

Assessing Long-Term Neurodevelopment among Children with Non-Syndromic Single Suture Craniosynostosis

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ABSTRACT

Background: Single suture craniosynostosis (SSC) is a disorder, affecting brain growth. Reviewing literature reveals controversialists of papers in this field.

Methods: This prospective study was conducted from 2014 to 2016. All the individuals, aged 2 to 16 years, whose medical records files were complete, with SSC from 1999 to 2013 were included. All patients had undergone cranial vault remodeling at Mofid Hospital, Tehran, Iran. Wechsler questionnaires, WPPSI-III and WISC-IV, were completed for each child based on his/her age.

Results: Seventy children were included, with the mean age of 6.7 (± 2.9) years. Forty-six (65.7%) children were boys while 24 (34.3%) were girls. Mean FSIQ for all of children was 95.5 (± 13.2). Mean verbal IQ, performance IQ, verbal comprehension, perceptual reasoning, processing speed, and working memory are 93.4 (± 14.1), 96.1 (± 13.3), 97.5 (± 13.9), 102.2 (± 12.5), 94.5 (± 9.8), and 97.5 (± 12.9), respectively. There was statistically significant difference between FSIQ of children with SSC and that of unaffected children (P -value <0.05). There was significant difference between verbal IQ of children with SSC and that of unaffected ones (P -value <0.007). There was significant difference between in processing speed between affected children and unaffected children (P -value <0.012).

Conclusion: Children, aged 2 to 6 years, with SSC had a significantly lower Verbal IQ, and children, aged 6 to 16 years, with SSC had a significantly lower processing speed than their healthy counterparts. Though FSIQ of children with SSC falls within normal range, it is a little lower than healthy peers.

Keywords: IQ; Single suture craniosynostosis; Neurodevelopment, WISC, WPPSI, Wechsler.

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INTRODUCTION

Craniosynostosis is a pathologic condition characterized by premature fusion of one or more cranial sutures, leading to abnormal shape of skull. Single suture craniosynostosis (SSC) is defined when only one suture—either sagittal, metopic, right or left coronal, or right or left lambdoid—is prematurely fused^{1,2}. Craniosynostosis is divided into syndromic or nonsyndromic. Syndromic craniosynostosis—accompanied by extracranial anomalies—is less frequent than nonsyndromic craniosynostosis. Moreover, in contrast to nonsyndromic

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craniosynostosis, syndromic craniosynostosis most often involves multiple sutures of cranial³⁻⁵.

A number of patients with craniosynostosis may develop, either short or long term, some complications. Increased intracranial pressure (IICP) which commonly affects patients with multiple suture craniosynostosis is a serious complication. However, IICP may lead to papilledema and optic nerve atrophy causing visual disruption. Although hydrocephalus is an uncommon complication in these patients, patients with syndromic craniosynostosis are more prone to develop it. Neurodevelopmental delay is a major concern in such patients. Several craniofacial syndromes are associated with both neurodevelopmental and intellectual delay, but, up to now, the definite etiology is not obvious^{4,6-10}.

Reviewing literature reveals that reports on different aspects of intellectual functioning in these patients are controversial. Many studies have demonstrated that such patients may suffer from lower development/function than normal counterparts, but some studies have showed that these patients have normal function as healthy ones¹¹⁻¹³.

Herein, we conducted a prospective study to assess the intellectual functioning among patients with craniosynostosis in several age groups in comparison to normal counterparts.

MATERIALS AND METHODS

This prospective study was conducted from 2014 to 2016. All the individuals, aged 2 to 16 years, whose medical records files were complete, with SSC from 1999 to 2013 were included. All patients had undergone cranial vault remodeling at Mofid Hospital, Tehran, Iran. Those patients agreed to participate in the study were interviewed by a psychologist. Three different questionnaires, based on their age group, were used.

This study was approved by ethical committee of Shahid Beheshti University of Medical Sciences (SBMU; Ethical Registration Number: SBMU.REC.1392.258).

