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REVIEW

Exploration of Key Brain Regions Involved in Acupuncture and Moxibustion Analgesia: An Imaging-Based Study

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Background: Acupuncture and moxibustion, as traditional therapies in Chinese medicine, are widely recognized for their therapeutic effects, particularly in pain relief. Nevertheless, the exact mechanisms underlying their analgesic effects remain to be fully elucidated. Advancements in neuroimaging techniques have opened a novel pathway for investigating alterations in brain function resulting from acupuncture and moxibustion analgesia.

Purpose: The purpose of this study was to investigate the brain regions activated during acupuncture and moxibustion treatment for pathological pain using neuroimaging, to better understand the underlying analgesic mechanisms.

Patients and Methods: An electronic search of PubMed was conducted using the keywords "acupuncture", "moxibustion", "analgesia", and "neuroimaging". A total of 37 articles, focusing on 14 diseases, were identified and analyzed.

Results: Acupuncture primarily activated regions in the frontal, parietal, and temporal lobes, with key areas including the anterior cingulate cortex (ACC), insula, prefrontal cortex (PFC), and primary somatosensory cortex (S1). Different stimulation modes and disease types produced distinct patterns of brain region activation.

Conclusion: Acupuncture and moxibustion modulate key brain regions involved in pain perception, emotional regulation, and cognitive functions. Acupuncture predominantly affects the sensory cortex, enhancing pain perception, while moxibustion has a more pronounced effect on the limbic system and thalamus, influencing emotional and cognitive aspects of pain. The findings indicate that acupuncture and moxibustion serve as effective non-pharmacological therapies for pain management, offering valuable insights into their underlying analgesic mechanisms. Future research should focus on further elucidating these mechanisms and optimizing clinical applications.

Keywords: acupuncture, moxibustion, analgesia, neuroimaging, brain regions

Introduction

Pain is a major global public health issue that significantly impacts patients' quality of life and drives the continuous rise in global healthcare expenditures.[1] According to the Global Burden of Disease Study (GBD 2019),[2] chronic pain has become one of the leading causes of disability worldwide, with musculoskeletal pain, neuropathic pain, and migraines being the most prevalent types. Currently, approximately 20–30% of the global population suffers from chronic pain, with particularly high incidence rates among elderly individuals, women, and low-income populations.[3] The International Association for the Study of Pain (IASP) defines pain as an unpleasant sensory and emotional experience associated with actual or potential tissue damage.[4] Chronic pain not only limits patients' mobility and daily activities but is also closely

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linked to mental health issues, such as anxiety, depression, and sleep disorders. Although pharmacological treatments (such as nonsteroidal anti-inflammatory drugs and opioids) play a crucial role in pain management, their long-term use is often accompanied by tolerance, dependence, and side effects, prompting researchers to explore safer and more effective non-pharmacological approaches. Understanding the mechanisms underlying pain development and its treatment is crucial for addressing this significant public health challenge.

Acupuncture and moxibustion, rooted in traditional Chinese medicine's meridian theory, involve stimulating specific acupoints to regulate qi and blood flow. Its analgesic mechanism involves multiple levels and systems, mainly including the coordinated regulation of the nervous, immune, and endocrine systems. In recent years, clinical and neurophysiological studies have shown that acupuncture and moxibustion has a significant analgesic effect in the treatment of chronic pain, musculoskeletal pain, neuropathic pain, and other diseases.[5,6] Studies have found that acupuncture and moxibustion can activate the endogenous analgesic pathway, promote the release of endorphins, 5-hydroxytryptamine (5-HT) and other analgesic substances, thus regulating pain perception and inflammatory response.[7] In addition, acupuncture and moxibustion can achieve analgesic effect by promoting the release of endogenous opioid peptides, up regulating the expression of local endorphins and peripheral opioid receptors, and inhibiting the effect of endogenous pain causing substances.[8] This process enhances the nervous system's regulatory functions, ultimately providing pain relief.[9] Acupuncture and moxibustion have been approved and recommended as primary analgesic methods by the World Health Organization (WHO) and have been listed as WHO-recommended, nonpharmacological options for pain management. They have been recognized as green analgesic methods both domestically and internationally due to their advantages, including few adverse reactions, wide applicability, and fast effectiveness under standardized diagnostic and treatment criteria compared with modern drug therapy.[10] In view of opioid addiction and drug side effects, acupuncture and moxibustion has shown great potential in pain management as an alternative or adjuvant therapy. However, the mechanism underlying acupuncture and moxibustion analgesia is not completely clear, and its exploration has always been a hotspot in alternative and complementary medicine research.

In recent years, neuroimaging techniques have undergone rapid advancements, significantly enhancing our comprehension of pain processing within the central nervous system (CNS).[11] These techniques offer advantages, such as being non-invasive, free of radiation, and providing high spatial resolution, making them valuable tools in modern neuroscience and acupuncture research. Through the use of neuroimaging, researchers can non-invasively observe the effects of acupuncture on brain activity and visualize specific brain regions involved in neuronal processes. This approach offers abundant visual evidence, shedding light on the central mechanisms behind acupuncture and moxibustion analgesia.

The CNS response to acupuncture and moxibustion can enhance the clinical effectiveness of their analgesic properties, likely through changes in CNS functional connectivity, restoration of normal plasticity, and consequent pain relief. In this study, we aimed to analyze brain activity changes linked to acupuncture and moxibustion in the treatment of pathological pain, summarize the CNS regions activated by their analgesic effects across different pain types, explore the underlying central mechanisms of pain relief, and offer insights for future research.

Methods

Database Data Source and Search Strategies

The PubMed database was searched on April 15, 2024, using the keywords "acupuncture", "analgesia", and "neuroimaging", and studies on regional information in the brain were selected. Without limiting the country of publication, only English literature was included, and duplicates and publications without full text availability were excluded. Two authors independently screened titles and abstracts, resolving disagreements through discussion, with the final decision being made by senior authors. To ensure comprehensive coverage, a secondary reference search was performed. After the initial screening, 1012 articles were excluded, and 65 full text articles were reviewed. Ultimately, 37 studies met the inclusion criteria. The search strategy is detailed in the Supplementary Materials.

Selection Criteria for Literature Screening

Inclusion Criteria

Articles were reviewed based on their abstracts and full texts and selected if they met the following criteria: original research, inclusion of patients with pathological pain, and use of neuroimaging to study brain changes resulting from acupuncture or moxibustion.

Exclusion Criteria

Articles meeting any of the following criteria were excluded: non-acupuncture, non-pain, and non-imaging studies; non-experimental articles, such as protocols, systematic reviews, meta-analyses, and syntheses; and experimental pain research.

Statistical Analysis

Excel software was used to establish a literature file database to count the characteristics of the publications related to acupuncture and moxibustion analgesia research (including the publication title, corresponding author, disease name, sample size, intervention mode, acupoint selection, acupuncture and moxibustion mode, imaging method, analysis method, and activation of brain regions after acupuncture). The study selection process diagram is shown in Figure 1.

Results

Study Selection

The search was conducted on April 15, 2024, and a total of 1012 relevant records were retrieved. After title and abstract screening, 947 articles were excluded. The remaining 65 articles were fully reviewed and assessed for quality. Through discussion and consensus, 37 neuroimaging studies focusing on pathological pain were ultimately included in this review.

Study Characteristics

Since 1997, there have been clinical research publications on acupuncture and moxibustion analgesia using imaging technology, and the overall number of publications has been increasing. The results are shown in Figure 2A comparison of all included studies in terms of acupoint use, control interventions, number of participants, and outcomes is presented in Table 1.

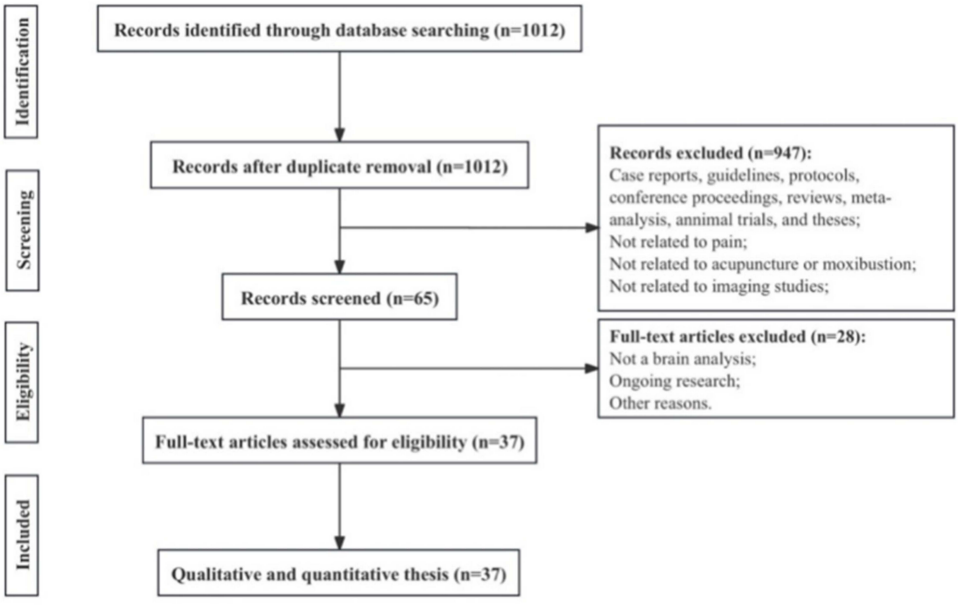

Figure 1 Flow diagram of the review process.

