**Table 1.** Study demographics and prior publications

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **No** | **Study name** | ***N*** | **Gender** | **Ages** | **Prior publications** | **Other experimental manipulations** |
| Study 1 | bmrk3 | 33 | 22 F | 27.9 (9.0) | Woo et al., 2015 Plos Biology, Lindquist et al. 2017, \*Woo et al. 2017, Geuter 2020 Cerebral cortex | Cognitive self-regulation intervention to increase or decrease pain |
| Study 2 | bmrk4 | 28 | 10 F | 25.2 (7.4) | Chang et al., 2015, Krishnan et al. 2016 eLife, Lindquist et al. 2017, \*Woo et al. 2017, Geuter 2020 Cerebral cortex | Combination of painful stimuli with heat-predictive visual cues |
| Study 3 | bmrk5 | 93 | 49 F | 28.7 (5.7) | Losin et al., 2020 Nature Human Behavior, Geuter 2020 Cerebral cortex | None |
| Study 4 | exp | 17 | 9 F | 25.5 (?) | Atlas et al., 2010 Journal of Neuroscience; Lindquist et al. 2017, \*Woo et al. 2017, Geuter 2020 Cerebral cortex | Combination of painful stimuli with heat-predictive auditory cues |
| Study 5 | ie | 50 | 27 F | 25.1 (6.9) | Roy et al., 2014 Nature Neuroscience, Lindquist et al. 2017, \*Woo et al. 2017, Geuter 2020 Cerebral cortex | Combination of painful stimuli with heat-predictive visual cues and with a placebo manipulation |
| Study 6 | ie2 | 19 | 10F | 25.5(9.5) | Jepma et al., 2018 Nature Human behaviour, Geuter 2020 Cerebral cortex | Combination of painful stimuli with heat-predictive visual cues |
| Study 7 | ilcp | 29 | 16 F | 20.4 (3.3) | Lindquist et al. 2017, \*Woo et al. 2017 | Combination of painful stimuli with intervention for perceived control (making vs. observing cue choice) and expectancy (80% vs. 50% probabilities of low pain) |
| Study 8 | nsf | 26 | 9 F | 27.8 (7.5) | Wager et al., 2013; Atlas et al., 2014, \*Lindquist et al. 2017, \*Woo et al. 2017, Geuter 2020 Cerebral cortex | Combination of painful stimuli with masked emotional faces evenly crossed with temperature |
| Study 9 | scebl | 26 | 11 F | 28 (9.3) | Koban 2019 Nature Communication; Lindquist et al. 2017, \*Woo et al. 2017 | Combination of painful stimuli with heat-predictive visual cues and unreinforced social information |

