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Quality of life and neuropsychological development at school age in Hirschsprung's disease

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ABSTRACT

Purpose: To determine the quality of life and neuropsychological development of school-aged children with Hirschsprung's disease.
Methods: In this observational monocentric study, a multidisciplinary team prospectively assessed quality of life, neuropsychometric development and bowel functional outcomes. This study was registered on ClinicalTrial.gov (NCT03406741). Kidscreen and VSP-A questionnaires assessed the quality of life and were compared to the reference population (Eurostat database). Intelligence, attention and executive functions, perceptual organization and memory were evaluated using the Wechsler Children's Intelligence Scale, the NEuroPSYchological assessment, and the Rey figure test. Bowel functional outcomes were obtained using the Krickenbeck score.
Results: Fifteen patients were included, with a mean age of 10.25 years. The children's Kidscreen-assessed quality of life index was higher than the reference population ($p = 0.01$). The Full-Scale Intelligent Quotient was dissociated in 64% of children. The Perceptional Reasoning Index and the Processing Speed Index were observed at lower levels. There were no disturbances in executive functions. A satisfactory bowel functional outcome was noted in 46.7% of children.
Conclusion: Children with Hirschsprung's disease have been shown to have subtle decreased performances in some areas of intelligence. Performing a neuropsychological assessment upon entering elementary school could help to detect these specific learning disabilities.
Levels of evidence: Level II, prognosis study.

In Hirschsprung's disease (HD), even after a complete surgery and in the absence of complications related to this surgery, the postoperative evolution is currently unpredictable. Postoperative Hirschsprung-associated enterocolitis (HAEC) occurs in up to 25% of patients and is the first cause of mortality. Functional intestinal disorders, mainly obstructive symptoms (constipation, fecal impaction, straining with defecation, abdominal distension or bloating) and continence disorders are present in up to 50% of patients [1]. These chronic defecation difficulties can impact long-term quality of life (QOL) for all age groups and have been reported in the literature [2]. In addition, repeated anesthesia, hospitalizations and infectious complications, such as enterocolitis in the neonatal period, may impact long-term neurodevelopment. There is only one recent study of 20 patients that showed that, despite normal intelligence, school-aged children with HD received more academic and educational support, and encountered attention deficit problems [3]. Moreover, these patients' QOL was slightly impaired. Finally, relatively little is known about the combined assessment of QOL, health status and cognitive development of school-aged children with HD. This age period represents a time of great academic achievements and new autonomy for a child, with acquisition of self-competencies. Additionally, their cognitive development and school integration may foretell their future psychosocial skills.

Our aims were to evaluate and compare the QOL of school-aged children with HD to the normal French population, as well as to describe their health status and psycho-cognitive profiles.

1. Patients and methods

1.1. Study population

This monocentric observational study was prospectively conducted between 2017 and 2018. Each included patient came to our hospital (Assistance Publique-Hôpitaux de Marseille, tertiary referral hospital)

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for a one-day evaluation workshop. A multidisciplinary team collected patient data, and assessed quality of life, neuropsychometric development and bowel functional outcomes.

Inclusion criteria were children born between January 2005 and December 2010, with HD confirmed by histopathology, who underwent curative surgery at the Assistance Publique-Hôpitaux de Marseille. Five experienced surgeons in colorectal surgery performed the surgery over this 6-year period. The children and their parents had to be able to answer a questionnaire in French, and the parents had to give informed consent and sign the study's consent form. Patients were not included if they had severe cerebral palsy, autism, amblyopia, hearing loss or chromosomal abnormality. Patients were excluded if their anamnestic data were not available. After compliance with the inclusion criteria was verified, the investigating physician telephoned the families to arrange an evaluation at the center.

Patients' characteristics (perinatal data, HD presentation and management, anesthetic data) were collected from medical records, as well as sociodemographic and family data (Tables 1 and 2).

1.2. Somatic evaluation

History of ongoing pathologies, treatments and education level were collected. During clinical examination, height and weight were measured and a neurological and fine motor evaluation by the Touwen Infant Neurological Examination was performed. Body mass index (BMI) was calculated by dividing the body mass by the square of the body height, and was expressed in kg/m^2. Overweight (including obesity) is defined by a BMI above the 97th percentile of the French reference curves and obesity by a BMI above the IOTF-30 (International Obesity Task Force) threshold.

