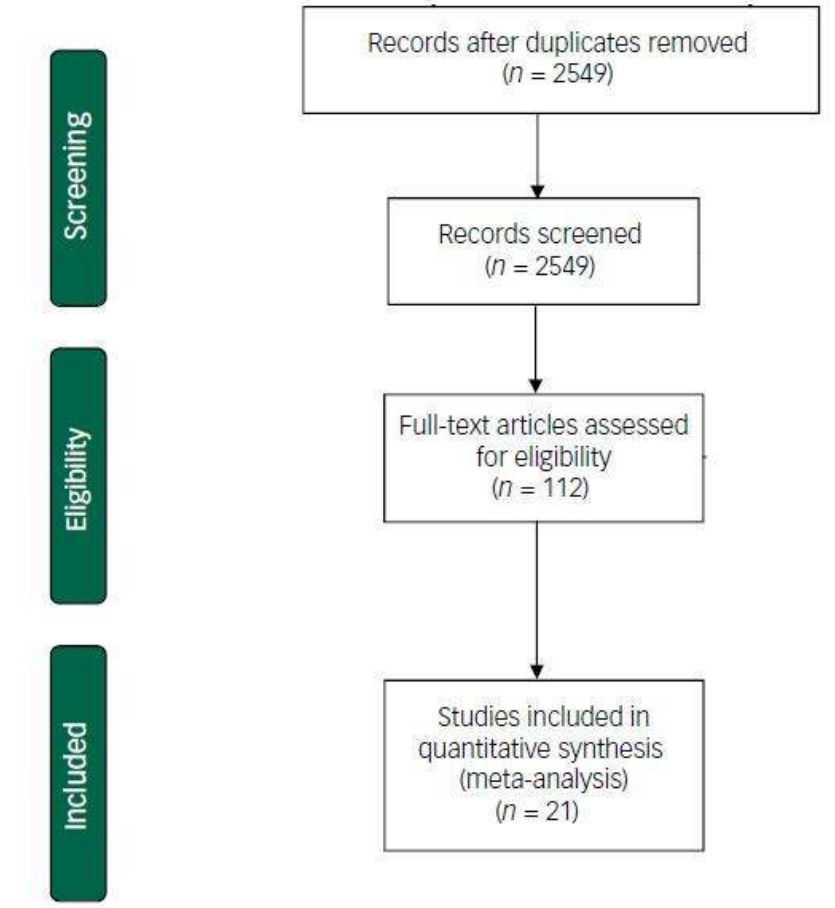
BJPsych Open (2020)
6, e53, 1–8. doi: 10.1192/bjo.2020.30

Impact of dissociation on the effectiveness of psychotherapy for post-traumatic stress disorder: meta-analysis

C. M. Hoeboer, R. A. De Kleine, M. L. Molendijk, M. Schoorl, D. A. C. Oprel, J. Mouthaan, W. Van der Does and A. Van Minnen

*Hoeboer et al 2020*

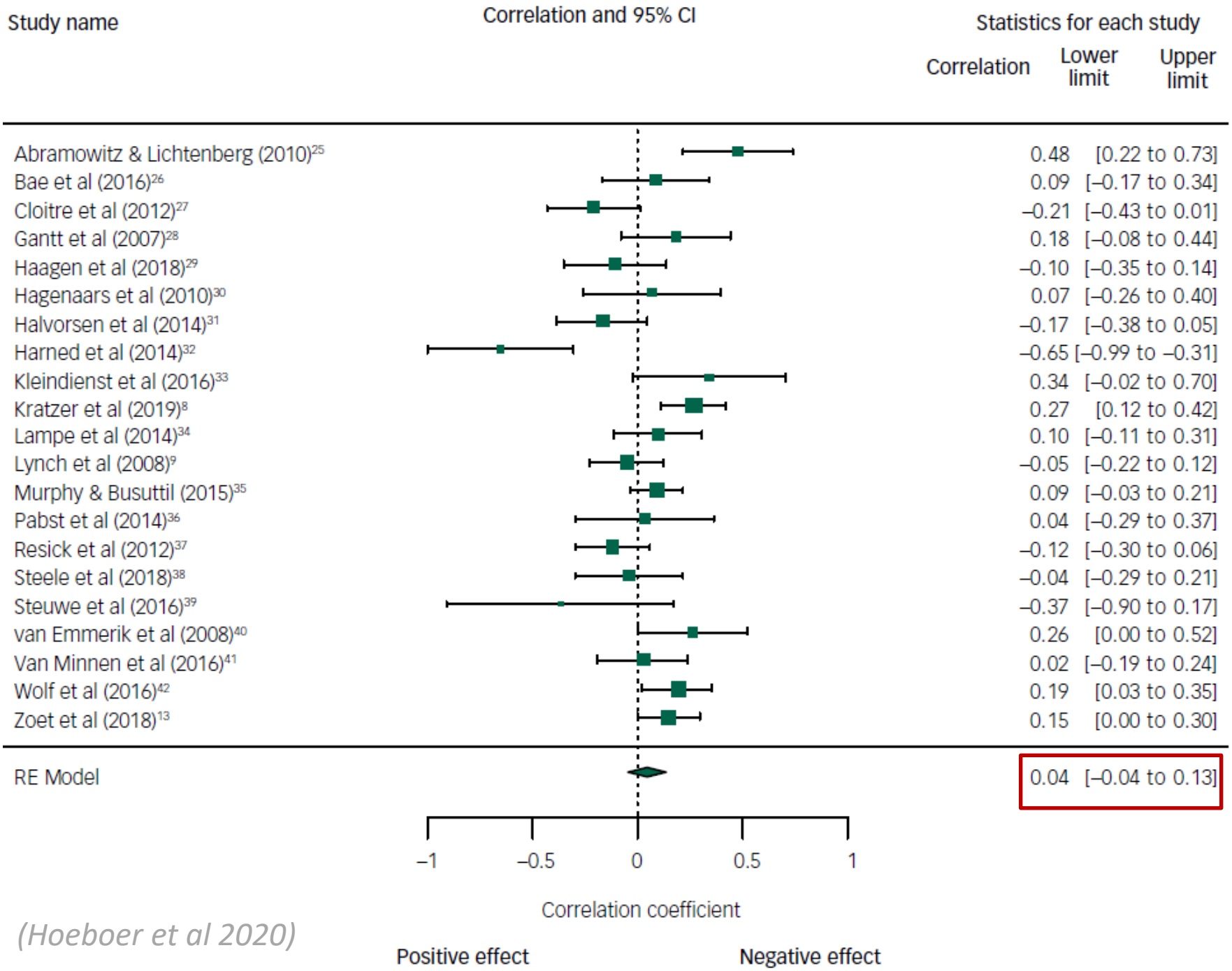
# Meta-Analysis: Dissociation → Outcome in PTSD




Flow chart of inclusion of studies.

- N=1714 patients (all PTSD)
- From k=21 trials

*Hoeboer et al 2020*




*(Hoeboer et al 2020)*

Review

BJPsych open

BJPsych Open (2020)
6, e53, 1–8. doi: 10.1192/bjo.2020.30

# Impact of dissociation on the effectiveness of psychotherapy for post-traumatic stress disorder: meta-analysis

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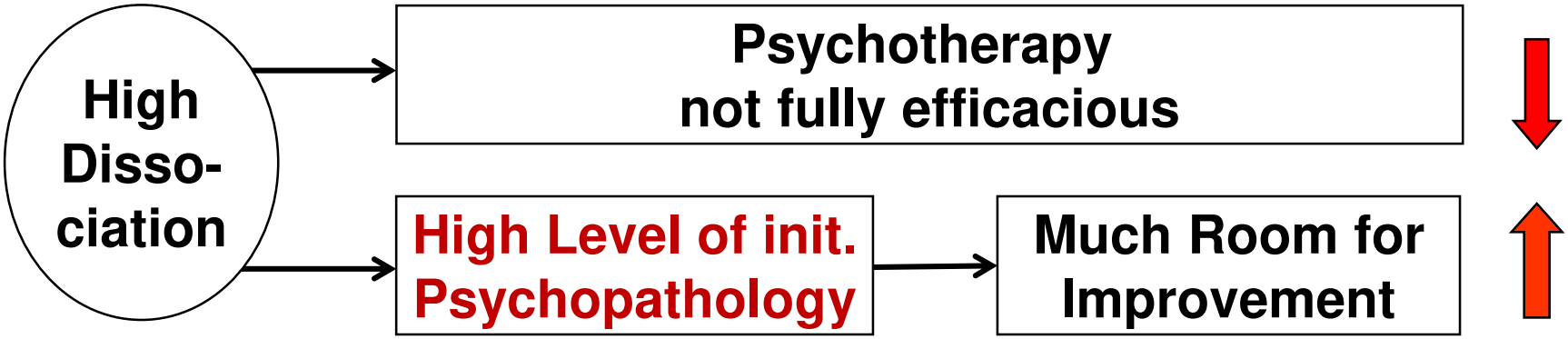
## Conclusions

We found no evidence that dissociation moderates the effectiveness of psychotherapy for PTSD. The quality of some of the included studies was relatively low, emphasising the need for high-quality clinical trials in patients with PTSD. The results suggest that pre-treatment dissociation does not determine psychotherapy outcome in PTSD.

*(Hoeboer et al 2020)*

# Methodological Limitation: Confounders

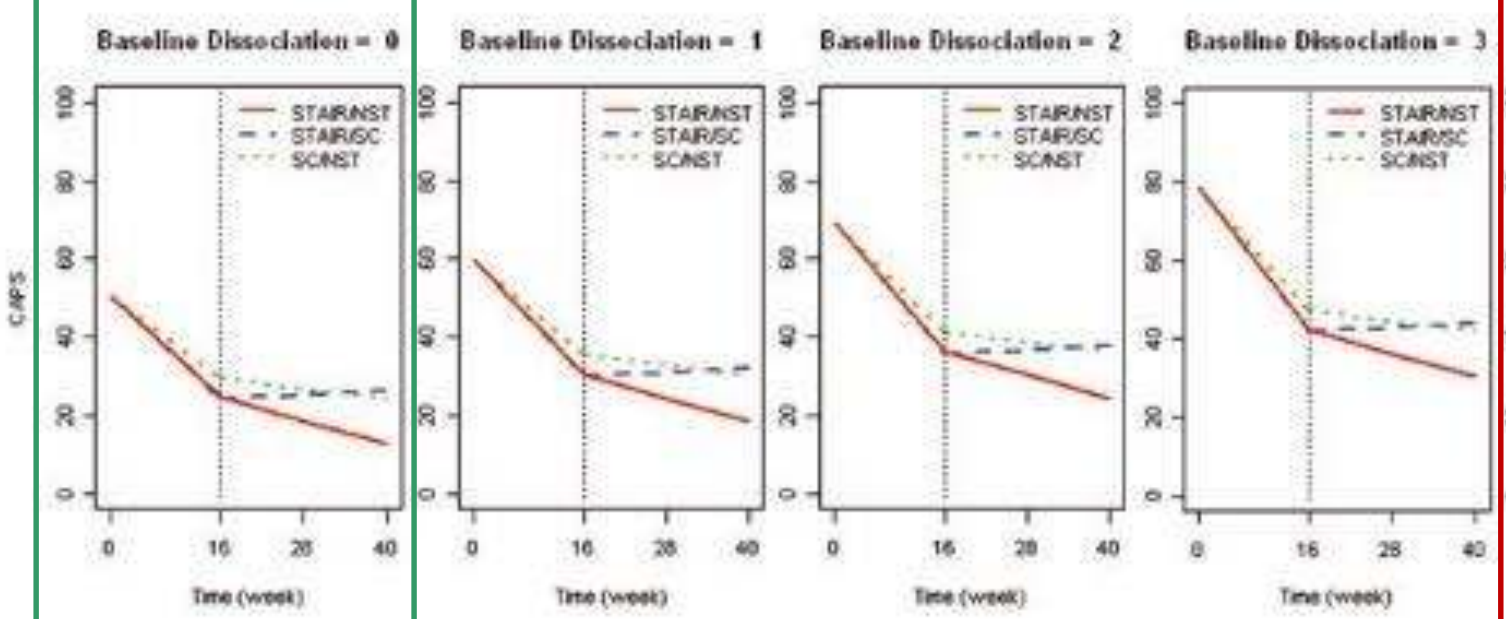



⇨ **Multivariate model accounting for the confounding effects of baseline severity**

# Dissociation means High Level of Psychopathology

**Low**

Dissociation




**High**

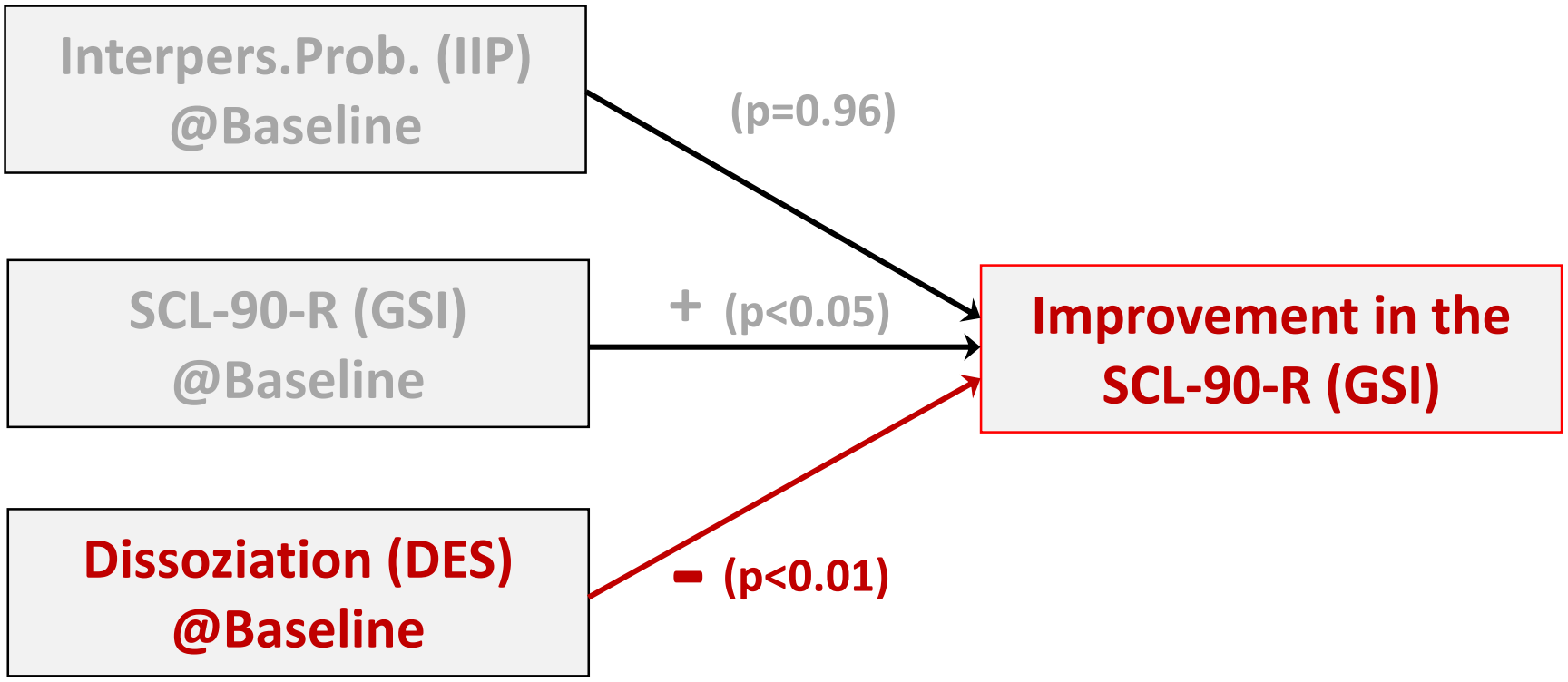
**start:** 50
**end:** …
**delta:** …

**start:** 90
**end:** 38
**delta:** **52**

*(Cloitre et al 2012)*

# Study 1: DBT for BPD (n=57)

**Dissociation (Baseline) → Predictor for Treatment Outcome (SCL-90-R)**

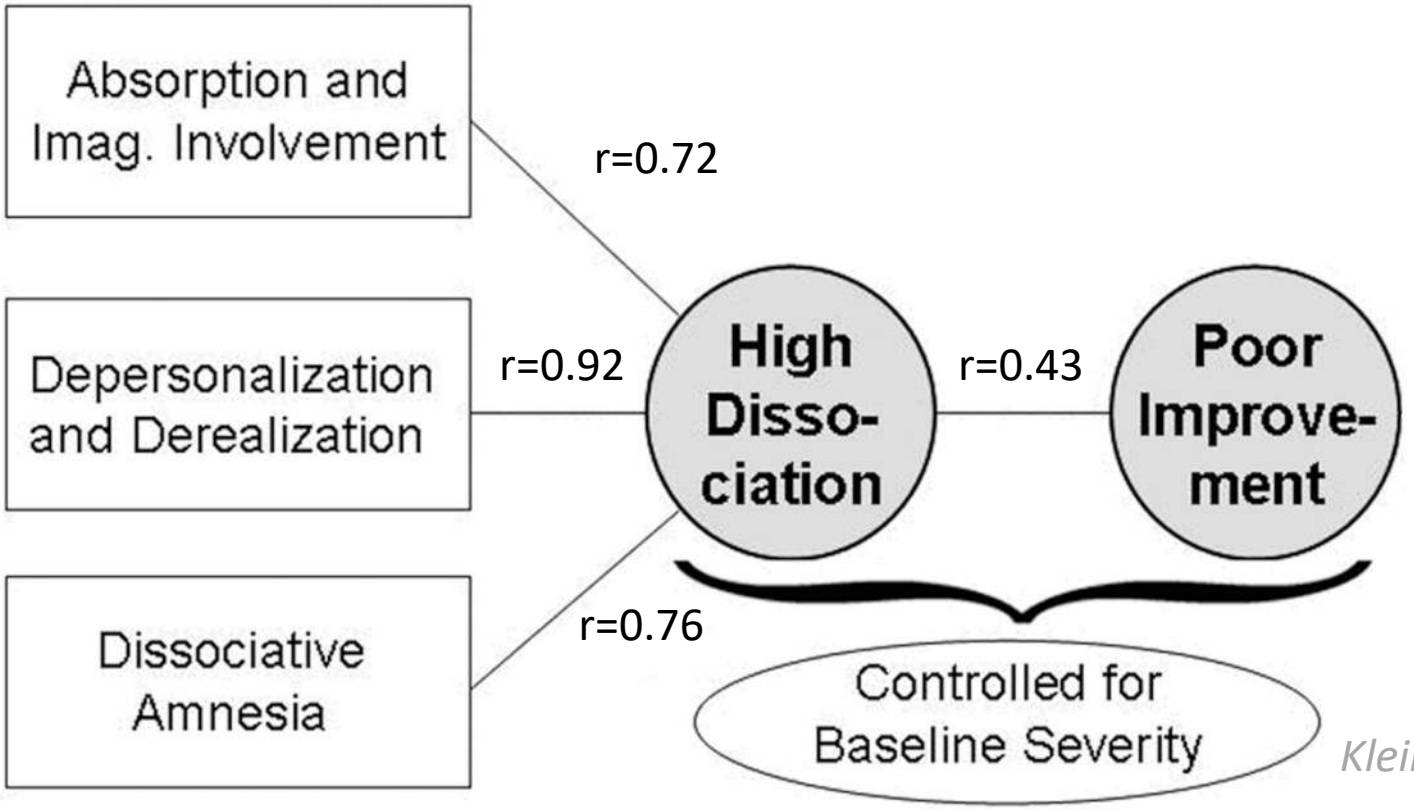



→ Dissociation emerged as a negative predictor

*Kleindienst et al 2011*

# Study 1: DBT for BPD (n=57)

## Quantification of the Effect | Which Facets matter most?




*Kleindienst et al 2011*

→ Little evidence for a differntial effect of the three facets

→ Canonical correlation r=0.43, i.e. quite a large effect

# Study 2: DBT-PTSD vs CPT for CPTSD (n=193)

**Dissociation → Improvement in the CAPS?**

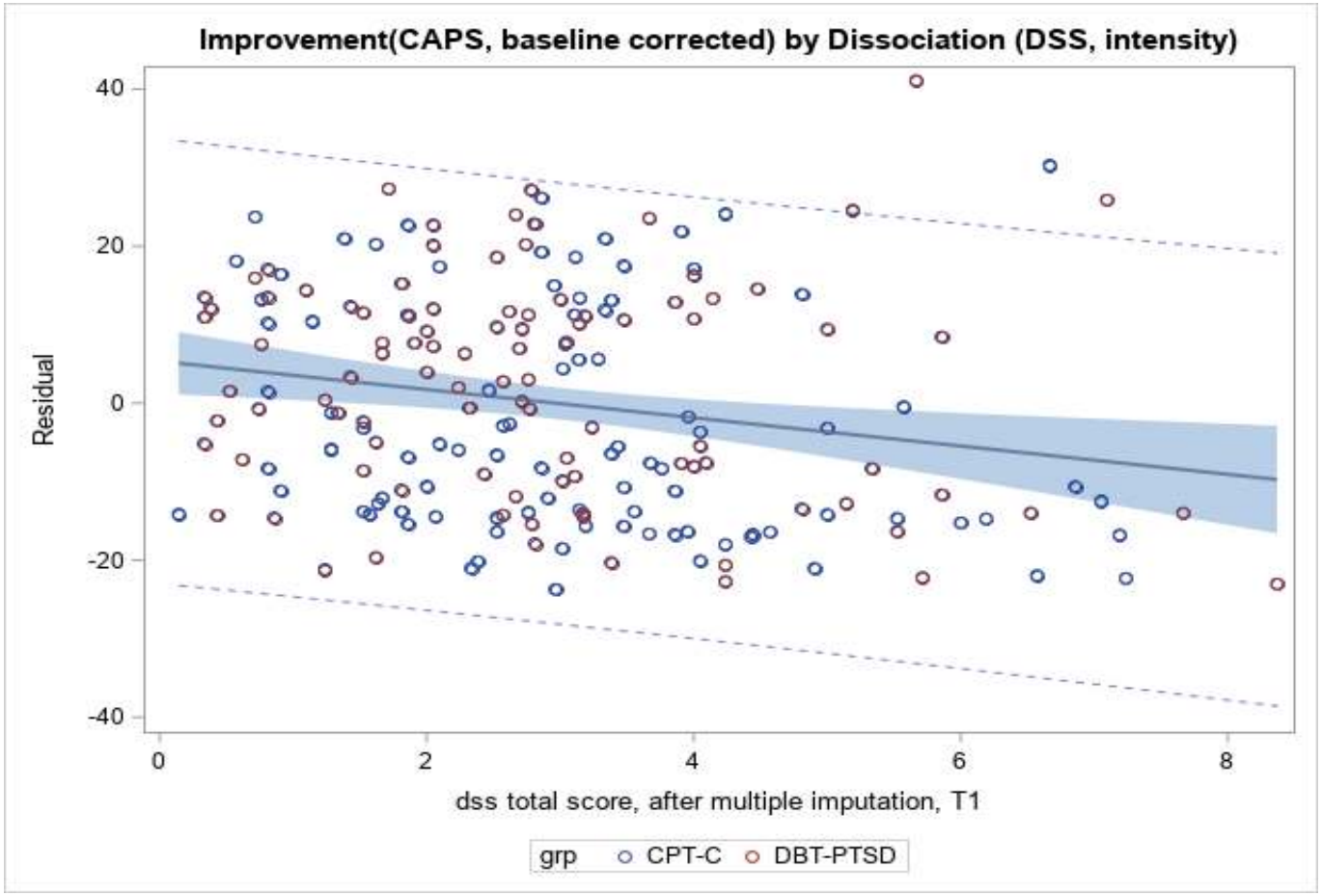
- N=193 women with PTSD related to sexual/physical CA
  with ≥ 3 diagnostic criteria of BPD
  incl. criterion 6 (affective instability)

  } ≈ CPTSD

- completed 45+3 sessions of outpatient treatment
  with either DBT-PTSD or CPT

# Study 2: DBT-PTSD vs CPT for CPTSD (n=193)

## Dissociation → Improvement in the CAPS?




- Dissociation emerged as a neg. predictor
- Stat. significant in both groups (DBT-PTSD and CPT)
- But the effect of dissociation was not very large

→ Why?

