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The Long-Term Neuropsychological Outcomes in Sagittal Craniosynotosis: Limited-Strip Craniectomy Vs. Whole-Vault Cranioplasty

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By

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Abstract

The "functional" morbidity in nonsyndromic craniosynostosis is not obvious. Because of this disconnect between cranial deformity and "functional" disability, cranial reconstructive surgery in patients with single-suture sagittal craniosynostosis has been regarded as a "cosmetic" intervention. However, it has been observed in a preliminary study that children with simple craniosynostosis often have a higher proportion of learning disabilities and cognitive problems as compared to nonafflicted children. The influence of modern comprehensive surgical treatment including the optimal age to perform surgery has not been well-documented.

This study examined long-term neuropsychological outcomes of children and adolescents with isolated sagittal craniosynostosis undergoing either limited-strip craniectomy or whole-vault cranioplasty. Furthermore, it assessed if a relationship between the age of surgery on children with isolated sagittal craniosynostosis and neuropsychological effects exists. It is hypothesized those children with isolated sagittal craniosynostosis will have a lower incidence of neuropsychological abnormalities, albeit at a higher incidence than the general population, the earlier in age they undergo the more comprehensive surgical whole-vault cranioplasty. If this study can confirm this hypothesis, then whole-vault cranioplasty at an early age may reduce the long-term neuropsychological effects of children with isolated craniosynostosis.

Retrospective inspection of the Yale-New Haven Hospital medical records from 1987 to 2002 identified eleven patients who underwent whole-vault cranioplasty and four patients who underwent limited-strip craniectomy. In terms of surgical age, eight patients underwent surgery younger than six months and seven patients who underwent surgery older than six months. The

small sample size of patients in the limited strip-craniectomy group circumvented comparisons between the types of surgery. The study demonstrated that patients undergoing surgery prior to six months of age had improved general cognitive function, academic achievement, executive functioning, and behavior compared to patients undergoing surgery after six months of age. These preliminary findings illustrate that the age of surgery impacts long-term neuropsychological outcomes with further studies necessary to explore the consequences of the type of surgery and specific-suture involvement in craniosynostosis.

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Background

Introduction:

Craniosynostosis is the pathological condition that arises from the premature fusion of one or more sutures in the cranial vault (**See Figure 1 and Figure 2**).(1) This is associated with deformation of the vault and base. Craniosynostosis may be either isolated or syndromic with a respective incidence of 0.4 and 1 per 1,000 live births.(2, 3) While both can involve the fusion of single or multiple sutures, syndromic craniosynostosis tends to be associated with multiple sutures. The premature fusion of the suture restricts the skull and growing brain underneath the affected suture, leading to expansion of the skull in unrestricted regions. More specifically, the compensatory growth of the skull occurs in planes parallel to the fused suture resulting in predictable and consistent cranial deformities.

History and Pathogenesis:

While premature closure of the sutures had been first described by Hippocrates (4), it was only centuries later that the pathogenesis of craniosynostosis became elucidated when Sommerring, in 1791, noted abnormalities of bone growth at suture lines in the disease.(5) Moreover, if a suture was fused prematurely, this limited growth in the skull perpendicular to the suture's axis. Based on their independent observations, Otto and Virchow came to similar conclusions in 1831 and 1851, respectively.(6, 7) Virchow added that compensatory expansion in the skull occurred to accommodate the growing brain. He observed that the growth in the skull was restricted perpendicular to the suture line, but increased parallel to it (**See Figure 3**).

This conclusion became the guiding principle to understanding craniosynostosis related skull deformities for the next 100 years.

Yet, van der Klaauw, in 1946 (5), and Moss, in 1959 (8, 9), challenged the rational that the etiology of cranial vault deformities resulted from the calvarial suture. Moss remained skeptical of the Virchow's hypothesis due to four findings: i) despite skulls consistent with craniosynostosis, clinical observations demonstrated the patency of a suture suspected to be prematurely fused (10); ii) characteristic cranial base abnormalities that are associated with individual stenosis of vault sutures (8); iii) observation that removal of a normal vault suture did not lead to significant skull deformity (11); and iv) the cranial base develops and matures prior to the calvarial suture.(8) Thus, Moss implicated the cranial base abnormality as the primary abnormality in craniosynostosis, and this lead to secondary cranial vault deformation. He proposed that brain enlargement served as the primary impetus for the expansion and shaping in the skull. This hypothesis became popularly known as the "functional matrix" theory.(12)

To validate which of the proposed hypotheses correctly explained the pathogenesis of craniosynostosis, experiments were conducted that documented the subsequent growth in the skull following the premature fusion of a suture. Animal studies highlighted that restriction of cranial vault sutures could cause irregular skull deformities that paralleled those observed in craniosynostosis of humans.(13, 14) Furthermore, Babler and Persing demonstrated unequivocally that the cranial base and facial skull deformities happened secondarily to the premature fusion of the cranial vault suture.(15) These studies suggest the cranial vault suture is a major factor responsible for craniosynostosis, particularly in the nonsyndromic cases.

Yet, neither Virchow's nor Moss's hypothesis fully explicate the range and pattern of abnormalities observed in craniosynostosis. A retrospective analysis of patients with individual cranial vault stenosis sought to define abnormality(ies) in the cranial vault and to postulate a mechanism that could explain the spectrum of findings.(5) Four tenets resulted from this study to explain deformities witnessed in the skull: i) cranial vault bones next to the prematurely fused sutures act as a single "plate" with decreased growth potential along all borders; ii) abnormal bone deposition occurs at the perimeter of the bone plate with increasing deposition the further the distance from the plate; iii) bone deposition occurs symmetrically at nonperimeter sutures "in line" with the fused suture; and iv) perimeter and abutting (in line) sutures have compensatory bone deposition in greater amounts the nearer the suture is to the prematurely fused suture.

Psychosocial Aspects of Cranial Deformities:

The skull or cranium has long been associated with the intellectual sense of the self.(16) Many cultures, such as Mayans, believed that the larger the skull, the greater the spiritual self. The Mayans applied external restraining devices to strengthen the spiritual value. Egyptians elongated the heads of children expected to become leaders, i.e., the Pharoahs, through towering headgear. In fact, it has been speculated that Nefertiti may have had craniosynostosis and acrocephaly. Modern societal norms rejects these ancient beliefs and cultural values, instead, appreciating a symmetrically, rounded headshape. Any aberration from this standard -- wide, tall, or narrow skull shapes -- is perceived as intellectual and spiritual weakness.

Berger identified the mental reformation process that one undertakes to determine and perceive skull form.(17) Visual receptors in the eye detect the shape of one's head with the objective image internalized and compared to the mind's subjective image. The discrepancies between the objective and subjective image can lead to negative psychological perceptions, despite corrective surgeries. This may be more pronounced in the adult cases of craniosynostosis, where the unfavorable perception of the skull has become deeply ingrained by the affected individual. Thus, a combined psychological and surgical intervention is advocated in craniosynostosis, particularly long-term cases.

The sense of self-esteem is closely related to the perceptual-cognitive assessment of body image.(18) During childhood, the body image remains dynamic.(16) The preschool child cares for how the body functions rather than looks. Around the age of four, the child develops a concern for how the body, particularly the face and skull, look. The full effect of the deformity may not occur until the child enters school supporting the decision to perform surgery prior to school age to allow adaption to physical and surgical changes. Otherwise, treatment postponed past this age permits defective perceptions of body image to become ingrained into the child's personality and psychology.

Neuropsychological Development:

Much debate surrounds whether or not children with craniosynostosis incur neurodevelopmental deficits. It has been documented that syndromic, multi-suture craniosynostosis commonly causes significant learning deficits including mental retardation.(19,

20) Yet, whether or not nonsyndromic, single-suture craniosynostosis results in aberrant neuropsychological developmental remains unclear. In 1961, Hemple et al. suggested that isolated sagittal craniosynostosis rarely caused mental retardation, and given the morbidity and mortality rates associated with craniectomy at the time, questioned surgical intervention for otherwise purely cosmetic reasons.(20) A year later Freeman and Borkowf employed developmental measures and intelligence quotients (IQs) to support Hemple et al.'s claims.(4) Barritt highlighted that craniosynostosis can result in disfigurement that could lead to potential psychosocial issues for children approving of surgical treatment even only for cosmetic purposes.(21) This controversy surrounding surgery in patients with nonsyndromic, single-suture craniosynostosis has initiated many studies involving intracranial pressure (ICP) and neuropsychological measurements all attempting to characterize the impact of surgical intervention on mental function.