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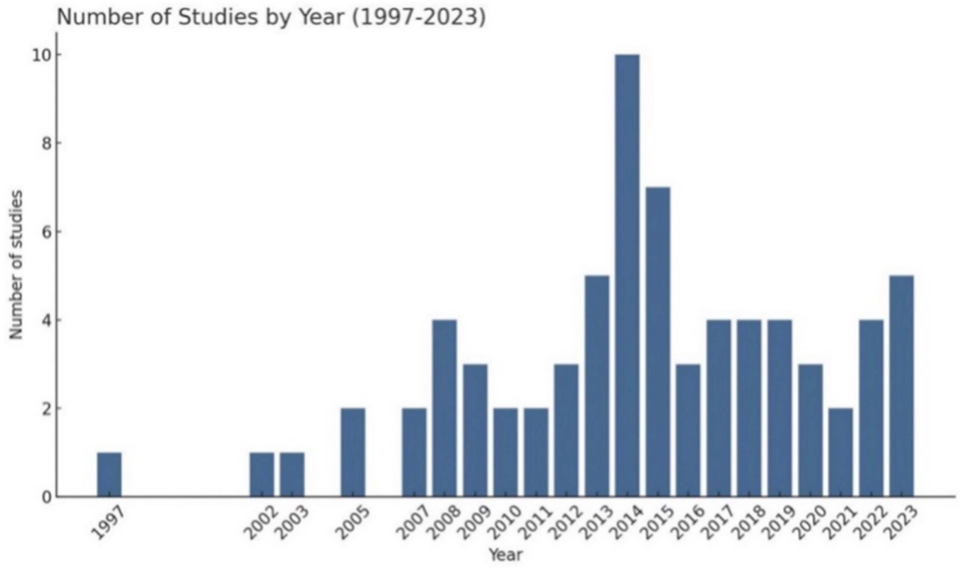

Figure 2 Annual distribution of clinical research publications in the field of acupuncture and moxibustion analgesia using imaging technology.

Participants

The 37 reviewed articles involved a total of 14 diseases, including eight articles on migraine without aura; seven articles on knee osteoarthritis; five articles on lower back pain; four articles each on carpal tunnel syndrome and primary dysmenorrhea; and one article each on sciatica, lumbar disc herniation with lower back and leg pain, chronic shoulder pain, chronic neck pain, stable angina, Parkinson's disease, fibromyalgia, endometriosis, and acute pain after knee replacement surgery. The proportion of diseases is shown in Figure 3.

Interventions

A total of 34 studies employed acupuncture stimulation methods, with 22 utilizing manual acupuncture and 12 opting for electroacupuncture as the intervention. Only two studies chose moxibustion as the treatment, and just one study combined both acupuncture and moxibustion.

Acupoints

The specific selection of acupoints for pathological conditions is presented in Table 2.

Cerebral Response to Stimulation

This review categorized and summarized the clinical study results based on the corresponding brain structures. The frequency of acupuncture and moxibustion activation of brain regions was 51 times in the frontal lobe, 39 times in the limbic lobe, 36 times in the parietal lobe, 25 times in the temporal lobe, 15 times in the occipital lobe, 13 times in the insular lobe, 11 times in the basal nucleus, 9 times in the cerebellum, 9 times in the thalamus, 6 times in the aqueduct gray matter of the mesencephalic island, 7 times in the brainstem, and one time each in the hypothalamus and ventral dorsal tegmental area. The detailed frequency of activated brain lobes is shown in Figure 4A-F.

Outcomes

Comparative Study of Brain Region Activation in Acupuncture and Moxibustion

For analgesia, acupuncture was used more frequently than moxibustion. Acupuncture mainly activated the frontal lobe, parietal lobe, limbic lobe, temporal lobe, insular lobe, occipital lobe, basal nucleus, cerebellum, dorsal thalamus, periaqueductal gray matter (PAG), brainstem, hypothalamus, and ventral dorsal tegmental area (Figure 4G). The brain areas activated by hand acupuncture and electroacupuncture mostly overlapped. Moxibustion mainly activated the limbic

Table 1 Study Characteristics

Source	Diagnosis	Sample Size (n)	Gender (Male/ Female)	Age (y)	Type of Intervention	Acupoints	Imaging Method	Brain Region
[12]	ALBP	ALBP: 28	ALBP: 17/11	-	MA	BL40	fMRI	S1, M1, S2, frontal eye field, frontal lobe, dmPFC, SMA, HIP, PHG, AG, pACC, pMCC, DMN, insula, temporal lobe, lateral temporal cortex, THA, mammillary body, supramarginal gyrus, PAG
[13]	CNP	TA: 66 SA: 33	-	-	MA	SJ15, SI14, SI15, BL11, LI16	fMRI	DR, thalamus, MR, parahippocampal gyrus, amygdala, insula, lingual gyrus, middle frontal gyrus, middle frontal gyrus
[14]	CSAP	CSAP: 37 HCs: 65	CSAP: 20/17 HCs: 26/39	CSAP: 65.05 ± 7.23 HCs: 56.71 ± 5.49	MA	PC6, HT5, LI5, LI6	fMRI	right orbitofrontal gyrus, HIP, PHG, left calcarine, L-MCC, brain stem, ITG, THA, cerebellum crus, left cuneus
[15]	CSP	Contra-group: 12 Ipsi-group: 8	Contra-group: 6/6 Ipsi-group: 4/4	Contra-group: 53.33 ± 5.26 Ipsi-group: 54.13 ± 7.45	MA	ST38	fMRI	limbic lobe, IPL, IFG, L-MFG, SMA, pACC, brain stem, THA, PoCG
[16]	CTS	CTS: 37 HCs: 30	CTS: 7/30 HCs: 11/19	CTS: 48.5 ± 10.0 HCs: 47.5 ± 9.6	EA	TW5, LV4, PC7, SP6	fMRI	PAG, S1, S2, SMA, insula
[17]	CTS	CTS: 59	CTS: 10/49	CTS: 49.1 ± 9.8	EA	TW5, LV4, PC7, SP6	fMRI	S1, S2, PFC, SMA, PCC, insula
[18]	CTS	CTS: 80 HCs: 34	CTS: 15/65 HCs: 6/28	CTS: 49.3 ± 8.6 HCs: 49.7 ± 9.9	EA	TW5, PC7	fMRI	S1
[19]	CTS	CTS: 10 HCs: 9	CTS: 4/6 HCs: 3/6	CTS: 51.1 HCs: 46.9	EA	TW5, PC7, HT3, PC3, SI4, LI5, LI10, LU5	fMRI	S1, M1
[20]	EMT	Tret: 30 Con: 30	Tret: 0/30 Con: 0/30	Tret: 35.2 ± 4.7 Con: 36.4 ± 4.8	MA, MOX	CV3	fMRI	HIP
[21]	FM	-	-	-	EA	LI11, LI4, GB34, SP6, ST36, LV3, DU20	fMRI	S1, insula
[22]	HID	HID: 20	HID: 8/12	-	BA	BL40, BL25, BL26	fMRI	limbic lobe, insula, MFG, SFG, orbit of superior frontal gyrus, IFG, ventral anterior nucleus, ventrolateral nucleus, putamen, CG, brain stem, STG, MTG, THA, AMY
[23]	KOA	KOA: 15 HCs: 15	KOA: 7/8 HCs: 4/11	KOA: 59.13 ± 10.27 HCs: 58.53 ± 8.15	MA	EXLE5	fMRI	right putamen, right lingual gyrus, striatum, RPN
[24]	KOA	KOA: 30	KOA: 17/13	KOA: 58 ± 8	MA	ST35, GB34, SP9, GB39, SP6	fMRI	mFP, L-pMPFC, rACC, PAG

(*Continued*)

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Table 1 (Continued).

Source	Diagnosis	Sample Size (n)	Gender (Male/ Female)	Age (y)	Type of Intervention	Acupoints	Imaging Method	Brain Region
[25]	KOA	Boosted Acu: 17 Standard Acu: 17 TAU: 12	Boosted Acu: 8/9 Standard Acu: 7/10 TAU: 4/8	Boosted Acu: 61.3 ± 6.9 Standard Acu: 61.2 ± 7.7 TAU: 60.1 ± 7.1	MA	ST35, GB34, SP9, GB39, SP6	fMRI	L-mPFC, vmPFC, Nac, rACC, PoCG, PaCG
[26]	KOA	VA: 21 SA: 22	VA: 10/11 SA: 7/15	VA: 57 ± 7 SA: 59 ± 7	EA	LI3, LI4	fMRI	OPFC, R-S2, IPL, DLPFC, mPFC, putamen, ACC, insula, STG, supramarginal gyrus
[27]	KOA	PCs: 30	-	-	MOX	ST35	fMRI	parietal lobe, frontal lobe, THA, cerebellum, occipital lobe, PreCG
[28]	KOA	PCs: 30	PCs: 17/13	PCs: 58 ± 8	MA	GB34, SP9, GB39, SP6, ST35	fMRI	rFPN, mPFC, pACC, ECN
[29]	KOA	PCs: 44	PCs: 17/13	PCs: 57.5 ± 8.3	MA	ST35, GB34, SP9, GB39, SP6	fMRI	MFC, HIP, PAG
[30]	LBP	VA: Augmented: 12 Limited: 12 SA: Augmented: 13 Limited: 13	VA: Augmented: 4/8 Limited: 4/8 SA: Augmented: 5/8 Limited: 5/8	VA: Augmented: 43.00 (11.09 Limited: 34.98 (13.16) SA: Augmented: 40.02 (13.51) Limited: 39.51 (14.40)	MA	GV3, BL23, BL40	fMRI	SPL, mPFC, VTA, AG, ACC, insula, PCU, AMY, PAG
[31]	LBP	cLBP: 20 HCs: 10	cLBP: 10/10 HCs: 5/5	cLBP: 38.1±6.4 HCs: 38.1±6.4	MA	BL23, GV3, BL40, KI3	fMRI	DLPFC, mPFC, ACC, DMN, PCU
[32]	LBP	TA: 24 SA: 26	TA: 8/16 SA: 11/15	TA: 39.0 ± 12.6 SA: 40.0 ± 13.7	MA	GV3, BL23, BL40, KI3	fMRI	mPFC, AG, putamen, insula, caudate nucleus
[33]	LBP	LBP: 102 HCs: 50	LBP: 44/58 HCs: 16/34	LBP: 41.2 ± 12.0 HCs: 41.4 ± 12.3	MA	GV3, BL23, BL40, KI3	fMRI	S1
[34]	Migraine	PCs: 30	PCs: 12/18	PCs: 32.87 ± 8.71	EA	TE5, GB34, GB20, ST8, LI6, ST36	FDG-PET/CT	OFC, MFG, HIP, PHG, AG, MCC, PCC, insula, STG, MTG, fusiform gyrus, cerebellum, PCU, supramarginal gyrus, PoCG
[35]	MwoA	MwoA: 48 HCs: 48	MwoA: 11/37 HCs: 11/37	MwoA: 21.29 ± 1.89 HCs: 21.17 ± 0.93	MA	GB34, GB40, SJ5, GB33, GB42, SJ8, ST36, ST42, LI6	MRI	insular lobe, IPL, SFG, MFG, CG
[36]	MwoA	CM: 14 HCs: 18	CM: 5/9 HCs: 9/9	CM: 42.91 ± 10.18 HCs: 38.59 ± 7.96	MA	SJ5, GB20, GB8, ST8	fMRI	L-SPFG, R-TPL, L-ACC, SMG, L-PCU
[37]	MwoA	MwoA: 70 HCs: 43	MwoA: 15/56 HCs: 9/34	MwoA: 21.51 HCs: 22.23	MA	GB34, GB40, SJ5, GB35, GB42, SJ8, ST36, ST42, LI6	fMRI	L-MFG, L-STG, MTG, lingual gyrus, cuneus