# Gap of Precision

Previous Research:

- Investigated the potential impact of dissociation (baseline) on outcome

In Theory:

- What matters most is the impact of **dissociation during the therapy** (which is crucial for relearning)

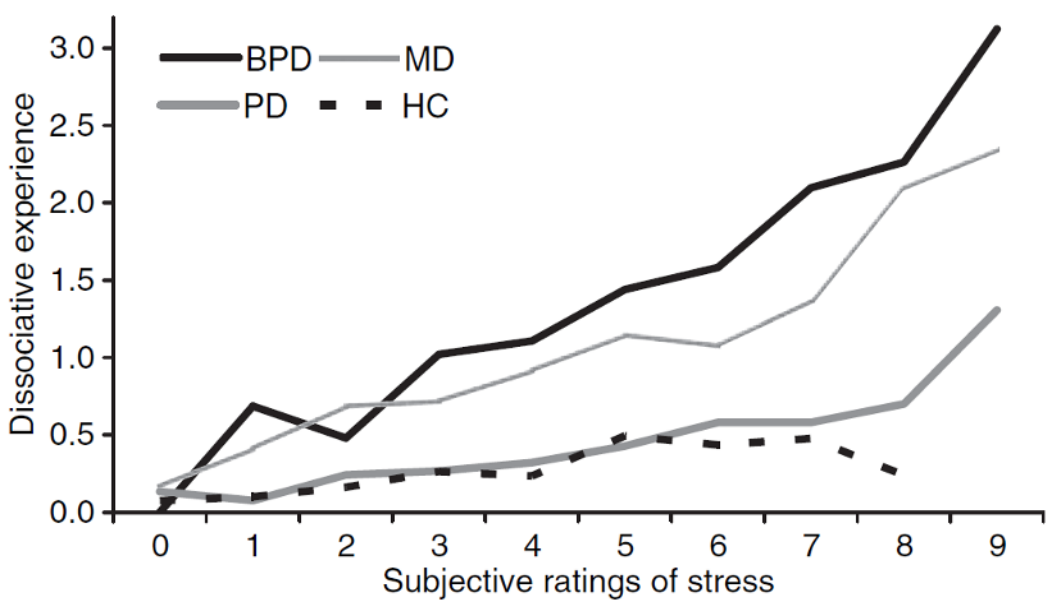
- Dissociation assessed at baseline may be too far away from the actual mechanism to provide an accurate estimate of the impact of dissociation

- There is good reason to assume that dissociation is particularly high during psychotherapy sessions:
  - dissociation is typically triggered by high levels of stress
    … in particular in patients with BPD

# Dissociative symptoms are positively related to stress in borderline personality disorder

C. E. Stiglmayr, U. W. Ebner-Priemer, J. Bretz, R. Behm, M. Mohse, C.-H. Lammers, I.-G. Anghelescu, C. Schmahl, W. Schlotz, N. Kleindienst, M. Bohus

- Ambulatory assessment study evaluating both dissociation and stress every 60min for 48h in the daily lives of n=164 individuals
- 4 diagnostic groups including n=50 with BPD




In particular patients with BPD are prone when experiencing stress

*Stiglmayr et al 2008*

# Gap of Precision

Previous Research:

- Investigated the potential impact of dissociation (baseline) on outcome

In Theory:

- What matters most is the impact of dissociation during the therapy (which is crucial for relearning)
- Dissociation assessed at baseline may be too far away from the actual mechanism to provide an accurate estimate of the impact of dissociation

Next Step

→ Investigate whether dissociation during the psychotherapeutic sessions significantly affects outcome in PTSD patients?

# Study 3: DBT-PTSD for CPTSD (n=36)

**Trait vs State Dissociation → Improvement in the CAPS?**

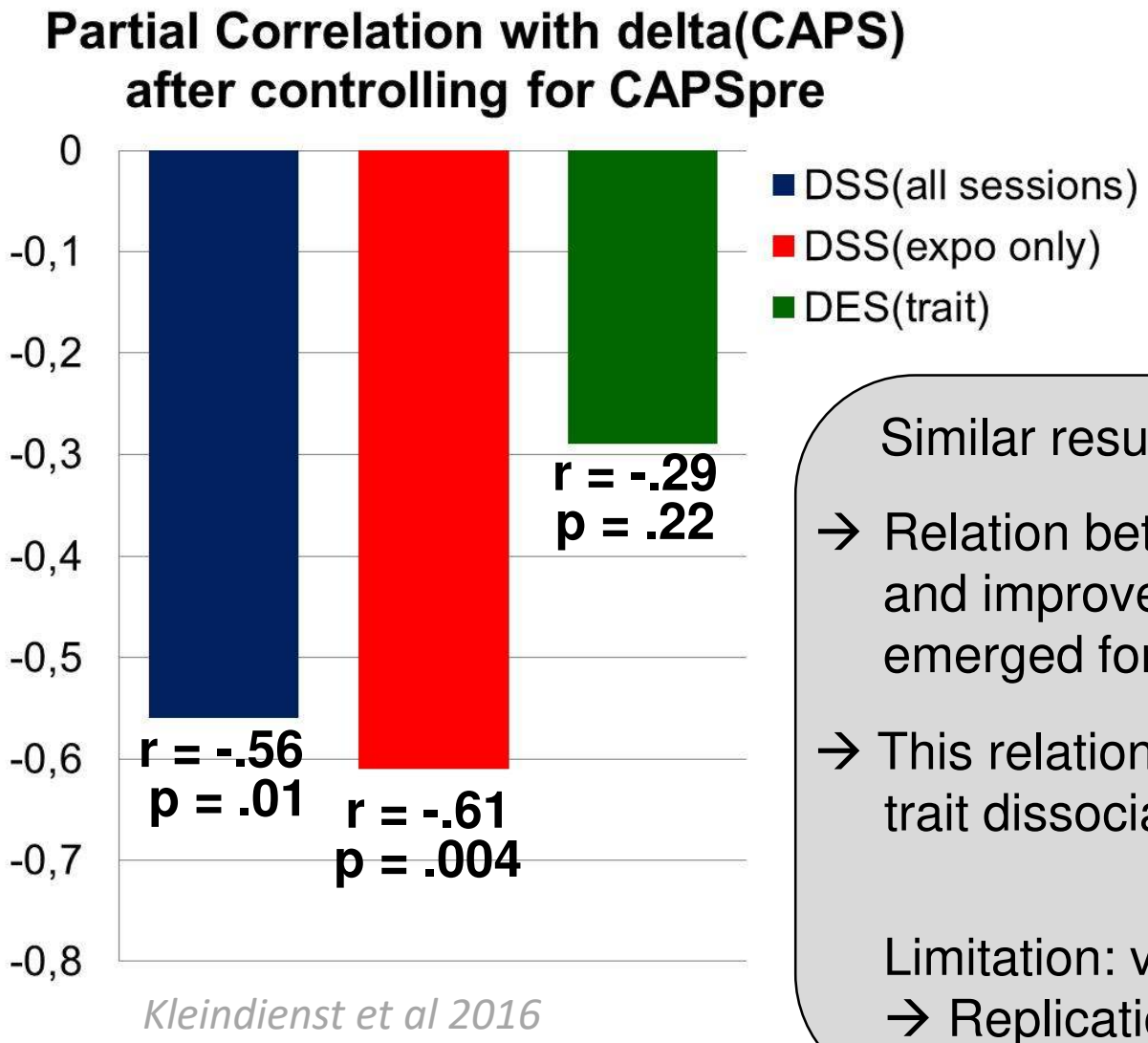
- N=36 women with PTSD related to CSA
  about 50% with co-occurring BPD
- N=24 completed 12 weeks of residential treatment
  with DBT-PTSD
- Outcome: Improvement in the CAPS
- Dissociation:
  - DES (trait dissociation)
  - DSS (state dissociation assessed directly after every session)

≈ CPTSD

e.g. “During the session I felt like people, or things, or the world surrounding me are not real.“

→ Mean score reflecting the patients’ level of dissociation during psychotherapeutic sessions

# Study 3: DBT-PTSD for CPTSD (n=36)




*Kleindienst et al 2016*

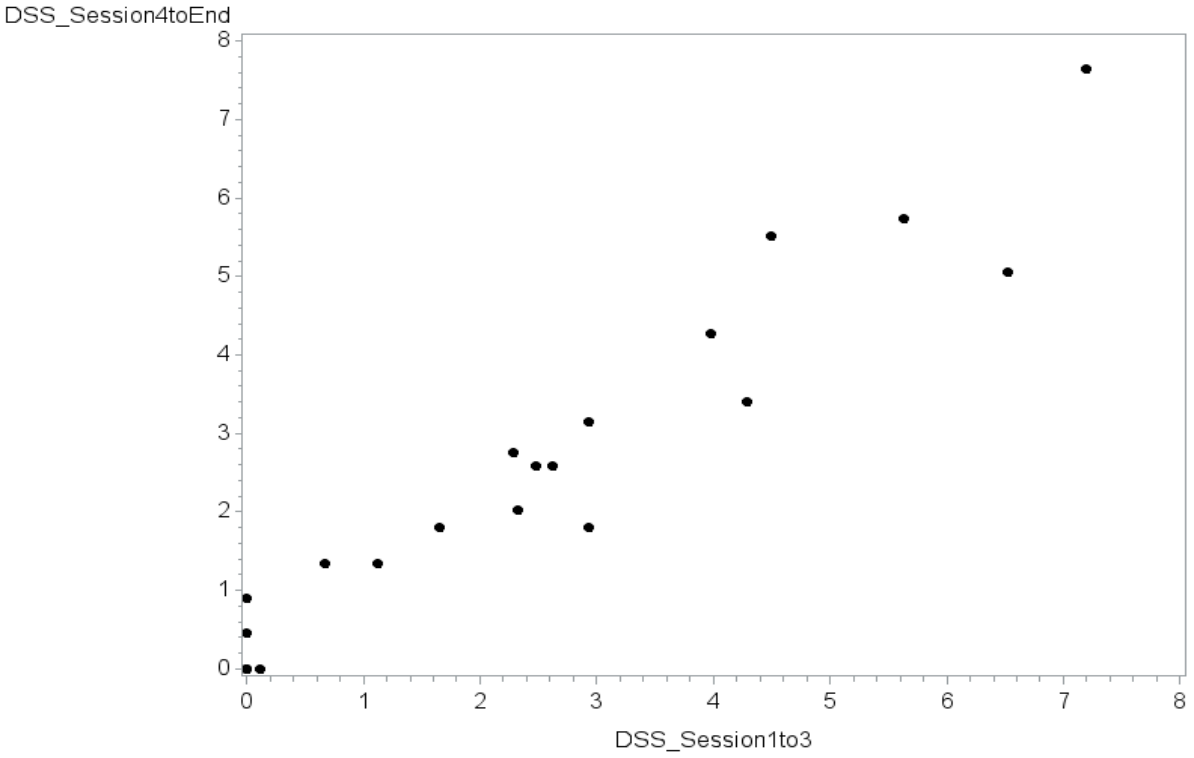
Similar results for the PDS & SCL

→ Relation between dissociation and improvement clearly emerged for state dissociation

→ This relation did not emerge for trait dissociation at baseline

Limitation: very small sample size
→ Replication required.

# Dissociation in Early vs Late Sessions of Psychotherapy




High dissociation during the first 3 psychotherapeutic sessions of DBT-PTSD

=

High dissociation during the entire treatment program

→ Treatment module that identifies and addresses dissociation at an early stage of therapy

→ Systematic evaluation of new strategies for addressing dissociation

# Interim Summary for Section 2.1
## (Applied Basic Research, Dissociation: Pathomechanism → Tx)

- **Dissociation empedes emotional learning**
- Dissociation **may prevent psychotherapies** of BPD, CPTSD, and PTSD **from being fully effective**
- The **impact of dissociation might be substantially larger than previously thought** considering
  - that inaccurate modelling might mask the detrimental effects of d.
  - that (state) dissociation might be particularly pronounced during psychotherapeutic sessions
- A **subgroup of patients tend to dissociate** as soon as a psychotherapy session starts

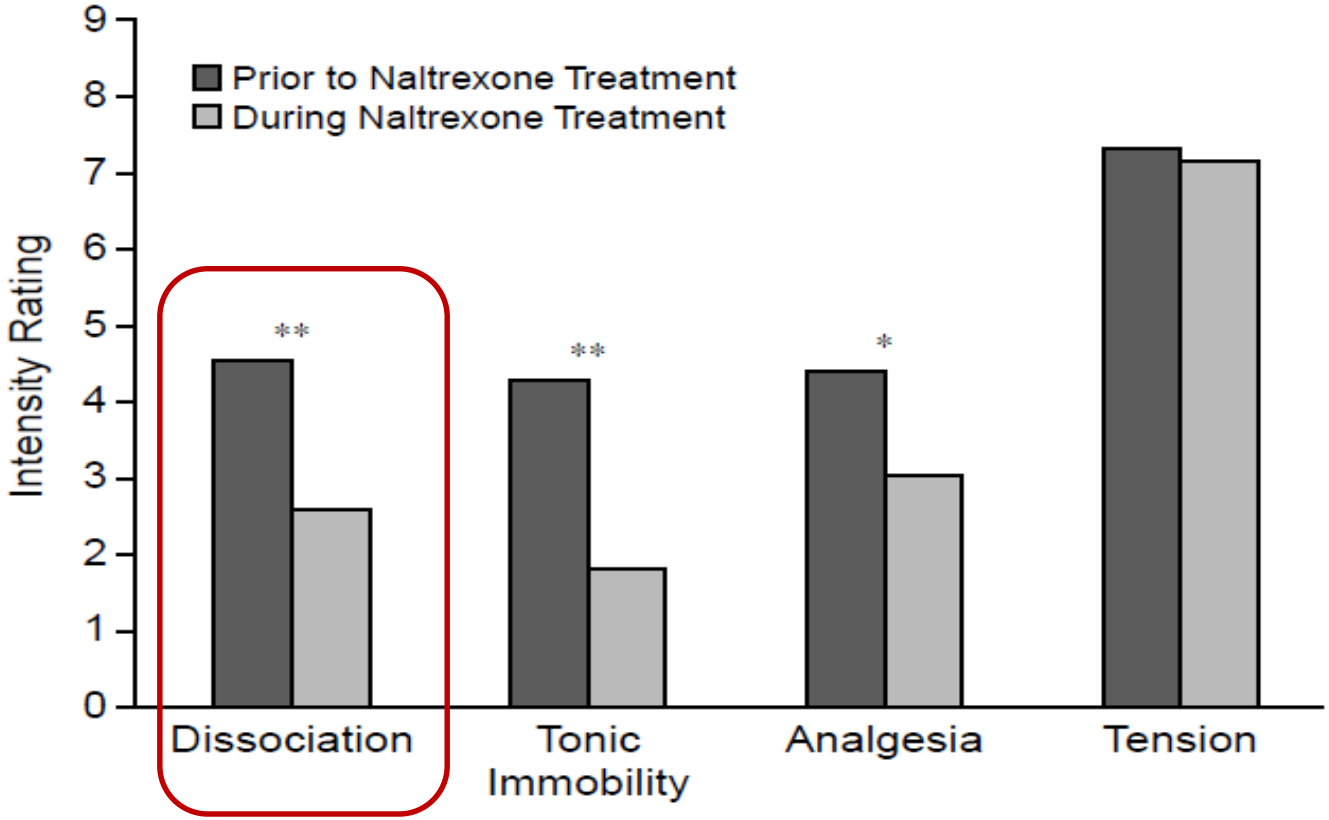
→ **During psychotherapy dissociation** should be monitored and eventually **addressed**. → ***How?***

# Naltrexone as a Treatment of Dissociation?

- Naltrexone is an opioid antagonist
  (mainly blocking κ- and μ-opioid receptors)
- Data from the 1980s (Pfeiffer et al., van der Kolk et al.)
  indicated that **opioid receptor blockers might antagonize**
  experimentally induced **depersonalization and analgesia**
- Simeon et Knutelska (2005) reported a significant reduction
  in the DES for patients with **depersonalization disorder**

→ Systematic evaluation in patients with BPD
- open trial
- RCT

# Naltrexone in the Treatment of Dissociative Symptoms in Patients With Borderline Personality Disorder

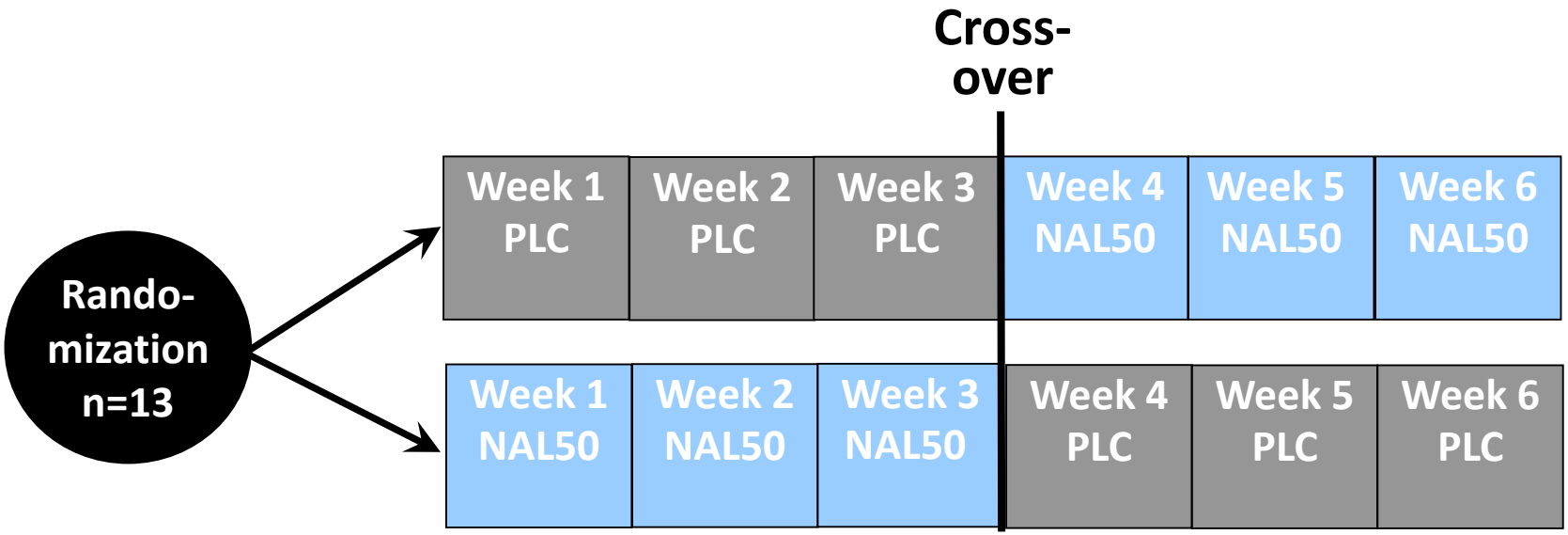



- Strong, highly significant reduction in DSS-scores *Bohus et al 1999*
- However, evidence is from one small, uncontrolled study → RCT

# Naltrexone for Treating Dissociation in BPD

## Pair of RCTs

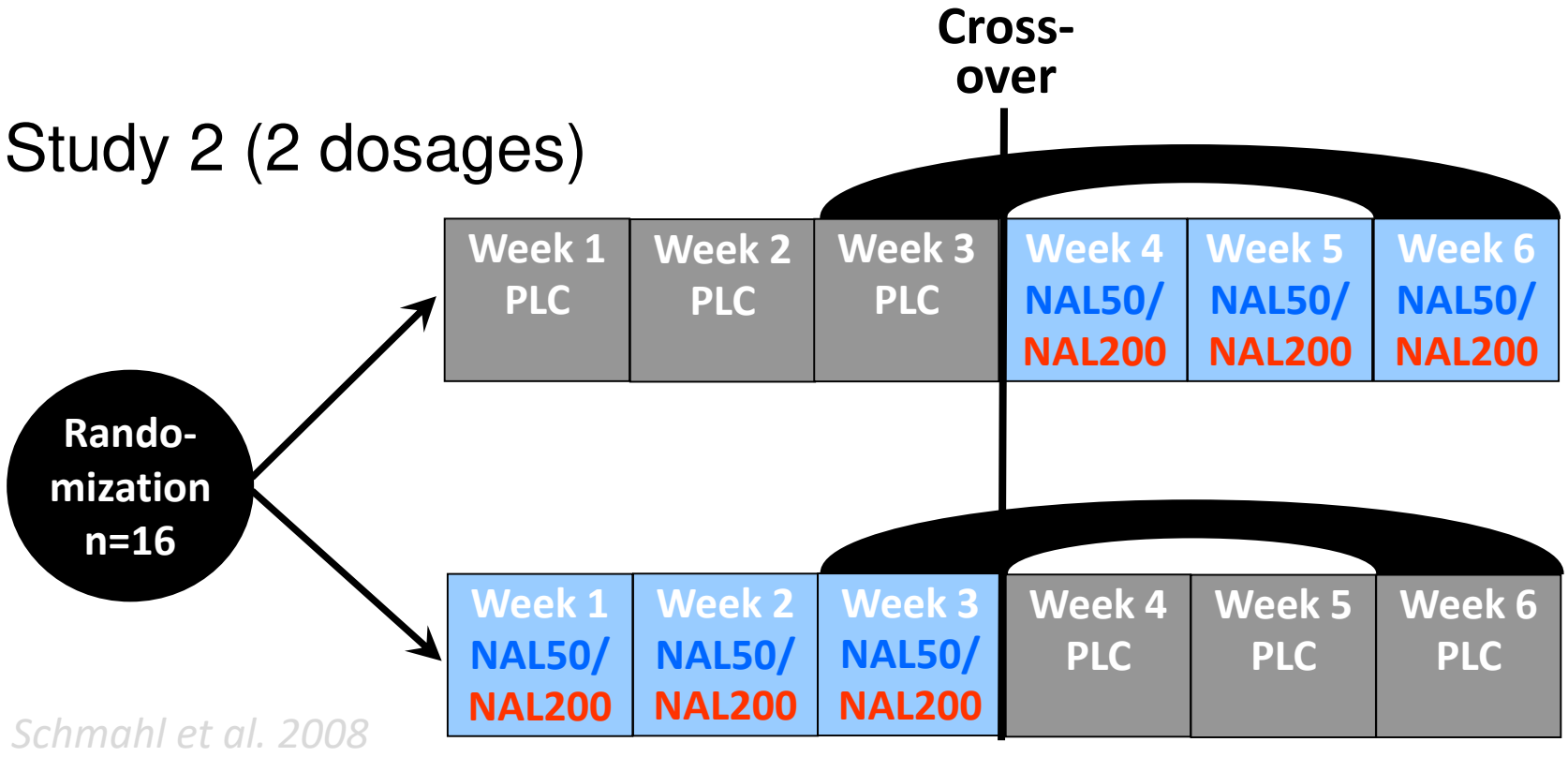
Study 1 (single dose)




