Review Article

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The Impact of Neurosurgery on the Neuropsychological Development of Patients with Craniosynostosis: A Scoping Review

Jéssica Luchi Ferreira [1], Igor José Nogueira Gualberto [2], Mariani da Costa Ribas [1], Michele Madeira Brandão [1], Cristiano Tonello [1]

[1] Department of Craniofacial Surgery, Hospital of Rehabilitation of Craniofacial Anomalies, University of São Paulo, Bauru, São Paulo, Brazil.

[2] Medical School of São Paulo, University of São Paulo, Bauru, São Paulo, Brazil

✉ Jéssica Luchi Ferreira, MD

e-mail: jessicaluchif@usp.br

Available at:
http://www.archpedneurosurg.com.br/

Introduction: Neuropsychological assessment evaluates the cognitive profile by identifying deficits and enabling monitoring. At HRAC-USP, patients with craniosynostoses undergo this assessment due to impacts on neuropsychomotor development (DNPM). These conditions may cause cranial fusion, restricting brain growth and adversely affecting cognitive functions. Evaluation is crucial for guiding therapeutic and surgical approaches and ensuring better outcomes. Objective: To identify how surgical procedures impact the neuropsychological profile of patients with syndromic and isolated craniosynostoses through a scoping review.
Methodology: This scoping review was conducted in March 2024 using PubMed, Embase, BVS/Lilacs, and Scopus databases; 1,215 articles were found and 18 original articles (E1-18) in English were selected that addressed the question: "What is the impact of surgery on neuropsychological aspects in patients with craniosynostoses?"
Results: Studies on craniosynostosis highlighted the predominance of isolated cases (83.3%), with surgeries performed before one year of age associated with better cognitive outcomes. The cranial expansion technique (38.8%) was effective in non-syndromic cases, while cranial remodeling showed varied results. After surgery, there were overall improvements in DNPM, but also risks of language delay and motor deficits, especially in patients operated on at older ages.
Conclusion: Surgery for craniosynostosis can improve neuropsychological outcomes, especially when performed early and with appropriate surgical techniques. More invasive procedures may lead to better outcomes, including increased Total Intelligence Quotient and better academic performance. It is crucial to consider such factors to optimize outcomes, reduce neurodevelopmental risks, and continuously monitor language and executive functions.

Keywords: neuropsychological tests, craniosynostoses, neuropsychology

INTRODUCTION

Neuropsychological assessment consists of cognitive evaluation, which allows qualitative and quantitative analysis of the cognitive profile - cognitive functions (praxis, executive functions, etc.) and intellectual functions of the individual, identifying early deficits and ensuring adequate follow-up [1,2].

This practice addresses demands regarding the patient's condition; therefore, cognitive evaluation assists in complementing medical exams, serving as a parameter for the cognitive functions' baseline in surgical procedures or providing support in the elaboration of therapeutic/rehabilitative approaches after the patient's discharge, aiming to benefit this process [3,4].

Given that congenital conditions affecting the skull cause adversities in neuropsychomotor development (NPMD) and the execution of certain cognitive functions [5-7], neurosurgery patients undergo this assessment at the Hospital for Rehabilitation of Craniofacial Anomalies, University of São Paulo (HRAC-USP). The largest evaluated population consists of patients diagnosed with craniosynostoses, isolated or syndromic, such as Apert Syndrome, Crouzon, Pfeiffer, and Saethre-Chotzen.

Due to their syndromic nature, great variability exists in clinical and neurocognitive characteristics [8]. Within these conditions, the predominance of the fusion of more than one cranial suture is observed, restricting brain growth, and increasing intracranial pressure (ICP), negatively impacting NPMD [7,9,10].

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It is known that neuropsychological functions (cognition, executive functions, praxis, language, behavior, among others) can suffer impacts, even subtle ones, due to increased ICP. Still, these can be reduced with early surgical intervention. However, debates regarding the optimal age for intervention remain; some authors define it as between 9 and 12 months of age [8,10,11].

In this context, through a scoping review, the present study aims to identify how surgery procedures impact the neuropsychological profile of patients with syndromic and isolated craniosynostoses.

MATERIALS AND METHODS

This study constitutes a scoping review per the methodology outlined by the Joanna Briggs Institute [12], and to ensure methodological rigor, the PRISMA tool adapted for Scoping Review was employed [13] (Figure 1).

