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*Original Article*

# The novel affiliation treatment for children with deprivation amblyopia after congenital cataract surgery

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**Abstract:** Background: To compare the effect among different treatment for deprivation amblyopia after congenital cataract extraction and IOL implantation. Material/Methods: Totally 38 subjects diagnosed of deprivation amblyopia (aged from 5 a to 10 a) were divided into three groups and treated with different therapeutic methods: conventional treatment (group A), the video game treatment (group B), and combination of the video game and heat-sensitive moxibustion treatment (group C). After 60 days of above treatment, all cases received therapy with red light flicker, luster, and light brush for 120 days at home. In addition, visual acuity and visual evoked potentials (VEP) were measured in all cases at pre-therapy and 20 d, 40 d, 60 d, 180 d post-therapy during the period of treatment. Results: There was no significant difference in age, course and visual acuity in three groups (P>0.05). After 180 days of treatment the visual acuity of all case in three groups were higher than pre-therapy, and the best-corrected visual acuity (BCVA) of group B and group C were higher than group A at every time point (P<0.05). The BCVA was improved from baseline by an average of 0.87 lines in the group A, 3.00 lines in the group B and 6.06 lines in the group C. Comparing with before treatment, the latency of P100 of VEP elicited by reversing checkerboard with different spatial frequencies were shortened significantly in three groups at 180 d. In addition, the latency of P100 of VEP elicited in group C were shorter than other cases in group A and B (all P<0.05). Conclusions: Compared two conventional treatment, heat-sensitive moxibustion affiliation treatment is better therapeutic tool for deprivation amblyopia after congenital cataract extraction and IOL implantation, and it should be widely applied in clinical treatment.

**Keywords:** Deprivation amblyopia, visual evoked potentials, heat-sensitive moxibustion

## Introduction

Congenital cataract is a common eye disease causing vision loss and amblyopia in children. With the advancement of cataract surgery techniques, congenital cataract is well managed by surgeries. However, postoperative amblyopia is still an unavoidable complication. Following implantation of intraocular lens, the development and recovery of visual function is a long-term process, and postoperative amblyopia treatment remains the key to improve eyesight.

Deprivation amblyopia, is the most common cause of monocular blindness, affecting approximately 3% to 5% of the population worldwide [1]. It is difficult to find the advance therapy for deprivation amblyopia after congenital cataract surgery, which severely damages vision and causes the exotropia [2]. Studies have shown that intrinsic neural connections and synaptic structures can be altered after birth by adjusting the visual system according to environmental stimulation [3, 4]. This sensitive period of visual development is called the critical period [5]. The impact on visual pathways and the