Early studies to assess intellectual acumen utilized ICP measurements. The premature fusion in craniosynostosis assumes a restriction in skull growth, and in turn, a rise in ICP, due to limitation in the space for brain growth. While Gault et al. demonstrated that low intracranial volume did not always correlate with increased ICP, the authors found that reduced intracranial volume did identify a population with higher likelihood of raised ICP.(22) The increased ICP causes neurological sequelae determined by the degree of fusion and particular suture involvement. Renier et al. found that one-third of patients with craniosynostosis in their study had increased ICP, albeit higher in children with multi-suture involvement.(23) More specifically, this group observed that 13% and 16% of patients with isolated sagittal craniosynostosis (23, 24) and with frontal plagiocephaly (25), respectively, had increased ICP.

Yet, whether an inverse relationship exists between ICP and neurobehavorial status has been equivocal. Renier et al. examined ICP in patients with developmental quotients (DQ) above and below 90 and found that only those with unilateral coronal craniosynostosis had an inverse relationship between ICP and DQ.(23) The study provided no details to analyze whether this association was statistically significant. Later studies by Arnaud et al. (24) and Gewalli et al. (26) failed to identify significant associations between ICP and developmental tests in patients with isolated sagittal craniosynostosis.

Regardless, Cohen and Persing indicated problems with interpreting ICP data due to paucity of noninvasive testing preventing normative data.(27) In addition to the difficulty of quantifying ICP, the value depends highly on a person's activities with rapid-eye movement (REM) sleep, coughing or sneezing leading to increases up to 60 mmHg. Furthermore, cases with elevated ICP do not necessarily have clinical indicators of increased ICP including irritability, retinal changes, and head banging. Whether an inverse relationship characterizes ICP and neurobehavioral outcomes continues to be explored and is currently unresolved.

Controversy surrounds whether the linkage between craniosynostosis and neurobehavioral outcomes has a direct, linear pathway.(28) Those advocating secondary brain malformation from craniosynostosis note that radiographical studies of patients with craniosynostosis show compression of the ventricular system underneath the pathological suture suggesting potential damage of the cortical and subcortical brain tissue.(29) David et al. utilized single positron emission computed topography (SPECT) to highlight the asymmetry of cerebral perfusion in single-suture craniosynostosis that corrects following surgery.(30) But, others contend that craniosynostosis and the cortical and subcortical deformations may be causally unrelated, instead attributable to neuropathology originating as early as in the embryonic stages of development.(31) Certain craniofacial studies demonstrate the central nervous system develops earlier and quicker than the cranial elements lending credence that a primary malformation occurs in the central nervous system.(32-34) Regardless, hypotheses regarding the specific brain malformation related to a pathologic suture dictate the selection of neuropsychological tests for evaluating neurobehavioral outcomes.

Neuropsychological Testing:

Studies examining the neuropsychological or behavioral development of children with single-suture craniosynostosis can be grouped in two ways: 1) those that classified results based on outcomes (learning disability, language impairment, behavioral abnormality, or test scores below a defined threshold); and 2) those that drew between group comparisons of average scores on a test or symptom checklist. Many in the former group utilized the Bayley Scales of Infant Development (BSID, 1969), in particular its Mental Developmental index (MDI) and Psychomotor Developmental index (PDI). The multiple studies directed by Kapp-Simon and by Speltz et al. revealed that no differences existed between test norms and children with single-suture craniosynostosis.(35-38) These findings led Kapp-Simon to claim that surgery in single-suture craniosynostosis was primarily a cosmetic intervention. While the Kapp-Simon studies omitted the PDI, other studies that employed the PDI noted that synostotic patients had lower-than-average scores on this subtest.(39, 40)

Nevertheless, Renier and Marchac rebuked the claim by Kapp-Simon et al., i.e., nonsyndromic craniosynostosis does not lead to aberrant mental development, criticizing the studies' small sample size and omission of testing older children lead to erroneous conclusions.(41) Instead, these authors demonstrated that young children tend to have normal mental development but this decreases with increasing age. They stressed the importance of performing early surgery in circumventing the regression in mental function that occurs with increasing age.

Generally, the early neurodevelopmental studies failed to examine the long-term consequences, particularly during the school-age period, of mental development. In fact, the testing remained rather rudiment never examining learning disabilities or cognitive impairment. Moreover, none of these studies assessed the psychosocial impact including socialization and behavioral issues of the disfigurement arising from craniosynostosis. Yet, over the last decade, as more sophisticated neuropsychological testing including the ability to detect subtle learning disabilities has become available, recent studies have incorporated these measures into their methodologies.(36, 42-44)

Virtanen et al. demonstrated that children with sagittal craniosynostosis older than seven years scored lower on three of the Wechsler Intelligence Scale of Children (WISC) Revised subtests (similarities, reading comprehension, and digit span) as compared to a matched control-group.(44) This study, however, may have not reached statistical significance had the data been analyzed more conservatively. Boltshauser et al. using the WISC 3rd edition and the Wechsler Adult Intelligence Scale (WAIS) showed that children and adults with unoperated sagittal craniosynostosis between the ages of two and twenty-five years displayed deficits in processing speed and tasks, assessing learning, memory, or memory span compared to their siblings.(45) Using similar neuropsychological measures, DaCosta et al. showed that in patients with single-suture craniosynostosis aging from seven to sixteen years that these patients showed lower-than-expected performance on tasks assessing sustained attention, visual-spatial planning ability, and planning/problem solving ability.(46) Magge et al. revealed that in sixteen sagittal craniosynostosis patients a significantly higher verbal IQ than nonverbal IQ suggesting problems in learning tasks that require visual-spatial abilities or related nonverbal abilities (perceptual organization and reasoning, visual attention, and memory.(42) These studies highlighted that patients with nonsyndromic, isolated craniosynostosis are at least at higher risk than the general population for developing long-term neuropsychological outcomes.

Nonetheless, these conclusions have been criticized for their small sample sizes, widely differing ages of patient tested, cross-section analysis, or limited assessment of global mental function. Thus, it has been recommended that future studies assess sizeable number of children within a narrow school-age range corresponding to the late-elementary to high school levels followed for an extended period of time. More specifically, the testing within this population should involve multiple domains of functioning including expressive language problems and nonverbal learning disorders characterized by visuospatial impairment, poor arithemetic skills, and interpersonal and emotional problems.

Impact of Age of Surgery:

The issue is further complicated by the schism that exists among those who advocate surgery as means to improve neuropsychological outcomes regarding the optimal age to perform surgery in isolated craniosynostosis. Persing et al. typically perform cranial reconstructive surgery at five to six months of age when the body can withstand the extent of surgery and anticipated blood loss; others tends to perform surgery at nine to ten months when the cranium has approximated its adult size, and requires less overcorrection of the cranial reconstruction.(3, 47) Researching how the age of surgery impacts long-term neuropsychological outcomes may provide insight in recommending to patients the optimal age for surgical intervention.

Statement of Purpose

The "functional" morbidity in nonsyndromic craniosynostosis is not obvious. Because of this disconnect between cranial deformity and "functional" disability, cranial reconstructive surgery in patients with single-suture sagittal craniosynostosis has been regarded as a "cosmetic" intervention.(37, 48, 49) However, it has been observed in a preliminary study that children with simple craniosynostosis often have a higher proportion of learning disabilities and cognitive problems as compared to nonafflicted children.(42) The influence of modern comprehensive surgical treatment including the optimal age to perform surgery has not been well-documented.

This study will examine long-term neuropsychological outcomes of children and adolescents with isolated sagittal craniosynostosis undergoing either (endoscopic) strip craniectomy (**See Figure 4**) or whole-vault cranioplasty (**See Figure 5**). While previous studies comparing (endoscopic) strip craniectomy and cranioplasty have documented blood loss, intensive care unit stay, hospital costs, and reoperative rate, this study will go further evaluating how each surgery affects mental function outcome and long-term educational costs. Lastly, this study will determine if a relationship between the age of surgery on children with isolated sagittal craniosynostosis and neuropsychological effects exists. Understanding these issues will better ensure appropriate management and sound health policy decisions including reimbursement patterns with regards to surgical intervention in isolated craniosynostosis.

