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How do placebo effects contribute to mindfulness-based analgesia? Probing acute pain effects and interactions using a randomized balanced placebo design.

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Further information and data: Open Science Framework (<https://osf.io/6mgxy/>)

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SUPPLEMENTARY METHODS

Materials and Measures

The following self-report instruments were additionally administered at pre-treatment and post-treatment.

Pain-related Cognitive Processes were measured using the Pain-related Cognitive Processes Questionnaire (PCPQ) [3]. The PCPQ measures cognitive processes across nine subscales: Suppression, Distraction, Enhancement, Dissociation, Reappraisal, Absorption, Rumination, Nonjudgment, and Acceptance; with adequate to good internal consistency ($\alpha \geq 0.70$) [2]. Higher scores (out of 4) on each of the subscales indicate higher involvement of specific cognitive processes.

Depression, Anxiety and Stress were measured using the Depression, Anxiety and Stress Scale short-form (DASS-21) [4]. It has good internal consistency ($\alpha=.88$) [1]. Higher subscale scores (-/21) indicate increasing levels of state depression, anxiety or stress, categorised by severity.

SUPPLEMENTARY RESULTS

Baseline Data

There were no statistically significant differences in the additional baseline outcome measures of pain-related cognitive processes ($F_s < 1.76$, $p_s > 0.14$), depression, anxiety or stress ($F_s < 0.78$, $p_s > 0.54$) across groups (Table S1 and S2).

Pain-related cognitive process outcomes

As shown in Table S2, of the nine pain-related cognitive processes measured, there was a small-to-medium increase in *Reappraisal* ($F(1,147)=4.73$, $p=.031$, $\eta_p^2=.03$) and a small-to-medium decrease in *Rumination* ($F(1,147)=4.04$, $p=.046$, $\eta_p^2=.03$) for any intervention vs no treatment but no effects of treatment, instruction or interaction between treatment and instruction ($F_s > 2.42$, $p_s < .12$). No other effects or interactions were seen for the remaining seven pain-related cognitive processes: *Suppression*, *Distraction*, *Enhancement*, *Dissociation*, *Absorption*, *Non-judgement* or *Acceptance* ($F_s > 3.86$, $p_s < .051$).

Depression, Anxiety and Stress

As shown in Table S2, for anxiety there was an effect of any intervention vs no treatment ($F(1,147)=5.56$, $p=.02$, $\eta_p^2=.04$) but no effects of treatment, instruction nor interaction between treatment and instruction ($F_s > 1.61$, $p_s < .021$). There were no effects of any intervention vs no treatment, treatment, instruction nor interaction between treatment and instruction for either depression ($F_s > 0.50$, $p_s < .48$) or stress ($F_s > 3.28$, $p_s < .07$).

SUPPLEMENTARY REFERENCES

- [1] Crawford JR, Henry JD. The Depression Anxiety Stress Scales (DASS): Normative data and latent structure in a large non-clinical sample. *British Journal of Clinical Psychology* 2003;42:111–131.
- [2] Day MA, Ward LC, Jensen MP. A Multivariate Validity Analysis of the Pain-related Cognitive Processes Questionnaire. *The Clinical Journal of Pain* 2018;34:723.
- [3] Day MA, Ward LC, Thorn BE, Lang CP, Newton-John TRO, Ehde DM, Jensen MP. The Pain-Related Cognitive Processes Questionnaire: Development and Validation. *Pain Medicine* 2018;19:269–283.
- [4] Lovibond SH, Lovibond PF. Manual for the depression anxiety stress scales. Psychology Foundation of Australia, 1996.

SUPPLEMENTARY TABLES

Full pre-treatment and post-treatment data for all outcomes are shown in [Table S1](#).

Full analyses for all outcomes are shown in [Table S2](#).

Manipulation check results are shown in [Table S3](#).

Pain outcomes by perceived treatment allocation are shown in [Table S4](#).