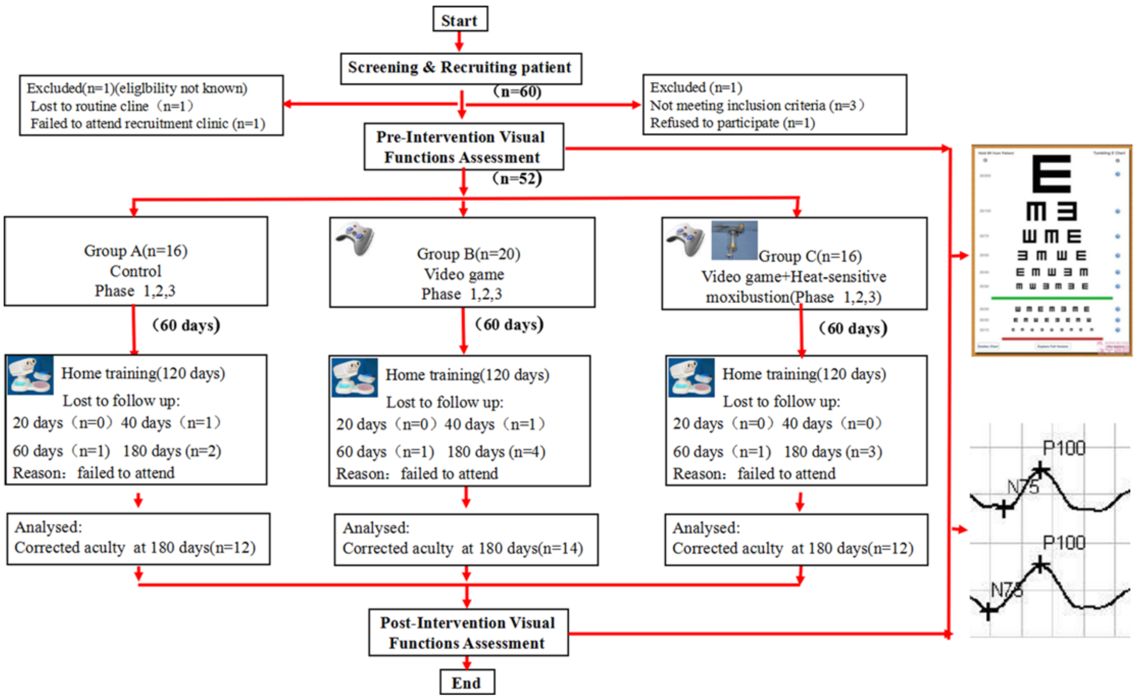


**Figure 1.** Outline of study procedures.

development of visual function that has been formed by congenital cataract during the critical period becomes irreversible when this period ends in older children [6]. A better knowledge of irreversible deprivation amblyopia and its treatment is also important. The treatment of congenital cataract remains a challenge because deprivation early in life leads to amblyopia. Visual outcomes after congenital cataract extraction and IOL implantation have improved dramatically with earlier surgery, yet greater attention is required for optical correction and therapy of the phakic eye.

Moxibustion is a traditional Chinese method that treats diseases through thermal stimulation generated by burning Moxa at special acupuncture and moxibustion points [7]. Different from other suspended moxibustion treatments, heat-sensitive moxibustion can stimulates a unique of Deqi and administers moxibustion on heat-sensitive acupuncture points, which are strong response to be produced by weak stimulation of burning moxa [8].

From August 2010 to August 2014, totally 38 deprivation amblyopia children post congenital cataract extraction and IOL implantation surgeries were selected from the ophthalmology department of our hospital. The selected patients were randomly divided into three groups: group A was untreated, group B was treated with video game, group C was treated with a combination of video game and heat-sensitive moxibustion. The results are shown below.

## Materials and methods

### *The experimental design*

This research was commenced in mid-2010 and completed in mid-2014. Health care division (L.C.) was responsible for conducting the clinical procedures in screening patients and assigning participants to interventions. Totally 60 children previously diagnosed as having deprivation amblyopia after congenital cataract surgery at our hospital from January 2009 to January 2014 were divided into three groups. Totally 52 subjects diagnosed of deprivation amblyopia were treated with different therapeutic methods: conventional treatment (n=16), the video game treatment (n=20), and combination of the video game and heat-sensitive moxibustion treatment (n=16). The treatment program consisted of a continuous 10-day course with daily administration. At the end of the course, children were instructed to go home to do exercises for 10 days. Then the

**Table 1.** The common condition of deprivation amblyopia after congenital cataract surgery patients at pre-therapy in three groups (x±s)

| Variables | A | B | C |
|---|---|---|---|
| N (Right/Left) | 12 (4/8) | 14 (6/8) | 12 (4/8) |
| Age (Range, year) | 7.78 ± 2.12 (6-10) | 8.02 ± 2.16 (6-10) | 7.84 ± 2.04 (6-10) |
| Sex (Male to female) | 8/4 | 9/5 | 8/4 |
| Axial length (mm) | 20.96 ± 2.18 | 21.38 ± 2.56 | 19.96 ± 3.34 |

next phase of treatment begun afterwards. Three phases of treatment/home exercises were conducted successively. After 60 days of above treatment, all cases received therapy with red light flicker, luster, and light brush for 120 days at home. After 180 days of treatment, 38 children were recruited and analyzed (Group A: n=12; Group B: n=14; Group C: n=12, **Figure 1**). All of the children had previously undergone manual anterior capsulorhexis, irrigation and aspiration of cataracts, posterior capsulectomy, and anterior vitrectomy. The secondary postponed IOL implantations were performed via a 2.6-3.2 mm superior limbal tunnel incision. A three-piece hydrophobic, acrylic, foldable IOL was placed in the ciliary sulcus, and an anterior vitrectomy was performed. The tunnel incision was sealed with one 10-0 nylon suture. After surgery, the operated eyes were treated with topical antibiotics, corticosteroids, and non-steroidal anti-inflammatory drugs. All of the surgeries (including initial cataract extraction and secondary IOL implantation) were performed by the same experienced surgeon (Yi Shao), with the patients under general anesthesia.