It is hypothesized those children with isolated sagittal craniosynostosis will have a lower incidence of neuropsychological abnormalities, albeit at a higher incidence than the general population, the earlier in age they undergo the more comprehensive surgical whole-vault cranioplasty. If this study can confirm this hypothesis, then whole-vault cranioplasty at an early age may reduce the long-term neuropsychological effects of children with isolated sagittal craniosynostosis, and in the process, decrease the need for special educational support for delays in achievement potentially lowering long-run costs.

Specific Aims and Hypotheses

The impact of cranial reconstructive surgery in patients with isolated craniosynostosis on long-term neuropsychological outcomes remains a source of significant debate.(24, 37, 42, 48, 49) Previous studies attempting to understand neuropsychological sequalae pre- and post-operative in this population by examining developmental quotient (DQ), intelligence quotient (IQ), intracranial pressure (ICP) have been equivocal.(20, 23, 24, 35, 44) This disconnect between functional ability and cranial deformity has provoked controversy with a few surgeons and neuropsychologists proclaiming surgery in isolated craniosynostosis as a "cosmetic" intervention.(37, 48, 49) Furthermore, among those who believe surgery improves neuropsychological outcomes, there exists a divide on what is the optimal age to perform surgery in this patient population. The group espousing delaying surgery until the cranium reaches adult size believes this mitigates the overcorrection necessary when performing cranial reconstruction at younger ages. Finally, with the current healthcare climate, there has been a rise (endoscopic) strip craniotomy has risen in popularity due to its lower blood loss, intensive care unit (ICU) stay, and hospital costs when compared to the more extensive whole-vault cranioplasty.

- *Aim #1:* To examine how the age of surgery impacts neuropsychological outcomes in patients with isolated sagittal craniosynostosis within the narrow school-aged group of six to twenty years amenable to testing of multiple domains of mental functioning. *Rationale:* No study has documented how the age of surgery impacts long-term neuropsychological outcomes, which may be crucial for determining at which age to perform surgery.

Hypothesis #1: It is hypothesized those children with isolated sagittal craniosynostosis undergoing surgery at an earlier age will have a lower incidence of neuropsychological issues, albeit at a higher incidence than the general population.

Aim #2: To examine how the type of surgery, strip craniectomy versus and whole-vault cranioplasty, impacts neuropsychological outcomes in patients with isolated sagittal craniosynostosis within the narrow school-aged group of six to twenty years amenable to testing of multiple domains of mental functioning.

Rationale: A need exists to assess how strip craniectomy and whole-vault cranioplasty affect neuropsychological outcomes and related schooling interventions influencing the treatment of isolated craniosynostosis.

Hypothesis #2: It is hypothesized those children with isolated sagittal craniosynostosis undergoing the more comprehensive whole-vault cranioplasty will have a lower incidence of neuropsychological issues requiring fewer special education classes that potentially may offset the initially higher surgical costs.

Methodology

Overview:

The study took place as a joint collaboration among the Yale School of Medicine (SOM) Yale SOM Department of Neurosurgery, Yale SOM Child Study Center, and Yale SOM Section of Plastic Surgery. Following approval from the Yale SOM Human Investigation Committee (HIC), the identification and recruitment of patients began in June 2008 and ended in November 2008. Neuropsychological testing commenced in July 2008 and ended in December 2008. The subsequent statistical analysis of the data occurred in January 2009. The Yale SOM Office of Student Research provided six months of research support facilitating my ability to fully participate in all phases of the project from the study design to the recruitment and identification of patients to the administration of the tests to the statistical analysis of the data.

Identification of Patients:

Retrospective inspection of the Yale-New Haven Hospital medical record located in the Yale SOM Department of Neurosurgery and the Yale SOM Section of Plastic Surgery, from 1987 to 2002 was used to identify subjects born with nonsyndromic, sagittal craniosynostosis. All patients had been surgically treated by either neurosurgeons with the Yale SOM Deparment of Neurosurgery or craniofacial plastic surgeons with the Yale SOM Section of Plastic Surgery. The operative summaries of all patients undergoing linear strip craniectomy or whole-vault cranioplasty for craniosynostosis during this 15 year period were systematically reviewed to confirm both the diagnosis and the treatment of choice. Exclusion criteria were the following:

current age of less than 6 years or greater than 20 years, syndromic craniosynostosis, non-English speakers, or presence of additional neurological complications such as seizures or mental retardation related to hydrocephalus or traumatic brain injury. The review of the medical records identified 56 patients fitting our inclusion criteria, of whom 42 patients underwent whole-vault cranioplasty and 14 patients underwent strip craniectomy.

Recruitment of Patients:

While the optimal control group would have consisted of patients who had nonsyndromic, sagittal craniosynostosis *without* undergoing corrective surgery, the vast majority of children born with this disease in the United States are treated within the first six months after birth. This necessitated the use of comparing both surgical groups to each other and to the norms established for the general population.

The medical record number (MRN) of these patients was noted from their charts and entered into the Yale-New Haven Hospital computer system to obtain their most up-to-date address and phone number. A letter inviting the patient to participate in the study was mailed to the address listed in the computer system. The letter provided the patient and the parent(s) information regarding the purpose of the study, the evaluative procedures, the details of the financial compensation, and the potential benefits and risks of study participation. The patient and parent(s) were informed that their participation in this study was voluntary and had the right to withdraw from the project at any time without affecting any medical and/or intervention services they may be receiving from the recruitment sites. The patients and their parent(s) willing to participate in the study were asked to contact me either through phone or email to set up a mutual date and time for the study to take place on. Sixteen patients with nonsyndromic, single-suture sagittal craniosynostosis, of whom twelve patients underwent whole-vault cranioplasty and four patients underwent strip craniectomy, scheduled a time for neuropsychological testing.

Twenty-nine letters came back to the Yale SOM Section of Plastic Surgery due to patients moving from the address listed in the computer system. Those twenty-nine patients were attempted to be reached via telephone using the number listed in the Yale-New Haven Hospital computer system. None of the patients could be reached because the phone numbers were incorrect.

Participants:

Prior to conducting statistical analyses, individual participant performance on intellectual functioning was examined to identify any potential participants who were functioning in the intellectually deficit range (IQ < 70). This excluded one participant who had received a strip craniectomy at three months of age and one who had received whole-vault cranioplasty at 31 months of age. This is done because individuals functioning in the lower ranges of IQ tend to have greater difficulties in academic achievement, executive functions, and increased behavioral difficulties than individuals functioning in relatively higher IQ ranges. Furthermore, individuals, who are functioning in the intellectually deficit range, may experience higher or lower than expected performance on other measures due to limited sampling of participants that are lower functioning during normative development of the measures.

Testing Site:

Patients and their parent(s) came to the Yale Craniofacial Center for a two hour and thirty minute testing session. The first fifteen minutes were used to explain the need for the study, the types of testing being conducted, the procedure for receiving the financial compensation, and the timeline for receiving the patient's testing results. It was stressed to the patients and their parent(s) that participation in this study was voluntary and that they have the right to withdraw from the project at any time without affecting any medical and/or intervention services they may be receiving from the recruitment sites. Following this, the patients and their parent(s) were asked to complete the appropriate forms in accordance with the Yale SOM Human Investigations Committee (HIC). More specifically, patients aged between six and twelve years completed the HIC-approved consent form, while patients aged between thirteen and twenty years completed the HIC-approved assent form. Parents of patients under eighteen years completed the HIC-approved parental form. Afterwards, the testing commenced with the patient according to the testing guidelines. During the period of testing, the parent(s) of each patient simultaneously completed surveys assessing the patient's behavior and socialization among family members, school classmates, and peers.

Neuropsychological Tests Administered:

The neuropsychological tests administered for this study were selected by Dr. Linda Mayes, a pediatric psychiatrist, Dr. Nancy Close, a child psychologist, and Dr. John Persing, a neurosurgeon and craniofacial surgeon, who are all familiar with the literature regarding the impact of single-suture sagittal craniosynostosis on anatomical regions of the brain. The tests aimed to measure subtle neuropsychological outcomes including learning disorders, attention disorders, and socialization issues. These tests are extremely useful in children and adolescents within the school-age range. Based on the recommendations in the literature, age criteria, and time constraints, the battery of tests listed in "Description of Tests" sections were administered. All of these tests have a strong reliability coefficient. For further information regarding other reliability (i.e, intertest and interrater reliability coefficients) and validity measures, please refer to the appropriate training manual for each test.