[38]	MwoA	MwoA: 37 HCs: 15	MwoA: 6/31 HCs: 2/13	MwoA: 37.97 ± 9.82 HCs: 34.88 ± 6.66	EA	DU20, EXHN5, GB20, GB8, GB5, GB15, LI4, LR3	fMRI	AG, cerebellum
[39]	MwoA	Active acupoint: 40 Inactive acupoint: 40	Active acupoint: 12/28 Inactive acupoint: 11/29	Active acupoint: 33.35 ± 11.69 Inactive acupoint: 33.23 ± 9.73	MA	SJ5, GB20, GB34, GB40, SJ22, PC7, GB37, SP3	fMRI	IPL, MFG, SMA, L-HIP, AG, pACC, R-PCC, insula, brain stem, STG, ITG, MTG, THA, lingual gyrus, cerebellum, cuneus, R-PoCG
[40]	MwoA	TA: 24 SA: 20	PCs: 0/44	TA: 33.04 ± 6.43 SA: 35.30 ± 9.43	MA	GB20, GB8, PC6, SP6, LR3	fMRI	R-SFG, R-IFG, R-MFG, L-ACC, R-STG, left cuneus
[41]	MwoA	MMoA: 38 HCs: 10	MMoA: 16/22 HCs: 3/7	37.6	MA	GB20, LR3, EX-HN5, GV20, EX-HN1	fMRI	lingual gyrus, DMN, cerebellum
[42]	Sciatica	Sciatica: 12 HCs: 15	Sciatica: 6/6 HCs: -	Sciatica: 61.42 ± 14.84 HCs: -	MA	BL23, GB30, BL40, GB34, BL60, GB39, BL23, BL25, BL27, GB30, BL37, BL54, BL36, GB31, BL40, ST36, GB34, SP9, BL58, SP6, GB39, BL60, KI3, BL62	fMRI	mPFC, PCC, cerebellum, L-PCU
[43]	PD	Tret: 9 Con: 7	Tret: 4/5 Con: 5/2	Tret: 60.7 ± 6.3 Con: 70.4 ± 8.2	MA	GV20, GB34, BL52	fMRI	S1, insular gyrus, L-MFG, L-STG, MTG, right flocculus of cerebellum, supramarginal gyrus, PoCG, PreCG
[44]	PDM	VA: 18 SA: 18	VA: 0/18 SA: 0/18	VA: 24.89 ± 4.59 SA: 26.13 ± 4.54	MA	SP6	fMRI	R-MFG, L-dACC, ACC, R-CAU, left cerebellum, cuneus, R-MFG, PAG, L-PoCG
[45]	PDM	PDM: 29	PDM: 0/29	VA: 24.86 ± 1.75 SA: 24.53 ± 2.07	MA	SP6, GB39	PET	SMN, SN, DMN
[46]	PDM	TA: 19 SA: 34	TA: 0/19 SA: 0/34	TA: 25.37 ± 2.41 SA: 24.20 ± 2.01	MA	SP6	fMRI	SMA, rACC, L-PreCG
[47]	PDM	PDM: 23 HPs: 23	PDM: 0/23 HPs: 0/23	PDM: 21.74 ± 2.01 HPs: 22.26 ± 2.12	MOX	CV4, CV8, SP6	fMRI	L-IFG, L-PHG, MCC, pACC, L-PCC, PCU
[48]	TKA	EA: 16 SA: 15 HCs: 32	EA: 2/14 SA: 2/13 HCs: 10/21	EA: 71.4 ± 6.1 SA: 69.4 ± 5.0 HCs: 68.8 ± 4.4	EA	ST32, ST36, SP9, GB34	fMRI	R-AG, L-MTG, PCU, right cuneus, MOG

Abbreviations: fMRI, functional magnetic resonance imaging; PET-CT, Positron emission tomography with computed tomography; FDG-PET/CT, fluorodeoxyglucose positron emission tomography combined with computed tomography; ALBP, acute low back pain; CNP, Chronic neck pain; CSAP, chronic stable angina pectoris; CSP, chronic shoulder pain; CTS, carpal tunnel syndrome; EMT, Endometriosis; FM, fibromyalgia; HID, lumbar disc herniation; KOA, knee osteoarthritis; LBP, low back pain; MwoA, migraine without aura; PD, Parkinson's disease; PDM, Primary dysmenorrhea; TKA, total knee arthroplasty; PFC, prefrontal cortex; OFC, orbitofrontal cortex; mPFC, medial prefrontal cortex; L-mPFC, left- medial prefrontal cortex; DLPFC, dorsolateral prefrontal cortex; L-pMPFC, left-posterior medial prefrontal cortex; SMA, supplementary motor area; SMN, the sensorimotor network; SN, salience network; DMN, default mode network; ECN, executive control network; rFPN, right-frontoparietal network; SFG, superior frontal gyrus; MFG, middle frontal gyrus; R-MFG, right- middle frontal gyrus; IFG, inferior frontal gyrus; L-IFG, left-inferior frontal gyrus; R-IFG, right-inferior frontal gyrus; PreCG, precentral gyrus; L-PreCG, left-precentral gyrus; M1, primary motor cortex; PCU, precuneus; L-PCU, left-precuneus; SPL, superior parietal lobule; IPL, inferior parietal lobule; PoCG, postcentral gyrus; L-PoCG, left-postcentral gyrus; R-PoCG, right-postcentral gyrus; S1, primary somatosensory cortex; S2, secondary somatosensory cortex; R-S2, right-secondary somatosensory cortex; AG, angular gyrus; R-AG, right-angular gyrus; STG, superior temporal gyrus; L-STG, left-superior temporal gyrus; R-STG, right-superior temporal gyrus; SFG, superior frontal gyrus; R-SFG, right-superior frontal gyrus L-SPFG, left-superior prefrontal gyrus; MTG, middle temporal gyrus; ITG, inferior temporal gyrus; MOG, middle occipital gyrus; MFG, middle frontal gyrus; L-MFG, left-middle frontal gyrus; R-MFG, right-middle frontal gyrus; HIP, hippocampus; PHG, parahippocampus; L-PHG, left-parahippocampus; CG, cingulated gyrus; CAU, caudate nucleus; Nac, nucleus accumbent; AMY, amygdala; THA, thalamus; RPN, raphe nuclei; ACC, anterior cingulate gyrus; rACC, rostral anterior cingulate cortex; L-ACC, left-anterior cingulate cortex; pACC, pregenual anterior cingulate gyrus; PCC, posterior cingulate cortex; R-PCC, right-posterior cingulate cortex; MCC, middle cingulate cortex; L-MCC, left-middle cingulate cortex; pMCC, posterior midcingulate cortex; R-TPL, right-temporal lobe; VTA, ventral tegmental area; DR, dorsal raphe nucleus; MR, median raphe nucleus.

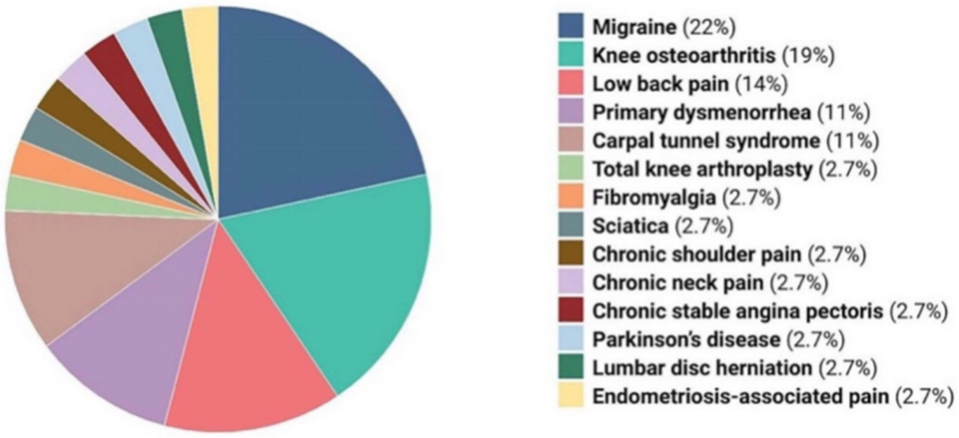

Figure 3 Proportion of diseases subjected to acupuncture and moxibustion analgesia research using imaging technology.

frontal lobe, parietal lobe, occipital lobe, thalamus, and cerebellum (Figure 4G). These findings indicate that, while different intervention methods activate specific brain regions, they also share common areas of activation.