All children (18 females and 20 males) in this study were 5-10 years old with an average age of 8 years old. Eyes were checked and analyzed in each case. In total, there were 10 eyes with mild amblyopia, 10 eyes with moderate amblyopia, and 8 eyes with severe amblyopia. There were 32 cases with center fixation and 6 cases with eccentric fixation. The study was conducted in accordance with the principles of the Declaration of Helsinki. For each patient, the study protocol and procedure was fully explained, and consent was obtained, according to the Ethical Committee of our hospital.

*Treatment methods*

Fengchi thermal positioning and heat-sensitive moxibustion operations were performed according to the moxibustion method reported by Chen Rixin [9-11]. During the recovering period for Group C, heat-sensitive moxibustion at bilateral Fengchi therapy (30 days) was implemented as follows: the heat-sensitive zone was probed near the Fengchi area; the heat-sensitive moxibustion moxa [12, 13] (produced by Affiliated Hospital of Jiangxi TCM University) was lit about 3 cm over the skin with swing moxibustion; and the heat-sensitive state was defined as when the patient felt moxibustion perfusion into the skin or moxibustion sensor [14, 15]. All patients were trained and mastered the skill before treatment so that they could perform moxibustion at the Fengchi for the heat-sensitive state (as described above). The treatment was conducted once a day, and each treatment period lasted until the sensation of heat-sensitive moxibustion disappeared, which took about 20-40 minutes. The best-corrected VA and the amplitude and latency of the P100 peak of each patient were measured and analyzed.

*Clinical data analysis*

All the subjects underwent the axial length measurement by partial coherence interferometry (IOL Master500, Carl Zeiss Shanghai Co.,Ltd) and pattern-reversal VEP stimulation in a dark and quiet room for both eyes by using the RETLPORT electrophysiological instrument (RET1-Port/Scan21, ROLAND CONSULT Stasche & Finger GmbH). The average value of the axial length of the eye was automatically obtained by IOL Master after 5 times of measurement [15].

The VEP amplitude was evaluated based on the laboratory-designed reference value of visual evoked potential [16]: a checkerboard pattern reversal was applied with the reversal frequency of 1.6 Hz. There were four kinds of checkerboard stimulating spatial frequency, and the contrasts were held at a constant 0.95. The distance from the monitor screen to the eye during measurement of visual evoked potentials was 0.74 m [17]. Subjects had a follow-up at 6 months to observe the changes of vision

**Table 2.** Mean treatment group improvement in best-corrected visual acuity atfollow-up visits (Lines)

| Group | N | 0 d | 20 d | 40 d | 60 d | 180 d |
|---|---|---|---|---|---|---|
| A | 12 | 7.40 ± 2.44 | 7.33 ± 2.48 | 7.20 ± 2.66 | 7.24 ± 2.59 | 6.53 ± 3.09 |
| B | 14 | 7.50 ± 2.37 | 6.03 ± 2.85 | 5.50 ± 3.07 | 4.87 ± 3.10*,# | 4.50 ± 2.71*,# |
| C | 12 | 7.43 ± 2.43 | 5.80 ± 2.70 | 3.47 ± 2.83*,# | 2.17 ± 2.07*,# | 1.37 ± 1.03*,# |

Data are shown as mean ± SD. Before therapy vs. after therapy, *P<0.05; Group B and C vs. Group A, #P<0.05.

