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ORIGINAL PAPER

Cognitive and functional outcome in spina bifida–Chiari II malformation

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Abstract
Purpose The long-term outcome in spina bifida–Chiari II–hydrocephalus complex is poorly understood. Traditional neurosurgical outcome measures are crude. Neuropsychological testing is increasingly important in outcome assessment. We investigated the health, disability, lifestyle and cognitive function in adults who had myelomeningocoele closure at birth.
Methods Adult patients under routine follow-up were assessed in a joint neurosurgery/neuropsychology clinic. Patients completed lifestyle questionnaires, the hydrocephalus outcome questionnaire (HOQ) and underwent cognitive testing. Clinical variables including number of shunt revisions, shunt infection and surgical decompression of foramen magnum, which may influence outcome, were investigated.
Results Twenty-one adults with a median age of 35 years were investigated. All had treated hydrocephalus, and eight had foramen magnum decompression for headache or progressive brainstem symptoms with stabilisation of symptoms in seven and improvement in one. Only eight patients were living independently, five were in paid employment and five work voluntarily. HOQ scores for cognitive function were lower (0.56 ± 0.20; mean ± standard deviation (SD)) than those for physical (0.64 ± 0.15) and social–emotional (0.65 ± 0.17) health. Cognitive function varied across the cohort with attention most severely affected (73.9 ± 17.0; mean ± SD). Repeated episodes of shunt malfunction or foramen magnum decompression were not associated with a worse cognitive function.
Conclusions Despite intervention in childhood and adequate cerebrospinal fluid diversion the prognosis for independent living into adulthood remains poor. All patients have elements of cognitive impairment. Structural brain abnormalities may be more important determinants of cognitive outcome than shunt malfunction.

Keywords Spina bifida · Chiari · Hydrocephalus · Cognitive function · Outcome

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Introduction

Spina bifida is the commonest central nervous system birth defect encountered in neurosurgery and comprises a heterogeneous range of abnormalities affecting the spinal cord, cerebrum and brainstem. Whilst the incidence of open spina bifida has decreased, probably due to improved maternal diet, pre-conception folic acid supplementation and improved antenatal screening [1–3], myelomeningocoele remains the commonest form. In myelomeningocoele, the dorsal midline mass contains meninges and neural

tissue, and is almost always associated with Chiari II malformation and hydrocephalus. The Chiari II malformation comprises congenital abnormalities of the hindbrain structures with bowing and elongation of the medulla oblongata and pons, and descent of the cerebellar vermis below the craniocervical junction (Fig. 1).

The spina bifida—Chiari II complex is associated with a reduced life expectancy [4–6] and during the first few years of life the major causes of death are related to brainstem dysfunction, and frequently include apnoea attacks, cardiac arrhythmias, vocal cord paralysis and opisthotonos, however, the symptoms of brainstem dysfunction and hindbrain abnormality may occur at any time in the life of a person with spina bifida—Chiari II [7, 8]. Long-term outcome data in spina bifida patients is mainly derived from a longitudinal cohort of 117 babies with open spina bifida who have been followed from birth. In this study, lifestyle was assessed by postal questionnaire and telephone interview; the 35-year follow-up revealed 46% survival with 40% living independently in the community, 40% driving a car, 20% in competitive employment and 20% ambulant to 50 m [4–6].

As well as improved survival for babies born with open spina bifida, cerebrospinal fluid (CSF) diversion means that patients are more likely to have an intelligence quotient (IQ) within the normal range, compared to historical series [9, 10]. Cognitive impairment in spina bifida–Chiari II complex has been attributed to the severity of associated hydrocephalus and shunt-related complications [11, 12]. Since the Chiari II malformation and hydrocephalus occur together, hydrocephalus alone may not explain the impaired cognitive function in these patients. Indeed studies of cognitive function in patients with isolated cerebellar damage due to other causes have demonstrated significant deficits in intellectual function [13], and the cerebellum has been implicated in a variety of cognitive functions [14]. More recently, two studies of paediatric patients have addressed cognitive function in Chiari II malformation and demonstrated that specific intellectual deficiencies may be attributed to structural brain defects [15, 16]. However, the cognitive function in adult survivors is only now starting to be addressed with assessments of memory, numeracy and language skills [17–20]. Therefore, the study aims were to investigate the long-term cognitive and functional outcome in adults with treated spina bifida–Chiari II–hydrocephalus malformation.

