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Acupuncture at Bi'nao increases the recovery of hypophasis in patients with incomplete recovered Bell's palsy: a randomized controlled clinical trial and task-state fMRI study

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ABSTRACT

Objectives: To evaluate the efficiency of acupuncture at the acupoint of Bi'nao for hypophasis and the mechanisms responsible for effect in the cerebral cortex.
Methods: Participants with hypophasis were selected from patients with incompletely recovered Bell's palsy and randomly allocated into Bi'nao group, Sham Bi'nao group and healthy control group with 33 participants per group. Acupuncture therapy was applied at the real or sham Bi'nao acupoint to compare efficiency. Clinical effects were evaluated by the House-Brackman Scale (HBS), Eye Crack Width Measurement (ECWM) scale and Eyelid Strength Assessment (ESA) before and after therapy. Regions of the brain cortex that were stimulated by acupuncture were detected by task-state functional magnetic resonance imaging.
Results: HBS and ESA scores in the Bi'nao group were lower than in the other two groups ($P<0.05$) while ECWM scores were higher ($P<0.05$). The cingulate cortex and cerebellum were activated during acupuncture stimulation in the Bi'nao group when compared to both the Sham Bi'nao group and the healthy control group ($P<0.05$).
Conclusion: Acupuncture at the acupoint Bi'nao increased the recovery of hypophasis in patients with incomplete recovered Bell's palsy. The underlying mechanism might be associated with the activation of the cingulate cortex and cerebellum.

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INTRODUCTION

Bell's palsy (BP) is regarded as a type of self-limited peripheral neuropathy caused by unspecified pathogens in which patients generally suffer from dysfunctional facial nerves and non-flexible muscle movements.[1-2] However, some patients will undergo a long recovery period and may experience certain sequelae symptoms, including hypophasis, hemifacial spasm or deviation in the angle of the mouth.[3-4] Hypophasis is considered as a significant clinical challenge with a high incidence.

Acupuncture, as well as electrical acupuncture therapy, has been widely used for the treatment of BP in China and across the world. [5-8] The efficacy of such therapy has been gradually proven by systematic reviews[9] and its application is considered as a reasonable resolution for the management of the sequelae associated with BP, [10-12] including hypophasis.

KEYWORDS:
acupuncture;
hypophasis;
Bell's palsy;
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Bi'nao, an acupuncture point located on the large intestine meridian of hand Yangming was previously reported to be useful for treating eye diseases according to the classical records of Traditional Chinese Medicine and some modern literature. [13-20] This acupoint is also used in clinical practice for the treatment of ophthalmoplegia and hypophasis. [21]

In the present study, the effect of acupuncture at Bi'nao in the treatment of hypophasis among patients with BP was evaluated via a randomized controlled trial (RCT) [22]. In addition, we used functional magnetic resonance imaging(fMRI) to identify potential mechanisms underlying the brain response to treatment.

METHODS

Clinical trial

Study design

This study was a single-center, three-arm, randomized, patient and assessor-blinded clinical trial with parallel groups. The research protocol of this study (version 1.0, 30th of June 2017) which followed the CONSORT, STRICTA[23] and SPIRIT[24] guidelines, was registered with the Chinese Clinical Trials Registry (ChiCTR-INR-17012955) and has also been published. [22]

Participants and recruitment

Participants were selected from the Departments of Acupuncture, Neurology, and Geratology of Baoshan Hospital, Shanghai University of Traditional Chinese Medicine. Recruitment spanned from September 2017 to December 2020. We enrolled both male and female patients aged 18–60 years. The participants were recruited by posters displayed in the hospital registration hall and by brochures sent out to those visiting these departments. The study title, research target, period, location, and contents of the intervention was introduced clearly to each participant.

The participants were informed of the potential benefits, risks, alternatives, and responsibilities of the study by the researchers during the consent process. The participants were fully aware that they were free to withdraw from the study at any time. Any adverse events (described as unfavorable or unintended signs, symptoms, or diseases occurring after treatment) that were related to acupuncture treatment were reported by the patients and practitioners during each patient visit. In addition, all vital signs and adverse events were measured and recorded during each visit.

All participants were randomized into Bi'nao group, Sham Bi'nao group and healthy control group with a 1:1:1 allocation ratio according to the protocol. Sample size was determined as 33 per group in accordance with a published protocol. [22]

Inclusion and exclusion criteria

The inclusion and exclusion criteria are listed in the study protocol[22]. Patients with Bell's palsy, who fulfilled the following inclusion criteria, were enrolled in the study: unilateral facial paralysis, aged between 18 and 60 years; Bell's palsy onset >1 month but <3 months; most symptoms recovered but hypophasis was present; the distance between the upper and lower eyelids was >2 mm; and no pathological signs.

Exclusion criteria

Participants meeting any of the following criteria were excluded from the study: pregnancy or breastfeeding; women who were pregnant during the study period; patients who had received medicine or acupuncture therapy in other hospitals before this study; diabetes for ≥5 years, grade 3 hypertension or hyperlipidemia ≥ 3 years; a history of malignant tumors, sexually transmitted disease, chronic renal or hepatic disease, glaucoma, acute otitis, ipsilateral chronic otitis, tuberculosis, immunodeficiency syndromes, recent head injury, psychiatric disease, infectious diseases, or any other conditions that may influence the treatment regimen being tested or that may have affected the completion of the study. We also excluded patients who had participated in other clinical trials within the previous 3 months.

