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Activated and deactivated functional brain areas in the *Deqi* state

A functional MRI study☆

Yong Huang[1], Tongjun Zeng[2], Guifeng Zhang[3], Ganlong Li[4], Na Lu[5], Xinsheng Lai[6], Yangjia Lu[7], Jiarong Chen[8]

1 *Traditional Chinese Medicine School, Southern Medical University, Guangzhou 510515, Guangdong Province, China*
2 *Rehabilitation Department, First People's Hospital, Shunde District, Foshan 528300, Guangdong Province, China*
3 *Academic Affairs Department, Xinxing Chinese Medicine School, Xinxing 527400, Guangdong Province, China*
4 *Traditional Chinese Medicine Department, Huarui Hospital, Southern Medical University, Guangzhou 510360, Guangdong Province, China*
5 *Medicophysics Department, Guangzhou Medical University, Guangzhou 510182, Guangdong Province, China*
6 *Acupuncture and Massage College, Guangzhou Traditional Chinese Medicine University, Guangzhou 510405, Guangdong Province, China*
7 *Traditional Chinese Medicine Department, Guangdong Medical College, Dongguan 523808, Guangdong Province, China*
8 *First School of Clinical Medicine, Southern Medical University, Guangzhou 510515, Guangdong Province, China*

Abstract
We compared the activities of functional regions of the brain in the *Deqi* versus non-*Deqi* state, as reported by physicians and subjects during acupuncture. Twelve healthy volunteers received sham and true needling at the *Waiguan* (TE5) acupoint. Real-time cerebral functional MRI showed that compared with non-sensation after sham needling, true needling activated Brodmann areas 3, 6, 8, 9, 10, 11, 13, 20, 21, 37, 39, 40, 43, and 47, the head of the caudate nucleus, the parahippocampal gyrus, thalamus and red nucleus. True needling also deactivated Brodmann areas 1, 2, 3, 4, 5, 6, 7, 9, 10, 18, 24, 31, 40 and 46.

Key Words
needling; sham needling; *Waiguan* (TE5); sham point; *Deqi*; functional MRI; brain region activation; deactivation; neural regeneration

Research Highlights
(1) The present study measured brain activity during true needling accompanied by *Deqi* sensation (soreness, numbness, heaviness, and distension) in physician and subjects, and compared it to brain activity accompanying non-sensation during sham needling.
(2) Functional MRI identified activated and deactivated brain areas in the *Deqi* state.

Abbreviations
fMRI, functional MRI; BA, Brodmann area

Yong Huang☆, M.D., Professor, Chief physician, Doctoral supervisor, Traditional Chinese Medicine School, Southern Medical University, Guangzhou 510515, Guangdong Province, China

Corresponding author: Xinsheng Lai, M.D., Professor, Chief physician, Doctoral supervisor, Acupuncture and Massage College, Guangzhou Traditional Chinese Medicine University, Guangzhou 510405, Guangdong Province, China
Lai1023@163.com

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INTRODUCTION

Deqi, also called needling sensation, is a special phenomenon that occurs following needling. When a needle is inserted, the physician feels a subsidence of the tip of the needle, while the person who receives the needling feels local soreness, numbness, heaviness and distension, or a spread of the sensation along a certain route[1-2]. *Deqi* is a unique sensation essential for clinical

efficacy according to traditional Chinese medicine. It has been proven by recent clinical practice[1, 3-4], but there is a lack of scientific evidence of *Deqi*.

Deqi relies on subjective descriptions from both patient and acupuncturist, and can therefore not be objectively assessed. Recent studies of *Deqi* have mainly focused on two aspects: (1) objective quantitative determination of *Deqi*, and (2) the essence of *Deqi* [5].

Large-sample studies of subjective sensations in the *Deqi* state have found that the nature of *Deqi* (a comfortable feeling in the patient) is distinct from pain[5-8]. In addition to the visual analogue scale, special scales have been developed for the identification of *Deqi* and for assessment of its strength[9-10]. Furthermore, it has been shown that *Deqi* should be induced by insertion of the needle to a certain depth and stimulation with twirling manipulation[11]. This is different from the shallow insertion with sham twirling used in studies utilizing the visual analogue scale.