Table S1. Pain and Process Outcome Means and Standard Deviations for all Groups from Pre-treatment and Post-treatment

Outcome	Time	Group									
		MM+		MM-		SHAM+		SHAM-		NTC	
		Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Pain Outcomes											
Pain Unpleasantness (VAS) (Primary Outcome)	Pre	4.14	1.01	5.03	1.14	4.25	1.33	4.59	1.59	4.73	1.37
	Post	3.43	1.23	4.05	1.73	3.79	1.70	4.06	1.77	4.76	2.01
	Post (Adj)	3.44	1.72	4.04	1.71	3.81	1.73	4.06	1.71	4.72	1.76
Pain Intensity (VAS)	Pre	4.79	0.88	5.22	0.90	4.77	0.85	5.07	1.01	5.11	1.02
	Post	4.06	1.27	4.63	1.56	4.10	1.73	4.29	1.61	5.08	1.71
	Post (Adj)	4.23	1.54	4.45	1.54	4.23	1.54	4.28	1.52	4.98	1.56
Pain Threshold (°C)	Pre	42.68	1.11	42.70	1.70	42.61	1.57	43.02	1.60	43.35	1.60
	Post	43.10	1.67	42.52	1.89	42.91	1.97	43.31	2.06	42.97	2.07
	Post (Adj)	43.05	1.96	42.52	1.95	42.83	1.95	43.30	1.93	43.11	1.98
Pain Tolerance (°C)	Pre	47.76	1.45	47.15	1.68	47.23	1.73	47.57	1.52	47.76	1.70
	Post	48.19	1.73	47.44	1.79	47.64	1.81	47.96	1.37	47.65	1.83
	Post (Adj)	48.27	1.71	47.32	1.71	47.67	1.71	47.95	1.69	47.67	1.73

Outcome (cont'd)	Time	Group									
		MM+		MM-		SHAM+		SHAM-		NTC	
		Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Process Outcomes											
<i>Placebo Effect</i>											
Response Expectancy (%)	General	68.30	10.20	63.20	21.66	67.10	13.95	64.80	16.30	65.30	15.02
	Specific	58.22	22.94	43.44	25.39	67.63	21.62	43.66	20.12	18.22	22.60
<i>Mindfulness (FFMQ15)</i>											
Observing	Pre	10.43	1.48	10.48	2.00	10.71	2.00	10.58	2.06	11.07	1.96
	Post	10.93	1.87	10.55	2.11	11.06	1.65	10.68	2.14	10.83	2.15
Describing	Pre	10.73	2.10	10.16	2.40	10.97	2.03	10.35	2.36	9.17	2.20
	Post	11.33	2.25	10.39	2.25	10.52	1.73	10.81	2.52	9.40	1.85
Acting with Awareness	Pre	9.03	2.33	9.10	2.15	9.58	2.45	8.71	2.04	9.73	1.89
	Post	9.33	2.28	8.81	1.89	9.68	2.14	9.16	1.99	9.10	2.35
Nonjudging	Pre	10.80	2.83	9.84	2.34	10.65	2.65	10.03	2.69	9.63	2.46
	Post	11.30	2.56	10.00	2.31	10.97	2.92	10.06	2.76	8.70	2.40
Nonreactivity	Pre	9.73	2.03	9.23	2.14	9.65	2.54	9.35	1.92	9.77	2.00
	Post	10.23	2.25	9.06	2.45	9.58	2.06	9.29	2.34	8.87	1.83
<i>Pain Catastrophizing (PCS)</i>											
PCS Total	Pre	15.23	9.50	17.03	9.80	17.97	10.22	18.32	9.56	15.23	8.77
Rumination	Pre	5.93	3.70	6.68	3.68	7.55	3.39	7.03	3.66	5.20	2.91
Magnification	Pre	3.37	2.50	3.68	2.57	3.77	2.70	4.13	2.73	3.77	2.54
Helplessness	Pre	5.93	4.09	6.68	4.63	6.65	5.38	7.16	4.97	6.27	4.20
<i>Depression, Anxiety, Stress (DASS21)</i>											
Depression	Pre	3.03	3.56	4.35	3.64	3.23	3.25	4.19	3.56	3.93	4.39
	Post	2.83	3.58	3.45	3.14	2.97	4.40	4.00	4.71	3.83	3.80
Anxiety	Pre	2.93	3.15	3.52	3.13	3.26	2.58	3.58	3.80	4.30	3.71
	Post	2.67	2.82	3.10	2.73	3.48	3.68	3.58	4.17	5.03	3.37
Stress	Pre	5.47	3.67	6.65	3.91	5.90	3.43	5.77	3.48	6.33	4.00
	Post	5.63	3.86	5.55	3.71	5.29	4.64	6.13	4.09	7.07	4.19