Randomization and blinding

The enrolled participants were randomly assigned to Bi'nao group, Sham Bi'nao group and healthy control group (in a 1:1:1 ratio). An independent statistician generated the block randomization scheme in a blinded manner. The table was managed by another independent researcher who was not involved in the recruitment, acupuncture treatment, or assessment. The clinical research coordinator sent the assignment information to the researcher who conducted random allocation; subsequently, the researcher only provided assignment information to the TCM doctors who performed the acupuncture treatment. To ensure the concealment of allocation, the information was recorded in an allocation log by the researcher which was not opened until the data were locked. The participants were blinded to the type of acupuncture treatment, and the assessor, data managers, statisticians, and study monitors were blinded to the allocation. The blinding was maintained until the data were locked. For evaluation in a blinded manner, the allocation guessing was assessed immediately after the final treatment. The practitioners and assessors were instructed to treat the participants according to predefined standard operating procedures (SOPs) during the trial to maintain blinding.

Interventions

All participants received conventional acupuncture therapy performed by specialists in TCM following the STRICTA 2010 checklist. Acupuncture therapy was applied on the Cuanzhu (BL2), Yangbai (GB14), Sizhukong (SJ23), Shangming, Waiguan (SJ5), and Zhaohai (KI6) acupoints for all patients as basic therapy. Participants assigned to the Bi'nao group received additional acupuncture at the real Bi'nao acupoint, while the participants assigned to the Sham Bi'nao group were given extra acupuncture therapy at a point 1 cm backwards from the Bi'nao acupoint as a placebo point. Participants in the healthy control group did not receive additional acupuncture on any other acupoint. Acupuncture therapy was manipulated strictly in accordance with the study protocol three times per week for a duration of one month. The participants were separated independently and were not aware of the interventions performed on each other.

Outcome measures

Primary outcome

The eye crack width measurement (ECWM) test was performed using a graduated ruler; this was defined as the width (mm) between the upper and lower eyelids when the patient attempted to close his/her eyes; measurements were taken three times and the mean value was determined. ECWM was performed before acupuncture therapy as the primary time measurement, weekly during the treatment duration, and at the first month after the first therapy by three physicians, and the mean value was determined. The mean values and standard deviations for the participants in each group were calculated and the differences in eye crack width (mm) between the intervention and healthy control groups were then compared statistically.

Secondary outcomes

The eyelid strength assessment (ESA) test was conducted based on the muscle strength when the eyes were closed. The evaluator placed an index finger on the patient's upper eyelids and asked the patient to close his/her eye. The difference in muscle strength between the two eyelids was recorded according to the following standard: level 5, normal contraction on the affected side which was symmetrical when compared to the healthy side; level 4, approximately normal contraction and slightly asymmetrical when compared with the healthy side; level 3, strength was approximately 50% of the healthy side; level 2, strength was approximately 25% of the healthy side; level 1, a slight muscular contraction in the affected side; level 0, no sign of muscle contraction in the affected side. Assessments were performed at the time points mentioned above and at one month after therapy by three physicians and the mean value was recorded. Levels 0 5 were given numeric values of 0 to 5 as an ESA score and the mean scores for participants in each group were calculated. The mean values and standard deviations of ESA scores between the intervention and healthy control groups were then compared statistically.

Follow-up

Follow-up was performed in strict accordance with the study protocol. All participants were followed up three months after the first acupuncture therapy, including those who completely recovered from hypophasis within one month. Follow-up involved a clinic visit or telephone survey relating to the progress and recurrence of hypophasis.

Statistical analysis

Statistical analysis was performed using IBM SPSS Windows version 22.0. Tests were two-sided and $P < 0.05$ was considered as statistically significant. For the primary and secondary outcome measurements, we applied one-way analysis of variance (ANOVA) to identify statistical differences between the HBS, ESA and ECWM scores of different groups. In the case of data that did not conform to a normal distribution, we applied the Kruskal-Wallis H test.

fMRI studies

Participants

Thirty BP patients were selected from the included participants and thirty healthy individuals were recruited from colleagues at Baoshan Hospital, Shanghai University of Traditional Chinese Medicine. All the healthy volunteers were right-handed and aged between 22 and 55 years. Task-state fMRI data were collected during three tasks: the blink task, acupuncture at the real Bi'nao task and acupuncture at the sham Bi'nao task.

Data acquisition for task-state fMRI

In this study, we used a Siemens Verio 3.0T MRI whole body scanner with a standard head coil. A total of seven sequences were scanned, as follows: (1) Pilot images; (2) T2-weighted images which were used to identify obvious disease in the brain; (3) T1-weighted two-dimensional (2D) anatomical images which were obtained from the axial position parallel to the AC-PC line with a total of 36 slices that covered the whole brain. This involved a T1-weighted spin-echo sequence, a TR/TE of 2000/11 ms, a FOV of 230 × 230 mm, a slice thickness/interval of 4.0/0.4 mm, and a resolution of 64×64; (4) Task-state eye blinking fMRI using EPI-BOLD sequences. The scanning direction and the number of slices were the same as those for the 2D anatomical images, with a TR/TE/FA of 2600 ms/30 ms/90°, a FOV of 230 × 230 mm and a resolution of 64 × 64; (5) Task-state placebo acupuncture fMRI for the sham Bi'nao group with the same detection parameters as step 5; (6) Task-state real acupuncture fMRI at the Bi'nao acupoint with the same detection parameters as step 5 and 6, and (7) T1-weighted 3D anatomical images; for these, the sagittal position was taken, and a total of 176 slices were scanned which covered the whole brain. We used a spoiled gradient echo sequence with a TR/TE/FA of 2300 mm/2.27 mm/13°, a FOV of 230 × 230 mm, slice thickness/spacing of 1.0/0.5 mm and a resolution of 64 × 64. The entire data acquisition process took about 60 min.

