Supplemental Materials for

Cognitive self-regulation influences pain-related physiology

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This PDF file includes:

Supplemental Methods

Full script for the Regulation practice

(Ask participant to close their eyes)

Let's take a moment and tune in to how things are for you right now. As we're sitting here, we can create a space where you can have control over what you're feeling, in a way that allows you to control the pain you experience. Are you ready? To begin, focus on the sensation of your left forearm that does not hurt at all in this moment, and become aware of how it feels, of the sensations that come from that region. If you are able to bring awareness to any aspects of this experience, even for the briefest of moments, you can develop a powerful relationship with your sensations, for example, pain, and even more importantly, with your mind and body.

(Pause)

Regulate-up

Now, we want you to practice increasing a painful sensation by using the power of your mind. Our research indicates that one of the most effective ways to do this is by changing the meaning of the painful sensation using the power of your imagination. Take a moment and try to imagine what it might feel like if this part of your body hurt (left forearm). As if something very hot or sharp was pushing on it, perhaps like one of the stimulations you just felt. Imagine how unpleasant the pain is, for instance, how strongly you would like to remove your arm from it. You can increase pain by imagining your arm burning from something very hot being put on it, and the stinging and shooting sensations that go along with that image. As you feel the pain rise, imagine it rising faster and faster, and going higher and higher. Think of how disturbing it is to be burned, and visualize your skin sizzling, melting, and bubbling as a result of the intense heat.

(Pause)

As you're imaging this, slowly become aware of what this feels like. Don't worry if you had trouble imagining this, it will become much easier once you have real sensations

you can manipulate. With the real painful heat, you will be able to exert your power of mind over your painful sensation.

Regulate-down

Take a moment to return to the sensation on your forearm. Now we want you to practice decreasing the painful sensation using the power of your mind. Imagine once again the burning, stinging, and shooting sensations that go along with strong heat being applied to your left forearm.

(Pause)

Now focus on the part of that pain that feels pleasant, like the warmth on your skin of hot clothes being taken out of the dryer. Allow the pain and heat to be carried away, flowing away from your body as if being taken downstream if you were to plunge that part of you into a cold river. Think of what it might feel like to be very cold, and have the heat on your arm warm you up. Once again, even if you were able to become aware of and control any aspects of this experience even for the briefest of moments, you have already come a long way in being able to build a powerful relationship with pain in such a way that you are able to change your experience of it. Now, open your eyes.

(open eyes)

If you found this difficult, don't worry: this was just a practice, and it will become much easier to manipulate your experience once you have stronger sensations to work with. How was it?

Study 2 Task Design

The experiment involved five task conditions. Each condition consisted of 10 trials of painful thermal stimulation delivered in a pseudorandom order to three different sites on the main participant's left leg. Moment-by-moment pain intensity ratings were collected from the main participant each trial. Overall pain intensity and unpleasantness ratings were collected from the main participants at the end of each condition. The first condition was a "Pre-manipulation" condition where the main participant experienced the pain

stimulations alone, without their partner present. The presentation order of the next three conditions was pseudorandomized so that there were six total orders. These conditions were (a) a "Present" condition, where the partner was present but did not touch or significantly interact with the main participant, (b) a "Hand-holding" condition, where the partner held the main participant's left hand, and (c) a "Gentle stroking" condition, where the supportive participant gently stroked the forearm of the main participant in a pleasurable and soothing way. Lastly, the main participant underwent a "Post-manipulation" condition, where they again experienced pain without their partner present. Skin conductance responses were recorded from both participants (main participants and partners) during each block they participated in. The current study uses data only from the "Present" condition.

