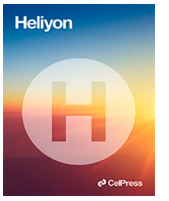
Heliyon 10 (2024) e26197

Contents lists available at ScienceDirect

Heliyon

journal homepage: www.cell.com/heliyon



Research article

Abnormal occipital and frontal activity during voluntary convergence in intermittent exotropia: A task-fMRI study

Lin Xia [a], Yanming Wang [b], Sha Luo [a], Yong Zhang [c], Bensheng Qiu [b,d], Xiaoxiao Wang [b,**], Lixia Feng [a,*]

[a] Department of Ophthalmology, First Affiliated Hospital of Anhui Medical University, Hefei, China
[b] Centre for Biomedical Imaging, University of Science and Technology of China, Anhui, China
[c] MR Research, GE Healthcare, Shanghai, China
[d] Institute of Artificial Intelligence, Hefei Comprehensive National Science Center, Hefei, China

ARTICLE INFO

Keywords:
Convergence
Cortical function
fMRI
Intermittent exotropia
MFG

ABSTRACT

Intermittent exotropia (IXT) is characterized by intermittently outward deviation of the eye and involved with vergence dysfunction. This study aimed to investigate the brain areas related to voluntary convergence and cortical activation changes between IXT patients and normal subjects. A total of 21 subjects, including 11 IXT patients and 10 age- and sex-matched normal subjects, were recruited for this study. A voluntary convergence task was employed, with changes in brain function measured by functional magnetic resonance imaging (fMRI). Correlations between cortical activation and clinical measurements were conducted by Pearson's correlation analysis. fMRI results showed that during voluntary convergence, the medial frontal gyrus (MFG) and bilateral occipital cortex were activated in the normal group, whereas only activation of the occipital cortex in IXT patients. Compared with the normal, IXT patients showed hypo-activation of both the MFG and cuneus during the task. The activation of MFG was negatively correlated to the duration of IXT. This study demonstrates that both MFG and occipital cortex may participate in voluntary convergence in normal subjects, while IXT patients have an aberrant cortical function of the MFG and cuneus, and the duration of IXT likely influences the severity of MFG. These findings may provide valuable insights for understanding the relationship between convergence and IXT.

1. Introduction

Intermittent exotropia (IXT), a subtype of exotropia, is characterized by divergent misalignment of the visual axis in ophthalmology. Its prevalence is estimated to be approximately 3% worldwide, with a higher prevalence in Asia [1–3]. Patients with IXT may have an exodeviation of one eye when tired or exposed to bright light, which could be controlled with attention. As a result, IXT can not only deteriorate visual function and stereopsis but also impact the appearance and overall quality of life. The etiology of IXT involves

Abbreviations: fMRI, functional magnetic resonance imaging; IXT, intermittent exotropia; MFG, medial frontal gyrus.

* Corresponding author.
** Corresponding author.
E-mail addresses: rogerxl@163.com (L. Xia), ming1258@ustc.edu.cn (Y. Wang), 18755270859@163.com (S. Luo), yongzhang@hotmail.com (Y. Zhang), bqiu@ustc.edu.cn (B. Qiu), wang506@ustc.edu.cn (X. Wang), lixiafeng@163.com (L. Feng).

https://doi.org/10.1016/j.heliyon.2024.e26197
Received 8 August 2023; Received in revised form 6 February 2024; Accepted 8 February 2024
Available online 10 February 2024

changes in ocular muscles and visual processing and remains uncovered [4,5].

The visual system's ability to maintain alignment of the eyes and coordinate their movements, with the cooperation of "vergence eye movements" and "binocular fusion", plays a crucial role in facilitating single and clear vision. Convergence, maintaining binocular fixation on the same object, is essential for eye position control, and its dysfunction may cause diplopia and further correlate with exodeviations [6]. Studies have suggested a potential link between IXT and deficits in convergence ability. Children with IXT had reduced convergence amplitudes detected at both distance and near [7]. Patients with IXT exhibited deficits in convergence and showed a strong correlation between fusion reserve ratio and control score [8]. Meanwhile, restoration of convergence is essential to recovery after strabismus surgery [9]. Given that convergence involves complex interactions among sensory input, ocular motor control, and cognitive processing, disturbances in these mechanisms could contribute to developing or exacerbating IXT. However, the exact nature of this relationship and its underlying mechanisms require further exploration.

