

Supplemental material

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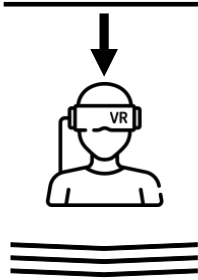
Table S4: Pre-Analysis tests

Figure S1: Illustration of test conditions

Participants went through four conditions including an immersive VR scenario of an island (VR), a non-immersive 2D video presentation of the island scenario (video), and a mental imagery of the island scenario instructed via audio file.

All three scenarios were selected and constructed in such a way that the intended psychophysical recording of pressure pain thresholds using pressure cuff algometry could be well integrated in them. The condition to which the participants were first exposed was counterbalanced, and the order of conditions following was randomized after generating six sequences to control for time effects. Participants were able to stop the pressure stimulation using a controller. The figure includes two representative screenshots of VR landscape scenario.

Immersive VR



2D-Control



Imagination



Standardized instructions for the imagination journey:

“Please close your eyes to increase your concentration. If you do not wish to close your eyes, keep them open and rest your eyes on a point at the front of the room. If possible, sit in a comfortable position. Your back should be in contact with the backrest, and your hands and forearms should rest loosely on your thighs or armrests, so that you do not have to use force to hold your arms and hands. Adjust your sitting position until the contact with the floor or chair feels as comfortable as possible. -short break

You are on an island with a white sandy beach. Your toes feel the sand warmed by the sun. - Pause - The wind caresses your skin with a light breeze. Your eyes turn to the sea and you feel the brightness of the colours. - Pause - You see the little waves. You breathe in the salty smell of the sea and taste it on your lips. Large, smooth rocks rise out of the water, protecting the bay from storms and blending pleasantly into the landscape. You look around. Your eyes are drawn to the interior of the island. The island is lined with palm trees with lush green leaves and shrubs, as if in an oasis. You walk on, quite pleasantly. -At your own pace you reach a clearing. A hammock has been set up for you between two palm trees. There is a cushion and a blanket in the hammock. - Pause - you lie down in it. The pillow feels soft under your head. The blanket is light as a feather. You make yourself comfortable. - Pause - Perhaps there is a bright, clear, fresh light - Pause - Perhaps there is a warm, friendly twilight. Now change the brightness in that place. Make it brighter or darker until the light is OK for you and as comfortable as possible. - Pause - Notice the colours in this place. Pause - Maybe they are bright, bold colours or maybe they are pastels. Change the colours until they are right for you. And look around. Notice the different colours. Discover new colours. Now notice the temperature in this place. Maybe there is a light breeze and it is a bit cool and refreshing. Maybe a ray of sunlight is shining on you and warming your skin. -Pause - Do you notice how comfortable and safe the warmth feels? -Pause - And also notice how comfortable and safe you feel. -Pause- Allow this place to affect you again in its entirety. - Pause - And feel it with full intensity. -Pause - You are on an island with a white sandy beach. -Pause - and in the midst of this sandy beach and this pleasant place together with this hammock, look around you and change the place in your imagination so that it feels pleasant to you. Be it in the hammock or let your imagination create a chair that is in the middle of this fantasy landscape. -Pause - And you sit in that chair or hammock and let your legs dangle. -Pause - And at the same time you let the whole situation have an effect on you. -Pause - The colours - Pause - The sounds - Pause - The temperature - Pause - The colourful colours - Pause - You can also imagine a jetty reaching into the sea and imagine your legs dangling down from the jetty, perceiving the blue of the sea, the green of the plants

or the yellow and flashing of the sandy beach as you wish. Let your imagination create a pleasant situation in this island landscape and in the sea. And feel a sense of health, strength and well-being in this place. - Pause - Feel a sense of health, strength and wellbeing move from this place to you. Now slowly bring your attention to your legs where the pressure cuffs are located. Focus all your attention on the pressure of the cuffs and the physical sensations they create. Let the place work on you and at the same time notice the sensation caused by the pressure cuffs on your legs. Notice how this sensation feels to you: Does it still feel like neutral pressure or is it already unpleasantly painful? Please pay close attention to the moment when the sensation becomes uncomfortable and therefore painful for you. This is your pain threshold!"