**Table 2.** Stimulation protocol

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Study number** | **Stimulated locations** | **Number of sites** | **Mean pain ratings by intensity level (within-subjects SEM)** | **Number of intensity levels** | **Fixed vs. calibrated** | **Stimulus Duration (seconds)** | **Rating Scale** | **Other experimental manipulations** |
| Study 1 (bmrk3) | Arm | 2 | 49.1, 56.6, 74.3, 99.4, 133.0, 159.3 (3.12) | 6 (44.3-49.3ºC) | Fix | 12.5 | 0-200 VASa | Cognitive self-regulation intervention to increase or decrease pain |
| Study 2 (bmrk4) | Arm, Foot | Arm: 4, Foot:4 | UL: 31.7, 40.5, 53.6 (0.9787) LL: 31.5, 40.2, 53.3 (0.96) | 3 (46-48ºC) | Fix | 11 | 0-100 LMSb | Heat-predictive viCombination of painful stimuli with heat-predictive visual cues sual cues for low, medium, and high pain |
| Study 3 (bmrk5) | Inner forearm | 4 | L: M=32.10, SD= 20.22; M: M= 41.94, SD= 20.36;  H: M=50.34, SD= 21.20\* | 3 (47°C, 48°C, 49°C) | Fix | (8 and) 11 | 0-100 LMSb | none |
| Study 4 (exp) | Arm | 4 | 2.5, 4.3, 7.4 (0.13) | 4 (L/M/H) | Cal | 10 | 0-10 VASc | Combination of painful stimuli with heat-predictive auditory cues |
| Study 5 (ie) | Arm | 6 | 29.4, 38.9, 51.9 (0.64) | 3 (46-48ºC) | Fix | 11 | 0-100 VASd | Combination of painful stimuli with heat-predictive visual cues and with a placebo manipulation |
| Study 6 (ie2) | Lower leg | 5 | L: M = 27.59, SD = 10.35  H: M = 31.82, SD = 11.12 | 2 (L48 ºC/H49 ºC) | Fix | 1.85 | 0-100 VASd | Combination of painful stimuli with heat-predictive visual cues |
| Study 7 (ilcp) | Arm | 2 | 24.3, 46.7 (1.14) | 2 (L44.7°/H46.7) | Cal | 10 | 0-100 VASd | Combination of painful stimuli with intervention for perceived control (making vs. observing cue choice) and expectancy (80% vs. 50% probabilities of low pain) |
| Study 8 (nsf) | Arm | 3 | 2.0, 2.8, 4.2, 6.6 (0.14) | 4 (PT/L/M/H) | Cal | 10 | 0-10 VASc | Combination of painful stimuli with masked emotional faces evenly crossed with temperature |
| Study 9 (scebl) | Leg | 6 | 26.0, 33.3, 40.4 (1.12) | 3 (48, 49, 50) | Fix | 1.85 | 0–100 VAS | Combination of painful stimuli with heat-predictive visual cues and unreinforced social information |

Note: PT, pain threshold; L, Low painful heat; M, Medium painful heat; H, High painful heat; F, Fixed; C, Calibrated; VAS, visual analog scale. LMS, labelled magnitude scale. aPain vs. no-pain decision followed by 0-100 VAS for either warmth or pain rating (=2x100). b:0, no sensation; 1.4, barely detectable; 6.1, weak; 17.2, moderate; 35.4, strong; 53.3, very strong; 100, strongest imaginable sensation. c:0, no sensation; 1, non-painful warmth; 2, lopain; 5, moderate pain; 8, maximum tolerable pain. d:0, no pain; 100, worst imaginable pain. \*The data of study 3 (bmrk5) in the rating column it is not AUC of the continuous rating transformed into a 0-100 scale but the “rating” measure is actually the peak of the continuous rating.