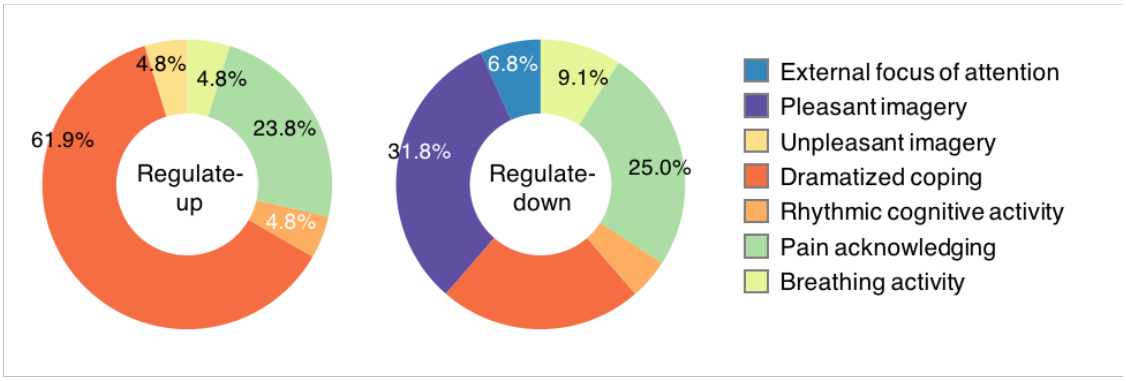

Figure S1. Analysis of post-experiment questionnaire on cognitive regulation strategies used by participants. The pie chart showing the proportions of regulation categories used by participants. To examine the actual regulation strategies used by participants, a post-experimental survey was administered. In the survey, we asked participants to describe the most effective strategy they used to regulate pain up or down. 38 participants responded (e.g. "For the up condition, I imagined that the thermode was burning a hole in my skin", or "For the down, I thought of drinking a hot cup of hot chocolate on a cold day"). We then asked emotion and pain researchers (n = 11) to categorize these responses into one of the eight categories. Six categories were taken from Fernandez & Turk (Fernandez & Turk, 1989): "External focus of attention", "Neutral imagery", "Pleasant imagery", "Dramatized coping", "Rhythmic cognitive activity", "Pain acknowledging." Plus, we added two more categories based upon the responses: "Unpleasant imagery" and "Breathing activity."

Categories are defined as the following. "External focus of attention": strategies involving a redirection of attention away from the site of stimulation. "Neutral imagery": strategies involving imagery of neither a pleasant nor unpleasant quality. "Pleasant imagery": strategies centering around the use of pleasant imagery. "Unpleasant imagery": strategies centering around the use of unpleasant imagery. "Dramatized coping": strategies involving a dramatized reconstruction of the context in which nociception occurs. "Rhythmic cognitive activity": strategies involving cognitive activity of a repetitive or systematized nature. "Pain acknowledging": strategies involving a reappraisal of the nociceptive stimulation in terms of objective sensations. "Breathing activity": regulating breathing, for example "I tried to slow down my breathing and remain calm".

We made the final decision about the regulation categories for each participant's response based on consensus across experimenters G.M. and C.W.

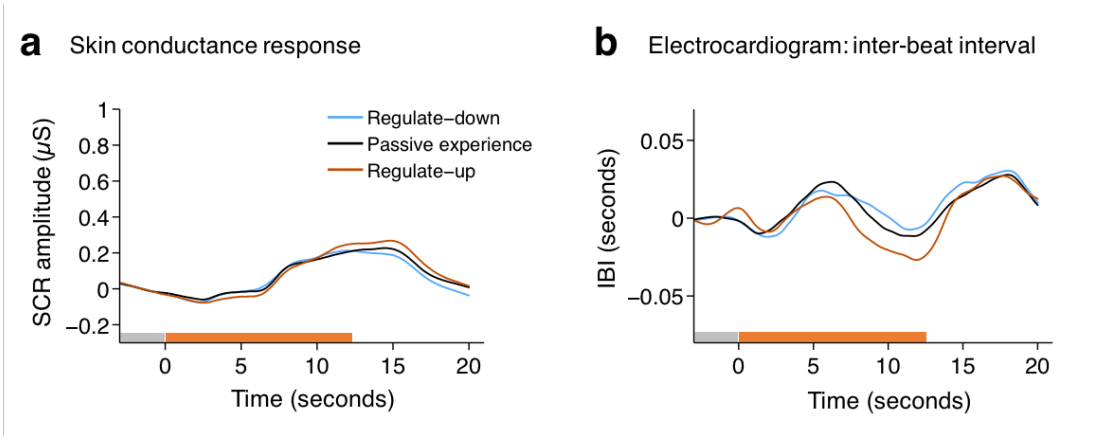

Figure S2. Mean physiological responses in different regulation conditions. Stimulus-locked grand average of **(a)** skin conductance responses (SCR) and **(b)** electrocardiogram's inter-beat intervals (IBI) across participants for each regulation condition. Data from 3 seconds prior to the thermal stimulation onset were used as a baseline.