Standard instructions for pressure cuff algometry

General Information:

"This device is used to measure personal pain tolerance."

"I will now place the pressure cuffs around your calf. The cuffs should be applied with equal pressure."

"Which is your dominant leg? (If you were to kick a football, which leg would you use?)"

"I will now give you the controller. Use the controller to indicate the intensity of the pain from minimum to maximum."

Spatial summation:

"We will now start a series of tests."

"First, the pressure cuffs are calibrated and you experience for the first time how the pressure cuffs feel."

"When the test starts, both cuffs will be filled with air evenly and you will feel pressure on both calves."

"The pressure will gradually increase and become more intense. It will feel more and more uncomfortable."

"The feeling will go from uncomfortable to painful. This is what we call the pain threshold. At this point, you will begin to move the slider to the right to indicate the intensity of the pain you feel on the numerical rating scale."

"I will now show you the slider. The slider is used to indicate the intensity of pain from minimum to maximum. The "0" corresponds to "no pain felt" and from the point where you feel pain, you should move the slider away from "0" to the right. The "10" corresponds to the point at which the pain is no longer tolerable for you ("maximum pain tolerated") - at this point the measurement stops and the pain stimulus is immediately removed."

"Therefore, please move the slider during the measurement from "0" (no pain felt) to "10" (maximum pain tolerated) so that the slider reaches the correct area of the scale with "10" exactly when the pain has reached the maximum tolerable level for you and the measurement should stop for you."

"Notice how this sensation feels to you: Does it still feel like neutral pressure, or is it already uncomfortably painful? Please pay close attention to the moment when the sensation becomes uncomfortable and therefore painful for you. This is your personal pain threshold! At this point, start moving the dial away from the "minimum" of 0 towards 10."

"We want to follow the course of your perceived pain intensity. To do this, move the slider according to the numerical rating scale as the pain intensity changes. Move the slider from 0

(no pain felt) to 10 (maximum pain tolerated). Speak out the numbers corresponding to your pain from 0 to 10, i.e. 1,2,3,4,5,... in ascending order, as the pain changes. For example, if the intensity of the pain increases from a 1 to a 2, please tell us by saying '2' on the scale from 0 to 10."

"When you have reached your maximum tolerable pain intensity, move the slider all the way to the right to "maximum"/10 and say "10"."

" In the next round, I will hold the slider and enter your pain level for you. The "minimum" now corresponds to the number "0", the "maximum" to "10". "

" During the measurement, please tell me how much pain you can tolerate using the scale from 0 to 10 in ascending order. As soon as you say 10, the measurement is finished."

SR curve 1:

" Pressure is now applied only to the dominant leg, no pressure is applied to the non-dominant leg."

" Please tell me where on the scale of 0-10, in ascending order, you feel your pain."

SR curve 2:

" Now pressure is applied to the non-dominant leg, no pressure is applied to the dominant leg."

" Please tell me where you feel the pain on a scale of 0-10 in ascending order."

Spatial summation:

" now pressure is applied to both legs as the first time"

" Please tell me where you feel the pain on a scale of 0-10 in ascending order."

Temporal summation:

" Pressure is applied to the dominant leg pulse by pulse"

" 10 pulses in total"

" Please tell me where on the scale of 0-10 in ascending order you feel the pain."

" Please only tell me if the pain is getting worse."

Conditioned pain modulation:

" Constant pressure applied to the non-dominant leg"

" The pressure is slowly increased on the dominant leg."

" Please concentrate on your dominant leg only."

" Please tell me where you feel the pain on a scale of 0-10 in ascending order."