**Table 3.** Imaging Acquisition parameters

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Study number** | **No. of trials/ subjects** | **Mean No. of excluded trials  (high VIFs)** | **Study location** | **Scanner details** | **EPI parameters** | **Voxel size (mm3)** | **Acquisition parameters** | **Discarded volumes** | **Stimulus software** | **Analysis software** |
| **Study 1** (bmrk3) | 97 | 6.8 | Columbia | 3T Phillips Achieva TX | TR = 2000ms; TE = 20ms; FOV = 224mm; Matrix = 64 x 64; Flip angle = 72° | 3.0 x 3.0 x 3.0 | 42 Slices Interleaved SENSE = 1.5 | 4 | E-prime | SPM8 |
| **Study 2** (bmrk4) | 81 | 6.1 | CU Boulder | 3T Siemens Tim Trio | TR = 1300ms; TE = 25ms; FOV = 220mm Matrix = 64 x 64; Flip angle = 50° | 3.4 x 3.4 x 3.4 | 26 Slices Interleaved iPAT = 2 | 6 | MATLAB | SPM8 |
| **Study 3** (bmrk5) | 36 heat trials | 3.5 | CU Boulder | 3T Siemens Tim Trio | \*TR = 460ms; TE = 29ms; FOV = 248mm; Flip angle = 44° | \*3.0 x 3.0 x 3.0 | 56 slices, multiband factor: 8 | 20\*\* | MATLAB | SPM8 |
| **Study 4** (exp) | 64 | 2.1 | Columbia | 1.5T GE Signa TwinSpeed Excite HD | TR = 2000ms; TE = 40ms; FOV = 224mm Matrix = 64 x 64; Flip angle = 84° | 3.5 x 3.5 x 4.55 | 24 Slices T2\*-weighted spiral in/out pulse | 5 | E-prime | SPM5 |
| **Study 5** (ie) | 48 | 5.7 | CU Boulder | 3T Siemens Tim Trio | TR = 1300ms; TE = 25ms; FOV = 220mm Matrix = 64 x 64; Flip angle = 75° | 3.4 x 3.4 x 3.0 | 26 Slices Interleaved iPAT = 2 | 6 | E-prime | SPM8 |
| **Study 6** (ie2) | 70 | 1.1 | CU Boulder | 3T Siemens Tim Trio | TR = 1300ms; TE = 25ms; FOV = 220mm Matrix = 64 x 64; Flip angle = 75° | 3.4 x 3.4 x 3.0 | 26 Slices Interleaved iPAT = 2 | 6 | E-prime | SPM8 |
| **Study 7** (ilcp) | 64 | 1 | CU Boulder | 3T Siemens Tim Trio | TR = 1980ms; TE = 25ms; FOV = 220mm Matrix = 64 x 64; Flip angle = 75° | 3.4 x 3.4 x 3.0 | 35 Slices Interleaved iPAT = 0 | 5 | E-prime | SPM8 |
| **Study 8** (nsf) | 48 | 2.7 | Columbia | 1.5T GE Signa TwinSpeed Excite HD | TR = 2000ms; TE = 3 ms; FOV = 224mm Matrix = 64 x 64 | 3.5 x 3.5 x 4.0 | 29 Slices | 5 | E-prime | SPM5, 8 |
| **Study 9** (scebl) | 96 | 4 | CU Boulder | 3T Siemens Tim Trio | TR = 1300 ms; TE = 25ms; FOV = 220mm Matrix = 64 x 64; Flip angle = 50° | 3.4 x 3.4 x 3.4 | 26 Slices Interleaved iPAT = 2 | 3 | E-prime | SPM8 |

Note: R, Time to repeat; TE, Time to echo; FOV, Field of view. \*First 25 participants were assessed with TR = 460ms, TE = 29ms, FOV = 248mm, and a Flip angle = 44°, than because of inference problems between multiband sequence and thermal stimulator after software uptdate, the remaining 63 participants were assessed with TR = 1300ms, TE = 25ms, FOV = 220mm, a Flip angle = 50°, and a voxel size of 3.4 x 3.4 x 3.4 mm; standard EPI; \*\* Discarded volumes for the remaining 63 subjects: 7.