A surgeon who did not participate in the initial surgical management completed an abdominal and perineal examination (abdominal palpation, position of the anus, search for hypertonic anal sphincter), and an evaluation of fecal continence and defecation using the Krickenbeck score. This continence score takes into account three criteria: the existence of voluntary defecation, the presence and intensity of soiling and/or constipation. Concerning soiling, grade 1 is occasional fecal staining (once or twice per week), grade 2 is every day staining with no social problem, and grade 3 is constant staining with social problems. Concerning constipation, grade 1 means it's manageable by changes in diet, grade 2 requires laxatives, and grade 3 is resistant to laxatives and diet.

We defined a satisfactory bowel functional outcome as:

- voluntary defecation AND
- absence of fecal staining or grade 1 fecal staining AND
- absence of constipation or grade 1 constipation

Stool consistency was evaluated using the Bristol Stool Form Scale: types 1 and 2 indicate constipation, types 3 and 4 are normal stool, and types 5/6 and 7 indicate diarrhea.

1.3. Neuropsychometric evaluation

The evaluation was conducted by a neuropsychologist using the Wechsler Children's Intelligence Scale, 4th Edition (WISC-IV), a test which calculates the full scale intelligent quotient (FSIQ) and four subindices (mean of 100 and standard deviation of 15) (Verbal comprehension index, perceptual reasoning index, working memory index, processing speed index), the Rey Figure Test evaluating perceptual organization and memory, and the NEuroPSYchological Assessment (NEPSY) subtests evaluating attention and executive functions (mean of 10 and standard deviation of 3). The assessment of the child's behavior was conducted using the Strengths and Difficulties Questionnaire (SDQ), which is well correlated to the «Child Behaviour Check List» d'Achenbach; it incorporates 25 items answered by the parents and divided between 5 scales of 5 items each, generating scores for conduct problems, hyperactivity–inattention, emotional symptoms, peer problems and prosocial behavior. All but the last one are summed to generate a total difficulties score, which ranges from 0 to 40. Each 1-point increase in the total difficulties score corresponds with an increase in the risk of developing a mental health disorder. Finally, the parents and children's anxieties were assessed by the Spielberg State–Trait Anxiety Inventory questionnaire (STAI and STAI-C), a self-evaluation questionnaire containing 20 items.

1.4. Quality of life evaluation

QOL was evaluated using Adolescents' Health and Perceived Health (VSP-A) and Kidscreen 10, both standardized and validated in the

Table 1
Individual characteristics of evaluated patients.

Patient	Gender	Hirschsprung's disease type	Number of anesthesia	Age at evaluation (months)	Body mass index (kg/m^2)	Functional Evaluation			WISC IV					
						Soiling grade	Constipation grade	Bristol stool form scale	VCI	PRI	WMI	PSI	FSIQ	Dissociated
1	M	Rectosigmoid	3	101	Normal	0	0	4	110	102	112	73	100	Yes
2	F	Rectosigmoid	1	92	Normal	1	0	4	106	73	103	93	90	Yes
3	F	Rectosigmoid	4	120	Obesity	1	3	3	132	96	79	100	106	No
4	M	Rectosigmoid	3	145	Normal	2	0	6	78	90	127	73	86	Yes
5	M	Rectosigmoid	2	141	Normal	3	0	5	108	88	112	81	96	Yes
6	M	Rectosigmoid	7	154	Normal	1	0	3,5	106	99	70	76	86	Yes
7	M	Rectosigmoid	5	154	Normal	3	2	4,5	96	94	73	81	83	No
8	F	Transverse Colic	2	84	Normal	1	0	3,5						
9	M	Transverse Colic	3	123	Overweight	1	0	3,5	116	71	97	93	92	Yes
10	F	Rectosigmoid	1	149	Obesity	1	0	3	98	82	88	103	89	Yes
11	F	Rectosigmoid	5	143	Overweight	1	0	4	108	90	103	100	92	No
12	M	Rectosigmoid	7	136	Normal	0	3	4	99	82	64	79	79	Yes
13	M	Rectosigmoid	10	106	Obesity	1	0	3,5	92	92	91	90	89	No
14	F	Rectal	1	93	Normal	1	0	3,5	120	116	94	96	112	Yes
15	M	Rectosigmoid	2	108	Overweight	1	0	4	103	94	106	109	104	No

