Effectiveness of an Emotional Working Memory Training in Borderline Personality Disorder: A Proof-of-Principle Study

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Borderline personality disorder (BPD) is a severe mental disorder, characterized by emotion dysregulation (affective hyper-sensitivity and instability), identity disturbance, interpersonal difficulties, and impulsivity [1, 2]. Despite successful treatment, only a minority of patients with BPD achieve good psycho-social integration, and emotional problems often persist [3, 4].

The ability to deploy working memory (WM) in emotionally stressful contexts (emotional WM, eWM) plays a critical role in affective-cognitive control and self-regulation [5, 6]. Emotional distraction was found to interfere with WM in BPD [7, 8]. Neuroimaging research suggests that eWM relies to a great extent on a fronto-parietal brain network which is fundamentally involved in emotion regulation (ER) [5, 6]. A computer-assisted eWM training (eWMt) (affective dual-n-back-task), developed by Schweizer and colleagues, previously showed beneficial effects on ER in healthy adults [9] and adolescents with post-traumatic stress disorder [10]. Since this training can be easily applied in different settings and made widely available to the broader population via internet, eWMt might be a cost-effective online intervention, augmenting ER in BPD.

This proof-of-principle study aimed to investigate the effectiveness of an adapted eWMt in BPD. We expected improvements in ER, measured by a cognitive reappraisal task, after eWMt compared to a placebo training [8]. We hypothesized that improvements in ER were predicted by improvements in eWM (performance on an adapted Sternberg task).

For this randomized controlled trial, 68 participants were recruited at the Department of Psychosomatic Medicine and Psychotherapy, Central Institute of Mental Health (CIMH), Mannheim, Germany, through the outpatient treatment unit and existing databases [2]. Interested participants were invited for extensive screening by trained clinical psychologists. Inclusion criteria were female gender, age between 18 and 55 years, and a DSM-IV-TR diagnosis of BPD. We excluded patients with current hospitalization, acute suicidal crisis, lifetime diagnosis of schizophrenia, bipolar I disorder, organic brain diseases, severe neurological diseases, change of psychotropic medication during training, and those living ≥150 km outside of Mannheim. From those, who had been randomly allocated to the two training conditions, 18 participants (eWM: $n = 12$, 32%; cognitive feature match [CFM]: $n = 6$, 19%) did not start or dropped out of the training and 5 participants were excluded due to changes in medication (complete participant flow: online suppl. Fig. 1; for all online suppl. material, see www.karger.com/doi/10.1159/000504454). The final two groups (eWM: $n = 22$; CFM: $n = 23$) did not differ significantly in age, intelligence, education, comorbidities, and medication status (online suppl. Table 1).

In the adapted eWMt, participants first alternately trained an n-back task with visual distractor stimuli (negative vs. neutral facial) and auditory distractors (neutral vs. negative vs. positive words), respectively, before starting the affective dual n-back training. Depending on the achieved n-back level, daily training sessions lasted between 20 and 30 min, consisting of 20 blocks (for detailed description, see online suppl. Material). The placebo training was a CFM task (CFMt) with minimal WM demands, without emotional material. Both groups trained on their personal computer for a 28-day period (min 16 days, max 20 days). Before the training (T1) and within 1 week after completion (T2), participants performed two experimental laboratory tasks at the CIMH: (1) a cognitive reappraisal task measuring ER, and (2) an adapted emotional Sternberg task measuring eWM (see online suppl. Material).

Logins and training duration were documented on a local server of the Medical Research Council Cognition and Brain Sciences Unit, Cambridge, UK, ensuring that both groups trained for a similar duration (eWMt: $17,558 \pm 10,035$, CFMt: $18,947 \pm 7,542$; $t_{(48)} = 0.53$, $p = 0.601$).

Both groups significantly improved their training-related performance (eWMt: 3.82 ± 0.76 vs. 5.14 ± 1.08, $t_{(21)} = 6.54$, $p < 0.0001$, $d = 1.34$; CFMt: $1,556.11 \pm 1,200.59$ vs. $4,218.21 \pm 2,951.99$, $t_{(18)} = 3.47$, $p = 0.003$, $d = 1.18$)[1]. Total training duration was positively

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[1] Due to different training conditions, these training scores were not directly comparable.

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Table 1. Results of the 2 × 2 × 2 rm-ANCOVA for the ER task

Ratings for negative pictures	F	$df\ 1, 2$	p	η_p^2
Group (training)	0.55	1, 39	0.463	0.01
Time	0.06	1, 39	0.805	0.02
Instruction	10.30	1, 39	0.003	0.21
Group × Time	1.34	1, 39	0.259	0.03
Group × Instruction	1.79	1, 39	0.189	0.04
Time × Instruction	2.32	1, 39	0.136	0.06
Group × Time × Instruction	5.15	1, 39	0.029	0.12

rm-ANCOVA, repeated measure analysis of covariance; ER, emotional regulation; BPD, borderline personality disorder. A 2 × 2 × 2 rm-ANCOVA was performed with Group (Emotional Working Memory vs. Placebo training) as between-subject factor and Time (before vs. after training) and Instruction (attend, regulate) as within-subject factors. Due to baseline differences in BPD symptom severity (Borderline Symptom List 23, BSL-23), depressive symptoms (Beck Depression Inventory, BDI), Anxiety (State Trait Anxiety Inventory, STAI), and dissociation (Dissociation Experience Scale, DES) (online suppl. Table 1), these variables were controlled for in the statistical analyses. These covariates had no significant effects (BSL: $F_{(1,39)}$ = 1.68, p = 0.202; BDI: $F_{(1,39)}$ = 0.95, p = 0.337; STAI: $F_{(1,39)}$ = 0.00, p = 0.985; DES: $F_{(1,39)}$ = 0.80, p = 0.378).

correlated to training success in the eWMt group (r = 0.431, p = 0.016, R^2 = 0.190), but not in the CFMt group (r = 0.263, p = 0.262).