Eye blinking and acupuncture stimulation protocol

A modified block design was used in the task-state acupuncture fMRI experiment (**Figure 1**). For the task-state eye blinking fMRI, participants were asked to blink their eyes with an interval of 26s each time; this was repeated three times during fMRI scanning. The next step of the sham acupuncture stimulation was performed after 30 min of rest.

When we began fMRI for the sham Bi'nao, a needle (85% silver purity) was inserted to a point 0.5 inches outside the Bi'nao point on the horizontal plane with a depth of approximately 1.0 cm and without de-qi sensation; this was retained while the fMRI data acquisition commenced. Stimulation consisted of rotating the needle bidirectionally with an even motion to an amplitude of approximately 180° at the rate of one cycle per second. After remaining at rest for 26 s, the needle was rotated again for another 26 s. Needle manipulation was repeated in a similar manner for a total of three repetitions. Subsequently, the needle was removed, and scanning continued for 4 minutes. Then, participants had a half-hour of rest before the next step.

As with the last step, task-state fMRI was performed in patients receiving acupuncture at the real Bi'nao acupoint at a depth of approximately 1.0cm with de-qi sensation. Subsequently, the procedures were the same as for sham Bi'nao fMRI. All acupuncture operations were performed by the same professional acupuncturist.

Data processing

For data preparation, we first used MRIConvert, MRIcron (dcm2niiX) and DCM2AsiszImg to convert the format of the original data. Then, MRIcron and SPM were used to check image quality. MRIcron is a cross-platform NIfTI format image viewer and can load multiple layers of images, generate volume renderings, and draw volumes of interest; it also provides dcm2nii for converting DICOM images to NIfTI format and NPM for statistical analysis.

Then, task-state fMRI data processing was performed using a combination of RESTplus and SPM. Each brain volume was corrected for motion. Where TR=3s, the number of scanning layers was 60, even odd ascending scanning. Functional images were then registered, smoothened, and de-noised (detrend, filter). Functional images were registered to each individual T1 image by 6-parameter rigid transformation and then registered to the MNI space with an affine algorithm. The normalized images were smoothened with a Gaussian kernel full width at half maximum of 8 mm and then band-pass filtered with a cutoff frequency of 0.01 Hz - 0.08Hz.

To control motion and physiological noise effects, the individual 4-dimensional time series using 8 parameters was regressed: by 2 for white matter and CSF mean signals and by 6 for possible motion parameters (3 translation and 3 rotation). In addition, SPM 12 was used to correct the origin prior to registration.

Index calculation and statistics

For this part of the analysis, we used SPM and xjview software. The full model was estimated for first-level analysis by SPM. Next, a second level GLM with images containing weighted parameter estimates was created. Then, we applied a design matrix with a one-sample T-test or two-sample t-test.

Task-state activation (one-sample T-test)

One-sample t-test was performed on the obtained images containing weighted parameter estimates to check the status of task-state activation in each group. A design matrix was obtained by using SPM 12 for two-level analysis. Then, the beta-value of the GLM model was estimated. Finally, the corresponding results of the contrast matrix were checked. The cluster size was determined by SPM and xjview software was used for statistical correction and generate an output.

Inter-group/intra-group comparison (2-sample t-test or paired t-test)

Images were analyzed with a two-sample t-test (between subjects) or a paired t-test (within subjects). A design matrix was obtained by applying the second level of SPM. Then, the beta value of the GLM model was estimated. Finally, we checked the corresponding results of the contrast matrix. Cluster size was determined by SPM and xjview software was used for statistical correction and generate an output.

RESULTS

A total of 126 participants diagnosed with BP and mainly suffering from hypophasis were recruited from the outpatients or inpatients departments. However, 21 of these patients were not enrolled for interview because they were of an inappropriate age (< 18 years or >60 years, n=13), had an inappropriate disease onset duration (< 1 month or >3 months, n=3), had a slighter severity of the disease (distance between the upper and lower eyelids < 2mm, n=5). Six participants were excluded by the interview: two refused to take part in our randomized controlled study and four had participated in other clinical trials during the previous three months. Finally, 99 participants were included in this study; none dropped out. **Fig. 2** illustrates the schedule of enrolment, allocation, interventions, and assessments in this trial.

The gender, proportion and age of all subjects (99 participants in total) included in this trail are shown in **Table 1** below. Statistical analysis indicated that there was no significant difference between the three groups in terms of gender proportion, age, or HB/ECWM/ESA scores.

Acupuncture therapy augmented the recovery of hypophasis

A test for homogeneity of variance for the HBS scores was not significant (P=0.206) and one-way ANOVA showed that there was a statistical difference between the three groups (P=0.000). As can be seen from **Figure 3. A**, the scores for the Bi'nao group were significantly lower than the other groups.

Tests for homogeneity of variance for the ECWM and ESA values were significant (P=0.000); therefore, non-parametric tests for independent samples were used for statistical comparisons. The rank-sum test for multiple independent samples (Kruskal-Wallis and one-way ANOVA) showed that there was a statistical difference between the three groups (P=0.000). As can be seen from **Figure 3. B and C**, the values for the Bi'nao group were significantly lower than those for the other two groups. No adverse reactions were reported in this study.