Over the span of a week, Dr. Nancy Close trained me to administer the tests including remaining aware of certain behavioral signs to understand when to repeat or curtail testing questions. This enabled me to conduct testing with each patient independently. Each test was scored according to the rubrics and scales outlined in the training manual. Dr. David Bridgett, a child psychologist fellow, provided an interpretation of these scores in context of long-tem neuropsychological outcomes and conducted statistical data analysis.

Analytical Strategy:

A combination of approaches was used to address the two following questions: 1) the impact of type of surgery on long-term neuropsychological outcomes; and 2) the impact of the age of surgery on long-term neuropsychological outcomes. First, mean differences between participants who received limited-strip craniectomy and who received whole-vault cranioplasty were examined using analysis of covariance (ANCOVA). All analyses statistically controlled for the age of the participant at the time of surgery and full-scale IQ (FSIQ). To examine the association between age at the time of surgery and cognitive, achievement, and behavioral outcomes, partial correlations were used for all analyses controlling for type of surgery. Partial correlations between achievement functioning and age of surgery were conducted controlling for both type of surgery and FSIQ; partial correlations examining associations between age of surgery and Behavior Rating Inventory of Executive unction (BRIEF) controlled for the type of surgery and FSIQ. Associations between scales of the Behavior Assessment for Children, Second Edition (BASC-2) and age at the time of surgery controlled for type of surgery, FSIQ, and the BRIEF General Executive Control (GEC) scale. Mean differences on cognitive, achievement, and behavioral outcomes between those participants who received surgical intervention when they younger than six months and those participants who received surgical intervention when they older than six months were examined using ANCOVA's. Covariates in the ANCOVA analyses correspond to the strategy used in determining covariates in the partial correlation analyses outlined above (covariates consisted of type of surgery, FSIQ, and BRIEF GEC, depending on the specific outcome examined).

As small sample sizes tend frequently occur in studies involving rare craniofacial abnormalities, we anticipated our study would have limited statistical power to detect effects. Thus, a less conservative probability value of 0.15 was adopted for determining statistical significance in the present investigation. Likewise, statistical trends were characterized and discussed when probability values were between 0.20 and 0.16. Furthermore, to identify potentially important effects, findings are also characterized by effect sizes. Partial correlations can be interpreted as effect sizes using Cohen's (Cohen, 1988) criteria for small ($r_p \leq 0.10$), medium ($r_p = 0.25$), and large ($r_p \geq 0.40$) effects. However, it is important to recognize that when interpreting partial correlations, the effect is what is remaining after accounting for covariates. Cohen's *d,* which measures the size of the effect when mean differences are examined, was used to determine the effect size of comparisons between surgical groups and age of surgery. Cohen's *d* effect size is interpreted such that values ≤ 0.20 are considered small effects, values = 0.50 are considered medium effects, and values ≥ 0.80 are considered large effects (Cohen, 1988).

Despite the steps noted above, the findings should be cautiously interpreted. Statistically, as sample sizes increase, samples are expected to more and more closely reflect the population as a whole. Thus, differences between groups could reflect unequal sample sizes, small sample sizes, or a combination of both as well as effects from other sources. In short, our data should be viewed as preliminary findings.

Description of Tests:

- **Wechsler Abbreviated Scale of Intelligence** (WASI, Wechsler 1999): This is an individually administered assessment of a child's ability to measure verbal, performance, and full scale IQ scores. The verbal IQ score is determined by a vocabulary subtest and a similarities subtest that measures verbal reasoning and word knowledge. The performance score is determined by matrix reasoning and block design measuring abstract reasoning skills and ability to separate figure and ground in visual stimuli. The WASI has been used to estimate IQ scores for research purposes. The test is administered to children aged 6 to 89 years. The average length of time to administer the test will be approximately 30 minutes.

- **Wechsler Fundamentals** (WF; Wechsler): This is an individually administered assessment of a child’s verbal, spelling, and mathematical abilities. The verbal component consists of word reading and reading comprehension. The spelling test asks the child to write dictated letters and words. The mathematical section measures a child's skills in numerical operations. The test is administered to children in grades from kindergarten to grade 12. The average length of time to administer the test will be approximately 45 minutes.
- **Beery-Buktencia Developmental Test of Visual Motor Integration, Fifth Edition** (Beery VMI-V; Beery, 2004): This is an individually administered assessment of a child’s ability to integrate visual and motor abilities. Furthermore, by presenting drawings of geometric forms arranged in order of increasing difficulty that the child is asked to copy, this test assists in identifying visual-motor deficits that can cause neuropsychological problem. The test is administered to children aged 2 to 18 years with the reliability coefficient relatively high (i.e, ranges from r=0.96 to r=0.97). The average length of time to administer the test will be approximately 10 minutes.

- **Behavior Rating Inventory of Executive Function** (BRIEF; Isquith, 2004) This is a test compromised of two rating forms, a parent questionnaire and teacher questionnaire, aimed to assess executive functioning in the home and school surroundings. The BRIEF questionnaire contains 86 questions in eight nonoverlapping clinical scales and two validity scales. These indices consist of a behavioral regulation index (BRI) and a metacognition index (MI) comprising a global executive composite. The BRI measures the ability of a child to shift cognitive set and modulate emotions and behavior applying appropriate inhibitory control, while the MI measures the ability of a child to initiate plan, organize, and sustain future-orientated problem solving in working memory. Furthermore, the test provides a measure of executive function in an everyday behavioral perspective rather than a clinic-based performance test. The test is administered to children aged 5 to 18 years with the reliability coefficient relatively high (i.e, ranges from r=0.80 to r=0.98). The average length of time for both parent and teacher to complete will be approximately 40 minutes.
- **Behavior Assessment System for Children, Second Edition** (BASC-2; Reynolds & Kamphaus, 2004): This measure provides a multimethod, multidimensional rating system that can be completed by both parents and teachers for children and young. It is administered in a questionnaire format that lists numerous aspects of behavior and personality functioning. The BASC-2 Parent Rating Scales (PRS) yields four primary composites: Externalizing Problems; Internalizing Problems; Behavioral Symptoms Index; and Adaptive Skills. These four composites are further broken down into nine

clinical scales: (i.e., Hyperactivity; Aggression; Conduct Problems; Anxiety; Depression; Somatization; Atypicality; Withdrawal; and Attention Problems). In addition, three Adaptive Scales (i.e., Adaptability; Social Skills; and Leadership) and three validity indices are derived, which address issues concerning response bias. The test is administered to children aged 2 to 25 years with the reliability coefficient relatively high (i.e, ranges from r=0.83 to r=0.87). The average length of time for both parent and teacher to complete will be approximately 40 minutes.

Results

Based on the rationale outlined in the methodology participants section, two participants were removed from further consideration in the current study due to low IQ scores. One participant had received a strip craniectomy at three months of age and one had received whole-vault cranioplasty at 31 months of age. This resulted in four patients who underwent limited-strip craniectomy and nine patients who underwent whole-vault cranioplasty. In terms of surgical age, eight patients underwent surgery younger than six months and seven patients who underwent surgery older than six months. Of note, three patients did not turn in both the BRIEF survey.

ANCOVA findings examining differences between those participants who received limited-strip craniectomy and who received whole-vault cranioplasty on measures of general cognitive potential including FSIQ, verbal IQ (VIQ), and performance IQ (PIQ), academic achievement, and broad externalizing and internalizing difficulties were not statistically significant (all *p's* > 0.15; See **Table 1** and **Table 2**). Comparisons between groups based on surgery type were not conducted on BRIEF scales because only one participant in the limited-strip craniectomy group completed the BRIEF survey.

Two partial correlations between measures of intellectual functioning and age (in months) at time of surgery were significant. After accounting for type of surgery, results indicated that those who received surgical intervention earlier in life obtained higher FSIQ and PIQ than those who received surgical interventions relatively later in life ($r_p = -0.48$, $p < 0.15$ and $r_p = -0.50$, $p < 0.15$, respectively; See **Table 3**). Controlling for type of surgery and FSIQ, findings indicated that those who received earlier surgical intervention obtained significantly higher reading composite, word reading, reading comprehension, and numerical operation scores relative to those who received surgical intervention at older ages (See **Table 4**).

