Bilateral Congenital Cataract: Deprivation Amblyopia and its relation to development

Catarata congénita bilateral: ambliopía por privación y su relación con el desarrollo

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Abstract

Purpose: To determine the impact of age at the time of bilateral congenital cataract (BCC) surgery, regarding changes in cognitive, language and motor development, considering the results of visual function. **Methods:** This is an ambispective descriptive longitudinal study of the evolution of visual acuity and development, using Teller Acuity Cards, Retinoscopy, and the Bayley Scales of Infant and Toddler Development, Third edition. Eight patients with BCC were included to establish the general conditions of onset with longitudinal follow-up after surgery. Patients were divided into two groups, considering the age of treatment (early treatment < 6 months; late treatment > 6 months). We used non-parametric statistics with trend tests in the two groups, using a significance level of $p < 0.05$. A description of visual development was made through a qualitative analysis. **Results:** Refractive errors decreased progressively, with a statistically significant difference between both groups ($p < 0.01$). The cognitive area showed improved outcomes with a significant difference ($p = 0.012$) in the early treatment group. **Conclusions:** Late surgical treatment led to severe disturbances in the organization of visual function, as well as in observable behaviors of the motor, cognitive, and language areas, limiting a comprehensive and adequate development of children. It is necessary to implement strategies that include visual rehabilitation and early intervention for developmental disturbances.

Key words: Congenital cataract. Visual deprivation. Amblyopia. Visual function. Development.

Resumen

Objetivo: Determinar el impacto de la edad de cirugía en la catarata congénita bilateral (CCB) sobre los cambios en el desarrollo cognitivo, motor y del lenguaje, considerando los resultados de la función visual. **Método:** Se trata de un estudio descriptivo, longitudinal y ambispectivo de la evolución de la agudeza visual y del desarrollo, que utilizó las cartillas de agudeza visual de Teller, retinoscopia y la Escala de Desarrollo Infantil Bayley III. Fueron incluidos ocho pacientes con CCB para establecer las condiciones generales de inicio, con un seguimiento longitudinal después de la cirugía. Los pacientes

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fueron divididos en dos grupos según la edad de tratamiento (tratamiento temprano < 6 meses y tratamiento tardío > 6 meses). Se utilizó estadística no paramétrica mediante la prueba de tendencia a través de grupos ordenados utilizando un nivel de significancia de $p < 0.05$. A través de un análisis cualitativo se realizó una descripción del desarrollo visual.

Resultados: El error refractivo disminuyó de manera progresiva y mostró una diferencia estadísticamente significativa entre ambos grupos ($p < 0.01$). El área cognitiva mostró mejores resultados en el grupo de tratamiento temprano ($p = 0.012$).

Conclusión: El retraso en el tratamiento quirúrgico conduce a graves alteraciones en la organización de la función visual, así como en los comportamientos observables en el área motora, cognitiva y del lenguaje, lo que limita el desarrollo integral y adecuado en el individuo. Es necesaria la implementación de estrategias que incluyan la rehabilitación visual y la intervención temprana de alteraciones del desarrollo.

Palabras clave: Catarata congénita. Deprivación visual. Ambliopía. Función visual. Desarrollo.

Introduction

Worldwide, it is estimated that the number of children with visual disabilities is 19 million, of which 12 million suffer from refractive errors that could be easily diagnosed and correctable¹; more than 90% live in developing countries and more than two thirds could have been avoided². It is estimated that 1.4 million children under 15 years of age suffer irreversible blindness and need visual rehabilitation for their full psychological and personal development¹. The main causes of blindness in children vary from one region to another and are largely associated with socioeconomic development and the availability of health care services³. It is estimated that in almost half of blind children the underlying cause could have been avoided if there was a visual detection program³.

However, there are important causes that are indistinct in all countries, such as congenital cataracts (CC), congenital ocular anomalies and hereditary retinal dystrophies.