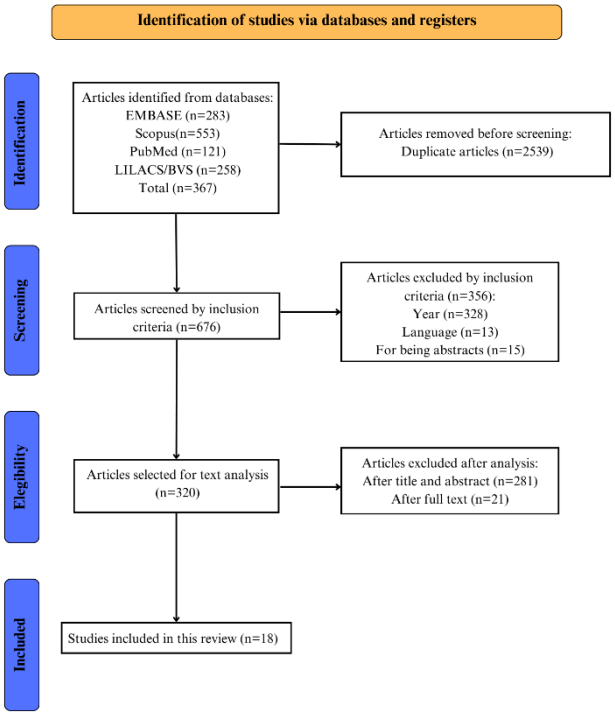

Figure 1- Flowchart of the study selection process, adapted from PRISMA-Sc

This research followed the 22 sub-steps outlined by Tricco et al. [13] to maintain scientific rigor which includes Title; Structured Abstract; Introduction - rationale and objectives -; Methods - protocol and registration, eligibility criteria, information sources, search, study selection, data collection process, data items, risk of bias in each study, summary measures, synthesis of results, risk of bias across studies, additional analyses -; Results - study selection, characteristics; critical appraisal; individual study results and synthesis of results; Discussion - summary of evidence, limitations, conclusions -; and Funding.

The Patient, Intervention, Comparison, and Outcome (PICO) [14] framework was used to devise the search strategy, as follows: P - individuals with syndromic and isolated craniosynostosis; I- surgical correction; C- individuals with typical neurodevelopment; and O- studies that testes neurodevelopmental and cognition outcomes in children after and/or before surgery. Considering this definition, the following guiding question was formulated: "What is the impact of surgery on neuropsychological aspects in patients with craniosynostosis?".

Research studies published in English or Portuguese after 2015 were eligible for inclusion, provided they contained information regarding surgery and developmental assessment. Review articles were excluded, as studies do not address the research question, posters from conference proceedings, expert opinions, and brochures.

The articles were researched with librarian assistance from March 05th to 7th, 2024 using the following databases: National Library of Medicine (PubMed/MEDLINE), Embase, Scopus, and Latin American and Caribbean Health Sciences Literature (LILACS/BVS).

Health descriptors (DeCS/MESH), keywords, and their alternative terms were used for the search. Boolean operators "or" and "and" were employed, and the following terms were defined: (Acrocephalosyndactylia OR Craniofacial Dysostosis OR Craniosynostoses) AND (Neuropsychological Test OR Cognitive Tests OR Neuropsychology OR Neurosurgery).

The search yielded 1215 articles via databases. After removing 539 duplicates with Mendeley software, 676 articles remained for screening. Through the Rayyan - Intelligent Systematic Review tool, 354 studies were excluded for failing to meet the inclusion criteria. After screening titles and abstracts, 281 articles were deleted, leaving 41 for full-text screening. Ultimately, eighteen studies met the criteria for inclusion (Figure 1).

The articles numbered 01 to 18 were called "study" for analysis. The results were presented in the form of tables and discursive reports.

RESULTS

Of the 18 studies included in the analysis, all were written in English. Over the last decade, 8 (44.4%) were published in the United States, followed by South Korea with 3 (14.2%) publications on the subject, and with one publication (4.7%) in Brazil, United Kingdom, Mexico, Turkey, France, Netherlands, and India (Chart 1).