*Schmahl et al. 2008*

# Naltrexone for Treating Dissociation in BPD

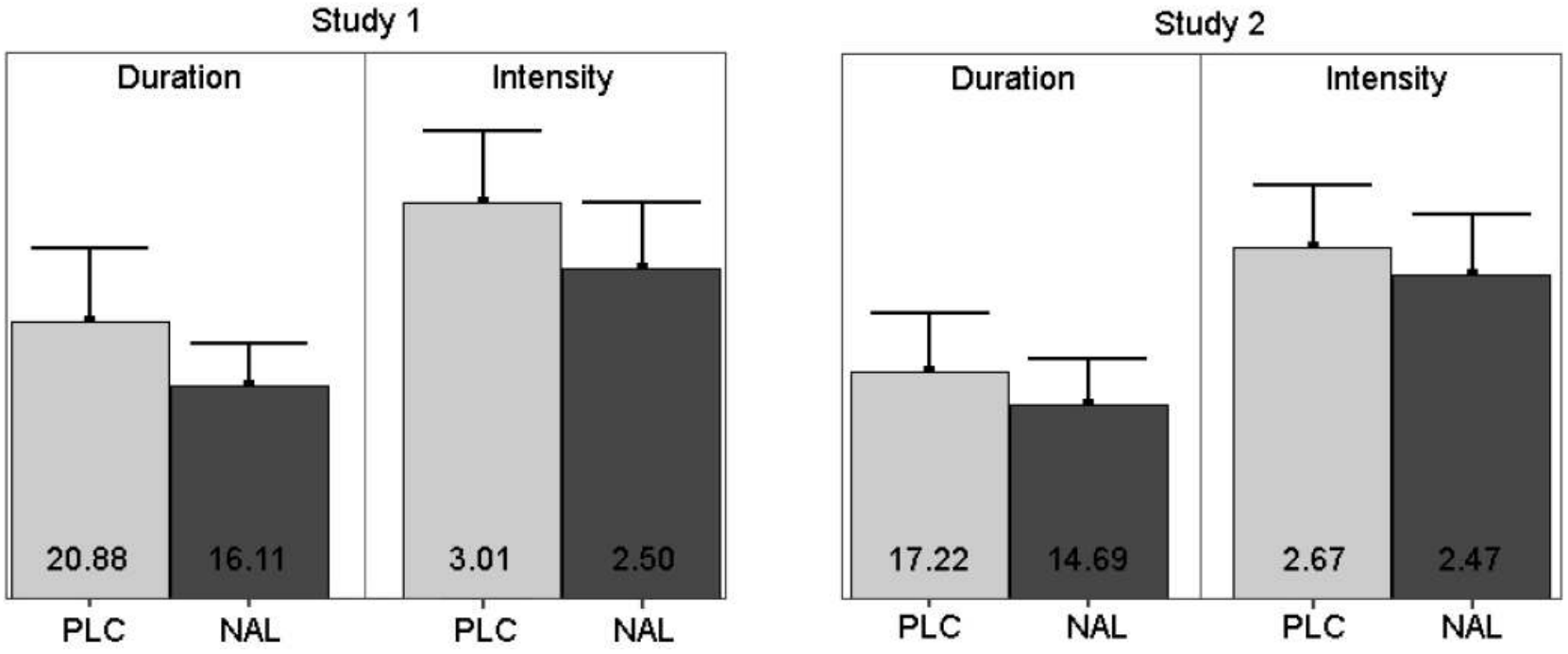
## Pair of RCTs




To avoid carry-over and withdrawal-effects, evaluation in both Studies 1 and 2 was based on the final weeks of PLC and NAL, respectively

# Naltrexone for Treating Dissociation in BPD

## Pair of RCTs




**F(1,9)=0.023**
**p=.88**

**F(1,9)=0.126**
**p=.73**

**F(1,12)=2.051**
**p=.18**

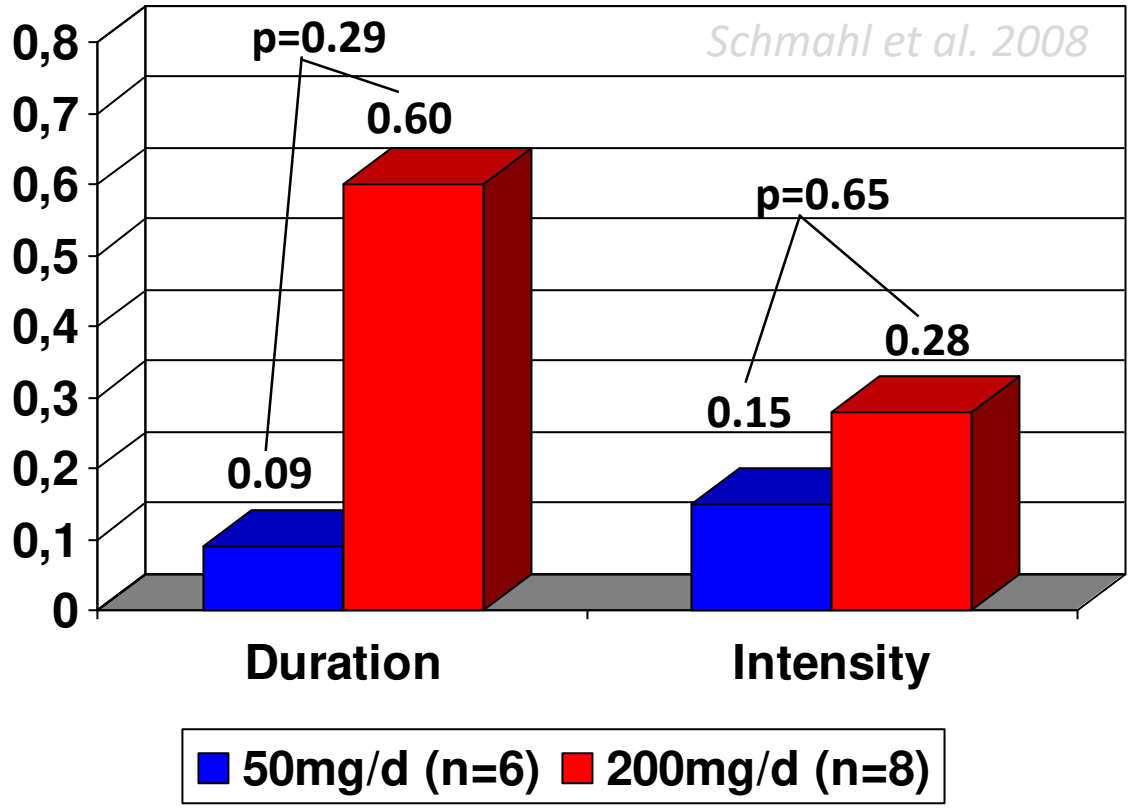
**F(1,12)=0.613**
**p=.45**

Between-group effect-sizes were in the range of d=0.1 to d=0.4

In contrast to the large pre-post effects in the Bohus et al. study between-group effects were small and not significant

# Naltrexone for Treating Dissociation in BPD

## Effect-sizes (NAL vs PLC) by dosage

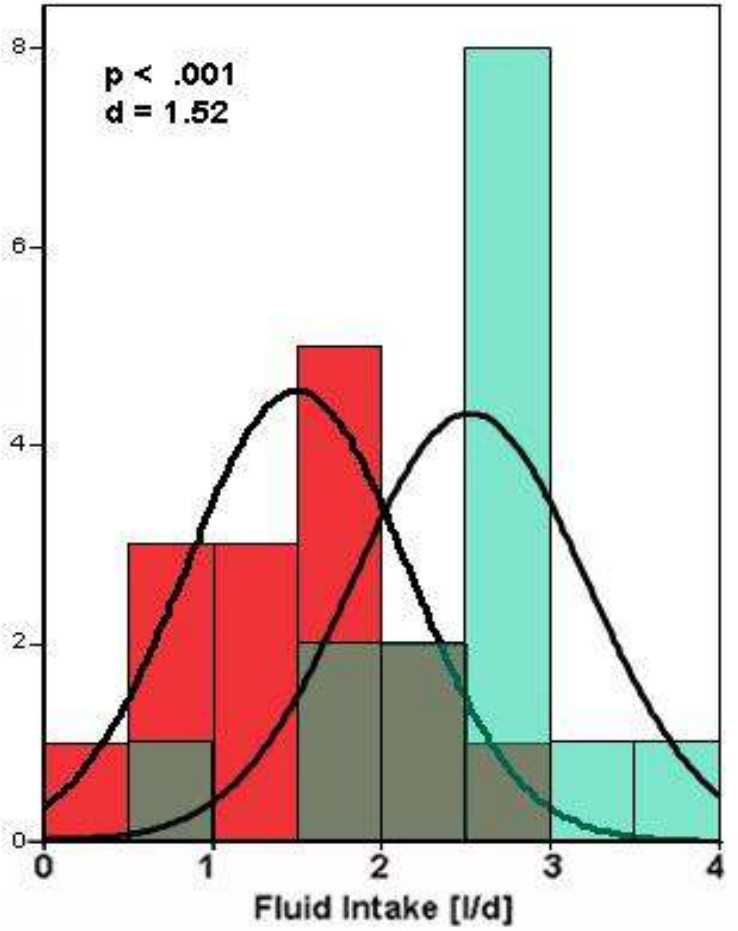



The results numerically favor 200mg/d, but the samples are too small (6 vs 8) to yield significance

Evidence for a pure pharmacological effect is far from being conclusive.
Small pharmacological effect? Large pre-post effects & clin. exp. → worth a try?

# Fluid Intake in BPD Patients (vs HCs)

BPD Patients (n=15)  Healthy Controls (n=15)

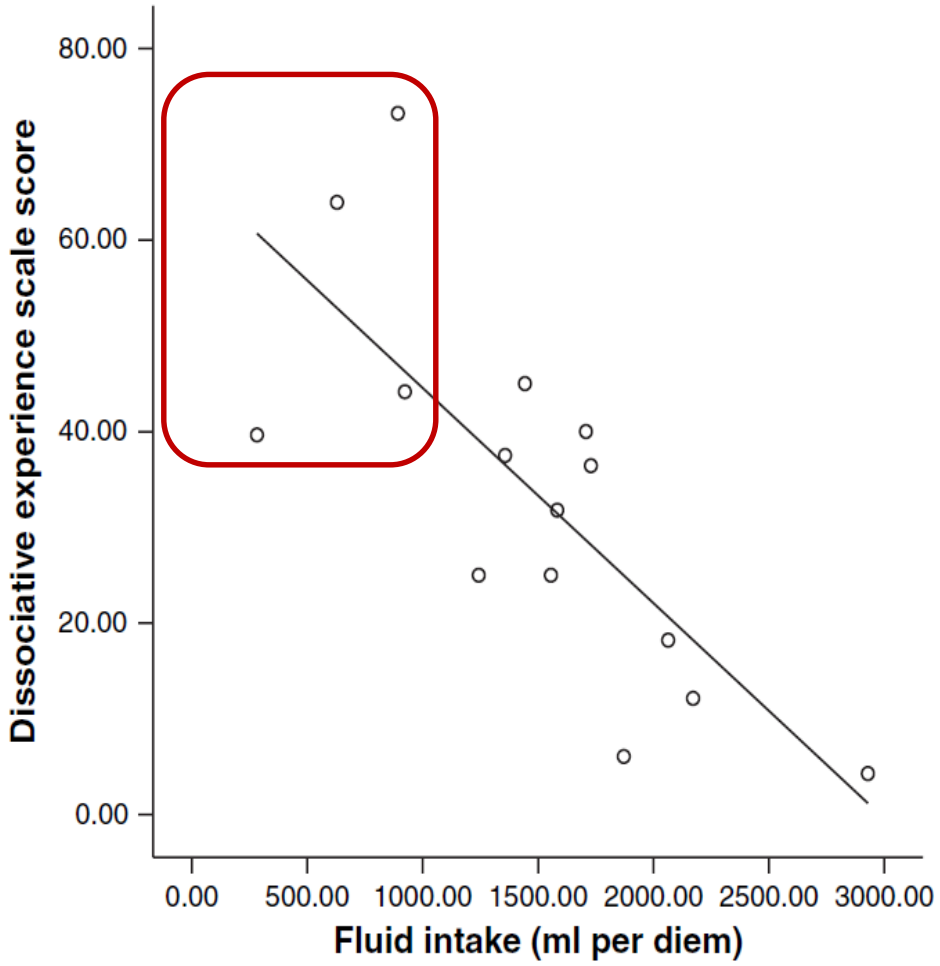



- Fluid intake in BPD patients was much lower than in HCs (about 1.5 vs. 2.5 l/d, p<0.001)
- … and was at a very low level (< 1 l/d) in several patients

→ Is fluid intake related to dissociation?

*Höschel et al. 2008*

# Fluid Intake in n=15 BPD Patients



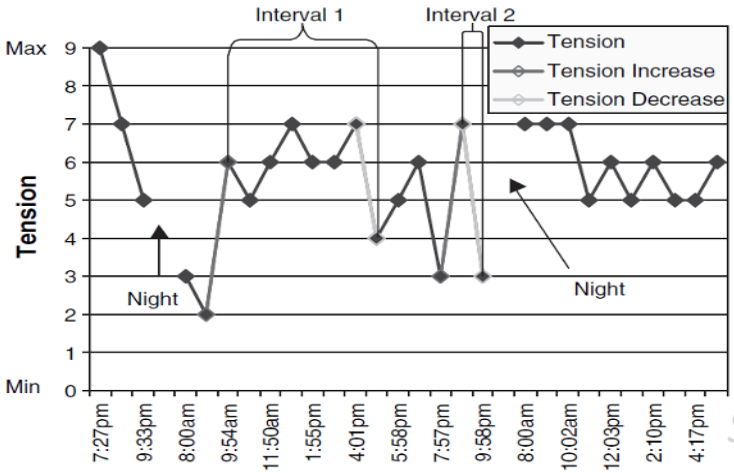

- Very strong relation (r=-.76, p=.001) between daily fluid intake and dissociation
- Those who were drinking less than 1 liter per day had extremely high scores of dissociation

→ Interventional study testing the hypothesis that supplementing fluid intake reduces dissociation in BPD

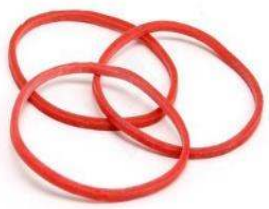
*Höschel et al. 2008*

# Further Measures for Addressing Dissociation

- Psychoeducation
- Cooperation with patients
- Mindfulness
- Reducing vulnerabilities
- Skills
  - antidissociative skill
  - emotion regulation skills
  - stress tolerance skills




Stiglmayr et al. 2005


# Further Measures for Addressing Dissociation

- For patients who tend to dissociate during psychotherapeutic sessions combined
  - sensory input
  - proprioceptive input
  - vestibulary input

  … was found to be helpful for blocking dissociation:

# Summary for Section 2.1 (Dissociation)

- Dissociation **may prevent psychotherapies** of BPD, CPTSD, and PTSD **from being fully effective**
- Dissociation should be monitored & eventually addressed.
- The scientific evidence for add-on measures for treating dissociation is scant. Treatment options include:
  - **Skills**!
  - Patients and the team should take care that the patients **drink** and **sleep** sufficiently
    → **Psychoeducation** and **cooperation** with the patient
  - **Naltrexone** (200mg/d) may be a pharmacological option

... It would be very interesting to me to hear about your experience with blocking dissociation.

# Overview

1) What has been achieved in the treatment of BPD?

2) Starting points for improving treatment efficacy
   - Model of BPD / CPTSD

   2.1) Applied basic research: Dissociation

   **2.2) Applied basic research: NSSI**

   2.3) Neuro-biologically informed approach: Neurofeedback

3) Supporting the patient in building a life worth living

   3.1) patients‘ perspective / feedback

   3.2) positive body image

4) Deficits in current therapies of BPD

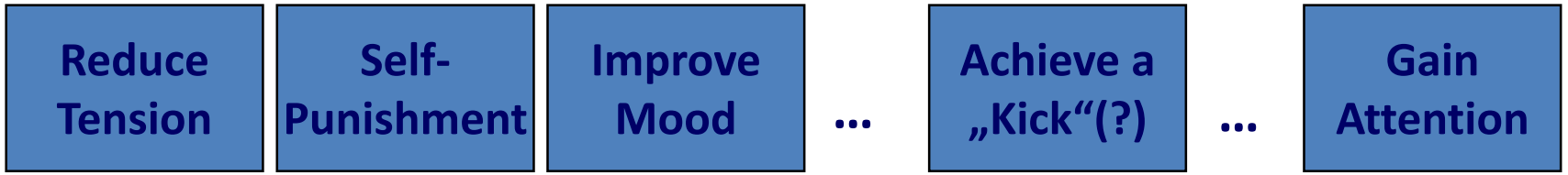
   4.1) Excess mortality

   4.2) Somatic comorbidities

   4.3) Psychiatric comorbidities

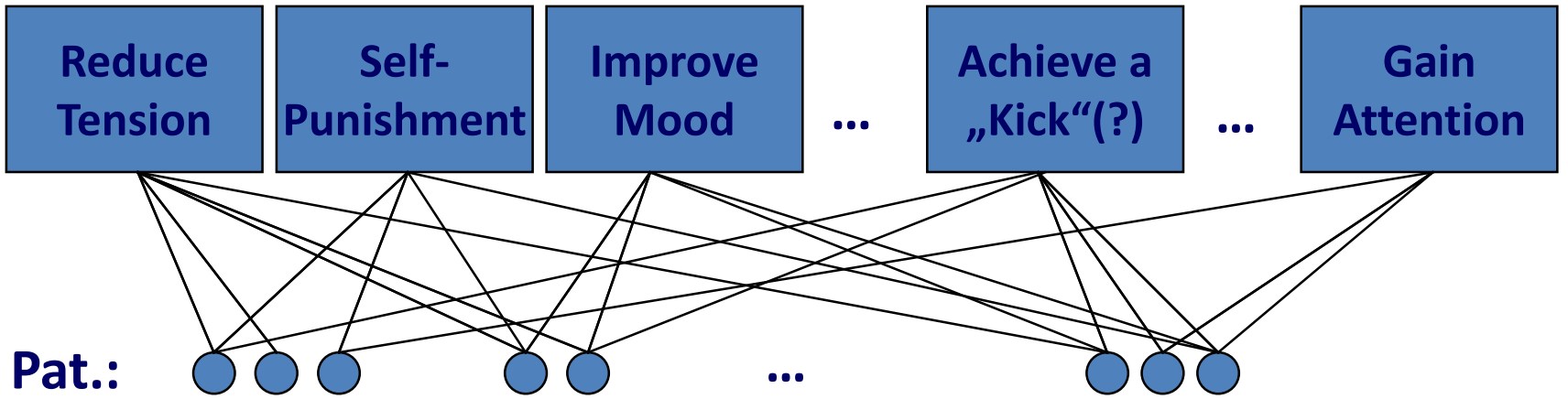
# Study on the Reasons for NSSI

Various motives for NSSI have been described:




However, there was clinical debate in our department regarding

- the relative importance of these motives
- about the distribution of these motives among the patients



# Study on the Reasons for NSSI

The optimal procedure for addressing NSSI will be different when

- (a) there are subgroups of patients,
  e.g., those cutting to reduce tension
  vs those cutting for achieving a kick or high

- (b) or most patients engage in NSSI for multiple reasons

We developped a questionnaire assessing 12 potential motives related to an act of NSSI and asked n=101 women with BPD

1. to **rank** these motives
2. which motives play a role *never – rarely – sometimes – often – always*
3. to report ther emotional states **before and after** an act of NSSI