CC refers to an opacity of the lens acquired during prenatal development⁴. It represents 13% of the causes of visual decline in children and is considered the most frequent cause of treatable visual deprivation. It has a prevalence of 1 to 4 per 10,000 children in developed countries and of 5 to 15 in developing countries⁴⁻⁸, with a global report of 200,000 blind children due to CC^{2,3,5,9}. It is the most important cause of blindness and is responsible for 5 to 20% of blindness in children worldwide⁹. In a systematic review of the prevalence of CC in several countries, an average prevalence of 1.03 per 10,000 children was identified, with an average incidence of 1.8 to 3.6 per 10,000 children per year¹⁰. In Latin America, it is estimated that one out of every 300 births per year present CC, and is responsible for 20% of the causes of blindness in childhood¹¹. In Mexico, a compilation of data from different ophthalmological hospitals in Mexico City and the Instituto Nacional de

Pediatría shows that in the last 10 years, 260 CC diagnoses were made before two years of age, from which only 18.46% underwent surgery¹²⁻¹⁵. In the Hospital General de México it is reported that bilateral CC (BCC) is more frequent (65%) than unilateral CC (35%), and strabismus appears as the most frequent sequela after surgery (25%)¹¹. The main cause of CC is idiopathic, followed by the inherited one; however, it may be due to a metabolic alteration (galactosemia, hemolytic anemia and hypoglycemia), or even have an infectious origin when it occurs during the first trimester of pregnancy (TORCH syndrome). However, there is a large variety of chromosomal and dysmorphic syndromes with a high risk of developing cataract (trisomy 21 and Turner syndrome)^{4,16}.

The management of CC will depend on the etiology, laterality, type of cataract and the degree of visual impairment⁵. The decision to perform surgery will depend on the clinical judgment of the ophthalmologist, who will take into account the presence of significant visual deprivation or if the cataract is visually significant, which will depend on its morphology, size, position and density⁴. In most cases, the diagnosis is usually late because there is no single universal model for the evaluation of visual development in children; however, there are tests that determine the integrity of visual function, such as the observation of the fixation pattern and visual monitoring¹⁷.

Deprivation amblyopia can be defined as an interruption in the development of visual acuity caused by a lack or inappropriate visual stimulation. Critical and sensitive periods have an important role in visual development¹⁸. Amblyopia caused by CC¹⁶ is due to anatomical and physiological structural abnormalities¹⁹ that are accompanied by visual loss²⁰. Amblyopia's reversibility will depend on the maturation states of the visual system¹⁸, the restriction's duration and the age of treatment²¹. If amblyopia is present during the critical period of visual development, optical and oculomotor

deficiencies will cause the loss of neural connections involved in the visual pathway that will affect binocular vision, which influences the control and manipulation of tasks that require three-dimensional vision. Mainly, it will affect visual-motor integration of tasks that require deep perception and fine motor skills that require hand-eye and foot-eye coordination²².

Detection and early treatment in patients with CC are important because child's development in the first two years of life is mainly linked to movement and perception. Cognitive schemes related to the construction of object permanence, the perception of space and gestural imitation could be delayed by visual difficulties when performing movements that limit the reach, manipulation and exploration of objects²².

Some studies have established that children with visual impairment have a delay in neuro psychomotor development due to a limited interaction with their environment and with objects that favor learning²³. The development of sensory functions requires the experience obtained during early childhood, so a congenital abnormality can modify visual, auditory and tactile abilities, disturbing the interaction with the environment^{24,25}. Therefore, the importance of the study lies in determining the impact of visual function restoration in the cognitive, motor and language areas to implement specific intervention strategies in CC.

Materials and methods

Study design

This is an observational, descriptive, longitudinal and ambispective study²⁶ to identify the effect of age of treatment on the restoration of visual function after CC surgery and the development of a follow-up program. In all cases, the parents signed the informed consent form and the protocol was approved by the ethics and research committees of the Instituto Nacional de Pediatría with registration number 047/2015.

Study population

The study population was patients under two years of age with a diagnosis of BCC that underwent phacemulsification from the Anterior Segment Department of the Fundación Hospital Nuestra Señora de la Luz, IAP, during the period from October 2012 to September 2014. Children who did not attend the developmental evaluation before surgery and those in whom the specialist determined concurrent ophthalmological

conditions that may affect follow-up were excluded. Two children that presented post-surgical complications associated with a significant visual decrease or that were diagnosed with systemic alterations that anticipate a developmental delay were excluded. The research was conducted at the Neurodevelopment Monitoring Laboratory of the Instituto Nacional de Pediatría in Mexico City.