Material and methods

Study population

Adult patients with known spina bifida–Chiari II malformation undergoing routine clinical follow-up under the care of the senior author (CLM) were identified from hospital records. As part of this routine follow-up process, 21 patients consented to be assessed in a joint neurosurgery and neuropsychology clinic. Cases were characterised by the following criteria: (1) myelomeningocele closed at birth; (2) age over 18 years; (3) able to read and write.

Outcome measures

Clinicopathological data were collected and included details on hydrocephalus treatment, brainstem and lower cranial nerve palsies, foramen magnum decompression and current clinical problems. Patient's current clinical status was classified as follows: (1) stable; (2) requiring surgery (e.g. for shunt malfunction or brainstem symptoms); (3) under investigation (i.e. for new symptoms); (4) progressive (i.e. symptoms not amenable or suitable for further surgery); and (5) chronic (i.e. symptoms requiring additional medical input e.g. chronic pain). Lifestyle questionnaires were administered to determine levels of independent living, self-caring, mobility and employment [5, 6]. The

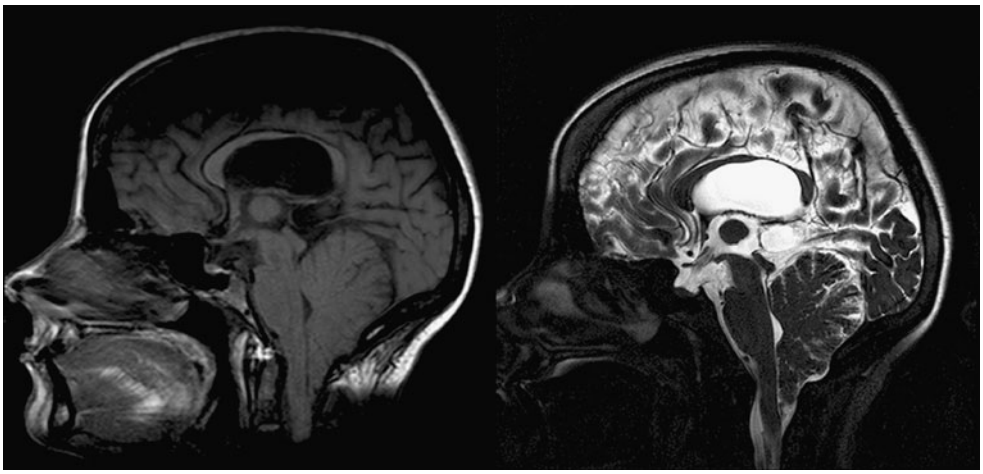

Fig. 1 Sagittal T1- and T2-weighted MRI showing typical features of Chiari II malformation associated with myelomeningocoele

hydrocephalus outcome questionnaire (HOQ), developed by Kulkarni et al. [21, 22], was modified with permission and administered to generate objective physical, social–emotional, cognitive and overall health scores. Cognitive function was assessed using the Repeatable Battery for the Assessment of Neuropsychological Status (RBANS). This measure assesses immediate and delayed memory, visuospatial construction, language and attention and produces an index score for each cognitive domain and a total score derived from a combination of all five domains.

Data analysis and statistics

The following outcomes were converted to binary data for statistical analysis: (a) stable clinical status (yes = stable; no = requiring surgery, under investigation, progressive, chronic); and (b) RBANS parameters for immediate and delayed memory, visuospatial construction, language, attention and the overall score were classified as equal to or less than one standard deviation below the normal cohort mean. The following clinical variables which may influence outcome were investigated: number of shunt revisions (>5 versus <5), previous shunt infection and surgical decompression of foramen magnum. Due to the small sample size non-parametric tests were used. Fisher's exact test was used to identify factors that could significantly affect the following outcomes: stable clinical status, independent living, employment (paid or voluntary), driving a car and RBANS parameters. Mann–Whitney *U* test was used to determine whether the explanatory variables influenced HOQ score. Probability values less than 0.05 were considered significant. Data were analysed using SPSS version 16 (SPSS, UK).