Functional magnetic resonance imaging (fMRI) is a non-invasive technique to evaluate brain function changes. Some cortical areas with abnormal activation in IXT have been reported using fMRI. Previous studies showed higher functional connectivity between brain regions related to vision and eye movement [10], as well as altered brain activation in patients with IXT during fusion stimulus [11]. Our previous studies also found cortical alterations in patients with constant exotropia [12]. However, the cortical activation changes related to convergence function in IXT remain unclear. It is a worthwhile endeavor to study which brain area is involved in convergence and how it changes in IXT.

The present study aimed to investigate the brain areas related to convergence and their functional alterations in IXT. Hence, we designed a voluntary convergence task and obtained related cortical activation changes with task-fMRI. The correlations between exodeviation angle or strabismic duration and cortical activations were also analyzed. These findings provide new evidence of impaired convergence function in patients with IXT and shed light on the underlying neural mechanisms of IXT.

2. Methods

2.1. Subjects

A total of 11 patients diagnosed with IXT and 10 healthy volunteers were recruited in this study from September 2020 to March 2022 at the First Affiliated Hospital of Anhui Medical University. All participants underwent a complete series of binocular examinations by an experienced ophthalmologist, including slit-lamp and fundus examination, eye motility, angle of deviation and convergence function. Participants' binocular best-corrected visual acuity was at least 0.2 logMAR or better. The angle of deviation was measured both at near (33 cm) and distance (5 m) by the prism and alternate cover test. The convergence function is examined by the near point of convergence (NPC). Subjects were asked to look at a fixation target 50 cm away. Then the examiner pushed the target along the two eyes' midline slowly until the subject reported diplopia. The distance between the target and the patient was recorded for analysis [13]. All participants had no history of amblyopia, anisometropia, psychiatric disorders, or other central nervous system dysfunction. The IXT and normal groups were matched for age, sex, BCVA of each eye, and NPC (all, $p > 0.1$). The detailed demographics are shown in Table 1. The study was approved by the ethics committee of the First Affiliated Hospital of Anhui Medical University (PJ2023-01-53). All participants wrote informed consent after understanding the purpose and risks of this study.

2.2. fMRI experiment design

We designed an eye-movement task with a block design paradigm in this study. As shown in Fig. 1a, the image stimuli were projected on a translucent projector screen superior to (anatomical position) the subject's head. Subjects could see the entire screen through an angle-adjustable mirror fixed on the head coil anterior to their eyes. The total distance between the screen and the subjects' eyes was 81 cm. The audio stimuli were played through an MRI-compatible headset. The visual and audio stimuli were presented with E-prime 2.0 (Psychology Software Tools, Pennsylvania, USA) and an audiovisual stimulation system for fMRI (Sinorad Medical Electronics Inc., Shenzhen, China). A trigger pulse from the MRI scanner synchronized the onset of the audio and video stimuli with the start of image acquisition.

Table 1
Demographics and clinical details of IXT and normal individuals.

Characteristic	IXT	Normal	Statistic	*P*-values
Number	10	8	N/A	N/A
Age (years)	24.60 ± 4.79	23.63 ± 1.19	t = 0.56	0.584
Gender (Male/Female)	6/4	3/5	N/A	0.637
Duration of IXT (years)	16.00 ± 7.29	N/A	N/A	N/A
Angle of deviation at near	−75.00 ± 10.27	N/A	N/A	N/A
Angle of deviation at distance	−71.00 ± 13.29	N/A	N/A	N/A
BCVA of the right eye (logMAR)	0.031 ± 0.062	0.0022 ± 0.047	U = 30	0.375
BCVA of the left eye (logMAR)	0.029 ± 0.047	0.0121 ± 0.034	U = 37	0.588
NPC (cm)	4.540 ± 0.955	3.913 ± 0.491	U = 22	0.104

Abbreviations: IXT: intermittent exotropia; BCVA: best corrected visual acuity; logMAR: logarithm of minimal angle of resolution; NPC: near point of convergence; N/A: not applicable.