Similarities and Differences in Brain Areas Activated by Acupuncture and Moxibustion Treatment for Acute and Chronic Pain

Pain can be categorized as either acute or chronic, depending on the duration of the condition. In the current review, acute pain diseases included acute low back pain,[12] acute pain after total knee arthroplasty,[48] and acute migraine without aura.[34] Chronic pain diseases included migraine without aura,[35–41] knee osteoarthritis,[23–29] carpal tunnel

Table 2 Literature Research of the Disease Details and Acupoint Selection in the Clinical Research Field of Acupuncture and Moxibustion Analgesia Based on Imaging Technology

Investigated Diseases	Selection of Acupoints
Migraine	TE5, GB34, GB20, ST8, LI6, GB40, SJ5, GB33, GB42, SJ8, ST36, ST42, GB35, GB8, DU20, EXHN5, GB5, GB15, LI4, LR3, SJ22, PC7, GB37, SP3, PC6, SP6, LR3, GV20, EX-HN1
Knee osteoarthritis	EXLE5, ST35, GB34, SP9, GB39, SP6, LI3, LI4
Low back pain	BL40, GV3, BL23, KI3
Carpal tunnel syndrome	TW5, LV4, PC7, SP6, GB34, KD3, SP5, HT3, PC3, SI4, LI5, LI10, LU5
Primary dysmenorrhea	SP6, GB39, CV4, CV8
Chronic neck pain	SJ15, SI14, SI15, BL11, LI16
Chronic stable angina pectoris	PC6, HT5, LI5, LI6
Chronic shoulder pain	ST38
Endometriosis-associated pain	CV3
Fibromyalgia	LI11, LI4, GB34, SP6, ST36, LV3, DU20, HT7
Lumbar disc herniation	BL40, BL25, BL26
Sciatica	BL23, GB30, BL40, GB34, BL60, GB39, BL23, BL25, BL27, GB30, BL37, BL54, BL36, GB31, BL40, ST36, GB34, SP9, BL58, SP6, GB39, BL60, KI3, BL62
Parkinson's disease	GV20, GB34, BL52
Total knee arthroplasty	ST32, ST36, SP9, GB34

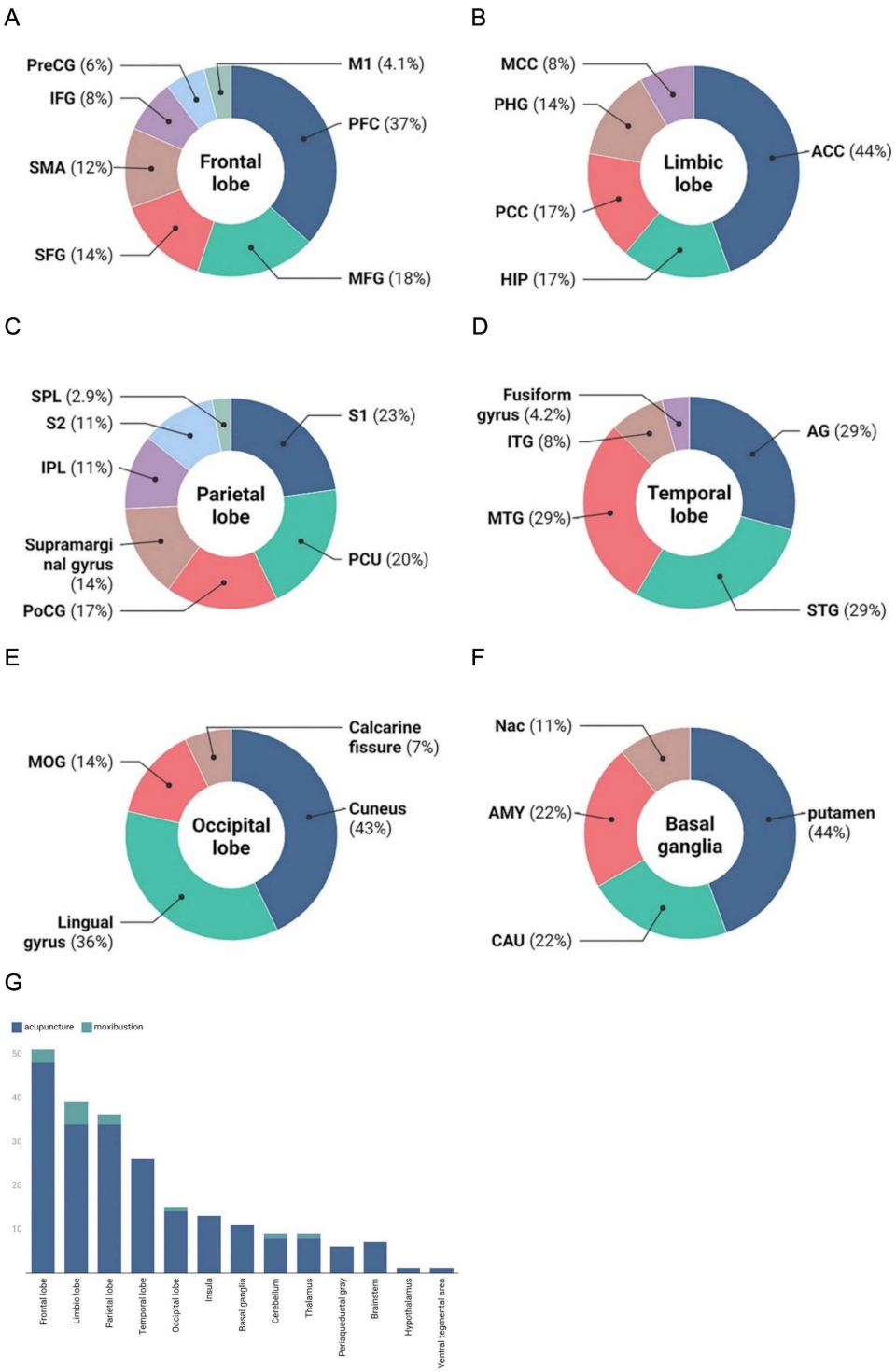

Figure 4 Total frequency of brain region appearances in articles included in the analysis.

Notes: (**A**) The proportion of brain regions activated in the frontal lobe. (**B**) The proportion of brain regions activated in the limbic lobe. (**C**) The proportion of brain regions activated in the parietal lobe. (**D**) The proportion of brain regions activated in the temporal lobe. (**E**) The proportion of brain regions activated in the occipital lobe. (**F**) The proportion of brain regions activated in the basal ganglia. (**G**) The total frequency of brain region appearances in the articles.

Abbreviations: PFC, prefrontal cortex; SMA, supplementary motor area; SFG, superior frontal gyrus; MFG, middle frontal gyrus; IFG, inferior frontal gyrus; PreCG, precentral gyrus; M1, primary motor cortex; PCU, precuneus; SPL, superior parietal lobule; IPL, inferior parietal lobule; PoCG, postcentral gyrus; S1, primary somatosensory cortex; S2, secondary somatosensory cortex; AG, angular gyrus; STG, superior temporal gyrus; MTG, middle temporal gyrus; ITG, inferior temporal gyrus; MOG, middle occipital gyrus; HIP, hippocampus; PHG, parahippocampus; CG, cingulated gyrus; CAU, caudate nucleus; Nac, nucleus accumbent; AMY, amygdala.

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syndrome,[16–19] chronic low back pain,[30–33] Parkinson's disease,[43] chronic stable angina pectoris,[14] a herniated lumbar disc with low back and leg pain,[22] non-acute sciatica,[42] chronic shoulder pain,[15] fibromyalgia,[21] chronic neck pain,[13] primary dysmenorrhea[44–47] and endometriosis.[20]

Both acute and chronic pain engage multiple brain regions, including the temporal lobe, limbic system (such as the insula and amygdala), frontal lobe, parietal lobe, and cerebellum. These areas are crucial for pain perception, emotional regulation, and motor responses associated with pain. Notably, both types of pain strongly activate parts of the limbic system, such as the insula and amygdala, highlighting the emotional processing of pain. However, acute pain primarily activates regions involved in sensory and motor processing, like the parietal lobe and primary somatosensory cortex. In contrast, chronic pain predominantly engages areas linked to pain evaluation, processing, and attention, such as the frontal lobe and insula. Additionally, chronic pain activates regions within the basal ganglia, including the striatum, which may be related to non-pain symptoms like movement disorders. Chronic pain also shows broader activation within the limbic system, including the hippocampus and amygdala, indicating a possible role in emotional memory processing (Figure 5A and B).