Examination of partial correlations between age at time of surgery and BRIEF ratings yielded two noteworthy trends. Participants who were relatively older at the time of surgery obtained higher scores on the BRIEF Inhibit and Behavior Rating Inventory (BRI) scales indicative of greater executive functioning difficulties ($r_p = .53$, $p < .20$ and $r_p = .51$, $p < .20$, respectively; See **Table 5**). Associations between age at time of surgery and BASC-2 scores also yielded several important findings. After accounting for type of surgery, FSIQ, and BRIEF GEC, partial correlations indicated that participants who were older at the time of their surgery obtained higher externalizing problems scores ($r_p = 0.61$, $p < 0.15$; See **Table 6**), higher somatic complaint scores ($r_p = 0.66$, $p < 0.15$) and marginally higher aggression problems scores ($r_p = 0.56$, $p < 0.20$) than participants who were relatively younger at the time of surgery (See **Table 7**).

To further understand the impact of the age of surgery, participants were split into two groups: those who received surgery prior to six months of age and those who received surgery after six months of age. ANCOVA's examining differences in intellectual functioning between groups indicated that participants in the younger age group obtained significant higher FSIQ scores ($F\ (1,2) = 5.25$, $p < 0.05$), marginally higher VIQ ($F\ (1,2) = 2.30$, $p = 0.16$), and significantly higher PIQ scores ($F\ (1,2) = 5.09$, $p < 0.05$) than participants in the older age group after controlling for the type of surgical intervention (See **Table 8**). After accounting for FSIQ and type of surgery, participants from the younger age group at time of surgery obtained significantly higher numerical operations scores than participants who were older than 6 months of age at the time of surgery (F (1,3) = 3.56, $p < 0.10$; See **Table 8**). No other achievement differences were statistically significant. Participants who were younger at the time of surgery performed marginally better on the BRIEF initiate scale relative to participants who were older than six months of age at the time of surgery (F (1,3) = 2.38, $p < 0.20$; See **Table 9**) after accounting for FSIQ and type of surgery. Individuals who received surgery after six months of age had greater difficulties with hyperactivity, as measured on the BASC-2, compared to participants who received surgery before six months of age (F (1,4) = 2.48, $p < 0.20$; See **Table 10**) after accounting for FSIQ, type of surgery, and BRIEF GEC. Although relatively few effects were statistically or marginally significant, examination of the effect sizes (see **Tables 8-10)** suggest that surgical intervention by the time individuals reach the age of six months have better clinical outcomes in terms of general cognitive functioning, academic achievement, executive functions, and behavioral problems relative to participants who were older than six months of age at the time of surgery.

Discussion

Surgical release of the prematurely fused suture has been advocated as the definitive treatment in craniosynostosis. The indication for surgery in multi-suture craniosynostosis remains straightforward due to the documented complications from non-treatment. Yet, the disconnect between cranial deformity and "functional" disability in patients with single-suture craniosynostosis foments debate whether surgery provides any benefit other than cosmetic restoration. Early studies measured global intelligence using developmental quotient (DQ) and intelligence quotient (IQ) failing to consider subtle neuropsychological outcomes including learning disabilities. This study examined how the type of surgery and age of surgery impacted patients with sagittal craniosynostosis in terms of general cognitive functioning, academic achievement, executive functioning, and behavioral problems.

Studies testing general cognitive functioning including DQ or IQ revealed patients with single-suture craniosynostosis score lower-than-average compared to the mean of the standardization group.(24, 40) In this study, general cognitive functioning was evaluated using the WASI to measure FSIQ, VIQ, and PIQ through subtests involving vocabulary, similarities, block design, and matrix reasoning. While there were no significant differences in general cognitive functioning between patients undergoing limited-strip craniectomy and whole-vault cranioplasty, general cognitive functioning inversely correlated with the age of surgery.

Those younger than six months at the time of surgery obtained significant higher FSIQ scores (F (1,2) = 5.25, $p < 0.05$), marginally higher VIQ (F (1,2) = 2.30, $p = 0.16$), and significantly higher PIQ scores (F (1,2) = 5.09, $p < 0.05$) as compared to those older than six months at time of surgery.

Based on the recommendations on the literature (28, 42, 50), the study attempted to examine subtle neuropsychological outcomes. Using the Wechsler Fundamentals, our study examined spelling, word reading, reading comprehension, and numerical operations finding that those with surgery performed before six months of age scored higher than those with surgery performed after six months of age based on partial correlations. Participants who were younger than six months of age at the time of surgery obtained significantly higher numerical operations scores than participants who were older than six months of age at the time of surgery (F (1,3) = 3.56, $p < 0.10$). Yet, no differences existed between the two types of surgical groups.

Studies examining problems with executive functioning including working memory, impulse control, and planning have been limited. The BRIEF used in this study measures the following aspects of executive functioning: Inhibit, Shift, Emotional Control, Initiate, Working Memory, Plan/Organize, and Monitor. The clinical scales form three broad indexes (Inhibitory Self-Control, Flexibility, and Emergent Metacognition) and one composite score (Global Executive Composite). Participants who were younger than six months at the time of surgery performed marginally better on the BRIEF initiate scale relative to participants who were older than six months of age at the time of surgery (F (1,3) = 2.38, $p < 0.20$; See **Table 9**). The type of surgery had no statistical significant impact on scores of the BRIEF scales.

Behavioral characteristics regarding patients with craniosynostosis have been ambiguous. While certain studies found behavioral adjustment as noted by parents and teachers roughly equivalent to those in the standardization sample (36, 44), Speltz et al. demonstrated higher levels of parent- and teacher-reported behavioral problems compared to a matched group of children.(38) Our study utilized the BASC-2 to evaluate the following scales: hyperactivity, aggression, conduct problems, anxiety, depression, somatization, atypicality, withdrawal, and attention problems. These scales are grouped into categories measuring difficulties in externalizing problems, internalizing problems, and behavior. Of note, those receiving surgery after six months had higher externalizing problems scores ($r_p = .61$, $p < .15$), higher somatization scores ($r_p = .66$, $p < .15$), and marginally higher aggression problems scores ($r_p = .56$, $p < .20$) compared to those receiving surgery prior to six months. More specifically, those receiving surgery prior to six months tended to be less hyperactive compared to those receiving surgery after six months (F (1,4) = 2.48, $p < .20$). The type of surgery did not produce any statistical significant effect on the BASC-2 scales.

This study went beyond previous investigations that aimed to characterize neurodevelopment indirectly through ICP measurements.(22, 51) Our findings demonstrated that patients who receive surgery after six months tend to have increased problems with numerical operations, initiation, and hyperactivity. While no significant differences occurred between PIQ and VIQ suggestive of specific learning disabilities, the issues with numerical operations cannot rule out future issues in mathematically-intensive coursework.(52) High scores on the BRIEF initiate scale prove concerning for the ability to start tasks and generate novel information and ideas.(53, 54) Early issues of hyperactivity if not addressed can lead to delinquent and antisocial behavior during adolescence and interpersonal relationships in childhood.(55) A recent study documented that hyperactivity, albeit less than attention problems, can be a significant predictor of college GPA.(56) Our preliminary findings seem to indicate surgical intervention prior to six months of age in those patients with single-suture craniosynostosis mitigate adverse long-term neuropsychological outcomes.

The type of surgery was not shown to impact the neuropsychological outcomes, possibly due to our small sample size having 13 patients, but the age of surgery did affect outcomes involving general cognitive functioning, academic achievement, executive functioning, and behavioral problems. The principal investigator of this study advocates performing surgery on patients with craniosynostosis at approximately six months of age when the body can withstand the impact of surgery and the potential blood loss that can occur. Thus, we used this age to divide the patients into two groups when examining the impact of the age of surgery on neuropsychological outcomes.

We acknowledge two potential vulnerabilities in inferring causality from correlation data. First, correlation is sensitive to the range of values of the variables being measured. Second, age of surgery may be confounded by other parameters affecting neuropsychological outcomes. For example, those patients receiving surgery at a younger age may represent a different sample than the patients receiving surgery at an older age. The former may have better access to a craniofacial center, more vigilant parents, and parents more confident about surgery compared to the latter group. No studies, however, as of yet have been able to separate the effects of the age of diagnosis from the age of surgery.

