ARTICLE

Surgically Restoring Portal Blood Flow to the Liver in Children With Primary Extrahepatic Portal Vein Thrombosis Improves Fluid Neurocognitive Ability

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ABSTRACT

OBJECTIVES. Children with primary extrahepatic portal vein thrombosis (EHPVT) have portal-systemic shunting, which may lead to disturbed neurocognitive function similar to portal-systemic encephalopathy (PSE) seen with chronic liver disease and cirrhosis. The functions most affected are those involving fluid cognitive ability, which comprise neurocognitive domains such as attention, processing speed, and short-term memory, that are particularly vulnerable to systemic illness or diffuse neurologic insult. We determined the fluid cognitive ability of children with EHPVT and whether surgically restoring portal blood flow by mesenteric left portal vein bypass (MLPVB) improved it.

DESIGN. Twelve children with EHPVT and no overt PSE underwent comprehensive neurocognitive testing before and 1 year after undergoing surgery with intent to perform MLPVB. The evaluations sampled 4 functional domains at both time points: (1) neurobehavioral (behavior, emotional, executive functioning); (2) broad cognitive (intelligence, achievement); (3) fluid ability (attention, mental speed, working memory, memory encoding); and (4) visual motor (drawing, fine motor). Tasks in the fluid-ability and visual-motor domains were expected to be especially sensitive to adverse effects of EHPVT and to be most likely to show improvement with MLPVB. The test group consisted of 8 subjects who underwent successful MLPVB, and the comparison group was composed of 3 patients who received distal splenorenal shunts and one whose MLPVB failed.

RESULTS. Both groups demonstrated similar fluid cognitive ability at initial evaluation. Successful MLPVB resulted in significantly improved fluid cognitive function: in the fluid cognitive domain, significant improvements were seen for the hit reaction time variability in the Conner's Continuous Performance Test, the attention scale of the Cognitive Assessment System, and immediate verbal memory in the Children's Memory Scale. In the visual-motor domain, z scores on the Grooved Pegboard Test improved. No improvement was observed in the comparison group.

DISCUSSION. The results show that surgically restoring portal flow to the liver in children with primary EHPVT results in improved fluid cognitive ability. Subjects showed some neurocognitive abnormalities involving mainly fluid cognitive ability consistent with minimal PSE seen in adults with chronic liver disease. Cognitive defects in patients with minimal PSE seem to relate primarily to attention and fine motor skill, and although affected patients can function in everyday life, they are at risk for performance deficits in educational and vocational situations requiring the ability to pay close attention and react quickly (eg, driving, employment in manufacturing). The tests we administered in these domains are pediatric equivalents to measures used to detect minimal PSE in adults and should detect abnormalities in the same functional domains. Our results suggest that a narrow battery of tests could be used to detect minimal PSE in children in a manner similar to the 5-test battery used in adults, eliminating the need for the comprehensive and broad testing we performed. Our findings suggest that shunting of portal blood from the liver in primary EHPVT can result in PSE and question whether it is as benign a disease as previously thought. The importance of our findings is twofold. For understanding the pathophysiology of PSE, we have shown that restoring blood flow to the liver improves cognitive function in children with EHPVT. For therapy for EHPVT, it becomes clear that MLPVB is an excellent treatment option. It is effective for treating the complications of portal hypertension and provides effective portal blood flow that other medical and surgical therapies do not. The findings provide additional evidence that primary EHPVT should be considered curable by MLPVB. However, comparison of overall risks and benefits of MLPVB with those of other therapeutic options and longer-term outcome studies must be completed before MLPVB can be fully endorsed as the best treatment for EHPVT in children.

CONCLUSIONS. Surgical restoration of portal venous flow to the liver in children with primary EHPVT by MLPVB improves fluid cognitive ability. MLPVB should be considered in treating primary EHPVT, because it corrects portal blood flow and could optimize learning potential.