Similarities and Differences in Brain Regions Activated by Acupuncture and Moxibustion Treatment for Physical and Visceral Pain

Based on the location of pain in the body, it can be classified as visceral or somatic pain. In this review, primary dysmenorrhea[44–47] and endometriosis[20] were included in the analysis of visceral pain. Acute low back pain,[12] acute pain after total knee arthroplasty,[48] acute migraine without aura,[34] Migraine without aura, migraine without aura,[35–41] knee

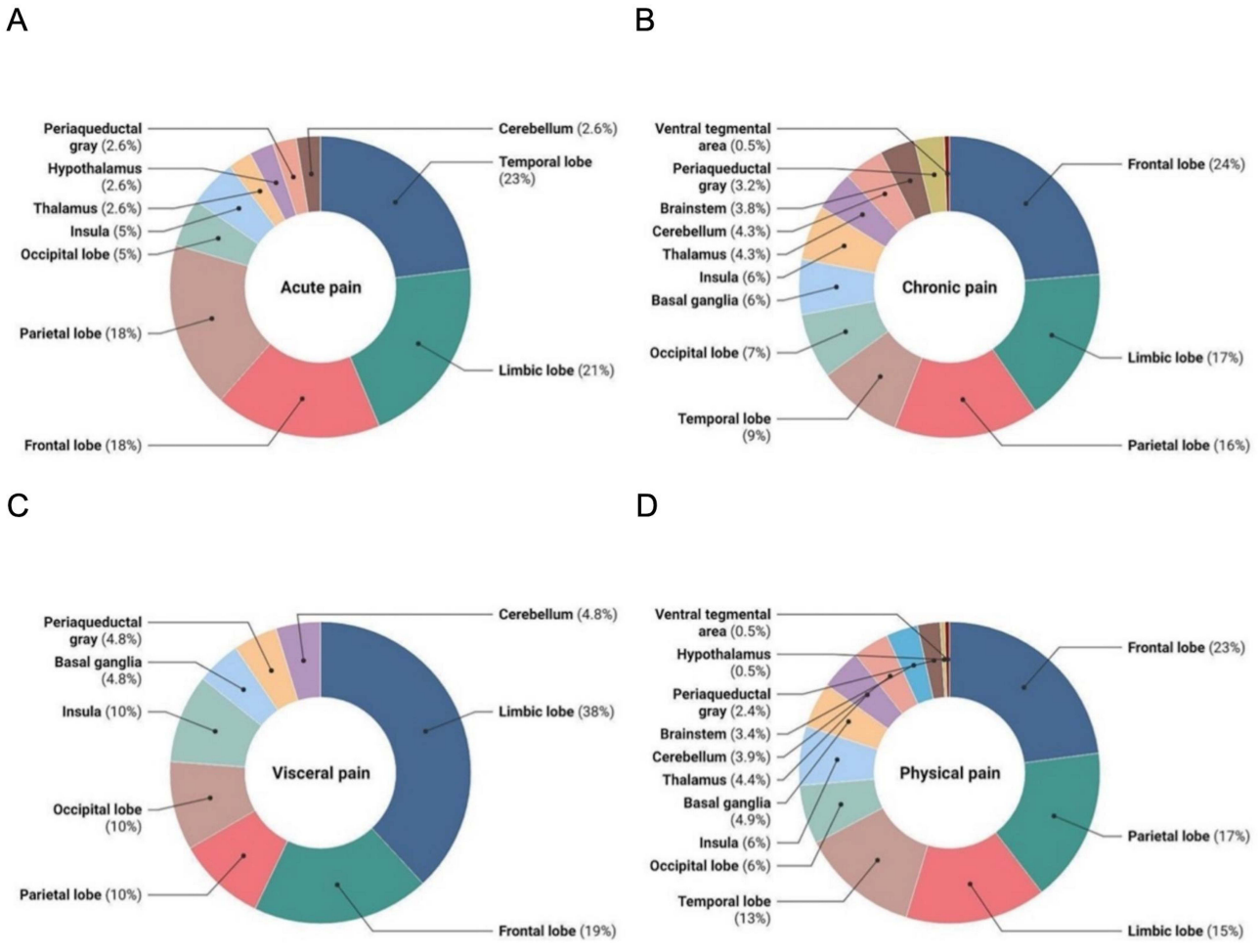

Figure 5 Brain response to acupuncture treatment for different pain types.
Notes: (**A**) Brain regions activated after acupuncture and moxibustion for acute pain. (**B**) Brain regions activated after acupuncture and moxibustion for chronic pain. (**C**) Brain regions activated after acupuncture and moxibustion for visceral pain. (**D**) Brain regions activated after acupuncture and moxibustion for physical pain.

osteoarthritis,[23–29] carpal tunnel syndrome,[16–19] chronic low back pain,[30–33] Parkinson's disease,[43] chronic stable angina pectoris,[14] a herniated lumbar disc with low back and leg pain,[22] non-acute sciatica,[42] chronic shoulder pain,[15] fibromyalgia,[21] chronic neck pain,[13] were included in the analysis of somatic pain.

Both visceral and somatic pain activated several brain regions, including the insular cortex, cerebellum, limbic system, basal ganglia, and the frontal, parietal, temporal, and occipital lobes. However, visceral pain activated more regions in the medial aspect of the limbic system, including the PAG matter, whereas somatic pain activated more regions in the motor and somatosensory cortex. Visceral pain showed a less widespread activation in the brain, mainly concentrated in the cortex and limbic system. In contrast, somatic pain had a broader activation range, including the cortex, limbic system, and deep structures, such as the thalamus and hypothalamus (Figure 5C and D).

Similarities and Differences in Brain Region Activation With Different Treatment Methods Used for the Same Disease

In this study, both migraine and knee osteoarthritis were treated with acupuncture and moxibustion, making them suitable for comparing different brain region responses to these two treatment methods.

For migraine, electroacupuncture and hand acupuncture both activated the frontal lobe, parietal lobe, temporal lobe, insular lobe, basal ganglia, and other cortical areas and subcortical structures related to pain, attention, and motor functions. In addition, electroacupuncture activated the limbic system and thalamus. Electroacupuncture focused more on the frontal lobe, temporal lobe, and other anterior regions, whereas hand acupuncture focused more on the parietal lobe, thalamus, and other posterior regions (Figure 6A).

For knee osteoarthritis, acupuncture and moxibustion co-activated areas including the frontal lobe, parietal lobe, occipital lobe, and thalamus. However, acupuncture-induced activation was more pronounced in the anterior regions, such as the prefrontal lobe, frontoorbital gyrus, and anterior cingulate gyrus, whereas moxibustion-induced activation was more pronounced in the middle and posterior regions, such as the parietal lobe, putamen, and thalamus (Figure 6B).

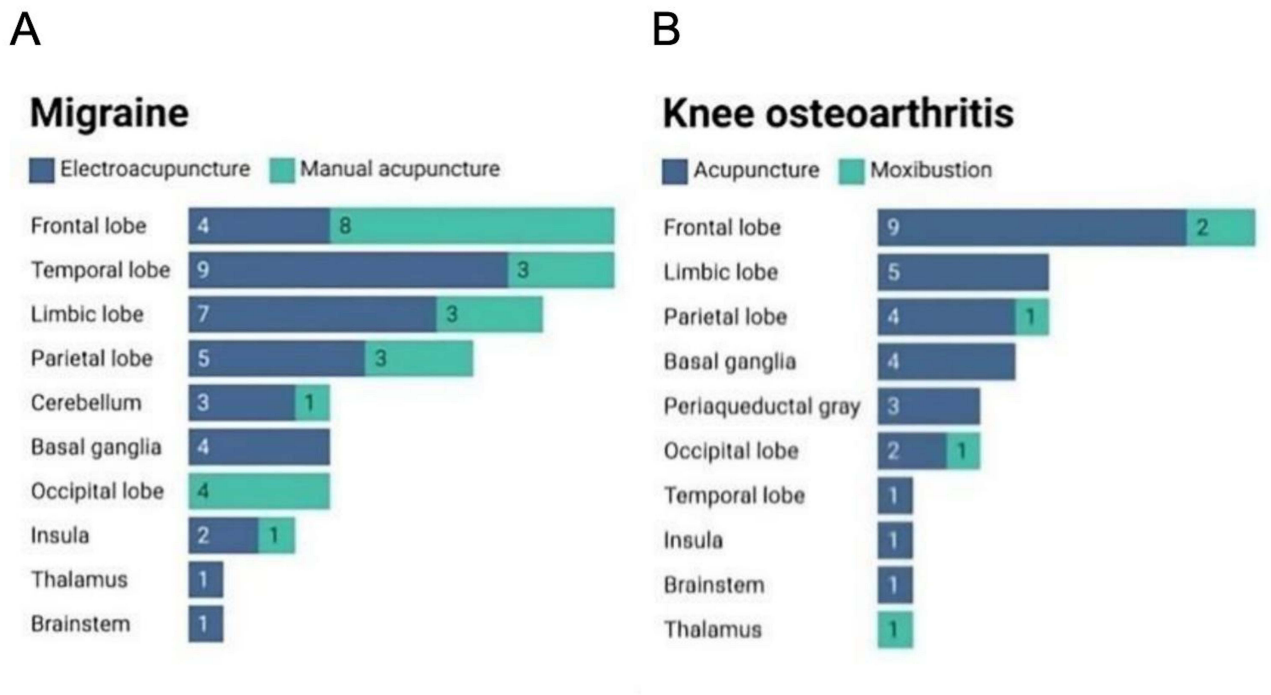

Figure 6 Brain region activation in response to different treatment methods used for the same disease.
Notes: (**A**) Differences in brain areas responding to electroacupuncture and hand-acupuncture in migraine. (**B**) Differences in brain regions responding to acupuncture and moxibustion in knee osteoarthritis.

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Imaging Methods

The articles included in this review were categorized based on the imaging methods used. The majority employed functional magnetic resonance imaging (fMRI) to investigate the mechanisms of acupuncture analgesia, while only two studies utilized positron emission tomography (PET).

Discussion

This review analysed the literature on changes of brain function associated with acupuncture and moxibustion analgesia determined using imaging technology.

Acupuncture and Moxibustion Can Activate Key Brain Regions Closely Related to Pain Regulation

Acupuncture and moxibustion exert their analgesic effects by stimulating different areas of the CNS and modulating neurotransmitters, signaling pathways, and immune responses.[49] Neuroimaging studies have demonstrated that acupuncture influences various brain regions involved in pain perception, emotional regulation, and cognitive functions. The following sections highlight key findings from neuroimaging research on the brain areas affected by acupuncture analgesia.