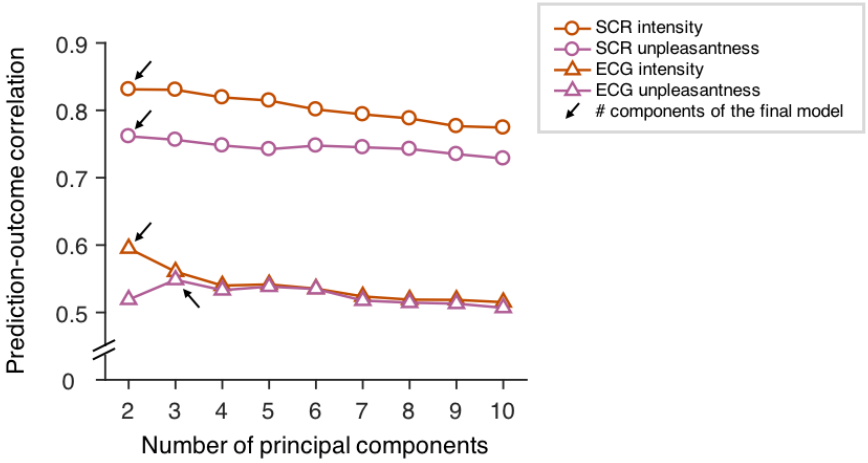

Figure S3. Selection of the number of components for physiological markers. Shown here are the mean prediction-outcome correlations (i.e., correlations between the actual outcome values, y and predicted values, $\hat{y}$) for different physiological predictive models with different numbers of components. To select the number of components for the final models that maximized the predictive performance, we used the leave-one-participant-out cross-validation procedure. The final number of components used in each model is indicated by the black arrow.