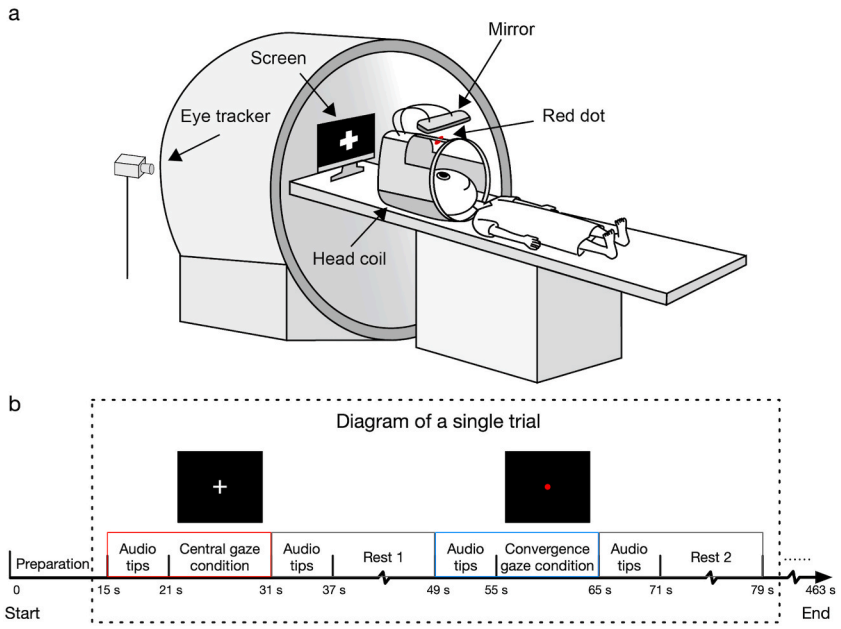


Fig. 1. Diagram of the experimental set-up and task-fMRI design. (a) The schematic of the experimental set-up. Subjects fix the red dot for the convergence gaze condition or fix the white cross through the mirror for the central gaze condition. The distance between the red dot and eyes is 6 cm and between the display and eyes is 81 cm. Both the screen and eye tracker are MRI-compatible. **(b)** The timeline shows the process and content of a single trial in the voluntary convergence task. There is a 15-s preparation before the first trial. Before each condition, there is a 6-s audio tip about the following condition. The duration of the central gaze or convergence gaze is 10 s. The duration of rest is about 8–12 s by pseudorandom, and the sum of the rest1 and rest2 in a trial is 20 s. Hence, the total duration of a single trial is 64 s. Following the rest 2, another trial starts without an interval. There are 7 trials in a run. The fixation of each gaze condition was drawn above the timeline. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

Each participant received 2 successive runs with a short interval. There are 7 trials in a run, with each trial having 3 different conditions: a central gaze, a convergence gaze, and a closed-eye rest condition. During the central gaze condition, subjects were asked to fix their eyes on a white cross with a black background displayed on the screen. During the convergence gaze condition, subjects were asked to fix a red dot placed on the head coil and 6 cm in front of the subjects' midline while the screen was black. The schematic of a trial is shown in Fig. 1b. To avoid practice effects, each rest was pseudo-randomized and was approximately 8–12 s in duration. Before formal fMRI scanning, all participants had enough practice to make sure, that they were familiar with the conditions and audio tips. Subjects were told to change their gaze after the audio but not during it. Throughout the scan, researchers could monitor participants' eyes with an eye tracker (EyeLink 1000 Plus, SR Research, Canada) to ensure their gaze is correct in different conditions (Fig. S1). Meanwhile, to ensure participants' adduction ability, we examined participants' voluntary convergence before scanning, like the NPC assessment.

2.3. Image acquisition

MRI scanning was performed by a GE 3.0T MR scanner (Discovery MR750, GE Medical Systems, Wisconsin, USA) with a standard 8-channel head coil at the Information Science Center of the University of Science and Technology of China. Some comfortable sponges were used to fill gaps between the subjects' heads and the head coil to avoid tiny head motion. Earplugs were used to reduce scanner noise.

The functional images were collected with an echo planar imaging sequence with the following scan parameters: repetition time (TR) = 2400 ms, echo time (TE) = 30 ms, flip angle = 90°, field of view = 192 × 192 mm^2, matrix size = 64 × 64, slice thickness = 3 mm, number of slices = 46, voxel size = 3 × 3 × 3 mm^3. The three-dimensional T1-weighted images were acquired with the following scan parameters: TR = 8.2 ms, TE = 3.2 ms, flip angle = 12°, field of view = 256 × 256 mm^2, matrix size = 256 × 256, slice thickness = 1 mm, number of slices = 192, voxel size = 1 × 1 × 1 mm^3.