According to this study, the frontal lobe is frequently activated by acupuncture. The prefrontal cortex (PFC) is responsible for executive functions, such as working memory, decision-making, and emotional regulation.[50] Acupuncture and moxibustion have been found to alter the functional connectivity of the PFC, thereby reducing cognitive and emotional responses to pain. At the molecular level, this effect is linked to the modulation of neurotrophic factors, like the brain-derived neurotrophic factor (BDNF), which plays a crucial role in promoting neuronal survival and synaptic plasticity.[51] Changes in the levels of BDNF and other neurotrophic factors contribute to the PFC's role in pain and stress reduction.[11] Moreover, the primary somatosensory cortex (S1) is a key region within the brain responsible for processing sensory information, including pain signals.[52] Neuroimaging studies have revealed that acupuncture can modulate the activity of S1, resulting in altered pain perception.[16,43] This modulation is associated with alterations in synaptic activity and neurotransmitter release, particularly involving glutamate and gamma-aminobutyric acid (GABA).[53,54] Glutamate is typically associated with excitatory signals, which increase the chances that a neuron will fire, while GABA serves as an inhibitory neurotransmitter, decreasing neuron firing. The balance between these neurotransmitters is essential for proper brain function and pain processing.[55] In the context of acupuncture, altering the activity of glutamate and GABA might modify how intensely pain is felt. The S1's role in encoding the intensity and location of pain makes it a crucial target for these therapies. Acupuncture and moxibustion can also affect pain-related cerebral cortex areas, such as the motor cortex and sensory cortex, change their functional connections, and reduce pain perception and transmission.[56]

The limbic system, including the anterior cingulate cortex (ACC), insula, and hippocampus, is another critical area influenced by acupuncture. The ACC plays a central role in emotional processing and pain perception.[57] Acupuncture and moxibustion have been shown to alter the functional connectivity of the ACC, leading to a reduction in the emotional and cognitive components of pain.[24,47] Molecularly, this effect is associated with the regulation of neurotransmitters, such as serotonin and dopamine, which are involved in mood and pain modulation.[58,59] The insula integrates sensory and affective aspects of pain.[60] The hippocampus, associated with memory and emotional responses,[61] also shows altered activity patterns under acupuncture and moxibustion.[20] These alterations in the limbic system emphasize acupuncture's capacity to regulate both the sensory and emotional aspects of pain, offering a more holistic approach to pain management.

Acupuncture also affects other brain regions, including the parietal, temporal, and occipital lobes, basal ganglia, cerebellum, thalamus, and brainstem. Within the parietal lobe, the postcentral gyrus (PoCG) and superior parietal lobule (SPL) are components of the somatosensory cortex, playing a crucial role in processing sensory information and localizing pain.[62] The temporal lobe regions, such as the superior temporal gyrus (STG) and middle temporal gyrus (MTG), are involved in sensory integration and memory, contributing to the overall perception of pain.[63] The activation of the occipital lobe suggests a potential integration of visual and sensory information. Moreover, the basal ganglia, particularly the caudate nucleus and putamen, play a vital role in motor control and pain modulation.[64,65] The cerebellum's role in motor coordination and the thalamus's function as a relay center for sensory signals further

emphasize acupuncture's comprehensive impact on the brain.[66] The brainstem, particularly the PAG, is involved in the endogenous pain modulation system, facilitating the release of endogenous opioids and contributing to pain relief.[67] Endogenous opioid peptides are important analgesic neurotransmitters, which can inhibit pain generation and transmission. Moreover, the thalamus is also a key component of the descending inhibitory system.[68] Therefore, acupuncture inhibits pain transmission and perception by activating endogenous analgesic systems in these regions.[69]

The brain regions influenced by acupuncture are primarily concentrated in the default mode network and basal ganglia. The default mode network is linked to spontaneous thought and introspection, while the basal ganglia are involved in motor control and conditioned learning.[70,71] This suggests that acupuncture not only modulates brain regions directly associated with pain, but also affects higher brain functions more broadly. This may be related to the overall acupuncture-induced regulation. In addition to physiological regulation, acupuncture and moxibustion affect the psychological state of individuals, reducing anxiety and depression, increasing pleasure, and diminishing the degree and duration of pain. This highlights the complex interaction between physiological and psychological processes in pain management through acupuncture and moxibustion.

Acupuncture and Moxibustion Regulation Reflects the Similarities and Differences of Brain Region Responses in Different Types of Pain

The study analyzed and compared acute, chronic, somatic, and visceral pain, demonstrating that acupuncture and moxibustion activate specific brain regions depending on the nature of the experienced pain.

Both acute and chronic pain activated certain common brain regions, but chronic pain affected a wider range of brain regions because of its persistence, complexity, and accompanying symptoms. In particularly, chronic pain involved more areas of the PFC, limbic system, and basal ganglia, further underscoring the widespread effects of chronic pain on the CNS. Chronic pain differs from acute pain with regards to the implicated neurologic mechanisms, mainly related to the duration of pain and extent of its effects on the nervous system. Acute pain is usually a sudden, short-lived pain experience, in which pain signals are transmitted from injured tissues to the CNS, activating brain regions associated with pain perception and triggering corresponding physiological and behavioral responses.[72] Pain caused by injury or illness is considered chronic if it lasts for more than three months.[1] Chronic pain has more complex and persistent manifestations and symptoms than acute pain.[73] At the same time, chronic pain is often accompanied by numerous comorbid symptoms and conditions, such as mood disorders and cognitive decline.[74] From a neurologic perspective, pain signals triggered by chronic pain activate more brain regions, including the PFC, limbic system, and basal ganglia. These brain regions play important roles in pain perception, emotional regulation, and attention control. For example, the PFC is involved in the cognitive processing and emotional regulation of pain,[75] the limbic system in the attentional and emotional responses to pain,[76] and the basal ganglia in the motor and behavioral responses to pain.[77] Chronic pain not only affects the CNS at the perceptual and cognitive levels, but also induces a wide range of physiological and psychological changes. Long-term pain stimulation can cause plasticity changes in the CNS, making the transmission of pain signals more sensitive and resulting in increased persistence and prolonged duration of pain.[78] Therefore, the therapeutic approach to chronic pain needs to consider its extensive effects on the CNS.

Both somatic and visceral pain involve the same areas of the brain. However, visceral pain and somatic pain differ in the extent and focus of activation of specific brain regions due to their different locations and symptoms.[79] This distinction underscores the intricate nature of pain processing within the brain. The current study suggests that visceral pain is more likely to trigger the activation of brain regions associated with mood and emotion,[80] which may explain why visceral pain is often accompanied by strong emotional responses. In contrast, somatic pain tends to activate areas associated with sensory perception and movement. These findings underscore the intricate and multifaceted nature of pain processing in the brain.

Different types of pain activate distinct brain regions, and by assessing brain changes in patients with various pain conditions treated with acupuncture and moxibustion, we can reveal disease-specific neuromodulation effects. The above results indicate that differences in activated brain regions during acupuncture and moxibustion treatment may reflect characteristics of different pain types and disease specificity. The high correlation of common brain regions reflects the stability of acupuncture and moxibustion regulation of brain functional connectivity.

Electroacupuncture and manual acupuncture were found to activate a wider range of sensory cortex areas, including the parietal, temporal, and occipital lobes, which are closely linked to somatosensory processing and pain perception. However, moxibustion activated more prominently the limbic system and occipital lobe, possibly due to the mild heat sensation associated with moxibustion. These findings suggest that acupuncture and moxibustion exhibit distinct patterns of brain function regulation, providing unique perspectives for exploring their mechanisms in pain treatment.

Application of Imaging Technology in Acupuncture and Moxibustion Analgesia Research

According to this study, medical imaging techniques have been used in clinical research on acupuncture analgesia since 1997. With the continuous development of medical imaging technology, an important milestone occurred in 2014, which was the first publication peak. This indicates that advances in medical imaging techniques have facilitated in-depth research into the mechanism of acupuncture analgesia. fMRI has high and comprehensive spatial and temporal performance and can provide detailed imaging information to help researchers observe brain changes during acupuncture and moxibustion treatment. However, limitations of current technology have impeded the progress in visualizing acupuncture and moxibustion analgesia mechanisms. Nevertheless, with the continuous advances of medical imaging techniques, we believe that we can overcome these limitations in the future and further reveal the mechanism of acupuncture and moxibustion analgesia.

Limitations and Perspectives

The study revealed that acupuncture produces a notable analgesic effect. However, the analysis was constrained by a small sample size, with only 37 included articles, and the range of examined disease types was relatively limited. Variations in stimulation parameters may also have influenced changes in functional connectivity. Additionally, the control group design had certain limitations. Future studies should aim to increase the sample size, expand the range of disease types, standardize stimulation parameters, and optimize control group design to enhance the study's reliability.

Conclusion

Acupuncture and moxibustion are distinctive therapeutic methods in traditional Chinese medicine. However, current research on their mechanisms, aided by imaging technology, is notably imbalanced. The academic focus has heavily favored acupuncture over moxibustion, leading to a limited scientific understanding of moxibustion's therapeutic mechanisms. This research bias has resulted in a deeper exploration of acupuncture's CNS effects, covering various physiological and neurologic aspects. Yet, as moxibustion is an integral part of acupuncture therapy, its mechanisms also warrant thorough investigation within modern medical contexts. Researchers are encouraged to use imaging technology to explore moxibustion's unique mechanisms, aiming to fully uncover the potential and value of acupuncture and moxibustion in contemporary medicine.

This study provides a comprehensive analysis of the central mechanisms underlying acupuncture and moxibustion analgesia, highlighting the significant brain regions affected by these traditional Chinese medicine practices. Neuroimaging studies indicate that acupuncture predominantly activates the frontal lobe, limbic system, parietal lobe, and other areas crucial for pain perception, emotional regulation, and cognitive function. Both acupuncture and moxibustion stimulate the ACC and PFC, which are essential in modulating pain and emotional responses. Moreover, the activation of the brainstem and PAG highlights the role of the endogenous opioid system in pain relief. These findings underscore the potential of acupuncture and moxibustion as effective non-pharmacological approaches for pain management and offer valuable insights for future research and clinical applications.

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Disclosure

The authors affirm that this research was conducted without any commercial or financial affiliations that might be perceived as a potential conflict of interest.