In addition to the studies of the subjective experience of *Deqi*, some research has focused on identifying anatomical correlates of *Deqi* induction. Shi *et al* [12] used light and electron microscopy to observe guinea pig tissue after needling, and reported that *Deqi* experienced by the acupuncturist was related to insertion into local connective tissue. Kimura *et al* [13] found that when the needle was withdrawn immediately upon the onset of *Deqi*, the transparent tissues attached to the needle tip contained many collagen fibers and mast cells, as confirmed by electron microscopy and immunohistochemistry. Analysis of the relationship between *Deqi* and peripheral afferent nerve fibers showed that *Deqi* induction was associated with needle insertion into slow conduction fibers[14-16].

Some studies have focused on changes in brain activity in the state of *Deqi*. Yin *et al* [17] observed that the strength of the subjective feeling was correlated to the power of α and δ activity on electroencephalography. Takamoto *et al* [18] found that blood oxygen concentration decreased in the supplementary motor area upon *Deqi* induction, based on functional near-infrared spectroscopy. Using functional MRI (fMRI), Asghar *et al* [19] observed that *Deqi* was associated with decreased activity of limbic subcortical structures and cerebellum compared with activity during uncomfortable pain. The sensation of *Deqi* is different in human beings than in animals[20]. Studies should focus on the brain, because it is pivotal in integrating afferent signals induced by the needling and mediating the therapeutic actions on target organs[20-21].

fMRI is superior for space-time discrimination, and is well suited to identifying changes in cerebral function in the *Deqi* state[21]. In contrast to the previous study[19], which compared *Deqi* with uncomfortable pain, the present study focused on comparing non-feeling with typical *Deqi*, to test the hypothesis that *Deqi* produces a specific pattern of cerebral activation/deactivation compared with sham needling.

RESULTS

Quantitative analysis of participants

A total of 12 healthy participants were included in the analysis.

Classification of subjective sensations of physician and subjects

Of the 12 participants, 6 were subjected to needling at *Waiguan* (TE5) and the others received needling at a sham point. All subjects received true and sham needling. Upon completion of the needling, subjects and physicians were asked to report on their experience during the needling. The subjects were asked to choose between “no feeling”, “soreness, distension or heaviness”, and “uncomfortable sharp pain”, and the physician was asked to choose between “empty” or “tenseness and heaviness” around the tip of the needle.

The physician claimed that he did not experience any tenseness or heaviness during sham needling of either the *Waiguan* or the sham point, but that there was a feeling of tenseness and heaviness during true needling of either points (Table 1). Patients were assigned to groups according to their reported sensation, and the activity of functional brain areas was compared between the *Deqi* state (true needling: soreness, numbness, distending; n = 10) and non-*Deqi* (sham needling: no feeling, n = 7).

Table 1 Needling sensation reported by physician and subjects

Point	Needling	Physician feeling		Subject feeling		
		Non-*Deqi*	*Deqi*	Non-*Deqi*	*Deqi*	Uncomfortable pain
Waiguan	Sham	6	0	6	0	0
	True	0	6	0	4	2
Sham	Sham	6	0	1	3	2
	True	0	6	0	6	0

There were six cases in each group.

Activated brain areas in the *Deqi* state

True needling with *Deqi* activated the right Brodmann areas (BA) 3, 6, 8, 9, 10, 11, 20, 37, 39, and 47 compared with sham needling. It also activated the head of caudate nucleus, the parahippocampal gyrus, thalamus red nucleus, and the left BA 3, 6, 9, 10, 13, 21, 40, 43, 47, (Table 2, Figure 1).