Soiling and constipation grades were defined according to the Krickenbeck score. WISC-IV (Weschler Intelligence Scale-4th Edition) was used for neuropsychometric evaluation (VCI: Verbal Comprehension Index; PRI: Perceptual reasoning index; WMI: Working memory index; PSI: Processing speed index; FSIQ: Full Scale Intelligence Quotient) (mean of 100 and standard deviation of 15), and NEPSY (NEuroPSYchological assessment) for evaluating attention and executive functions (mean of 10 and standard deviation of 3). K10-P/K10-E (Kidscreen-10 child/Kidscreen parents) and VSP-Ae/VSP-Ap (evaluated by children and parents, respectively) are quality of life questionnaires (range from 0 to 100).

French language. The scores of these two questionnaires range from 0 to 100, with higher scores reflecting a higher QOL [4,5].

The VSP-A is a self-assessment questionnaire with a total index obtained from nine scores. The measured dimensions are vitality, psychological well-being, physical well-being, relationships with friends, leisure, relationships with family, relationships with teachers, schoolwork and self-esteem. We used the child's (VSP-Ae, 35 items) and the parents' version (VSP-Ap, 34 items) of the VSP-A. In the VSP-Ae, the physical and psychological well-being dimensions are grouped together to form an overall general well-being dimension.

The full version of Kidscreen explores the following dimensions: physical well-being, psychological well-being (positive and negative), emotions, relationship with parents and autonomy, relationships with friends, and social and academic support. Our study used the child and parents' versions with 10 items in order to obtain a total index.

1.5. Reference population

The reference population for the analysis of QOL scores is from a European database that was established in 2003, including a French sample ($n = 989$) obtained by the random dialing of telephone numbers, which was then compared to Eurostat data [5]. This sample included children aged 8 to 10 who responded to QOL VSP-A and Kidscreen questionnaires. It provided a basic sample comparable to our study's population, taking into account the confounding factors of age and sex.

1.6. Ethics

This study was approved by the Personal Protective Committee at our institution on 7 May 2017 and was registered on ClinicalTrial.gov under number NCT03406741. With respect to the use and storage of computer data, this study was entered in the CIL/AP-HM registry under the number 2018-04.

1.7. Statistical analysis

A descriptive analysis was performed using qualitative variables presented as numbers and percentages. Quantitative data were presented as means and standard deviations. Chi-square tests or Fisher's exact tests were used for qualitative variables, and Student t-tests or Mann–Whitney U tests were used for continuous variables. Data were analyzed using SPSS software on Windows. Concerning QOL, the scores, as well as the subscores of the different dimensions of the questionnaires were established on the basis of an algorithm realized by the designers of these questionnaires. The normal distribution of QOL scores was verified using a Shapiro–Wilk test. A p-value below 0.05 was considered statistically significant.

2. Results

2.1. Study population

Thirty-six children born between January 2005 and December 2010 have been operated for Hirschsprung disease in our institution One patient have been excluded because of a Down syndrome. Thirty-five were eligible for this study, and a total of 15 (43%) completed all the study assessments (Fig. 1). Among the 15 patients, 13 underwent a transanal pull-through procedure, one a laparotomy associated with transanal pull-through and one a Deloyer procedure [6]. Individual characteristics of the evaluated patients are described in Table 1. The mean age at the time of assessment was 10.25 [7; 12.8] years. The perinatal characteristics of children with HD were not different between patients who were included and patients who were lost to follow-up (Table 2).

2.2. Somatic and neuropsychometric evaluations

Data are reported in Table 3. A satisfactory bowel functional outcome was found in 7 of the 15 patients (46.7%). Three children used retrograde rectocolic irrigations (Peristeen©), two for grade 3 constipation and one for grade 3 fecal staining. The large majority of the children (80%) had a normal stool consistency (types 3 and 4). No children had type 1 or 2 stool consistency. Six children (40%) had a BMI more than the 97th percentile, three (20%) and three (20%) were, respectively, classified as overweight and obese. Six patients (40%) followed a diet adapted to HD.