References

1. Treede RD, Rief W, Barke A, et al. Chronic pain as a symptom or a disease: the IASP classification of chronic pain for the international classification of diseases (ICD-11). *Pain*. 2019;160(1):19–27. doi:10.1097/j.pain.0000000000001384
2. GBD 2019 Diseases and Injuries Collaborators. Global burden of 369 diseases and injuries in 204 countries and territories, 1990-2019: a systematic analysis for the global burden of disease study 2019. *Lancet Lond Engl*. 2020;396(10258):1204–1222. doi:10.1016/S0140-6736(20)30925-9.
3. Pitcher MH, Von Korff M, Bushnell MC, Porter L. Prevalence and profile of high-impact chronic pain in the United States. *J Pain*. 2019;20(2):146–160. doi:10.1016/j.jpain.2018.07.006
4. Raja SN, Carr DB, Cohen M, et al. The revised international association for the study of pain definition of pain: concepts, challenges, and compromises. *Pain*. 2020;161(9):1976–1982. doi:10.1097/j.pain.0000000000001939
5. Vickers AJ, Vertosick EA, Lewith G, et al. Acupuncture for chronic pain: update of an individual patient data meta-analysis. *J Pain*. 2018;19(5):455–474. doi:10.1016/j.jpain.2017.11.005
6. Takakura N, Takayama M, Kawase A, et al. Acupuncture for Japanese katakori (chronic neck pain): a randomized placebo-controlled double-blind study. *Med Kaunas Lith*. 2023;59(12):2141. doi:10.3390/medicina59122141
7. Ma X, Chen W, Yang NN, et al. Potential mechanisms of acupuncture for neuropathic pain based on somatosensory system. *Front Neurosci*. 2022;16:940343. doi:10.3389/fnins.2022.940343
8. Chen Y, Li D, Li N, et al. Role of nerve signal transduction and neuroimmune crosstalk in mediating the analgesic effects of acupuncture for neuropathic pain. *Front Neurol*. 2023;14:1093849. doi:10.3389/fneur.2023.1093849
9. Ifrim Chen F, Antochi AD, Barbilian AG. Acupuncture and the retrospect of its modern research. *Romanian J Morphol Embryol*. 2019;60(2):411–418.
10. Kelly RB, Willis J. Acupuncture for pain. *Am Fam Physician*. 2019;100(2):89–96.
11. Kong L, He Q, Li Q, Schreiber R, Kaitin KI, Shao L. Rapid progress in neuroimaging technologies fuels central nervous system translational medicine. *Drug Discovery Today*. 2023;28(3):103485. doi:10.1016/j.drudis.2023.103485
12. Shi Y, Liu Z, Zhang S, et al. Brain network response to acupuncture stimuli in experimental acute low back pain: an fMRI study. *Evid Based Complement Alternat Med*. 2015;2015:210120. doi:10.1155/2015/210120
13. Wang X, Ni X, Ouyang X, et al. Modulatory effects of acupuncture on raphe nucleus-related brain circuits in patients with chronic neck pain: a randomized neuroimaging trial. *Cns Neurosci Ther*. 2024;30(3):e14335. doi:10.1111/cns.14335
14. Lan L, Yin T, Tian Z, et al. Acupuncture modulates the spontaneous activity and functional connectivity of calcarine in patients with chronic stable angina pectoris. *Front mol Neurosci*. 2022;15:842674. doi:10.3389/fnmol.2022.842674
15. Zhang S, Wang X, Yan CQ, et al. Different mechanisms of contralateral- or ipsilateral-acupuncture to modulate the brain activity in patients with unilateral chronic shoulder pain: a pilot fMRI study. *J Pain Res*. 2018;11:505–514. doi:10.2147/JPR.S152550
16. Maeda Y, Kettner N, Lee J, et al. Acupuncture evoked response in contralateral somatosensory cortex reflects peripheral nerve pathology of carpal tunnel syndrome. *Med Acupuncture*. 2013;25(4):275–284. doi:10.1089/acu.2013.0964
17. Maeda Y, Kettner N, Lee J, et al. Acupuncture-evoked response in somatosensory and prefrontal cortices predicts immediate pain reduction in carpal tunnel syndrome. *Evid Based Complement Alternat Med*. 2013;2013:795906. doi:10.1155/2013/795906
18. Maeda Y, Kim H, Kettner N, et al. Rewiring the primary somatosensory cortex in carpal tunnel syndrome with acupuncture. *Brain*. 2017;140(4):914–927. doi:10.1093/brain/awx015
19. Napadow V, Liu J, Li M, et al. Somatosensory cortical plasticity in carpal tunnel syndrome treated by acupuncture. *Hum Brain Mapp*. 2007;28(3):159–171. doi:10.1002/hbm.20261
20. Beissner F, Preibisch C, Schweizer-Arau A, Popovici RM, Meissner K. Psychotherapy with somatosensory stimulation for endometriosis-associated pain: the role of the anterior hippocampus. *Biol Psychiatry*. 2018;84(10):734–742. doi:10.1016/j.biopsych.2017.01.006
21. Mawla I, Ichesco E, Zöllner HJ, et al. Greater somatosensory afference with acupuncture increases primary somatosensory connectivity and alleviates fibromyalgia pain via insular γ-aminobutyric acid: a randomized neuroimaging trial. *Arthritis Rheumatol*. 2021;73(7):1318–1328. doi:10.1002/art.41620
22. Ye Y, Liu B. Analgesic effects of balanced acupuncture versus body acupuncture in low-back and leg pain patients with lumbar disc herniation, as assessed by resting-state functional magnetic resonance imaging. *Neural Regen Res*. 2012;7(21):1624–1629. doi:10.3969/j.issn.1673-5374.2012.21.004
23. Gao N, Shi H, Hu S, et al. Acupuncture enhances dorsal raphe functional connectivity in knee osteoarthritis with chronic pain. *Front Neurol*. 2021;12:813723. doi:10.3389/fneur.2021.813723
24. Chen X, Spaeth RB, Retzepi K, Ott D, Kong J. Acupuncture modulates cortical thickness and functional connectivity in knee osteoarthritis patients. *Sci Rep*. 2014;4:6482. doi:10.1038/srep06482
25. Kong J, Wang Z, Leiser J, et al. Enhancing treatment of osteoarthritis knee pain by boosting expectancy: a functional neuroimaging study. *NeuroImage Clin*. 2018;18:325–334. doi:10.1016/j.nicl.2018.01.021
26. Gollub RL, Kirsch I, Maleki N, et al. A functional neuroimaging study of expectancy effects on pain response in patients with knee osteoarthritis. *J Pain*. 2018;19(5):515–527. doi:10.1016/j.jpain.2017.12.260
27. Xie H, Xu F, Chen R, et al. Image formation of brain function in patients suffering from knee osteoarthritis treated with moxibustion. *J Trad Chin Med*. 2013;33(2):181–186. doi:10.1016/s0254-6272(13)60122-3
28. Chen X, Spaeth RB, Freeman SG, et al. The modulation effect of longitudinal acupuncture on resting state functional connectivity in knee osteoarthritis patients. *mol Pain*. 2015;11:67. doi:10.1186/s12990-015-0071-9
29. Egorova N, Gollub RL, Kong J. Repeated verum but not placebo acupuncture normalizes connectivity in brain regions dysregulated in chronic pain. *NeuroImage Clin*. 2015;9:430–435. doi:10.1016/j.nicl.2015.09.012