Acupuncture-induced activation of functional domains in the cerebral cortex

As shown in **Table 2** and **Figure 4**, acupuncture therapy performed on the real Bi'nao acupoint in BP patients with hypophasis showed increased activation in the left superior cerebellum and the right anterior cingulate cortex when compared to that in the healthy control group. The left middle temporal gyrus was seen to be activated in healthy controls when compared to BP patients when performing acupuncture therapy at the Bi'nao acupoint.

When performing acupuncture therapy at the Bi'nao acupoint in BP patients with hypophasis showed increased activation in the left superior temporal gyrus when compared to that in the healthy control group. The left middle temporal gyrus was found to be activated in the healthy controls when compared to BP patients when performing acupuncture therapy at the sham Bi'nao acupoint.

When making blinking movements in BP patients with hypophasis, we observed increased activation in the right calcarine and left precentral gyrus when compared to that in the healthy control group. In addition, the left calcarine, right middle frontal gyrus, left precentral gyrus, right thalamus, and left middle frontal gyrus were found to be activated in healthy controls when compared to BP patients when making blinking movements.

DISCUSSION

With regards to the efficacy of the Bi'nao acupoint, the book 'Acupuncture and Moxibustion of Tongren Acupoints in Ancient China' describes the therapeutic scope of treating several symptoms, including coldness and heat, scrofula of the neck, pain of the shoulders and back, weakness of the arms, and wind of the shoulders. However, since publication of the fourth edition of the Textbook of Traditional Chinese Medicine Colleges in Modern High Education. [25] The main form of treatment for this acupoint not only refers to shoulder and arm pain, it also refers to eye disease but without describing the specific forms of eye disease that can be treated.

When reviewing the literature, we found that acupuncture at the Bi'nao acupoint has been used to treat hordeolum, acute ocular conjunctivitis, viral keratitis, optic nerve atrophy, early cataract, glaucoma, electro-optic ophthalmia, amblyopia and extra-ocular diseases.[13-20] Our present findings demonstrate that the Bi'nao acupoint can also be used to treat hypophasis.

The task-state data results of our fMRI study showed that acupuncture at the Bi'nao and sham Bi'nao acupoints in healthy subjects activated the temporal gyrus; this was also the case for acupuncture performed at the sham Bi'nao acupoint in patients with facial paralysis. Acupuncture at the Bi'nao acupoint in patients with facial paralysis activated the ipsilateral upper cerebellar arch, anterior cingulate cortex (ACC) and collateral cingulate cortex. Although these results were acquired from non-adjusted data, our findings were consistent with a previous study [26] and indicated that during the early stages of recovery from facial paralysis, acupuncture and moxibustion can strengthen the function of the ipsilateral cingulate cortex.

The ACC has been demonstrated to be involved in error detection and conflict monitoring.[27] One of the key functions of the ACC is to detect the occurrence of errors that may lead to further control or movement processing.[28] Because there is a normal sensory afferent pathway on the side of the lesion, the ACC on the lesion side can detect state or sensory information and inform the ACC on the non-lesion side. Then, the ACC on the injured side can assist the non-injured side to compensate by designating the sensorimotor area to reduce bilateral asynchronous movement. Through the ability of the cingulate gyrus to perform error correction and integration, the cerebral cortex can improve the function of muscle movement innervated by the optic nerve to treat facial paralysis.

However, this study also has some limitations that need to be considered. For example, there is a clear absence of research on resting-state fMRI. Previous studies have shown that cortical reorganization may supplement the recovery of facial paralysis by changing functional connectivity (FC); this is mainly manifested by the early blocking and late strengthening of error detection, sensory motor integration, motor integration and other related areas.[29]

Related fMRI studies showed that regulatory mechanisms can differ between patients with left and right early BP, with positive or negative co-relationships with the superior temporal gyrus, right supramarginal, left and right middle cingulate cortex, superior frontal gyrus and precentral gyrus.[30-31] The connectivity of the middle cingulate cortex was found to be decreased during the early stages but increased in the late stages of BP. [32] In a previous study, Hu reported that the FC of the ACC was positively correlated with the duration of BP,[26;33] thus suggesting that the ACC may play a crucial role in the process of cortical reorganization during the recovery from BP.

In addition, the study results also suggest that the mechanism of acupuncture at the Bi'nao acupoint is also related to the cerebellum. However, how acupuncture could treat facial paralysis by activating part of the cerebellum may be complicated by its action circuit; this requires further investigation.

CONCLUSION

Acupuncture at the Bi'nao acupoint improves the recovery from hypophasis in patients with incomplete recovered BP. The underlying mechanism might be associated with the activation of the cingulate cortex and cerebellum.

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Availability of data and materials

The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

Ethical Statement and Approval

The study was conducted in accordance with the Declaration of Helsinki. The study protocol was approved by the Institutional Review Board of Medical Ethics Committee Board of Baoshan Hospital, Shanghai University of Traditional Chinese Medicine (Reference: 201709-02).

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Informed Consent

All participants provided written and informed consent for their data to be published.

Conflict of Interests

The authors declare no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Authorship contributions

Zhidan Liu designed the study protocol and conceived the study; Zhidan Liu, Chuang Zhao and Xiaoyan Li wrote the manuscript; Zhidan Liu and Xiaoyan Li sought funding and ethical approval; Chunlan Chen, Zunyuan Li, and Wenge Huo reviewed and modified the manuscript; Jiangbo He accomplished the acquisition of functional magnetic resonance imaging and Zunyuan Li,Wenge Huo performed the statistical analyses. All authors read and approved the final manuscript. The corresponding author has the sole responsibility of submission of the manuscript for publication.