Chart 2 categorizes the studies based on the neuropsychological assessment methodology used and the functions evaluated in the population. The predominant cognitive assessment methodology applied across the 18 studies reviewed was the Wechsler Intelligence Scale and its various iterations, utilized in nine studies (50%) to evaluate the intelligence quotient (IQ) [6,15-22]. Afterward, the Bayley Scales of Infant and Toddler Development were employed in six studies (33.3%) to evaluate NPMD [23-28], and the Behavior Rating Inventory of Executive Function (BRIEF) was utilized in four articles (22.2%) aiming to appraise executive functions [15-17,21].

However, in Verlut et al. [21], two tools were applied to evaluate emotions and anxiety: the Positive and Negative Affect Schedule and the Revised Children's Manifest Anxiety Scale. One study did not specify the instruments used in the assessment [29].

Chart 3 presents the studies according to diagnosis, surgical procedures, ages, and outcomes.

Only three studies (16.6%) included patients diagnosed with syndromic craniosynostoses, such as Apert syndrome [6,30], Crouzon syndrome [6,30], Pfeiffer Syndrome [30], and Saethre-Chotzen syndrome [29,30]. Among the 15 (83.3%) studies that investigated isolated craniosynostosis, sagittal (12; 29.7%) [16-24,26-28], and metopic (10; 27%) [18-26,32] craniosynostosis were the most studied type, followed by unicoronal synostosis (8; 21.6%) [15,18-20,22-23,25-26], Lambdoid (5; 13.5%) [18-20,22,24], bicoronal (2; 5.4%) [24,26], and multisuture (1; 2.7%) [20] craniosynostosis were less frequently represented.

Considering the type of surgical procedure, a few studies associated more than one surgical technique[16,23,25-26,30], nevertheless the most common technique used was cranial vault expansion (CVE) related in seven (38.8%) studies [16-19,23,25,29], followed by six (33.3%) articles that mentioned cranial vault remodeling (CVR) [15,20,22,24,26,30].

Other three techniques were mentioned in other studies, such as fronto-orbital advancement (4; 22.2%) [23,25-26,30] distraction osteogenesis (3; 16.6%) [16,27-28], and Le Fort III osteotomy (1; 5.5%) [30]. Another three (16.6%) did not specify the surgical technique used [6,21,31].

Regarding the age during surgery, nine studies (50%) involved populations operated on when they were less than or equal to 1 year old [15-18,20-21,24,26,29]. In comparison, four studies (22.2%) involved patients who underwent surgery after turning 1 year old [19,22,23,25]. Three studies (16.7%) showed high variability in age, ranging from 3 months to 8 years old [27-28,30]. Two studies (11.1%) did not provide information about the age at the time of procedure [6,31].

As stated in chart 2 above, the most evaluated functions were IQ, NPMD, and executive functions. Notably, the results described below consider the assessment outcomes after the surgery.

Of the nine studies (50%) that assessed the Full-Scale Intelligence Quotient (FSIQ) [6,15-22], only two (22.2%) [18-19] did not present results regarding the FSIQ, separately investigating verbal and memory functions. Meanwhile, of the remaining seven studies, three (33.3%) reported below-average FSIQ [6,16,22], while the remaining four (44.4%) studies indicated FSIQ within the expected range for the age group [15,17,20-21].

In the six studies (33.3%) [23-28], employing the Bayley Scales of Infant and Toddler Development [32] to assess NPMD, improvement was observed across all sections of the tool: "Personal Social Development," "Fine Motor Development," "Gross Motor Development," and "Language Cognitive Development." Despite the improvement all authors described nonsignificant changes before and after surgery, also some authors noted a potential risk of language and motor delay compared to typical subjects, even after surgery [23-24,26].

Among the four studies (22.2%) [15,17-18,21], that assessed executive functions using the BRIEF instrument, three (75%) indicated deficits in the evaluated function even after surgery [17-18,21].

DISCUSSION

When identifying the type of craniosynostosis, 83.3% of the studies focused on isolated craniosynostosis [15-28,31], this prevalence may be attributed to its higher occurrence in the population when compared to syndromic cases, with a prevalence rate of one in 2,000 to 2,500 live births [33].

While debates persist regarding the optimal age for surgery, there is a consensus that it is most beneficial to perform the procedure before the child reaches one year of age [8,10,11,34]. This can be observed in the results among the studies assessing FSIQ (50%) [6,15-22], where 33.3% reported below-average FSIQ, particularly in patients operated on later in childhood [6,16,22]. It is noteworthy that two of the studies [6] focused solely on patients with syndromic craniosynostosis, a group known to face heightened neurodevelopmental risks due to additional complications associated with their syndromes [8-10].

