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Cognitive and Adaptive Functioning after Liver Transplantation for Maple Syrup Urine Disease: A Case Series

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Abstract

MSUD is a complex metabolic disorder that has been associated with central nervous system damage, developmental delays, and neurocognitive deficits. Although liver transplantation provides a metabolic cure for MSUD, changes in cognitive and adaptive functioning following transplantation have not been investigated. In this report we present data from 14 patients who completed cognitive and adaptive functioning testing pre- and one year and/or three years post-liver transplantation. Findings show either no significant change or improvement in IQ scores pre- to post-liver transplantation. Greater variability was observed in adaptive functioning scores, but the majority of patients evidenced either no significant change or improvement in adaptive scores. In general, findings may indicate that liver transplantation curtails additional central nervous system damage and neurocognitive decline providing an opportunity for stabilization or improvement in functioning.

INTRODUCTION

It is estimated that approximately 1 in 185,000 infants worldwide are born with maple syrup urine disease (MSUD), an inherited deficiency of branched chain alpha-ketoacid dehydrogenase activity that impairs the degradation of the branched chain amino acids (BCAAs) valine, leucine, and isoleucine and results in their accumulation in plasma and body tissues (1,2). The accumulation of BCAAs can have devastating effects on cognition, behavior, psychosocial functioning, and overall quality of life (1,3,4). Strict control of

protein intake and close monitoring of plasma BCAA levels are essential for optimal outcome (5). However, even with close supervision, patients with MSUD can deteriorate quickly into metabolic crises as a result of common viral illnesses, infections, injuries, exercise, or physiologic stress (5). Due to the unpredictability of such events, metabolic crises cannot be completely prevented. These episodes alongside chronic amino acid imbalances characteristic of MSUD, have been associated with brain damage, developmental delays, and poor neurocognitive outcomes (3–5).

Previous studies demonstrated greater compromise in cognitive function with prolonged exposure to elevated plasma leucine levels and increasing patient age (1), whereas other studies have shown that age at diagnosis is the best predictor of cognitive functioning (3).

Most have focused on cognitive and developmental outcomes with little attention to “real life functioning”, i.e., adaptive functioning. Such studies typically focus on measures of “innate ability” (e.g., IQ) as opposed to the practical application of skills within community life. A study by Simon and colleagues (6) suggests significant deficits in the real world functioning of adults with MSUD, including lower educational and professional attainment as well as disruptions in personal relationships. Despite the clear deficits described in the literature (1,3–5,7–13) data on tasks of daily living have yet to be consistently discussed.

After biliary atresia, metabolic conditions such as urea cycle defects, tyrosinemia, Wilson’s Disease and crigler najjar syndrome are the second most common disease category leading to liver transplantation in children. A serendipitous finding led to the addition of MSUD to this list of indications for liver transplantation (4). Liver transplantation in patients with MSUD successfully corrects BCAA levels, eliminates metabolic crises, and allows for the liberalization of diet restrictions (4). The experience at our center has provided good evidence of the medical benefits of liver transplantation for patients with MSUD and suggests that liver transplantation holds promise for improving the long-term outcomes for individuals with MSUD (4).

The initial research on liver transplantation for MSUD focused primarily on medical outcomes (4). However, given the similarities reported in the literature suggesting the association of neurocognitive deficits with other diseases typically treated with liver transplantation, e.g., biliary atresia and infantile hepatic cirrhosis, (14) and the reported cognitive outcomes for these populations (14–17), we expect generally comparable results. For example, previous research suggests that pediatric patients perform in the “low normal range” of cognitive and developmental functioning following transplantation (14–17) The few studies that have examined pre- and post-transplant findings in pediatric populations have suggested general stability in cognitive functioning scores following liver transplantation (18,19).

The primary aims of the current study are to provide information on markers of adaptive and cognitive functioning for a group of patients with MSUD who underwent liver transplantation. To our knowledge, this is the first report of functional outcomes following liver transplantation in this patient population.

MATERIALS AND METHODS

DESIGN

This is a case series of 14 patients with MSUD describing their cognitive and adaptive functioning prior to transplantation and one year post-liver transplantation. We also include data on six of the 14 patients who have also completed cognitive and adaptive functioning three years post liver transplantation.