Outcome (cont'd)	Time	Group									
		MM+		MM-		SHAM+		SHAM-		NTC	
		Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
<i>Pain Processing (PCPQ)</i>											
PCPQ Total	Pre	1.94	0.42	1.94	0.41	2.05	0.40	1.93	0.53	2.05	0.39
	Post	2.22	0.39	2.10	0.36	2.23	0.38	2.11	0.56	2.19	0.41
<u>Pain Diversion</u>	Pre	1.91	0.60	1.96	0.50	2.16	0.63	2.06	0.74	2.11	0.61
	Post	2.10	0.66	2.00	0.54	2.16	0.46	2.18	0.75	2.16	0.50
<i>Suppression</i>	Pre	1.61	0.60	1.62	0.59	1.81	0.65	1.71	0.72	1.87	0.63
	Post	1.86	0.71	1.65	0.57	1.80	0.55	1.85	0.77	1.83	0.49
<i>Distraction</i>	Pre	2.13	0.75	2.23	0.65	2.39	0.72	2.37	0.84	2.28	0.69
	Post	2.21	0.74	2.25	0.76	2.25	0.60	2.39	0.82	2.35	0.61
<i>Enhancement</i>	Pre	1.97	0.87	2.02	0.61	2.26	0.68	2.10	0.85	2.21	0.75
	Post	2.28	0.78	2.06	0.73	2.49	0.50	2.30	0.80	2.30	0.67
<u>Pain Distancing</u>	Pre	1.41	0.72	1.37	0.63	1.46	0.59	1.23	0.70	1.61	0.51
	Post	1.86	0.65	1.61	0.55	1.76	0.64	1.52	0.82	1.72	0.66
<i>Dissociation</i>	Pre	1.12	0.78	1.08	0.66	1.05	0.58	0.86	0.58	1.30	0.66
	Post	1.65	0.70	1.29	0.77	1.34	0.77	1.12	0.88	1.50	0.80
<i>Reappraisal</i>	Pre	1.67	0.83	1.65	0.79	1.87	0.73	1.59	0.97	1.91	0.63
	Post	2.06	0.82	1.93	0.68	2.18	0.62	1.90	1.02	1.93	0.72
<u>Pain Focus</u>	Pre	1.97	0.64	1.99	0.68	1.97	0.60	1.94	0.55	1.73	0.49
	Post	2.03	0.58	2.08	0.65	1.87	0.57	1.98	0.54	1.97	0.51
<i>Absorption</i>	Pre	2.17	0.66	2.08	0.74	2.01	0.59	2.10	0.65	1.89	0.58
	Post	2.21	0.69	2.22	0.74	2.04	0.57	2.17	0.57	2.05	0.63
<i>Rumination</i>	Pre	1.77	0.75	1.88	0.80	1.92	0.74	1.77	0.74	1.58	0.69
	Post	1.84	0.68	1.90	0.70	1.69	0.67	1.78	0.70	1.88	0.64
<u>Pain Openness</u>	Pre	1.71	0.68	1.65	0.60	1.65	0.52	1.68	0.69	1.76	0.52
	Post	1.96	0.74	1.86	0.64	2.06	0.62	1.81	0.76	1.95	0.59
<i>Non-Judgmental</i>	Pre	1.70	0.95	1.55	0.73	1.57	0.68	1.62	0.85	1.73	0.68
	Post	2.02	0.86	1.80	0.85	2.05	0.78	1.74	1.03	1.96	0.69
<i>Acceptance</i>	Pre	1.68	0.56	1.75	0.55	1.72	0.55	1.71	0.64	1.78	0.56
	Post	1.87	0.74	1.89	0.59	2.06	0.59	1.86	0.60	1.93	0.62

Table S2. Pain and Process Outcome Results from Baseline Between Groups ANOVAs and Pre-treatment to Post-treatment Orthogonal Contrasts

