Supplemental materials

Title: Abnormal anatomical and functional connectivity of the thalamo-sensorimotor circuit in chronic low back pain: resting-state fMRI and diffusion tensor imaging study

Cui Ping Mao[1], Georgia Wilson[1], Jin Cao[1], Nathaniel Meshberg[1], Yiting Huang, Jian Kong[1]

Department of Psychiatry, Massachusetts General Hospital and Harvard Medical School, Charlestown, MA, USA 02129

The Inclusion/Exclusion criteria of chronic low back pain

Inclusion Criteria

a) Volunteers 18-60 years of age.

b) Meet the Classification Criteria of chronic low back pain (having low back pain for more than 3 months).

c) At least 4/10 clinical pain on a 0-10 continuous visual analogue scale (VAS) before the MRI scan.

d) Participants have had a prior evaluation of their low back pain by a health care provider, which may have included radiographic studies. Documentation of this evaluation will be sought from Partners or outside medical records and kept in the subject's research record.

e) At least a 10th grade English-reading level; English can be a second language, provided that the patients feel they understand all the questions used in the assessment measures.

Exclusion Criteria

a) Specific causes of back pain (e.g. cancer, fractures, spinal stenosis, infections).

b) Complicated back problems (e.g. prior back surgery, medicolegal issues).

c) Conditions making study participation difficult (e.g. paralysis, psychoses, or other severe psychological problems as per the judgment of a study investigator during Session 1).

d) The intent to undergo surgery during the time of involvement in the study.

e) History of cardiac, respiratory, or nervous system disease that, in the investigator's judgment, precludes participation in the study because of a heightened potential for adverse outcome. For example: asthma or claustrophobia.

f) Presence of any contraindications to MRI scanning. For example: cardiac pacemaker, metal

implants, fear of closed spaces, pregnancy.

g) Unresolved medical legal/disability/workers compensation claims in connection with low back pain.

h) Radicular pain extending below the knee.

i) Use of prescription opioids or steroids for pain.

j) Active substance abuse disorder in the past 24 months, as determined by self-report and/or urine toxicology.

Supplemental Table 1 Brain areas included in 6 cortical regions of interest.

Cortical ROI	Regions included	Label
Prefrontal cortex	Frontal Pole	1
	Superior Frontal Gyrus	3
	Middle Frontal Gyrus	4
	Inferior Frontal Gyrus (pars triangularis)	5
	Inferior Frontal Gyrus (pars opercularis)	6
	Frontal Medial Cortex	25
	Subcallosal Cortex	27
	Paracingulate Gyrus	28
	Cingulate Gyrus (Anterior division)	29
	Frontal Orbital Cortex	33
	Frontal Operculum Cortex	41
	Central Operculum Cortex	42
Motor Cortex	Precentral Gyrus	7
	Juxapositional Lobule Cortex (Supplementary Motor Area)	26
Somatosensory Cortex	Postcentral Gyrus	17
Parietal Cortex	Superior Parietal Lobule	18
	Supramarginal Gyrus (anterior division)	19
	Supramarginal Gyrus (posterior division)	20
	Angular Gyrus	21
	Precuneous Cortex	31

	Parietal Operculum Cortex	43
Temporal Cortex	Temporal Pole	8
	Superior Temporal Gyrus (anterior division)	9
	Superior Temporal Gyrus (posterior division)	10
	Middle Temporal Gyrus (anterior division)	11
	Middle Temporal Gyrus (posterior division)	12
	Middle Temporal Gyrus (Temporo-occipital part)	13
	Inferior Temporal Gyrus (anterior division)	14
	Inferior Temporal Gyrus (posterior division)	15
	Inferior Temporal Gyrus (Tempero-occipital part)	16
	Parahippocampal Gyrus (anterior division)	34
	Parahippocampal Gyrus (posterior division)	35
	Temporal Fusiform Cortex (anterior division)	37
	Temporal Fusiform Cortex (posterior division)	38
	Temporal Occipital Fusiform Cortex	39
	Planum Polare	44
	Planum Temporale	46
Occipital Cortex	Lateral Occipital Gyrus (Superior division)	22
	Lateral Occipital Gyrus (Inferior division)	23
	Intracalcarine Cortex	24
	Cuneal cortex	32
	Lingual Gyrus	36

	Occipital Fusiform Gyrus	40
	Supracalcarine Cortex	47
	Occipital Pole	48

ROI, region of interest.

Supplemental Table 2 Anatomical connectivity of the thalamocortical pathways revealed by probabilistic tractography.

Cortical region	Hemisphere	Group		*P* value
		HC	CLBP	
Prefrontal cortex	Left	0.32 ± 0.05 [a]	0.31± 0.06	0.204
Prefrontal cortex	Right	0.37 ± 0.06	0.38 ± 0.06	0.887
Parietal cortex	Left	0.12 ± 0.03	0.12 ± 0.04	0.516
Parietal cortex	Right	0.12 ± 0.03	0.12 ± 0.03	0.345
Temporal cortex	Left	0.17 ± 0.05	0.17 ± 0.05	0.792
Temporal cortex	Right	0.15 ± 0.04	0.16 ± 0.05	0.811
Occipital cortex	Left	0.16 ± 0.04	0.15 ± 0.04	0.11
Occipital cortex	Right	0.14 ± 0.03	0.14 ± 0.03	0.347

HC, healthy control; CLBP, chronic low back pain; [a]: mean ± standard deviation.

Supplemental Table 3 Correlation between anatomical/functional connectivity of the thalamus and clinical measures in patients with chronic low back pain

Clinical measures	Hemisphere	RsFC				Anatomical connectivity	
		Thalamo-motor		Thalamo-somatosensory		Thalamo-motor	
		R1	*P1*	*R2*	*P2*	*R3*	*P3*
BDI scores	Left	0.177	0.2	0.223	0.106	-0.141	0.308
	Right	0.181	0.191	0.164	0.237	NA	NA
Pain intensity (past week)	Left	0.24	0.219	0.12	0.563	0.1	0.71
	Right	0.193	0.431	0.15	0.399	NA	NA
Pain intensity (during MRI scan)	Left	0.2	0.219	0.17	0.563	0.05	0.74
	Right	0.15	0.431	0.32	0.036*	NA	NA
Pain duration	Left	-0.186	0.12	0.093	0.441	0.19	0.59
	Right	0.143	0.235	0.014	0.091	NA	NA

RsFC, resting-state functional connectivity; BDI, Beck Depression Inventory II; MRI, magnetic resonance imaging; NA, not available. R1, R2 and R3 represent the correlation coefficients between the thalamic connectivity and clinical measures in patients with chronic low back pain.