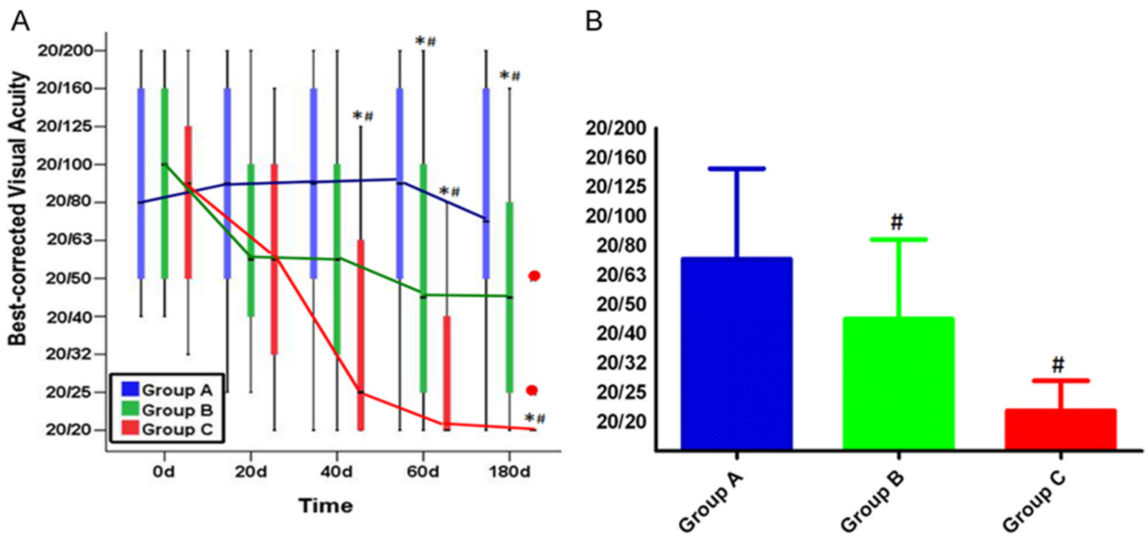


**Figure 2.** Mean best-corrected visual acuity from baseline to 180 days. At each time point, the box on the left demonstrated the distribution of best-corrected visual acuity for the group A, the one on the middle represented the data for the group B and the one on the right represented the data for the group C. The top and bottom of each box represented the 25th and 75th percentiles of the data and the line in the box showed the median. The three groups means are represented by a blue (group A), green (group B), red (group C) and are connected across the visits with lines. The bars extending above and below each box represented 1.5 times the interquartile range (difference between the 25th and 75th percentiles), and the open circles are outlier values. A: The BCVA increased with time in three groups. After 180 d treatment, the BCVA of Group B and C was higher than in Group A at every time point. However, there were no significant differences in either Group B or Group C. B: Analysis of the BCVA among the three groups at 180 days after treatment. Data are shown as mean ± SD. Data are shown as mean ± SD. Before therapy vs. after therapy, *P<0.05; Group B, C vs. Group A, #P<0.05.Group A: n=12; Group B: n=14; Group C: n=12.

and VEP, and to evaluate the therapeutic effects of deprivation amblyopia with different causes.

*Diagnostic criteria*

The diagnosis was made in accordance with the 1999 Criteria for Children with Oblique deprivation Amblyopia, except for those with deprivation amblyopia caused by nystagmus. The diagnostic classification for deprivation amblyopia included mild (VA 0.8-0.6), moderate (VA 0.5-0.2), and severe (VA≤0.1). The evaluation of treatment criteria were as follows: patients were considered to be cured if the VA was improved to 0.9 or more; the treatment was regarded as effective if VA improved by two lines or more; and treatment was regarded as ineffective if VA improved by only one line or remained unchanged.

*Statistical analysis*

Repeated measure ANOVA was used for all indexes comparisons before and after treatment, and SNK-Q test was applied for all indexes between the two groups of the multiple comparisons. All continuous values are expressed as means ± standard deviation (SD). A value of $P$<0.05 was considered statistically significant. Calculations and statistical analyses were performed using the SPSS 19.0 software package for Windows (SPSS, China).

## Results

*The best corrected visual acuity (BCVA)*

The average patient age was 8, ranging from 5 to 10 y. There was no significant difference in the age, sex and axial length among three