REFERENCES

1. Danesh, A., & Ouanounou, A. (2022). Bell's Palsy: Etiology, Management and Dental Implications. Journal (Canadian Dental Association), 88, m8.
2. Heckmann, J. G., Urban, P. P., Pitz, S., Guntinas-Lichius, O., & Gágyor, I. (2019). The Diagnosis and Treatment of Idiopathic Facial Paresis (Bell's Palsy). Deutsches Arzteblatt international, 116(41), 692-702. https://doi.org/10.3238/arztebl.2019.0692
3. Picard, D., Leroy, R., Poussy, T., Tankéré, F., & Gatignol, P. (2021). Facteurs prédictifs des séquelles de paralysie faciale idiopathique : suivi longitudinal [Sequelae in bell's palsy: Prognostic factors for recovery]. Annales de chirurgie plastique et esthetique, 66(5), 364-370. https://doi.org/10.1016/j.anplas.2020.09.003
4. Shokri, T., Saadi, R., Schaefer, E. W., & Lighthall, J. G. (2020). Trends in the Treatment of Bell's Palsy. Facial plastic surgery : FPS, 36(5), 628-634. https://doi.org/10.1055/s-0040-1713808
5. Zhong, W., Yu, H., Rao, X., Wu, J., Gou, Y., Cui, H., Huang, X., & Wang, L. (2020). Efficacy of Manipulative Acupuncture Therapy Monitored by LSCI Technology in Patients with Severe Bell's Palsy: A Randomized Controlled Trial. Evidence-based complementary and alternative medicine: eCAM, 2020, 6531743. https://doi.org/10.1155/2020/6531743
6. Zhang, C. Y., Xu, S. B., Huang, B., Du, P., Zhang, G. B., Luo, X., Huang, G. Y., Xie, M. J., Zhou, Z. K., & Wang, W. (2016). Needle Sensation and Personality Factors Influence Therapeutic Effect of Acupuncture for Treating Bell's Palsy: A Secondary Analysis of a Multicenter Randomized Controlled Trial. Chinese medical journal, 129(15), 1789-1794. https://doi.org/10.4103/0366-6999.186640
7. Liang, F., Li, Y., Yu, S., Li, C., Hu, L., Zhou, D., Yuan, X., & Li, Y. (2006). A multicentral randomized control study on clinical acupuncture treatment of Bell's palsy. Journal of traditional Chinese medicine = Chung i tsa chih ying wen pan, 26(1), 3-7.
8. Li, Y., Liang, F. R., Yu, S. G., Li, C. D., Hu, L. X., Zhou, D., Yuan, X. L., Li, Y., & Xia, X. H. (2004). Efficacy of acupuncture and moxibustion in treating Bell's palsy: a multicenter randomized controlled trial in China. Chinese medical journal, 117(10), 1502-1506.
9. Shi, J., Lu, D., Chen, H., Shu, M., Xu, Y., Qian, J., Ouyang, K., Huang, H., Luo, Z., Wang, C., & Zhang, Y. (2022). Efficacy and Safety of Pharmacological and Physical Therapies for Bell's Palsy: A Bayesian Network Meta-Analysis. Frontiers in neurology, 13, 868121. https://doi.org/10.3389/fneur.2022.868121
10. Öksüz, C. E., Kalaycıoğlu, A., Uzun, Ö., Kalkışım, Ş. N., Zihni, N. B., Yıldırım, A., & Boz, C. (2019). The Efficacy of Acupuncture in the Treatment of Bell's Palsy Sequelae. Journal of acupuncture and meridian studies, 12(4), 122-130. https://doi.org/10.1016/j.jams.2019.03.001
11. Kwon, H. J., Choi, J. Y., Lee, M. S., Kim, Y. S., Shin, B. C., & Kim, J. I. (2015). Acupuncture for the sequelae of Bell's palsy: a randomized controlled trial. Trials, 16, 246. https://doi.org/10.1186/s13063-015-0777-z
12. Fabrin, S., Soares, N., Regalo, S. C., & Verri, E. D. (2015). The Effects of Acupuncture on Peripheral Facial Palsy Sequelae after 20 Years via Electromyography. Journal of acupuncture and meridian studies, 8(5), 245-248. https://doi.org/10.1016/j.jams.2015.01.006
13. Zhang Z.L.(1991).Clinical observation of acupuncture on Bi'nao point in treating 32 cases of hordeolum. New Journal of Traditional Chinese Medicine (Chin) , 6, 33-34.
14. Li Z.R.(2008).Clinical experience and consideration on acupuncture treatment for difficult eye diseases. Zhongguo zhenjiu (Chin), 28(2),137-139.
15. Cao L, Gao Y.(2010).Acu-point by triple direction needling in treatment of A case of diplopia treated by Professor Lian Yulin with Hegu needling acupuncture on Bi'nao. New Journal of Traditional Chinese Medicine (Chin), 42(10),101.
16. Bai Y.F. (2011).The effect on visual M, P channel by acupuncture therapy on point Bi'nao. Nanjing: Nanjing University of Traditional Chinese Medicine.
17. Huang L.X., Huang Y.M. (2011).Research on acupuncture points. Beijing: People's Medical Publishing House.
18. Zhang Y.L., Tian Z.C. (2010). Acupuncture on Bi'nao point in treating electric ophthalmia. Shanxi Med J (Chin), 1979, 5, 41.
19. Li F.M. (1984).Acupuncture therapy on Bi'nao point for external oculopathy. Hebei J Trad Chin Med (Chin), 1,35.
20. Cao R.F. (2012).Acupuncture therapy for Ophthalmological diseases. Beijing: People's Medical Publishing House.
21. Liu Z.D., Hu J., Zhou W.K. (2017). Electroacupuncture therapy for ophthalmoplegia: a case series. World J Acupunct Moxibustion, 27(2), 6-10.
22. Li, X., Chen, C., Zhao, C., Li, Z., Liang, W., & Liu, Z. (2018). Augmentation effect of acupuncture on Bi'nao for hypophasis in patients with Bell's palsy: study protocol for a randomized controlled trial. Trials, 19(1), 316. https://doi.org/10.1186/s13063-018-2699-z
23. MacPherson, H., Altman, D. G., Hammerschlag, R., Youping, L., Taixiang, W., White, A., Moher, D., & STRICTA Revision Group (2010). Revised STandards for Reporting Interventions in Clinical Trials of Acupuncture (STRICTA): extending the CONSORT statement. Journal of alternative and complementary medicine (New York, N.Y.), 16(10), ST1-ST14. https://doi.org/10.1089/acm.2010.1610
24. Chan, A. W., Tetzlaff, J. M., Gøtzsche, P. C., Altman, D. G., Mann, H., Berlin, J. A., Dickersin, K., Hróbjartsson, A., Schulz, K. F., Parulekar, W. R., Krleza-Jeric, K., Laupacis, A., & Moher, D. (2013). SPIRIT 2013 explanation and elaboration: guidance for protocols of clinical trials. BMJ (Clinical research ed.), 346, e7586. https://doi.org/10.1136/bmj.e7586
25. Nanjing College of Traditional Chinese Medicine.(1979). Acupuncture. Shanghai: Shanghai Science and Technology Press.
26. Hu, S., Wu, Y., Li, C., Park, K., Lu, G., Mohamed, A. Z., Wu, H., Xu, C., Zhang, W., Wang, L., Yang, J., & Qiu, B. (2015). Increasing functional connectivity of the anterior cingulate cortex during the course of recovery from Bell's palsy. Neuroreport, 26(1), 6-12. https://doi.org/10.1097/WNR.0000000000000295
27. Botvinick, M. M., Cohen, J. D., & Carter, C. S. (2004). Conflict monitoring and anterior cingulate cortex: an update. Trends in cognitive sciences, 8(12), 539-546. https://doi.org/10.1016/j.tics.2004.10.003
28. Paus, T., Petrides, M., Evans, A. C., & Meyer, E. (1993). Role of the human anterior cingulate cortex in the control of oculomotor, manual, and speech responses: a positron emission tomography study. Journal of neurophysiology, 70(2), 453-469. https://doi.org/10.1152/jn.1993.70.2.453
29. Klingner, C. M., Volk, G. F., Brodoehl, S., Burmeister, H. P., Witte, O. W., & Guntinas-Lichius, O. (2012). Time course of cortical plasticity after facial nerve palsy: a single-case study. Neurorehabilitation and neural repair, 26(2), 197-203. https://doi.org/10.1177/1545968311418674
30. Han, X., Li, H., Wang, X., Zhu, Y., Song, T., Du, L., Sun, S., Guo, R., Liu, J., Shi, S., Fu, C., Gao, W., Zhang, L., & Ma, G. (2018). Altered Brain Fraction Amplitude of Low Frequency Fluctuation at Resting State in Patients With Early Left and Right Bell's Palsy:

Do They Have Differences?. Frontiers in neuroscience, 12, 797. https://doi.org/10.3389/fnins.2018.00797
31. Han, X., Li, H., Du, L., Wang, X., Zhu, Y., Yu, H., Song, T., Sun, S., Guo, R., Liu, J., Shi, S., Fu, C., Gao, W., Zhang, L., Yan, R., & Ma, G. (2019). Differences in functional brain alterations driven by right or left facial nerve efferent dysfunction: Evidence from early Bell's palsy. Quantitative imaging in medicine and surgery, 9(3), 427-439. https://doi.org/10.21037/qims.2019.02.13
32. He, X., Zhu, Y., Li, C., Park, K., Mohamed, A. Z., Wu, H., Xu, C., Zhang, W., Wang, L., Yang, J., & Qiu, B. (2014). Acupuncture-induced changes in functional connectivity of the primary somatosensory cortex varied with pathological stages of Bell's palsy. Neuroreport, 25(14), 1162-1168. https://doi.org/10.1097/WNR.0000000000000246
33. Hu, S., Kan, H., Kan, J., Li, C., Yuan, A., Xu, C., Wang, A., Wang, Y., Bao, X., Shen, T., & Wu, H. (2019). Longitudinal Changes in Functional Connectivity of the Caudate Is Associated With Recovery From Bell's Palsy. Frontiers in aging neuroscience, 11, 295. https://doi.org/10.3389/fnagi.2019.00295