Procedure

Teller visual acuity cards were used to measure visual acuity, retinoscopy was used for the refractive state; the Bayley-III Scale of Infant Development was used to determine cognitive, motor and language development. Refractive value was assessed in each evaluation and the necessary changes to the prescription were made. The behaviors that require visual function for their development and expression were selected from the Bayley-III scale in the clinical examination.

The visual rehabilitation program included the use of contact lenses after surgery until one year of age; in the second year, the use of eyeglasses with a prism was implemented to correct ocular deviation, and after two years, it was modified to use bifocal lenses to compensate for distant and near vision.

The intervention program consisted of strategies to favor cognitive, motor (fine/gross), language (expressive/receptive) and social personal development²⁷. Strategies were used to favor the development of visual function involving tasks of fixation, visual tracking, oculomotor coordination, gross and fine manipulation and hand-eye/foot-eye coordination. Attendance and participation in the intervention program and the use of prescription glasses were evaluated. A preoperative evaluation was performed based on the initial conditions and it was applied every two months until 42 months of age.

Data analysis

The patients were divided in two groups according to the age at surgery: early treatment (<6 months) and late treatment (> 6 months). In each group the median of each test to which they were subjected was calculated, and the trend was calculated by means of a non-parametric test for ordered groups, which is an extension of the Wilcoxon rank test, using a level of significance of $p < 0.05$. Statistical software Stata® (StataCorp 2013, Stata Statistical Software) was used for the analysis.

Table 1. General characteristics

Patient	Age at follow-up start (months)	Sex	Cataract type	Age at surgery in OD (months)	Age at surgery in OS (months)	Ocular disorders		Socioeconomic status		
						Ocular deviation	Nystagmus	Monthly income (# minimum wage)	Mother's Education Level	Siblings
1	2.9	M	Nuclear	5.6	6.0	No	No	7.3	Bachelor's degree	Yes
2	2.2	F	Nuclear	4.7	4.9	XT OS	No	2.5	High school	Yes
3	4.1	F	Nuclear	5.8	6.0	ET OD	No	3.4	Technical degree	Yes
4	3.6	F	Nuclear	4.6	5.6	ET OS	Yes	4.7	Bachelor's degree	No
5	7.5	F	Nuclear	8.8	9.0	XT OS	No	2.5	Secondary school	No
6	10.5	M	Nuclear	11.2	11.7	ET OD	Yes	4.2	Technical degree	Yes
7	6.1	M	Nuclear	7.7	10.4	ET OD	Yes	1.3	High school	No
8	5.8	H	Nuclear	7.1	14.1	ET OS	Yes	2.6	High school	No

OD: Right eye, OS: Left eye, M: Male, F: Female, XT: Exotropia, ET: Esotropia

The visual acuity estimation was converted to logMAR units and the refractive error was used in spherical equivalent for its analysis.

In the qualitative analysis, according to the evaluation of the selected behaviors that promote the visual function, three typologies were identified²⁸: 1) good evolution (the development reached values close to normal); 2) regular evolution (development, although improved, only fluctuated near the average), and 3) poor evolution (development remained below average).

Results

We included eight cases (4 girls and 4 boys) with 118 evaluations (average of 14.75 evaluations per patient), with a follow-up up to 42.1 months of age. The average age at surgery in the early treatment group was 5.6 months (range 4.9-6.0 months) and in the late treatment group, it was of 11.3 months (range 9.0-14.1 months). Table 1 shows the demographic variables of the cases.

Four patients presented nystagmus from the beginning of the follow-up and seven presented ocular deviation before and after the BCC surgery.

Visual function

Figure 1 shows the evolution of visual acuity for each eye separately by groups. Visual acuity was measured during follow-up with the use of optical correction. In the early treatment group, visual acuity shows a greater

gain despite the presence of strabismus, which persists after surgery. In this group, at the end of follow-up, cases were classified with mild to moderate amblyopia, while those in the late treatment group were classified with moderate to severe amblyopia.

The visual acuity gains in each eye separately showed better results in the right eye both in the early treatment and in the late treatment groups (Fig. 1); however, statistical tests showed no significant difference ($p = 0.459$ and $p = 0.882$).

