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Research Paper

Visual Restoration after Cataract Surgery Promotes Functional and Structural Brain Recovery

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ABSTRACT

Background: Visual function and brain function decline concurrently with aging. Notably, cataract patients often present with accelerated age-related decreases in brain function, but the underlying mechanisms are still unclear. Optical structures of the anterior segment of the eyes, such as the lens and cornea, can be readily reconstructed to improve refraction and vision quality. However, the effects of visual restoration on human brain function and structure remain largely unexplored.
Methods: A prospective, controlled clinical trial was conducted. Twenty-six patients with bilateral age-related cataracts (ARCs) who underwent phacoemulsification and intraocular lens implantation and 26 healthy controls without ARC, matched for age, sex, and education, were recruited. Visual functions (including visual acuity, visual evoke potential, and contrast sensitivity), the Mini-Mental State Examination and functional magnetic resonance imaging (including the fractional amplitude of low-frequency fluctuations and grey matter volume variation) were assessed for all the participants and reexamined for ARC patients after cataract surgery. This trial was registered with ClinicalTrials.gov (NCT02644720).
Findings: Compared with the healthy controls, the ARC patients presented decreased brain functionality as well as structural alterations in visual and cognitive-related brain areas preoperatively. Three months postoperatively, significant functional improvements were observed in the visual and cognitive-related brain areas of the patients. Six months postoperatively, the patients' grey matter volumes in these areas were significantly increased. Notably, both the function and structure in the visual and cognitive-related brain areas of the patients improved significantly and became comparable to those of the healthy controls 6 months postoperatively.
Interpretation: We demonstrated that ocular reconstruction can functionally and structurally reverse cataract-induced brain changes. The integrity of the eye is essential for maintaining the structure and function of the brain within and beyond the primary visual pathway.

1. Introduction

Aging is accompanied by concurrent declines in visual and brain functions. Studies in humans and animal models provide converging evidence that these functional changes are often accompanied by specific structural alterations of the eye and brain regions (Knezovic et al., 2015; Hsu et al., 2016; Ferreira et al., 2017). The eyes and brain are anatomically and functionally connected (Ochoa-Urdangarain et al., 2001). On the one hand, the retina and optic nerve are extensions of the brain that can be directly observed from the surface of the body. On the other hand, as visual information accounts for a large proportion of brain inputs, visual skills, such as stereopsis and form perception, are highly and consistently correlated with intellectual development (Gottfried and Gilman, 1985).

Ocular diseases have been shown to contribute to cognitive decline and abnormal changes in brain structure. Subjects with untreated poor vision showed a 5- to 9·5-fold increased risk of developing Alzheimer's disease (AD) or other cognitive disorders (Rogers and

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Langa, 2010). Impairment of the brain's short-range and long-range functional connections in visual pathways, the frontal cortex, visual areas, posterior parietal, and frontal cortices was also detected in children with anisometropic amblyopia (Wang et al., 2014). Furthermore, widespread structural abnormalities in the central nervous system extending beyond the visual cortex were observed in patients with advanced primary open-angle glaucoma, an irreversible disease involving the retina and optic nerve (Dai et al., 2013).

Age-related cataract (ARC), the most common cause of vision decline or loss in the general aging population, is due to lens opacification (Asbell et al., 2005). A retrospective study in Taiwan of 19,954 ARC patients revealed a marked increase in the overall incidence of AD after an 8-year follow-up, suggesting that ARC is associated with structural and functional impairments of the brain (Lai et al., 2014). The vision loss of most cataract patients can be readily corrected via phacoemulsification and intraocular lens (IOL) implantation. However, whether functional and structural changes in the brain can be reversed after visual restoration is largely unknown. Previous studies have reported cognitive improvements in elderly patients after cataract surgery (Tamura et al., 2004; Ishii et al., 2008). However, most of these functional analyses were based on subjective questionnaire investigations and lacked objective evidence, such as neuroimaging. Furthermore, whether ocular reconstruction can promote functional and structural changes in specific brain regions remains unclear.

In the present study, we conducted a prospective, controlled clinical trial with consecutive patients presenting bilateral ARC. These patients exhibited significantly decreased visual function and underwent phacoemulsification with IOL implantation. We measured changes in brain function and structure before and after cataract surgery using functional magnetic resonance imaging (fMRI), a well-established neuroimaging technology that not only evaluates grey matter (GM) variation but also detects functional changes in the brain by monitoring blood oxygen level-dependent signals (Tambini et al., 2017), and the Mini-Mental State Examination (MMSE), a classic measurement of cognitive impairment (Predictors, 2017; Dixon et al., 2017a). We demonstrate that patients with ARC display impaired brain function and structure, but these changes can be fully reversed by visual acuity restoration.