**Table S1.** Inferential statistics for four types of NPS effects in Studies 1-9

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Study number** | **Mean response of NPS** | | | |  | **Within subject correlation with temperature** | | | | |  | **Within subject correlation with pain** | | | | |  | **Between subject correlation with pain** | | |
|  | t | df | p | d |  | Within-r | t | df | p | d |  | Within-r | t | df | p | d |  | Between-r | p | d |
| **Study 1** (bmrk3) | 10.19 | 32 | 1.44e-11 | 1.77 |  | 0.27 | 6.25 | 32 | 5.28e-07 | 1.09 |  | 0.28 | 6.39 | 32 | 3.51e-07 | 1.11 |  | -0.13 | 0.46 | -0.27 |
| **Study 2** (bmrk4) | 13.86 | 27 | 8.65e-14 | 2.62 |  | 0.30 | 10.98 | 27 | 1.85e-11 | 2.07 |  | 0.33 | 8.69 | 27 | 2.64e-09 | 1.64 |  | 0.16 | 0.40 | 0.33 |
| **Study 3** (bmrk5) | 19.05 | 91 | 1.66e-33 | 1.99 |  | 0.22 | 9.20 | 91 | 1.20e-14 | 0.96 |  | 0.23 | 9.83 | 91 | 5.82e-16 | 1.02 |  | 0.04 | 0.70 | 0.08 |
| **Study 4** (exp) | 5.02 | 16 | 0.13e-3 | 1.22 |  | 0.31 | 6.91 | 16 | 3.50e-06 | 1.68 |  | 0.34 | 6.58 | 16 | 6.31e-06 | 1.59 |  | 0.74 | 0.69e-3 | 2.20 |
| **Study 5**  (ie) | 17.07 | 49 | 2.92e-22 | 2.41 |  | 0.42 | 18.91 | 49 | 3.72e-24 | 2.67 |  | 0.35 | 13.56 | 49 | 3.30e-18 | 1.92 |  | 0.19 | 0.18 | 0.39 |
| **Study 6** (ie2) | 6.97 | 18 | 1.64e-06 | 1.60 |  | 0.05 | 2.32 | 18 | 0.03 | 0.53 |  | 0.14 | 5.22 | 18 | 5.77e-05 | 1.20 |  | 0.31 | 0.20 | 0.65 |
| **Study 7** (ilcp) | 8.91 | 28 | 1.15e-09 | 1.65 |  | 0.30 | 11.65 | 28 | 2.99e-12 | 2.16 |  | 0.35 | 11.49 | 28 | 4.11e-12 | 2.13 |  | 0.04 | 0.86 | 0.07 |
| **Study 8** (nsf) | 10.76 | 25 | 7.14e-11 | 2.11 |  | 0.41 | 13.98 | 25 | 2.56e-13 | 2.74 |  | 0.42 | 10.57 | 25 | 1.04e-10 | 2.07 |  | 0.55 | 0.38e-2 | 1.31 |
| **Study 9** (scebl) | 10.60 | 25 | 9.69e-11 | 2.08 |  | 0.13 | 4.20 | 25 | 0.29e-3 | 0.82 |  | 0.17 | 4.81 | 25 | 6.04e-05 | 0.94 |  | 0.22 | 0.27 | 0.46 |
| **Mean** |  |  |  | **1.94** |  |  |  |  |  | **1.64** |  |  |  |  |  | **1.52** |  |  |  | **0.58** |

