

Supplementary Materials for **Specific reduction in cortisol stress reactivity after social but not attention-based mental training**

Veronika Engert, Bethany E. Kok, Ioannis Papassotiriou, George P. Chrousos, Tania Singer

Published 4 October 2017, *Sci. Adv.* **3**, e1700495 (2017)

DOI: 10.1126/sciadv.1700495

The PDF file includes:

- Supplementary Materials and Methods
- fig. S1. Parameter estimates from hierarchical linear models showing effects of study duration on self-reported and cortisol stress reactivity and recovery.
- table S1. Number of participants with available data (and winsorized outliers) per stress marker and measurement time point.
- table S2. Descriptive statistics per group.
- table S3. Mean number (SD) of weekly practice sessions for each mental training exercise per training module.
- table S4. Omnibus F tests in linear mixed models for habituation effects on self-reported and HPA axis stress responses.
- table S5. Coefficients from a linear regression examining improvement in psychoendocrine covariance (association of Δ STAI and Δ cortisol) in each training group relative to the no training group.

Other Supplementary Material for this manuscript includes the following:
(available at advances.sciencemag.org/cgi/content/full/3/10/e1700495/DC1)

- Source data (Excel file)

Supplementary Materials and Methods

Supplementary statistical analysis

Associations of self-reported stress scores. To show that the state scale of the State Trait Anxiety Inventory (STAI, 25) goes beyond merely measuring anxiety, we calculated a linear regression predicting the STAI score from the six subscores (tension-anxiety, depression-dejection, anger-hostility, vigor-activity, fatigue-inertia, confusion-bewilderment) of the Profile of Mood States (POMS, 61) assessed at the peak in subjective stress experience (-5 minutes).

Habituation effect in the retest control group. Throughout the *ReSource* study, participants came to the laboratory for training and testing purposes on a weekly basis. Stress reduction over time may thus originate from participants habituating to the laboratory setting, not the effect of mental training. To detect a potential training-independent habituation effect, participants from the retest control group were tested at different phases of the study. We applied the main model to the cortisol and self-report stress data of only the retest control group using test phase (baseline=T0, test phase 1=T1, test phase 2=T2) instead of group as a level 2 predictor.

Psychoendocrine covariance in younger versus older participants. To explore whether age has an influence on training-induced changes in psychoendocrine covariance, participants were split into two groups based on their age (below/above the mean of 40.68 years) and the linear regression as described in the statistical analysis section was executed in both groups.

Supplementary results

Missing data and outliers. An overview of the available data and winsorized outliers per stress marker and measurement time-point is given in table S1. Missing data are attributable to insufficient saliva volume [cortisol, α -amylase (AA)], technical difficulties with data collection and movement artifacts [heart rate (HR), high frequency heart rate variability (HF-HRV)], inability to draw blood [interleukin-6 (IL-6) and high-sensitive C-reactive protein (hsCRP)] and incompletely filled questionnaires (self-reported stress). In the autonomic and immune models, four respectively three participants had to be excluded because information on the covariate body mass index was not provided.

Association of self-reported stress scores. Confirming that the state scale of the STAI measures facets of distress other than anxiety, a linear regression ($F(6,301)=211.69, P\leq.001, R^2=.81$) showed that next to POMS tension-anxiety ($b=.77, t=18.56, P\leq.001$), the depression-dejection ($b=.10, t=2.34, P=.020$), vigor-activity ($b=-.27, t=-9.19, P\leq.001$) and fatigue-inertia subscores ($b=-.08, t=-2.63, P=.009$) significantly predicted the STAI score, all assessed at -5 minutes in anticipation of the stressor. Anger-hostility ($b=-.01, t=-0.27, P>.70$) and confusion-bewilderment subscores ($b=-.02, t=-0.37, P>.70$) were unassociated with the STAI state scale.

Habituation effect in the retest control group. Regarding a potential habituation effect, linear mixed models revealed no significant differences in the self-reported and cortisol stress responses of retest control participants tested at different test phases (T0, T1 or T2). In fact, contrary to a habituation effect, participants showed marginally higher cortisol stress reactivity

when tested at T1 or T2 rather than T0 (table S4, fig. S1 A+B). Thus, training effects on stress reactivity cannot be attributed to participants habituating to frequent laboratory visits.

Psychoendocrine covariance in younger versus older participants. Consistent with Mendes' idea of weakened mind-body connections with age (30), we see that the training-dependent increase in psychoendocrine covariance is only present in the younger participants. Older participants consistently show null correlations of subjective and cortisol stress reactivity scores (table S5). Future research may wish to further explore the interaction between age and psychoendocrine covariance in mental training research.

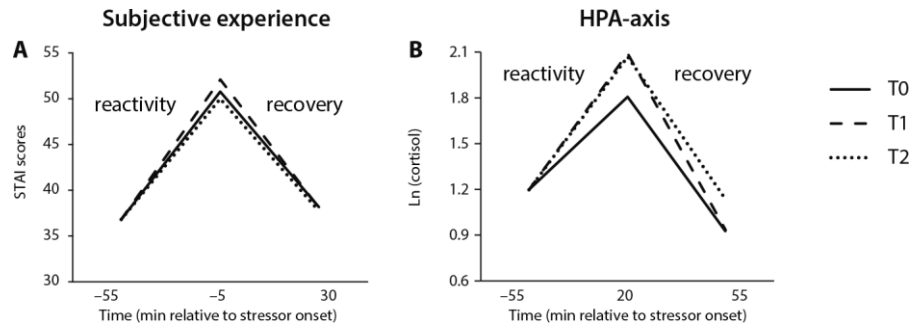


fig. S1. Parameter estimates from hierarchical linear models showing effects of study duration on self-reported and cortisol stress reactivity and recovery. Values at the first measurement time-point are equalized, representing statistical control for baseline scores. Retest control participants tested at baseline (T0), in the first (T1) or the second test phase (T2) did not differ significantly in **(A)** self-reported stress responses as measured by the state scale of the STAI (all P -values $>.10$). **(B)** Hypothalamic-pituitary-adrenal (HPA) axis stress responses as measured by cortisol release were marginally higher at T1 and T2 rather than T0 ($P=.054$). Training effects on stress reactivity cannot be attributed to participants habituating to frequent laboratory visits.

table S1. Number of participants with available data (and winsorized outliers) per stress marker and measurement time point.