In both groups, the refractive error decreased progressively and consistently, with a greater decrease in the early treatment group, which started with values of around +5.00 diopters that decreased to -0.50 diopters; however, the late treatment group started with values close to +10.00 diopters that decreased to +5.00 diopters (Fig. 2). The statistical test shows a significant difference between both groups for each eye ($p < 0.01$ and $p < 0.01$).

Development

Delays were observed in all areas before surgery in all the patients. Regarding cognitive development, the early treatment group reached a development classified as average from 13 months. In contrast, the late treatment group evolved below the average, reaching values above the average at 31 months (Fig. 3). The statistical test shows results that reflect a significant difference between both groups ($p = 0.012$).

Figure 1. Postoperative visual acuity in the right eye is slightly better than in the left eye in both groups, with better performance in the early treatment group. AL: mild amblyopia; AM: moderate amblyopia; AS: severe amblyopia; N: normal; VB: low vision.

Figure 2. Refractive error using spherical equivalent is very similar in both eyes. The early treatment group shows lower onset values, maintained during follow-up. Tx: treatment.

Regarding language development, both groups evolved in a similar way. The early treatment group remained under

average development until 37 months, when they reached average levels. These remained until the end of follow-up.

Figure 3. Bayley III Scale of Infant Development. Cognitive scale. The early treatment group starts with borderline development reaching an average value after 12 months. The late treatment group begins with an extremely low development, not reaching an average value until 31 months. AbP: below average; ArP: above average; EB: extremely low; L: borderline; MS: very superior; P: average; S: superior; Tx: treatment.

Table 2. Typology

Adequate evolution	Regular evolution	Poor evolution
Mother Bachelors degree/ High school	Mother Technical degree/ Secondary school	Mother Technical degree/ Secondary school
General visual characteristics		
1. Age at surgery < 6 months 2. Ocular alignment 3. Without nystagmus 4. Constant use of optical aid	1. Age at surgery > 6 months 2. Ocular deviation 3. Nystagmus 4. Non constant use of optical aid	1. Age at surgery > 6 months 2. Ocular deviation 3. Nystagmus 4. Non constant use of optical aid
Family characteristics		
1. Main caregiver = Mother / Both parents 2. Siblings = Yes 3. Economic contribution = Both parents / Father 4. Income = 4.7 – 7.1 minimum wages 5. Attended kindergarten = Yes	1. Main caregiver = Mother 2. Siblings = Yes 3. Economic contribution = Father / Aunts 4. Income = 2.5 – 3.4 minimum wages 5. Attended kindergarten = Yes	1. Main caregiver = Both parents / Mother 2. Siblings = No 3. Economic contribution = Both parents / Father / Grandparents 4. Income = 1.4 / 4.2 5. Attended kindergarten = No

However, the late treatment group showed lower scores up to 32 months, when they reached average scores (Fig. 4). However, the statistical test does not reflect a significant difference between both groups ($p = 0.677$).

Regarding motor development, cases of early treatment showed an extremely low development from the preoperative period to 12 months after surgery, when they reached a borderline score and achieved average levels up to 18 months. The late treatment group

obtained a borderline score at 4 months that improved until 22 months, when it reached an average value (Fig. 5). The statistical test shows no significant differences between both groups ($p = 0.398$).

For typologies construction, the general visual and familiar characteristics were taken into consideration (Table 2).

The visual functioning and its intervention in the clinical and behavioral expression during the follow-up

Figure 4. Bayley III Scale of Infant Development. Language scale. The early treatment group achieves an average development at 37 months, unlike the late treatment group that reaches it from 32 months. AbP: below average; ArP: above average; EB: extremely low; L: borderline; MS: very superior; P: average; S: superior; Tx: treatment.

Figure 5. Bayley III Scale of Infant Development. Motor scale. The early treatment group reaches an average value from 19 months, unlike the late treatment group that achieves it until 33 months. AbP: below average; ArP: above average; EB: extremely low; L: borderline; MS: very superior; P: average; S: superior; Tx: treatment.

were described in four time-points: pre-surgical, postoperative, during the follow-up and in the last recorded evaluation (Table 3).