# Reasons for engaging in NSSI

## (As reported by N=101 BPD Patients)

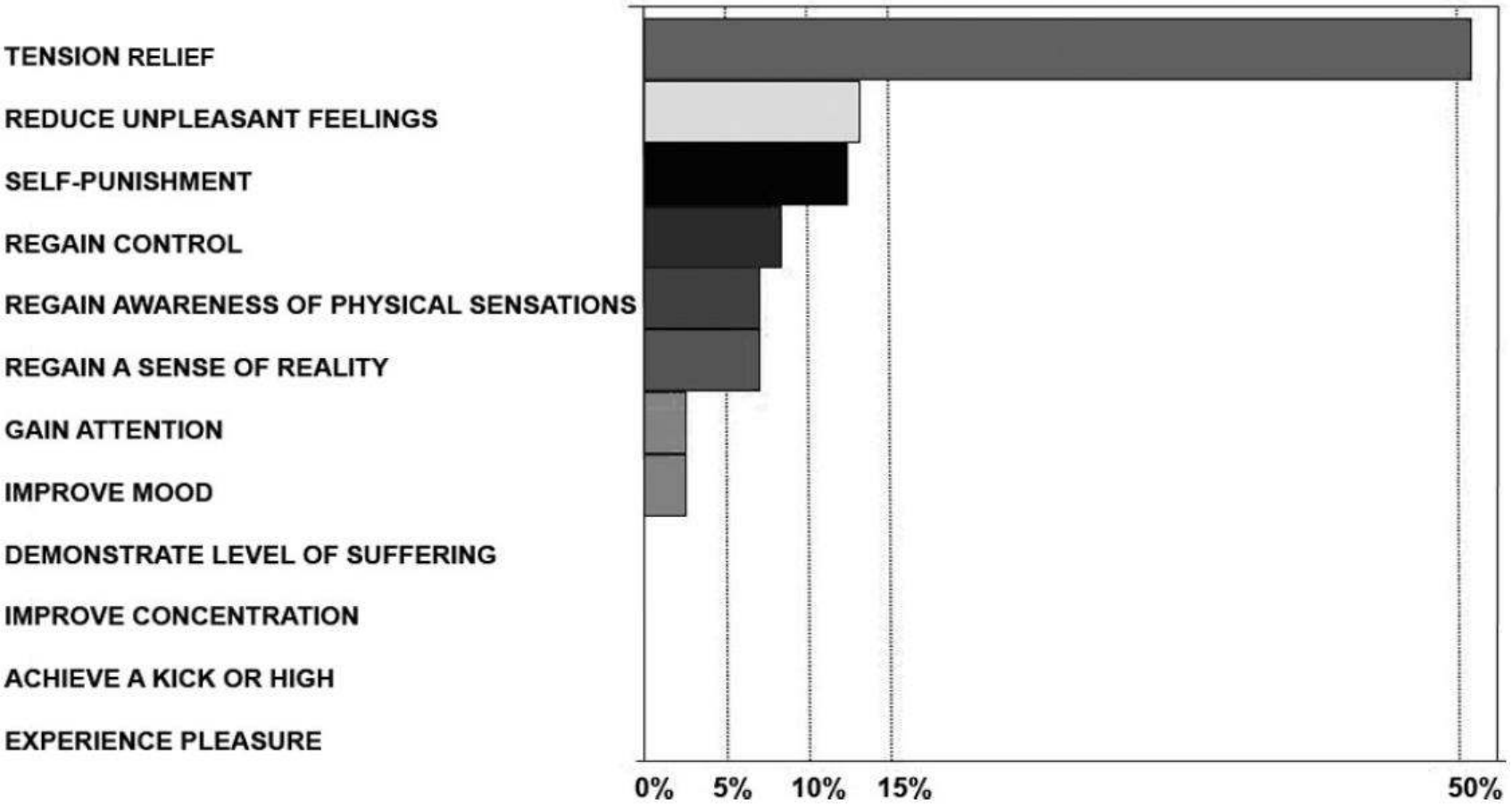



**FIGURE 1.** Primary expectations or motives related to NSSI.

*(Kleindienst et al 2008)*

„I would always ☒ – frequently ☒ – sometimes ☒ like to …“

ACHIEVE TENSION RELIEF

REDUCE UNPEASANT FEELINGS

PUNISH MYSELF

REGAIN CONTROL

REGAIN SENSE OF REALITY

REGAIN BODILY AWARENESS

GAIN ATTENTION

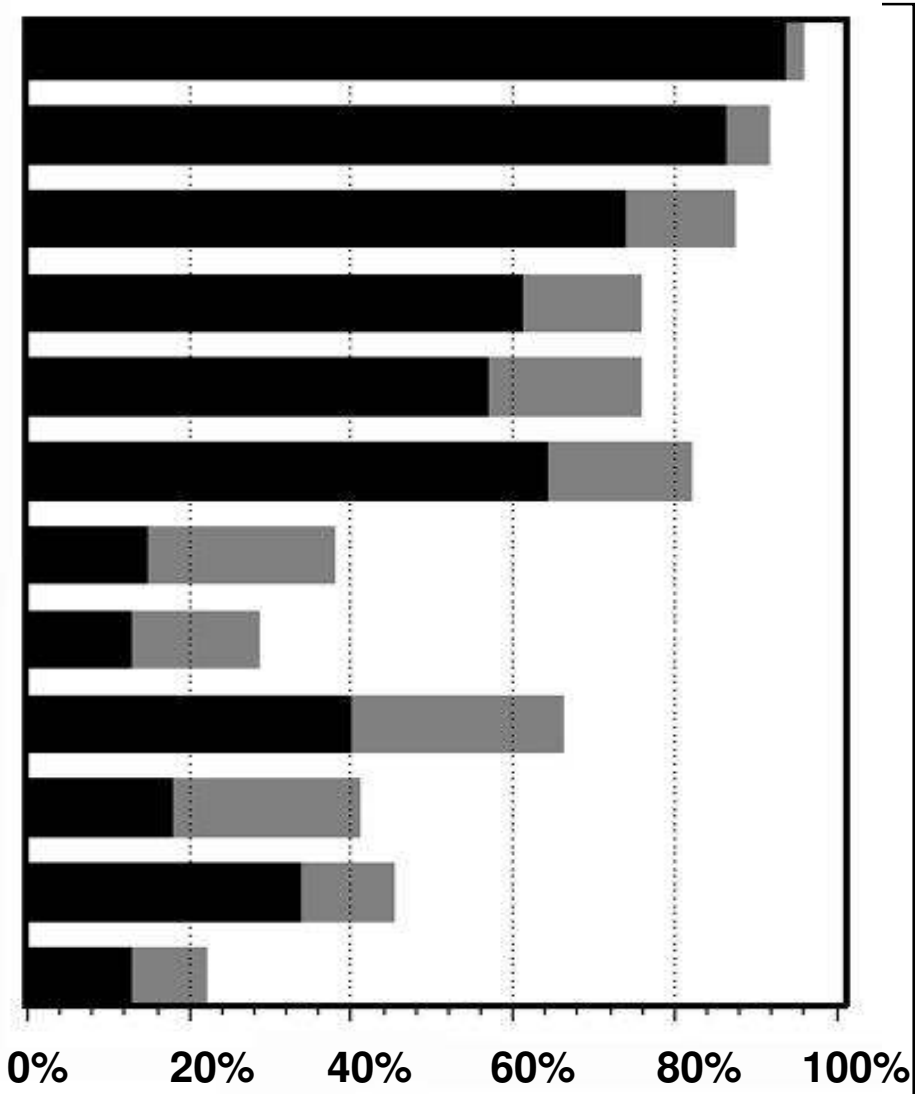
DEMONSTRATE SUFFERING

IMPROVE MOOD

IMPROVE CONCENTRATION

ACHIEVE A KICK OR HIGH

EXPERIENCE LUST




Ø no. of motives
(sometimes/frqtl./always): 7.5
(frqtl./always): 5.7

*Kleindienst et al 2008*

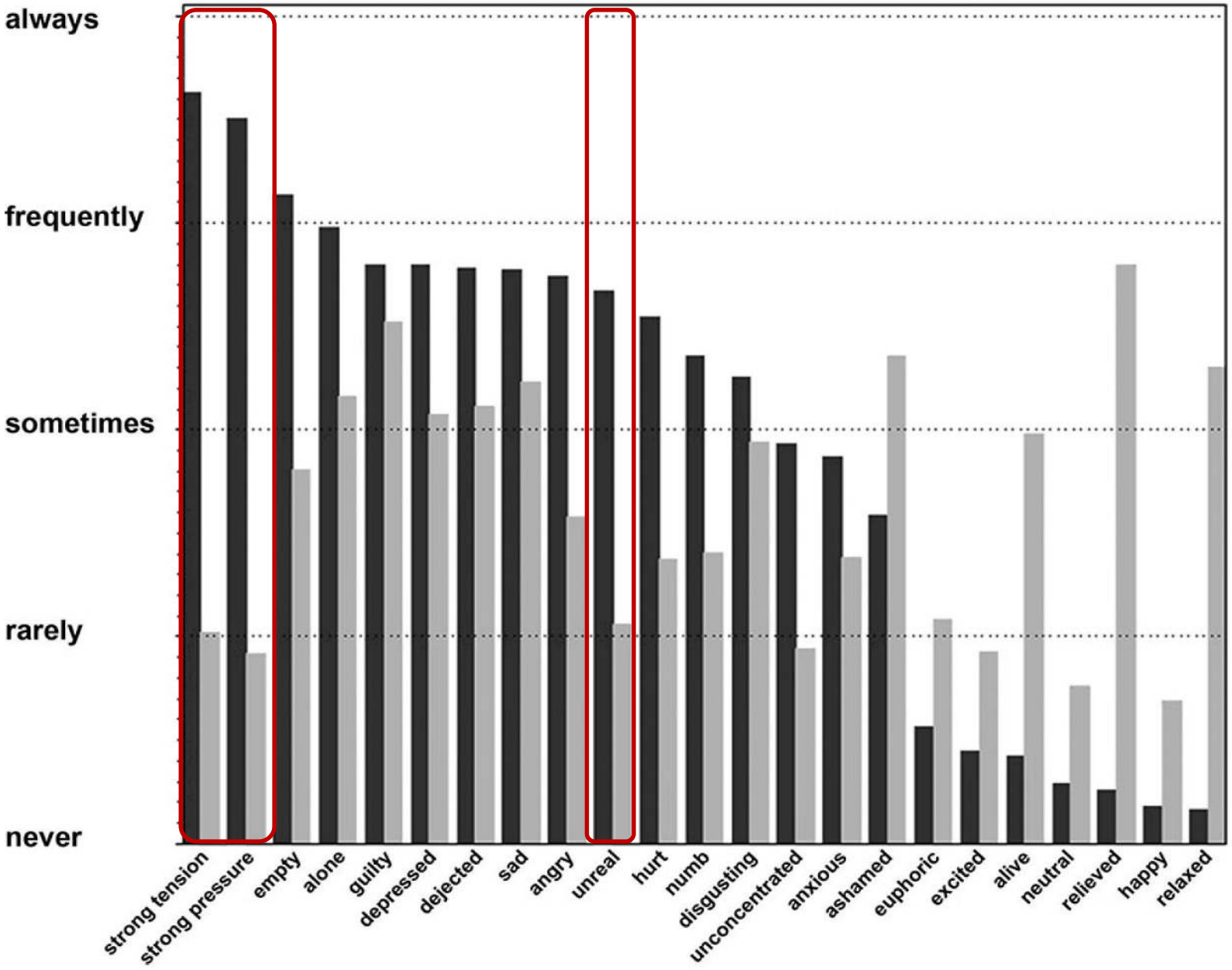


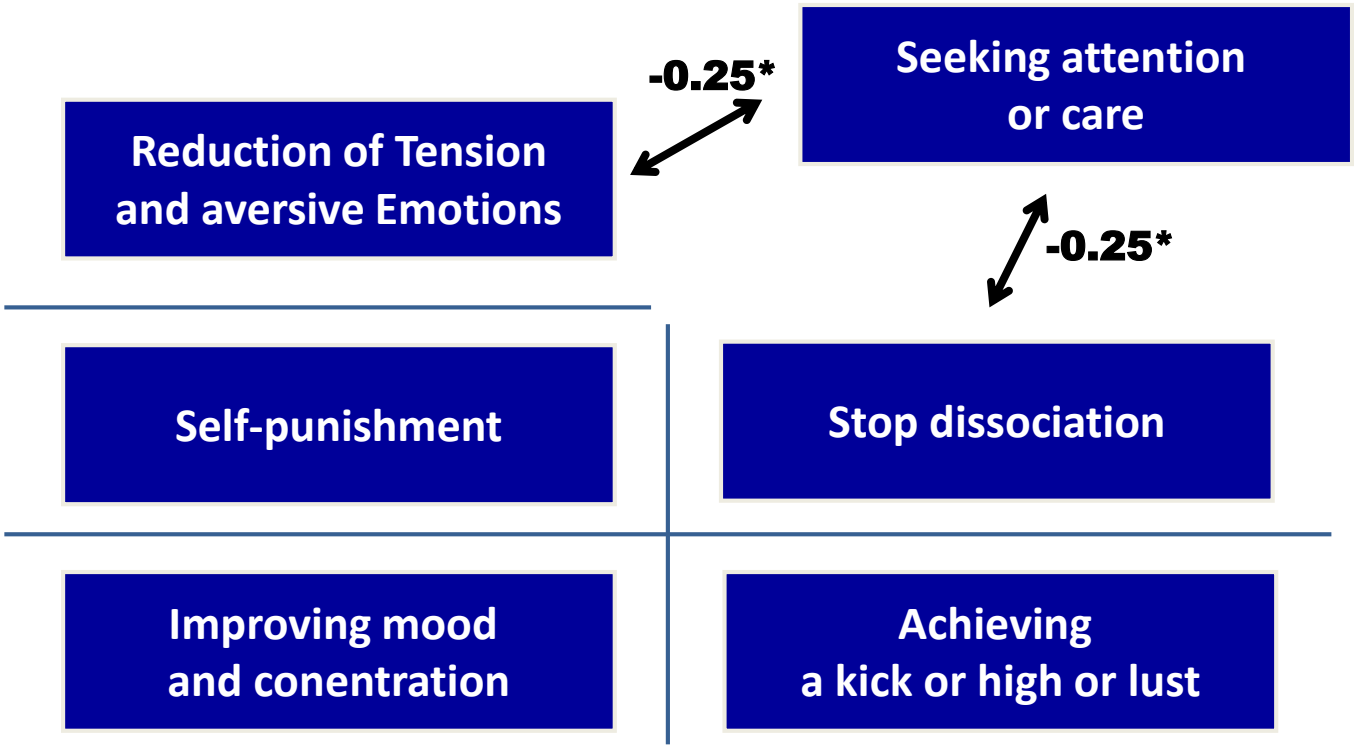

**FIGURE 3.** Average intensity of items characterizing the emotional state before (■) and after (□) an act of NSSI.

# Factorial Structure of the Motives for NSSI

- Each 1-3 items (e.g., „reduce tension“, „reduce unpleasant feelings“) were intercorrelated (r‘s ≈ 0.3-0.5) and can be grouped (≈ factors)

| | |
|---|---|
| **1) Reduce tension**<br>**2) Reduce unpleasant feelings** | **1) Gain attention**<br>**2) Demonstrate suffering** |
| **1) Self-punishment** | **1) Regain control**<br>**2) Regain bodily awareness**<br>**3) Regain a sense of reality** |
| **1) Improve mood**<br>**2) Improve concentration** | **1) Achieving a kick or high**<br>**2) Experiencing lust** |

# Factorial Structure of the Motives for NSSI




- Those 6 factors were mostly uncorrelated
  - with the exception of „seeking attention or care“, which was negatively correlated to the high-stress factors

# Clinical Implications and Section Summary (2.2)

- Relief from a state of high tension and of highly unpleasant feelings is almost always a motive for an act of NSSI

- Typically, several other motives
  (e.g., gain attention + regain bodily awareness)
  are part of the motivation

→ If you only address the primary motive identified in the behavioral analysis, NSSI will likely persist as it is still driven by other motives

→→ Proactive exploration of a broad spectrum of possible motives should be included in the behavioral analysis.

# Overview

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   4.1) Excess mortality

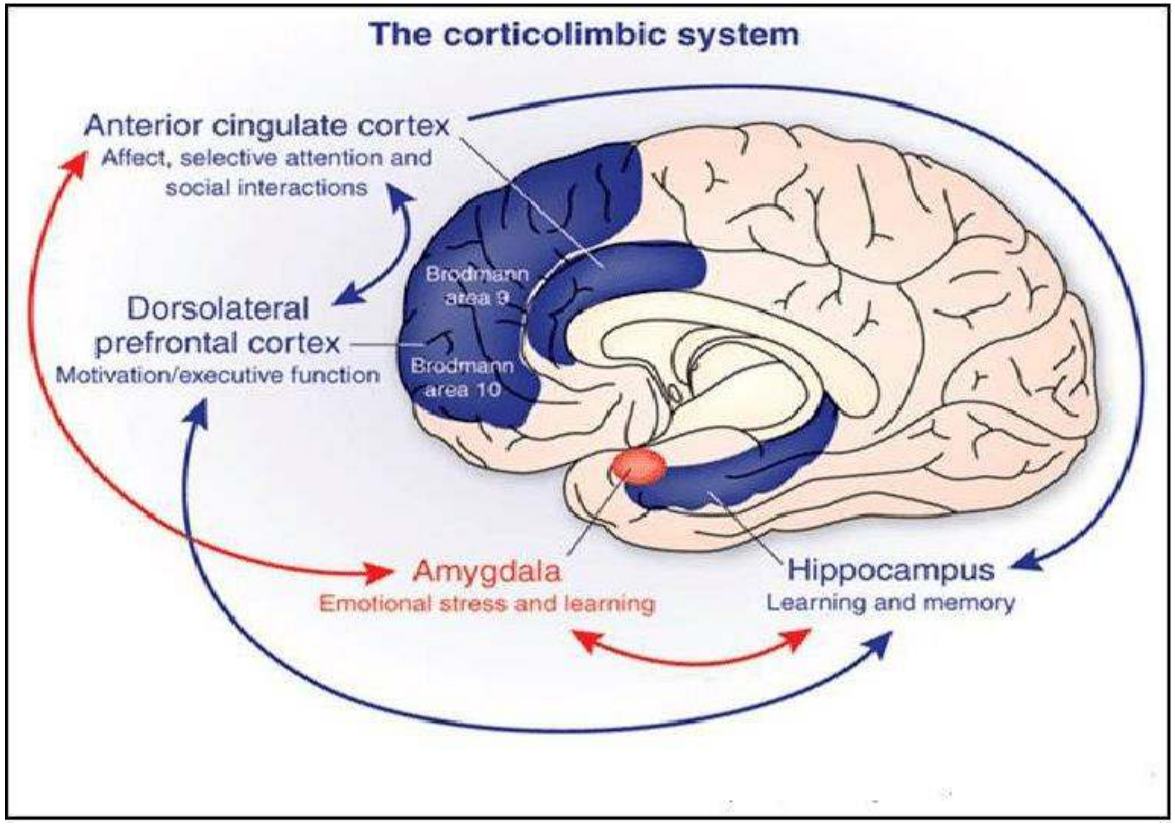
   4.2) Somatic comorbidities

   4.3) Psychiatric comorbidities

# Disturbed Corticolimbic Function in BPD and PTSD

The corticolimbic system is crucial for regulating emotions and attention.

Disturbances in the corticolimbic system are among the best supported neurological substrates for **disturbed emotion regulation** in BPD.



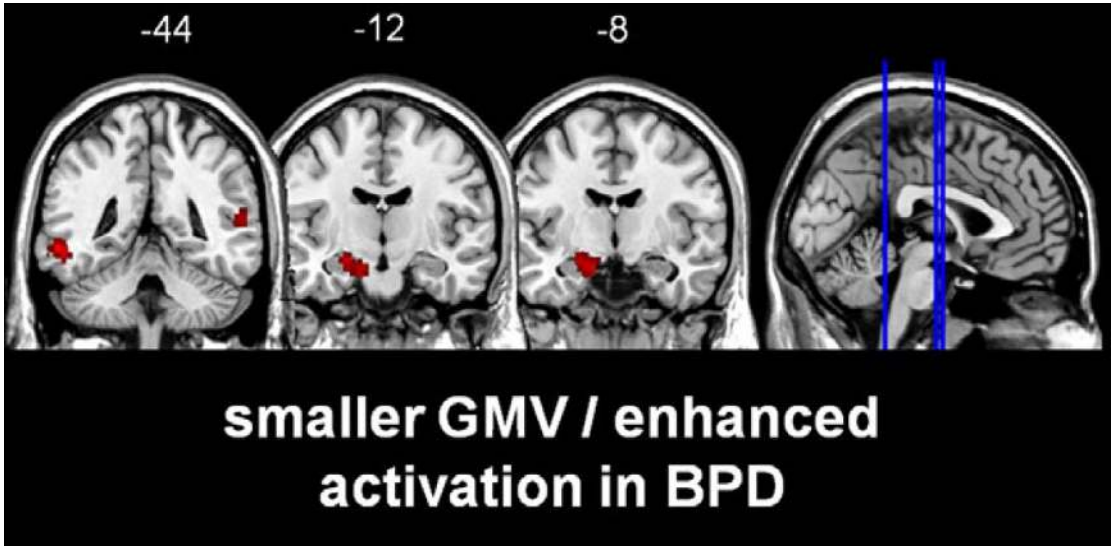

*Leisman & Melillo 2013*

# Neural Correlates of Disturbed Emotion Processing in Borderline Personality Disorder: A Multimodal Meta-Analysis

Lars Schulze, Christian Schmahl, and Inga Niedtfeld

Biological Psychiatry January 15, 2016

- k=19 fmrI-studies (processing of negative vs neutral stimuli) in 281 patients with BPD and 293 HC
- k=10 studies investigating gray matter abnormalities in 263 patients with BPD and 278 HC

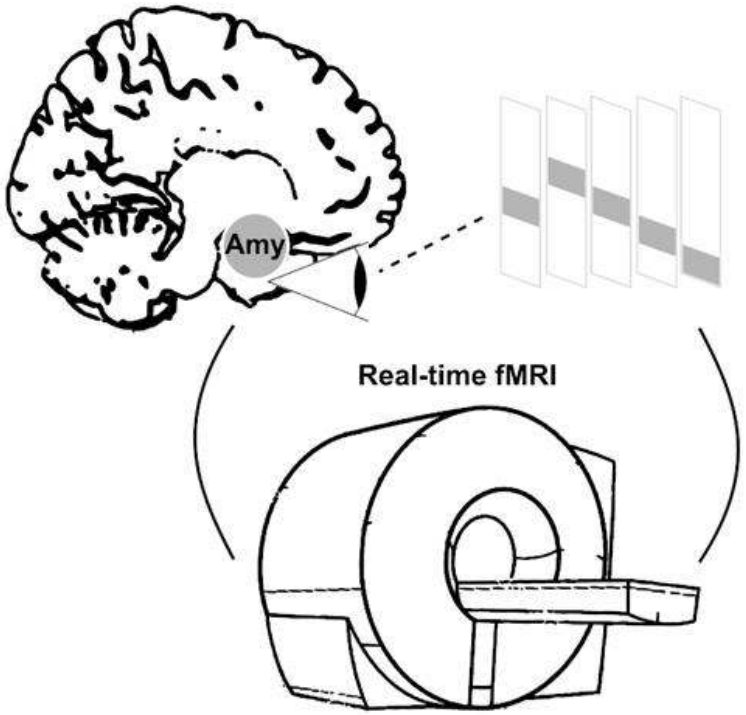



<u>Functional level:</u>
Amygdala was hyperactivated in BPD

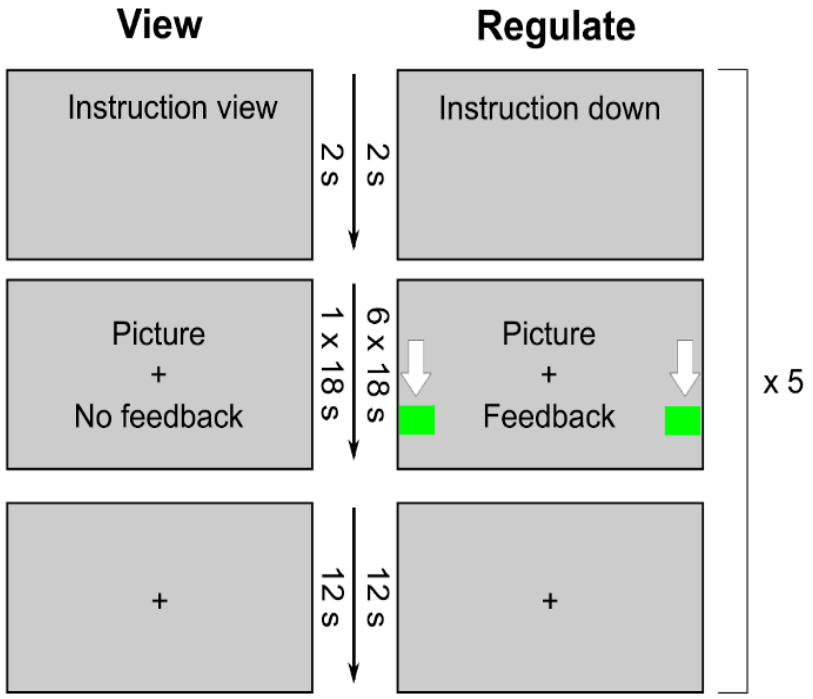
<u>Morphological level:</u>
Amygdala had reduced volume in participants with BPD

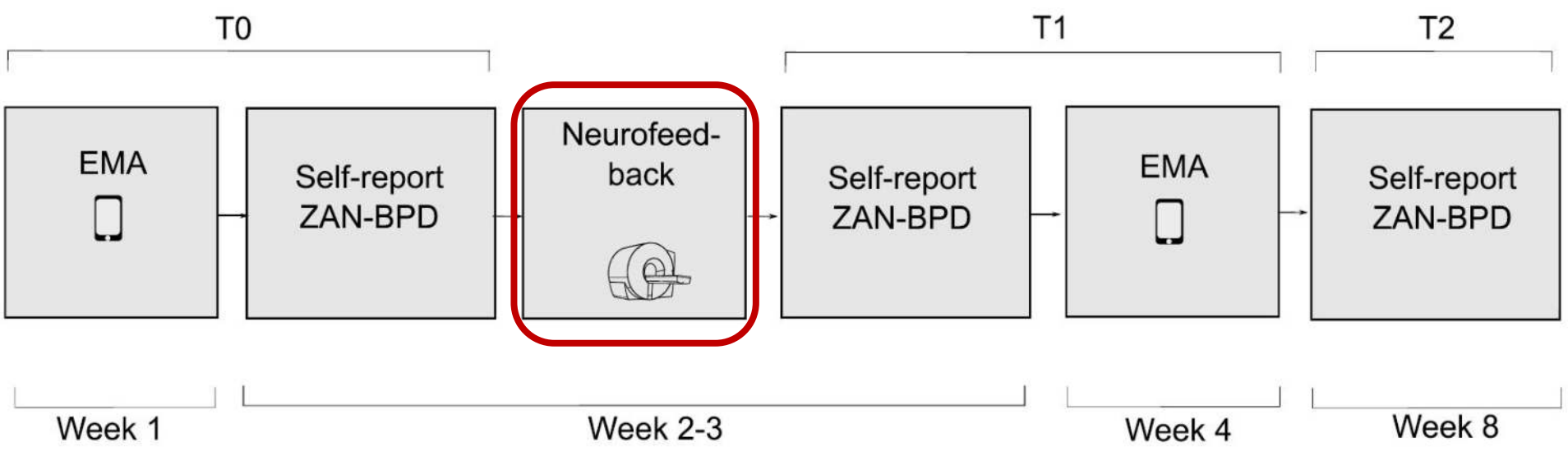
Basic idea consistently followed by Chris Paret :

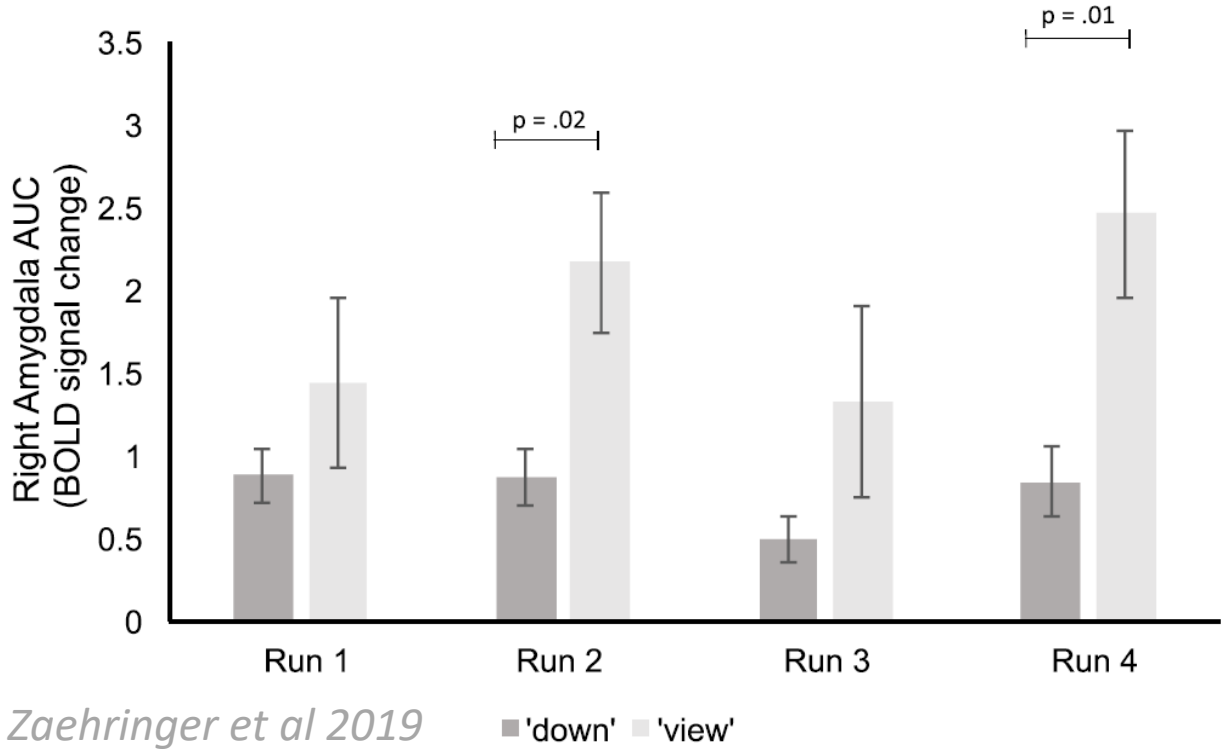
- Enabeling BPD patients to downregulate their hyperactivated amygdala via neuro-feedback.
- While watching aversive pictures in the scanner BPD patients repeatedly receive neuro-feedback displaying the activity of their amygdala