	Cortisol	AA	HR	HF-HRV	hsCRP	IL-6	STAI
	Measurement time-point						
BL	312 (1)	308 (3)	267 (3)	263 (2)	291	281 (6)	309 (5)
Peak	310 (1)	304 (3)	271 (1)	271 (4)	290	283 (7)	313
Rec1	310 (1)	305 (2)	263 (1)	263 (2)	283		309 (3)
Rec2	311	304 (2)					312 (4)
Rec3	311 (2)	307 (3)					313 (4)

table S2. Descriptive statistics per group.

	NT	Prs	Aff	Prs/Aff	Prs/Per
	Frequency				
Sex (male/female)					
	56/74	19/27	17/29	20/24	16/31
Hormonal status (no cycle/natural menstrual cycle/hormonal contraceptives)					
	23/36/15	8/17/2	4/19/6	4/14/6	10/15/6
City (Berlin/Leipzig)					
	62/68	23/23	21/25	23/21	23/24
Smokers (yes/no)					
	14/116	7/39	2/44	6/38	8/39
	Mean (SD)				
Age	40.13 (9.06)	40.76 (10.02)	40.22 (9.79)	41.64 (8.63)	41.70 (9.57)
MDI	52.23 (5.71)	52.89 (5.49)	51.54 (5.31)	51.39 (6.83)	51.72 (5.10)
STAI	35.98 (7.09)	35.67 (7.93)	37.28 (8.42)	37.32 (7.76)	36.09 (6.63)
PSS	13.62 (5.96)	13.73 (5.74)	12.98 (6.16)	14.89 (5.32)	13.09 (5.48)

Aff: Affect; MDI: Major Depression Inventory (62); NT: no training; Per: Perspective; Prs: Presence; PSS: Perceived Stress Scale.

table S3. Mean number (SD) of weekly practice sessions for each mental training exercise per training module.

	Presence		Affect		Perspective	
	BM	Body Scan	LKM	Dyad	OTM	Dyad
Practice sessions/week	4.71 (1.23)	4.36 (1.22)	3.78 (1.38)	3.59 (1.10)	3.63 (1.23)	3.24 (1.15)

BM: Breathing Meditation; LKM: Loving-kindness Meditation; OTM: Observing-thoughts Meditation.

table S4. Omnibus *F* tests in linear mixed models for habituation effects on self-reported and HPA axis stress responses.

	STAI		Cortisol	
Fixed effects				
	<i>F</i> (<i>df</i>)	<i>P</i>	<i>F</i> (<i>df</i>)	<i>P</i>
Intercept (peak)				
Intercept	3789.60 (197)	≤.001	797.82 (122)	≤.001
Test phase	0.44 (197)	>.600	2.99 (122)	.054
Baseline	51.60 (198)	≤.001	12.66 (122)	≤.001
Hormones/Sex	3.52 (113)	.063	1.64 (121)	>.100
Age	0.98 (113)	>.300	4.33 (121)	.034
Time of day			2.43 (121)	>.100
Recovery slope				
Intercept	313.06 (200)	≤.001	257.20 (125)	≤.001
Test phase	0.46 (200)	>.600	2.14 (125)	>.100
Baseline	3.44 (200)	.065	0.25 (126)	>.600
Random effects				
	Estimate (<i>SE</i>)		Estimate (<i>SE</i>)	
Subject	28.34 (4.73)		0.33 (0.04)	
Recovery slope	.007 (.005)		≤.001 (≤.001)	

Removing the covariates from a respective model did not change the pattern of significance.

table S5. Coefficients from a linear regression examining improvement in psychoendocrine covariance (association of Δ STAI and Δ cortisol) in each training group relative to the no training group.

	40.68 years and below			Above 40.68 years		
	<i>F</i> (9,137)= 4.61, <i>P</i> ≤.001, <i>R</i> ² =.23			<i>F</i> (9,149)=1.03, <i>P</i> >.40, <i>R</i> ² =.06		
	<i>b</i>	<i>t</i>	<i>P</i>	<i>B</i>	<i>t</i>	<i>p</i>
Δ STAI	.05	0.46	>.600	-.004	-.03	>.900
Presence	-.37	-2.59	.011	-.03	-.16	>.800
Presence/Perspective	-.41	-2.81	.006	-.14	-.75	>.400
Presence/Affect	-.27	-2.39	.018	-.30	-1.81	.073
Affect	-.21	-1.82	.071	-.17	-1.15	>.200
Δ STAI*Presence	.50	3.59	<.001	.08	0.51	>.600
Δ STAI*Presence/Perspective	.34	2.43	.016	.08	0.50	>.600
Δ STAI*Presence/Affect	.11	1.05	>.20	.20	1.35	>.100
Δ STAI*Affect	.18	1.66	.099	.01	0.08	>.900

Δ : baseline-to-peak change.