Wechsler Preschool and Primary Scale of Intelligence (WPPSI-III)

The Wechsler Preschool and Primary Scale of Intelligence, consisting of 14 subtests, was designated by Wechsler. Subsets are one of three following types: core, supplemental, or optional. The core subtests are used to calculate the Verbal, Performance, and

Full Scale IQ. The supplemental subtests provide additional information about cognitive abilities or can be used as replacement for inappropriate subtests. The optional subtests are those which are providing additional information about cognitive functioning but cannot be used as replacements for core subtests¹⁴.

Wechsler Intelligence Scale for Children-Fourth Edition (WISC-IV)

The WISC-IV is a test assessing intellectual ability, only individuals aged 6 to 16 years. This test contains 15 subtests while each one is allocated to either the Verbal Comprehension (VC), Perceptual Reasoning (PR), Working Memory (WM), or Processing Speed (PS) subscales. Each subscale has a standardized mean and SD of 100 and 15, respectively. The Full Scale IQ (FSIQ) is consists of 10 core sub tests: 3 VC (Vocabulary, Similarities, and Comprehension), 3 PR (Block Design, Picture Concepts, and Matrix Reasoning), 2 WM (Digit Span and Letter-Number Sequencing), and 2 PS (Coding and Symbol Search). This scale, including the FSIQ, four indices, and subsets, has high reliability and validity¹⁵⁻¹⁷.

Data Analysis

All statistical analyses were performed using statistical package for social science (SPSS 16, Chicago, IL, USA). Variables are expressed as number (%) or mean (\pm SD). One sample *t*-test was used in calculating *P*-value for FSIQ, verbal IQ, performance IQ, verbal comprehension, perception reasoning, processing speed, and working memory. A *P* value less than 0.05 was considered statistically significant (*P*-value<.05).

RESULTS

A total of 130 patients were informed, but only 70 (53.8%) patients agreed to participate in the study. Forty-six (65.7%) children were boys while 24 (34.3%) were girls, with the mean age of 6.7 (\pm 2.9) years (Table 1). Mean FSIQ for all of children was 95.5 (\pm 13.2), ranging from 65 to 122. Thirty-one (44.2%) of patients had an IQ from 86 to 100 (Table 2). As Table 3 outlines, mean verbal IQ, performance IQ, verbal comprehension, perceptual reasoning, processing speed, and working memory are 93.4 (\pm 14.1), 96.1 (\pm 13.3), 97.5 (\pm 13.9), 102.2 (\pm 12.5), 94.5 (\pm 9.8), and 97.5 (\pm 12.9), respectively. There was statistically significant difference between FSIQ of children with

Table 1: Demographics of children based on each relevant questionnaire.

Variable	WPPSI-III	WISC-IV
	2-6 years	6 to 16 years
Number of Children (%)	42 (60%)	28 (40%)
Mean age (\pm SD)	3.7 (\pm 0.79)	9.6 (\pm 2.4)
Sex	Female	13 (46.4%)
	Male	31 (73.8%)
		15 (53.6%)

Table 2: Number of children in each FSIQ group and mean of IQ in each one.

Variable	Full Scale IQ				
	<70	71-85	86-100	101-115	>115
Number of Children (%)	2 (2.8%)	13 (18.5%)	31 (44.2%)	21 (30%)	3 (4.2%)
Mean FSIQ (\pm SD)	65.5 (0.7)	77.8 (3.15)	94.2 (\pm 5.1)	107.7 (\pm 3.9)	120 (\pm 3.4)

Table 3: Outcomes of Wechsler's questionnaires.