Table S1A: Inhibitory and facilitatory response rates for conditioned pain modulation of PDT stratified according to test condition

	Baseline			Imagery			View			VR		
	No effect	Negative CPM	Positive CPM	No effect	Negative CPM	Positive CPM	No effect	Negative CPM	Positive CPM	No effect	Negative CPM	Positive CPM
	n = 4	n = 20	n = 31	n = 1	n = 26	n = 28	n = 1	n = 35	n = 19	n = 0	n = 34	n = 21
Pain-free controls (n = 28)	4 (14.3%)	9 (32.1)	15 (53.6%)	1 (3.6 %)	17 (60.7%)	10 (35.7%)	0	19 (67.9%)	9 (32.1%)	0	21 (75%)	7 (25.0%)
Individuals with pain (n = 27)	0	11 (40.7%)	16 (59.3%)	0	9 (33.3%)	18 (66.7%)	1 (3.7%)	16 (59.3%)	10 (37.0%)	0	13 (48.1%)	14 (51.9%)

Legend: Participants divided into those with positive CPM values, indicating inhibitory CPM activity, and those with negative CPM values, indicating facilitative CPM activity.

CPM: conditioned pain modulation; PDT: pain detection threshold.

Table S1B Inhibitory and facilitatory response rates for conditioned pain modulation of PTT stratified according to test condition

	Baseline			Imagery			View			VR		
	No effect	Negative CPM	Positive CPM	No effect	Negative CPM	Positive CPM	No effect	Negative CPM	Positive CPM	No effect	Negative CPM	Positive CPM
	n = 5	n = 17	n = 33	n = 8	n = 28	n = 19	n = 8	n = 30	n = 17	n = 8	n = 33	n = 14
Pain-free controls (n = 28)	4 (14.3%)	9 (32.1%)	15 (53.6%)	5 (17.9%)	16 (57.1%)	7 (25%)	3 (10.7%)	20 (71.4%)	5 (17.9%)	5 (17.9%)	20 (71.4%)	3 (10.7%)
Individuals with pain (n = 27)	1 (3.7%)	8 (29.6%)	18 (66.7%)	3 (11.1%)	12 (44.4%)	12 (44.4%)	5 (18.5%)	10 (37.0%)	12 (44.4%)	3 (11.1%)	13 (48.1%)	11 (40.7%)

Legend: Participants divided into those with positive CPM values, indicating inhibitory CPM activity, and those with negative CPM values, indicating facilitative CPM activity.

CPM: conditioned pain modulation; PTT: pain tolerance threshold.

Table S2: Post-hoc tests between the groups for every condition

<i>DV</i>	<i>Condition</i>	<i>Group_1</i>	<i>Group_2</i>	<i>n1</i>	<i>n2</i>	<i>t</i>	<i>df</i>	<i>p</i>	<i>p_sig</i>	<i>d</i>	<i>low</i>	<i>high</i>
PDT	VR	HC	CP	31	28	4.66	56.94	0.00	***	1.234	0.652	1.767
PDT	View	HC	CP	31	28	4.62	52.36	0.00	***	1.223	0.643	1.756
PDT	Imagery	HC	CP	31	28	4.52	53.81	0.00	***	1.198	0.62	1.73
PDT	Baseline	HC	CP	31	28	3.77	56.97	0.00	**	1	0.438	1.522
CPM_PDT	Imagery	HC	CP	28	27	-1.49	39.87	0.24	ns			
CPM_PDT	Baseline	HC	CP	28	27	1.17	52.98	0.35	ns			
CPM_PDT	VR	HC	CP	28	27	-2.96	45.88	0.01	*	-0.814	-1.346	-0.246
CPM_PDT	View	HC	CP	28	27	-2.62	46.12	0.03	*	-0.72	-1.249	-0.158

Legend: Post-hoc t-test between the HC and CP group for the dependent variables (DV) PDT and CPM_PDT stratified for every condition.