Table 2 Activation of brain areas in the *Deqi* state compared between true and sham needling

Brain area	Brodmann area	Talairach (mm)			*t*
		x	*y*	*z*	
Right cerebrum, frontal lobe, superior frontal gyrus	10	10	62	16	4.16
Right cerebrum, frontal lobe, superior frontal gyrus	11	20	56	–12	3.93
Right cerebrum, frontal lobe, superior frontal gyrus	6	8	14	54	4.29
Right cerebrum, frontal lobe, precentral gyrus	6	38	–12	66	3.80
Right cerebrum, frontal lobe, precentral gyrus	6	44	–6	52	3.58
Right cerebrum, frontal lobe, middle frontal gyrus	6	38	8	52	3.30
Right cerebrum, frontal lobe, middle frontal gyrus	8	52	22	42	4.01
Right cerebrum, frontal lobe, middle frontal gyrus	9	58	18	34	2.87
Right cerebrum, frontal lobe, inferior frontal gyrus	47	52	30	–10	4.32
Right cerebrum, parietal lobe, supramarginal gyrus	40	54	–54	26	4.77
Right cerebrum, parietal lobe, post central gyrus	3	30	–32	66	2.87
Right cerebrum, temporal lobe, middle temporal gyrus	39	56	–66	26	5.32
Right cerebrum, temporal lobe, middle temporal gyrus	39	52	–58	8	4.99
Right cerebrum, temporal lobe, inferior temporal gyrus	20	54	–10	–20	6.31
Right cerebrum, temporal lobe, inferior temporal gyrus,	20	58	–12	–20	5.13
Right cerebrum, inferior temporal gyrus	37	50	–66	–2	3.63
Right cerebrum, sub-lobar, caudate head		14	18	–6	3.73
Left cerebrum, frontal lobe, superior frontal gyrus	6	–10	8	55	4.38
Left cerebrum, frontal lobe, middle frontal gyrus	6	–44	2	52	3.14
Left cerebrum, frontal lobe, middle frontal gyrus	47	–46	34	–8	4.50
Left cerebrum, frontal Lobe, medial frontal gyrus	10	–2	60	20	4.40
Left cerebrum, frontal lobe, inferior frontal gyrus	9	–46	0	20	3.58
Left cerebrum, frontal lobe, inferior frontal gyrus	47	–52	26	–4	4.78
Left cerebrum, frontal lobe, inferior frontal gyrus	47	–46	28	–14	4.55
Left cerebrum, parietal lobe, postcentral gyrus	3	–62	–12	22	2.98
Left cerebrum, parietal lobe, postcentral gyrus	43	–64	–10	14	2.81
Left cerebrum, parietal lobe, supramarginal gyrus	40	–64	–48	30	4.69
Left cerebrum, parietal lobe, supramarginal gyrus	40	–60	–60	32	2.85
Left cerebrum, parietal lobe, inferior parietal lobule	40	–62	–26	30	3.01
Left cerebrum, middle temporal gyrus	21	–62	–58	0	4.94
Left cerebrum, sub-lobar, insula	13	–38	–2	–2	3.39
Left cerebrum, limbic lobe, parahippocampal gyrus		–34	–14	–12	2.56
Left cerebrum, thalamus		–2	–14	–2	3.12
Left brainstem, midbrain, red nucleus		–4	–16	–10	2.82

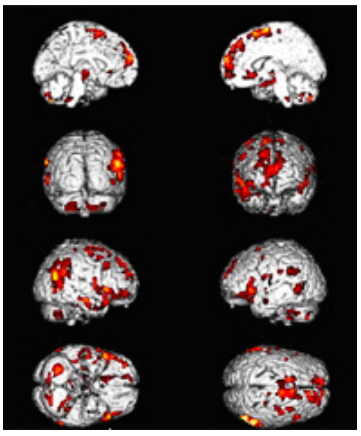

Figure 1 Activation of brain areas in the *Deqi* state compared between true and sham needling.

Row 1: Sagittal plane; row 2: occipital area; row 3: lateral plane; row 4: inferior and superior surfaces. The color shows the activated areas (low to high degree showed by red to yellow).

fMRI showed that true needling with *Deqi* decreased the activity in the right BA 1, 3, 4, 7, 9, 18 and 24, and the left BA 2, 3, 5, 6, 9, 10, 31, 40 and 46 (Figure 2 and Table 3).