Variable	Number of children	Mean (\pm SD)	Median	Minimum	Maximum	P-value	
FSIQ	70 (100%)	95.5 (\pm 13.2)	95	65	122	0.006	
WPPSI-III	42 (60%)	Verbal IQ	93.4 (\pm 14.1)	95	66	122	0.007
		Performance IQ	96.3 (\pm 13.3)	96	67	119	0.09
WISC-IV	28 (40%)	Verbal comprehension	97.5 (\pm 13.9)	99	75	130	0.39
		Perception reasoning	102.2 (\pm 12.5)	104	77	127	0.38
		Processing Speed	94.5 (\pm 9.8)	98	78	117	0.012
		Working Memory	97.7 (\pm 12.9)	96	76	120	0.402

SSC and that of unaffected children (P -value: 0.006, t : -2.8, df : 69). There was not statistically significant difference between performance IQ of children with SSC and that of normal children (P -value: 0.09, t : -1.7, df : 41). There was significant difference between verbal IQ of children with SSC and that of unaffected ones (P -value: 0.007, t : -2.8, df : 41). There was no significant difference between working memory of affected children and that of normal ones (P -value: 0.402, t : -0.85, df : 27). There was significant difference between in processing speed between affected children and unaffected children (P -value: 0.012, t : -2.7, df : 27). There was no significant difference in perceptual reasoning between children with SSC and

normal children (P -value: 0.38, t : 0.88, df : 27). There was no significant difference in verbal comprehension between affected children and unaffected children (P -value: 0.39, t : -0.86, df : 27).

DISCUSSION

In contrast to many craniofacial disorders, craniosynostosis is a common congenital disorder of craniofacial region, with an incidence of 1 in 2000 to 2500 births^{5, 18, 19}. Majority of cases, approximately 85%, occur without any genetic background, most probably due to a spontaneous mutation^{20, 21}. The diagnosis is often made within the first months

of life, and the mainstay of treatment is surgical approach in which the fused suture/sutures are released to reshape the calvarium, allowing brain growth and normal neurodevelopment. Although the precise time of surgery is debated, craniotomy is performed for all patients in the first year of life²². However, based on some studies, these children may show some neurodevelopment delays. In here, FSIQ of children with SSC was around 95, and there was statically significant difference between FSIQ of patients with craniosynostosis and unaffected children (P -value<0.05). FSIQ of children with SSC is significantly lower than normal counterparts, but their FSIQ falls within normal range. Children, aged 2 to 6 years, with SSC had significantly lower verbal IQ, some 93, than unaffected peers (P -value<0.05). Moreover, processing speed, approximately 94, of children, aged 6 to 16 years, with SSC was significantly lower than normal ones (P -value<0.05). Yet, in performance IQ, verbal comprehension, and working memory the difference was not statistically significant (P -value>0.05). Although children with SSC had a little higher perception reasoning, the difference was not statistically significant.

Chieffo et al evaluated 65 children who had undergone surgery for sagittal or unicoronal craniosynostosis concluded that such children will manifest lower than average 6 cognitive level²³. Mendonca et al demonstrated that 30% of patients with metopic synostosis had speech and language delays, and delays were not associated with severity of disorder²⁴. Shipster et al evaluated 76 children with isolated sagittal synostosis and concluded that such children are at increased risk developing speech and language delays²⁵. Magge et al retrospectively reviewed 16 patients with sagittal synostosis and found out that their IQ was in normal range but learning disabilities were significantly prominent within them²⁶. Boltshauser et al prospectively assessed 30 children with isolated sagittal synostosis, and concluded that their school performance, behavior and quality of life were reassuring²⁷. Kelleher et al assessed 63 children with trigonocephaly, concluded that they had high frequency of developmental, educational, and behavioral problems²⁸. Wallace ER et al evaluated 179 children with SSC and concluded that such children have deficits in manual dexterity but their visual processing are similar to that of normal ones²². The cognitive, behavioral, and psychological outcomes of children with metopic synostosis were worse than their normal counterparts²⁹. There was no significant

difference between healthy children and children with SSC in language, memory, and learning tasks in early elementary school ages³⁰. FSIQ of children in a study was around 96 which was similar to normal children, and, in addition, VIQ was greater than PIQ³¹. Collett et al in a prospective study evaluated 179 school-aged children, but their study outcomes were variable to definitely conclude³². In another study it is indicated that there is no definitive relation between size of brain and intelligence, so this is the reason why FSIQ of children is not far lower than healthy counterparts²¹.