Table S3: Post-hoc tests between the conditions for each group

<i>DV</i>	<i>Group</i>	<i>Condition_1</i>	<i>Condition_2</i>	<i>n</i>	<i>t</i>	<i>df</i>	<i>p</i>	<i>p_sig</i>	<i>d_z</i>	<i>low</i>	<i>high</i>
SSP_PDT	All	View	VR	59	2.10	58	0.08	ns			
SSP_PDT	All	Imagery	View	59	1.40	58	0.26	ns			
SSP_PDT	All	Baseline	VR	59	1.60	58	0.20	ns			
SSP_PDT	All	Baseline	View	59	-0.40	58	0.83	ns			
SSP_PDT	All	Baseline	Imagery	59	-1.41	58	0.26	ns			
SSP_PDT	All	Imagery	VR	59	2.78	58	0.02	*	0.362	0.097	0.624
PTT	All	View	VR	59	-2.30	58	0.05	ns			
PTT	All	Imagery	View	59	-1.77	58	0.16	ns			
PTT	All	Baseline	Imagery	59	-1.71	58	0.17	ns			
PTT	All	Imagery	VR	59	-3.08	58	0.01	*	-0.401	-0.665	-0.135
PTT	All	Baseline	VR	59	-5.74	58	0.00	***	-0.747	-1.033	-0.455
PTT	All	Baseline	View	59	-3.72	58	0.00	**	-0.485	-0.753	-0.213
PDT	CP	Imagery	View	28	-0.45	27	0.83	ns			
PDT	CP	Baseline	View	28	-0.69	27	0.65	ns			
PDT	CP	Baseline	Imagery	28	-0.41	27	0.83	ns			
PDT	HC	View	VR	31	-1.38	30	0.27	ns			
PDT	HC	Imagery	View	31	-1.57	30	0.22	ns			

PDT	CP	View	VR	28	-2.68	27	0.03	*	-0.506	-0.896	-0.108
PDT	CP	Imagery	VR	28	-3.09	27	0.01	*	-0.583	-0.98	-0.177
PDT	CP	Baseline	VR	28	-2.53	27	0.04	*	-0.479	-0.867	-0.083
PDT	HC	Imagery	VR	31	-3.38	30	0.01	**	-0.606	-0.986	-0.218
PDT	HC	Baseline	VR	31	-6.78	30	0.00	***	-1.217	-1.678	-0.744
PDT	HC	Baseline	View	31	-4.07	30	0.00	**	-0.73	-1.122	-0.328
PDT	HC	Baseline	Imagery	31	-3.82	30	0.00	**	-0.686	-1.074	-0.289
CPM_PTT	All	View	VR	55	0.36	54	0.83	ns			
CPM_PTT	All	Imagery	VR	55	0.39	54	0.83	ns			
CPM_PTT	All	Imagery	View	55	0.08	54	0.94	ns			
CPM_PTT	All	Baseline	VR	55	3.31	54	0.01	**	0.446	0.167	0.721
CPM_PTT	All	Baseline	View	55	3.12	54	0.01	*	0.421	0.143	0.695
CPM_PTT	All	Baseline	Imagery	55	2.96	54	0.01	*	0.399	0.123	0.672
CPM_PDT	CP	View	VR	27	-0.11	26	0.94	ns			
CPM_PDT	CP	Imagery	VR	27	-0.18	26	0.92	ns			
CPM_PDT	CP	Imagery	View	27	-0.08	26	0.94	ns			
CPM_PDT	CP	Baseline	VR	27	0.23	26	0.89	ns			
CPM_PDT	CP	Baseline	View	27	0.31	26	0.84	ns			

CPM_PDT	CP	Baseline	Imagery	27	0.34	26	0.84	ns			
CPM_PDT	HC	View	VR	28	0.80	27	0.60	ns			
CPM_PDT	HC	Imagery	VR	28	1.35	27	0.28	ns			
CPM_PDT	HC	Imagery	View	28	0.76	27	0.61	ns			
CPM_PDT	HC	Baseline	VR	28	5.19	27	0.00	***	0.981	0.522	1.428
CPM_PDT	HC	Baseline	View	28	3.15	27	0.01	*	0.595	0.188	0.994
CPM_PDT	HC	Baseline	Imagery	28	2.62	27	0.03	*	0.495	0.098	0.884

Legend: Post-hoc (paired) t-tests between the different conditions for the dependent variables (DV) PDT, CPM_PDT/PTT and SSP_PDT stratified for group in case of a significant interaction effect.