30. Yu S, Ortiz A, Gollub RL, et al. Acupuncture treatment modulates the connectivity of key regions of the descending pain modulation and reward systems in patients with chronic low back pain. *J Clin Med*. 2020;9(6):1719. doi:10.3390/jcm9061719
31. Li J, Zhang JH, Yi T, Tang WJ, Wang SW, Dong JC. Acupuncture treatment of chronic low back pain reverses an abnormal brain default mode network in correlation with clinical pain relief. *Acupuncture Med*. 2014;32(2):102–108. doi:10.1136/acupmed-2013-010423
32. Tu Y, Ortiz A, Gollub RL, et al. Multivariate resting-state functional connectivity predicts responses to real and sham acupuncture treatment in chronic low back pain. *NeuroImage Clin*. 2019;23:101885. doi:10.1016/j.nicl.2019.101885
33. Kim H, Mawla I, Lee J, et al. Reduced tactile acuity in chronic low back pain is linked with structural neuroplasticity in primary somatosensory cortex and is modulated by acupuncture therapy. *NeuroImage*. 2020;217:116899. doi:10.1016/j.neuroimage.2020.116899
34. Yang J, Zeng F, Feng Y, et al. A PET-CT study on the specificity of acupoints through acupuncture treatment in migraine patients. *BMC Complementary and Alternative Medicine*. 2012;12:123. doi:10.1186/1472-6882-12-123
35. Tian Z, Guo Y, Yin T, et al. Acupuncture modulation effect on pain processing patterns in patients with migraine without aura. *Front Neurosci*. 2021;15:729218. doi:10.3389/fnins.2021.729218
36. Zou Y, Tang W, Li X, Xu M, Li J. Acupuncture reversible effects on altered default mode network of chronic migraine accompanied with clinical symptom relief. *Neural Plast*. 2019;2019:5047463. doi:10.1155/2019/5047463
37. Li Z, Zhou J, Cheng S, et al. Cerebral fractional amplitude of low-frequency fluctuations may predict headache intensity improvement following acupuncture treatment in migraine patients. *J Trad Chin Med*. 2020;40(6):1041–1051. doi:10.19852/j.cnki.jtcm.2020.06.016
38. Liu S, Luo S, Yan T, et al. Differential modulating effect of acupuncture in patients with migraine without aura: a resting functional magnetic resonance study. *Front Neurol*. 2021;12:680896. doi:10.3389/fneur.2021.680896
39. Zhao L, Liu J, Zhang F, et al. Effects of long-term acupuncture treatment on resting-state brain activity in migraine patients: a randomized controlled trial on active acupoints and inactive acupoints. *PLoS One*. 2014;9(6):e99538. doi:10.1371/journal.pone.0099538
40. Zhang Y, Wang Z, Du J, et al. Regulatory effects of acupuncture on emotional disorders in patients with menstrual migraine without aura: a resting-state fMRI study. *Front Neurosci*. 2021;15:726505. doi:10.3389/fnins.2021.726505
41. Li C, Li X, He K, et al. Discovery of the mechanisms of acupuncture in the treatment of migraine based on functional magnetic resonance imaging and omics. *Front Med*. 2023;17(5):993–1005. doi:10.1007/s11684-023-0989-7
42. Liu CH, Yeh TC, Kung YY, et al. Changes in resting-state functional connectivity in nonacute sciatica with acupuncture modulation: a preliminary study. *Brain Behav*. 2020;10(2):e01494. doi:10.1002/brb3.1494
43. Yu SW, Lin SH, Tsai CC, et al. Acupuncture effect and mechanism for treating pain in patients with parkinson's disease. *Front Neurol*. 2019;10:1114. doi:10.3389/fneur.2019.01114
44. Tu CH, Lee YC, Chen YY, et al. Acupuncture treatment associated with functional connectivity changes in primary dysmenorrhea: a resting state fMRI study. *J Clin Med*. 2021;10(20):4731. doi:10.3390/jcm10204731
45. Xu J, Xie H, Liu L, et al. Brain mechanism of acupuncture treatment of chronic pain: an individual-level positron emission tomography study. *Front Neurol*. 2022;13:884770. doi:10.3389/fneur.2022.884770
46. Wang Y, Xu J, Zhang Q, et al. Immediate analgesic effect of acupuncture in patients with primary dysmenorrhea: a fMRI study. *Front Neurosci*. 2021;15:647667. doi:10.3389/fnins.2021.647667
47. Yang H, Li X, Guo XL, et al. Moxibustion for primary dysmenorrhea: a resting-state functional magnetic resonance imaging study exploring the alteration of functional connectivity strength and functional connectivity. *Front Neurosci*. 2022;16:969064. doi:10.3389/fnins.2022.969064
48. Kang B, Zhao C, Ma J, et al. Electroacupuncture alleviates pain after total knee arthroplasty through regulating neuroplasticity: a resting-state functional magnetic resonance imaging study. *Brain Behav*. 2023;13(3):e2913. doi:10.1002/brb3.2913
49. Huang L, Xu G, He J, et al. Bibliometric analysis of functional magnetic resonance imaging studies on acupuncture analgesia over the past 20 years. *J Pain Res*. 2021;14:3773–3789. doi:10.2147/JPR.S340961
50. Ong WY, Stohler CS, Herr DR. Role of the prefrontal cortex in pain processing. *mol Neurobiol*. 2019;56(2):1137–1166. doi:10.1007/s12035-018-1130-9
51. Ibarra IL, Ratnu VS, Gordillo L, et al. Comparative chromatin accessibility upon BDNF stimulation delineates neuronal regulatory elements. *mol Syst Biol*. 2022;18(8):e10473. doi:10.15252/msb.202110473
52. Kim W, Kim SK, Nabekura J. Functional and structural plasticity in the primary somatosensory cortex associated with chronic pain. *J Neurochem*. 2017;141(4):499–506. doi:10.1111/jnc.14012
53. Jin Y, Meng Q, Mei L, et al. A somatosensory cortex input to the caudal dorsolateral striatum controls comorbid anxiety in persistent pain. *Pain*. 2020;161(2):416–428. doi:10.1097/j.pain.0000000000001724
54. Li H, Chalavi S, Rasooli A, et al. Baseline GABA+ levels in areas associated with sensorimotor control predict initial and long-term motor learning progress. *Hum Brain Mapp*. 2024;45(1):e26537. doi:10.1002/hbm.26537
55. Sears SM, Hewett SJ. Influence of glutamate and GABA transport on brain excitatory/inhibitory balance. *Exp Biol Med*. 2021;246(9):1069–1083. doi:10.1177/1535370221989263
56. Zhang J, Lu C, Wu X, Nie D, Yu H. Neuroplasticity of acupuncture for stroke: an evidence-based review of MRI. *Neural Plast*. 2021;2021:2662585. doi:10.1155/2021/2662585
57. Sun G, McCartin M, Liu W, et al. Temporal pain processing in the primary somatosensory cortex and anterior cingulate cortex. *mol Brain*. 2023;16(1):3. doi:10.1186/s13041-022-00991-y
58. Bliss TVP, Collingridge GL, Kaang BK, Zhuo M. Synaptic plasticity in the anterior cingulate cortex in acute and chronic pain. *Nat Rev Neurosci*. 2016;17(8):485–496. doi:10.1038/nrn.2016.68
59. Li XH, Matsuura T, Xue M, et al. Oxytocin in the anterior cingulate cortex attenuates neuropathic pain and emotional anxiety by inhibiting presynaptic long-term potentiation. *Cell Rep*. 2021;36(3):109411. doi:10.1016/j.celrep.2021.109411
60. Horing B, Büchel C. The human insula processes both modality-independent and pain-selective learning signals. *PLoS Biol*. 2022;20(5):e3001540. doi:10.1371/journal.pbio.3001540
61. Segev A, Korem N, Mizrachi Zer-Aviv T, et al. Role of endocannabinoids in the hippocampus and amygdala in emotional memory and plasticity. *Neuropsychopharmacol*. 2018;43(10):2017–2027. doi:10.1038/s41386-018-0135-4
62. Wang B, Hao Y, Zhan Q, et al. Dynamic reconfiguration of functional brain networks supporting response inhibition in a stop-signal task. *Brain Imaging Behav*. 2020;14(6):2500–2511. doi:10.1007/s11682-019-00203-7

63. Liu L, Lyu TL, Fu MY, et al. Changes in brain connectivity linked to multisensory processing of pain modulation in migraine with acupuncture treatment. *NeuroImage Clin*. 2022;36:103168. doi:10.1016/j.nicl.2022.103168
64. Yuan Z, Wang W, Zhang X, et al. Altered functional connectivity of the right caudate nucleus in chronic migraine: a resting-state fMRI study. *J Headache Pain*. 2022;23(1):154. doi:10.1186/s10194-022-01506-9
65. Rukavina K, Mulholland N, Corcoran B, et al. Musculoskeletal pain in Parkinson's disease: association with dopaminergic deficiency in the caudate nucleus. *Eur J Pain*. 2024;28(2):244–251. doi:10.1002/ejp.2172
66. Bostan AC, Strick PL. The basal ganglia and the cerebellum: nodes in an integrated network. *Nat Rev Neurosci*. 2018;19(6):338–350. doi:10.1038/s41583-018-0002-7
67. Bagley EE, Ingram SL. Endogenous opioid peptides in the descending pain modulatory circuit. *Neuropharmacology*. 2020;173:108131. doi:10.1016/j.neuropharm.2020.108131
68. Meeker TJ, Schmid AC, Keaser ML, et al. Tonic pain alters functional connectivity of the descending pain modulatory network involving amygdala, periaqueductal gray, parabrachial nucleus and anterior cingulate cortex. *NeuroImage*. 2022;256:119278. doi:10.1016/j.neuroimage.2022.119278
69. Cabioğlu MT, Cetin BE. Acupuncture and immunomodulation. *Am J Chin Med*. 2008;36(1):25–36. doi:10.1142/S0192415X08005552
70. Zhang Y, Zhang H, Nierhaus T, Pach D, Witt CM, Yi M. Default mode network as a neural substrate of acupuncture: evidence, challenges and strategy. *Front Neurosci*. 2019;13:100. doi:10.3389/fnins.2019.00100
71. Pereira CR, Criado MB, Machado J, Pereira CT, Santos MJ. Acute effects of acupuncture in balance and gait of Parkinson disease patients - a preliminary study. *Complementary Therap Clin Pract*. 2021;45:101479. doi:10.1016/j.ctcp.2021.101479
72. Bell A. The neurobiology of acute pain. *Vet j*. 2018;237:55–62. doi:10.1016/j.tvjl.2018.05.004
73. Kuner R, Kuner T. Cellular circuits in the brain and their modulation in acute and chronic pain. *Physiol Rev*. 2021;101(1):213–258. doi:10.1152/physrev.00040.2019
74. Bushnell MC, Ceko M, Low LA. Cognitive and emotional control of pain and its disruption in chronic pain. *Nat Rev Neurosci*. 2013;14(7):502–511. doi:10.1038/nrn3516
75. Qi X, Cui K, Zhang Y, et al. A nociceptive neuronal ensemble in the dorsomedial prefrontal cortex underlies pain chronicity. *Cell Rep*. 2022;41(11):111833. doi:10.1016/j.celrep.2022.111833
76. Hogri R, Teuchmann HL, Heinke B, Holzinger R, Trofimova L, Sandkühler J. GABAergic CaMKIIα+ amygdala output attenuates pain and modulates emotional-motivational behavior via parabrachial inhibition. *J Neurosci*. 2022;42(27):5373–5388. doi:10.1523/JNEUROSCI.2067-21.2022
77. Chudler EH, Dong WK. The role of the basal ganglia in nociception and pain. *Pain*. 1995;60(1):3–38. doi:10.1016/0304-3959(94)00172-B
78. Li XY, Wang N, Wang YJ, et al. Long-term temporal imprecision of information coding in the anterior cingulate cortex of mice with peripheral inflammation or nerve injury. *J Neurosci*. 2014;34(32):10675–10687. doi:10.1523/JNEUROSCI.5166-13.2014
79. Cervero F. Visceral versus somatic pain: similarities and differences. *Dig Dis Basel Switz*. 2009;27 Suppl 1:3–10. doi:10.1159/000268115
80. Mayer EA, Gupta A, Kilpatrick LA, Hong JY. Imaging brain mechanisms in chronic visceral pain. *Pain*. 2015;156 Suppl 1(0 1):S50–S63. doi:10.1097/j.pain.0000000000000106

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