**Table 3.** P100 of VEP at pre-therapy and post-therapy 180 d in three groups at follow-up visits

| | A | | B | | C | |
|---|---|---|---|---|---|---|
| | Pretherapy | 180 d | Pretherapy | 180 d | Pretherapy | 180 d |
| Latency of P100 | | | | | | |
| 1 cycle/degree | 104.24 ± 5.71 | 104.31 ± 6.96 | 103.92 ± 6.15 | 102.37 ± 6.59 | 105.12 ± 6.24 | 103.04 ± 6.87 |
| 2 cycle/degree | 109.78 ± 6.16 | 110.12 ± 7.88 | 110.92 ± 5.98 | 109.79 ± 6.77 | 111.94 ± 6.73 | 109.28 ± 5.98 |
| 4 cycle/degree | 117.12 ± 6.92 | 116.97 ± 7.45 | 118.13 ± 6.54 | 110.42 ± 6.59*,# | 119.02 ± 6.27 | 99.98 ± 3.28*,# |
| 8 cycle/degree | 122.36 ± 6.89 | 116.81 ± 7.37* | 121.42 ± 6.82 | 114.02 ± 7.74*,# | 121.33 ± 6.98 | 102.46 ± 5.72*,# |
| Amplitude of P100 | | | | | | |
| 1 cycle/degree | 9.87 ± 4.64 | 9.85 ± 4.53 | 9.93 ± 5.15 | 9.86 ± 5.83 | 9.98 ± 5.32 | 9.28 ± 6.22 |
| 2 cycle/degree | 10.01 ± 6.12 | 10.81 ± 5.02 | 10.27 ± 6.93 | 10.31 ± 5.88 | 10.82 ± 6.01 | 10.17 ± 6.42 |
| 4 cycle/degree | 11.08 ± 5.84 | 11.15 ± 6.12 | 11.13 ± 5.72 | 11.67 ± 6.19 | 11.92 ± 5.82 | 11.16 ± 5.63 |
| 8 cycle/degree | 12.25 ± 5.66 | 12.36 ± 6.12 | 12.32 ± 5.83 | 12.27 ± 5.97 | 12.56 ± 5.19 | 12.71 ± 6.06 |

Data are shown as mean ± SD. Before therapy vs. after therapy, *P<0.05; Group B, C vs. Group A, #P<0.05.