**Table S2.** Inferential statistics comparing whole-NPS with local NPS responses in Studies 1-9

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Rank** | **Mean response** | | | |  | **Within subject correlation with temperature** | | | |  | **Within subject correlation with pain** | | | |  | | **Between subject correlation with pain** | | | | |
|  |  | Brain region | Mean (se) | t | p (fdr) |  | Brain region | Mean (se) | t | p (fdr) |  | Brain region | Mean (se) | t | p (fdr) | |  | | Brain region | Mean (se) | t | p (fdr) |
|  |  | NPS | 1.94 (0.14) |  |  |  | NPS | 1.64 (0.27) |  |  |  | NPS | 1.52 (0.15) |  |  | |  | | NPS | 0.58 (0.25) |  |  |
| **Positive regions** | **Rank 1** | rIns | 1.69 (0.17) | 2.10 | 6.95e-02 |  | rIns | 1.24 (0.23) | 1.11 | 2.82e-01 |  | dACC | 1.20 (0.11) | 1.67 | 1.16e-01 | |  | | rdpIns | 0.42 (0.27) | 1.12 | 0.31 |
| **Rank 2** | rdpIns | 1.46 (0.10) | 4.22 | 3.15e-03 |  | dACC | 1.14 (0.19) | 2.13 | 6.37e-02 |  | rIns | 1.15 (0.13) | 1.82 | 9.42e-02 | |  | | rIns | 0.39 (0.13) | 1.08 | 0.31 |
| **Rank 3** | rS2 | 1.26 (0.14) | 6.24 | 5.34e-04 |  | rdpIns | 0.98 (0.14) | 2.82 | 2.17e-02 |  | lIns | 1.06 (0.09) | 2.59 | 2.64e-02 | |  | | rThal | 0.34 (0.15) | 1.50 | 0.24 |
| **Rank 4** | lIns | 1.15 (0.17) | 6.57 | 4.38e-04 |  | lIns | 0.97 (0.16) | 2.10 | 6.37e-02 |  | rdpIns | 1.01 (0.12) | 2.61 | 2.46e-02 | |  | | dACC | 0.31 (0.16) | 1.60 | 0.22 |
| **Rank 5** | dACC | 1.01 (0.16) | 10.43 | 4.66e-05 |  | rS2 | 0.78 (0.13) | 1.48 | 1.72e-01 |  | rS2 | 0.87 (0.08) | 3.68 | 4.07e-03 | |  | | vermis | 0.30 (0.10) | 1.25 | 0.29 |
| **Rank 6** | rThal | 0.66 (0.15) | 7.69 | 1.74e-04 |  | rThal | 0.74 (0.12) | 2.97 | 1.89e-02 |  | rThal | 0.83 (0.08) | 4.01 | 2.73e-03 | |  | | rS2 | 0.29 (0.18) | 2.46 | 0.12 |
| **Rank 7** | vermis | 0.43 (0.10) | 11.33 | 4.66e-04 |  | vermis | 0.61 (0.13) | 3.36 | 9.78e-03 |  | vermis | 0.76 (0.11) | 4.06 | 1.89e-03 | |  | | lIns | 0.28 (0.10) | 1.41 | 0.25 |
| **Rank 8** | rV1 | -0.77 (0.29) | 8.23 | 1.74e-04 |  | rV1 | 0.19 (0.17) | 4.46 | 1.24e-03 |  | rV1 | 0.20 (0.17) | 5.66 | 8.13e-05 | |  | | rV1 | 0.19 (0.07) | 1.68 | 0.22 |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | |  | |  |  |  |  |
| **Negative regions** | **Rank 1** | rIPL | 0.84 (0.24) | 4.34 | 3.11e-03 |  | rIPL | 0.30 (0.19) | 4.02 | 2.31e-03 |  | rIPL | 0.23 (0.20) | 5.15 | 2.17e-04 | |  | | pgACC | 0.13 (0.14) | 2.06 | 0.16 |
| **Rank 2** | lLOC | 0.62 (0.30) | 4.21 | 3.15e-03 |  | lSTS | 0.17 (0.18) | 4.80 | 1.20e-03 |  | pgACC | 0.18 (0.13) | 6.70 | 2.33e-05 | |  | | rLOC | 0.03 (0.15) | 2.47 | 0.12 |
| **Rank 3** | rpLOC | 0.50 (0.28) | 4.93 | 1.93e-03 |  | pgACC | 0.13 (0.14) | 5.03 | 1.20e-03 |  | lSTS | 0.07 (0.18) | 6.17 | 4.34e-05 | |  | | rpLOC | 0.02 (0.11) | 1.84 | 0.19 |
| **Rank 4** | rLOC | 0.50 (0.28) | 4.73 | 2.23e-03 |  | rLOC | 0.12 (0.18) | 4.63 | 1.20e-03 |  | rpLOC | 0.06 (0.12) | 7.42 | 1.78e-05 | |  | | lLOC | -0.00 (0.13) | 2.56 | 0.12 |
| **Rank 5** | pgACC | 0.49 (0.20) | 5.93 | 6.58e-04 |  | rpLOC | 0.10 (0.14) | 4.89 | 1.20e-03 |  | lLOC | 0.05 (0.15) | 6.90 | 1.81e-05 | |  | | lSTS | -0.01 (0.11) | 2.22 | 0.14 |
| **Rank 6** | PCC | 0.45 (0.25) | 4.49 | 2.78e-03 |  | lLOC | 0.07 (0.18) | 4.95 | 1.20e-03 |  | rLOC | 0.04 (0.19) | 6.00 | 5.57e-05 | |  | | rIPL | -0.18 (0.17) | 3.24 | 0.12 |
| **Rank 7** | lSTS | 0.18 (0.17) | 7.85 | 1.74e-04 |  | PCC | -0.13 (0.23) | 4.45 | 1.24e-03 |  | PCC | -0.25 (0.19) | 7.26 | 1.78e-05 | |  | | PCC | -0.25 (0.15) | 2.58 | 0.12 |