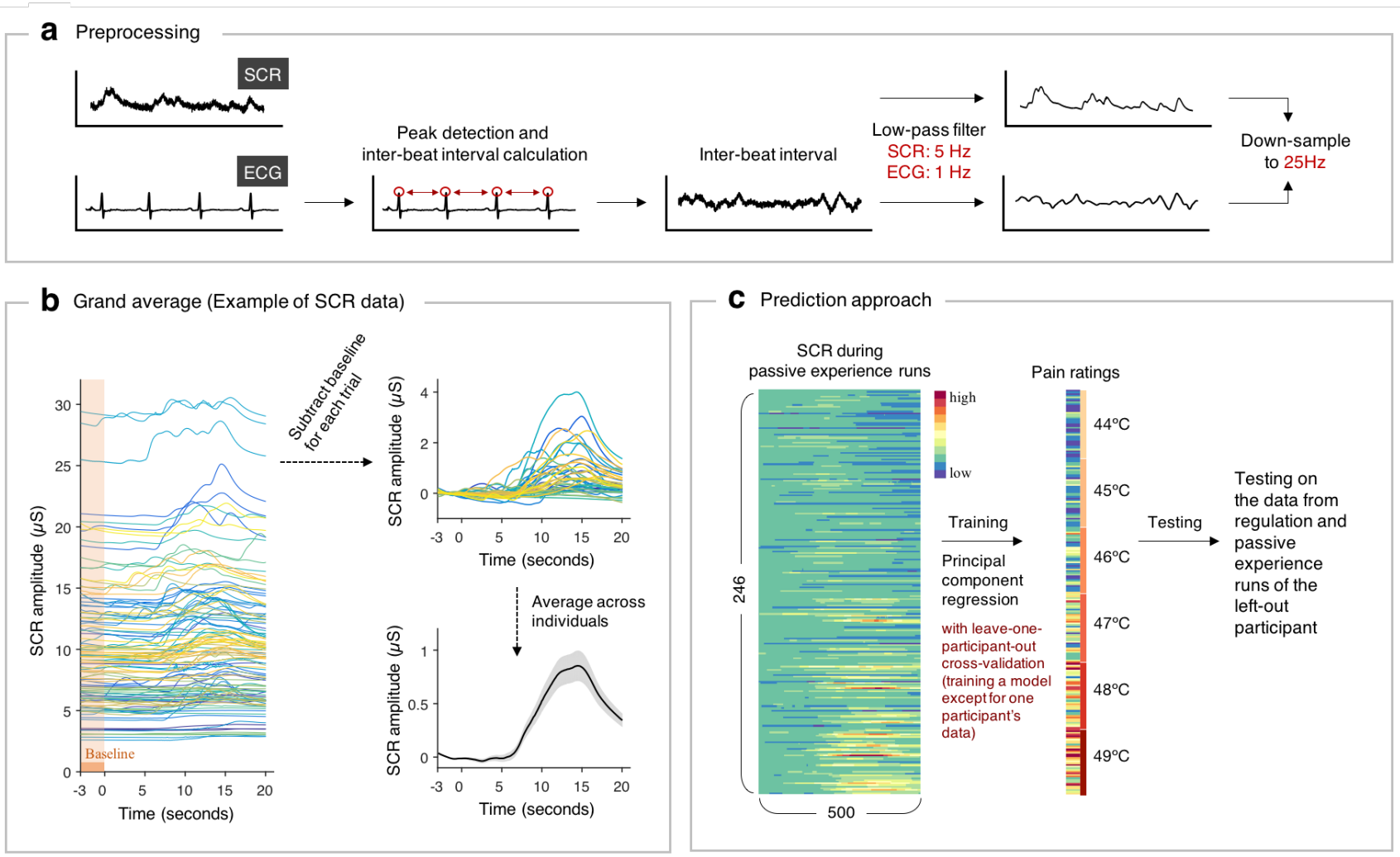

Figure S4. Data analysis pipeline. (a) Preprocessing pipeline. Electrocardiogram (ECG) data was converted into an inter-beat interval time-series. The raw SCR and IBI data were then both put through a low-pass filter (5 Hz for SCR, 1 Hz for IBI) and down-sampled to 25 Hz. **(b)** Stimulus-locked grand averages (an example of SCR data). Mean values of the three second baseline period before stimulation onset were subtracted from the stimulation epoch, and then time courses were averaged across individuals. Shades represent standard

errors of the mean (s.e.m.). **(c)** Prediction approach. Using concatenated stimulus-locked average responses in only the passive experience runs as features, SCR and ECG time-course models that are predictive of pain ratings were derived with principal component regression (PCR). A leave-one-participant-out cross-validation procedure was used for testing of data from Study 1: SCR/ECG models were derived based on physiological data from passive experience conditions for all participants except for one out-of-sample participant, and the models were then tested on the out-of-sample participant's data in all three conditions by calculating the dot-product between the time-series weights and stimulus-locked physiological data. This process was done iteratively for each participant. Note that the data from regulation runs were not included in the model developing procedure at all.