**2 conditions:**



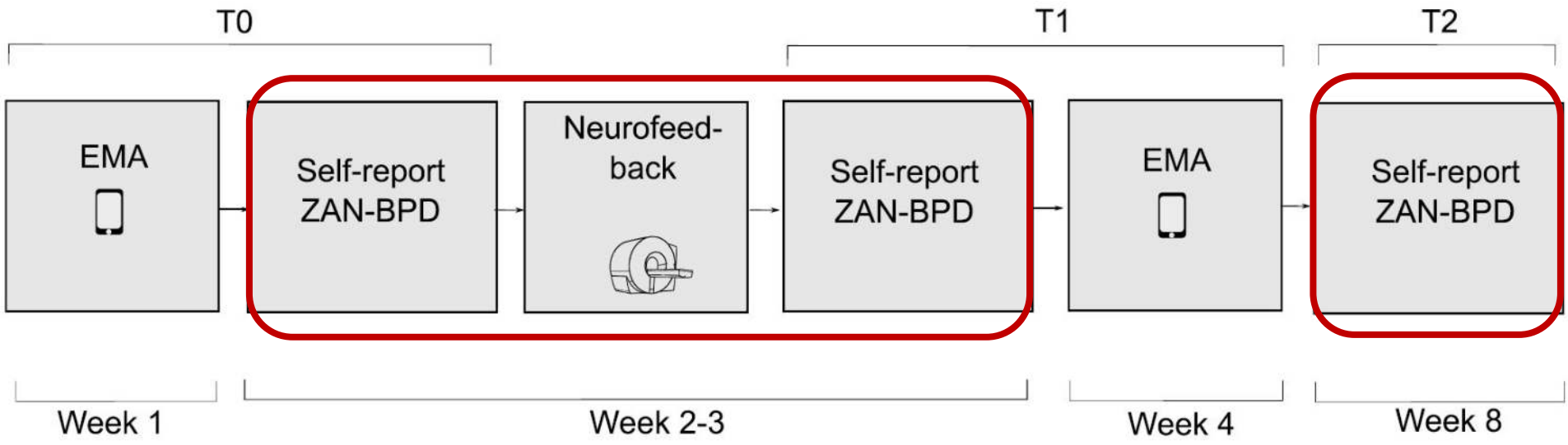


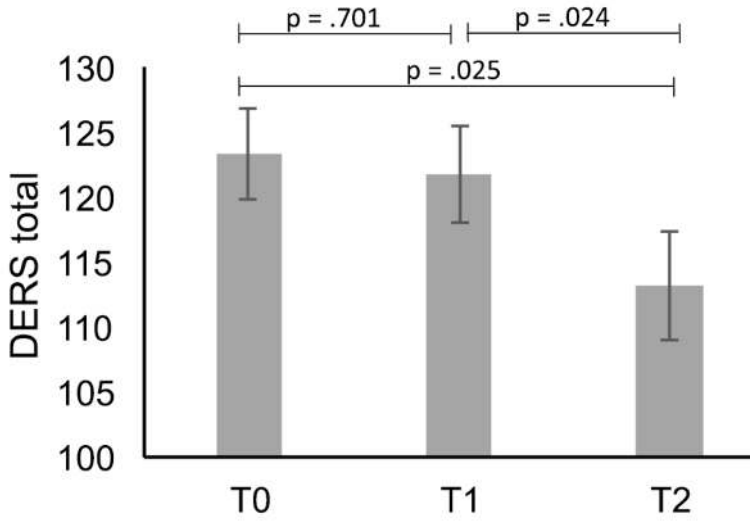



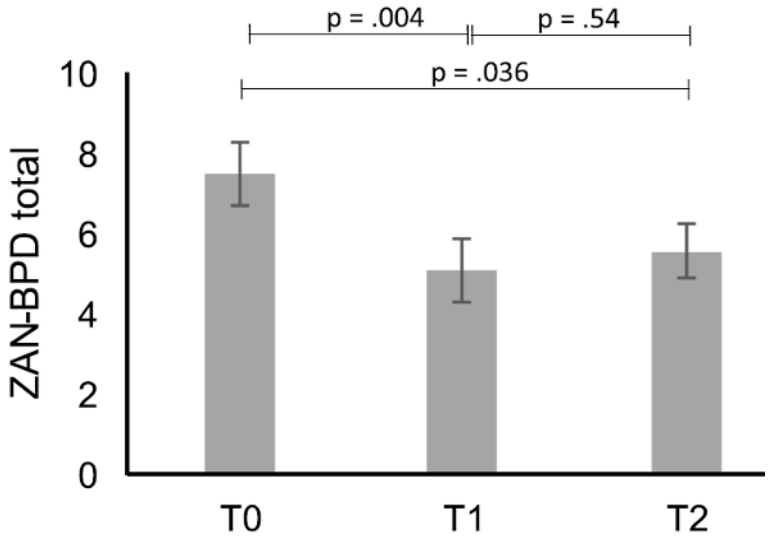

*Zaehringer et al 2019*

Participants were able to downregulate their amygdala

→ Does the amygdala regulation translate into improved emotion regulation?

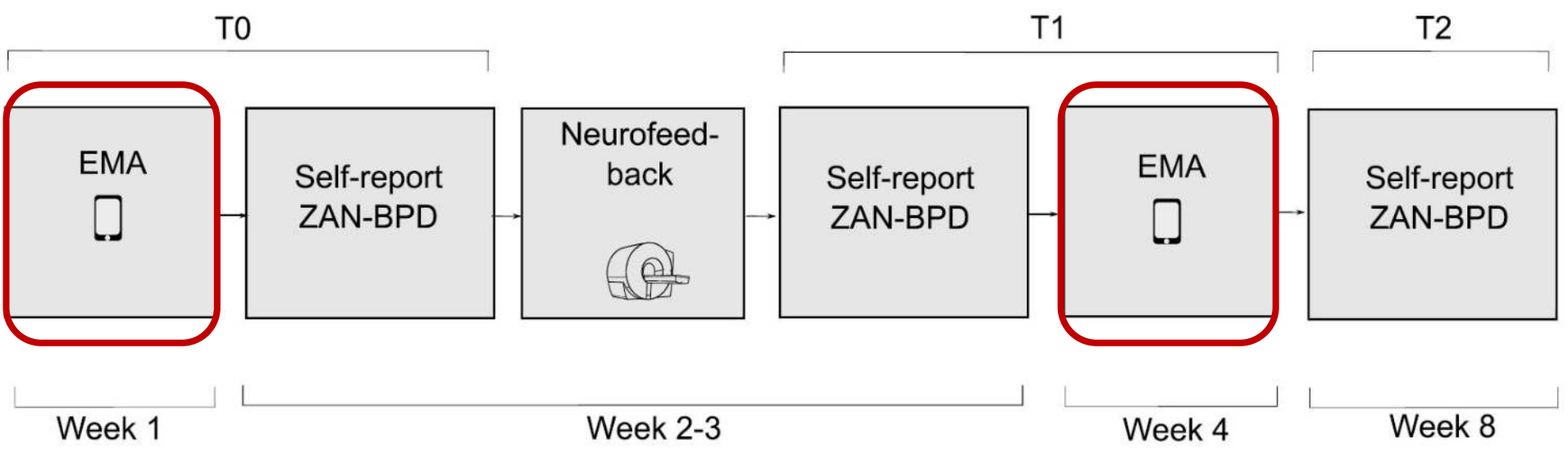


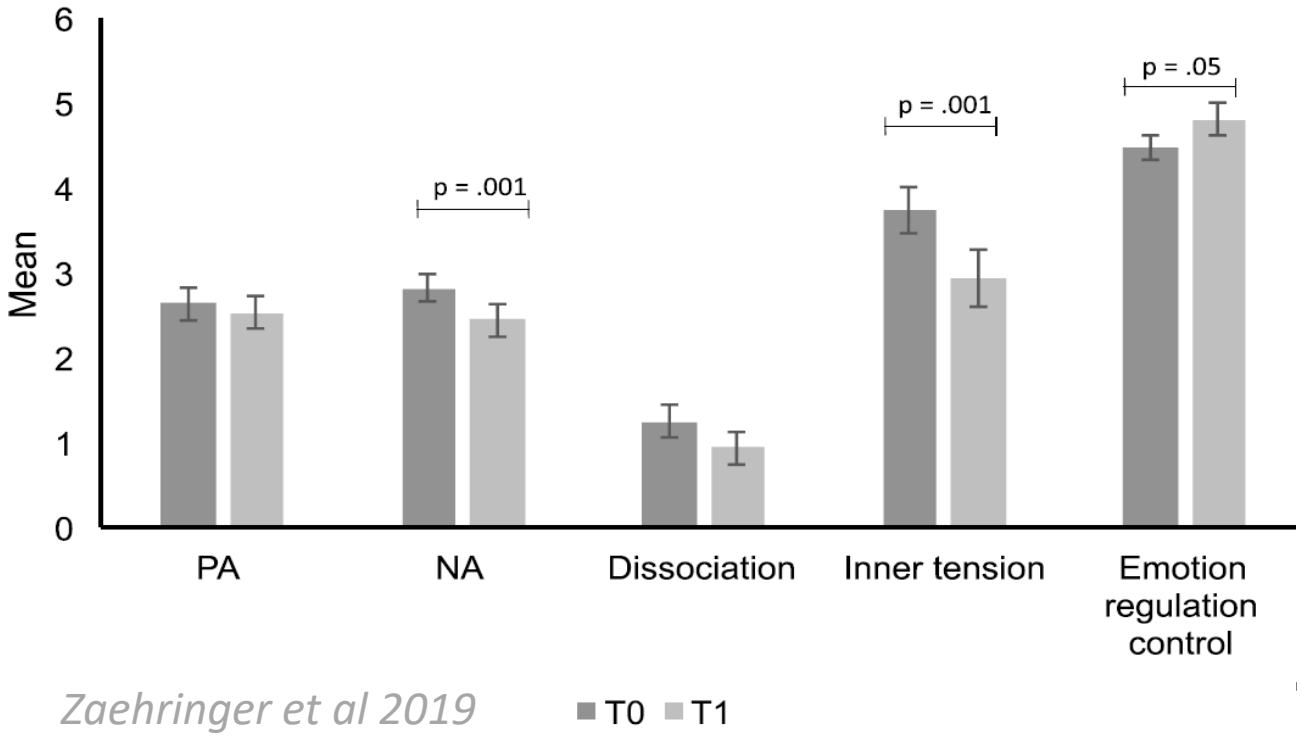




Both the Difficulties in Eemotion Regulation Scale (DERS) and the overal severity of BPD-symptoms (ZAN-BPD) significantly improved.

*Zaehringer et al 2019*




EMA: 12 random prompts /day on 4 consecutive work days




*Zaehringer et al 2019*

Significant improvements related to amy-NF in particular in terms of
- mean neg. affect
- inner tension

# Section Summary (2.3), Limitations, Next Steps

Summary:

Patients who received amygdala-NF

- learned to down-regulate their amygdala
- improved with respect to BPD symptoms (emotion reg., ZAN-BPD)
- had less negative emotions and states of high tensions in their daily lives

Major limitations:

1) lack of control group

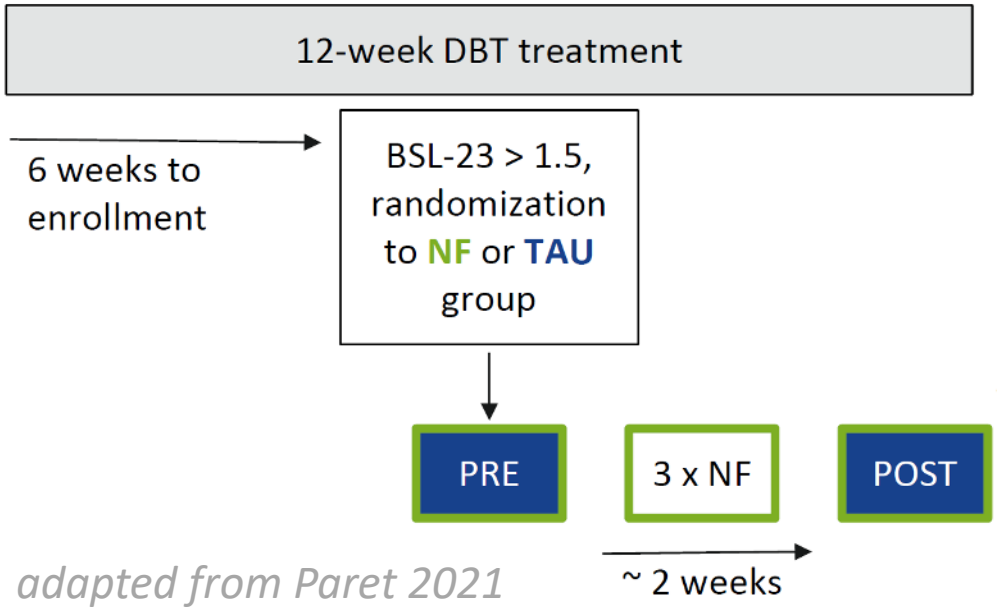
→ do the effects originate from NF or from something else?

2) scanners are not widely availble → restricted availability

# Amygdala NF for BPD: Next Steps

1) Replacing fmrI with EEG
   - defining a EEG signature
   - providing and evaluating EEG feedback

2) Evaluating the effects of **amygdala NF in RCTs**
   - e.g., to assess efficacy of NF as an adjuvant therapy supporting DBT in those patients with relatively high levels of psychopathology (n=44)




*adapted from Paret 2021*

# Overview

1) What has been achieved in the treatment of BPD?

2) Starting points for improving treatment efficacy
   - Model of BPD / CPTSD
   2.1) Applied basic research: Dissociation
   2.2) Applied basic research: NSSI
   2.3) Neuro-biologically informed approach: Neurofeedback

3) Supporting the patient in building a life worth living
   3.1) patients‘ perspective / feedback
   3.2) positive body image

4) Deficits in current therapies of BPD
   4.1) Excess mortality
   4.2) Somatic comorbidities
   4.3) Psychiatric comorbidities

# Improving Psychotherapies for BPD

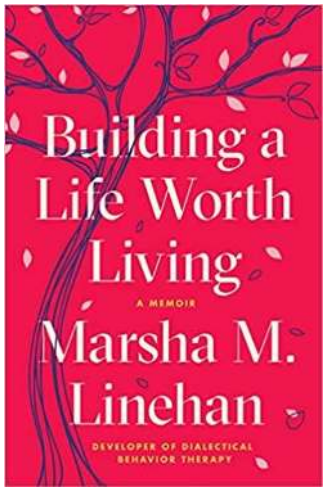
As important it is to…

- prevent suicides
- prevent and address crisis generating behaviors
- prevent patients from prematurely quitting therapy
- to achieve symptomatic remission (=no longer meeting BPD criteria)

We should keep in mind that building a live worth living is more than getting rid of the diagnosis

| Criterion - Borderline Personality Disorder |
| --- |
| 1. Frantic efforts to avoid real or imagined abandonment. |
| 2. A pattern of unstable and intense interpersonal relationships characterised by alternating between extremes of idealisation and devaluation. |
| 3. Identity disturbance: markedly and persistently unstable self-image or sense of self. |
| 4. Impulsivity in at least two ares that are potentially self-damaging (e.g., spending, sex, substance abuse, reckless driving, binge eating). |
| 5. Recurrent suicidal behaviour, gestures, threats or self-mutilating behaviour. |
| 6. Affective instability due to a marked reactivity of mood (e.g., intense episodic dysphoria, irritability or anxiety usually lasting a few hours and only rarely more than a few days). |
| 7. Chronic feelings of emptiness. |
| 8. Inappropriate, intense anger or difficulty controlling anger (e.g. frequent displays of temper, constant anger, recurrent physical fights). |
| 9. Transient, stress-related paranoid ideation or severe dissociative symptoms. |

≠



# Improving Psychotherapies for BPD

Moving beyond “Borderline-relevant outcomes include borderline symptoms, self- harm and parasuicidal behavior, and suicide.“

*(Cristea et al., 2017)*

To better know the patients‘ perspective we systematically asked them

- whether they have a name for their problem
- about their individual expectations related to the therapy
- about their goals they would like to achieve

*Görg, Kiegelmann et al., in preparation*

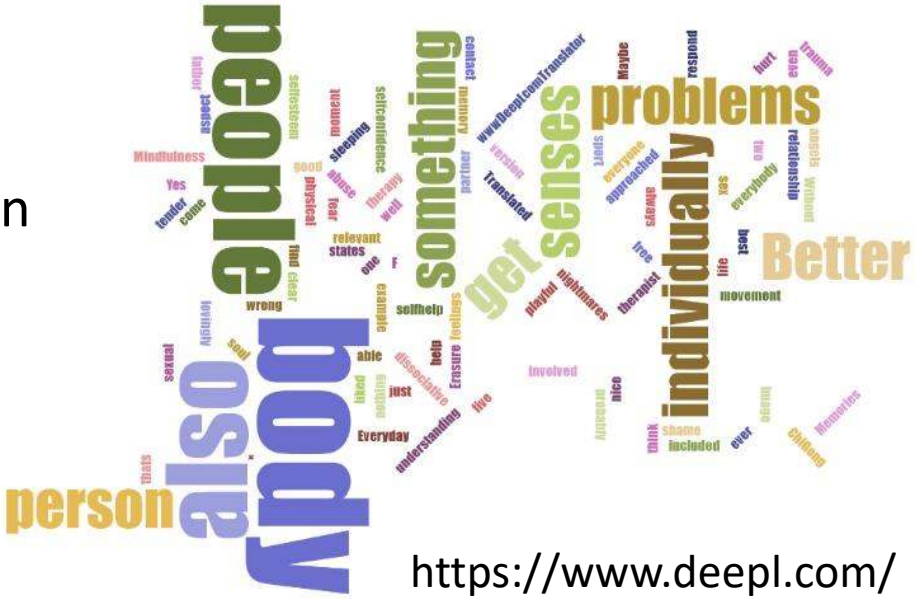
# Content Analysis

*N. Görg, M. Kiegelmann, M.-L. Zeitler.*

Systematic qualitative content analysis of n=149 interviews is on the way

… no definite results yet, but as illustrated in the word cloud based on the patient‘s input initial several patients would like

- a **more individualized therapy**
- more emphasis on **bodily aspects**



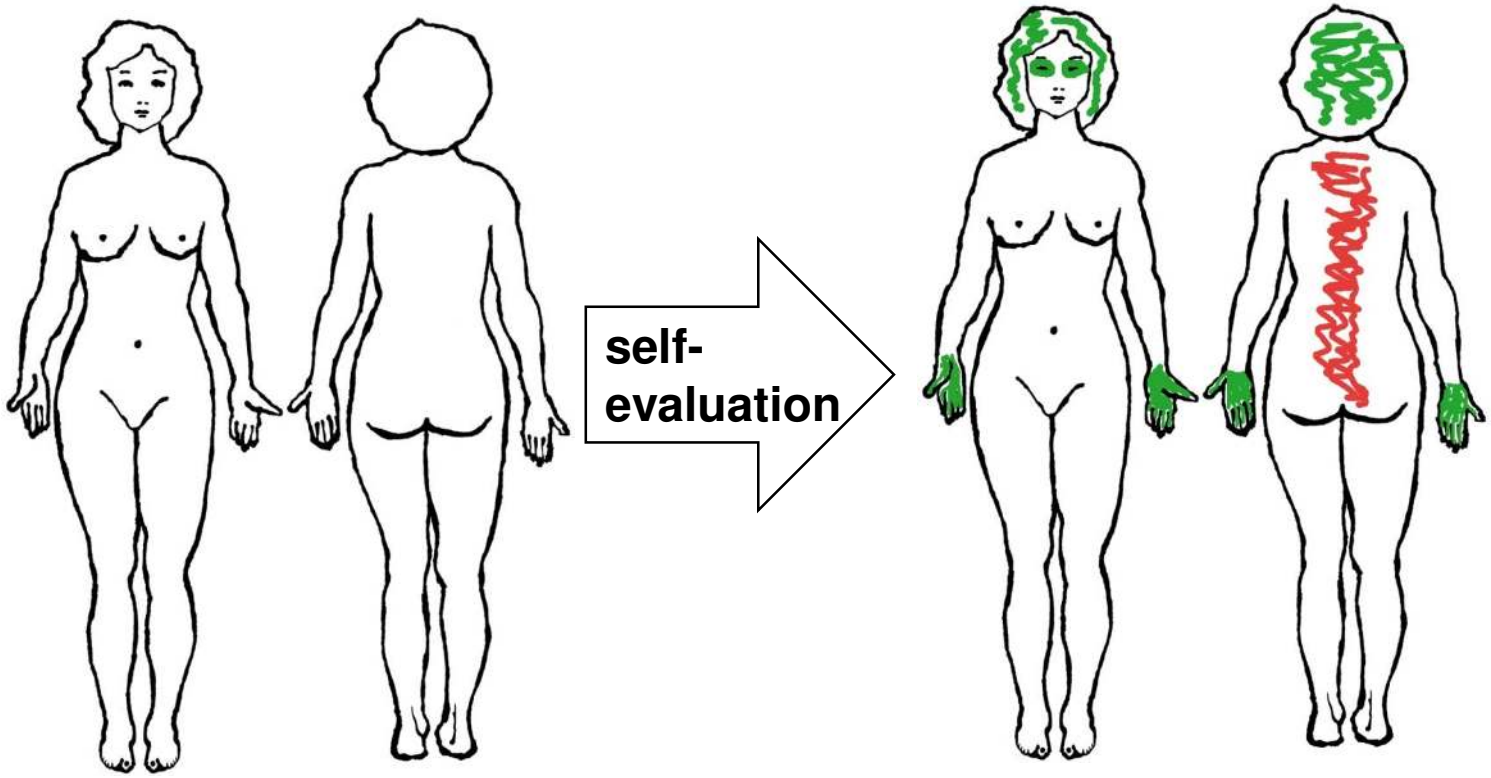

https://www.deepl.com/
https://www.jasondavies.com/wordcloud/

# Body Self-Evaluation

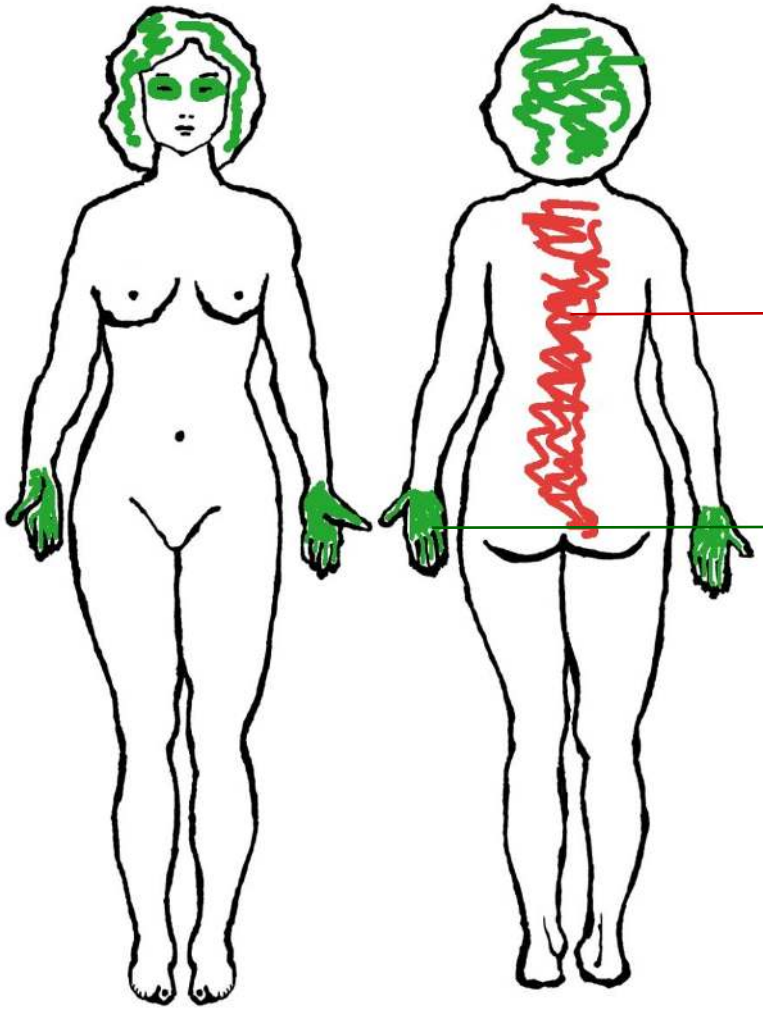
*Anne Dyer*

How to assess body self-evaluation?