EXTRAHEPATIC PORTAL VEIN thrombosis (EHPVT) is a common cause of chronic portal hypertension in children.[1] Patients with primary EHPVT have no underlying liver disease, as opposed to secondary EHPVT, which is seen in patients with cirrhosis. Portal hypertension, therefore, results entirely from the resistance to blood flow into the liver that results from the thrombosis. Collaterals formed in the hilum of the liver, so-called cavernous transformation of the portal vein, are insufficient to fully restore effective portal blood flow, so portal hypertension persists.[2] As in other forms of portal hypertension, primary EHPVT results in the formation of extrahepatic collaterals to return mesenteric blood to the systemic circulation without passing through the liver. EHPVT is considered to be a benign disorder if portal hypertension and its complications are managed appropriately.[2,3]

Hepatic encephalopathy is defined as brain dysfunction resulting from liver disease.[4] Portal-systemic encephalopathy (PSE) refers to brain dysfunction resulting from portal-systemic shunting and is usually observed in the context of advanced chronic liver disease.[5] Chronic liver disease–related cognitive dysfunction in the absence of overt PSE has been termed minimal PSE.[5] The functions most affected are those involving fluid cognitive ability, which is composed of neurocognitive domains such as attention, processing speed, and short-term memory, which are particularly vulnerable to systemic illness or diffuse neurologic insult.[6] Intelligence and long-term memory are minimally affected.[7,8] The degree of PSE in adults with chronic liver disease has been correlated with the magnitude of shunting.[9] Therapeutic shunts to treat portal hypertension (eg, portocaval shunt and transjugular intrahepatic portal-systemic shunt) are intended to increase portal-systemic shunting. However, increasing the shunting of blood often has the unintended consequence of precipitating PSE,[10] which serves to confirm the importance of shunting in the pathogenesis of PSE.

A mesenterico-left portal vein bypass (MLPVB) redirects blood from the superior mesenteric vein to the intrahepatic portal system via the left portal vein and is an effective approach to treating children with idiopathic EHPVT.[11–14] Originally designed to correct acute portal vein thrombosis in liver transplant recipients, the operation entails using an autologous vein as a jump graft from the mesenteric vein to the well-developed left portal vein in the Rex recessus and has been called a meso-Rex shunt.[15] Children with primary idiopathic EHPVT often have a small underdeveloped or atrophic intrahepatic portal venous system, which has caused some technical problems in performing MLPVB. However, we and others[14,16] have shown that the intrahepatic portal venous system rapidly adapts to permit normal mesenteric flows into the liver. It is not a "shunt" per se, because it does not perform the primary function of a portosystemic shunt, which is to facilitate the reduction of portal hypertension by surgically directing all or part of the portal blood flow to the systemic venous system, bypassing the liver. It is a bypass operation, and, with its use, portal hypertension is eliminated, portal flow to the liver is restored, and portal-systemic shunting and its pathophysiologic effects are eliminated.[12,17] Having observed several children with EHPVT who had symptoms consistent with minimal brain dysfunction/attention-deficit disorder, we hypothesized that careful neurocognitive testing would show a substantial proportion of children

with EHPVT to have deficits in fluid cognitive ability consistent with minimal PSE. In addition, we hypothesized that restoring portal blood flow and reducing portal-systemic shunting by MLVPB would improve fluid cognitive ability. To test our hypotheses, we designed a prospective study to characterize the neurocognitive function of children with primary EHPVT and to determine if surgical restoration of portal venous flow into the liver would improve function, particularly fluid cognitive ability.

METHODS

Patient Enrollment

This was a prospective study designed to compare fluid cognitive ability in children with primary EHPVT before and 1 year after surgery. All of the children with primary EHPVT referred to Children's Memorial Hospital from 2000 to 2002 for consideration of an MLPVB procedure were interviewed for enrollment into the study. Exclusion criteria for this study included an age of <6 years, history of prematurity, underlying liver disease, neurologic disease or history of central nervous system trauma, primary hypercoagulable state, and acute gastrointestinal bleeding or hospitalization within 2 weeks of neurocognitive testing. All of the children underwent surgery with the intent to perform MLPVB and, if that was found to not be feasible, to have a distal splenorenal shunt (DSRS). The patients receiving successful MLPVB constituted the test population, and children who received a DSRS or whose MLPVB failed functioned as a comparison population. This study was approved by the Children's Memorial Hospital Institutional Review Board. Informed consent was obtained from parents and from subjects who were >12 years of age.

Patient Assessment

All of the patients underwent extensive evaluation to exclude underlying or coexisting liver disease. We confirmed that liver histology results were normal at the time of the procedure. Patients underwent Doppler ultrasound evaluation of the mesenteric and portal venous systems. Magnetic resonance and computed tomographic angiography were used as noninvasive approaches to obtain accurate images of the intrahepatic veins before surgery. A standard hepatic-function panel, prothrombin time, and random nonfasting venous ammonia level were obtained at the time of initial evaluation.

