Supplementary Materials:

Modulating Subjective Pain Perception with Decoded MNI-space Neurofeedback: A Proof-of-Concept Study

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Supplementary methods

Data Analysis

Induction Success.

We used multilevel modeling to examine if each group was able to successfully modulate SIIPS induction. Furthermore, we evaluated if NPS activity (which was not the target of training) was also affected by the intervention. In this model, trial and log(trial) are included as level 1 predictors in order to control for habituation/sensitization, while day (1 to 4) is at level 1 to control for changes in induction success across time. In this model, group (up- or downregulation) and decoder type (SIIPS or NPS) are level 2. Trial and log(trial) are grand mean centered, group and decoder type are effect coded, and day is continuous. Bootstrapped estimates were computed using the *tab_model* function in the *sjPlot* package [24] for all models based on bootstrapped distributions (10000 replications, resampled at the trial level). The same function was used to compute marginal and conditional R^2 values. All multilevel models were built using fixed predictors that should influence the outcome variable based on theory. Additional random effects were tested, but only those that improved the overall model fit were included in the final model. The null model had an ICC of .003.

The multilevel model can be represented by the following equation:

$$
\begin{aligned}
&\text{Level 1:} \quad Induction_{ij} = \beta_{0j} + \beta_{1j} Trial_{ij} + \beta_{2j} \log(Trial)_{ij} + \beta_{3j} Day_{ij} + R_{ij} \\
&\text{Level 2:} \quad \beta_{0j} = \gamma_{00} + \gamma_{01} Group_j + \gamma_{02} DecoderType_j + U_{0j} \\
&\qquad\qquad \beta_{1j} = \gamma_{10} \\
&\qquad\qquad \beta_{2j} = \gamma_{20} \\
&\qquad\qquad \beta_{3j} = \gamma_{30} + \gamma_{31} Group_j + \gamma_{32} DecoderType_j + \gamma_{33} Group_j DecoderType_j
\end{aligned}
\tag{1}
$$

In model 1, induction success ($Induction_{ij}$) for each participant (denoted by *j*) on each trial (denoted by *i*) is predicted by the level 1 variables trial (γ_{10}), log(trial) (γ_{20}), and day (γ_{30}), and

the level 2 variables group (γ_{01}) and decoder type (γ_{02}). There are also cross-level interactions examining groups across days (γ_{31}), decoder type across days (γ_{32}), as well as group and decoder type across days (γ_{33}). This model also contains the fixed component of the intercept (γ_{00}), a random component which is the intercept variance for each person (U_{0j}) with total variance τ^2, and the level 1 residual (R_{ij}) with variance σ^2.

In order to further investigate the interactions, we next ran two different multilevel models - one for each decoder - to determine if participants were able to modulate SIIPS and NPS induction separately across days. In these models, trial, log(trial), and day are level 1 predictors, while group is level 2. The ICCs for the null models were .006 for SIIPS (i.e., model 2) and .117 for NPS (i.e., model 3). The following equations represent the models:

$$\begin{aligned} &\text{Level 1:} \quad Induction_{ij} = \beta_{0j} + \beta_{1j} Trial_{ij} + \beta_{2j} \log(Trial)_{ij} + \beta_{3j} Day_{ij} + R_{ij} \\ &\text{Level 2:} \quad \beta_{0j} = \gamma_{00} + \gamma_{01} Group_j + U_{0j} \\ &\qquad\qquad \beta_{1j} = \gamma_{10} \\ &\qquad\qquad \beta_{2j} = \gamma_{20} \\ &\qquad\qquad \beta_{3j} = \gamma_{30} + \gamma_{31} Group_j \end{aligned} \tag{2, 3}$$

In models 2 and 3, SIIPS and NPS induction ($Induction_{ij}$) for each participant on each trial is predicted by the level 1 variables trial (γ_{10}), log(trial)(γ_{20}), and day (γ_{30}), and the level 2 variable group (γ_{01}). There is also a cross-level group by day interaction (γ_{31}). These models also contain a fixed intercept (γ_{00}), random intercept variance for each person (U_{0j}) with total variance τ^2, and a level 1 residual error (R_{ij}) with variance σ^2.