Future studies will have to address these vulnerabilities as well as other shortcomings. Studies should include significantly more patients, particularly from each type of surgical group, to allow for increased statistical power. Patients should be evaluated pre- and post-operatively to determine the effect of surgery. This would allow not only an evaluation of the impact of the age of surgery, but the impact of the surgery itself on neuropsychological outcomes. Admittedly, this remains challenging given the rudiment assessments of cognitive functioning early in life. Finally, rigorous studies examining neuropsychological outcomes of different synostoses are necessary for understanding specific suture-brain-behavior associations.

Conclusion

Fewer neuropsychological deficits were observed in patients with sagittal craniosynostosis undergoing surgery prior to six months than those after six months. These findings suggest not only the need for surgery to be performed early on in life, but also appropriate academic and behavioral interventions be accessible for patients with nonsyndromic, single-suture craniosynostosis.

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Figures

Figure 1. Vertex view of infant cranium demonstrating unfused sutures and open fontanelles. AF is the Anterior Fontanelle and PF is the Posterior Fontanelle.(From Huang, M. H., Gruss, J. S., Clarren, S. K., et al. The differential diagnosis of posterior plagiocephaly: true lambdoid synostosis versus positional molding. *Plast Reconstr Surg*. 98: 765-774; discussion 775-766, 1996.)

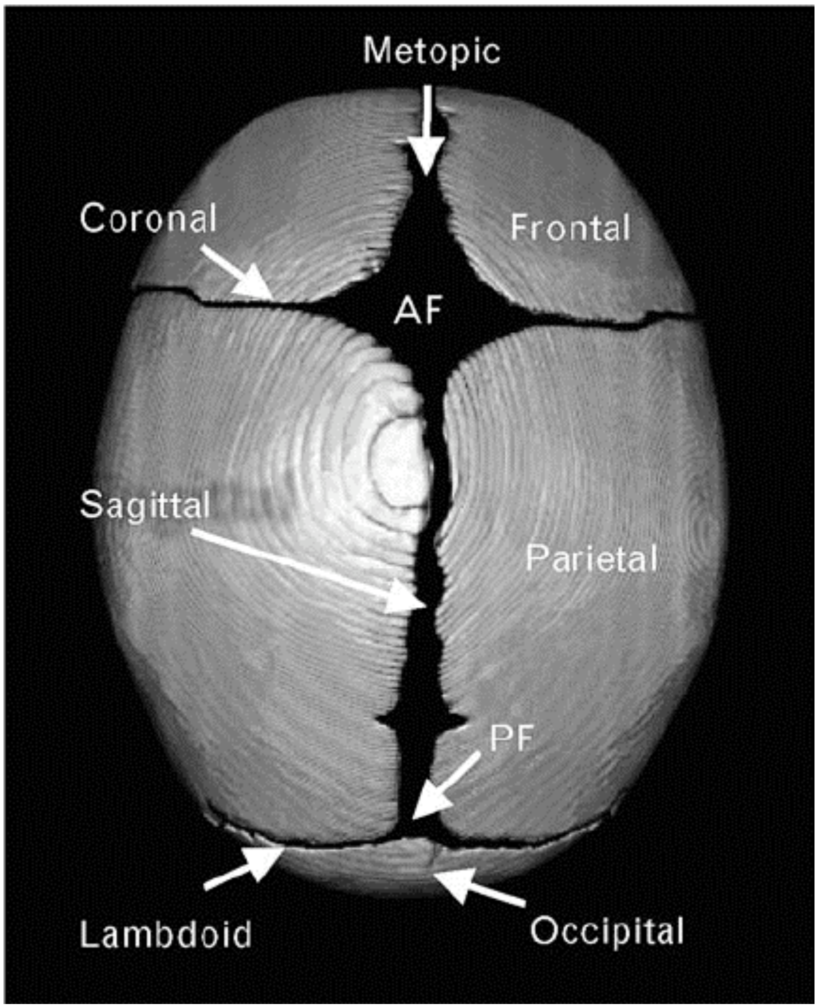


Figure 2. Sagittal Craniosynostosis: The digital image and radiograph represent an infant with premature fusion of the sagittal suture. (From Huang, M. H., Gruss, J. S., Clarren, S. K., et al. The differential diagnosis of posterior plagiocephaly: true lambdoid synostosis versus positional molding. *Plast Reconstr Surg*. 98: 765-774; discussion 775-766, 1996.)

Figure 3. A. Major cranial sutures. B. Growth of the brain that is reflected in expansion of the cranial vault is always perpendicular to cranial sutures as demonstrated by arrows. (From Carson BS, Dufresne CR. Craniosynostosis and neurocranial asymmetry. In: Dufresne CR, Carson BS, Zinreich SJ, eds. *Complex Craniofacial Problems*. New York: Churchill Livingston; 1996:169)

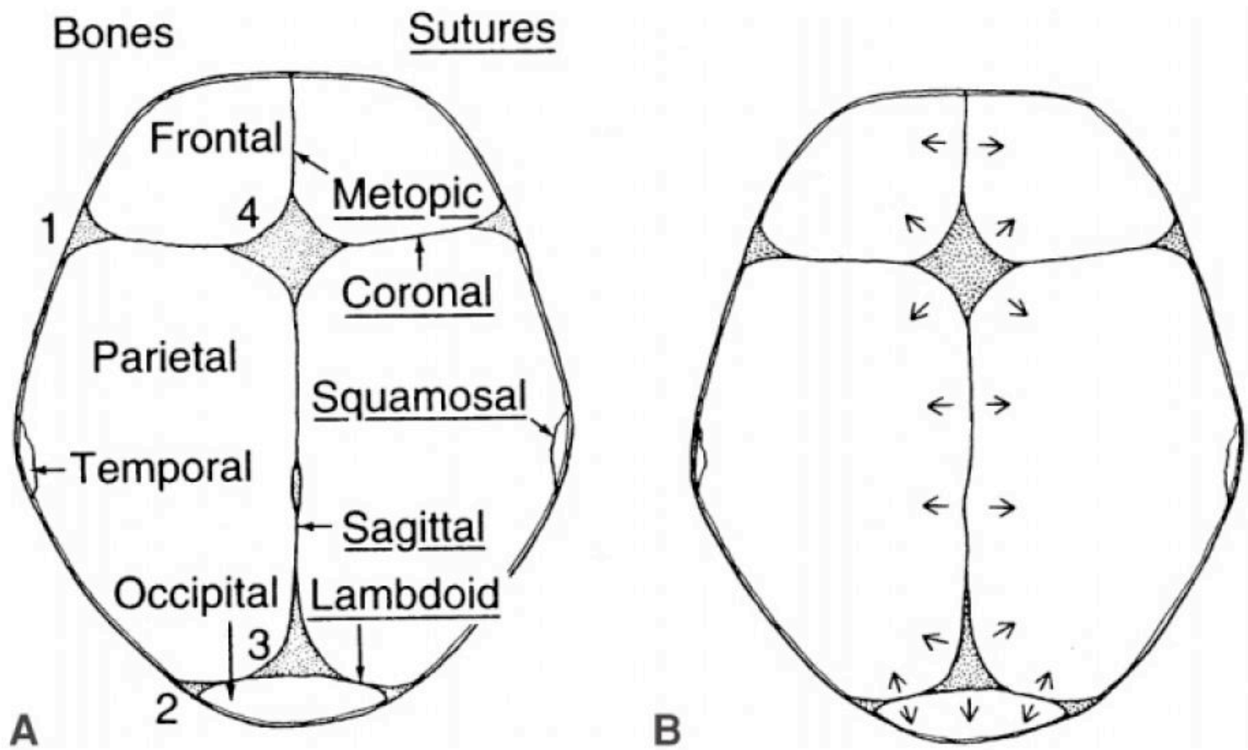


Figure 4. Limited Strip-Craniectomy in Sagittal Craniosynostosis. Two small incisions are placed medially over the anterior fontanelle and lambda. The endoscope and dissector are inserted anteriorly followed by subgaleal and epidural dissection. After paramedian osteotomies have been completed a mid-line strip of bone is removed. Barrel-stave osteotomies are then extended bilaterally and normocephaly is achieved with postoperative helmet-molding therapy. (From Jimenez, D. F., Barone, C. M. Endoscopic craniectomy for early surgical correction of sagittal craniosynostosis. *J Neurosurg* 88: 77-81, 1998.)