CONCLUSION

Children, aged 2 to 6 years, with SSC had a significantly lower Verbal IQ, and children, aged 6 to 16 years, with SSC had a significantly lower processing speed than their healthy counterparts. However, children with SSC had a higher perception reasoning than healthy peers. Although FSIQ of children with SSC falls within normal range, it is a little lower than healthy peers.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interests.

REFERENCES

1. Knight SJ, Anderson VA, Spencer-Smith MM, Da Costa AC. Neurodevelopmental outcomes in infants and children with single-suture craniosynostosis: a systematic review. *Dev Neuropsychol* 2014;**39**(3):159-186.
2. Aldridge K, Birgfeld C, Austin JR, Regina YM, et al. Structural brain differences in school-age children with and without single-suture craniosynostosis. *J Neurosurg Pediatr* 2017;**19**(4):479-489.
3. Cornelissen M, Ottelander B, Rizopoulos D, Hulst RVD, Molen AMVD, Horst CVD, et al. Increase of prevalence of craniosynostosis. *J Craniomaxillofac Surg*. 2016;**44**(9):1273-1279.
4. Tahiri Y, Bartlett SP, Gilardino MS. Evidence-Based Medicine: Nonsyndromic Craniosynostosis. *Plast Reconstr Surg* 2017;**140**(1):177e-191e.
5. Timberlake AT, Persing JA. Genetics of Nonsyndromic