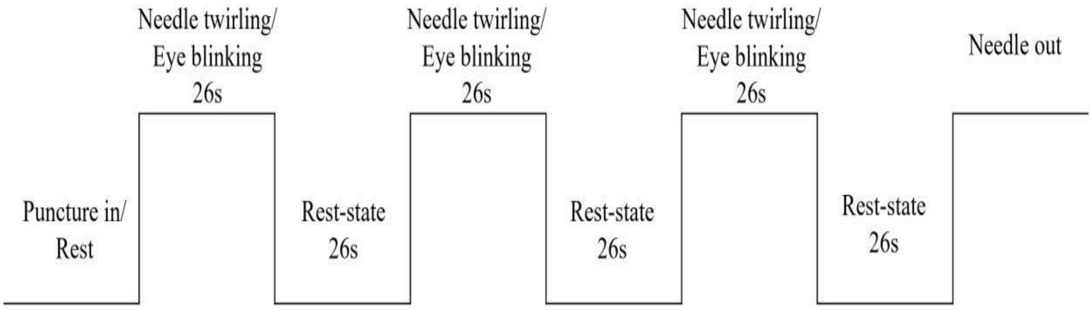

Figure 1: The block design of task-state fMRI research

A modified block design was used in the task-state acupuncture fMRI experiment with a three cycles stimulation and rest of 26 seconds.

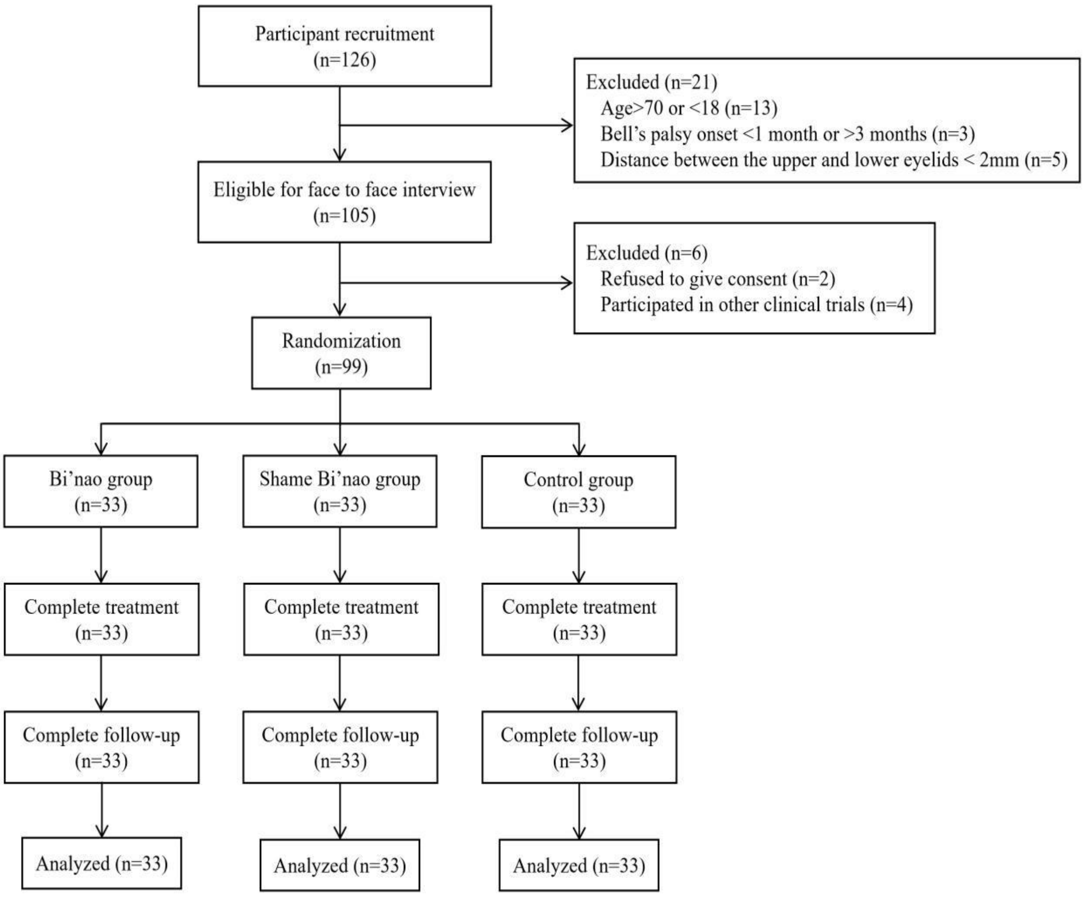

Figure 2: The road-map of this clinical trial

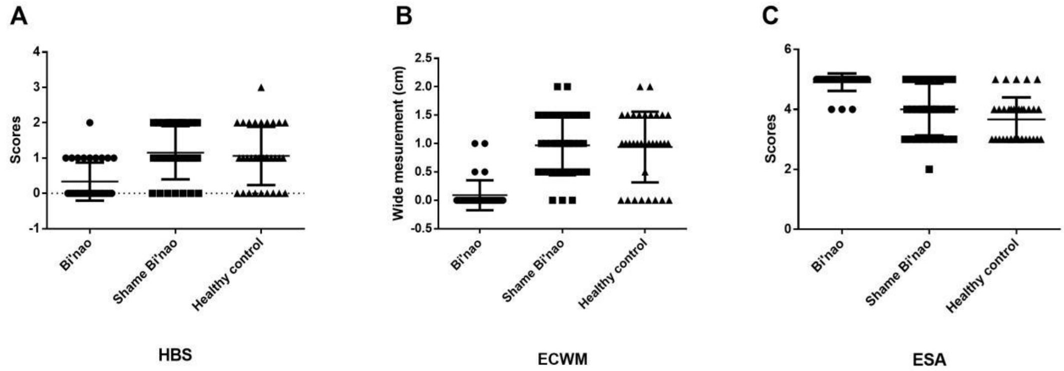

Figure 3: Clinical changes of the study population after intervention

The mean ± variance of the HBS scores (A) and ECWM values (B), ESA values(C) in Bi'nao group was significantly lower than those of the other two groups, with statistically significant differences (P=0.000).