SAMPLE

Patients with classical MSUD (i.e., the severe form of MSUD) were recruited between 2005 and 2009 from the Hillman Center for Pediatric Transplantation at the Children's Hospital of Pittsburgh of UPMC. Recruitment and study procedures were approved by Committees for the Protection of Human Subjects. The series is comprised of the 14 patients who completed all standard cognitive and adaptive testing pre- and at least one year post-liver transplantation. In addition, a subset of 6 patients who also completed all standard cognitive and adaptive testing three years post-transplantation is included in the series.

MEASURES

The specific measures used to assess functioning have varied over time but have consistently included measures that are typically used with populations from early childhood to late adulthood, exhibit robust psychometric properties, and for which normative data are available.

Cognitive functioning (i.e., innate intellectual abilities that are typically expected to remain stable throughout the lifetime of an individual) was determined by using either the Abbreviated Battery IQ of the Stanford-Binet Intelligence Scales--Fifth Edition (20) or the Wechsler Abbreviated Scale of Intelligence (WASI; (21)). Scores for both cognitive measures are based on a mean of 100 and a standard deviation of 15 (20,21). Both scales were standardized on nationally representative samples and are highly correlated with other Wechsler full scale measures of intelligence ranging from 0.69 to 0.81 for the Abbreviated Battery IQ of the Stanford Binet to 0.81 to 0.92 for the WASI (20,21). The Abbreviated Battery IQ of the Stanford-Binet shows correlations ranging from 0.81 to 0.87 with the overall Stanford Binet Full Scale IQ, and the Full Scale IQ of the Stanford Binet has reliability coefficients ranging from 0.97 to 0.98 (20). Reliability coefficients for the WASI range from 0.92 to 0.98 for its full scale IQ (21). All participants received the Abbreviated Battery IQ of the Stanford Binet pre-transplantation, and 10 out of 14 participants were re-tested one year post-transplantation with the same measure.

Adaptive functioning (i.e., the real life functioning of participants) was determined by using either the Vineland Adaptive Behavior Scale--Second Edition (22) or the Adaptive Behavior Assessment System--Second Edition (ABAS-II; (23)). Both measures are based on a mean of 100 and a standard deviation of 15 (22,23). Both scales are highly correlated with correlations ranging from 0.78 to 0.84 between the Adaptive Behavior Composite of the Vineland and the General Adaptive Composite of the ABAS-II (22,23). Reliability coefficients for the Adaptive Behavior Composite of the Vineland Adaptive Behavior Scale--Second Edition range from 0.83 to 0.96 (22). Reliability coefficients for the General Adaptive Composite of the ABAS-II range from 0.93 to 0.99 (23). All participants received the Vineland Adaptive Behavior Scale--Second Edition pre-transplantation, and 11 out of 14 participants were re-tested one year post-transplantation with the ABAS-II.

Cognitive and adaptive functioning measures were administered by a licensed clinical psychologist.

In addition to the cognitive and adaptive measures, participants also completed a brief demographics form as well as a full battery of medical tests as part of their pre-transplantation work-up including lab studies, echocardiogram, and genetic consultation.

RESULTS

This case series sample included 10 males and 4 females, with a mean age of 11.5 years (SD= 7.1, range 2–22 years) at the time of transplantation (Table 1). Patient and graft survival is 100% and liver function was normal at follow-up.

Ninety-three percent of the participants reported at least one lifetime hospitalization related to their MSUD diagnosis (range 0–35 hospitalizations) and the majority of participants (57%) had four or more hospitalizations. The majority of participants (72%) reported at least one “metabolic crisis episode” prior to transplantation. Mean leucine levels for the sample were 271 $\mu\text{mol/L}$ (Range = 85–480; SD = 124) prior to liver transplantation on a protein restricted intake diet, and 164 $\mu\text{mol/L}$ (Range = 70–440; SD = 113) post-liver transplantation on an unrestricted protein intake diet. Mean leucine to valine ratios were 0.89 (range = 0.21–1.73; SD = 0.40) prior to liver transplantation and 0.69 (range = 0.41–0.94; SD = 0.14) post-liver transplantation. Mean leucine to isoleucine ratios were 2.07 (range = 0.39–4.64; SD = 1.2) prior to liver transplantation and 2.23 (range = 1.30–7.0; SD = 1.48) post-liver transplantation (Table 2).