Note: Paired t-tests treating study as the unit of observation (i.e., study is a random effect). Ins denotes Insula, V1 primary visual area, S2 secondary somatosensory cortex, ACC anterior cingulate cortex, Thal thalamus, STS superior temporal sulcus, PCC posterior cingulate cortex, LOC lateral occipital complex, and IPL inferior parietal lobule. Direction is indicated with preceding lowercase letters as follows: r denotes right, l left, d dorsal, p posterior, pg perigenual.

**Table S3.** Paired t-tests of reliability ICC(3,k) between NPS and local brain areas

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | **Rank** | Brain region | Mean (se) | t | p (fdr) |
|  |  | NPS | 0.83 (0.03) |  |  |
| **Positive Region** | **Rank 1** | rIns | 0.80 (0.04) | 0.72 | 0.49 |
| **Rank 2** | rV1 | 0.79 (0.05) | 0.81 | 0.47 |
| **Rank 3** | rS2 | 0.78 (0.05) | 1.26 | 0.30 |
| **Rank 4** | rdpIns | 0.74 (0.05) | 2.19 | 0.13 |
| **Rank 5** | dACC | 0.74 (0.07) | 1.57 | 0.23 |
| **Rank 6** | lIns | 0.72 (0.10) | 1.19 | 0.31 |
| **Rank 7** | vermis | 0.59 (0.14) | 1.80 | 0.18 |
| **Rank 8** | rThal | 0.59 (0.07) | 4.24 | 0.02 |
|  |  |  |  |  |  |
| **Negative Region** | **Rank 1** | lSTS | 0.69 (0.07) | 2.47 | 0.13 |
| **Rank 2** | PCC | 0.68 (0.07) | 2.56 | 0.13 |
| **Rank 3** | rpLOC | 0.65 (0.12) | 1.48 | 0.24 |
| **Rank 4** | lLOC | 0.64 (0.10) | 2.25 | 0.13 |
| **Rank 5** | rIPL | 0.64 (0.09) | 2.24 | 0.13 |
| **Rank 6** | rLOC | 0.58 (0.14) | 2.00 | 0.15 |
| **Rank 7** | pgACC | 0.54 (0.08) | 4.86 | 0.02 |

Note: Ins denotes Insula, V1 primary visual area, S2 secondary somatosensory cortex, ACC anterior cingulate cortex, Thal thalamus, STS superior temporal sulcus, PCC posterior cingulate cortex, LOC lateral occipital complex, and IPL inferior parietal lobule. Direction is indicated with preceding lowercase letters as follows: r denotes right, l left, d dorsal, p posterior, pg perigenual.

**Table S4.** Comparison of NPS performance among three computation methods

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Index** | **Mean response** | | |  | **Within subject correlation with temperature** | | |  | **Within subject correlation with pain** | | |  | **Between subject correlation with pain** | | |  | **Reliability** | | |
|  | Mean (se) | F | p |  | Mean (se) | F | p |  | Mean (se) | F | p |  | Mean (se) | F | p |  | Mean (se) | F | p |
| **dot product** | 1.94 (0.14) | 0.95 | 0.40 |  | 1.64 (0.27) | 0.14 | 0.87 |  | 1.52 (0.15) | 0.49 | 0.62 |  | 0.58 (0.24) | 0.12 | 0.89 |  | 0.83 (0.03) | 0.03 | 0.97 |
| **correlation** | 2.28 (0.20) |  | 1.46 (0.28) |  | 1.28 (0.21) |  | 0.42 (0.25) |  | 0.82 (0.03) |
| **cosine** | 2.18 (0.19) |  | 1.45 (0.27) |  | 1.30 (0.20) |  | 0.44 (0.26) |  | 0.83 (0.03) |

Note: study as rfx….(stats)