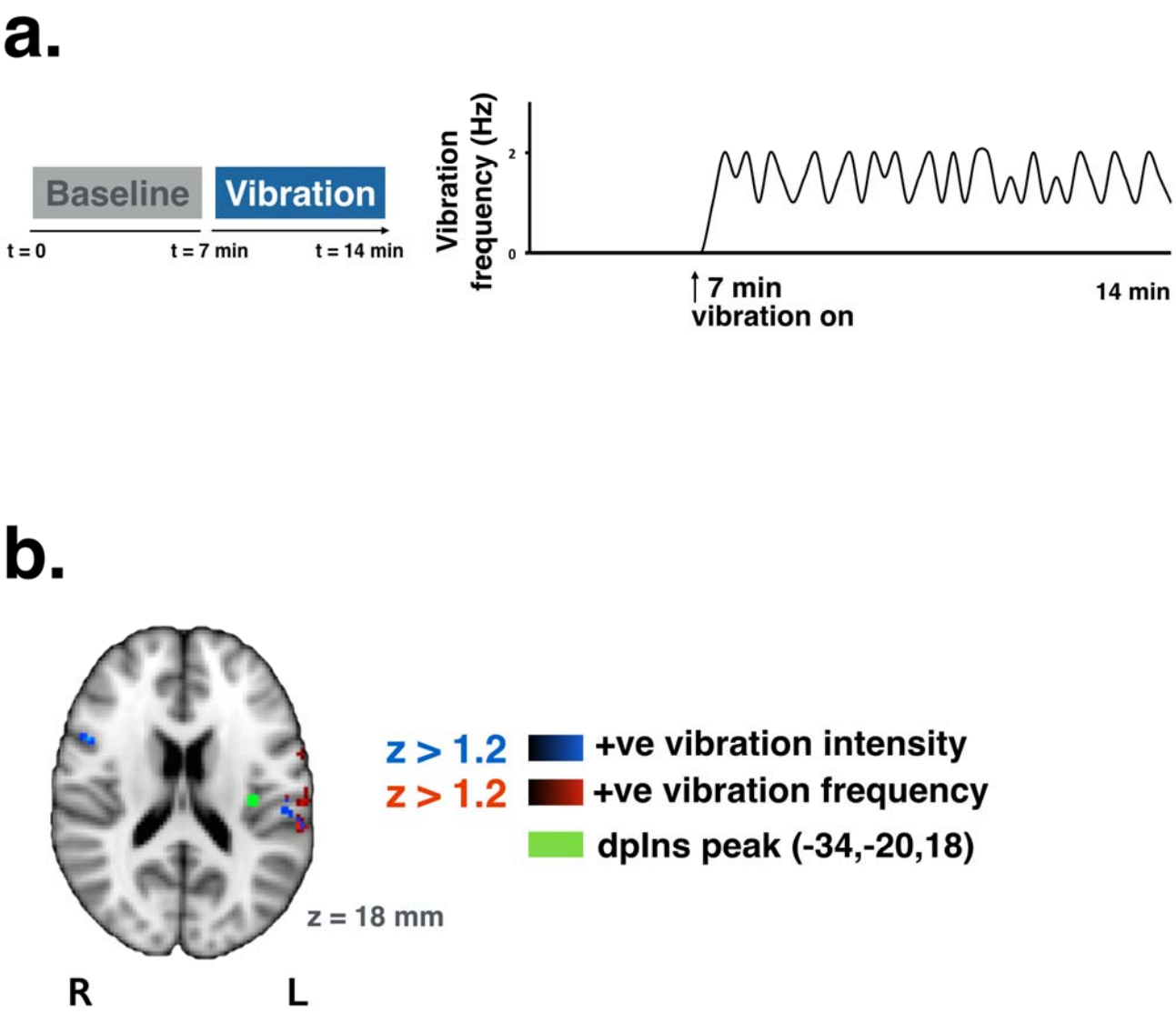
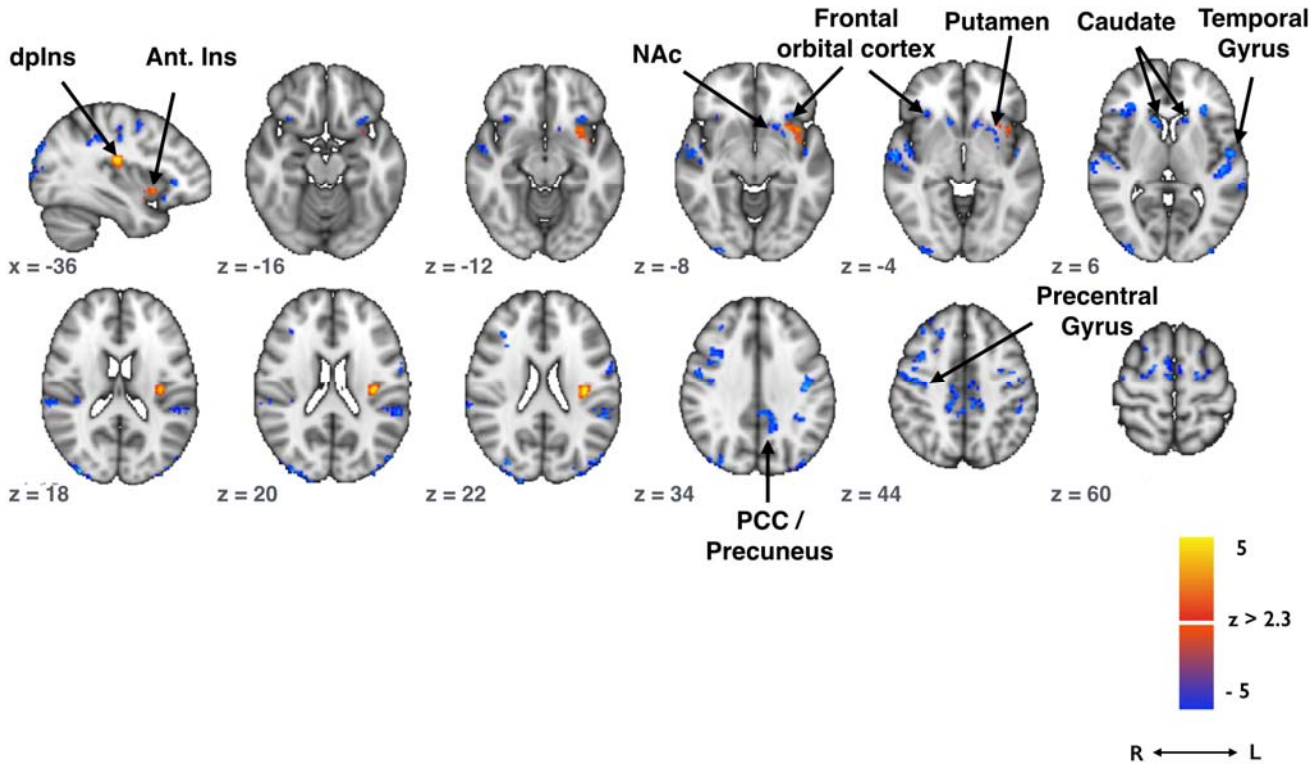