The majority of participants (86%) required early intervention services focused on the development of cognitive, social, physical, and emotional functioning that included speech therapy (71%), physical therapy (43%), and/or occupational therapy (43%) services. Six participants had secondary diagnoses of Attention Deficit Hyperactivity Disorder (ADHD), of which three also had cognitive impairments, developmental disabilities, or motor delay and spasticity. One participant had a secondary diagnosis of cerebral palsy and two other participants had developmental, motor, and speech delays (Table 2).

COGNITIVE FUNCTIONING

Pre-transplant IQ scaled scores (Figure 1) ranged from 61 to 100 (Median = 76, Interquartile Range = 66.3–91.8) with the majority of the participants (57%) scoring in the borderline to normal range of functioning (i.e., IQ ≥ 75). IQ scaled scores one year post-transplantation ranged from 58 to 103 (Median = 85, Interquartile Range = 69.3–97.3) with 71% of participants falling in the borderline to normal range of functioning. Nine participants (64% of the sample) showed an increase in scores (3–21 points), four participants (29% of the sample) showed a decrease in IQ scaled scores (3–9 points), and one participant showed no change in scores. For most participants (57% of the sample) the changes in IQ scaled scores were ≤ 6 points and within the range of typically observed confidence intervals of ± 4 –6 points for Full Scale IQs for Stanford Binet and Wechsler measures (24). For the remainder of the group (43%) changes in score ranged from 9–21 points with five out of six participants (36%) displaying a positive change in score pre- to post-liver transplantation and one participant (7%) displaying a 9 point drop in IQ score pre- to post-liver transplantation. Overall findings suggest that for the majority of participants (57%) IQ scaled scores remained stable (i.e., remained within the expected confidence interval) following liver transplantation.

ADAPTIVE FUNCTIONING

Adaptive functioning scaled scores (Figure 2) pre-liver transplantation ranged from 47 to 117 (Median = 84.5, Interquartile Range = 63–93.8) with 50% of the sample scoring in the borderline to above average range of functioning (Adaptive scaled score ≥ 75). Adaptive functioning scaled scores one year post-transplantation ranged from 40 to 110 (Median = 84.5, Interquartile Range = 67–100.8) with 71% of the sample scoring in the borderline to average range of functioning. Most participants evidenced changes in adaptive functioning scaled scores. Six participants (43% of the sample) showed increases in adaptive functioning

scaled scores (2–30 points), six participants (43% of the sample) showed decreases in adaptive functioning scaled scores (3–15 points), and two participants showed no change in score at all. For most participants (57% of the sample) the changes in adaptive functioning scaled scores were ≤ 8 points and not clinically significant. For three participants (21.4%) post-transplant adaptive functioning scaled scores were 14–30 points above their measured adaptive functioning scaled score pre-transplantation. For the other three participants (21.4%) post-transplant adaptive functioning scaled scores were 11–15 points below their measured adaptive functioning scaled score pre-transplantation. Overall findings suggest greater variability and change in adaptive functioning scores pre- to post-transplantation, with the majority of the sample (57%) showing no clinically significant change in adaptive functioning scaled scores.

Findings for the subgroup of six patients who also completed cognitive and adaptive functioning testing three years post-transplant (Figures 3 and 4) suggest a similar pattern to that found at one year post-transplantation. Of the six participants four showed increases in IQ scaled scores from one-year to three-years post-transplantation (1–12 points), and two showed decreases in IQ scaled scores from one-year to three-years post-transplantation (5–12 points). For half of this smaller group of six participants changes in IQ scaled scores were ≤ 6 points and within the range of typically observed confidence intervals signifying no significant change in scores (24). For the other three participants, two had significant increases in IQ scores (≥ 10 points) and one participant had a significant decrease in IQ score ($=12$ points). In regards to adaptive functioning all participants showed increases in adaptive functioning scaled scores from one-year to three-years post-transplantation (1–19 points), with the majority of this smaller sample of six participants (67%) showing changes ≤ 7 points. Overall the findings suggest that for the majority of participants scores either remained stable or improved following liver transplantation.