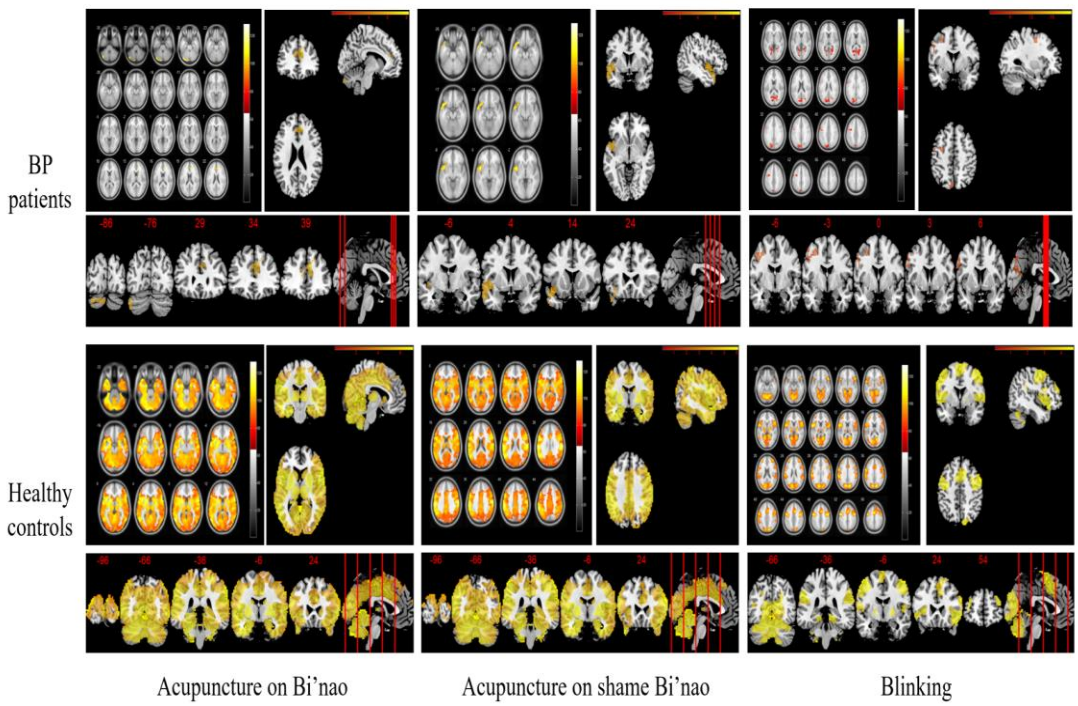

Figure 4: Functional domain of cerebral cortex activation by task-state acupuncture

As concluded from statistic result in Table 2, the task-state acupuncture activated Temporal_Mid_L (left middle temporal gyrus) in both real and shame Bi'nao stimulation in healthy controls, which was similar to the activation of stimulation during acupuncture on shame Bi'nao in BP patients, while activated Cerebelum_Crus1_L (left superior cerebellum) and Cingulum_Ant_R (right anterior cingulate cortex) when performing acupuncture at real Bi'nao in BP patients. However, Calcarine_R (right calcarine) and Precentral_L (left precentral gyrus) were both activated during blinking task in BP patients and healthy controls, but Frontal_Mid_R (right middle frontal gyrus), Thalamus_R (right thalamus), Frontal_Mid_L (left middle frontal gyrus) were additional activated in healthy controls.

Table 1: Demographic and clinical data of the study population

Group	N	Gender		Age (Years)	HB (scores)	ECWM (scores)	ESA (scores)
		Male	Female				
Bi'nao	33	17	16	44.58±9.98	2.82±0.64	2.35±0.73	3.06±0.50
shame Bi'nao	33	20	13	47.21±9.61	2.88±0.55	2.5±0.63	2.97±0.68
control	33	17	16	49.06±10.33	2.79±0.60	2.44±0.72	2.98±0.61

Table 2: Cortical activation in patients with facial paralysis and healthy subjects by task-state fMRI

Group	Task	Brain Regions	Cluster size	Peak intensity	Peak MNI Coordinate (mm) (x, y, z)
Patients	Acupuncture on Bi'nao	Cerebelum_Crus1_L (aal)	128	8.0957	-18, -90, -30
		Cingulum_Ant_R (aal)	136	8.2105	9, 39, 27
	Acupuncture on placebo Bi'nao	Temporal_Pole_Sup_L (aal)	321	8.71	-36, 21, -21
	Blinking	Calcarine_R (aal)	814	23.373	-21, -81, 33
		Precentral_L (aal)	105	8.7916	-54, 3, 36
Healthy control	Acupuncture on Bi'nao	Temporal_Mid_L (aal)	39733	11.5348	60, -27, 24
	Acupuncture on placebo Bi'nao	Temporal_Mid_L (aal)	36857	10.5503	-33, 18, -33
	Blinking	Calcarine_L (aal)	6253	8.4162	30, -51, -57
		Frontal_Mid_R (aal)	3309	8.3509	48, -6, 51
		Precentral_L (aal)	1955	10.0069	-54, 3, 9
		Thalamus_R (aal)	155	6.7448	21, -24, 3
		Frontal_Mid_L (aal)	255	7.4974	-39, 39, 30