Supplementary Figure 1

Innocuous, ongoing vibration induced CBF changes.

a) Schematic of the vibration scan paradigm design that consisted of two identical multi-TI pCASL scans (parameters identical to those described in the methods section). The baseline scan consisted of no vibration stimulation (grey); while the vibration scan (blue) consisted of a continuously oscillating non-noxious stimulation of the subject's foot for the duration of the 7min scan. To minimize habituation effects, the vibration stimulus frequency was oscillated between 1-2.0 Hz (fixed amplitude of 1mA) using 0.5Hz step changes, at pseudorandom intervals between 20-60 seconds. Subjects were prompted to rate the stimulus intensity using a COVAS scale as discussed previously. None of the subjects reported the vibration stimulation as painful (group mean pain intensity = 0). The group mean vibration saliency rating for the full vibration scan was 3.12 (s.e.m. =0.265). For clarity, a plot of vibration frequency over time is displayed in Figure (a) above. b) No significant correlation was observed between absolute CBF and either the ongoing vibration intensity levels applied or with the ongoing perceived stimulus intensity levels reported by the subjects (Mixed Effects, z>2.3,

p<0.05; cluster corrected; n=12). However, sub-threshold activation clusters are visible within the contralateral medial operculum; a subsection of the "posterior insular and adjoining medial operculum" (PIMO) region that Garcia-Larrea and others have highlighted as being linked to non-noxious sensory processing. For clarity, the non-significant sub-threshold clusters are shown in (b): red pixels represent the absolute CBF increases correlated with the ongoing vibration stimulus intensity applied to the subject's foot (i.e. stimulus frequency). Blue pixels represent the absolute CBF increases correlated with the perceived stimulus intensity ratings reported by the subjects. The cluster in green represents the peak dpIns cluster that shows a strong positive correlation with ongoing pain intensity reported in the current study. Statistical maps were overlaid on selected slices of the MNI brain. Radiological convention is used (L: left; R: right).



Supplementary Figure 2

Peak pain period perfusion changes.