Fourteen children were educated in ordinary schools and one in a medical–educational institute. Only one child had to repeat a class, but he had previously been one year younger than his grade level. For children enrolled in conventional schools, none received any school

NEPSY		K10-P	K10-E	VSPA-E						
Auditory attention	Visual Attention			Family relationships	Vitality	General well-being	Hobbies	Relationships with teachers	Relationships with caregivers	Index totals
9	7	63	50	79	100	83	80	100	100	85
10		58	48	64	85	79	65	88	0	63
10	10	50	55	82	75	60	60	88	58	65
8	11	50	75	96	100	88	90	63		
10	8	60	55	92	88	55	90	25	67	67
8	8	53	68	89	85	58	80	75	75	74
9	9	45	43	82	75	54	70	63	58	61
		53								
10	9	75	73	79	85	92	85	88	75	79
12	13	73	55	43	70	79	40	38		
8		60	48	100	55	79	65	88	92	79
12		68	54	42	71	68	70	75		
4		53	43	86	80	63	75	50	92	76
9	8	80	83	100	95	71	80	100	100	88
10	14	73	60	32	95	75	65	100	100	79

Table 2
Characteristics of « included » and « lost to follow up » patients during the neonatal period.

	Included ($n = 15$) n (%) or mean (±SD)	Lost to follow up ($n = 20$) n (%) or mean (±SD)	p-value
Perinatal Data			
Male	9 (60)	17 (85)	0.09
Premature (< 7 weeks of gestation)	0	0	0.42
Birth Weight (g)	3254 (±477)	3542 (±529)	0.13
Parents' age at birth			
Mother	28.2 (±6.3)	32.1 (±6.4)	0.05
Father	31.3 (±4.7)	34.5 (±9.5)	0.20
Parental occupation			
None	2 (13.3)	1 (5)	
One	4 (26.7)	8 (40)	
Both	9 (60)	11 (55)	
Type of Hirschsprung's disease			
Rectal	1 (6.7)	4 (21.1)	
Rectal–sigmoid	12 (80)	12 (63.2)	
Left Colic	0	1 (15.3)	0.18
Transverse Colic	2 (13.3)	0	
Total	0	2 (10.45)	
Enterocolitis			
Preoperative	2 (14.3)	3 (15.8)	1.00
Postoperative	2 (14.3)	4 (21)	0.33
Initial medical management			
Stoma Surgery	15 (33.3)	6 (31.6)	1.00
Curative surgery			
Age (days)	93 (±77)	84 (±67)	0.90
Weight (g)	5230 (±1275)	5598 (±1285)	0.45
Duration (min)	224 (±56)	242 (±69)	0.48
Postoperative medical management			
Intensive care unit stay (days)	7 (46.7)	9 (47.4)	0.96
Total length of stay (days)	14.4 (±13.9)	9.9 (±4.8)	0.97
Surgical revision	0	3 (15.8)	0.23
Total number of general anesthesia	3.7 (±2.6)	3.4 (±2.7)	0.68
Total number of hospitalizations	4.5 (±3.4)	5.9 (±8.1)	0.91

tutoring support. One child failed to complete all neuropychological assessments because of a nonlabeled developmental disorder. Moreover he wasn't able to fill the quality of life questionnaire for autoevaluation (VSPA-E and Kidscreen-E).

With respect to the WISC-IV evaluation, nine children (64%) had dissociated FSIQ (a dissociation of 1 SD between two subtests). The Perceptional Reasoning Index (PRI) and Processing Speed Index (PSI) were decreased to 91 (±11.6) and 91.5 (±11.9), respectively, and the Rey Figure was not successfully achieved in the copy and recall stages in one quarter of patients. Altogether, this suggested a visuoperception disorder. The NEPSY evaluation showed low mean auditory attention and low visual attention, suggesting a sustained attention defect. With