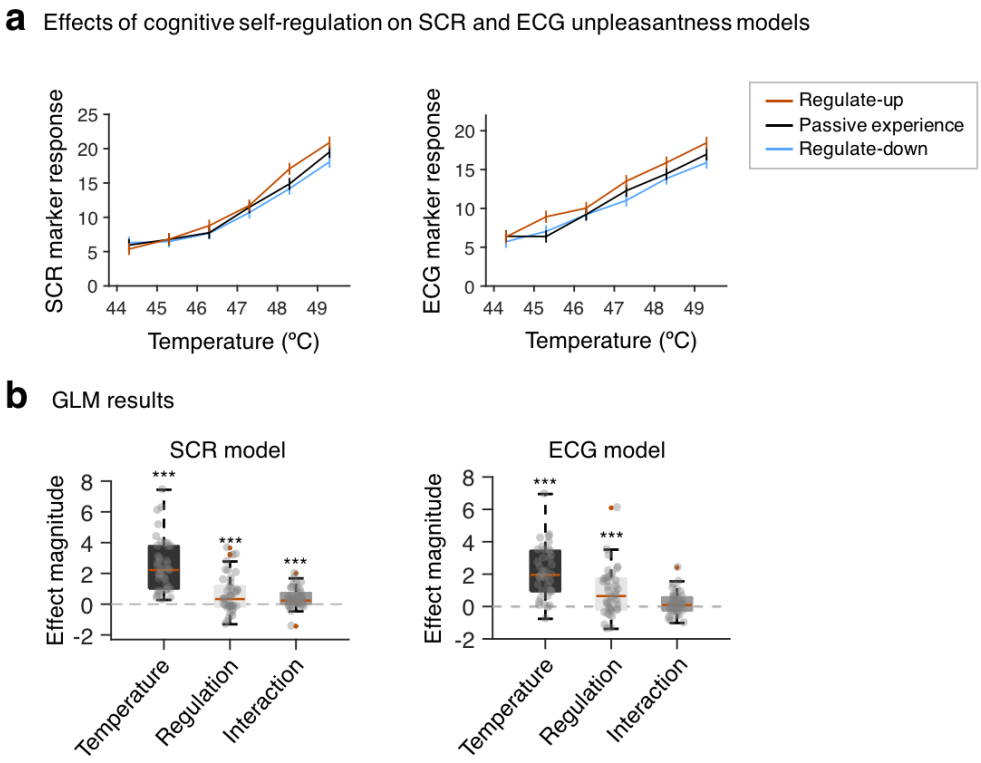

Figure S5. Effects of cognitive self-regulation on SCR and ECG unpleasantness markers. These are analogous plots to **Fig. 5**, except that these are the results for SCR and ECG unpleasantness markers. **(a)** Predicted pain scores by SCR and ECG pain unpleasantness models. Error bars represent within-subject S.E.M. **(b)** Multi-level general linear model results. Both stimulus intensity and cognitive self-regulation had significant effects on SCR and ECG unpleasantness marker responses. $^{***}p < .001$; Bootstrap tests (10,000 iterations) were used for significance testing.

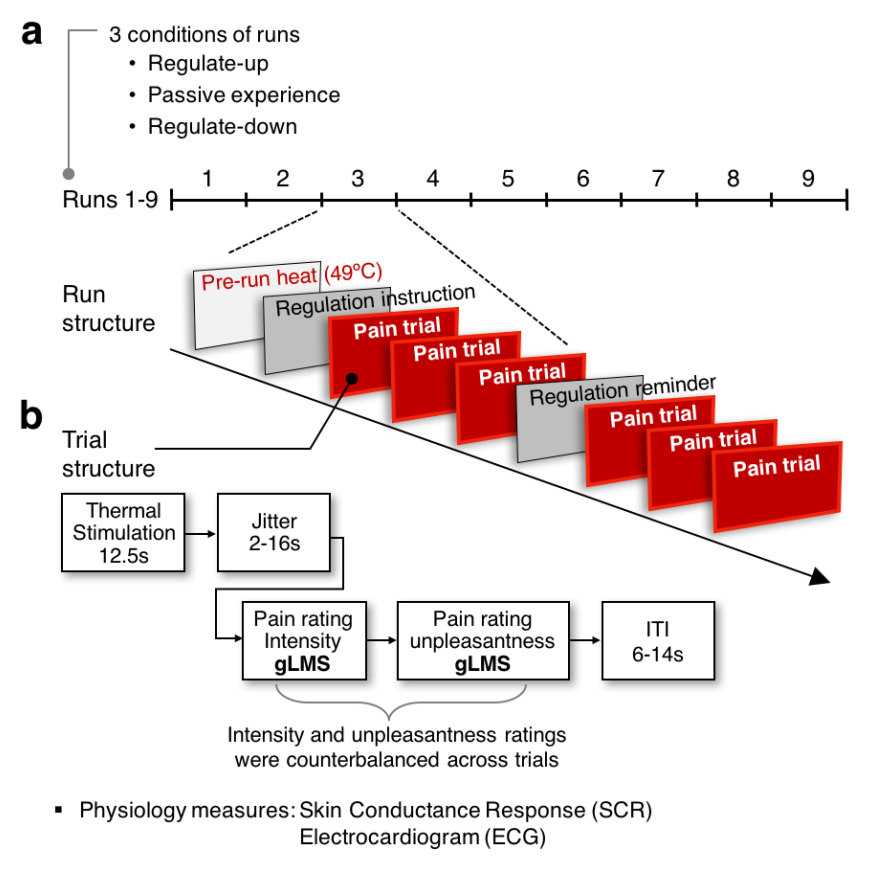

Figure S6. Experimental Design. (a) Run structure: Three different regulation conditions were pseudorandomized across 9 runs using a Latin square method. Each run began with a pre-run heat stimulation to minimize peripheral habituation effects on pain experience (Jepma, Jones, & Wager, 2014). After instructions for regulation were presented, six trials of heat pain were administered, and a regulation reminder was given in the middle of the run. **(b)** Trial structure: Each trial consisted of a thermal stimulation of 12.5 seconds (3s ramp-up, 7.5s plateau, 2.5s ramp-down), a jittered interval of 2-16 seconds, and then intensity and unpleasantness ratings, the order of which was counterbalanced. A jittered inter-trial interval (ITI) of 6-14 seconds separated the trials. gLMS = general Labeled Magnitude Scale.