2.4. Data preprocess and analysis

For the fMRI data, we used AFNI (Analysis of Functional Neuro Images, https://afni.nimh.nih.gov) for image process and data analysis [14]. After converting the data from DICOM to NIFTI format files, the first 5 vol of each subject were discarded to eliminate any unstable magnetic fields or subjects' fluctuating neural activities. The slice-timing and head motion corrections were conducted to improve the temporal and spatial resolution of the data. Slices with head motion greater than 0.3 mm were censored. Additionally,

subjects with more than 5% censored slices were excluded from further analysis, and a total of 3 subjects were excluded due to excessive head motion. Ten IXT patients and 8 normal controls participated in the fMRI analysis. Then, functional images were normalized to the respective native structure images and Montreal Neurological Institute (MNI) template. After spatial smoothing (FWMH = 6 mm) by a Gaussian kernel, the general linear model was used to calculate each voxel's regression factor (beta) in different gaze statuses for each participant [15].

2.5. Statistical analysis

For fMRI data, a paired-sample *t*-test was performed using AFNI to compare brain activation differences between the central gaze and convergence gaze within groups. The two-sample *t*-test was conducted to compare activation differences between IXT and normal. At the voxel level, statistical significance was set at $p < 0.005$. At the cluster level, $p < 0.05$ was set as the statistical threshold with AFNI 3dClustSim correction [16]. The statistical results were rendered into a three-dimensional cortical surface using SUMA [17].

In addition, Pearson's correlation analysis was performed to explore the relationship between the beta effect changes and clinical measurements in the IXT using GraphPad Prism 9.3. $P < 0.05$ was considered to indicate statistical significance.

3. Results

3.1. Brain activation changes in IXT and normal groups

To explore the brain areas related to voluntary convergence, we first computed the cortical activation during the convergence task in the IXT and normal groups, respectively. In patients with IXT, significantly increased brain activation during convergence versus a central gaze was observed mainly in the bilateral lingual gyrus (Fig. 2a, Table 2). In normal subjects, the substantially activated cortical regions during convergence versus a central gaze were observed in the bilateral cuneus and the left medial frontal gyrus (MFG) (Fig. 2b–Table 2).

A comparison of the activation changes between the two groups during the convergence task showed that the IXT subjects had decreased brain activation in the right cuneus and right MFG (Fig. 2c–Table 3). These findings suggest that patients with IXT exhibit altered cortical activation patterns during voluntary convergence, particularly in the visual and prefrontal areas, compared to normal subjects.

3.2. Relationship between the activated cortex and clinical measurements

To discover the potential influence of clinical measurements on cortex activation, we extracted the mean beta effect changes in the activated cortices during the task-fMRI for each participant of the IXT group and conducted correlation analysis. The activation of the MFG showed a negative correlation to the duration of strabismus marginally beyond statistical significance (Fig. 3, $p = 0.0535$, $r = -0.6247$) but not to the near/distance exodeviation angle (Fig. S2). However, cuneus activation showed no correlation to either of the clinical measurements (Fig. S3).

4. Discussion

According to previous studies, patients with IXT exhibit abnormal cortical function. To our knowledge, the present study is the first

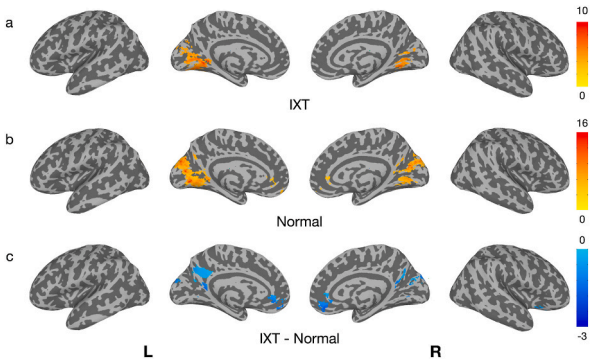


Fig. 2. Cortical activation changes during voluntary convergence task. The brain regions with significant activation are shown on the cortical surface. The red color indicates positively activated regions while the blue for negative. The activated cortical regions are distributed in **(a)** the bilateral partial occipital cortex among the IXT, and in **(b)** the medial prefrontal cortex and the bilateral occipital cortex among the normal. **(c)** Compared with the normal, the IXT had obviously hypo-activated cortices distributed in the medial prefrontal cortex and bilateral occipital cortex. The color bar represents the T value from the paired-sample *t*-test within **(a)** the IXT or **(b)** the normal subjects, and from **(c)** the two-sample *t*-test of the two groups. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

Table 2
Brain regions with significant activation during convergence in the IXT and normal groups.