Outcome	Time	Baseline		Contrast															
				Any Intervention vs NTC				Treatment (MM vs SHAM)				Instruction (+ vs -)				Interaction (Told vs Get)			
		F	p	F	p	np2	d	F	p	np2	d	F	p	np2	d	F	p	np2	d
Pain Outcomes																			
Unpleasant (VAS)	Pre	2.34	0.06																
	Post			6.40	0.01	0.04	0.42	1.01	0.32	0.01	0.17	0.12	0.74	0.00	0.06	0.00	0.95	0.00	0.00
	Post (Adj)			5.53	0.02	0.04	0.39	1.03	0.31	0.01	0.17	0.09	0.77	0.00	0.06	0.00	0.95	0.00	0.00
Intensity (VAS)	Pre	1.42	0.23																
	Post			5.55	0.02	0.04	0.39	0.15	0.70	0.00	0.06	0.51	0.48	0.00	0.11	0.34	0.56	0.00	0.09
	Post (Adj)			4.27	0.04	0.03	0.35	1.01	0.32	0.01	0.17	0.12	0.74	0.00	0.06	0.16	0.69	0.00	0.06
Threshold (°C)	Pre	1.23	0.30																
	Post			1.13	0.29	0.01	0.18	0.53	0.47	0.00	0.13	0.56	0.46	0.00	0.13	1.45	0.23	0.01	0.20
	Post (Adj)			0.34	0.56	0.00	0.09	0.33	0.57	0.00	0.09	0.07	0.80	0.00	0.00	1.13	0.29	0.01	0.18
Tolerance (°C)	Pre	0.98	0.42																
	Post			4.92	0.03	0.03	0.36	0.02	0.88	0.00	0.00	0.29	0.59	0.00	0.09	0.51	0.48	0.00	0.11
	Post (Adj)			4.40	0.04	0.03	0.35	0.01	0.92	0.00	0.00	0.08	0.78	0.00	0.06	0.31	0.58	0.00	0.09

Outcome	Time	Baseline		Contrast															
				Any Intervention vs NTC				Treatment (MM vs SHAM)				Instruction (+ vs -)				Interaction (Told vs Get)			
		F	p	F	p	np2	d	F	p	np2	d	F	p	np2	d	F	p	np2	d
Process Outcomes																			
Placebo Effect																			
Expectancy		0.48	0.75																
	Specific			57.90	0.00	0.28	1.25	1.40	0.24	0.01	0.19	22.61	0.00	0.13	0.78	1.27	0.26	0.01	0.19
Mindfulness (FFMQ15)																			
Observing	Pre	0.53	0.72																
	Post			1.27	0.26	0.01	0.19	0.00	0.99	0.00	0.00	1.84	0.18	0.01	0.22	0.06	0.81	0.00	0.00
Describing	Pre	2.97	0.02																
	Post			1.52	0.22	0.01	0.20	1.79	0.18	0.01	0.22	0.12	0.73	0.00	0.06	5.84	0.02	0.04	0.40
Awareness	Pre	1.13	0.34																
	Post			3.71	0.06	0.03	0.32	1.20	0.28	0.01	0.18	0.78	0.38	0.01	0.14	1.54	0.22	0.01	0.20
Nonjudging	Pre	1.17	0.33																
	Post			15.83	0.00	0.10	0.66	0.25	0.62	0.00	0.09	2.69	0.10	0.02	0.27	0.05	0.83	0.00	0.00
Nonreact	Pre	0.39	0.82																
	Post			8.21	0.00	0.05	0.47	0.70	0.40	0.01	0.14	2.47	0.12	0.02	0.26	1.72	0.19	0.01	0.22
Pain Catastrophizing (PCS)																			
PCS Total	Pre	0.72	0.58	-	-	-		-	-	-		-	-	-		-	-	-	
Ruminat	Pre	2.15	0.08	-	-	-		-	-	-		-	-	-		-	-	-	
Magnific	Pre	0.33	0.86	-	-	-		-	-	-		-	-	-		-	-	-	
Helpless	Pre	0.30	0.88	-	-	-		-	-	-		-	-	-		-	-	-	
Depression, Anxiety, Stress (DASS21)																			
Depression	Pre	0.78	0.54																
	Post			0.37	0.54	0.00	0.11	0.45	0.50	0.00	0.11	0.02	0.88	0.00	0.00	0.50	0.48	0.00	0.11
Anxiety	Pre	0.71	0.59																
	Post			5.56	0.02	0.04	0.39	1.61	0.21	0.01	0.21	0.06	0.81	0.00	0.00	0.03	0.87	0.00	0.00
Stress	Pre	0.48	0.75																
	Post			3.28	0.07	0.02	0.30	0.26	0.61	0.00	0.09	0.00	0.98	0.00	0.00	2.95	0.09	0.02	0.29