Absolute CBF changes during the 7-minute peak of the pain experience (peak pain period only vs baseline; Mixed Effects: $z>2.3, p<0.05$). Statistical maps were overlaid on selected slices of the MNI brain. Radiological convention is used. Orange pixels represent supra-threshold absolute CBF increases while blue pixels represent decreases. The anatomical locations for significant changes in CBF are listed in Supplementary table 2. These data highlight that the peak capsaicin pain relative to baseline is linked to positive and negative perfusion changes in a select group of brain regions, some of which have been previously shown as involved in pain processing (ref. 5 and Baliki, M.N. et al. Nat. Neurosci. **15**, 1117–1119, 2012). Importantly, the region that shows maximal hyper-perfusion during the 'peak pain' compared to baseline is localized to the contralateral dpIns (mean CBF change ± s.e.m; 15 ± 4.1% or 6.9 ± 1.9 ml / 100 g blood / min). This data supports the results from the regression analysis displayed in Figure 2; where the dpIns cluster reaches a peak of activity at the time point of maximum capsaicin-induced pain. Importantly, none of the other regions identified here show a significant correlation with the ongoing pain ratings, as we found was the case for the dpIns, even with a less strict statistical threshold. Radiological convention is used. L, left; R, right; dpIns, dorsal posterior insula; Ant. Ins, anterior insula; NAc, nucleus accumbens; PCC, posterior cingulate.

Supplementary Table 1

one-way ANOVA

Interactions	p-value (Bonferroni corrected)	F value	DOF
Time x Rating (Phase I)	0.046 *	4.201	6
Condition x Rating (full experiment)	<0.001 *	108.69	12

post hoc pairwise comparisons of pain conditions

Condition (A)	Condition (B)	Mean Difference (A-B)	p-value (Bonferroni corrected)
Baseline	Peak pain	-49.844 *	<0.001
	Habituation	-20.802 *	<0.001
	Rekindled	-56.146 *	<0.001
	Relief	-2.438 *	0.762
Peak pain	Baseline	49.844 *	<0.001
	Habituation	29.042 *	0.008
	Rekindled	-6	1
	Relief	47.406 *	<0.001
Habituation	Baseline	20.802 *	<0.001
	Peak pain	-29.042 *	0.008
	Rekindled	-35.344 *	<0.001
	Relief	18.365 *	0.002
Rekindled	Baseline	56.146 *	<0.001
	Peak pain	6	1
	Habituation	35.344 *	<0.001
	Relief	53.708 *	<0.001
Relief	Baseline	2	0.762
	Peak pain	-47.406 *	<0.001
	Habituation	-18.365 *	0.002
	Rekindled	-53.708 *	<0.001

Supplementary Table 2

	Volume	Anatomical label (COG)	COG MNI coordinates			*Peak Z-score*
CBF increases (peak > baseline)			**X**	**Y**	**Z**	
Cluster 1	728	L. insula cortex	-34	11	-9	4.36
Cluster 2	936	L. insula cortex	-35	-20	20	3.34

	Volume	Anatomical label (COG)	COG MNI coordinates			*Peak Z-score*
CBF decreases (peak < baseline)			**X**	**Y**	**Z**	
Cluster 1	968	L. post cingulate	-11	-25	42	3.39
Cluster 2	1024	L. putamen	-19	14	-2	3.18
Cluster 3	1024	R. caudate	13	18	5	3.63
Cluster 4	1032	R. trans. temporal gyrus	50	-20	10	3.56
Cluster 5	1056	R. post. cingulate	11	-26	43	3.37
Cluster 6	1096	L. supramarginal gyrus	-40	-39	39	3.35
Cluster 7	1128	L. inf. frontal gyrus	-32	26	-3	3.61
Cluster 8	1472	R. SMA	1	0	59	3.31
Cluster 9	1504	R. frontal orbital cortex	36	29	1	3.67
Cluster 10	1528	L. lat. occipital cortex	-37	-87	24	3.39
Cluster 11	1552	R. sup. frontal gyrus	29	27	46	3.44
Cluster 12	1936	L. precentral gyrus	-46	-11	36	3.77
Cluster 13	2000	L. sup. frontal gyrus	-29	-1	52	4.19
Cluster 14	2048	L. post. cingulate	-5	-43	32	3.25
Cluster 15	2872	R. lat. occipital cortex	35	-88	18	4.04
Cluster 16	3096	L. cent. opercular cortex	-51	-27	10	3.56
Cluster 17	3144	R. sup temporal gyrus	59	-16	2	3.73
Cluster 18	6136	R. mid. frontal gyrus	40	0	43	4.21