Group	No.	Brain regions	BA	Peak Z value	Voxels	MNI coordinates			Voxel p value	Cluster p value
						X	Y	Z		
IXT	Cluster 1	Left lingual gyrus	Left BA19	10.77	523	−13.5	+52.5	−1.5	0.005	≪0.01
	Cluster 2	Right lingual gyrus	Right BA19	8.40	180	+13.5	−55.5	−4.5	0.005	<0.01
Normal	Cluster 1	Right cuneus	Right BA19	16.00	1379	+4.5	−88.5	+34.5	0.005	≪0.01
	Cluster 2	Left medial frontal gyrus	Left BA10	5.90	102	−1.5	+46.5	−10.5	0.005	<0.05

Abbreviations: IXT: intermittent exotropia.

Table 3
Brain activation differences during convergence between the IXT and normal.

No.	Brain regions	BA	Peak Z value	Voxels	MNI coordinates			Voxel p value	Cluster p value
					X	Y	Z		
Cluster 1	Right cuneus	Right BA19	−6.56	447	+4.5	−91.5	+31.5	0.005	<0.01
Cluster 2	Right medial frontal gyrus	Right BA11	−5.44	272	+1.5	+34.5	−13.5	0.005	<0.01

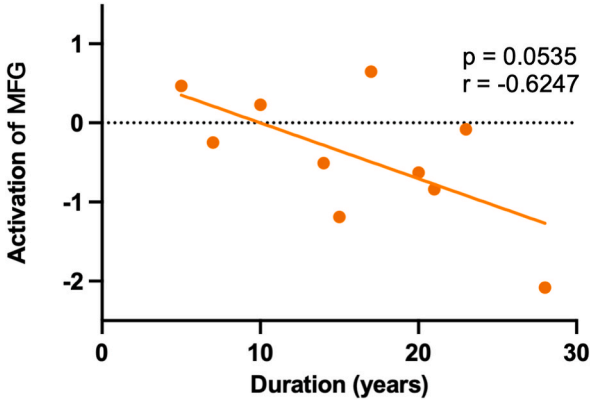


Fig. 3. Correlation between activation of MFG and duration of IXT. For IXT, the beta effect of the activated MFG correlates with the duration of IXT with slightly missing the significance (p = 0.0535, r = −0.6247). MFG: medial frontal gyrus; p, p-value; r, Pearson's correlation coefficient.

to explore the cortical activation changes relating to voluntary convergence among the IXT by fMRI. Our findings revealed that: (1) during the voluntary convergence task, patients with IXT showed significant activation in the bilateral lingual gyrus, while the normal group showed apparent activation in the cuneus and MFG; (2) compared with the normal group, the IXT group showed considerable hypo-activation in the right cuneus and MFG during the voluntary convergence task; (3) the activation of MFG was correlated with the duration of IXT. These results suggest that cuneus and MFG participated in voluntary convergence in normal subjects, while the function alterations in these areas might be involved in the IXT.

Vergence maintains the eyes in a converged or diverged position to stare at the close or far stimuli and establishes not only binocular single vision but also stereopsis. A previous study on vergence tasks has found that several brain regions are activated when participants are instructed to stare alternately at 1 of 3 fixation points (2°, 3°, or 4° centered along the subjects' midline) [18]. These regions include those associated with eye movement (e.g., frontal eye field, supplementary eye field), visual processing (e.g., cuneus, lingual gyrus, precuneus), and attention (cingulate). In this study, we asked participants to maintain a vergence situation for 10 s without moving their eyes, with a near fixation point of about 27° centered along the subjects' midline and a far point of about 2°. We found that the cuneus and lingual gyrus, previously implicated in vergence tasks, were activated during voluntary convergence. In the frontal lobe, the activated region we found was MFG, rather than frontal eye fields or dorsolateral prefrontal cortex identified in the previous research [18]. However, it's possible that these brain activation differences between this study and the previous research were due to the longer fixation duration in our work (i.e., 10 s in our study vs. 2 s in previous studies), where brain activity related to maintenance of converge was in dominance while brain activity related to eye movements was minimal. This is critical in the present study, as we aimed to discover the cortices related to voluntary convergence rather than eye movements.