Results

Clinical features, hydrocephalus and Chiari management

Twenty-one adults who had myelomeningocoele closure at birth were assessed (Table 1). There were 13 males and eight females, and the median age was 35 years (range, 19–45). Seventeen were shunted before 6 months, one by 18 months and one at 20 years. Two patients had primary endoscopic third ventriculostomy (ETV) as adults presenting with decompensated hydrocephalus. Fifteen had less than five shunt revisions (considered the low revision group), but one patient had over 100 shunt-related procedures. Patients presenting with shunt malfunction who have suitable ventricular anatomy are offered ETV in line with local practice and based on good outcome for secondary ETV in adults [23]. At the time of assessment four patients therefore had a functioning third ventroculostomy, and 17 patients a functioning ventriculoperitoneal shunt. Eight patients had undergone foramen magnum decompression for progressive brainstem symptoms (n = 2), symptomatic headache (n = 4) or symptomatic syrinx (n = 2). Seven patients had stabilisation of symptoms and one patient with headache reported significant improvement. Patient clinical status was classified as stable (n = 14), progressive (n = 2), chronic (n = 2) and under investigation (n = 3).

Disability and lifestyle

In terms of lifestyle, only eight are living independently in the community managing their own lives including transport, continence care, pressure sores and other medical needs. Three women had children of their own, none of whom had visible spina bifida. Seven are ambulant indoors either independently or with walking aids. Ten required help with showering/bathing as well as continence care. Eleven drove cars and an additional two had a licence but had given up driving. Sixteen had been hospitalised in the last 5 years; 10 for shunt-related symptoms requiring surgery. Six required hospital care for urinary tract infection, pneumonia, renal colic and deep venous thrombosis. Five are in paid employment, three of them wheelchairs dependent, and a further five work voluntarily.

Hydrocephalus outcome

Nineteen patients completed the HOQ form (patients 6 and 13 declined). The scores for each parameter for individual patients are shown in Table 2. The scores for the cohort were physical 0.64 ± 0.15 (mean ± standard deviation SD); social-emotional 0.65 ± 0.17; cognitive 0.56 ± 0.20; and overall 0.62 ± 0.13. The cohort overall scored well in all domains except cognitive function.

Cognitive function

Thirteen patients consented to undergo neuropsychological testing to determine cognitive function (patients 6, 13, 16–21 declined). The score for immediate memory was 84.9 ± 14.9 (mean ± standard deviation), for delayed memory 83.1 ± 16.8, for visuospatial construction 88.2 ± 17.4, for language 86.7 ± 11.6 and for attention 73.9 ± 17.0 (Fig. 2).

Outcome analysis

There was no significant relationship between shunt history (mechanical obstruction or infection) or foramen magnum decompression and outcome for lifestyle (Table 3), hydrocephalus outcome questionnaire scores (Table 4) and cognitive function (Table 5).

Table 1 Clinicopathological characteristics of study population including hydrocephalus and Chiari II status

ID	Sex	Age at study	Hydrocephalus status			Chiari II status				Overall clinical status
			Number of shunt revisions	Previous shunt infection	Current hydrocephalus status	Foramen magnum decompression	Age at Chiari surgery	Indication	Outcome from Chiari surgery	
1	Female	40	<5	No	ETV	Yes	34	Chiari headache	Stable	Progressive
2	Male	27	5 to 10	Yes	Shunt	No				Stable
3	Male	32	<5	No	Shunt	No				Stable
4	Male	35	<5	Yes	Shunt	Yes	32	Brainstem symptoms	Stable	Progressive
5	Female	35	5 to 10	No	Shunt	Yes	30	Chiari headache	Stable	Chronic
6	Female	25	>50	Yes	Shunt	Yes	9	Chiari headache	Improved	Stable
7	Male	45	<5	No	Shunt	No				Stable
8	Male	30	11 to 15	No	Shunt	No				Under investigation
9	Female	42	<5	No	Shunt	Yes	42	Syrinx progression	Stable	Under investigation
10	Male	20	<5	No	Shunt	Yes	12	Syrinx progression	Stable	Stable
11	Female	39	<5	No	Shunt	No				Under investigation
12	Female	42	<5	No	ETV	No				Stable
13	Male	22	<5	No	Shunt	No				Stable
14	Female	32	21 to 30	Yes	Shunt	Yes	17	Chiari headache	Stable	Chronic
15	Male	44	<5	No	Shunt	Yes	37	Brainstem symptoms	Stable	Stable
16	Male	40	<5	Yes	Shunt	No				Stable
17	Male	36	n/a	n/a	ETV	No				Stable
18	Male	37	<5	No	Shunt	No				Stable
19	Male	31	n/a	n/a	ETV	No				Stable
20	Male	29	<5	No	Shunt	No				Stable
21	Female	25	<5	No	Shunt	No				Stable

n/a, not applicable

Discussion

This study was undertaken to characterise the long-term functional and cognitive outcome in a cohort of patients with spina bifida–Chiari II–hydrocephalus complex. Utilising a battery of outcome measures and formal neuropsychological testing, this study objectively assessed cognitive function in adults who had myelomeningocoele closure at birth. Overall, cognitive function was poor especially in the domain of attention. There was no relationship between shunt malfunction and cognitive outcome in our cohort.