→ Survey of Body Areas



# Body Self-Evaluation



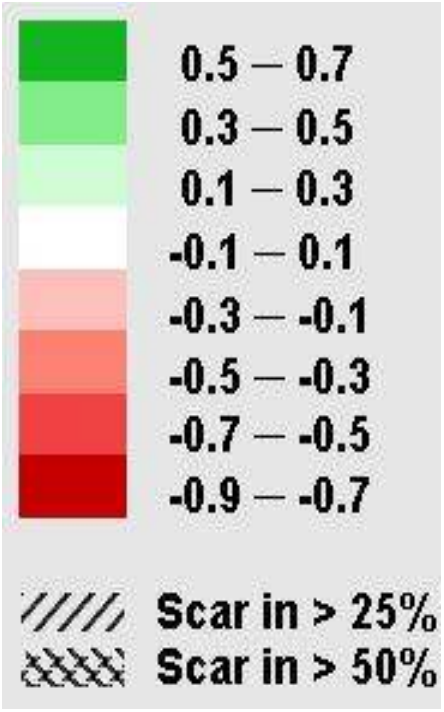
+1
+1
0
-1
+1

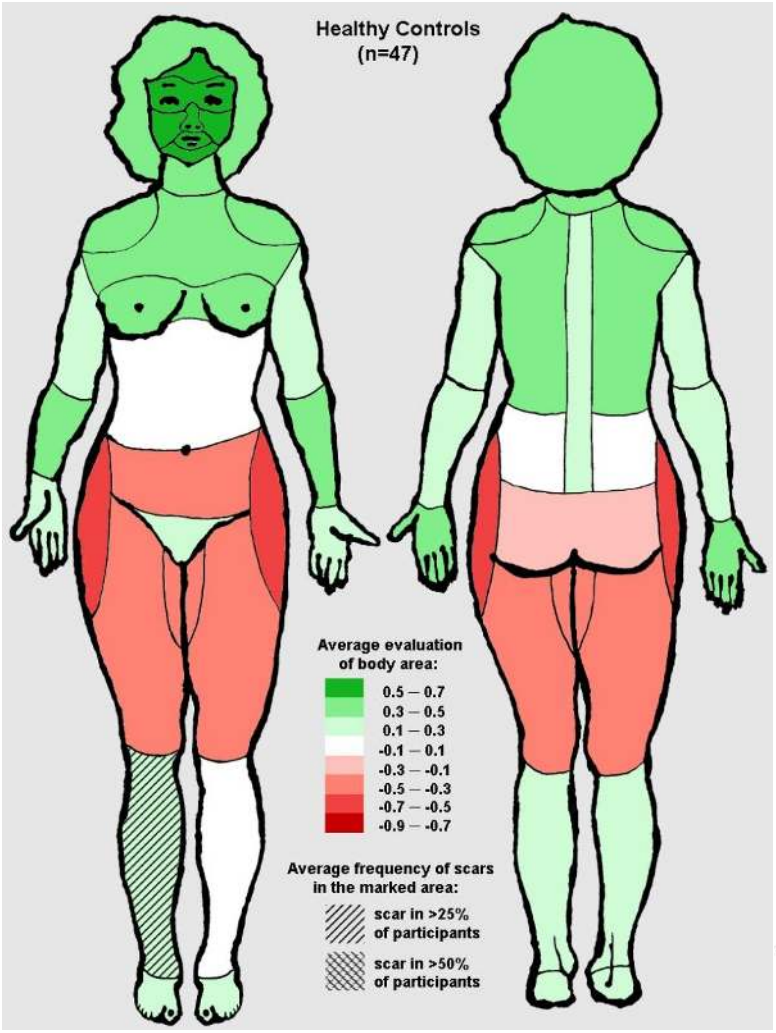
mean SBA

*Kleindienst et al. 2014*

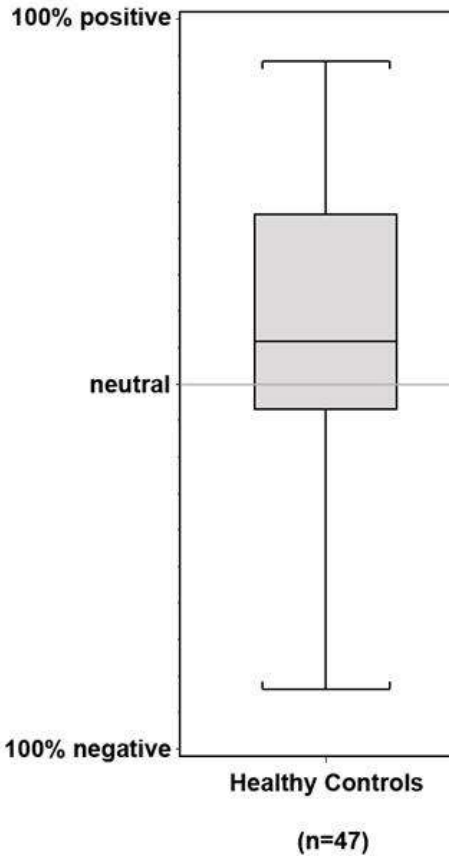
# SBA: Color Coding, Results for Healthy Controls

**Average evaluation of body areas:**



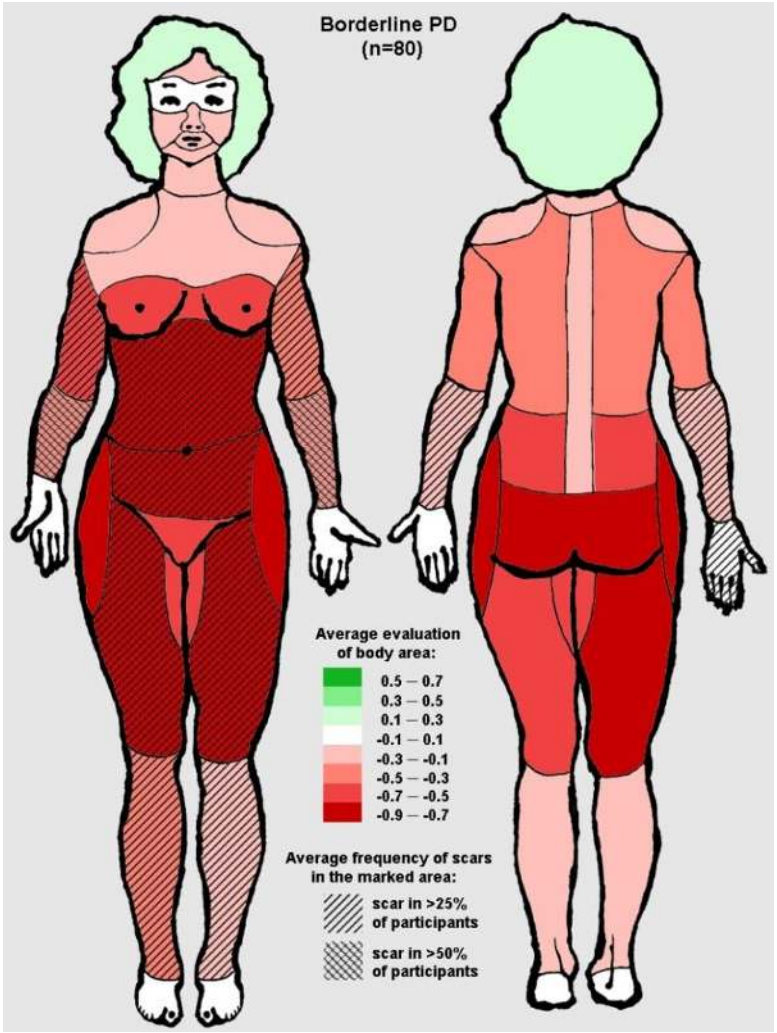




Mean SBA-score:
0.17±0.35, p<0.01

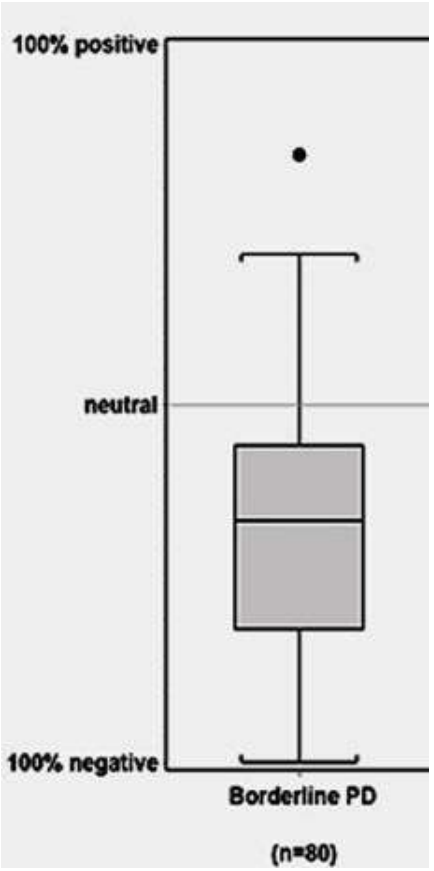



*Kleindienst et al. 2014*

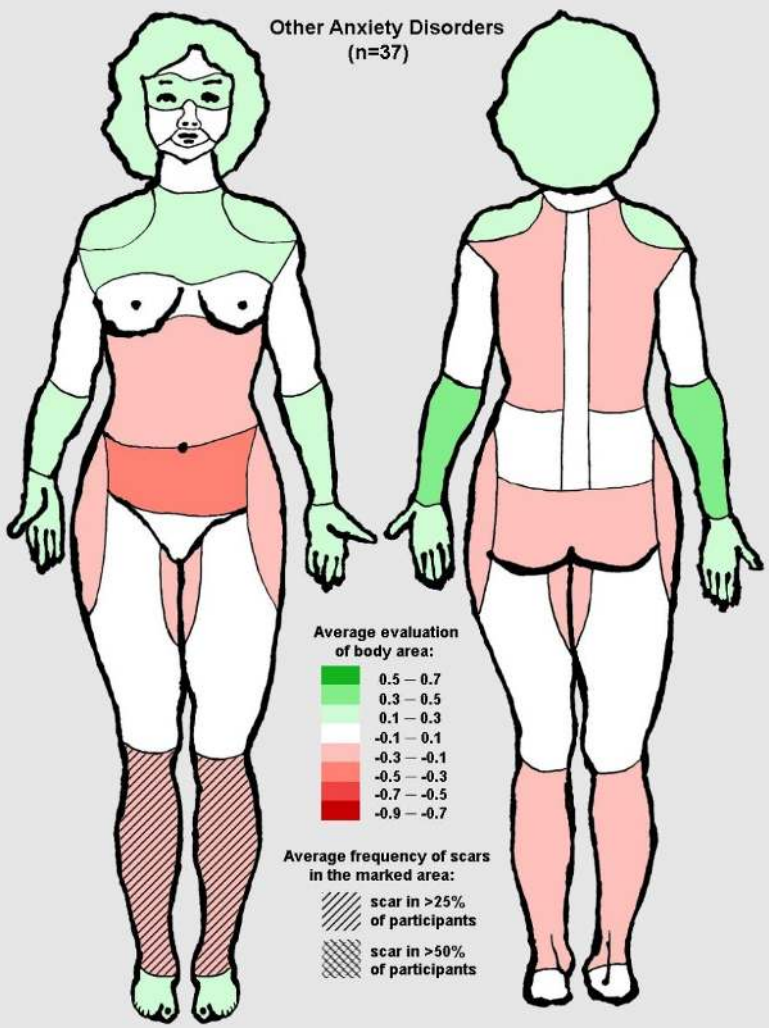
# SBA: Results for BPD



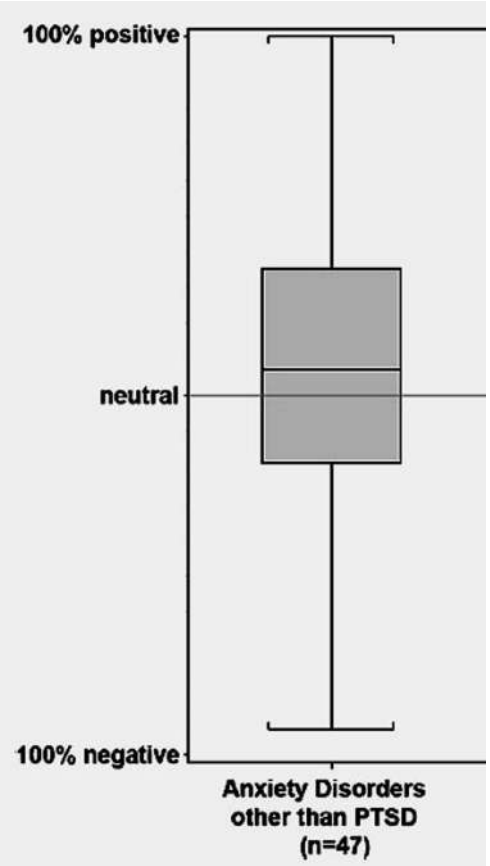

Mean SBA-score:
-0.34±0.37, p<0.001



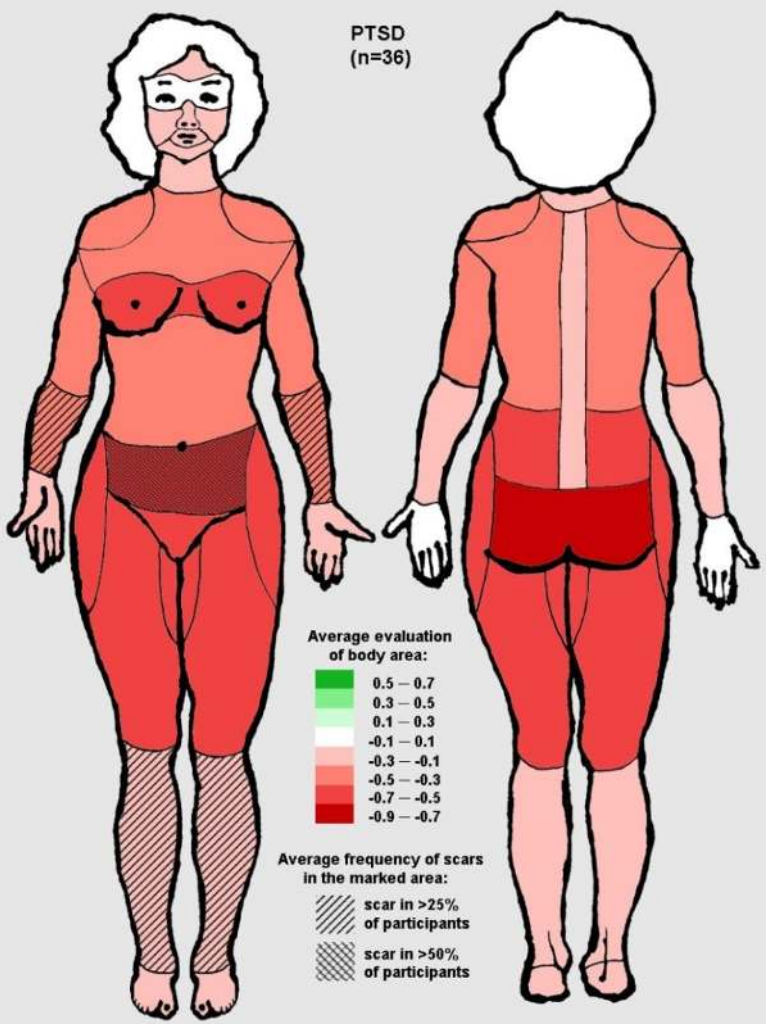
# Anxiety Disorders (mostly Social Phobia, Panic Do.)



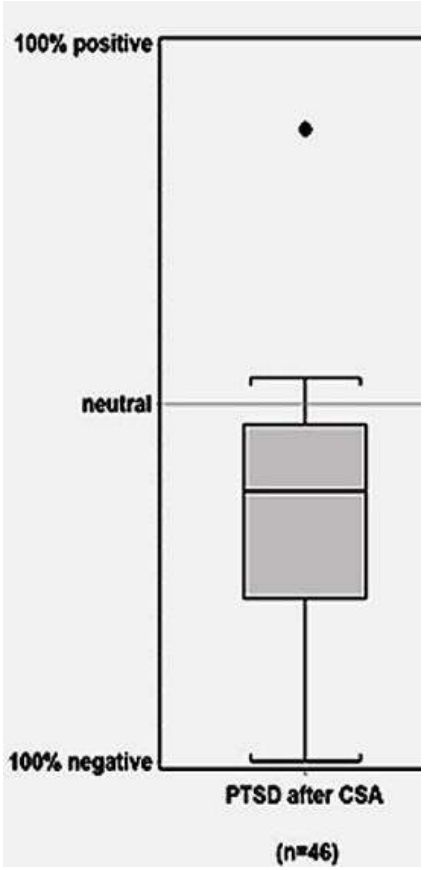

Mean SBA-score:
0.06±0.43, p=0.42



# PTSD after Childhood Sexual Abuse (CSA)



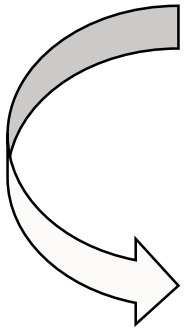

Mean SBA-score:
-0.24±0.40, p<0.001



# Body Self Evaluation: Interim Conclusion

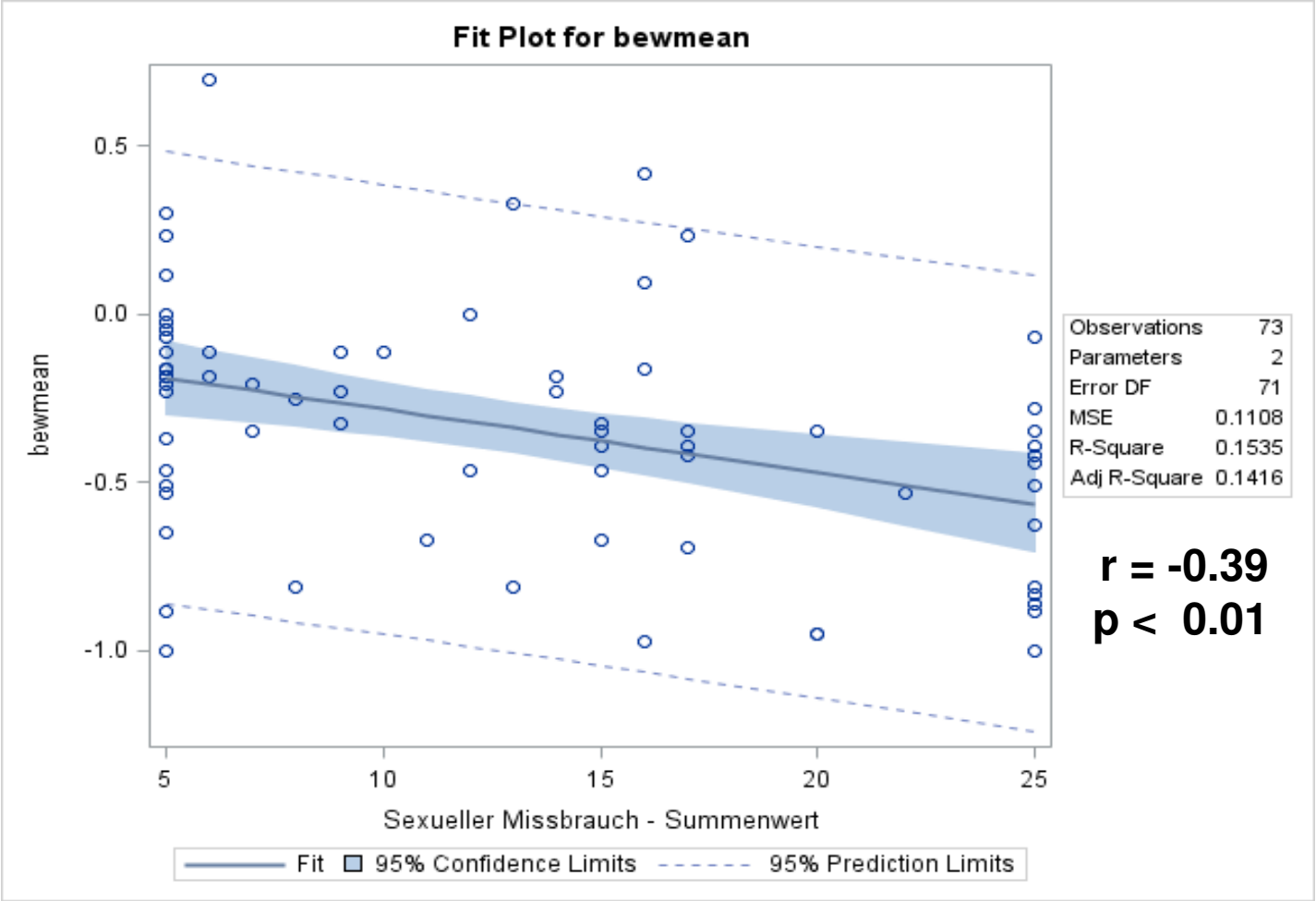
1) On average, BPD patients showed a highly negative body self-evaluation

2) Negative body self-evaluation was also seen in the other group affected by CSA (i.e. PTSD)