The visual cortex is involved in the visual information process and plays a role in eye position encoding, pursuit, and saccade behaviors [19,20], which are essential for normal visual acuity, stereopsis, and eye alignment [21]. Using task-fMRI, we found apparent and similar activating areas in visual cortex among both IXT and normal groups. Our sample size is similar to other task-fMRI studies related to vergence [22,23]. These suggest that the task paradigm is valid and the results are reproducible. Meanwhile,

convergence could lead to a prominent difference in observed images between two eyes, i.e., binocular rivalry. During the convergence task, we observed significant activation in the bilateral lingual gyrus among the IXT group and in the cuneus among the normal group. This might be due to binocular rivalry, which is also reported in a recent study [24]. Furthermore, we observed hypo-activation of the visual cortex in IXT when compared to the normal group. Our and other previous studies have identified visual cortical impairments in individuals with exotropia through resting state-fMRI [12,25,26]. This result suggests that IXT also suffers from deficits in binocular vision, especially during evident binocular rivalry, although they could have normal visual acuity.

MFG contributes to reorienting attention from exogenous to endogenous attentional control and anticipation tasks [27,28]. Interestingly, we found that MFG activated robustly during the voluntary convergence task in the normal group but not in the IXT. This result may indicate IXT's dysfunction in visual spatial attention and fixation maintenance related to the voluntary convergence task. By the way, we also found the beta effects of MFG were negatively correlated to the duration of IXT. This may be another evidence that MFG is involved in the occurrence of IXT, and the pathological severity in the MFG is influenced by the duration of IXT. A previous study reported increased activated areas in MFG after visual therapy among patients with convergence insufficiency, suggesting MFG's potent role in convergence function [29]. We did not find significant differences in the near point of convergence between the IXT and normal group. This may indicate different neural mechanisms between the IXT and convergence insufficiency. However, it is also a worthwhile endeavor for further studies to discover the relationship between convergence function and MFG to understand its role in IXT completely.

Anyway, there are still some limitations in this study. The participants in this study were adults beyond the critical period of visual development. Therefore, the generalizability of the findings to children or adolescents with IXT, whose brains exhibit greater plasticity, may be limited. Due to the strict inclusion criteria, the number of participants enrolled in this study is limited. Nevertheless, convergence activated similar brain areas in the two groups, suggesting that our experiment design is reliable. It is also important to note that the voluntary convergence task used in this study may only reflect some aspects of the vergence function, including tonic vergence, accommodative vergence, fusional vergence, and proximal vergence. The task in this study may correspond to proximal vergence, and therefore, caution should be taken when interpreting the findings in the context of the broader clinical features of IXT. In our future research, we plan to expand the participant pool and incorporate additional experimental conditions to enhance the robustness of our studies and explore more valuable results.

In this study, we designed a voluntary convergence task to investigate changes in cortical activity among the IXT and normal subjects. Our findings revealed significant hypo-activations rather than over-activations related to voluntary convergence among the IXT, including the bilateral visual cortex and parts of the medial prefrontal cortex. Moreover, we identified a potential relationship between MFG activation and the duration of IXT. We proposed that cuneus and MFG may take part in the process of voluntary convergence and are involved in the occurrence of IXT.

5. Data availability statement

Data will be made available on request.

Funding

This study was supported by the Postgraduate Innovation Research and Practice Program of Anhui Medical University (No. YJS20210268, LX); and the National Natural Science Foundation of China (No. 21876041, BQ).

Ethics statement

The study was approved by the ethics committee of the First Affiliated Hospital of Anhui Medical University (PJ2023-01-53).