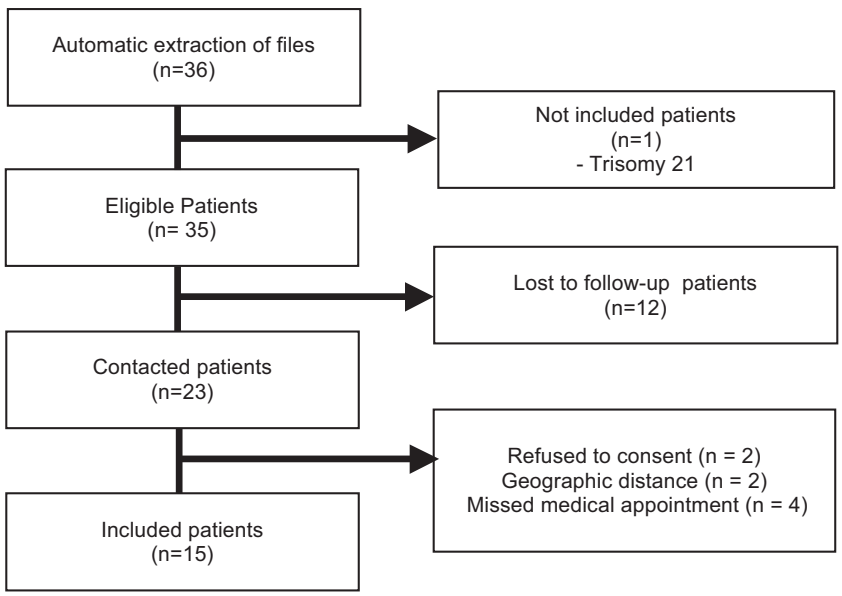

Fig. 1. Study's flow diagram. Abbreviations BMI: body mass index. ENS: enteric nervous system. FSIQ: full scale intelligent quotient. HD: Hirschsprung's disease. HAEC: Hirschsprung-associated enterocolitis. IOTF-30: internation obesity task force. NEPSY: Neuropsychological Assessment. PRI: perceptional reasoning index. PSI: processing speed index. QOL: quality of life. SDQ: Strengths and difficulties Questionnaire. STAI: State–Trait Anxiety Inventory questionnaire. VCI: verbal comprehension index. VSP-A: adolescent' Health and Perceived Health. WISC-IV: children's Intelligence Scale. WMI: working memory index.

respect to the STAI evaluation, low anxiety scores were noted both in children and parents.

2.3. Quality of life assessment (Table 4)

The QOL of HD children assessed by Kidscreen was significantly higher, from the parents' perspective, when compared to the reference population for children of the same gender and age ($p = 0.01$) and tended to be higher from the children's perspective ($p = 0.06$).

In addition, HD patients had higher QOL scores than the reference population in most dimensions of the VSP-A QOL. From the children's point of view, the largest increases, compared to the reference population, were noted for hobbies and relationships with both family and caregivers. From the parents' point of view, relationships with the family and caregivers had the largest increases. Self-esteem was the only domain significantly reduced ($p = 0.02$) when compared to children of the same gender and age in the reference population. This trend was also noted from the children's perspective ($p = 0.55$).

3. Discussion

Little is known about QOL and neuropsychometric functioning in school-aged HD patients. In our study, the QOL of school-aged children with HD was higher when compared to children of the same gender and age in the reference population, except for self-esteem as reported by parents. Neuropsychometric evaluation shows that these children maintained normal intelligence and did not have any dysexecutive disorders. Results to some subtests evoke visual perception and/or sustained attention deficits but this had little impact during children school-aged years. Only one child benefited from specific assistance and none had academic support sessions. To the best of our knowledge, this is the first study providing a concomitant assessment of QOL, health status and cognitive development in school-aged children with HD.

First, in our study, HD patients' characteristics were comparable to the literature, with a short-segment HD in most of the patients [1]. From a functional point of view, despite a high rate of fecal staining (86.7%) at a mean age of 10.25 years, the outcomes remained satisfactory for 46.7% of the patients. These results were also comparable to the published data in 7–12 year-old HD patients [7]. Nevertheless, 20% of the children were overweight and 20% were obese, which were much higher than the latest data presented by the French Institute for Public Health Surveillance in 2017, where 18.1% of pupils in primary education (5th grade) were overweight and 3.6% were obese.

One of our main results is in accordance with the only published study about neuropsychometric evaluation in school-aged HD; this study included 20 patients and noted the same specific neuropsychological disorders, but with a different academic impact [3]. Thus, nearly half of the included children with HD received adapted schooling methods and academic coaching or tutoring. This variation in managing minor neuropsychological disorders at school could be explained by the use of different educational methods between France and the Netherlands. Conversely, a population-based study comparing HD adults to a healthy reference group in Sweden did not show any difference in higher education levels. However, in this adult study, confounders such as socioeconomic and educational status were not monitored and might have influenced the results [8].