Next, we wanted to further examine if each group was able to separately modulate SIIPS

induction. To examine this, two multilevel models were run: one for the upregulation and one for the downregulation group. The ICCs for the null models were .001 for the upregulation group (i.e., model 4), and .044 for the downregulation group (i.e., model 5). These models can be represented by the below equations:

$$\begin{aligned}
&\text{Level 1:} \quad Induction_{ij} = \beta_{0j} + \beta_{1j}Trial_{ij} + \beta_{2j}\log(Trial)_{ij} + \beta_{3j}Day_{ij} + R_{ij} \\
&\text{Level 2:} \quad \beta_{0j} = \gamma_{00} + U_{0j} \\
&\qquad\qquad \beta_{1j} = \gamma_{10} \\
&\qquad\qquad \beta_{2j} = \gamma_{20} \\
&\qquad\qquad \beta_{3j} = \gamma_{30}
\end{aligned} \tag{4, 5}$$

Here - in models 4 and 5 - SIIPS induction for each individual in each group is being predicted. All other variables are the same as in the previous models.

Pain ratings.

To determine if pain ratings on day five were related to SIIPS induction, we employed multilevel modeling. In this model, condition (i.e., whether or not dot-motion was viewed during induction), trial, and log(trial) were all level 1 predictors, while group, pre-rating (i.e., pain ratings from day one), and SIIPS induction were all level 2. The ICC for the null model is .451. The following equations represents this model:

$$\begin{aligned}
&\text{Level 1:} \quad Rating_{ij} = \beta_{0j} + \beta_{1j}Condition_{ij} + \beta_{2j}Trial_{ij} + \beta_{3j}\log(Trial)_{ij} + R_{ij} \\
&\text{Level 2:} \quad \beta_{0j} = \gamma_{00} + \gamma_{01}Group_j + \gamma_{02}Pre - Rating_j + \gamma_{03}SIIPSInduction_j + \\
&\qquad\qquad \gamma_{04}Group_jSIIPSInduction_j + U_{0j} \\
&\qquad\qquad \beta_{1j} = \gamma_{10} \\
&\qquad\qquad \beta_{2j} = \gamma_{20} \\
&\qquad\qquad \beta_{3j} = \gamma_{30}
\end{aligned} \tag{6}$$

In model 6 pain ratings on day five (for each trial of each individual in each group) is being predicted by the level 1 variables condition (γ_{10}), trial (γ_{20}), and log(trial) (γ_{30}), and the level 2

variables group (γ_{01}), pre-rating (γ_{02}), SIIPS induction (γ_{03}), and group-by-SIIPS induction (γ_{04}). This model also contains a fixed intercept (γ_{00}), random intercept variance (U_{0j}) with total variance τ^2, and a level 1 residual error (R_{ij}) with variance σ^2.

To further investigate the interaction and group effect, two more models - one for each group - were run to determine if, in each group, SIIPS induction modulates pain ratings. The ICCs for the null models were .129 for the upregulation (i.e., model 7), and .634 for the downregulation (i.e., model 8), group. These models can be represented by the following equations:

$$\begin{aligned} \text{Level 1:} \quad & Rating_{ij} = \beta_{0j} + \beta_{1j} Condition_{ij} + \beta_{2j} Trial_{ij} + \beta_{3j} \log(Trial)_{ij} + R_{ij} \\ \text{Level 2:} \quad & \beta_{0j} = \gamma_{00} + \gamma_{01} Pre - Rating_j + \gamma_{02} SIIPSInduction_j + U_{0j} \\ & \beta_{1j} = \gamma_{10} \\ & \beta_{2j} = \gamma_{20} \\ & \beta_{3j} = \gamma_{30} \end{aligned} \qquad (7, 8)$$

In models 7 and 8, pain ratings on day five for each trial for each individual is being predicted. All other variables are the same as in the previous models. All multilevel analyses were conducted in the RStudio software for statistical analysis (RStudio Team, 2020, version 1.3.1056 [25] using the *lme4* package, version 1.1.32 [26]).

Results

Table S1

Multilevel model estimates for decoder induction. Estimates are bootstrapped 10 000 times.