CRediT authorship contribution statement

Lin Xia: Writing – original draft, Visualization, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation. **Yanming Wang:** Writing – review & editing, Validation, Supervision, Resources, Methodology. **Sha Luo:** Investigation. **Yong Zhang:** Software, Resources, Methodology. **Bensheng Qiu:** Software, Resources, Methodology, Funding acquisition. **Xiaoxiao Wang:** Writing – review & editing, Visualization, Supervision, Software, Resources, Methodology. **Lixia Feng:** Writing – review & editing, Validation, Supervision, Resources, Project administration, Data curation.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements

The authors thank all patients and volunteers involved in this study for their valuable participation. The authors would like to thank Information Science Laboratory Center of University of Science and Technology of China for the measurement services. We thank Dr.

Jinying Yang, Dr. Du Zhang, and other MRI technicians at the University of Science and Technology of China for their professional and excellent work. We would also like to express our gratitude to Dr. Yitian Fang for his assistance in diagrams.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2024.e26197.

References

[1] C.W. Pan, H. Zhu, J.J. Yu, et al., Epidemiology of intermittent exotropia in preschool children in China, Optom. Vis. Sci. 93 (1) (2016) 57–62, https://doi.org/10.1097/OPX.0000000000000754. Jan.
[2] A. Fiess, H.M. Elflein, M.S. Urschitz, et al., Prevalence of strabismus and its impact on vision-related quality of Life: results from the German population-based gutenberg health study, Ophthalmology 127 (8) (Aug 2020) 1113–1122, https://doi.org/10.1016/j.ophtha.2020.02.026.
[3] Y. Wang, A. Zhao, X. Zhang, et al., Prevalence of strabismus among preschool children in eastern China and comparison at a 5-year interval: a population-based cross-sectional study, BMJ Open 11 (10) (2021) e055112.
[4] A.B. Agarwal, C.Y. Feng, A.L. Altick, et al., Altered protein composition and gene expression in strabismic human extraocular muscles and tendons, Invest. Ophthalmol. Vis. Sci. 57 (13) (Oct 1 2016) 5576–5585, https://doi.org/10.1167/iovs.16-20294.
[5] E. Bui Quoc, C. Milleret, Origins of strabismus and loss of binocular vision, Front. Integr. Neurosci. 8 (2014) 71, https://doi.org/10.3389/fnint.2014.00071.
[6] H. Steffen, M.F. Walker, D.S. Zee, Rotation of Listing's plane with convergence: independence from eye position, Invest. Ophthalmol. Vis. Sci. 41 (3) (2000) 715–721. Mar.
[7] T. Fu, J. Wang, M. Levin, Q. Su, D. Li, J. Li, Fusional vergence detected by prism bar and synoptophore in Chinese childhood intermittent exotropia, J Ophthalmol 2015 (2015) 987048, https://doi.org/10.1155/2015/987048.
[8] S.R. Hatt, D.A. Leske, B.G. Mohney, M.C. Brodsky, J.M. Holmes, Fusional convergence in childhood intermittent exotropia, American journal of ophthalmology 152 (2) (2011) 314–319.
[9] Y. Wu, M. Xu, J. Zhang, et al., Can clinical measures of postoperative binocular function predict the long-term stability of postoperative alignment in intermittent exotropia? Journal of Ophthalmology (2020) 2020.
[10] X. He, J. Hong, Q. Wang, et al., Altered spontaneous brain activity patterns and functional connectivity in adults with intermittent exotropia: a resting-state fMRI study, Front. Neurosci. 15 (2021) 746882, https://doi.org/10.3389/fnins.2021.746882.
[11] Q. Li, J. Bai, J. Zhang, Q. Gong, L. Liu, Assessment of cortical dysfunction in patients with intermittent exotropia: an fMRI study, PLoS One 11 (8) (2016) e0160806.
[12] H. Shi, Y. Wang, X. Liu, et al., Cortical alterations by the abnormal visual experience beyond the critical period: a resting-state fMRI study on constant exotropia, Curr. Eye Res. 44 (12) (2019) 1386–1392, https://doi.org/10.1080/02713683.2019.1639767. Dec.