DISCUSSION

This is the first study of cognitive and adaptive functioning in patients with MSUD before and following liver transplantation. Previous research focused on the medical management and cognitive outcomes but provided limited longitudinal follow-up, or discussion of adaptive functioning.

Not surprisingly, a significant proportion of patients with MSUD in our series functioned below the normal range of intelligence and most had below average levels of adaptive functioning. These findings highlight the challenges faced by patients with MSUD. Furthermore the data show a pattern of high neurological comorbidity (e.g., ADHD, developmental delay, spastic diplegia) and special developmental needs (e.g., early intervention services, physical therapy, occupational therapy, and/or speech therapy needs).

The majority of participants had either stable IQ scores following liver transplantation or significant improvements. Adaptive functioning scores were more variable pre- to post-liver transplantation in our participants but showed no overall trend for improvement or deterioration. Examination of the six participants who provided three-year post-transplant data suggests stabilization or improvement in both IQ and adaptive functioning scores across time. The findings are encouraging given that the majority of our group was comprised of young children (i.e., children under 10 years of age) who continue to attain skills in parallel to a non-MSUD normative group, and given that IQ is generally expected to remain stable throughout a “normal individual’s lifetime”. The findings are positive signs of developmental gains. For most participants (8 out of 14) their post-transplant IQ scores remained within a few points of their pre-transplant score, suggesting that pre-transplant status could be the most powerful determinant of outcome. However, for a number of our

participants significant improvements were evident. Taken together, these findings suggest that patients transplanted early in life, before experiencing brain damage, may benefit most from liver transplantation with regard to neurocognitive outcome.

Despite the study's novelty in reporting on adaptive functioning in an MSUD sample and the relatively large size of this case series (given the rarity of MSUD), there are some limitations. First, the sample was not large enough to formally test hypotheses regarding change over time or associations between variables. Second, we included a broad range of participant age (2–22 years) in a small sample which limited our ability to explore the possible impact of age on outcomes. Third, we only report early (i.e., one year) outcomes for the full cohort, although six participants who were assessed at three years showed a similar pattern we do not know if further gains in cognitive or adaptive functioning scores could emerge with the passage of time. Lastly, we were not able to longitudinally examine patients who did not proceed to transplantation in order to compare their patterns of cognitive and adaptive functioning to those who did.

Despite these limitations, this study provides insight into the cognitive and adaptive functioning of patients with MSUD following liver transplantation. Findings are encouraging showing metabolic stability with diet liberalization and the potential for optimizing development and skill acquisition in our patient population which is one of the primary aims of treatment. Future research should focus on assessing the evolution of functioning in these areas over time in populations of patients with MSUD who forego liver transplantation.

References

1. Hoffmann B, Helbling C, Schadeewaldt P, Wendel U. Impact of longitudinal plasma leucine levels on the intellectual outcome in patients with classic MSUD. *Pediatric Research*. 2006; 59(1):17–20. [PubMed: 16326996]
2. Strauss, K.; Puffenberger, EG.; Morton, DH. Maple Syrup Urine Disease, GeneReviews, initial posting January 2006. [Last accessed Dec. 2009]. 2006 Available from: <http://www.ncbi.nlm.nih.gov/bookshelf/br.fcgi?book=gene&part=msud>
3. le Roux C, Murphy E, Hallam P, Lilburn M, Orlowska D, Lee P. Neuropsychometric outcome predictors for adults with maple syrup urine disease. *Journal Inherited Metabolic Disease*. 2006; 29(1):201–202.
4. Strauss K, Mazariegos GV, Sindhi R, Squires R, Finegold DN, Vockley G, Robinson DL, Hendrickson C, Virji M, Cropcho L, Puffenberger EG, McGhee W, Seward LM, Morton DH. Elective liver transplantation for the treatment of classical maple syrup urine disease. *American Journal of Transplantation*. 2006; 6(3):557–564. [PubMed: 16468966]
5. Morton DH, Strauss KA, Robinson DL, Puffenberger EG, Kelley RI. Diagnosis and Treatment of Maple Syrup Disease: A Study of 36 Patients. *Pediatrics*. 2002; 109(6):999–1008. [PubMed: 12042535]
6. Simon E, Schwarz M, Wendel U. Social outcome in adults with maple syrup urine disease (MSUD). *Journal Inherited Metabolic Disease*. 2007; 30:264.
7. Clow C, Reade TM, Scriver CR. Outcome of early and long-term management of classical maple syrup urine disease. *Pediatrics*. 1981; 68(6):856–862. [PubMed: 6798541]
8. Couce Pico M, Castineiras Ramos DE, Boveda Fontan MD, Iglesias Rodriguez AJ, Cocho de Juan JA, Fraga Bermudez JM. Avances en el diagnostico y tratamiento de la enfermedad de jarabe de arce, experiencia en Galicia. [Advances in the diagnosis and treatment of maple syrup urine disease: experience in Galicia (Spain)]. *Anales de Pediatría*. 2007; 67(4):337–343. [PubMed: 17949643]
9. Emory E, Brown RT, Savoie T, Sexson S. A case study of maple syrup urine disease, dietary treatment and neuropsychological performance. *Neuropsychiatry, Neuropsychology, and Behavioral Neurology*. 1992; 5(1):60–63.