Predictors	*Model Estimates*	*95% CI*	*p-values*	*Bootstrapped Estimates*	*Bootstrapped 95% CI*	*p-values*
(Intercept)	537.807	[-17.334, 1092.948]	.058	539.855	[-14.675, 1107.700]	.056
Trial	28.608	[12.475, 44.740]	<.001	28.656	[12.475, 44.842]	< .001
log(Trial)	-859.382	[-1474.588, -244.176]	.006	-860.561	[-1469.599, -244.421]	.006
Group	165.949	[-384.909, 716.807]	.555	168.237	[-373.337, 710.468]	.555
Day	61.066	[-238.584, 360.716]	.690	61.327	[-241.867, 364.559]	.684
Decoder Type	575.968	[137.345, 1014.591]	.010	580.615	[149.498, 1014.651]	.012
Group x Day	349.974	[56.355, 643.593]	.019	353.599	[58.433, 640.564]	.019
Group x Decoder Type	155.017	[-283.606, 593.640]	.488	151.731	[-287.244, 589.515]	.495
Day x Decoder Type	26.787	[-266.798, 320.371]	.858	27.368	[-259.170, 317.728]	.859
Group x Day x Decoder Type	355.742	[62.158, 649.326]	.018	358.141	[66.942, 650.002]	.016
Random Effects						
σ^2	262792755.53					
τ_0^2	454993.80					
Marginal/ Conditional R^2	.005/ .007					

Note. Group is effect coded where upregulation is 1 and downregulation is -1. Decoder type: SIIPS (1) and NPS (-1)

Table S2

Multilevel model estimates for SIIPS induction across days in the Downregulation Group. Estimates are bootstrapped 10 000 times.

Predictors	*Model Estimates*	*95% CI*	*p-values*	*Bootstrapped Estimates*	*Bootstrapped 95% CI*	*p-values*
(Intercept)	808.544	[-239.565, 1856.654]	.164	807.525	[-222.701, 1860.547]	.128
Trial	14.676	[1.683, 27.668]	.027	14.744	[1.631, 27.738]	.028
log(Trial)	-391.220	[-887.949, 105.508]	.123	-391.449	[-898.474, 112.763]	.126
Day	-630.537	[-871.207, -389.867]	<.001	-632.032	[-868.812, -385.656]	<.001
Random Effects						
σ^2	48385848.15					
τ_0^2	2276303.85					
Marginal/ Conditional R^2	.009/ .054					

Table S3

Multilevel model estimates for SIIPS induction across days in the Upregulation Group. Estimates are bootstrapped 10 000 times.

Predictors	*Model Estimates*	*95% CI*	*p-values*	*Bootstrapped Estimates*	*Bootstrapped 95% CI*	*p-values*
(Intercept)	1354.016	[-780.004, 3488.036]	.225	1363.166	[-769.601, 3463.894]	.211
Trial	113.210	[40.933, 185.487]	.002	114.152	[42.233, 186.722]	.001
log(Trial)	-3461.067	[-6208.277, -713,857]	.014	-3263.528	[-6263.641, -673.236]	.012
Day	871.926	[-451.828, 2195.690]	.197	875.656	[-442.724, 2194.109]	.199
Random Effects						
σ^2	1138615295.96					
τ_0^2	1249368.08					
Marginal/ Conditional R^2	.004/ .005					

Table S4

Multilevel model estimates for pain ratings on day 5 for the Downregulation Group. Estimates are bootstrapped 10 000 times.

Predictors	*Model Estimates*	*95% CI*	*p-values*	*Bootstrapped Estimates*	*Bootstrapped 95% CI*	*p-values*
(Intercept)	60.730	[49.447, 72.012]	<.001	60.729	[49.292, 71.583]	<.001
Trial	3.172	[2.106, 4.238]	<.001	3.176	[2.106, 4.226]	<.001
log(Trial)	-18.380	[-23.471, -13.288]	<.001	-18.408	[-23.471, -13.295]	<.001
Condition	.429	[-.764, 1.623]	.480	.446	[-.735, 1.604]	.464
Pre-Rating	-.092	[-1.028, .845]	.845	-.097	[-1.007, .836]	.841
SIIPS Induction	.009	[.004, .014]	.017	.009	[.004, .014]	.001
Random Effects						
σ^2	157.22					
τ_0^2	114.36					
Marginal R^2/ Conditional R^2	.447/.680					

Table S5

Multilevel model estimates for pain ratings on day 5 for the Upregulation Group. Estimates are bootstrapped 10 000 times.