Significantly, the remaining 44.4% of studies indicated that the FSIQ fell within the expected range for the respective age group, with all patients having undergone surgery before the age of one year [15,17,20-21].

One study [17] underscores the enhancement in FSIQ, academic performance, and visuomotor integration among patients who underwent reoperation between the ages of 5 to 16 years, after the initial surgery performed before the age of one.

Conversely, studies using the Bayley Scales of Infant and Toddler Development [32] for neurodevelopmental assessment observed improvement across various domains post-surgery, albeit with a potential language and motor delay risk compared to typical subjects [24,26-28]. Three of the selected studies that identified delays involved a mixed population, with some individuals having undergone surgery after one year old [23-24,28].

Additionally, studies assessing executive functions using the BRIEF instrument noted deficits persisting after surgery, particularly in patients operated on at older ages [10-17-18]. These findings underscore the importance of considering age in surgical decision-making and postoperative neurocognitive monitoring to optimize outcomes.

Some authors recognize age at surgical time as a significant factor in pursuing better outcomes because, during this period of development the skull bones are still flexible enough to undergo remodeling more easily, reducing the impacts of increased ICP and craniofacial dysmorphisms related to brain growth [8,35]. Also, Bruce et al. [36] highlight syndromic cases with elevated perioperative risk due to supplementary factors, which can be reduced in early-age surgery.

The correlation between age and surgical procedure in managing craniosynostosis involves multiple facets. Among the studies, CVE was the most common technique (38.8%), associated with improved neurodevelopmental outcomes in some cases, all populations included were not syndromic. Regarding age, three of five studies involved infants operated on within the first year of life [18,23,25], while a substantial portion included patients operated on after age one.

The CVE technique alleviates increased intracranial pressure by allowing skull expansion and facilitating brain growth [35,37]. Studies indicate that early whole vault cranioplasty, performed before 6 months of age, yields superior intelligence quotient and achievement scores compared to minor invasive surgery, such as strip craniectomy [38-41].

Unlike that, cranial vault remodeling (33.3%) [15,20,22,24,26,30] yielded mixed results regarding neurocognitive improvement. Five studies [15,20,22,24,26] described lower outcomes after the surgery; three of these studies [15,22,24] presented patients operated on after one year old.

The limited space for a developing brain and elevated intracranial pressure result in neuroanatomical changes extending beyond the areas directly affected by the fused suture [19]. This phenomenon is particularly notable among individuals with isolated craniosynostosis, who often experience persistent neuropsychological deficits that become more pronounced during school age [17-18,20,22].

Only one study [30] focused on individuals with syndromic craniosynostosis who underwent multiple surgeries using various techniques throughout their lifetime, including CVR with fronto-orbital advancement and Le Fort III osteotomy. Remarkably, all patients demonstrated FSIQ and academic skills within age-appropriate ranges. This positive outcome could be attributed to combining CVR with fronto-orbital advancement, which aims to reshape the skull and create additional space for brain growth [40].

CONCLUSION

Surgical intervention for craniosynostosis can positively impact neuropsychological outcomes, particularly when performed early in life and with appropriate selection techniques. Operative treatment performed before age one, combined with the selection of a proper surgical technique, is essential. More invasive procedures may offer better outcomes, enhancing neuropsychological results, including elevated FSIQ scores and enhanced academic performance. Overall, surgery for craniosynostosis management requires careful consideration of various factors to optimize results and minimize neurodevelopmental risks.

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none

DISCLOSURES

Ethical approval

This study was performed in line with the principles of the Declaration of Helsinki. Considering the present study is a review, there is no need for Ethic Committe evaluation.

Conflict of interest

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

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Artificial intelligence

No artificial intelligence was not used in this paper work

CONTRIBUTIONS

-**Jéssica Luchi Ferreira**: Formal Analysis, Investigation, Methodology, Writing – original draft, Writing – review & editing
-**Igor José Nogueira Gualberto**: Data curation, Methodology, Writing – review & editing
-**Mariani da Costa Ribas**: Conceptualization, Supervision, Writing – review & editing
-Michele Madeira Brandão: Supervision
-Cristiano Tonello: Conceptualization, Supervision

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