Table S4: Pre-Analysis tests

<i>DV</i>	<i>group</i>	<i>condition</i>	<i>n</i>	<i>df</i>	<i>t</i>	<i>p</i>	<i>p_sig</i>	<i>d_z</i>	<i>low</i>	<i>high</i>
TSP	CP	VR	21	20	5.14	0.00	***	1.122	0.563	1.663
TSP	HC	VR	20	19	2.77	0.01	*	0.619	0.132	1.092
TSP	CP	View	21	20	4.10	0.00	***	0.895	0.379	1.396

TSP	HC	View	20	19	2.37	0.03	*	0.529	0.054	0.992
TSP	CP	Imagine	21	20	4.71	0.00	***	1.028	0.488	1.552
TSP	HC	Imagine	20	19	2.32	0.03	*	0.518	0.044	0.98
TSP	CP	Baseline	21	20	5.21	0.00	***	1.137	0.576	1.681
TSP	HC	Baseline	20	19	3.06	0.01	**	0.683	0.188	1.165
Spat_PTT	CP	VR	28	27	-4.45	0.00	***	-0.84	-1.267	-0.402
Spat_PTT	HC	VR	31	30	-4.47	0.00	***	-0.803	-1.204	-0.392
Spat_PTT	CP	View	28	27	-4.18	0.00	***	-0.791	-1.211	-0.36
Spat_PTT	HC	View	31	30	-5.01	0.00	***	-0.9	-1.313	-0.476
Spat_PTT	CP	Imagine	28	27	-4.64	0.00	***	-0.876	-1.308	-0.433
Spat_PTT	HC	Imagine	31	30	-2.65	0.01	*	-0.476	-0.844	-0.1
Spat_PTT	CP	Baseline	28	27	-2.75	0.01	*	-0.52	-0.911	-0.12
Spat_PTT	HC	Baseline	31	30	-3.96	0.00	***	-0.712	-1.102	-0.312
Spat_PDT	CP	VR	28	27	-2.94	0.01	**	-0.555	-0.949	-0.152

Spat_PDT	HC	VR	31	30	-4.34	0.00	***	-0.78	-1.178	-0.372
Spat_PDT	CP	View	28	27	-3.09	0.00	**	-0.585	-0.982	-0.179
Spat_PDT	HC	View	31	30	-3.77	0.00	***	-0.677	-1.063	-0.281
Spat_PDT	CP	Imagine	28	27	-2.37	0.02	*	-0.448	-0.833	-0.055
Spat_PDT	HC	Imagine	31	30	-1.95	0.06	ns			
Spat_PDT	CP	Baseline	28	27	-2.41	0.02	*	-0.456	-0.842	-0.063
Spat_PDT	HC	Baseline	31	30	-2.06	0.05	*	-0.37	-0.732	-0.003
Cpm_PTT	CP	VR	27	26	-0.11	0.92	ns			
Cpm_PTT	HC	VR	28	27	-2.41	0.02	*	-0.455	-0.841	-0.062
Cpm_PTT	CP	View	27	26	1.64	0.11	ns			
Cpm_PTT	HC	View	28	27	-3.37	0.00	**	-0.637	-1.039	-0.225
Cpm_PTT	CP	Imagine	27	26	-0.56	0.58	ns			
Cpm_PTT	HC	Imagine	28	27	-1.57	0.13	ns			
Cpm_PTT	CP	Baseline	27	26	2.10	0.04	*	0.405	0.008	0.794

Cpm_PTT	HC	Baseline	28	27	1.14	0.27	ns			
Cpm_PDT	CP	VR	27	26	0.55	0.59	ns			
Cpm_PDT	HC	VR	28	27	-3.17	0.00	**	-0.599	-0.998	-0.192
Cpm_PDT	CP	View	27	26	0.56	0.58	ns			
Cpm_PDT	HC	View	28	27	-2.76	0.01	*	-0.522	-0.913	-0.122
Cpm_PDT	CP	Imagine	27	26	0.47	0.64	ns			
Cpm_PDT	HC	Imagine	28	27	-1.44	0.16	ns			
Cpm_PDT	CP	Baseline	27	26	0.61	0.55	ns			
Cpm_PDT	HC	Baseline	28	27	2.27	0.03	*	0.428	0.037	0.812

Legend: Pre-Analysis (paired) t-tests between the for the dependent variables (DV) CPM_PDT/PTT, TSP,SSP_PDT/PTT stratified for group and condition.