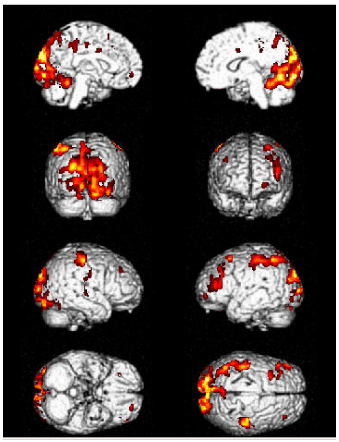

Figure 2 Deactivation of brain areas in the *Deqi* state compared between true and sham needling.

Row 1: Sagittal plane; row 2: occipital area; row 3: lateral plane; row 4: inferior surface and superior surface. The color shows the deactivated areas (low to high degree showed by red to yellow).

Table 3 Deactivation of brain areas in the *Deqi* state compared between true and sham needling

Brain area	Brodmann area	Talairach (mm)			*t*
		x	*y*	*z*	
Right cerebrum, parietal lobe, postcentral gyrus	1	54	–2	58	5.00
Left cerebrum, parietal lobe, precuneus	7	–10	–42	46	2.72
Left cerebrum, limbic lobe, cingulate gyrus	24	0	2	34	2.78
Right cerebrum, frontal lobe, middle frontal gyrus	9	40	40	38	3.49
Right cerebrum, frontal lobe, precentral gyrus	4	54	–12	32	3.10
Right cerebrum, parietal lobe, postcentral gyrus	3	45	–22	56	4.42
Right cerebrum, occipital lobe, lingual gyrus	18	18	–88	–12	5.18
Right cerebrum, occipital lobe, middle occipital gyrus	18	25	–95	8	5.12
Left cerebrum, frontal lobe, superior frontal gyrus	10	–24	56	–4	4.07
Left cerebrum, frontal lobe, medial frontal gyrus	6	–12	–16	46	2.97
Left cerebrum, frontal lobe, middle frontal gyrus	9	–42	28	30	3.47
Left cerebrum, frontal lobe, middle frontal gyrus	46	–46	44	14	4.22
Left cerebrum, frontal lobe, paracentral lobule	5	–4	–34	48	3.25
Left cerebrum, parietal lobe, postcentral gyrus	2	–44	–28	52	4.60
Left cerebrum, parietal lobe, postcentral gyrus	3	–46	–22	56	4.42
Left cerebrum, parietal lobe, inferior parietal lobule	40	–50	–44	54	4.10
Left cerebrum, limbic lobe, cingulate gyrus	31	–4	–36	40	3.28

DISCUSSION

The experimental design of studies of *Deqi* is difficult because of the reliance on the subjective experience of both physician and needling receivers. In the physician, *Deqi* might appear as soon as the needle is inserted, or after twirling, lifting and thrusting. Sensations in the needling receiver can be described as more than ten types of sensations with different degrees of strength. In addition, reports by the physician and the receiver do not always match.

The present study utilized fMRI to assess brain activation in the *Deqi* state[20, 22]. Strictly speaking, the study should also have included the following groups: *Deqi* in both physician and subject; *Deqi* in physician and non-sensation in subject; *Deqi* in physician and uncomfortable pain in subject; non-sensation in both physician and subject; non-sensation in physician and *Deqi* in subject; and non-sensation in physician and uncomfortable pain in the subject. In addition, we should have made a comparison between true and sham points. Asghar *et al* [19] studied the difference between *Deqi* and uncomfortable pain, but the present study focused on comparing *Deqi* with non-sensation, according to the post-needling feeling of both physician and subjects.

In this study, the physician reported *Deqi* during needling at both true and sham points, and reported non-sensation during sham needling at both true and sham points. However, the experience of the subjects was different. *Deqi* was mainly reported in the subjects who received needling at true and sham points, whereas non-sensation was reported during sham needling at the true point. Non-sensation, uncomfortable pain and *Deqi* were all reported during sham needling at the sham point. The results could not be processed statistically since the sample size was too small. However, the subjective feelings of the receivers of sham needling at the sham point varied, and the implications of these findings for clinical practice require further study.