**Is the negative body self-evaluation in BPD related to CSA?**

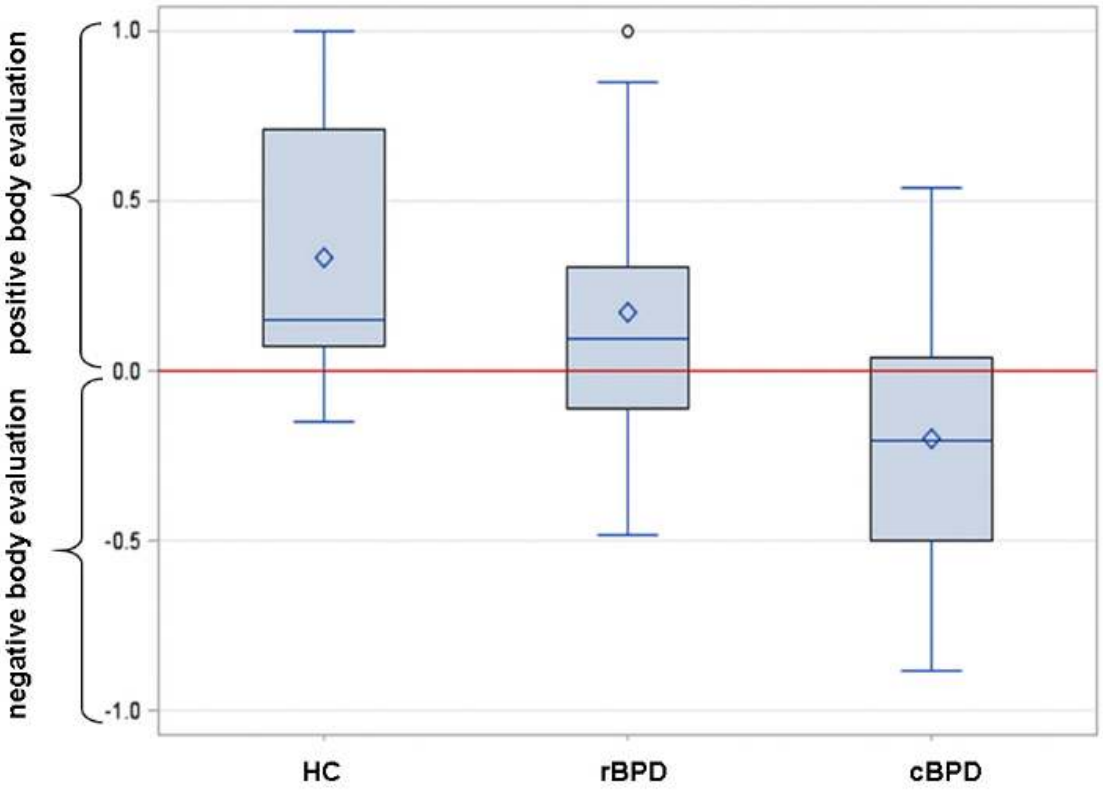
# BPD Patients: Body Self-Evaluation and CSA




In BPD patients CSA was related to negative body self-evaluation

# Body Self-Evaluation: What about remitted BPD-Pat‘s?

Three groups: HC (n=20), remitted BPD (n=22), current BPD (n=26)



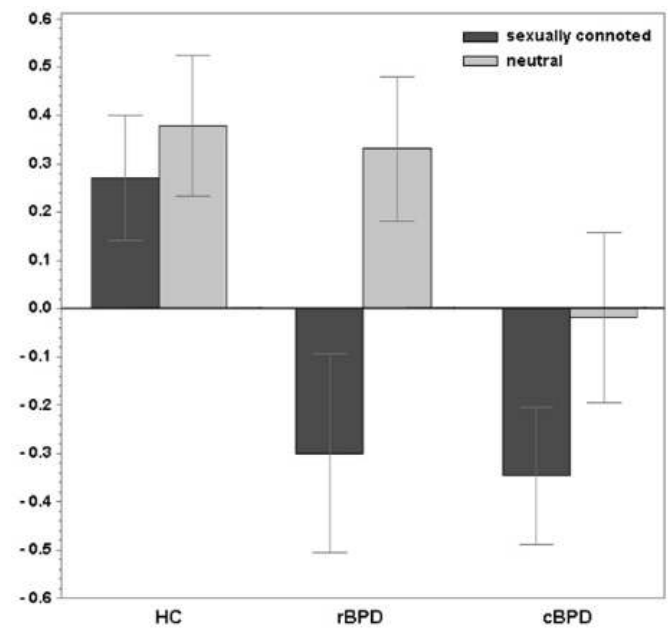

***Overall evaluation of the own body:***

<u>HC:</u>
clearly positive

<u>rBPD:</u>
not significant

<u>cBPD:</u>
clearly negative

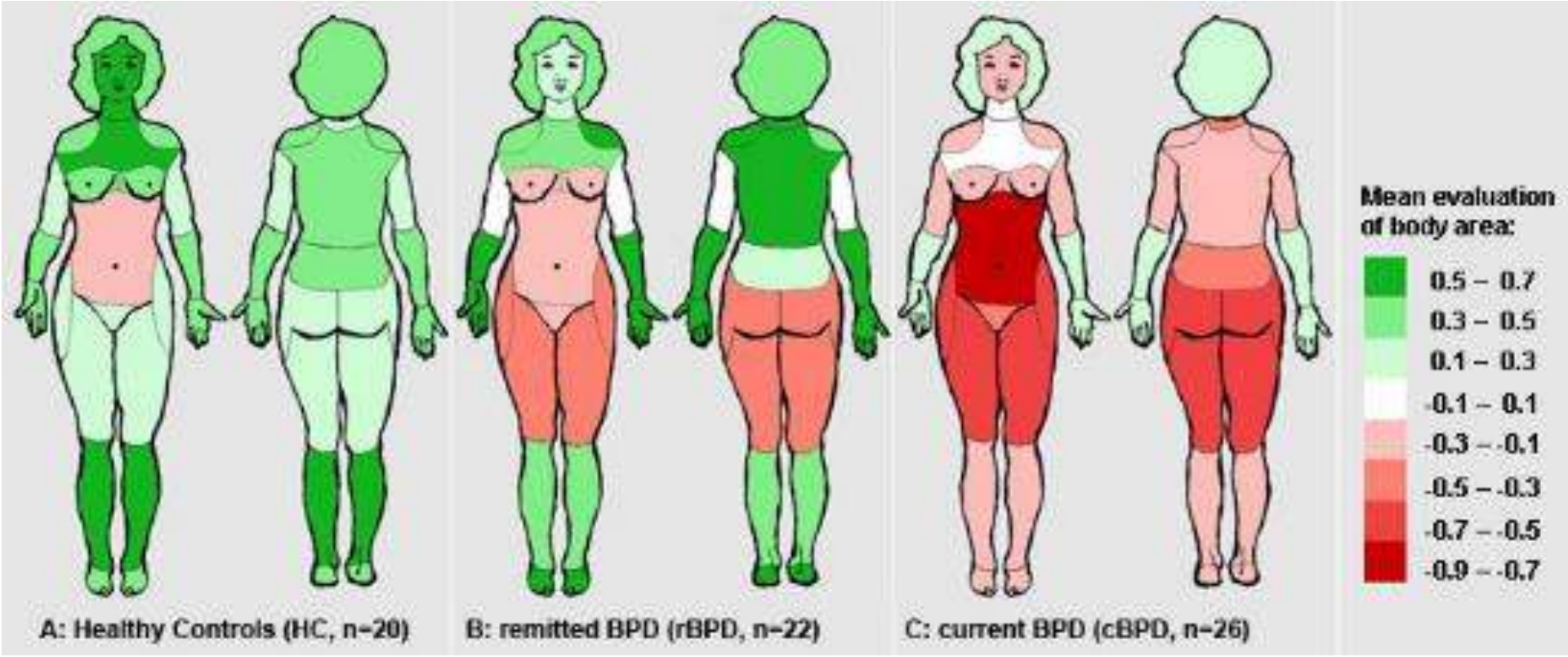
*Kleindienst et al. 2014*




With respect to neutral (=not sexually connoted) areas remitted BPD resembled HC participants

With respect to sexually connoted areas remitted BPD resembled BPD patients currently fulfilling the diagnostic criteria

*Kleindienst et al. 2014*



# Summary for Section 3

Ultimately, DBT is about supporting the patients to **build a life worth living**

- many ways to do that (DBT stages of treatment, DBT ACES, …)
- considering the patients‘ feedback and own formulations the relationship to the own body is not sufficiently addressed

This view is supported when **body maps** are used for evaluation

- **BPD patients generally dislike their own body**
- even after they have **remitted** they still **dislike sexually connoted areas**
- … herby highlighting the devasting effects of CSA

→ We need to evaluate and possibly improve extant programs.

→ I‘d be interested in hearing about approaches in Sweden.

# Overview

1) What has been achieved in the treatment of BPD?

2) Starting points for improving treatment efficacy
   - Model of BPD / CPTSD

   2.1) Applied basic research: Dissociation
   2.2) Applied basic research: NSSI
   2.3) Neuro-biologically informed approach: Neurofeedback

3) Supporting the patient in building a life worth living
   3.1) patients‘ perspective / feedback
   3.2) positive body image

4) Deficits in current therapies of BPD
   4.1) Excess mortality
   4.2) Somatic comorbidities
   4.3) Psychiatric comorbidities

# Excess Mortality in BPD

Well established that a diagnosis of BPD goes along with a significantly increased risk of suicide

**Current Meta-analytic evidence**

| Author | Completed Suicide | Years of follow-up | Studies |
|---|---|---|---|
| Álvarez-Tomás et al., 2019 | 2.4% (Range 0-8%) | 5-14 years | 10 |
| Pompilii et al., 2009 | 8% (Range 2-17%) | 3-27 years | 8 |

However, other causes of excess mortality in BPD patients are even more prevalent.

*Schneider et al. 2019*

# ALL-CAUSE MORTALITY OF HOSPITAL-TREATED BORDERLINE PERSONALITY DISORDER: A NATIONWIDE COHORT STUDY

Jesper Nørgaard Kjær, MD, Robert Biskin, MDCM, Claus Vestergaard, MSc, and Povl Munk-Jørgensen, MD, DrMSc

- Data from Danish nationwide registers of Causes of Death and of Psychiatric Disorders
- N=10,545 with a first-ever diagnosis of BPD (main diagoses) established during residential or outpatient treatment
- Followed up for ∅ 8 years
- Mortality rates were compared with the general population matched for age and sex

→ Standardized Mortality Ratios (SMRs) were calculated for the observation period from 1995-2011

# Standardized Mortality Ratio in BPD

## Compared to the General Danish Population

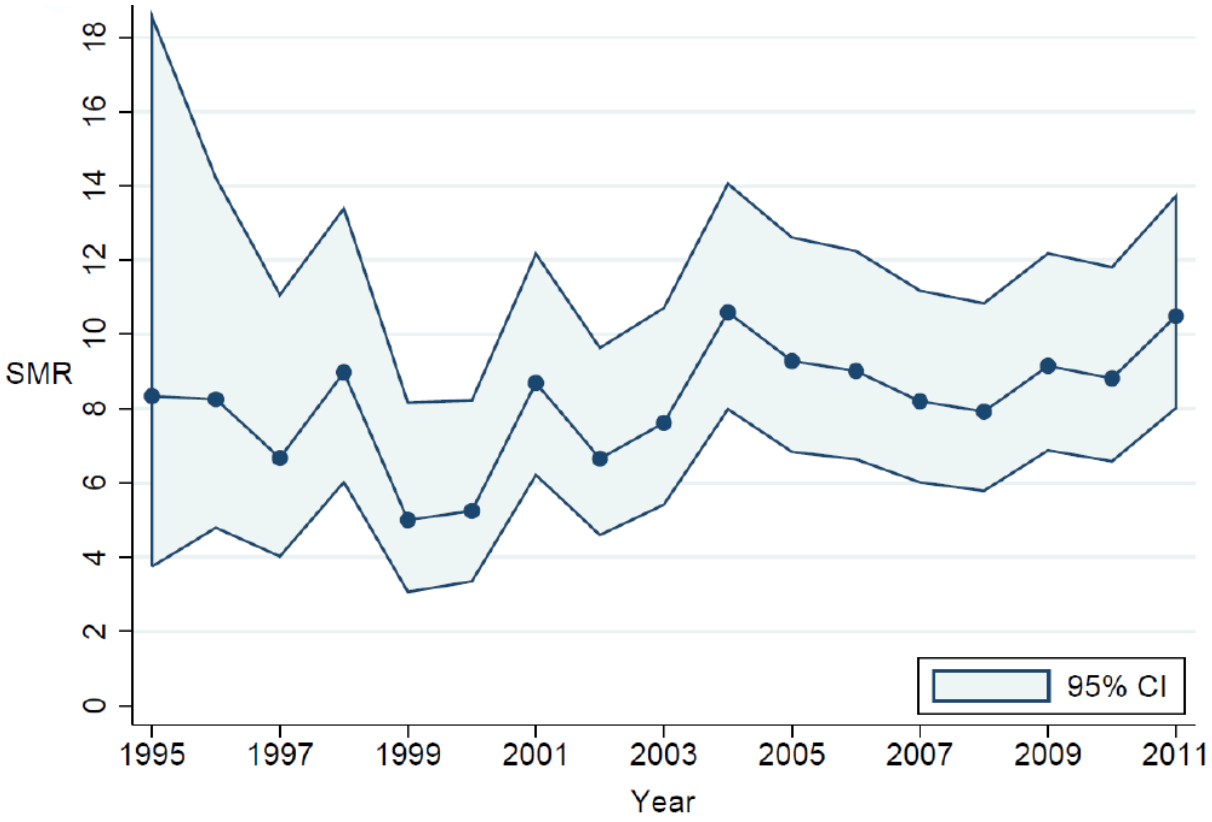



FIGURE 1. Standardized mortality ratio of patients with borderline personality disorder compared with the general Danish population and adjusted for age and sex.

→ Standardized Mortality Ratios (SMRs) of about 8 (!)

# Causes of Death in BPD by Sex and Age

## Compared to the General Danish Population

**TABLE 2. Causes of Death for the BPD Cohort, Mortality Rate per 10,000 Person Years [95% CI]**

| | Natural | Suicide | Accident | Violence or homicide | Unknown |
|---|---|---|---|---|---|
| Female | 27.91 [24.30, 32.06] | 14.67 [12.10, 17.79] | 7.34 [5.59, 9.63] | 1.13 [0.56, 2.26] | 3.25 [2.16, 4.88] |
| Male | 57.60 [46.18, 71.84] | 26.96 [19.42, 37.42] | 14.24 [9.08, 22.32] | 6.75 [3.51, 12.98] | 11.99 [7.34, 19.59] |
| 15-19 | 1.71 [0.24, 12.12] | 6.82 [2.56, 18.20] | 1.71 [0.24, 12.11] | 1.71 [0.24, 12.12] | 0.00 - |
| 20-29 | 5.82 [3.62, 9.37] | 12.66 [9.17, 17.49] | 4.79 [2.84, 8.09] | 2.40 [1.14, 5.03] | 1.37 [0.51, 3.65] |
| 30-39 | 15.35 [11.26, 20.92] | 16.88 [12.56, 22.70] | 11.52 [8.05, 16.47] | 2.30 [1.03, 5.13] | 4.61 [2.62, 8.11] |
| 40-49 | 50.46 [40.39, 63.04] | 25.59 [18.68, 35.05] | 13.79 [8.99, 21.14] | 0.66 [0.09, 4.66] | 9.19 [5.45, 15.52] |
| 50-59 | 128.45 [103.28, 159.76] | 20.98 [12.17, 36.16] | 4.84 [1.56, 15.05] | 3.23 [0.81, 12.91] | 12.92 [6.46, 25.82] |
| 60-69 | 326.83 [246.10, 434.02] | 20.73 [6.69, 64.24] | 13.82 [3.44, 55.58] | 0.00 — | 6.91 [0.97, 49.13] |
| +70 | 547.86 [316.91, 947.11] | 0.00 — | 0.00 — | 0.00 — | 0.00 — |

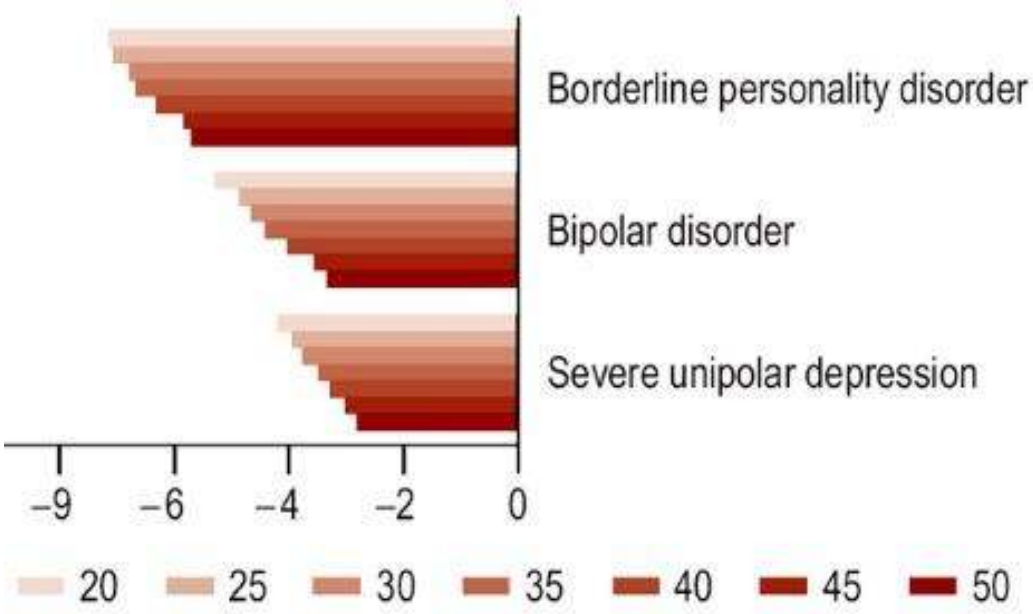
- Largely unknown how these „natural“ causes of death are related BPD
- Some of these „natural“ causes are related to BPD / CA

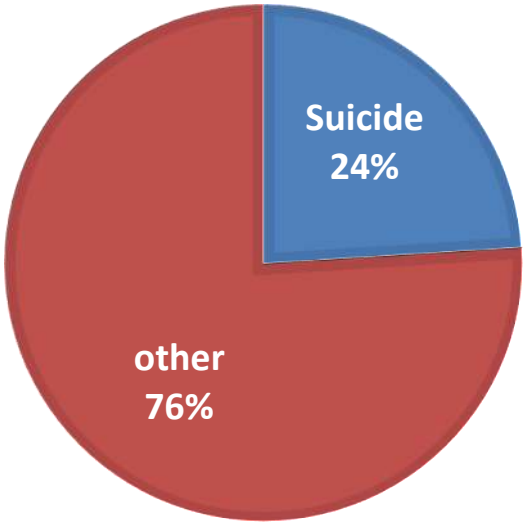
*Kjaer et al. 2020*

# Years of Life Lost by Age

## Compared to the General German Population

- Mortality data based on German health insurance data (N=15,590,107).




- Diagnosis of BPD is related with a loss of life between 5.1 and 7.1 years
- I.e. even more than in major affective disorders
- The authors estimate that other causes of death than suicide account for 76% of the observed excess mortality.

*Schneider et al. 2019*

# Somatic Comorbidities in BPD

## Compared to the General German Population (controlled for age and sex)

| | | Borderline personality disorder | | Psychotic disorders | | Bipolar disorder | | Severe unipolar depression | |
|---|---|---|---|---|---|---|---|---|---|
| **Medical morbidity / risk factor (base rate, i.e., prevalence in whole population)** | **ICD-10 code** | **OR*[2]** | **(95% CI)** | **OR*[2]** | **(95% CI)** | **OR*[2]** | **(95% CI)** | **OR** | **95-%-KI** |
| Hepatitis, human immunodeficiency virus (0.675%) | B15–B24 | **4.28** | **[4.15; 4.40]** | **2.39** | **[2.35; 2.44]** | **1.91** | **[1.84; 1.99]** | **2.08** | **[2.05; 2.12]** |
| MN of female genital organs (0.482%) | C51–C58 | **1.70** | **[1.61; 1.80]** | 1.08 | [1.05; 1.11] | 1.13 | [1.06; 1.19] | 1.34 | [1.32; 1.37] |
| Endocrine, nutritional and metabolic diseases (48.590%) | E00–E90 | **1.70** | **[1.69; 1.72]** | 1.42 | **[1.42; 1.43]** | **1.61** | **[1.59; 1.63]** | **1.75** | **[1.74; 1.76]** |
| Diabetes mellitus (12.801%) | E10–E14 | **1.85** | **[1.82; 1.88]** | **1.61** | [1.60; 1.62] | 1.27 | [1.25; 1.28] | 1.41 | [1.40; 1.41] |
| Obesity (12.442%) | E66 | **2.08** | **[2.06; 2.10]** | **1.60** | **[1.59; 1.61]** | **1.45** | **[1.43; 1.47]** | **1.53** | **[1.53; 1.54]** |
| Organic mental disorders and dementias (4.063%) | F0, G30–G31 | **4.60** | **[4.50; 4.71]** | **8.43** | **[8.37; 8.49]** | **3.85** | **[3.79; 3.92]** | **3.09** | **[3.07; 3.11]** |
| Mental and behavioral disorders due to alcohol (2.239%) | F10 | **12.23** | **[12.06; 12.40]** | **4.25** | **[4.22; 4.29]** | **4.10** | **[4.03; 4.17]** | **3.18** | **[3.15; 3.20]** |
| Mental and behavioral disorders due to psychotropic substances (except alcohol) (6.937%) | F11–F19 | **5.28** | **[5.22; 5.33]** | **3.02** | **[3.00; 3.03]** | **2.27** | **[2.24; 2.30]** | **2.18** | **[2.17; 2.20]** |

- Might partially relate to dysfunctional coping in BPD
- Might partially relate to unsafe sexual behaviors in BPD

We are just beginning to understand the mechanisms

RESEARCH ARTICLE Op

# Childhood maltreatment as a risk factor for cancer: findings from a population-based survey of Canadian adults

Wendy E. Hovdestad*, Margot Shields, Amanda Shaw and Lil Tonmyr

N=20,000 from the Canadian Community Health Survey

| Women | % reporting cancer (95% CI) | Odds ratios controlling for age | Odds ratios controlling for age, and other socio-demographic factors |
|---|---|---|---|
| No abuse (reference) | | Odds (95% CI) | Odds (95% CI) |
| 1 type of abuse | 8.3 ( 6.7, 9.8) | 1.3 * (1.0, 1.7) | 1.2 (1.0, 1.6) |
| 2 types of abuse | 10.5 * ( 7.5, 13.6) | 2.0 ** (1.4, 2.8) | 1.8 ** (1.2, 2.5) |
| 3 types of abuse | 13.9 * ( 8.5, 19.3) | 2.7 ** (1.6, 4.5) | 2.3 ** (1.4, 3.7) |

Source: Statistics Canada, Canadian Community Health Survey
*CPA* Childhood physical abuse, *CSA* Childhood sexual abuse, *CEIPV* Childhood exposure to intimate partner violence

Risk of cancer in women (not in men) increased with the number of childhood adversities

*Hovestad et al. 2020*

# The pediatric buccal epigenetic clock identifies significant ageing acceleration in children with internalizing disorder and maltreatment exposure

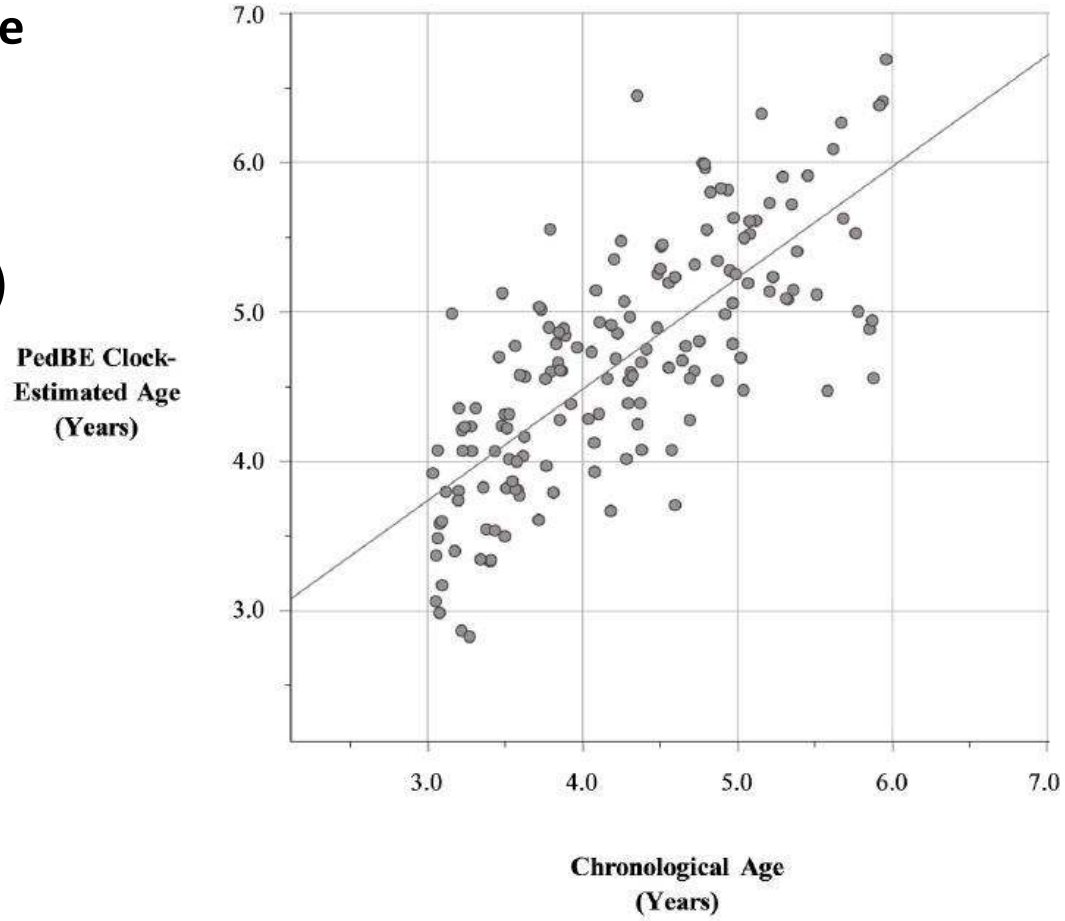
Felix Dammering [a], Jade Martins [b], Katja Dittrich [c], Darina Czamara [b], Monika Rex-Haffner [b], Judith Overfeld [a], Karin de Punder [a], Claudia Buss [a,d], Sonja Entringer [a,d], Sibylle M. Winter [c], Elisabeth B. Binder [b], Christine Heim [a,e,*]

- PedBE: **marker of epigenetic age**
- maltreatment categories
  (SA, PA, EA, … neglect)

N=158 children (73 girls, 85 boys)
Mean age: 4.25 years

1) epigenetic age by
   chronological age

2) is epigenetic age accelerated
   by abuse/neglect?