Predictors	*Model Estimates*	*95% CI*	*p-values*	*Bootstrapped Estimates*	*Bootstrapped 95% CI*	*p-values*
(Intercept)	45.539	[37.049, 54.030]	<.001	45.565	[37.248, 53.912]	<.001
Trial	3.111	[1.631, 4.591]	<.001	3.112	[1.621, 4.585]	<.001
log(Trial)	-20.992	[-28.052, -13.932]	<.001	-21.017	[-27.977, -13.987]	<.001
Condition	.769	[-.886, 2.423]	.361	.766	[-.901, 2.441]	.360
Pre-Rating	-.064	[-.957, .829]	.895	-.073	[-.978, .827]	.872
SIIPS Induction	.000	[-.002, .002]	.977	.000	[-.002, .003]	.963
Random Effects						
σ^2	236.12					
τ_0^2	63.69					
Marginal R^2/ Conditional R^2	.115/.303					

Table S6

Most effect neurofeedback strategies used by each participant on each day, and which group they belonged to.

Subject	*Day 2*	*Day 3*	*Day 4*	*Day 5*	*Group*
1	Recalled positive and strong memories	Recalled positive and strong memories	Recalled personal and nostalgic childhood memories	Recalled deep and personal memories	Downregulation
2	Focused on the centre and ignore everything else	Combination of relaxing and clearing your head, with focusing on the centre dot	Combination of relaxing and clearing your head, with focusing on the centre dot	Combination of relaxing and clearing your head, with focusing on the centre dot	Downregulation
3	Imagined wrist and finger movement	Imagined kneading dough with hands	Imagined swinging of the wrist	Imagined kneading of dough or beating a drum	Upregulation
4	Recalled emotionally strong memories and songs that reminded them of high school	Came up with a new idea or thought of different red items	Thought about an emotional song and what was important to them	Thought about an emotional song and pictured memories they enjoyed and things they want to do	Downregulation
5	Imagined the Princess and the frog dancing	Imagined the Starbucks logo and cup	Imagined a song from the *Madagascar* movie	Imagined flipping through a book from left to right	Downregulation
6	Focused on the screen and mentally described what they saw	Focused on the screen and mentally described what they saw	Mentally singing a song that was stuck in their head	Mentally singing songs that they like	Downregulation
7	Holding their breath	Tried to keep their eyes still	Tried to keep their eyes still	Tried to recreate what worked well previously	Upregulation
8	Focused only on the dots	Connected the moving dots in their minds	Connected the moving dots in their minds	Connected the moving dots in their minds	Upregulation
9	Went over a presentation for a class in their mind	Kept their mind busy by thinking of new things	Kept their mind busy by thinking of new things and making links between thoughts	Quickly kept thinking of new things	Upregulation

10	Zoning out	Imagined having a positive feeling through their arms and legs. Feeling happy	Felt grateful, trusting, calm, and happy	Imagined being happy and in love	Downregulation
11	Focused on tracking the moving dots	Focused on tracking the moving dots, rolling their eyes, and mind wandering	Tracked patterns of dots while being focused on and thinking “right to left”	Tracked patterns of dots while being focused on and thinking “right to left”	Upregulation
12	Imagined playing soccer	Focused on the headache they were experiencing	Thought of nothing and only concentrated during feedback	Did not concentrate on anything but the centre dot	Upregulation
13	Imagined doing things with their friends	Kept their mind as blank as possible	Kept their mind as blank as possible	Kept their mind as blank as possible	Downregulation
14	Imagined getting good feedback	Drew a path with their gaze between objects on the screen	Tried imagining the feedback circle	Picked an object on the screen to focus on	Downregulation
15	Moved their eyes from left to right	Looked around the screen	Thought about being scatter brained	Thought about being scatter brained	Upregulation
16	Focused on the centre dot and zoning out	Imagined having a conversation with someone	Focused on the centre dot	Changed focus on where they were looking on the screen	Downregulation