- Craniosynostosis. *Plast Reconstr Surg* 2018; **141**(6):1508-1516.
6. Governale LS. Craniosynostosis. *Pediatr Neurol* 2015; **53**(5):394-401.
 7. Spruijt B, Joosten KF, Driessen C, Rizopoulos D, Naus NC, Schroeff MP, et al. Algorithm for the Management of Intracranial Hypertension in Children with Syndromic Craniosynostosis. *Plast Reconstr Surg* 2015; **136**(2):331-340.
 8. Speltz ML, Collett BR, Wallace ER, Starr JR, Cradock MM, Buono L, et al. Intellectual and academic functioning of school-age children with single-suture craniosynostosis. *Pediatrics* 2015; **135**(3):e615-623.
 9. Speltz ML, Kapp-Simon KA, Cunningham M, Marsh J, Dawson G. Single-suture craniosynostosis: a review of neurobehavioral research and theory. *J Pediatr Psychol* 2004; **29**(8):651-668.
 10. Tamburrini G, Caldarelli M, Massimi L, Santini P, Di Rocco C. Intracranial pressure monitoring in children with single suture and complex craniosynostosis: a review. *Childs Nerv Syst* 2005; **21**(10):913-921.
 11. Costa ACD, Walters I, Savarirayan R, Anderson VA, Wrennall JA, Meara JG. Intellectual outcomes in children and adolescents with syndromic and nonsyndromic craniosynostosis. *Plast Reconstr Surg* 2006; **118**(1):175-181.
 12. Becker DB, Petersen JD, Kane AA, Cradock MM, Pilgram TK, Marsh JL. Speech, cognitive, and behavioral outcomes in nonsyndromic craniosynostosis. *Plast Reconstr Surg* 2005; **116**(2):400-407.
 13. Chieffo D, Tamburrini G, Massimi L, Di Giovanni S, Giansanti C, Caldarelli M, et al. Long-term neuropsychological development in single-suture craniosynostosis treated early. *J Neurosurg Pediatr* 2010; **5**(3):232-237.
 14. Wechsler D. The Wechsler Preschool and Primary Scale of Intelligence, 3rd Edition (WPPSI-III). 2002. San Antonio, TX: The Psychological Corporation.
 15. Wechsler D. Wechsler Intelligence Scale for Children, 4th Edition (WISC-IV). 2003. San Antonio, TX: The Psychological Corporation.
 16. Gomez R, Vance A, Watson SD. Structure of the Wechsler Intelligence Scale for Children - Fourth Edition in a Group of Children with ADHD. *Front Psychol*. 2016; **7**:737.
 17. Williams PE, Weiss LG, Rolfhus EL. Psychometric Properties (WISC-IV Technical Report No.2). 2003. San Antonio, TX: Psychological Corp 9.
 18. Kalantar-Hormozi A, Abbaszadeh-Kasbi A, Goravanchi F, Davai NR. Prevalence of Rare Craniofacial Clefts. *J Craniofac Surg* 2017; **28**(5): e467-e470.
 19. Kalantar-Hormozi H, Abbaszadeh-Kasbi A, Sharifi G, Davai NR, Kalantar-Hormozi A. Incidence of Familial Craniosynostosis Among Patients with Nonsyndromic Craniosynostosis. *J Craniofac Surg* 2019. **30**(6):e514-e517.
 20. Lajeunie E, Crimmins DW, Arnaud E, Renier D. Genetic considerations in nonsyndromic midline craniosynostoses: a study of twins and their families. *J Neurosurg* 2005; **103**(4):353-356.
 21. Cohen MM. Epidemiology of Craniosynostosis. In: Cohen MM Jr, MacLean RE, editors. *Craniosynostosis: Diagnosis, Evaluation and Management*. 2nd ed. New York: Oxford University Press; 2000. Pp:112-118.
 22. Wallace ER, Collett BR, Kapp-Simon K, Starr JR, Birgfeld C, Speltz ML. Visuomotor Function in School-Age Children with Single-Suture Craniosynostosis. *J Dev Behav Pediatr* 2016; **37**(6):483-490.
 23. Chieffo D, Ricci D, Baranello G, Martinelli D, Veredice C, Lettori D, et al. Early development in Dravet syndrome; visual function impairment precedes cognitive decline. *Epilepsy Res* 2011; **93**(1):73-79.
 24. Mendonca DA, White N, West E, Dover S, Solanki G, Nishikawa H. Is there a relationship between the severity of metopic synostosis and speech and language impairments? *J Craniofac Surg* 2009; **20**(1):85-88.
 25. Shipster C, Hearst D, Somerville A, Stackhouse J, Hayward R, Wade A. Speech, language, and cognitive development in children with isolated sagittal synostosis. *Dev Med Child Neurol* 2003; **45**(1):34-43.
 26. Magge SN, Westerveld M, Pruzinsky T, Persing JA. Long-term neuropsychological effects of sagittal craniosynostosis on child development. *J Craniofac Surg* 2002; **13**(1):99-104.
 27. Boltshauser E, Ludwig S, Dietrich F, Landolt MA. Sagittal craniosynostosis: cognitive development, behaviour, and quality of life in unoperated children. *Neuropediatrics*. 2003; **34**(6):293-300.
 28. Kelleher MO, Murray DJ, McGillivray A, Kamel MH, Allcutt D, Earley MJ. Behavioral, developmental, and educational problems in children with nonsyndromic trigonocephaly. *J Neurosurg* 2006; **105**(5):382-384.
 29. Osborn AJ, Roberts RM, Mathias JL, Anderson PJ, Flapper WJ. Cognitive, behavioral and psychological functioning in children with metopic synostosis: a meta-analysis examining the impact of surgical status. *Child Neuropsychol* 2019; **25**(2):263-277.
 30. Kapp-Simon KA, Wallace E, Collett BR, Cradock MM, Crerand CE, Speltz ML. Language, learning, and memory in children with and without single-suture craniosynostosis. *J Neurosurg Pediatr* 2016; **17**(5):578-588.
 31. Bellew M, Chumas P. Long-term developmental follow-up in children with nonsyndromic craniosynostosis. *J Neurosurg Pediatr* 2015; **16**(4):445-451.
 32. Collett BR, Kapp-Simon KA, Wallace E, Cradock MM, Buono L, Speltz ML. Attention and executive function in children with and without single-suture craniosynostosis. *Child Neuropsychol* 2017; **23**(1):83-98.