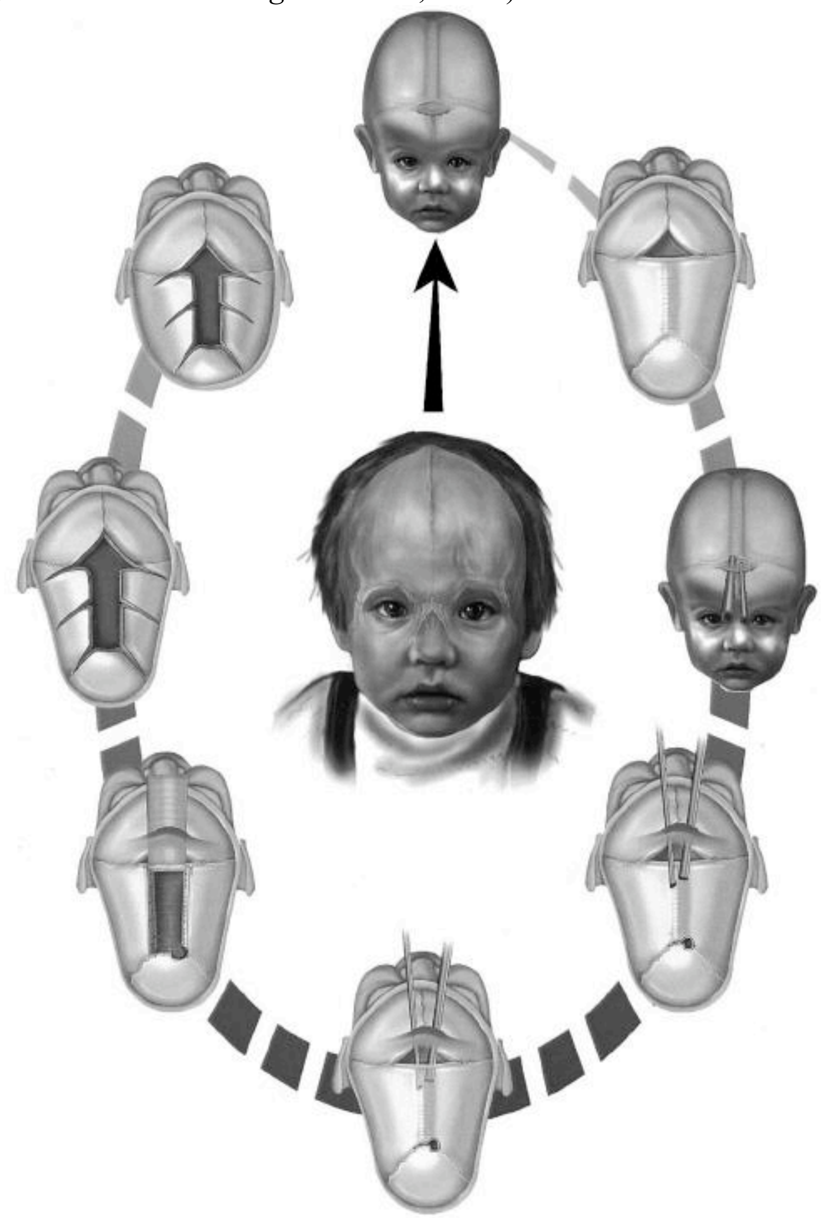
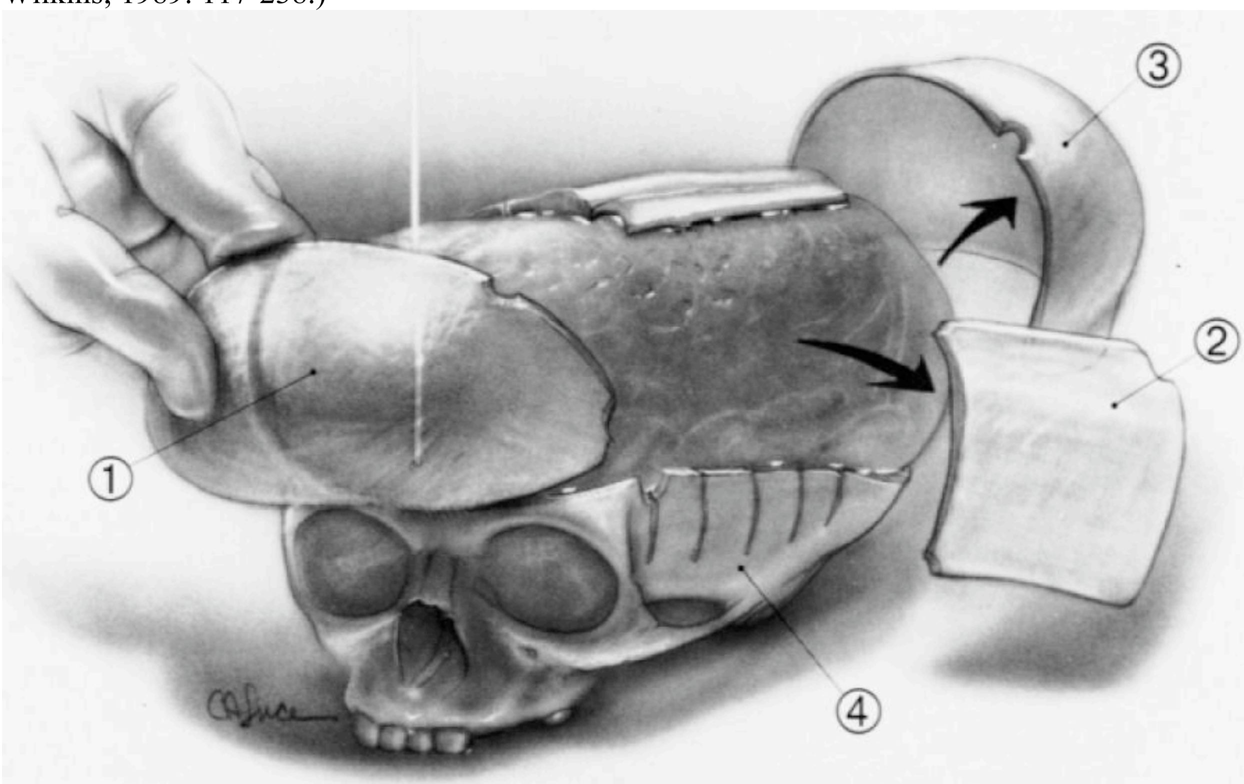


Figure 5. Whole-Vault Cranioplasty in Sagittal Craniosynostosis. Bifrontal (1), separate parietal (2), and biparietal occipital craniotomies (3), are performed in serial order. Laterally orientated barrel staves are placed in the temporal bone region (4). (From Persing, J. A., Edgerton, M.T., Jane, J.A. Surgical Treatment of Craniosynostosis. In: Persing, J. A., Edgerton, M.T., Jane, J.A., eds. Scientific Foundation and Surgical Treatment of Craniosynostosis. Baltimore: Williams & Wilkins; 1989: 117-238.)



Tables

Table 1. Comparison Between Strip Craniectomy and Whole Vault Cranioplasty on Cognitive[1] and Achievement[2] Measures

Measure	Strip (*n* = 4) Mean (SD)	Whole Vault (*n* = 9) Mean (SD)	p	*d*
Full Scale IQ	114.50 (15.67)	110.67 (18.53)	> .05	.22
Verbal IQ	112.50 (17.82)	111.00 (21.07)	> .05	.07
Performance IQ	113.00 (15.23)	108.67 (15.99)	> .05	.26
Reading Composite	115.25 (7.80)	102.67 (25.43)	> .05	.94
Word Reading	120.50 (6.76)	107.00 (26.43)	> .05	1.16
Reading Comp.	108.75 (10.56)	97.89 (25.61)	> .05	.60
Spelling	110.00 (22.64)	100.89 (30.24)	> .05	.22
Numerical Operations	111.00 (6.38)	94.67 (24.06)	> .05	1.49

1. Findings are based on ANCOVA's, with age in months at time of surgery controlled for in Cognitive findings and both age in months at time of surgery and FSIQ controlled for in Achievement Findings.