Neurocognitive Testing

Comprehensive neurocognitive testing was administered by a neuropsychologist or experienced neuropsychology technician within 2 weeks before surgery and at 1 year after surgery. The individuals who administered the tests were not part of the study per se and were unaware of the medical/surgical condition of the subjects. Standardized parent questionnaires were administered to obtain information about the child's academic history and neurobehavioral status. The evaluations sampled 4 functional domains at both time points: (1) neurobehavioral (behavior, emotional, and executive functioning); (2) broad cognitive (intelligence and achievement); (3) fluid ability (attention, mental speed, working memory, and memory encoding); and (4) visual motor (drawing and fine motor). Tasks in the fluid-ability and visual-motor domains were expected to be especially sensitive to adverse effects of EHPVT and to be most likely to show improvement with MLPVB.

Neurobehavioral

The Child Behavior Checklist (CBCL) is a standardized survey of parent concerns related to a child's behavioral and emotional status. The CBCL index of total behavior problems was examined as an indicator of overall adjustment.[18] The Behavior Rating Inventory of Executive Function (BRIEF) is a standardized parent questionnaire that samples behaviors related to executive functioning.[19] The global executive composite of the BRIEF was examined as an index of executive functioning. The Children's Depression Inventory was administered to subjects as a standardized self-report survey of depressive symptomatology.[20]

Broad Cognitive

The full-scale IQ index of the Donders revision of the Wechsler Intelligence Scale for Children, Third Edition (WISC-III) was used to measure general intelligence.[21,22] Academic skills mastery was sampled with the reading and arithmetic subtests of the Wide Range Achievement Test, Third Edition.[23]

Fluid Ability

The Conners Continuous Performance Test (CCPT) was administered as a computerized measure of the ability to sustain attention over time.[24] Four indices from the CCPT were examined: hit rate (percentage of correct responses), false-alarm rate (percentage of incorrect responses), hit reaction time (milliseconds), and hit reaction time standard error or variability (HRTV; milliseconds). The planning and attention scale indices of the Cognitive Assessment System (CAS) were examined as indicators of the ability to plan and to direct focal attention over brief intervals.[25] Immediate and delayed verbal and visual memory indices of the Children's Memory Scale (CMS) were examined as parameters of memory performance.[26] The overall index of the Brief Test of Attention was examined as an index of verbal working memory.[27]

Visual Motor

The Beery Developmental Test of Visual Motor Integration (BVMI) was administered as a pencil-and-paper test

TABLE 1	Patient Characteristics Before Surgery	
	Successful MLPVB (*n* = 8)	Comparison Group (*n* = 4) DSRS or Failed MLPVB
Age, mean ± SD, y	9.7 ± 1 .8	9.0 ± 2.6
Gender, male/female, *n*	6:2	4:0
Ethnicity, white/Latino/black, *n*	6:2:0	2:1:1
Liver histology	Normal in all	Normal in all
Serum ALT, mean ± SD, IU/L (reference: 2–30 IU/L)	24 ± 8	26 ± 12
Total serum bilirubin, mean ± SD, mg/dL (reference: 0.2–1.0 mg/dL)	1.1 ± 0.6	1.3 ± 0.1
Prothrombin time, mean ± SD, s (reference: 11.8–15.5 s)	16.5 ± 1.5	17.5 ± 0.8
Nonfasting venous ammonia, mean ± SD, μmol/L (no reference value available)	45 ± 16	35 ± 15

ALT indicates alanine aminotransferase.

of visuographic (drawing) skills.[28] Manual dexterity and speed were examined by using a summary measure of the performances of the dominant and nondominant hands on the Grooved Pegboard Test.[29]

Statistical Analysis

Inferential analyses of questionnaire and neurocognitive test data within each group at the 2 time points were based on the 2-tailed Student's *t* test for paired samples. A value of $P = .05$ was selected as the significance criterion.

RESULTS

Patient Characteristics

Twelve children met all of the entry criteria and underwent preoperative and follow-up neurocognitive testing. Eight children who underwent successful MLPVB constitute the test group. The comparison group consisted of 3 children who received DSRS because of anatomic limitations identified intraoperatively (left intrahepatic portal vein diameter too small: $n = 2$; aberrant location of left intrahepatic portal vein: $n = 1$) and 1 patient whose attempted MLPVB failed.