With respect to QOL, its measurement varies according to the evaluated concepts, patient age, the choice of instruments and the use of self- and/or heteroevaluations. We used instruments with a high degree of validity and reliability, such as Kidscreen and VSP-A, which are designed to measure QOL for both healthy and chronically ill children. The strength of these tools lies in their simultaneous development in several European countries, taking into account the adaptation of content to age and intercultural impact, and on the measurement of the most significant dimensions recommended by the World Health Organization to obtain a measure of an adapted QOL.

Table 3
School-age children characteristics.

	Evaluated patients (n)	n (%) or mean (±SD)
Age at evaluation (yrs)	15	10.25 (±2)
School data		
Repeating a school year	15	1 (6.6)
Specific education	15	1 (6.6)
Neuro-cognitive evaluation		
Touwen infant exam	14	
Healthy		12 (85.7)
Mild minor neuromotor dysfunctions (MND-1)		2 (4.3)
Moderate minor neuromotor dysfunction (MND-2)		0
WISC-IV	14	
Full Scale Intelligence Quotient (FSIQ)		91 (±9.4)
Verbal Comprehension Index (VCI)		106 (±13)
Perceptual Reasoning Index (PRI)		91 (±11.6)
Working Memory Index (WMI)		95.5 (±18.1)
Processing Speed Index (PSI)		91.5 (±11.9)
Dissociation		9 (64)
NEPSY		
Score executive function/ planning (tower)	10	11.2 (±1.6)
Auditory attention	14	9.2 (±1.9)
Visual attention	10	9.7 (±2.3)
Design fluency	14	10.2 (±1.7)
Rey figure	15	`
Copy total		
<10		2 (14.3)
Reproduction total		
<10		2 (14.3)
Behavior (SDQ)	15	
Hyperactivity score		3.8 (±2.6)
Total difficulties		10.7 (±4.8)
Anxiety		
STAI parents	15	
Trait		33.7 (±8.9)
State		37.2 (±8.2)
STAI child	14	
Trait		30.3 (±7.9)
Functional digestive outcomes		
Voluntary defecation	15	9 (60)
Constipation	15	3 (20)
Soiling	15	13 (86.7)
Bristol stool form scale	15	
Types 1-2		0
Types 3-4		12 (80)
Types 5-6-7		3 (20)
Body Mass Index (kg/m^2)		
Normal		9 (60)
Overweight	15	3 (20)
Obesity		3 (20)

WISC-IV (Weschler Intelligence Scale-4th Edition): mean 100, standard deviation 15. NEPSY (NEuroPSYchological assessment): mean 10, standard deviation 3. Rey figure: copy or reproduction <10th percentile defines a visuoperception disorder. SDQ (Strengths and Difficulties Questionnaire) total difficulties: closed to average 0–13, slightly above average 14–16, high 17–19 or very high 20–40. Hyperactivity score: close to average = 0–5, slightly above average = 6–7, high = 8, very high = 9–10. STAI: "State–Trait Anxiety Inventory" questionnaire (STAI and STAI-C), a self-evaluation questionnaire containing 20 items giving 2 scores (state and trait) ranging from 20 (no anxiety) to 80 (high anxiety).

Jardine et al. have shown that combined assessments of QOL, even among school-aged children, are necessary to evaluate divergent views between the parents and the child [9]. These divergent QOL scores have been observed in many pathologies [10]. Typically, parents report lower QOL than their children. Our work confirms this observation for school-aged children with HD, with a significantly decreased self-esteem score only noted from the parents' point of view.

In addition, HD patients' QOL is usually decreased in questionnaires that are centered on the disease and is identical or higher to generic questionnaires, such as the ones used in our study to compare to children of the same age and gender in the reference population. A generic questionnaire meta-analysis of 22 studies exploring the QOL of 6

Table 4
Quality of life (QOL) data at school age in HD patients compared to the reference population.