Outcome	Time	Baseline		Contrast															
				Any Intervention vs NTC				Treatment (MM vs SHAM)				Instruction (+ vs -)				Interaction (Told vs Get)			
		F	p	F	p	np2	d	F	p	np2	d	F	p	np2	d	F	p	np2	d
PCPQ (Pain Processing)	Pre	0.64	0.63																
	Post			0.48	0.49	0.00	0.11	0.21	0.65	0.00	0.06	2.21	0.14	0.02	0.25	0.92	0.34	0.01	0.16
<u>Diversion</u>	Pre	0.84	0.50																
	Post			0.00	0.98	0.00	0.00	0.04	0.84	0.00	0.00	0.11	0.74	0.00	0.06	1.78	0.18	0.01	0.22
<i>Suppression</i>	Pre	1.00	0.41																
	Post			0.27	0.60	0.00	0.09	0.02	0.90	0.00	0.00	0.29	0.59	0.00	0.09	2.90	0.09	0.02	0.28
<i>Distraction</i>	Pre	0.65	0.63																
	Post			0.42	0.52	0.00	0.11	0.01	0.92	0.00	0.00	0.38	0.54	0.00	0.11	0.54	0.46	0.00	0.13
<i>Enhancemen</i>	Pre	0.80	0.53																
	Post			0.36	0.55	0.00	0.09	1.23	0.27	0.01	0.18	3.20	0.08	0.02	0.29	0.76	0.39	0.01	0.14
<u>Distance</u>	Pre	1.45	0.22																
	Post			2.25	0.14	0.02	0.25	0.51	0.48	0.00	0.11	2.85	0.09	0.02	0.28	0.76	0.38	0.01	0.14
<i>Dissociation</i>	Pre	1.76	0.14																
	Pre			0.11	0.75	0.00	0.06	1.37	0.24	0.01	0.19	3.41	0.07	0.02	0.31	1.13	0.29	0.01	0.18
<i>Reappraisal</i>	Pre	1.01	0.40																
	Pre			4.73	0.03	0.03	0.36	0.01	0.92	0.00	0.00	0.98	0.32	0.01	0.17	0.07	0.79	0.00	0.00
<u>Focus</u>	Pre	0.94	0.44																
	Post			1.73	0.19	0.01	0.22	1.87	0.17	0.01	0.23	1.12	0.29	0.01	0.18	0.35	0.55	0.00	0.09
<i>Absorption</i>	Pre	0.81	0.52																
	Post			0.00	0.95	0.00	0.00	0.56	0.46	0.00	0.13	0.50	0.48	0.00	0.11	0.01	0.93	0.00	0.00
<i>Rumination</i>	Pre	0.93	0.45																
	Post			4.04	0.05	0.03	0.33	2.42	0.12	0.02	0.26	0.95	0.33	0.01	0.16	0.88	0.35	0.01	0.16
<u>Openness</u>	Pre	0.17	0.95																
	Post			0.12	0.73	0.00	0.06	0.11	0.74	0.00	0.06	3.14	0.08	0.02	0.29	1.32	0.25	0.01	0.19
<i>Non-Judgme</i>	Pre	0.31	0.87																
	Post			0.03	0.87	0.00	0.00	0.00	1.00	0.00	0.00	3.86	0.05	0.03	0.33	0.90	0.35	0.01	0.16
<i>Acceptance</i>	Pre	0.84	0.50																
	Post			0.09	0.76	0.00	0.06	0.84	0.36	0.01	0.16	1.41	0.24	0.01	0.19	0.76	0.39	0.01	0.14

Table S3. Manipulation Check Results Between Groups

Group	“I think I am in the group” (Manipulation Check)					“Did your training include mindfulness?” (Credibility Check)			
	MM	SHAM	NTC	NOT SURE	TOTAL	YES	NOT SURE	NO	TOTAL
MM+	25	2	1	2	30	25	3	2	30
MM-	0	31	0	0	31	18	6	7	31
SHAM+	26	4	0	1	31	26	4	1	31
SHAM-	0	30	0	1	31	23	4	4	31
NTC	0	0	30	0	30	1	6	23	30
Significantly Different?	$\chi^2(12, N=153)=269.28, p<.001$					$\chi^2(6, N=123)=8.71, p=.19$			

Table S4. Pain Outcomes and Expectancy by Perceived Treatment

Outcome	Did your training include mindfulness?		
	Mean (SD)		
	Yes	Not Sure	No
Δ Unpleasantness (VAS)	-0.60 (1.65)	-0.62 (1.62)	-0.30 (1.69)
Δ Intensity (VAS)	-0.70 (1.61)	-0.60 (1.55)	-0.18 (1.55)
Δ Threshold (°C)	+0.36 (1.98)	-0.35 (1.25)	-0.31 (1.34)
Δ Tolerance (°C)	+0.47 (1.04)	+0.21 (0.99)	-0.15 (0.88)
Specific Expectancy (%)	55.9 (23.9)	52.0 (22.9)	18.7 (21.4)