Table 1 gives the patient characteristics at the time of initial evaluation, none of which were different between groups. Parents reported that 4 patients in the MLPVB group and 3 in the comparison group required special education classes or supplemental tutoring. No patients in either group were receiving medical treatment for portal hypertension with medications (ie, propranolol) that might have negatively affected performance on tests. Both groups had mildly prolonged prothrombin times as reported previously,[17] and both groups demonstrated similar degrees of hyperbilirubinemia consistent with portal-systemic shunting.[30] Serum alanine aminotransferase levels and liver histology results were normal in all of the patients. At the 1-year follow-up, the MLPVB and DSRS were shown to be patent and functioning.

Neurobehavioral Domain

The results of neurobehavioral tests at the 2 time points are given in Table 2. The presurgical testing revealed normal overall scores for subjects in both groups, reflecting normal behavior and emotional status of the patients, and did not change significantly at the 1-year follow-up. No significant symptoms of depression or mood disturbances were identified in either group at either time point.

Broad Cognitive Domain

These results are shown in Table 2. Both groups had normal IQs and normal scores on tests of reading and arithmetic at baseline and at follow-up testing, without significant group or time effects. WISC-III full-scale IQ scores for the test subjects were 100.0 ± 15.0 at baseline and 99.7 ± 13.2 at the 1-year follow-up (reference: 100; SD: 15).

Fluid Cognitive Domain

The CCPT, which measures the ability to sustain attention over time, demonstrated abnormally large HRTV in both the test-group and comparison-group subjects before surgery, indicating difficulty maintaining a consistent level of alertness or arousal over time. There was considerable variation among subjects, with some test results being normal (8–10 milliseconds) and others being substantially above that level (Fig 1). At follow-up, the HRTV for the test group of subjects had improved substantially ($P = .024$). Subjects with the worst presurgical scores improved dramatically, whereas those with normal or near-normal scores did not change (Fig 1A). Postsurgical test scores were all normal or near normal. At follow-up, the HRTV did not consistently improve in the comparison group (Fig 1B).

Scores for the CAS attention scale, which measures focal attention over short periods of time, varied from normal to modestly abnormal in both groups at baseline (Fig 2). At follow-up, the MLPVB group showed significant positive change ($P = .0070$; Fig 2A), whereas the comparison group did not (Fig 2B).

Means and SDs for Neurobehavioral and Neurocognitive Indices in Subjects Before and 1 Year After MLPVB and in the Comparison Group

	Pre-MLPVB	Post-MLPVB	Pre-Comp	Post-Comp
Neurobehavioral indices				
CBCL total behavior problems (mean: 50; SD: 10)	54.7 ± 4.6	51.3 ± 8.5	59.3 ± 12.7	55.3 ± 9.7
BRIEF global executive composite (mean: 50; SD: 10)	48.3 ± 7.4	52.6 ± 8.6	60.0 ± 7.2	59.0 ± 7.2
Children's Depression Inventory (mean: 50; SD: 10)	54.0 ± 10.3	47.6 ± 11.6	54.33 ± 8.7	59.0 ± 12.2
Broad cognitive indices				
WISC-III FSIQ (mean: 100; SD: 15)	100.0 ± 15.0	99.7 ± 13.2	101.8 ± 20.6	94.5 ± 14.8
WRAT-3 reading (mean: 100; SD: 15)	106.6 ± 15.0	108.1 ± 21.8	104.3 ± 16.6	101.8 ± 15.7
WRAT-3 arithmetic (mean: 100; SD: 15)	96.3 ± 12.9	98.4 ± 7.8	94.5 ± 10.1	95.0 ± 18.1
Fluid-ability indices				
CCPT hit rate, raw data, %	96.3 ± 4.8	98.2 ± 1.9	91.9 ± 5.7	88.9 ± 13.2
CCPT false-alarm rate, raw data, %	50.7 ± 24.9	47.2 ± 18.2	52.8 ± 25.2	57.6 ± 15.3
CCPT hit reaction time, time in ms	428.3 ± 39.9	395.5 ± 58.1	476.3 ± 132.9	493.2 ± 205.9
CCPT HRTV, time in ms	12.8 ± 7.1	7.1 ± 1.9[a]	17.9 ± 10.4	20.1 ± 17.1
CAS planning index (mean: 100; SD: 15)	92.3 ± 17.9	92.7 ± 12.4	97.8 ± 11.3	94.0 ± 9.5
CAS attention index (mean: 100; SD: 15)	88.0 ± 15.6	98.4 ± 11.6[a]	97.0 ± 10.1	83.8 ± 5.3
CMS immediate verbal memory (mean: 100; SD: 15)	102.9 ± 12.8	111.0 ± 15.6[a]	104.0 ± 16.6	104.0 ± 15.4
CMS delayed verbal memory (mean: 100; SD: 15)	100.3 ± 13.4	110.1 ± 16.3[a]	101.0 ± 16.6	103.0 ± 24.4
CMS immediate visual memory (mean: 100; SD: 15)	106.3 ± 11.7	101.9 ± 8.3	92.3 ± 18.1	89.0 ± 22.3
CMS delayed visual memory (mean: 100; SD: 15)	106.5 ± 9.2	103.0 ± 10.8	92.0 ± 22.3	102.3 ± 18.6
BTA, z score (mean: 0; SD: 1)	−0.6 ± 0.5	−0.1 ± 0.9	−0.9 ± 0.6	−0.9 ± 1.0
Visual-motor indices				
BVMI (mean: 100; SD: 15)	85.6 ± 26.4	95.4 ± 11.1	86.0 ± 12.5	91.7 ± 13.3
Grooved Pegboard, z score (mean: 0; SD: 1)	−0.3 ± 1.23	0.05 ± 1.1[a]	−0.5 ± 1.2	−1.9 ± 3.9