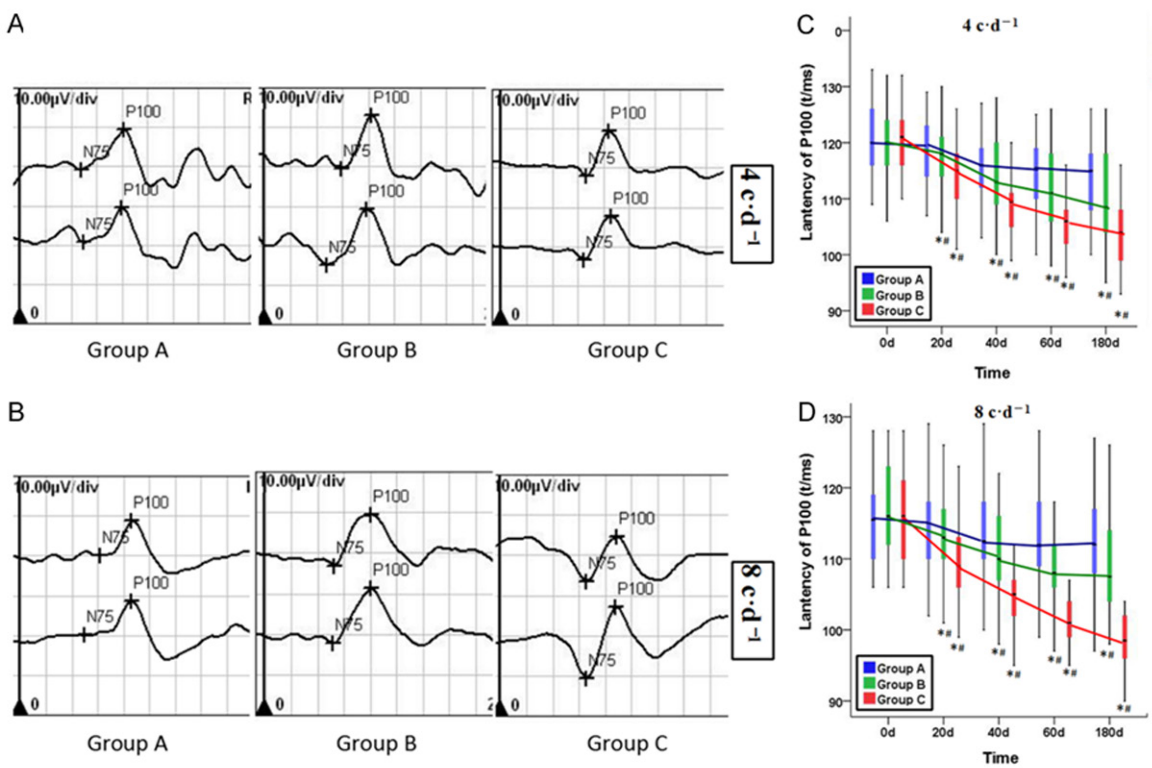


**Figure 3.** The change of VEP with deprivation amblyopic in 4 and 8 cycle/degree among three groups at follow-up visits. At follow-up visits, the latencies of P100-waves among three groups were examined at 6 (A) and 8 cycle/degree (B). Four bright flashes were used for stimulation, and the latencies of P100-waves (C, D) in the three groups were quantified. Data are shown as mean ± SD. Before therapy *vs.* after therapy, *P<0.05; Group B and C *vs.* Group A, #P<0.05. Group A: n=12; Group B: n=14; Group C: n=12.

groups (all P>0.05, **Table 1**). As shown in **Figure 2**, there were no significant differences in the BCVA of unilateral deprivation amblyopia among the three groups before treatment (all P>0.05). In all groups BCVA increased with time. After treatment, the BCVA of Group B and C was higher than in Group A at every time point (P<0.05). However, there were no significant differences in either Group B or Group C (P<0.05). The BCVA was improved from baseline by an average of 0.87 lines in Group A, 3 lines in Group B, and 6.06 lines in Group C (**Table 2**). The level of improvement was statistically different in the three treatment groups

(P=0.11, P=0.17, P=0.24, respectively; **Figure 2A**). During follow-up, the BCVA of 21 eyes improved to normal VA (Group A: 4 eyes; Group B: 7 eyes; Group C: 10 eyes); the differences of improved BCVA among the three groups before and after treatment were statistically significant (all P<0.05; **Figure 2B**).

*The Change of VEP with unilateral deprivation amblyopic at follow-up visits*

There were no significant differences in the amplitude of P100-waves among three groups before therapy and at 180 d after therapy in 1, 2, 4 and 8 cycle/degree (all P>0.05, **Table 3**). Under lower spatial frequencies (1 and 2 cycle/degree), the P100 peak latencies of both groups showed no significant differences among three groups before and after treatment. However, visual evoked potential test results showed that after 180 d, the VEPs P100 peak latency under higher spatial frequencies checkerboard reversal of the group B and group C was significantly reduced (**Figure 3A**, **3B**). The latencies before treatment of Group B under the spatial frequency of 4 and 8 cycles/degree were 117.12 ± 6.92 ms and 122.36 ± 6.89 ms, respectively. At 180 d after treatment, the latencies were 116.97 ± 7.45 ms and 116.81 ± 7.37 ms, respectively. The differences of latencies before treatment and 180 d after treatment were not significant [4 cycles/degree, t=10.6, P>0.05, **Figure 3C**; 8 cycles/degree, t=14.2, P>0.05, **Figure 3D**]. In Group B, when the spatial frequencies were 4 or 8 cycles/degree, the latencies before treatment were 118.13 ± 6.54 ms and 121.42 ± 6.82ms, respectively. At 180 d after treatment, the latencies were 110.42 ± 6.59 ms and 114.02 ± 7.74 ms, respectively [4 cycles/degree, t=1.3, P<0.05, **Figure 3C**; 8 cycles/degree, t=1.6, P<0.05, **Figure 3D**]. In Group C, when the spatial frequencies were 4 or 8 cycles/degree, the latencies before treatment were 119.02 ± 6.27 ms and 121.33 ± 6.98 ms, respectively. At 180 d after treatment, the latencies were 99.98 ± 3.28 ms and 102.46 ± 5.72 ms, respectively [4 cycles/degree, t=1.8, P<0.05, **Figure 3C**; 8 cycles/degree, t=2.4, P<0.05, **Figure 3D**]. However, the reduction in Group C was more significant than that of Group A and Group B. In this study, we confirmed that group B and group C treatment regime could partially recover the reduction in latency of P100-wave (4 cycles/degree and 8 cycles/degree) in deprivation amblyopia after congenital cataract surgery.