Considering the typology, the levels show that children with good evolution achieve expected values for age, mainly by acquiring and improving visual tasks

Table 3. Characteristics of visual functioning

Typology	Preoperative	Postoperative	Follow-up	Last assessment
Good Evolution Acquired	1. Response to light	1. Explores surroundings 2. Perceives small objects 3. Tracks moving objects 4. Detects and takes small objects with radial scan-path	1. Precise visual fixation 2. Coordinated horizontal and vertical eye tracking 3. Puts in and takes out small objects	1. Precise visual fixation 2. Coordinated eye tracking 3. Precision when manipulating small objects 4. Identifies forms and colors 5. Threads beads
With Alteration	2. Weak object fixation 3. Horizontal and vertical eye tracking is present but limited with fixation losses	5. More precise eye tracking	4. Manipulates small objects with radial scan-path 5. Compensatory head posture	
Regular Evolution Acquired	1. Response to light	1. Explores surroundings 2. Perceives small objects		
With Alteration	2. Weak object fixation 3. Slow horizontal and vertical eye tracking; limited with fixation losses 4. Upward eye movements when trying to fixate	3. More precise eye tracking 4. Difficulty taking objects 5. Does not track moving objects	1. Imprecise visual fixation 2. Imprecise horizontal and vertical eye tracking 3. Manipulates small objects with radial scan-path 4. Imprecision when putting in and taking out small objects 5. Compensatory head posture 6. Squinting when fixating	1. More precise visual fixation 2. Coordinated eye tracking 3. Precision when manipulating small objects 4. Identifies forms 5. Threads beads with difficulty 6. Difficulty to associate colors with forms
Poor Evolution Acquired	1. Response to light	1. Explores surroundings 2. Perceives small objects		
With Alteration	2. Weak object fixation 3. Slow horizontal and vertical eye tracking; limited with fixation losses 4. Upward eye movements when trying to fixate	3. More precise eye tracking 4. Difficulty taking objects 5. Does not track moving objects	1. Imprecise visual fixation 2. Imprecise horizontal and vertical eye tracking 3. Manipulates small objects with radial scan-path 4. Imprecision when putting in and taking out small objects 5. Compensatory head posture 6. Gets close to the exploration table to observe details	1. Imprecise visual fixation 2. Coordinated eye tracking with compensatory head posture 3. Difficulty when manipulating small objects 4. Difficulty to associate colors with forms 5. Threads beads with difficulty

involving fixation, precision, hand-eye and foot-eye coordination, unlike children with poor evolution who present difficulties in each area despite the age and the strategies implemented.

Discussion

CC is considered as one of the main causes of preventable visual decline and it is estimated that blindness in almost half of children could have been avoided if there was an adequate health service infrastructure,

where diagnosis and early treatment represent a window of opportunity for visual function development, as well as other skills that allow optimal child development^{3,29}.

Current evidence indicates that surgical intervention should be performed in the first weeks of life, since it is considered a period characterized by rapid changes at the level of the visual cortex³⁰. It has been established that BCC surgery should be carried out within the first 10 weeks, since it is considered a sensitive period for visual deprivation³¹; however, subsequent treatment

that includes therapeutic strategies to avoid strabismus and amblyopia is necessary^{32,33}.

In the case of Mexico diagnosis is still late, despite the fact that the Ministry of Health emphasizes the importance of visual exploration in the first 6 months of age³⁴. Both the investment in the health system³⁵ and the lack of trained personnel to perform a visual screening in the first weeks of life could affect long-term visual results, since visual loss in children considers particular strategies that are different from that of adults³⁵⁻³⁷.

The study of CC is relevant given its high frequency and the possibility of preventing blindness with timely surgical treatment; however, research on visual postoperative evolution and cognitive development of cases is a subject that has been poorly studied. In Mexico, as in other less developed countries, there are no strategies and programs for the detection of visual anomalies or early visual rehabilitation programs for this type of disorder³⁸.

The interest of this research lies in the analysis of developmental pathways over a prolonged period of 42 months, with several evaluated cases that did not have the opportunity to undergo surgery in the first weeks of life, whose recovery, both visual and cognitive, provides information regarding the sensitive period of functional recovery and the perspectives of late treatment, a frequent problem in developing countries.