This is a selected cohort of patients under long-term follow-up at the study institution. As such, more severe cases of spina bifida–Chiari II–hydrocephalus complex have either died or are too unwell to attend for follow-up, which represents an inherent population bias in our study. Whilst the overall survival rate for myelomeningocoele patients is not known, most patients in our study commented that they had friends with spina bifida who had died recently, and often contemplated their own death. In a recent American study of younger spina bifida patients with a mean age of 21.7 years, 76% were still alive, compared to only 46% in a UK cohort with a mean age of 35 years [6]. Whether patients are managed conservatively or actively at birth, quality of life is an important factor in those who survive. Despite our study being a selected cohort of survivors, the prospect for integration into society remained poor. Thirty-eight percent were living independently, 33% were ambulant unassisted or with aids, 52% drove a car and only 24% were in paid employment (a further 24% did voluntary work). Our figures are comparable to other studies in the literature [4–6, 24], although it is recognised

Table 2 Hydrocephalus outcome questionnaire data

			Modified HOQ score			
Study ID	Sex	Age at study	Physical	Social–emotional	Cognitive	Overall
1	Female	40	0.53	0.45	0.79	0.55
2	Male	27	0.88	0.60	0.63	0.69
3	Male	32	0.82	0.90	0.98	0.89
4	Male	35	0.28	0.52	0.46	0.44
5	Female	35	0.58	0.46	0.23	0.44
6	Female	25	n/a	n/a	n/a	n/a
7	Male	45	0.42	0.71	0.52	0.58
8	Male	30	0.72	0.57	0.73	0.65
9	Female	42	0.67	0.60	0.67	0.64
10	Male	20	0.77	0.85	0.50	0.75
11	Female	39	0.45	0.45	0.46	0.45
12	Female	42	0.77	0.80	0.58	0.74
13	Male	22	n/a	n/a	n/a	n/a
14	Female	32	0.62	0.55	0.58	0.58
15	Male	44	0.55	0.50	0.38	0.49
16	Male	40	0.73	0.88	0.92	0.84
17	Male	36	0.65	0.79	0.58	0.70
18	Male	37	0.70	0.61	0.56	0.63
19	Male	31	0.55	0.44	0.35	0.45
20	Male	29	0.77	0.80	0.46	0.71
21	Female	25	0.62	0.88	0.25	0.65

Patients 6 and 13 declined to complete the questionnaire

1, good health; *0*, poor health; *n/a*, not applicable

that the quality of life deteriorates with age and there is decreased life expectancy [25].

Chiari II malformation is invariably associated with open spina bifida and the features are readily demonstrated on MRI. Between 25 and 33% of patients are symptomatic from the Chiari II malformation and in the infant this manifests as brainstem dysfunction associated with sleep apnoea and lower cranial nerve palsies and a 15% mortality rate in those affected [8]. Whether early decompression improves symptoms remains controversial as surgery related morbidity and mortality is also high, up to 15–20%, in infants [7, 26]. Older children and young adults with Chiari II malformation may complain of symptoms related to foramen magnum impaction such as headache, neck pain and upper limb sensory disturbance. Brainstem dysfunction and lower cranial nerve palsies may also be present. Surgical treatment may be indicated in symptomatic patients, once adequate CSF diversion by either shunting or endoscopic third ventriculostomy has been established [23]. In our study, 38% of patients underwent foramen magnum decompression for progression at between nine and 37 years of age, and symptoms either improved or stabilised. There was no patient in our cohort who had undergone decompression as infants, which suggests that those patients may have been more severely affected and did not survive into adulthood. Nevertheless, our decompression rate is much higher than other series in the literature [24]; however there was no adverse effect on lifestyle, HOQ scores or cognitive function compared to those who had not undergone foramen magnum decompression. There is a subgroup of patients with progressive cranial nerve and brainstem failure for whom deterioration cannot be halted by surgical decompression.