	Hirschsprung's disease patients		Reference population	Difference		
	Average	Standard Deviation	Average	Mean	Standard Deviation	p-value
VSP-Ae (children)						
Vitality	83.65	12.85	77.14	6.51	11.65	0.087
General well-being	71.99	12.74	77.01	−5.02	13.87	0.173
Relationships with friends	53.85	29.01	63.16	−9.31	31.81	0.382
Hobbies	72.69	13.94	59.95	12.73	17.02	0.028
Relationships with the family	78.75	20.88	66.89	11.87	23.29	0.075
School work	74.04	24.71	72.28	1.75	21.31	0.507
Self esteem	79.49	13.44	81.60	−2.11	13.13	0.552
Relationship with caregivers	74.24	29.45	48.38	25.86	32.38	0.041
Index	74.11	8.87	71.86	2.45	8.44	0.424
VSP-Ap (parent)						
Vitality	78.65	11.52	73.84	4.80	9.88	0.136
Psychological well-being	71.11	15.51	76.86	−5.75	15.26	0.272
Relationship with friends	65.42	24.45	65.32	0.108	24.98	0.937
Hobbies	61.67	18.83	55.28	6.386	17.17	0.182
Relationships with the family	87.50	10.50	74.98	12.52	9.85	0.006
Physical well-being	73.96	20.26	74.21	−0.249	18.45	0.814
Relationships with teachers	75.69	21.45	66.77	8.929	17.41	0.099
School work	73.96	22.89	74.68	−0.718	21.41	0.695
Self esteem	64.93	18.33	79.79	−14.85	21.63	0.023
Relationship with caregivers	63.64	36.18	32.73	30.86	36.01	0.026
Index	72.54	11.51	71.42	1.19	9.54	0.754
Kidscreen-10 Infant						
Index	57.88	12.86	49.16	8.72	13.10	0.064
Kidscreen-10 Parent						
Index	60.67	11.10	45.53	15.23	10.65	0.01

VSP-Ae and VSP-Ap (evaluation by children and parents, respectively): scores ranging from 0 to 100. Kidscreen-10 child and Kidscreen-10 parents: scores ranging from 0 to 100.

to 16 year old patients with anorectal malformations and HD showed a slight decrease of QOL compared to same age and gender reference groups [11]. In comparison with adolescents, school-aged children have better QOL, but lower functional outcomes. The relationship between QOL and functional outcomes, as related to the disease, is poorly defined and highly heterogeneous. Unlike our work, no study in this meta-analysis measured the existence of comorbidities, such as obesity or neuropsychological fate, and their possible relationship with QoL.

In 2008, a qualitative QOL study of 152 HD children from 8 to 17 years of age was conducted by Hartman et al., who showed no difference in QOL in comparison to the reference population [12]. However, there were very large individual variations between patients with very low and very high QOL levels. These variations, especially regarding self-evaluation, also appear in our population characteristics. Hartman et al. also showed that a decrease in self-esteem was found in patients with severe HD forms, with additional genetic diseases, and in females. In our study, only the parents reported a decreased QOL with respect to self-esteem.

Moreover, as with a healthy population, QOL self-assessment is influenced by variable domains in accordance with the child's age. Between 8 and 12 years old, the psychosocial domain (self-esteem and relationships with others) is predominant and afterwards the physical domain takes over in the context of body changes and sexual problems. Finally, in a qualitative trajectory analysis study of 121 HD patients from 8 to 16 years old, Hartman et al. showed a QOL improvement over time in HD patients, along with a decrease of functional digestive symptoms and an increase of psychosocial skills, more particularly when there was better school integration that improved self-competencies [13]. Thus, to improve and maintain QOL in these patients, and more generally to improve their academic, behavioral and social skills, it is essential to minimize the long-term functional digestive symptoms in HD. Children and adolescents will have a better perception of their QOL if they develop better psychosocial skills and increase their ability to cope.

In fact, children with chronic illnesses complete the self-evaluation QOL questionnaires positively since they have learned to live with their pathology and have the desire to be considered ‘normal’.

In addition, we could discuss whether the existence of another chronic disorder such as obesity may decrease their psychosocial skills at school age and may affect their QOL. It seems that in HD, the children's QOL is mainly affected by the perception of the disease and their related psychosocial abilities [13].