Analyses revealed a significant interaction of Group by Time by Instruction on ER (Table 1). The eWMt group showed better down-regulation (compared to passive attendance) of negative emotions at T2 (– 3.33 ± 2.78) versus T1 (– 4.60 ± 2.53) ($t_{(21)}$ = 2.24, p = 0.036, d = 3.04) compared to the CFMt group (T1: – 4.77 ± 2.87, T2: – 4.81 ± 2.51, $t_{(22)}$ = 0.08, p = 0.938).

Increases in eWM performance (reaction times of correct trials) during the adapted Sternberg task predicted improvements in ER (B = –0.01, SE = 0.003, t = 2.22, p = 0.034 [–0.014, –0.001]), while this did not interact with the training group (B = 0.001, SE = 0.006, t = 0.166, p = 0.869 [–0.012, –0.014]).

Our study provides preliminary evidence for future research on the effectiveness of eWMt in BPD. In line with our hypothesis, eWMt led to better ER. Improvements were predicted by enhanced eWM performance (adapted Sternberg task), supporting the idea that enhanced inhibitory control of emotional material might underlie gains in ER. Against our expectation, this relationship was not specific to the training group, raising the question whether ER improvements may also be achievable through cognitive training without emotional distractors. Including corresponding neutral and emotion exposure training conditions in future studies may help elucidating which training components are essential for augmenting ER, keeping personal distress at a minimum. Future research may further use ecological ambulatory monitoring and apps for mobile devices to assess application of eWMt in everyday life compared to "cold" experimental settings. Neuroimaging studies in BPD might shed light on the idea that beneficial transfer effects of eWMt on ER are related to increased engagement of a fron-to-parietal-limbic brain network [5, 6] in line with Schweizer et al. [9].

To our knowledge, our study is the first to evaluate the effectiveness of an adapted eWMt in BPD using a randomized controlled design and well-established experimental paradigms to investigate transfer effects. While results need to be interpreted as preliminary, given the small sample size, findings point to a potentially promising effect of eWMt on ER in BPD. Since some subjects received outpatient treatment, potentially confounding results, future research should clarify the role of concurrent psychotherapy in ER gains and whether there are stable long-term effects.

Considering limited financial resources and treatment places as well as insufficient psychosocial integration after symptom reduction in BPD [3, 4], eWMt has promise as a cost-effective intervention for patients who experience a regular training routine as stabilizing.

Author Contributions
A.K.-U., J.-C.W., S.S., S.L., and M.B. designed the study. S.S. and A.H. designed the original version of the training and provided training material and resources. A.K.-U. and J.-C.W. adapted the training for its current use. J.-C.W. performed pre- and post-assessments, supervised by A.K.-U. and M.B. A.K.-U. designed the structure of the paper and its rationale, including statistical analyses, and wrote the first draft of the paper. S.S., S.L., and M.B. provided in depth feedback throughout each stage of writing. All co-authors provided further feedback that contributed toward the final version of the paper, which has been approved by all authors.

References

1 American Psychiatric Association. APA., Diagnostic and statistical manual of mental disorders: DSM-5. 5. Arlington (VA): American Psychiatric Association. XLIV; 2013. p. 947.
2 Schmahl C, Herpertz SC, Bertsch K, Ende G, Flor H, Kirsch P, et al. Mechanisms of disturbed emotion processing and social interaction in borderline personality disorder: state of knowledge and research agenda of the German Clinical Research Unit. Borderline Personal Disord Emot Dysregul. 2014 Sep;1:12.
3 Gunderson JG, Stout RL, McGlashan TH, Shea MT, Morey LC, Grilo CM, et al. Ten-year course of borderline personality disorder: psychopathology and function from the collaborative longitudinal personality disorders study. Arch Gen Psychiatry. 2011;68(8):827–37.

4 Zeitler ML, Bohus M, Kleindienst N, Knies R, Ostermann M, Schmahl C, et al. How to Assess Recovery in Borderline Personality Disorder: Psychosocial Functioning and Satisfaction With Life in a Sample of Former DBT Study Patients. J Pers Disord. 2018;4:1–19.

5 Koch SB, Mars RB, Toni I, Roelofs K. Emotional control, reappraised. Neurosci Biobehav Rev. 2018;95:528–34.

6 Cohen N, Ochsner KN. From surviving to thriving in the face of threats: the emerging science of emotion regulation training. Curr Opin Behav Sci. 2018 Dec;24:143–55.

7 Krause-Utz A, Oei NY, Niedtfeld I, Bohus M, Spinhoven P, Schmahl C, et al. Influence of emotional distraction on working memory performance in borderline personality disorder. Psychol Med. 2012;42(10): 2181–92.

8 Krause-Utz A, Elzinga BM, Oei NY, Spinhoven P, Bohus M, Schmahl C. Susceptibility to Distraction by Social Cues in Borderline Personality Disorder. Psychopathology. 2014;47(3):148–57.

9 Schweizer S, Grahn J, Hampshire A, Mobbs D, Dalgleish T. Training the Emotional Brain: Improving Affective Control through Emotional Working Memory Training. J Neurosci. 2013;33(12):5301–11.

10 Schweizer S, Samimi Z, Hasani J, Moradi A, Mirdoraghi F, Khaleghi M. Improving cognitive control in adolescents with post-traumatic stress disorder (PTSD). Behav Res Ther. 2017;93:88–94.