We found a large number of activated and deactivated regions in the brain during the *Deqi* state. An interesting finding was that the activated regions were concentrated in brain areas that control somatic sensation and motor output, vision, gustation, language, and spatial orientation. The deactivated regions were concentrated to brain areas controlling somatic sensation and motor output, vision, affection, cognition, and spatial orientation, as well as frontal anterior and limbic-parietal association areas. These results indicate that in the state of *Deqi*, the effect of needling at *Waiguan* to treat motor and sensory dysfunction of the upper limbs and disorders of the eyes and ears, and to reduce heat and regulate mental disorders, could be manifested more completely.

Another interesting finding was that both activated and deactivated regions appeared in a same BA, such as BA3, 6, 9, 10 and 40, suggesting that those brain areas are very active in *Deqi* state after needling.

Among areas with changed activity during *Deqi*, we focused on those showing mixed activation and deactivation. These areas process somatic sensorimotor information and are part of the association areas of the cortex. Under *Deqi* conditions, needling action included two aspects: effects on certain brain areas to cause curative

effects, and strengthening of limbic-cortex associations. In contrast to a previous study[19], we did not find any areas with changed activity in the cerebellum. Similar to the study of Asghar *et al* [19], *Deqi* was also found to be related to the association areas of the brain, indicating an effect of needling on functional connectivity of the brain. In fact, acupoint stimulation has different effects in physiological *versus* pathological states. Future studies should focus on pathological states. Also, there is a shortage of fMRI studies of needling that use a block design[23]. Subsequent studies could use scans of resting functional connectivity[24-26] to reveal the essence of *Deqi*.

SUBJECTS AND METHODS

Design

A block design, neuroimaging study.

Time and setting

The experiment was performed at the Guangzhou University of Chinese Medicine, and the Southern Medical University, China, from 2008 to 2010.

Subjects

Twelve right-handed healthy volunteers were recruited from different universities in Guangzhou, China. The inclusion criteria were as follows: (1) 21–28 years old undergraduate/postgraduate students majoring in a non-medical subject; (2) non-smokers with regular eating habits without excessive consumption of liquid, tea or coffee, normal sleep, and normal body structure; (3) no metal in his/her body (such as heart stents); (4) no acupuncture treatment within 3 months prior to the experiment; (5) passed a screening test performed 3 months before the experiment (all the volunteers received the screening test by true/sham needling); and (6) agreed to sign the informed consent. The study was ethically approved by declaration of Helsinki.

The subjects included 6 males and 6 females, with an average age of 22.83 ± 2.32 years (range 21–27 years), weight of 55.33 ± 8.44 kg (44–70 kg), and height of 165.42 ± 9.61 cm (155–183 cm).

Methods

True and sham needling

The 12 volunteers were equally assigned to two groups. Subjects in the *Waiguan* group received sham and true needling at *Waiguan*, while the subjects in the sham point group received sham and true needling at a sham point. The *Waiguan* acupoint was located on the forearm, 2 cun above the transverse crease of the dorsum of the wrist, between the radius and ulna (cun is a unit of length that refers to the width of the interphalangeal joint of the patient's thumb; Figure 3) [27].

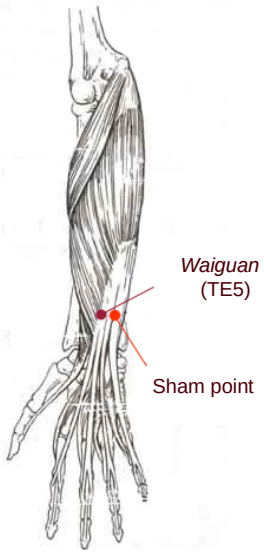

Figure 3 Location of *Waiguan* (TE5) and sham point. The directions of needling were perpendicular.