In this study, surgical treatment was performed according to international standards, an intraocular lens was placed and there were no postoperative complications. All were included in a visual rehabilitation and intervention program, and ideal scales and statistical methods indicated in small samples were used to evaluate development. We tried to compare the results of two groups depending on the moment of the surgical intervention: early (before 6 months of age) versus late (after 6 months of age) regarding the normalized age of the tests as historical witness.

The results show that visual function is structured according to the age of treatment, since each patient has acquired each process in a different way. Visual functioning before surgery was characterized by loss of fixation, with difficulty in visually directed tasks, using proprioceptive compensations that improved once the surgery was performed. Some authors report that, as age progresses, the visual experience and its functional changes contribute not only to the function itself but also facilitates the expansion of cognitive structures. Practice allows more precise discriminations that

facilitate the acquisition and permanence of structures linked to visual stimuli^{36,37}.

The rehabilitation process used was crucial to form an adequate development. The tasks involved in promoting development in all areas based on strategies to promote visual function allowed children to acquire and improve their skills, despite the initial biological condition. Parental support and persistence in rehabilitation allowed children operated at a younger age to achieve a better performance.

The literature discusses the results of surgery according to the age of treatment; however, several studies highlight the importance of performing treatment at an early age. It is estimated that 80% of CC patients in early stages achieve a visual acuity of 20/60, contrary to patients with late treatment that achieve 20/200 or worse³⁹. Therefore, after surgery, it is essential to perform an appropriate optical correction together with visual rehabilitation and multidisciplinary follow-up to reduce complications in terms of visual results⁶, considering the individual, the family and their environment⁴⁰. In the present study, the multidisciplinary therapeutic support of strategies to favor visual, cognitive, motor and language skills was crucial to achieve a better performance, regardless of the age at surgery, and in some children even allowed to reach normal values both in visual function and in the different areas of evaluation.

It has been reported that patients with BCC show a delay in hand-eye and hand-ear coordination as well as in sound localization that have a cognitive impact on the construction of object permanence. These restrictions can have cumulative impacts on postural control development, coordination and proactive mobility⁴¹, because vision is deeply integrated with the whole action system of the infant that involves posture, manual coordination, and even intelligence and personality⁴².

In recent decades, studies that address the impact of visual damage on child development in the areas of social adaptation, sensorimotor understanding, environmental exploration, verbal comprehension and expressive language have been published. However, there are few articles that continued researching this topic. The specialized literature on CC is abundant, but the interest is mainly focused on visual function outcomes^{43,44}.

The delays observed during follow-up are part of the developmental process. We postulate that the reorganization of previous behaviors facing the new demands, allow more complex behaviors closely related to visual function improvement, but of slower acquisition.

The study has the limitation of including a small number of cases, although the totality of those operated in

the hospital was investigated, whose follow-up covered a prolonged period.

The results obtained suggest that the age of treatment continues to be fundamental in visual prognosis. However, it is possible to observe that it also intervenes in global behavior, whose integrated diagnosis points to the need of establishing parallel early intervention strategies that, by involving the implementation of a systematized evaluation of visual functioning in response to standardized demands (development tests), allow timely and comprehensive intervention in children, including optical treatment in its different modalities, visual rehabilitation and early intervention of problems and motor, cognitive, linguistic and emotional disturbances, which would allow a comprehensive and adequate human development in the individual.

Conclusions

Delays in surgical treatment lead to serious alterations in visual functioning organization and leave sequelae such as the presence of strabismus, nystagmus and amblyopia. Overall development, measured by observable behaviors in the motor, cognitive and language areas, is also affected by the age at surgical intervention. It is also suggested that the duration of the sensitive period for visual function recovery seems not to be as limited and narrow as reported in the literature, where the intervention has serious influences on the final prognosis.

The age of treatment is still fundamental in visual acuity outcomes, but overall development also undergoes modifications: children operated at a higher age have a lower performance, which gradually improves thanks to the implementation of intervention strategies that favor their development.

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Ethical disclosures

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this study.

Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent. The authors have obtained the written informed consent of the patients or subjects mentioned in the article. The corresponding author is in possession of this document.

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Conflicts of interest

There was no conflicts of interest during this research.

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