WRAT-3 indicates Wide Range Achievement Test, Third Edition; BTA, Brief Test of Attention. Data are given as mean ± SD.
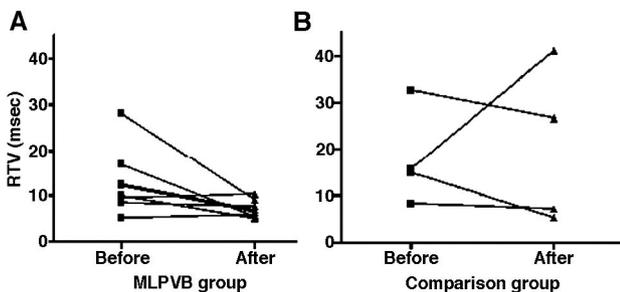[a] $P < .05$ versus pre-MLPVB value.

FIGURE 1
HRTV on the CCPT measures the ability to sustain a consistent level of alertness over time. This index is a particularly sensitive indicator of sustained attention failure and has a normal reference value of 7 to 8 milliseconds in the age range studied. Several subjects had highly abnormal HRTV before surgery. At the 1-year follow-up, there was a consistent improvement in HRTV in the MLPVB group (A) but not in the comparison group (B).

FIGURE 2
The CAS attention subscale measures focal attention, with a normal mean of 100 ± 15 (SD). Although the majority of subjects in both groups scored within the reference range on this test, the MLPVB patients had a significant improvement in CAS attention scores at the 1-year follow-up (A), whereas the comparison subjects did not (B).

CMS subtests tapping visual and verbal memory were used to assess immediate and delayed memory functions in both (visual and verbal) modalities. Significant variability was noted for immediate verbal memory at baseline, with only 1 subject falling clearly outside of the accepted reference range (Fig 3). Subjects in the MLPVB group showed significant improvement in scores after surgery ($P = .0021$; Fig 3A), whereas the comparison group showed no improvement (Fig 3B).

Visual-Motor Domain
The Grooved Pegboard Test of manual dexterity and speed showed mildly negative z scores in both groups at baseline, with 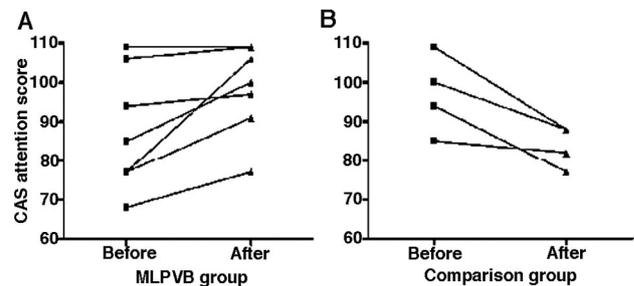some individuals falling well below the accepted norm (Fig 4). The MLPVB group showed a significant increase in manual speed as indicated by z scores at follow-up ($P = .0043$; Fig 4A), whereas the comparison group showed no improvement (Fig 4B). Both groups had normal scores on the BVMI of visuographic skills at baseline and no significant improvement in follow-up.