Historically, approximately 85–95% of patients with myelomeningocele have some degree of hydrocephalus requiring treatment [24], and almost half of meningocele patients shunted at birth require shunt revision in the first year of life, mostly due to mechanical failure [27]. The incidence of symptomatic hydrocephalus requiring shunting in more recent cohorts is ~50% [28]; however these patients require close follow-up to ensure cognitive function does not decline at the expense avoiding a shunt [29]. Endoscopic third ventriculosomy has also been used in some patients although the failure rate is high when performed as a primary procedure [30, 31]. In patients presenting with shunt malfunction, secondary ETV has a better success rate and is therefore best reserved for later management [23, 30]. Two patients in our cohort presented with late decompensated hydrocephalus in adulthood and were treated successfully with primary ETV.

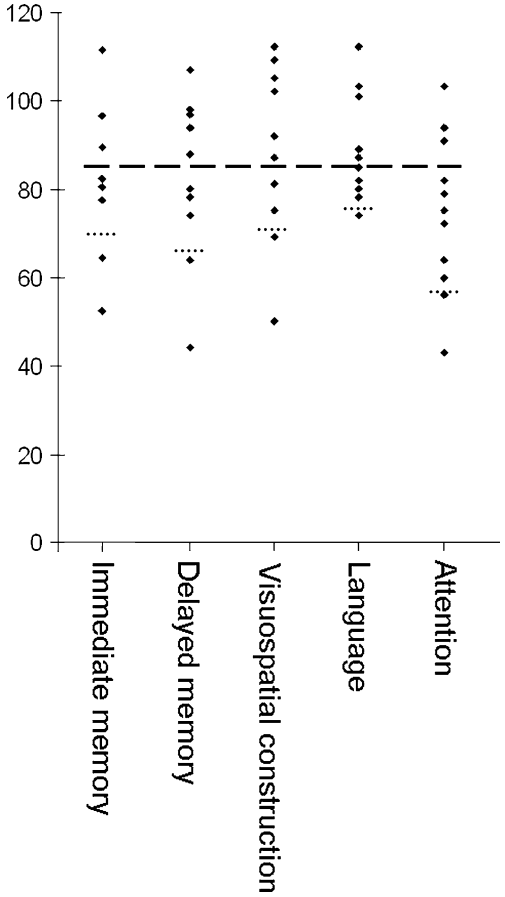

Fig. 2 Cognitive function of the study population in the five cognitive domains assessed by RBANS. The individual patient scores are represented and the *dotted line* is the study cohort mean minus 1 SD. The *dash line* represents the normative mean minus 1 SD

Whilst shunt revision in spina bifida patients has been associated with poorer lifestyle outcome [32], we found no relationship between the number of shunt operations, shunt infection and lifestyle and health scores derived from the hydrocephalus outcome questionnaire. Using the HOQ as a condition-specific measure that quantifies health and quality of life of patients with hydrocephalus, studies in paediatric cohorts identified both shunt infection and number of revisions as factors associated with lower HOQ scores, in particular cognitive health [22]. In our cohort, HOQ scores for overall health, physical health and cognitive health as similar, however the paediatric cohort scored more highly in the social-emotional health domain [22]. This may reflect a more optimistic outlook of parents and children compared to adults who may have accepted and recognised the difficulty integrating into normal society. As expected, the cognitive health scores in both adults and children are low.

Historically, it has been reported that patients who have associated hydrocephalus and episodes of shunt malfunction (blockage and infection) have lower intelligence than those who only have myelomeningocele [33]. However, two recent studies have demonstrated significant cognitive impairment in myelomeningocele patients in the paediatric population that have been attributed to the structural defects associated with the Chiari II malformation, rather than repeated episodes of hydrocephalus [15, 16]. Fibre tract anomalies in the limbic system were correlated with memory deficits [15]. Whilst we did not investigate structural abnormalities in relation to cognitive function in this study, we did demonstrate that episodes of shunt malfunction were not associated with worse cognitive outcome, which suggests that other structural factors may be important in determining levels of cognitive function on myelomeningocoele patients.