Table 2. Comparison[1] Between Strip Craniectomy and Whole Vault Cranioplasty on BASC Externalizing and Internalizing Problems

Measure	Strip (*n* = 2) Mean (SD)	Whole Vault (*n* = 9) Mean (SD)	p	*d*
Externalizing Problems	39.00 (0.00)	50.56 (10.62)	> .05	NA[2]
Internalizing Problems	40.00 (4.24)	53.78 (13.02)	> .05	-3.15

1. Findings are based on ANCOVA's, with both age in months at time of surgery and FSIQ controlled for in all analyses.
2. Cohen's *d* could not be calculated for externalizing because no variability in the Strip group.

Table 3. Relationship[1] between Age (Months) at Time of Surgery and Intellectual Functioning

Variable	Full Scale IQ	Verbal IQ	Performance IQ
Age at Surgery	-.48**	-.35	-.50**
FSIQ	---	.87***	.84***
VIQ	---	---	.46**

1. Associations are partial correlations controlling for type of surgery

* $p < .20$
** $p < .15$
*** $p < .05$

Table 4. Relationship[1] between Age (Months) at Time of Surgery and Achievement Functioning

Variable	Reading Composite	Word Reading	Reading Comprehension	Spelling	Numerical Operations
Age at Surgery	-.71***	-.54**	-.67***	-.34	-.47**
Reading Composite	---	.79***	.90***	.74***	.66**
Word Reading	---	---	.44*	.68***	.40
Reading Comp.	---	---	---	.59**	.68***
Spelling	---	---	---	---	.45*

1. Associations are partial correlations controlling for type of surgery and FSIQ

* $p < .20$

** $p < .15$

*** $p < .05$

Table 5. Relationship[1] between Age (Months) at Time of Surgery and BRIEF Ratings

Variable	Inhibit	Shift	Emotion Control	BRI	Initiate	Working Memory	Plan	Organize	Monitor	MI	GEC
Age at Surgery	.53*	.38	.48	.51*	.11	.07	.19	-.22	.23	.11	.39
Inhibit	---	.59*	.78***	.88***	.09	-.21	-.13	-.16	.53*	-.01	.54*
Shift	---	---	.91***	.90***	.44	.31	.20	.24	.53*	.36	.79***
Emotion Con.	---	---	---	.98***	.35	.10	.11	.27	.61**	.29	.79***
BRI	---	---	---	---	.31	.05	.06	.12	.61**	.22	.77***
Initiate	---	---	---	---	---	.88***	.75***	.73***	.76***	.91***	.79***
Working Mem.	---	---	---	---	---	---	.88***	.64**	.58*	.93***	.64**
Plan	---	---	---	---	---	---	---	.62**	.67**	.93***	.65*
Organize	---	---	---	---	---	---	---	---	.65**	.79***	.60**
Monitor	---	---	---	---	---	---	---	---	---	.81***	.91***
MI	---	---	---	---	---	---	---	---	---	---	.80***

1. Associations are partial correlations controlling for type of surgery and FSIQ

* $p < .20$

** $p < .15$

*** $p < .05$

Table 6. Relationship[1] between Age (Months) at Time of Surgery and BASC-2 Broad Internalizing and Externalizing Problems

Variable	Externalizing	Internalizing
Age at Surgery	.61**	.36
Externalizing	---	-.29

1. Associations are partial correlations controlling for type of surgery, FSIQ, and BRIEF Global Executive Control Index

* $p < .20$
** $p < .15$
*** $p < .05$

Table 7. Relationship[1] between Age (Months) at Time of Surgery and Specific BASC-2 Behavior Problem Scales

Variable	Hyperactivity	Aggression	Conduct Problems	Anxiety	Depression	Somatic Complaints	Atypicality	Withdrawn	Attention Problems
Age at Surgery	.13	.56*	.51	-.44	.36	.66**	.12	-.45	-.45
Hyperactivity	---	.02	.19	-.49	.48	.02	.71**	-.09	-.28
Aggression	---	---	.29	-.49	-.16	.12	.10	-.01	.30
Conduct Prob.	---	---	---	-.71**	.11	.18	-.26	.12	-.49
Anxiety	---	---	---	---	-.47	.01	.01	.11	.40
Depression	---	---	---	---	---	.11	.27	-.77***	-.62**
Somatic Comp.	---	---	---	---	---	---	-.12	-.01	-.61**
Atypicality	---	---	---	---	---	---	---	-.35	.23
Withdrawn	---	---	---	---	---	---	---	---	.20

1. Associations are partial correlations controlling for type of surgery, FSIQ, and BRIEF Global Executive Control Index

* $p < .20$

** $p < .15$

*** $p < .05$

Table 8. Cognitive and Achievement Outcome Comparisons[1] between those Participants Undergoing Surgery at Younger than Six Months of Age or Participants Undergoing Surgery at Older than Six Months of Age

Measure	6 Months (*n* = 7) Mean (SD)	Post 6 Months (*n* = 6) Mean (SD)	p	*d*
Full Scale IQ	119.87 (16.69)	102.50 (13.28)	< .05	1.06
Verbal IQ	117.71 (17.63)	104.17 (20.25)	< .20	0.67
Performance IQ	117.29 (13.92)	101.50 (12.85)	< .05	0.43
Reading Composite	119.00 (14.67)	92.00 (20.72)	> .05	0.70
Word Reading	125.57 (17.17)	95.50 (18.62)	> .05	0.46
Reading Comp.	111.57 (11.62)	89.17 (26.38)	> .05	0.73
Spelling	118.29 (24.76)	86.67 (20.87)	> .05	0.48
Numerical Operations	114.14 (12.27)	82.83 (16.87)	< .10	1.04

1. Findings are based on ANCOVA's, with type of surgery controlled for in Cognitive findings and type of surgery and FSIQ controlled for in Achievement Findings.

Table 9. BRIEF Outcome Comparisons[1] between those Participants Undergoing Surgery at Younger than Six Months of Age or Participants Undergoing Surgery at Older than Six Months of Age

Measure	6 Months (*n* = 4) Mean (SD)	Post 6 Months (*n* = 6) Mean (SD)	p	*d*
Inhibit	13.5 (2.51)	18.00 (6.81)	> .20	-0.80
Shift	9.75 (1.50)	14.17 (4.95)	> .20	-1.10
Emotional Control	11.75 (1.50)	17.50 (7.48)	> .20	-0.96
BRI	35.00 (2.83)	49.67 (18.06)	> .20	-1.02
Initiate	10.50 (2.08)	16.00 (2.53)	< .20	-2.32
Working Memory	12.25 (2.22)	21.67 (6.15)	> .20	-1.87
Plan	14.75 (1.25)	25.83 (7.14)	> .20	-1.95
Organize	11.75 (1.71)	14.67 (2.94)	> .20	-1.15
Monitor	11.75 (2.87)	17.33 (4.03)	> .20	-1.53
MI	61.00 (6.63)	95.50 (20.54)	> .20	-2.06
GEC	96.00 (8.41)	145.17 (31.01)	> .20	-1.96

1. Findings are based on ANCOVA's, with type of surgery controlled and FSIQ controlled for in all analyses.

Table 10. BASC-2 Outcome Comparisons[1] between those Participants Undergoing Surgery at Younger than Six Months of Age or Participants Undergoing Surgery at Older than Six Months of Age

Measure	6 Months (*n* = 4) Mean (SD)	Post 6 Months (*n* = 6) Mean (SD)	p	*d*
Externalizing T Score	41.40 (4.51)	54.33 (10.81)	> .20	-1.44
Internalizing T Score	43.50 (6.66)	58.83 (12.35)	> .20	-1.45
Hyperactivity	5.25 (4.11)	8.50 (5.01)	< .20	-0.69
Aggression	2.25 (2.22)	8.50 (5.71)	> .20	-1.33
Conduct Problems	1.25 (0.96)	6.17 (2.63)	< .20	-2.28
Anxiety	9.50 (4.80)	19.17 (6.49)	> .20	-1.64
Depression	2.25 (2.22)	7.50 (5.50)	> .20	-1.15
Somatic Complaints	3.50 (3.70)	7.67 (5.79)	> .20	-0.82
Atypicality	2.00 (1.83)	3.17 (2.32)	> .20	-0.54
Withdrawn	2.00 (2.00)	7.50 (5.28)	> .20	-1.26
Attention Problems	2.75 (3.20)	8.33 (3.93)	> .20	-1.52

1. Findings are based on ANCOVA's, with type of surgery controlled, FSIQ, and BRIEF GEC controlled for in all analyses.