True and sham needling was delivered by one acupuncturist who had been in charge of a needling sensation screen three months earlier. The volunteers were blinded to the type of needling they received. True needling: The skin was sterilized locally and the needle was inserted using the tube insertion method. The tubes were purchased from Dongbang AcuPrime Co. (Exeter, England) and the 0.3 cm × 40 cm silver needles from Zhongyan Taihe Co. (Beijing, China). The physician put the auxiliary part of the tube on the skin at the acupoint, inserted the needle into the tube, and tapped the end of the needle to insert its tip into the tube. Then, the tube was removed and the needle punctured to a depth of 15 ± 2 mm. The handle of the needle was twirled to induce the needling sensation. Then, the physician manually applied an even reinforcing and reducing manipulation, by twirling the needle ± 180°, at 60 times/min. Twirling and non-twirling stimulation was alternated in blocks of 30 seconds, and the stimulation was lasted for 360 seconds in total (Figure 4). Sham needling: Sterilization procedures and needling instruments were the same as the above. However, instead of subcutaneous insertion of the needle, the stimulation was designed to provide alternating 30 seconds blocks of touching the skin with the tip of the needle (tactile stimulation) and then lifting the needle. The stimulation lasted for 360 seconds (Figure 5).

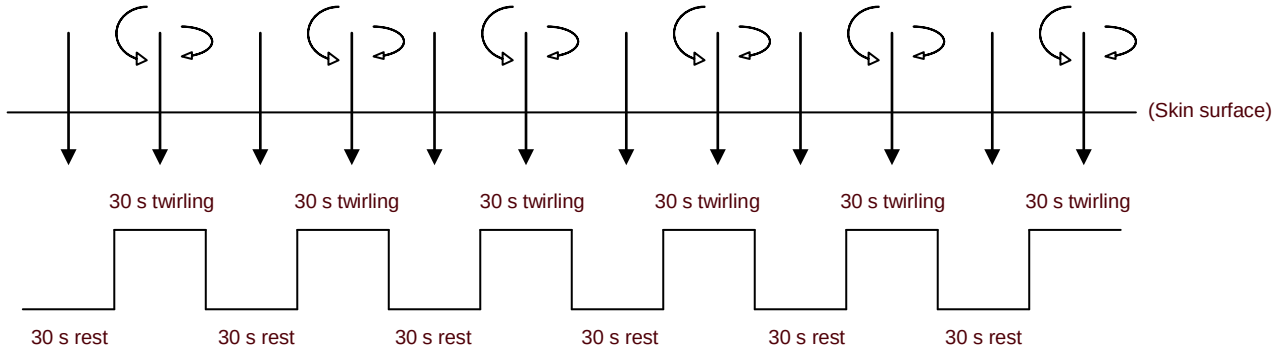

Figure 4 Block design of true needling at the *Waiguan* (TE5) and sham points. s: Second.

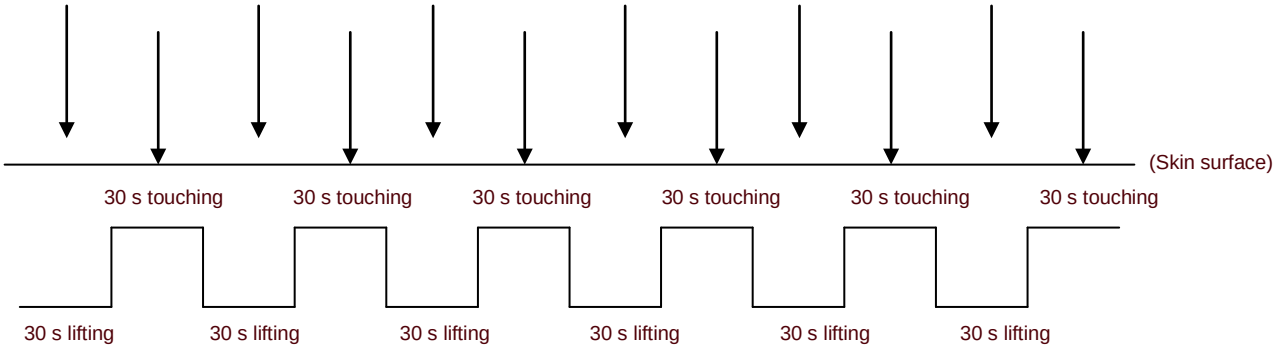

Figure 5 Block design of sham needling at the *Waiguan* (TE5) and sham points. s: Second.