[13] M.M. Ma, W. Long, Z. She, et al., Convergence insufficiency in Chinese high school students, Clin. Exp. Optom. 102 (2) (2019) 166–171, https://doi.org/10.1111/cxo.12838. Mar.
[14] R.W. Cox, AFNI: software for analysis and visualization of functional magnetic resonance neuroimages, Comput. Biomed. Res. 29 (3) (Jun 1996), https://doi.org/10.1006/cbmr.1996.0014, 162-73.
[15] K.J. Friston, A.P. Holmes, K.J. Worsley, J.P. Poline, C.D. Frith, R.S. Frackowiak, Statistical parametric maps in functional imaging: a general linear approach, Hum. Brain Mapp. 2 (4) (1994) 189–210.
[16] R.W. Cox, G. Chen, D.R. Glen, R.C. Reynolds, P.A. Taylor, FMRI clustering in AFNI: false-positive rates redux, Brain Connect. 7 (3) (Apr 2017) 152–171, https://doi.org/10.1089/brain.2016.0475.
[17] Z.S. Saad, R.C. Reynolds, Suma. Neuroimage 62 (2) (Aug 15 2012) 768–773, https://doi.org/10.1016/j.neuroimage.2011.09.016.
[18] Y. Alkan, B.B. Biswal, T.L. Alvarez, Differentiation between vergence and saccadic functional activity within the human frontal eye fields and midbrain revealed through fMRI, PLoS One 6 (11) (2011) e25866.
[19] T. Huff, N. Mahabadi, P. Tadi, Neuroanatomy, Visual Cortex, StatPearls Publishing, 2021. *StatPearls [Internet]*.
[20] A.E. Cavanna, M.R. Trimble, The precuneus: a review of its functional anatomy and behavioural correlates, Brain 129 (Pt 3) (2006) 564–583, https://doi.org/10.1093/brain/awl004. Mar.
[21] Y. Chen, J.D. Crawford, Cortical activation during landmark-centered vs. Gaze-centered memory of saccade targets in the human: an FMRI study, Front. Syst. Neurosci. 11 (2017) 44, https://doi.org/10.3389/fnsys.2017.00044.
[22] T.L. Alvarez, Y. Alkan, S. Gohel, B. Douglas Ward, B.B. Biswal, Functional anatomy of predictive vergence and saccade eye movements in humans: a functional MRI investigation, Vision Res 50 (21) (Oct 12 2010) 2163–2175, https://doi.org/10.1016/j.visres.2010.08.018.
[23] N. Fogt, A.J. Toole, X. Li, E. Owusu, S.T. Manning, M.T. Kulp, Functional magnetic resonance imaging activation for different vergence eye movement subtypes, Ophthalmic Physiol. Opt. 43 (1) (2023) 93–104, https://doi.org/10.1111/opo.13063. Jan.
[24] E.A. Bock, J.D. Fesi, J. Da Silva Castenheira, S. Baillet, J.D. Mendola, Distinct dorsal and ventral streams for binocular rivalry dominance and suppression revealed by magnetoencephalography, Eur. J. Neurosci. 57 (8) (2023) 1317–1334, https://doi.org/10.1111/ejn.15955. Apr.
[25] X. Yan, Y. Wang, L. Xu, et al., Altered functional connectivity of the primary visual cortex in adult comitant strabismus: a resting-state functional MRI study, Curr. Eye Res. 44 (3) (2019) 316–323, https://doi.org/10.1080/02713683.2018.1540642. Mar.
[26] X. He, J. Hong, Z. Liu, et al., Decreased functional connectivity of the primary visual cortex and the correlation with clinical features in patients with intermittent exotropia, Front. Neurol. 12 (2021) 638402, https://doi.org/10.3389/fneur.2021.638402.
[27] S. Japee, K. Holiday, M.D. Satyshur, I. Mukai, L.G. Ungerleider, A role of right middle frontal gyrus in reorienting of attention: a case study, Front. Syst. Neurosci. 9 (2015) 23, https://doi.org/10.3389/fnsys.2015.00023.
[28] C. Corradi-Dell'Acqua, F. Turri, L. Kaufmann, F. Clément, S. Schwartz, How the brain predicts people's behavior in relation to rules and desires. Evidence of a medio-prefrontal dissociation, Cortex 70 (2015) 21–34.
[29] T.L. Alvarez, V.R. Vicci, Y. Alkan, et al., Vision therapy in adults with convergence insufficiency: clinical and functional magnetic resonance imaging measures, Optom. Vis. Sci. 87 (12) (Dec 2010), https://doi.org/10.1097/OPX.0b013e3181fef1aa. E985-1002.