10. Hilliges CAD, Wendel U. Intellectual performance of children with maple syrup urine disease. *European Journal of Pediatrics*. 1993; 152(2):144–147. [PubMed: 8444223]
11. Kaplan P, Mazur A, Field M, Berlin JA, Berry GT, Heidenreich R, Yudkoff M, Segal S. Intellectual outcome in children with maple syrup urine disease. *Journal of Pediatrics*. 1991; 119(1 Pt 1):46–50. [PubMed: 2066858]
12. Nord A, vDW, Greene C. Developmental profile of patients with maple syrup urine disease. *Journal Inherited Metabolic Disease*. 1991; 14(6):881–889.
13. Nyhan W, Wulfeck BB, Tallal P, Marsden DL. Metabolic correlates of learning disability. *Birth Defects: Original Article Series*. 1989; 25(6):153–169. [PubMed: 2605319]
14. Stewart SM, Kennard BD, Waller DA, Fixler D. Cognitive function in children who receive organ transplantation. *Health Psychology*. 1994; 13(1):3–13. [PubMed: 8168468]
15. Gilmour S, Adkins R, Liddell GA, Jhangri G, Robertson CM. Assessment of Psychoeducational Outcomes After Pediatric Liver Transplant. *American Journal of Transplantation*. 2009; 9(2):294–300. [PubMed: 19067656]
16. Schulz KH, Wein C, Boeck A, Rogiers X, Burdelski M. Cognitive performance of children who have undergone liver transplantation. *Transplantation*. 2003; 75(8):1236–1240. [PubMed: 12717209]
17. Alonso EM, Sorensen LG. Cognitive development following pediatric solid organ transplantation. *Current Opinion in Organ. Transplantation*. 2009; 14:522–525.
18. Kennard B, Stewart S, Phelan-McAuliffe D, Waller D, Bannister M, Fioravani V, Andrews W. Academic outcome in long-term survivors of pediatric liver transplantation. *Journal of Developmental & Behavioral Pediatrics*. 1999; 20(1):17–23. [PubMed: 10071941]
19. Stewart SM, Uauy R, Waller D, Kennard B, Benser M, Andrews WS. One year follow-up of mental and motor development and social competence in pediatric patients receiving successful liver transplantation. *Journal of Pediatrics*. 1989; 114:574–581. [PubMed: 2647947]
20. Roid, GH. *Stanford Binet Intelligence Scales-Fifth Edition*. 5. Itasca: The Riverside Publishing Company; 2003.
21. PsychCorp. *Wechsler Abbreviated Scale of Intelligence (WASI) Manual*. 1. San Antonio: Harcourt Assessment, Inc; 1999.
22. Sparrow, SS.; Cicchetti, Domenic V.; Balla, David A. *Vineland Adaptive Behavior Scales*. 2. Circle Pines: AGS Publishing; 2005.
23. Harrison, PL.; Oakland, Thomas. *Adaptive Behavior Assessment System*. 2. San Antonio: Harcourt Assessment Inc; 2003.
24. Sattler, JM. *Assessment of Children Cognitive Foundations*. 5. La Mesa: Jerome M. Sattler, Publisher Inc; 2008.