2. Materials and Methods

2.1. Participants and Study Design

Twenty-six patients (13 males and 13 females) with ARC and 26 healthy controls matched for age, sex, and education, were recruited from Zhongshan Ophthalmic Center (ZOC). Written informed consent was obtained from all participants or their legal guardians. This study was approved by the Ethics Committee of ZOC at Sun Yat-sen University and followed the tenets of the Declaration of Helsinki. Twenty-six patients (52 eyes) were allocated to the Tecnis ZMB00 IOL (Abbott Medical Optics, Santa Ana, CA, USA) or ZCB00 IOL (Abbott Medical Optics, Santa Ana, CA, USA) arms depending on the patient's choice. The inclusion criteria for the study were as follows: cataracts in both eyes classified according to the Lens Opacity Classification System III, corneal astigmatism < 1·0 diopters (D), and IOL power between +18·0 and +25·0 D. The exclusion criteria included a medical history of neurological or psychiatric disorders, prior refractive, glaucoma, or penetrating keratectomy surgery, degenerative optical diseases, associated ocular or systemic diseases that may interfere with the results, significant vitreous loss during surgery that may hamper the implantation and performance of IOLs, and anterior chamber hyphema. Cataract surgery was performed in all patients by the same experienced ophthalmologist (WRC). The standard technique in all patients consisted of sutureless phacoemulsification using a Legacy 2000 Series and Infinity phacoemulsification machine (Alcon Laboratories Inc., Fort Worth, Texas, USA), with clear corneal incisions up to 3·2 mm and 5·0 to 5·5 mm capsulorhexis. Surgery was performed on the second eye 1 month after the first procedure in each patient. Structural and functional MRI scans were performed before surgery and at 1 week, 3 months, and 6 months after surgery on the second eye (Fig. 1). This trial was registered with ClinicalTrials.gov, NCT02644720.

2.2. Examination of Ocular Structure and Visual Function

At the 6-month follow-up visit, a slit-lamp examination was performed to examine the transparency of the posterior capsule and to exclude residual posterior capsule plaques. The locations of the IOLs were

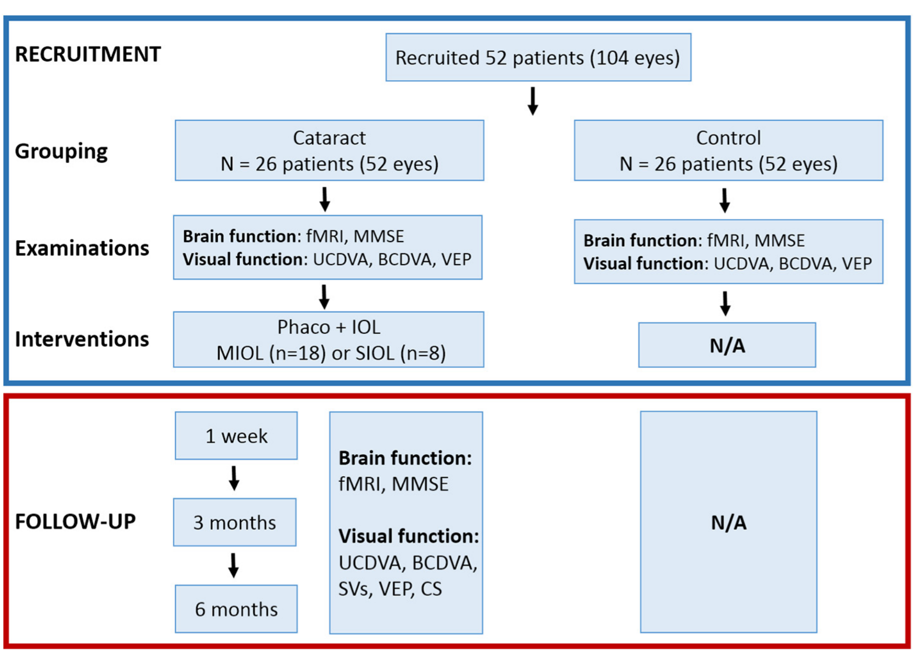

Fig. 1. Flowchart of recruitment and follow-up evaluations from 1 week after the second eye surgery. Notes: fMRI, functional magnetic resonance imaging; MMSE, Mini-Mental State Examination; UCDVA, uncorrected distance visual acuity; BCDVA, best-corrected distance visual acuity; CS, contrast sensitivity; SVs, straylight values; VEP, visual evoked potential; IOL, intraocular lens; SIOL, single-focus intraocular lens; MIOL, multifocal intraocular lens.

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