DISCUSSION
The results of this study demonstrate that surgically restoring portal flow to the liver in children with primary EHPVT results in improved fluid cognitive ability. The subjects showed some neurocognitive abnormalities involving mainly fluid cognitive ability that are entirely consistent with minimal PSE seen in adult subjects with
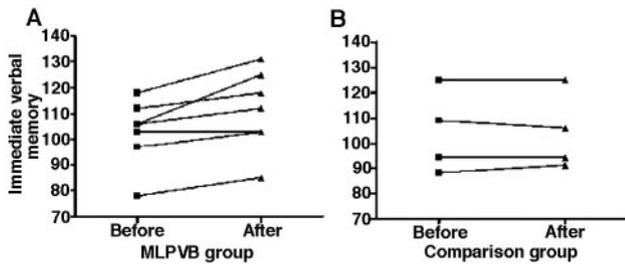
FIGURE 3
The CMS is a test of verbal and visual memory that measures immediate and delayed recall, with a normal mean score of 100 ± 15 (SD). Shown here are the scores of subjects for immediate verbal memory before and 1 year after MLPVB surgery. Although the majority of subjects in both groups scored within the reference range on this test, subjects in the MLPVB group had significant improvement in immediate memory recall 1 year after surgery (A), whereas the comparison group did not (B).
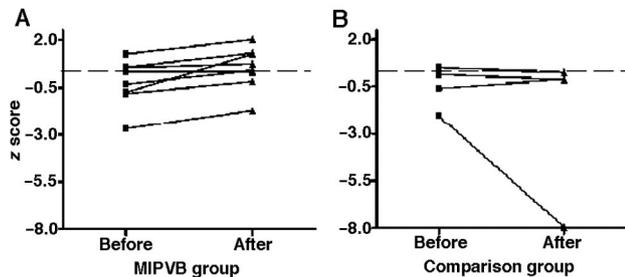

FIGURE 4
Manual dexterity in children with EHPVT before and after surgery was measured with the Grooved Pegboard Test. A, MLPVB patients showed significant improvement in fine motor skills of their dominant hand as shown by a shift in z scores from negative to positive. B, No improvement in z scores was observed in the comparison group.

chronic liver disease.[7] This latter finding suggests that shunting of portal blood from the liver in primary EHPVT can result in PSE and brings to question whether it is as benign a disease as previously thought. The findings provide additional evidence to support the idea that primary EHPVT should be considered as curable by MLPVB.

Many adults with cirrhosis and no overt PSE have minimal PSE that requires sophisticated neurocognitive testing to detect.[7] A recent consensus statement adopted temporarily a 5-test battery for studies of minimal encephalopathy, the psychometric hepatic encephalopathy score.[5] Cognitive defects in patients with minimal PSE seem to relate primarily to attention and fine motor skill, and, whereas affected patients can function in everyday life, they are at risk for performance deficits in educational and vocational situations that require the ability to pay close attention and react quickly (eg, driving and employment in manufacturing).

The battery of tests used in this study was comprehensive and expected to detect neurocognitive defects in 4 major functional domains. We expected the domains of fluid ability (attention, mental speed, working memory, and memory encoding) and visual-motor skills (drawing and fine motor) to be particularly vulnerable to

chronic portal-systemic shunting, as is the case in other chronic medical conditions in children.[6] Each of the subjects in this study had ≥1 test result in these critical domains that clearly fell outside of the reference range. The tests we administered in these domains are pediatric equivalents to measures that are used to detect minimal PSE in adults[5] and should detect abnormalities in the same functional domains. Our results suggest that a narrow battery of tests could be used to detect minimal PSE in children in a manner similar to the 5-test battery used in adults, eliminating the need for the comprehensive and broad testing we performed. The current data suggest that measures of fluid ability should be emphasized in assessments of the neurocognitive sequelae of portal-systemic shunting and, more broadly, of chronic liver disease in children. It should be pointed out that many of the subjects' individual fluid-ability and visual-motor domain test scores fell within the reference range at baseline, although each subject had ≥1 abnormal score. This highlights the need for a battery of tests to be performed to detect minimal PSE. These children did not have overt PSE and were not considered to be disabled, although several of them were receiving special educational assistance. Indeed, broad cognitive indices for the subjects were scored as normal and did not change after MLPVB, at least as judged by the generic tests applied. Additional studies will be needed to determine what group of tests can most effectively detect PSE and whether a global performance score can be developed to provide improved sensitivity and specificity for detecting minimal PSE in children.