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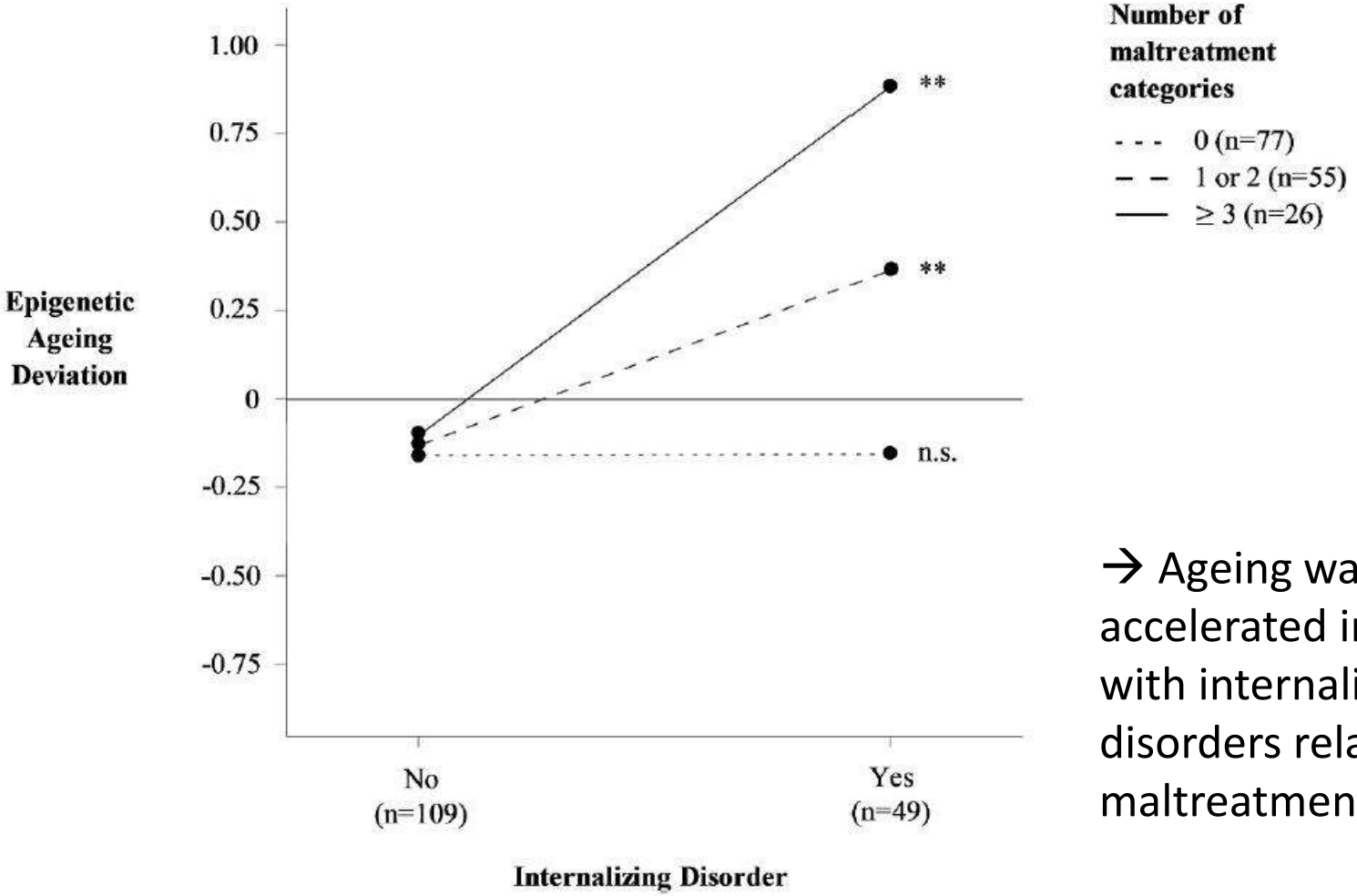



→ Ageing was accelerated in children with internalizing disorders related to maltreatment

# Summary for Sections 4.1 - 4.2

- The diagnosis of BPD is related to a loss of about 5-7 years of life
- About 25% of this loss of life are related to completed suicide
- We are just beginning to understand other (e.g., somatic) causes for excess mortality in BPD

# Overview

1) What has been achieved in the treatment of BPD?

2) Starting points for improving treatment efficacy
   - Model of BPD / CPTSD

   2.1) Applied basic research: Dissociation
   2.2) Applied basic research: NSSI
   2.3) Neuro-biologically informed approach: Neurofeedback

3) Supporting the patient in building a life worth living
   3.1) patients‘ perspective / feedback
   3.2) positive body image

4) Deficits in current therapies of BPD
   4.1) Excess mortality
   4.2) Somatic comorbidities
   **4.3) Psychiatric comorbidities**

# Why focus on the Subgroup of BPD+PTSD?

- **Prevalence:** In clinical samples of BPD the percentage of patients with a dual diagnosis of BPD+PTSD is about 40-80%
  *(Cackowski et al 2016, Harned et al 2010, Sack et al 2013, Zanarini et al 1998)*

- **Relevance:** The dual diagnosis of BPD+PTSD is **prognostically unfavorable**
  - in naturalistic studies *(Marshall-Berenz et al 2011, Wedig et al 2012)*
  - in controlled studies *(DBT: Harned et al 2010,*
    *MBT, DBT: Barnicot et al 2018, CBT for PTSD: McDonagh et al 2005)*
  - there is a lack of treatments with proven simultanous efficacy against BPD and PTSD

→ At least half of treatment seaking patients with BPD present with a dual diagnosis of BPD+PTSD
→ These patients need a treatment addressing both conditions

# Previous Approaches for treating BPD+PTSD

**Standard DBT** *(Harned et al, 2008)*

| | Full remission DBT (%) |
|---|---|
| MDD ($n$ = 59) | 67.6 |
| Panic disorder ($n$ = 32) | 47.4 |
| PTSD ($n$ = 40) | 34.8 |
| SDD ($n$ = 17) | 87.5 |
| ED ($n$ = 15) | 63.6 |

- relatively low when e.g., compared to the results from a meta-analysis reporting a remission for PTSD of 56%
  *(Bradley et al. 2005)*

→ standard DBT may not be sufficient for treating PTSD

# Previous Approaches for treating BPD+PTSD, ctd‘

**DBT + DBT-PE:**

- Start with **DBT** for treating BPD… then treat PTSD with
- **Prolonged Exposure (PE)** if sufficient control over dysfunctional behaviors has been achieved *(Harned et al 2010, 2012, 2014)*

Behaviour Research and Therapy 55 (2014) 7–17

Contents lists available at ScienceDirect

Behaviour Research and Therapy

journal homepage: www.elsevier.com/locate/brat


A pilot randomized controlled trial of Dialectical Behavior Therapy with and without the Dialectical Behavior Therapy Prolonged Exposure protocol for suicidal and self-injuring women with borderline personality disorder and PTSD

Melanie S. Harned*, Kathryn E. Korslund, Marsha M. Linehan

# Previous Approaches for treating BPD+PTSD, ctd‘

**DBT + DBT PE vs standard DBT: Results** *(Harned et al 2014)*

- medium to large pre-post effect sizes (PTSD, suicide attempts, NSSI, dissociation)
- 47.1% (8/17) of the patients did not achieve sufficient stability to enter the DBT PE phase or dropped out after they did

**Table 6**
Results of mixed-effects models.

| | Main effects | | | Interactions |
|---|---|---|---|---|
| | Time | Condition | Completer | Time × condition |
| PTSD[a] | $4.5_{3,42}$** | $0.4_{1,22}$ | $0.5_{1,21}$ | $0.3_{3,42}$ |
| Dissociation[a] | $2.8_{3,41}$* | $0.5_{1,20}$ | $0.3_{1,20}$ | $0.5_{3,41}$ |
| Trauma-related guilt cognitions | $0.0_{1,19}$ | $0.4_{1,87}$ | $9.0_{1,87}$** | $1.5_{1,19}$ |
| Shame | $21.5_{1,29}$*** | $0.1_{1,92}$ | $2.0_{1,92}$ | $0.0_{1,29}$ |
| Anxiety | $16.5_{1,22}$** | $0.7_{1,22}$ | $0.1_{1,22}$ | $0.6_{1,22}$ |
| Depression | $11.9_{1,28}$** | $2.5_{1,93}$ | $3.2_{1,93}$ | $0.0_{1,28}$ |
| Global severity | $17.9_{1,16}$** | $0.4_{1,23}$ | $0.2_{1,23}$ | $0.6_{1,16}$ |

- DBT + DBT PE was not statistically superior to DBT

→ promising approach, but the results are not yet conclusive

# Previous Approaches for treating BPD+PTSD, ctd‘

**NET** (Narrative Exposure Therapy) **based approaches**
*(Schauer et al 2011, Steuwe et al 2016)*

- Promising, but evidence is based on small pilot studies and not yet conclusive

**EMDR** (Eye Movement Desensitization and Reprocessing) **based approaches**
*(Slotema et al 2019)*

- Promising, but evidence is based on small pilot studies and not yet conclusive

→ Results show potential for both NET and EMDR in the treatment of BPD+PTSD when combined with treatment modules addressing BPD
→ However, these studies were small, lacked control groups, and did not assess overall severity of BPD

# DBT-PTSD vs CPT

## in Participants with a Dual Diagnosis of BPD+PTSD (n=93)

Inclusion criteria:

- Women, 18-65 years
- **PTSD** related to sexual/physical CA
- **≥ 5 diagnostic criteria of BPD** incl. criterion 6 (affective instability)

Exclusion criteria:

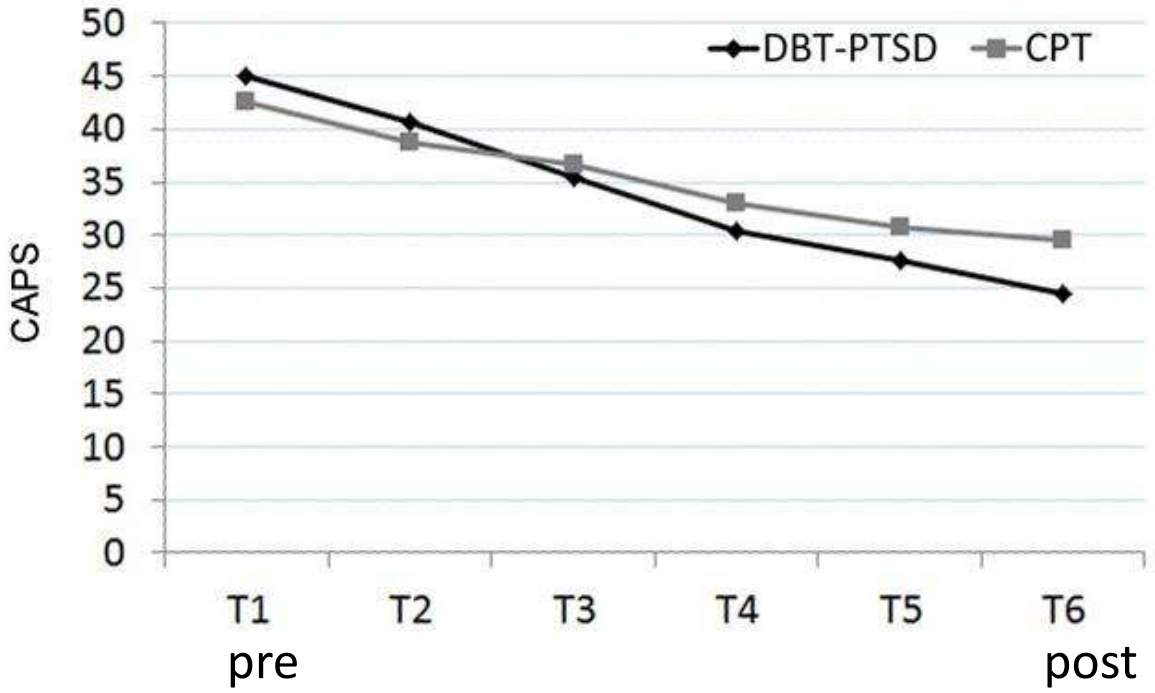
- Lifetime diagnosis of schizophrenia, bipolar I disorder, or mental retardation
- Severe psychopathology requiring immediate treatment (e.g., acute alcohol withdrawal syndrome, or BMI<16.5)
- Life threatening suicide attempts (very high medical risk to die) within the last 2 months

What about patients with ongoing self-harm or high risk behaviors?

→ No exclusion criterion. These patients were accepted for the study

# Primary Outcome 1: CAPS-Score

## Intent To Treat (ITT) after Multiple Imputation (MI), PTSD+BPD (n=93)



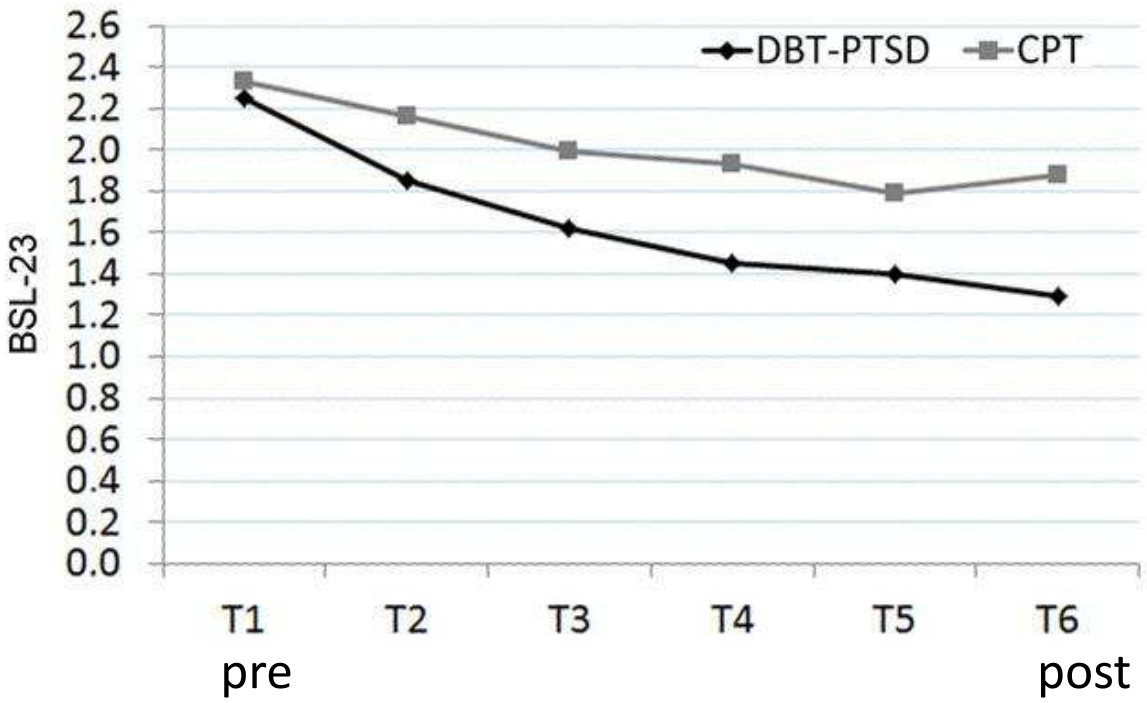

| Parameter | Estimate | Std-Error | Pr > \|t\| |
|---|---|---|---|
| time | -3.3001 | 1.0340 | <.0001 |
| group | -0. 2957 | 2.2316 | 0.8484 |
| time*group | 1.4020 | 0.6397 | 0.0310 |

Decline in the CAPS over time

… more pronounced under DBT-PTSD

# Primary Outcome 2: Symptoms of BPD (BSL-23)

## Intent To Treat (ITT) after Multiple Imputation (MI), PTSD+BPD (n=93)




| Parameter | Estimate | Std-Error | Pr > \|t\| |
|---|---|---|---|
| time | -0.2333 | 0.0515 | <.0001 |
| group | -0.1068 | 0.1368 | 0.4370 |
| time*group | 0.0808 | 0.0318 | 0.0128 |

Decline in the BSL-23 over time

... more pronounced under DBT-PTSD

# Suicides and Suicide Attempts

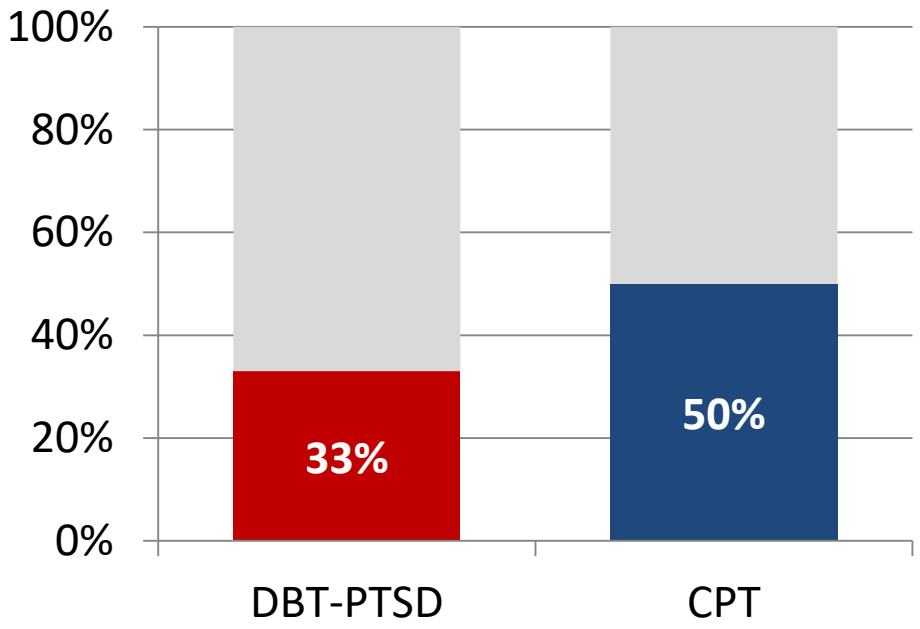
**(Available data for the Observation Period, n=93)**

During the observation period of 15 months there were

- 0 suicides
- 1 suicice attempts (CPT: 1; DBT-PTSD: 0)

# Drop-out Rates

## Participants with a Dual Diagnosis of BPD+PTSD (n=93)

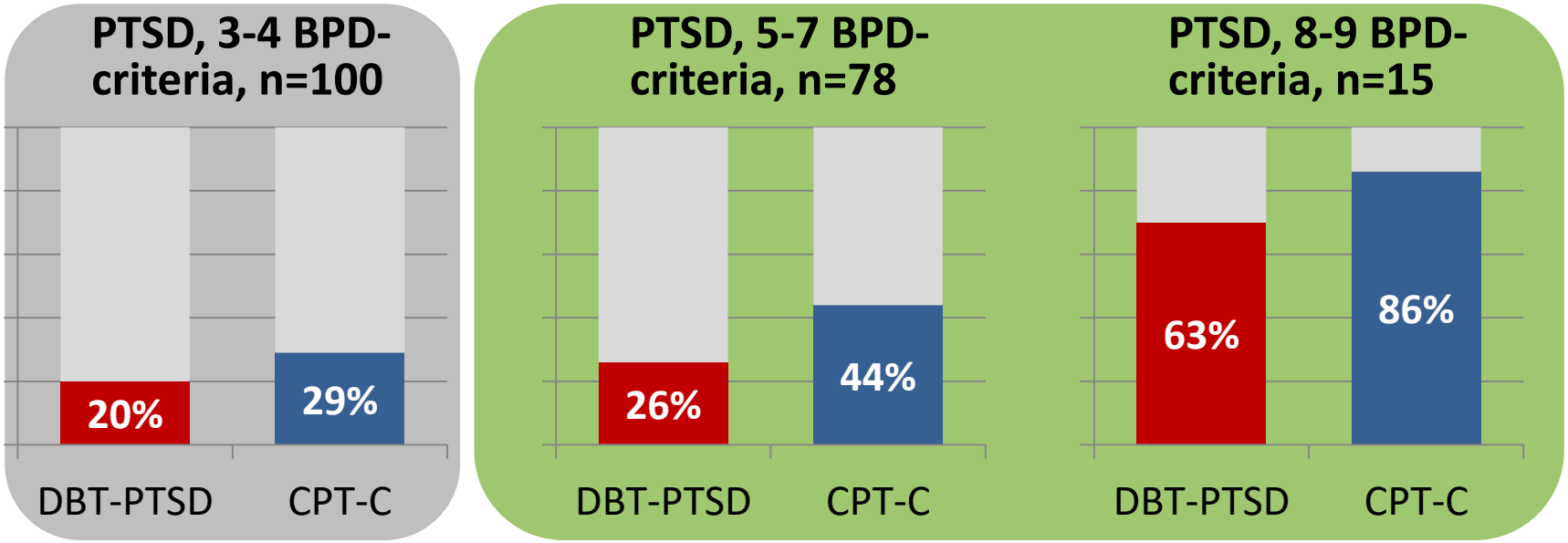



DBT-PTSD vs CPT: p=0.089

→ Drop-out rates in patients with BPD+PTSD need to be further addressed

# Drop-out Rates

## Depending on the number of BPD-Criteria (n=193)




| Parameter | Estimate | SE | ChiSq | Pr>ChiSq |
|---|---|---|---|---|
| Intercept | -2.7191 | 0.7655 | 12.616 | 0.0004 |
| CAPS_baseline | 0.0140 | 0.0175 | 0.6388 | 0.4242 |
| BPD_criteria | 0.2853 | 0.1025 | 7.7441 | 0.0054 |

Specific effect of BPD
(not just symptom severity)

# Drop-out Rates

## Depending on the number of BPD-Criteria (n=193)

Smartphone-Study for Predicting Dropout in BPD
(in Cooperation with TU Darmstadt)

Basic Idea: AI-based analysis of speech-samples recorded in response to brief input statements

# Summary of Section 4.3

- **About 50%** of treatment seeking BPD patients simultaneously require treatment for co-occurring PTSD

- In our RCT comparing **DBT-PTSD and CPT** in patients with a dual diagnosis we observed **change in both BPD- and PTSD symptomatology:**
  - medium to large effects within the CPT-group
  - large effects within the DBT-PTSD group
  - medium between-group effect ($d=0.6$, $p<0.01$)

→ At least DBT-PTSD is efficacious for patients with a dual diagnosis of BPD+PTSD.

- **Drop-out rates:**
  - high in both treatment groups, albeit somewhat lower in the DBT-PTSD (vs CPT) group (33% vs 50%, $p=0.089$)

  → the high drop-out rates are a limitation to be further addressed

---> Thank you very much for your attention <---

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