Educational mainstreaming, special counselling, improved understanding of the patient's potential and increased public awareness of spina bifida contribute to a reduction in stress through psycho-social problems originating within themselves, their families and society. In the large American cohort, 86% were attending or graduated from high school [24], and whilst 43% of our cohort were working, only 19% were in competitive employment. Previous

Table 3 Relationship between explanatory variables and lifestyle outcome

		Stable clinical status		*P* value[a]	Living independently		*P* value[a]	Drives a car		*P* value[a]	Employed		*P* value[a]
		No	Yes		No	Yes		No	Yes		No	Yes	
>5 Shunt revisions	No	4	10	0.305	9	5	1.0	7	7	1.0	9	5	0.603
	Yes	3	2		4	1		3	2		2	3	
Past shunt infection	No	5	9	1.0	10	4	1.0	8	6	0.628	9	5	0.603
	Yes	2	3		3	2		2	3		2	3	
Foramen magnum decompression	No	2	11	0.056	8	5	1.0	6	7	1.0	5	8	0.183
	Yes	5	3		5	3		4	4		6	2	

[a] Fisher's Exact test

Table 4 Relationship between explanatory variables and HOQ scores (values are mean ± SD)

HOQ domain	Shunt revision >5		*P* value[a]	Shunt infection		*P* value[a]	Foramen magnum decompression		*P* value[a]
	No (n = 13)	Yes (n = 4)		No (n = 13)	Yes (n = 4)		No (n = 10)	Yes (n = 7)	
Physical	0.62 ± 0.16	0.70 ± 0.13	0.55	0.64 ± 0.13	0.63 ± 0.26	0.87	0.69 ± 0.15	0.57 ± 0.15	0.17
Social-emotional	0.69 ± 0.17	0.54 ± 0.06	0.20	0.66 ± 0.17	0.64 ± 0.17	0.96	0.72 ± 0.16	0.56 ± 0.14	0.10
Cognitive	0.58 ± 0.21	0.54 ± 0.22	0.87	0.55 ± 0.21	0.65 ± 0.20	0.41	0.61 ± 0.22	0.52 ± 0.19	0.59
Overall	0.64 ± 0.14	0.59 ± 0.11	0.55	0.63 ± 0.13	0.64 ± 0.17	1.0	0.68 ± 0.13	0.56 ± 0.11	0.07

[a] Mann–Whitney U test

studies have demonstrated that reading and writing function remain deficient into adulthood [17] and that memory status is positively correlated with functional independence [19]. Indeed, patients though severely physically disabled but who have relatively mild cognitive impairment can be self-supporting and in competitive employment. Nevertheless, a significant proportion of patients in our cohort scored below the normative mean on formal cognitive testing.

Our study suffers from several limitations. Firstly, due to the small sample size the study lacks statistical power, which may reflect the lack of a significant relationship between the explanatory variables and outcome measures. Indeed, this contrast with previous studies that have demonstrated that patients who have more than four shunt revisions have lower performance IQ and are less likely to live independently [20], although patients reported that their quality of life was no worse. Secondly, our cohort represents a group of higher functioning individuals on the spina bifida–Chiari II–hydrocephalus spectrum. This inherent self-selection bias is a limitation of all studies of patient function in adulthood, but nevertheless may account for the lack a statistical relationship between variables and outcome. Despite being at the higher end of the spectrum marked heterogeneity in levels of function were observed in our cohort.

Conclusions

Despite intervention in childhood and adequate cerebrospinal fluid diversion, the prognosis for independent living into adulthood without symptoms is poor. All patients have elements of cognitive impairment, notably attention and memory function, which invariably influences social integration and employment prospects, both important components of wellbeing. This study provides a good baseline measure of cognitive function for comparison with future generations of patients with spine bifida–Chiari II complex.

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Table 5 Relationship between explanatory variables and cognitive function (≤mean + 1 SD)

		Immediate memory		*P* value[a]	Delayed memory		*P* value[a]	Visuospatial construction		*P* value[a]	Language		*P* value[a]	Attention		*P* value[a]
		No[b]	Yes		No[b]	Yes		No[b]	Yes		No[b]	Yes		No[b]	Yes	
>5 Shunt revisions	No	6	3	0.266	5	4	1.0	5	4	1.0	4	5	1.0	2	7	1.0
	Yes	1	3		2	2		3	1		1	3		1	3	
Past shunt infection	No	5	5	1.0	6	4	0.559	6	4	1.0	5	5	1.0	2	8	1.0
	Yes	2	1		1	2		2	1		0	3		1	2	
Foramen magnum decompression	No	4	2	0.592	3	3	1.0	5	1	0.266	3	3	0.592	2	4	0.559
	Yes	3	4		4	3		3	4		2	5		1	6	

[a] Fisher's Exact test

[b] <1 SD below normative mean

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