Portal-systemic shunting in the absence of liver disease is seen in patients with a variety of congenital vascular defects including persistence of the ductus venosus, intrahepatic veno-venous shunts, and the Abernathy malformation (complete portal-systemic shunt). Case studies in children and adults have shown substantial cognitive defects in patients with congenital portal-systemic shunts.[31–39] We investigated the cognitive function of 2 children with congenital shunts and essentially no effective portal blood flow and found major defects in attention and motor skills.[40] Staged closure of the shunts resulted in normal effective portal blood flow to the liver, and cognitive function substantially improved in follow-up. Although limited, this experience serves to demonstrate the importance of portal-systemic shunting and its inverse, effective portal blood flow, in influencing efficient cognitive processing.

A significant design flaw of the current investigation derives from the population studied. These were all children who were referred to our service and in need of treatment of portal hypertension because of EHPVT. As such, they could not be randomly assigned to "to-treat" or "not-to-treat" groups. The MLPVB offers complete cure of EHPVT, whereas the standard treatment offers only palliation of portal hypertension. Identifying a com-

parison group proved difficult given the "intent-to-treat" design. Other centers report that <50% of children with EHPVT can be treated with MLPVB based on the lack of an appropriate-sized intrahepatic portal vein,[13,14,41] which would suggest that we would identify equal or greater numbers of control subjects for our studies. However, that turned out to not be the case. With increasing experience, we are now able to perform MLPVB in >90% of the patients with primary EHPVT who are referred to our center. Thus, recruiting additional comparison subjects has become increasingly difficult. One could argue that the improvement in cognition may have occurred naturally over the 1-year time frame of this study, unrelated to the surgical therapy. We cannot postulate why that would have occurred. There is a potential "learning effect" if some psychometric tests are repeated too frequently or too soon in the same patient. However, for the measures of fluid brain function that improved in the MLPVB group, practice effects over the time interval studied in this investigation are likely to be minimal.[42] It is highly unlikely that the subjects in the MLPVB group "learned" how to take the tests better by taking them 1 year earlier. Furthermore, the cognitive function in the comparison group did not improve.

Although the specific pattern of test scores and their pattern of improvement with MLPVB were not consistent across individual subjects, improvements were clearly seen for our overall sample in the domains of fluid ability and visual-motor skills. The possibility that the changes observed after successful MLPVB represent regression to the mean cannot be dismissed, because a study design incorporating a control cohort was not possible. However, individual subjects did not score significantly worse on any of the tests in the domains of fluid ability and visual-motor skills that showed improvement for the group as a whole, which is the opposite of what would be expected if individual scores regressed to the group mean. Furthermore, we concurrently studied 4 similar-aged children in whom MLPVB could not be performed and compared the pattern of change after surgery with that seen after successful MLPVB. The limited data show no pattern of improved fluid cognitive ability in these subjects.

The importance of our findings is twofold. From a perspective of understanding the pathophysiology of PSE, we have shown that restoring blood flow to the liver improves cognitive function in children with EHPVT. These findings, along with those from studies in adult patients who have undergone transjugular intrahepatic portal-systemic shunt,[43–45] suggest an inverse relationship between effective portal blood flow and cognitive function. Increasing the efficiency of portal-systemic shunting worsens cognitive function and increases the incidence of PSE, whereas we have shown that increasing effective portal blood flow improves cognitive function. From a perspective of therapy for

EHPVT, it becomes clear that MLPVB is an excellent treatment option. It is similarly effective for treating the complications of portal hypertension[12] and provides effective portal blood flow that other medical and surgical therapies do not. By providing effective portal blood flow, the MLPVB helps to improve fluid cognitive ability and correct coagulation abnormalities.[17] This advantage does not necessarily imply that MLPVB should be performed unless indicated by major complications such as variceal bleeding and hypersplenism. However, if a child with EHPVT can be shown to have neurocognitive deficits in the domains of fluid ability and visual-motor skills, MLPVB surgery should be considered in advance of the onset of major complications.

CONCLUSIONS

Some children with EHPVT have deficits in fluid cognitive ability that are consistent with minimal PSE, and restoration of portal blood flow by MLPVB can improve fluid cognitive function in these patients. The results additionally demonstrate the added value of MLPVB in correcting EHPVT over traditional treatments that just palliate portal hypertension.

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