Cognitive Functioning

Fig. 1.
Cognitive functioning scores pre- and one year post-liver transplantation

Fig. 2.
Adaptive functioning scores pre- and one year post-liver transplantation

Cognitive Functioning

Fig. 3.
Cognitive functioning scores pre, one-year, and three years post-liver transplantation.

Fig. 4.
Adaptive functioning scores pre, one-year, and three years post-liver transplantation.

Table 1

Demographic Characteristics of Sample

Age at Transplantation Mean/SD (range)	11.5/7.1(2–22)
*Median Reported Family Income	\$71,000–80,000 (<\$12,000 to >\$80,000)
Gender N(%)	
Male	10 (71)
Female	4(29)
Ethnicity N(%)	
Asian	2(14)
Caucasian	11(79)
Latino	1(7)
**In Special Education N(%)	
Yes	9(64)
No	4(29)
Not in School	1(7)

* These figures are based on the median reported by participating families and are based on N=14.

Table 2

Clinical Data by Participant

Part. #	Age at MSUD Diagnosis in Days	Age at Transplant in Years	Number of Reported Hospitalizations prior to Transplant	Number of Reported Crises Prior to Transplant	Mean Leucine Levels (μmol/L) Pre-Transplant*	Leucine Levels (μmol/L) Day Post-Transplant	Required Early Intervention and/or PT/OT/ Speech Services	Enrolled in Special Education pre and/or post	Pt has ADHD diagnosis and/or has developmental delays
1	9	9.8	10	10	275	130	Y	Y	Y
2	10	20.5	35	31	85	70	Y	Y	Y
3	31	3.6	6	6	125	70	Y	Y	Y
4	15	2.2	1	0	370	100	Y	Not in school	N
5	600	21.7	5	4	325	170	Y	Y	Y
6	8	21.4	4	4	480	140	Y	N	Y
7	1	5.8	1	0	110	330	Y	Y	N
8	10	8.9	1	10	265	130	Y	Y	Y
9	12	7.6	0	0	330	130	Y	Y	Y
10	17	10.2	15	15	90	90	Y	Y	Y
11	6	14.3	2	2	405	310	Y	N	N
12	7	7.2	20	Not reported	285	80	Y	Y	Y
13	14	5.6	7	5	355	110	N	N	N
14	13	22	6	4	295	440	N	N	N

* Mean leucine levels pre-transplant were based on the average of two laboratory readings prior to transplantation except for Participant number 6 for whom only one reading was available in the medical record. Normal leucine ranges are 30–200 μmol/L for children (i.e., aged ≤18 years) and <220 μmol/L for adults.

Appendix IQ and Adaptive Functioning Scaled Scores by Participant Pre- and 1-year Post-Liver Transplantation

Part. #	Pre-transplant IQ Scaled Score (M=100, SD=15)	1 year Post-Transplant IQ Scaled Score	Change in IQ Scaled Score Pre- to Post-Transplant	Clinically significant Change	Pre- Transplant Adaptive Functioning Scaled Score (M = 100, SD = 15)	1 year Post-Transplant Adaptive Functioning Scaled Score	Change in Adaptive Functioning Scaled Score Pre- to Post-Transplant	Clinically Significant Change
1	61	58	-3	N	60	52	-8	N
2	70	67	-3	N	47	49	+2	N
3	67	58	-9	Y/-	55	40	-15	Y/-
4	70	91	+19	Y/+	83	80	-3	N
5	76	79	+3	N	90	76	-14	Y/-
6	91	100	+9	Y/+	107	107	0	N
7	97	97	0	N	86	100	+14	Y/+
8	61	70	+9	Y/+	64	72	+8	N
9	85	91	+6	N	86	86	0	N
10	100	103	+3	N	92	98	+6	N
11	76	89	+13	Y/+	73	103	+30	Y/+
12	64	79	+15	Y/+	69	85	+16	Y/+
13	94	98	+4	N	99	84	-15	Y/-
14	85	81	-4	N	117	110	-7	N