Subjects in both the sham and true needling groups initially received sham needling, and true needling began one week later. Their brains were scanned by fMRI during the sham/true needling. After the scan, the subjects were asked to report on his/her experience during the needling, selecting between “soreness, numbness and distention”, “uncomfortable pain” and “non-sensation”.

Re-grouping

The subjects were re-grouped based on their report on needling sensation. When non-sensation was reported from both the physician and the subject, the subject was assigned to the “non-*Deqi* group”. When typical *Deqi* occurred (soreness, numbness and distention reported by the subject; and tenseness and heaviness at the tip of the needle reported by the physician), the subject was assigned to the “*Deqi* group”. Brain activation and deactivation were compared between the two groups.

fMRI scan

fMRI scanning was performed with a 3.0 T whole-body MRI scanner (GE, Bethesda, MD, USA) and a standard head coil. The subjects were blindfolded (Xinhua Tourism Co., Hangzhou, China) and used earplugs (Aearo Co., Hartford, Connecticut, USA). The subject had a rest on the bed for 5–10 minutes before the scan. The scan covered the entire brain and the images were parallel to the anterior/posterior commissure (AC-PC) line. The scan was divided into two parts. The first part was the collection of three-dimensional anatomy images with T1-weighted three-dimensional gradient echo-pulse fast spin sequence for 3 minutes with axial view T1 fluid-attenuated-inversion-recovery scan; repetition time, 2 300 ms; echo time, 21 ms; time of inversion, 920 ms; slice thickness, 6.0 mm; gap 1.0 mm for 20 layers totally; field of view, 24 cm × 18 cm; matrix, 320 × 256; NEX = 2; field of view echo train length, 9; and band width 50. Another part of the scan was the collection of blood oxygenation level-dependent functional images with single provocation echo-planar imaging sequence for 6.5 minutes with gradient echo/echo-planar imaging/90 (90° pulse); repetition time, 3 000 ms; echo time, 20 ms; flip angle, 90°; field of view, 24 cm × 24 cm; slice thickness, 6.0 mm; slice gap, 1.0 mm; matrix, 96 × 96; NEX = 1; phase per location, 130, 2 600 phases for 6 minutes and 30 seconds.

Data analysis

The fMRI data were processed with the software Statistical Parametric Mapping (SPM2, http://www.fil.ion.ac.uk)

and a matched operating platform of Matlab 6.1 (Mathworks, Natick, MA, USA)[28]. Slight movements of the head were corrected by the Realign module; then, the images were normalized to the Montreal Neurological Institute space and smoothed spatially by a Gaussian kernel of 5 mm × 5 mm × 5 mm. The smoothed data were analyzed with a generalized linear model voxel by voxel. The *t* value of each voxel was calculated by two-sample *t*-tests, and statistical parametric mapping was based on the *t* values ($P < 0.001$, uncorrected, $K > 30$). Significant changes in different brain regions during non-sensation and *Deqi* were identified and superposed on the standard brain image mode of each subject's anatomic images. All the images of a group were combined into a standardized model. Then, the two-sample *t*-test model with the results from fixed effects analysis was used to compare the differences between *Deqi* and non-sensation. The results were reported by the coordinates of the Talairach space, and activated/deactivated areas were showed with red color in figures.

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Author contributions: Xinsheng Lai was in charge of funds. Yong Huang and Xinsheng Lai conceived and designed the study. Tongjun Zeng and Ganlong Li provided and integrated data. Guifeng Zhang was in charge of needling. Na Lu analyzed experimental data. Yong Huang and Jiarong Chen wrote and revised the manuscript. Yangjia Lu contributed to statistical analysis.

Conflicts of interest: None declared.

Ethical approval: The experiment was approved by the Ethics Committee of the First Affiliated Hospital of Guangzhou University of Chinese Medicine, China.

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