## Discussion

Amblyopia is a vision neurodevelopmental disorder associated with decreased visual acuity, poor or no stereopsis, and suppression of information from one eye. Amblyopia may be caused by strabismus (strabismic amblyopia), refractive error (anisometropic amblyopia), or deprivation from obstructed vision (deprivation amblyopia) [17]. In the developed world, amblyopia is the most common cause of childhood visual impairment, which reduces quality of life and also almost doubles the lifetime risk of legal blindness.

Congenital cataract, characterized by visual deprivation and formation of amblyopia, is an important, treatable cause of childhood visual handicap throughout the world. Bilateral congenital cataract is the most common cause of treatable childhood blindness. Human vision development depends on appropriate external stimulation, and early visual experience plays a key role in emmetropization [18]. Congenital cataract prevents the eyeball to receive enough light stimulation, resulting in incomplete development of optic nerve, which could eventually lead to the formation of deprivation amblyopia in children [19]. A better understanding of the sensitive periods in visual development and the timing of cataract removal are critical for the reversal of amblyopia. Early intervention is recommended [20, 21]. The decision to operate on bilateral partial cataracts after infancy should take into account the impact of the condition on the child's normal activities. Deprivation amblyopia is a developmental disorder of visual function, which is always caused after congenital cataract extraction and IOL implantation. The best treatment period for children is between 3 to 7 years old, which is also the critical period of vision development. The early diagnosis and timely treatment is the key to saving the vision acuity for affected children. Therefore, cooperation of parents and commitment to deprivation amblyopia treatment for preschool children are both essential for the effectiveness of this treatment [22].

In this study, the majority of young subjects were older than 6 years old and had been diagnosed with deprivation amblyopia after congenital cataract surgery. Regardless of the degree of amblyopia that might persist after treatment, recovery of some useful vision can be anticipated. The occlusion therapy is sometimes useful if one eye is more amblyopic than the other. Through covering, the inhibition of the dominant eye to the amblyopic eye is blocked to increase visual stimulation to the amblyopic eye, which ultimately leads to an improvement in visual acuity.

The pathogenesis of deprivation amblyopia is the dysfunction from retinal ganglion cells to the visual center. Fengchi (GB 20) belongs to the Gallbladder Meridian of Foot-shaoyang, which can significantly alter the excitability of the cerebral cortex and improve blood circulation in the eye, ultimately nourishing the retina and the optic nerve, stimulating visual cells, eliminating the inhibition on the visual pathway and the retinal cells, and improving and activating the visual pathway and the conduction of retinal cells. Fengchi has several rendezvous points, which is an important point in eliminating pathogenic wind since the point has the function of brightening the eye [23]. The heat-sensitive moxibustion is a type of Moxa moxibustion [24], which can produce nonlocal or nonsuperficial heat sensation in the related acupuncture and stimulate the brain's visual center to respond again to restore binocular vision [25-27]. We previously reported that Fengchi moxibustion is an efficacious treatment in patients with unilateral hyperopic anisometropic amblyopia [28]. The current study found that after heat-sensitive moxibustion affiliation treatment, the BCVA was statistically significantly lower ($P<0.05$) in Group A, but the improvement was greater ($P<0.05$) in Group B and C. In addition, the total effective rate rose to 83.3% by the moxibustion affiliation treatment, significantly higher than that in the treatment of occlusion of 33.3% and 57.2% of treating with a combination of video game.

Visual evoked potential is an objective evaluating method for deprivation amblyopia [29, 30]. Compared to the health subjects, the p100 peak's incubation of VEP amplitude was decreased, and the extended period was increased in deprivation amblyopia patients [31, 32]. Our research found that the evoked potential amplitude were increased and the p100 peaks incubation were shortened after treatment. The group C was the greatest changes, which indicated that moxibustion and occlusion therapy may change the evoked potential of the sick eye.

## Conclusion

Amblyopia treatment effect after intraocular lens implantation in cataract children is related to the degree of deprivation, age, and treatment compliance [33, 34]. Among them, the compliance plays a great role in the curative effect of amblyopia. A large number of clinical studies show that patients with good compliance have better treatment effect, and the duration of the treatment is shorter [35-39]. The moxibustion therapy is very safe and widely used for deprivation amblyopia in older children. Moreover, it improves the efficacy of treatment with affect learning. Further studies will be needed to recruiting the large subjects or assess the long-term effects on this multifactorial illness.

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## Disclosure of conflict of interest

None.

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