Table S1. Multi-level general linear model results for different contrasts.

Outcome (Y)	Contrasts (X)	*beta*	s.e.m	bootstrap test results	
				z	*p*
pain intensity ratings	stimulus intensity (temperature)[a]	5.01	0.32	3.70	0.0001
	regulate-up vs. regulate-down[a]	2.12	0.36	3.75	0.0001
	regulate-up vs. passive experience[b]	1.44	0.52	2.46	0.0069
	passive experience vs. regulate-down[c]	2.80	0.56	4.02	<.0001
pain unpleasantness ratings	stimulus intensity (temperature)[a]	5.50	0.38	3.49	0.0002
	regulate-up vs. regulate-down[a]	5.19	0.68	4.44	<.0001
	regulate-up vs. passive experience[b]	4.77	0.77	3.80	0.0001
	passive experience vs. regulate-down[c]	5.62	1.02	5.50	<.0001
SCR intensity marker	stimulus intensity (temperature)[a]	2.50	0.33	4.76	<.0001
	regulate-up vs. regulate-down[a]	0.61	0.18	4.12	<.0001
	regulate-up vs. passive experience[b]	0.70	0.38	1.64	0.0500
	passive experience vs. regulate-down[c]	0.51	0.30	1.53	0.0630
SCR unpleasantness marker	stimulus intensity (temperature)[a]	2.78	0.38	4.91	<.0001
	regulate-up vs. regulate-down[a]	0.61	0.19	3.95	<.0001
	regulate-up vs. passive experience[b]	0.72	0.42	1.55	0.0604
	passive experience vs. regulate-down[c]	0.49	0.33	1.19	0.1162
ECG intensity marker	stimulus intensity (temperature)[a]	1.50	0.23	4.85	<.0001
	regulate-up vs. regulate-down[a]	0.62	0.15	3.91	<.0001
	regulate-up vs. passive experience[b]	1.09	0.31	3.38	0.0004
	passive experience vs. regulate-down[c]	0.14	0.30	0.52	0.6968
ECG unpleasantness marker	stimulus intensity (temperature)[a]	2.27	0.29	4.13	<.0001
	regulate-up vs. regulate-down[a]	0.87	0.23	4.09	<.0001
	regulate-up vs. passive experience[b]	1.24	0.43	2.82	0.0024
	passive experience vs. regulate-down[c]	0.50	0.45	0.58	0.2800

Note. This table shows results from three different multi-level general linear models (MGLM) represented by different superscripts. All three MGLM models include three types of independent variables: (i) stimulus intensity (temperature, ˚C), (ii) regulation, and (iii) the interaction term between the stimulus intensity and regulation. For three different MGLM models, we used different contrasts for the "regulation" variable. [a] For the regulate-up vs. regulate-down contrast, the regulation was coded as 1, 0, and -1 for regulate-up, passive experience, and regulate-down, respectively. [b] For the regulate-up vs. passive experience contrast, the regulation regressor was coded as 0.5 and -0.5 for regulate-up and

passive experience, respectively to make the unit consistent with the other models. [c] For the passive experience vs. regulate-down contrast, the regulation regressor was coded as 0.5 and -0.5 for passive experience and regulate-down. For model [b] and [c], we only report the results of the regulation contrasts in this table.

References

Fernandez, E., & Turk, D. C. (1989). The utility of cognitive coping strategies for altering pain perception: a meta-analysis. *Pain, 38*(2), 123-135.

Jepma, M., Jones, M., & Wager, T. D. (2014). The dynamics of pain: evidence for simultaneous site-specific habituation and site-nonspecific sensitization in thermal pain. *J Pain, 15*(7), 734-746. doi:10.1016/j.jpain.2014.02.010