The main limitation of our study is the relatively small number of included patients. HD is a rare disease and the number of children that were lost to follow-up was high. To ensure that our population was representative of the target population, we demonstrated that the perinatal, clinical and socioeconomic characteristics of our population were not different from those of the lost to follow-up population. Similarly, we chose to compare our study population to a representative reference group of French children of the same age in a European sample.

4. Conclusion

Despite our small sample size, this study highlights that school-aged children with HD had normal cognitive functioning with subtle visuospatial and attention disorders that remained moderate and did not seem to impact their schooling, psychosocial skills, and therefore, their QOL. Performing a neuropsychological assessment prior to entering primary school could help detect possible specific learning disorders. Thus, children with HD could benefit from appropriate educational methods in order to improve their QOL by developing their academic and psychosocial competencies, as well as by reducing significant variations with their classmates. Neuropsychological disorders were demonstrated in a small and selected monocentric population. Larger multicenter studies are needed to objectively define the determinants of health that affect the QOL of school-aged children with HD.

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References

[1] Tam PKH. Hirschsprung's disease: a bridge for science and surgery. J Pediatr Surg 2016;51:18–22. https://doi.org/10.1016/j.jpedsurg.2015.10.021.
[2] Diseth TH, Bjornland K, Novik TS, et al. Bowel function, mental health, and psychosocial function in adolescents with Hirschsprung's disease. Arch Dis Child 1997;76:100–6. https://doi.org/10.1136/adc.76.2.100.
[3] Van Den Hondel D, Aarsen FK, Wijnen RMH, et al. Children with congenital colorectal malformations often require special education or remedial teaching, despite normal intelligence. Acta Paediatr Int J Paediatr 2016;105:e77–84. https://doi.org/10.1111/apa.13154.
[4] Landgraf J, Act H, Hopital C, et al. Development, Validation of HRQL measurement in children: VSP-AE author(s): Pascal Auquier, Audrey Clement, Christophe Sapin, Mohammed El Khammar, Jean-Louis San Marco and Mane-Claude Simeoni Source : Quality of Life Research 2016;10(No. 3):8–9.
[5] Berra S, Ravens-Sieberer U, Erhart M, et al. Methods and representativeness of a European survey in children and adolescents: the KIDSCREEN study. BMC Public Health 2007;7:1–14. https://doi.org/10.1186/1471-2458-7-182.
[6] Prévot J. Hirschsprung's disease: Deloyers' technic. Ann Chir Infant 1970;11:81–4.
[7] Ludman L, Spitz L, Tsuii H, et al. Hirschsprung's disease: functional and psychological follow up comparing total colonic and rectosigmoid aganglionosis. Arch Dis Child 2002;86:348–51. https://doi.org/10.1136/adc.86.5.348.
[8] Granström AL, Svenningsson A, Nordenskjöld A, et al. Population-based study shows that Hirschsprung disease does not have a negative impact on education and income. Acta Paediatr 2016;105:1508–12. https://doi.org/10.1111/apa.13594.
[9] Jardine J, Glinianaia SV, McConachie H, et al. Self-reported quality of life of young children with conditions from early infancy: a systematic review. Pediatrics 2014;134:e1129–48. https://doi.org/10.1542/peds.2014-0352.
[10] Hartman EE, Oort FJ, Aronson DC, et al. Children with anorectal malformations, Hirschsprung disease, and their siblings: proxy reports and self-reports. J Pediatr Gastroenterol Nutr 2015;61:630–5. https://doi.org/10.1097/MPG.0000000000000855.
[11] Hartman EE, Oort FJ, Aronson DC, et al. Quality of life and disease-specific functioning of patients with anorectal malformations or Hirschsprung's disease: a review. Arch Dis Child 2011;96:398–406. https://doi.org/10.1136/adc.2007.118133.
[12] Hartman EE, Oort FJ, Sprangers MA, et al. Factors affecting quality of life of children and adolescents with Anorectal malformations or Hirschsprung disease. J Pediatr Gastroenterol Nutr 2008;47:463–71. https://doi.org/10.1097/MPG.0b013e31815ce545.
[13] Hartman EE, Oort FJ, Aronson DC, et al. Explaining change in quality of life of children and adolescents with anorectal malformations or Hirschsprung disease. Pediatrics 2007;119:e374–83. https://doi.org/10.1542/peds.2006-0212.