UNIVERSITY OF MINNESOTA
Driven to Discover℠

Cognitive outcomes in Hurler syndrome following transplant before age 12 months

Spurlock, K.[1], Orchard, P.J.[2], Miller, W.[2], Lund, T.[2], Kaizer, A.[3], Eisengart, J.B.[2],

[1]College of Biological Sciences, University of Minnesota, [2]Department of Pediatrics, University of Minnesota Medical School, [3]Department of Biostatistics and Informatics, University of Colorado, Colorado School of Public Health

BACKGROUND

- Mucopolysaccharidosis (MPS) type I is a rare autosomal recessive LSD caused by deficiency in the enzyme α-L-iduronidase.
- Severe form of MPSI, Hurler syndrome, is characterized by progressive neurological involvement and multisystem disease resulting in death by end of early childhood if untreated.
- Individuals with Hurler syndrome follow a predictable trajectory of normal cognitive development in first year of life, slowing in second year, and rapid decline thereafter.
- Allogeneic hematopoietic stem cell transplantation (HCT) is the standard of care as it stabilizes deterioration and extends survival.
- Enzyme replacement therapy (ERT) as an adjunct to HCT reduces morbidity and mortality and may lead to more favorable cognitive outcomes.
- Overwhelming evidence that earlier treatment with HCT leads to improved cognitive outcomes.

OBJECTIVE

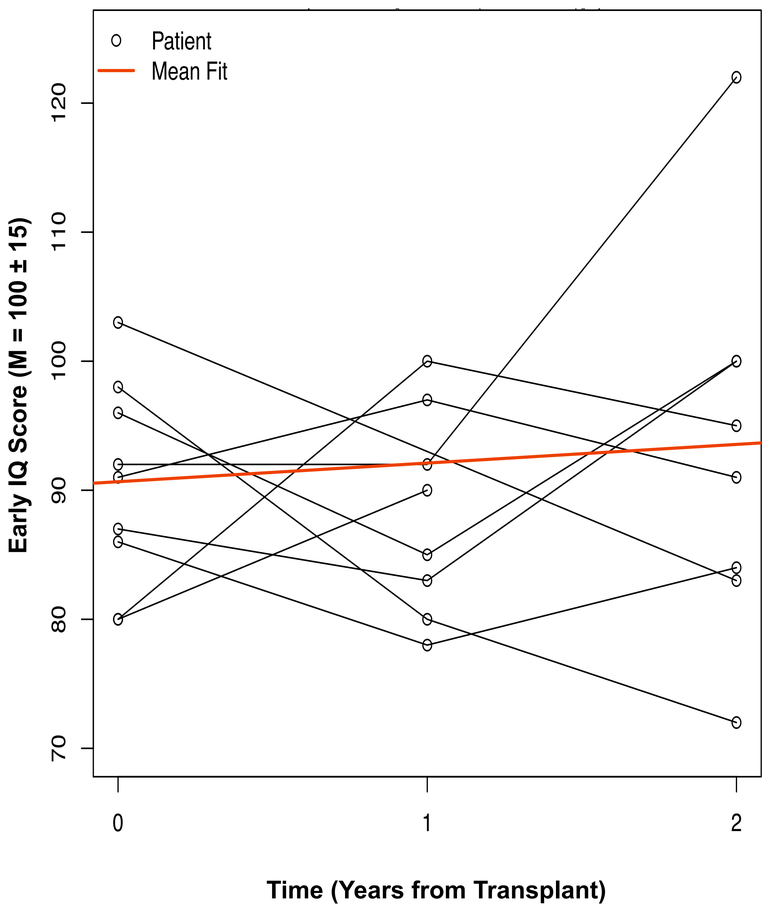
To characterize cognitive outcomes of patients with Hurler syndrome transplanted prior to 12 months of life.

METHODS

- Assessed cognitive outcomes of 8 patients with Hurler syndrome:
  - Transplanted at less than 12 months of age
  - Transplanted since 2005 to reflect modern HCT practice
  - All patients received ERT in peri tranplant period
- Longitudinal cognitive follow up data available at least 2 years following HCT for all patients.
- Examined cognitive scores before transplant and at 1 and 2 years following HCT.
- Early IQ scores (IQ) were measured with the Mullen Scales of Early Learning and Bayley Scales of Infant and Toddler Development, Third Edition.
- Early IQ scores were analyzed longitudinally. Generalized estimating equations were used with robust variance estimation to determine the mean fit and p-value with an autoregressive (AR1) correlation structure to account for correlated observations.

RESULTS

IQ OVER TIME



- IQ scores at 2 years following HCT were not different from baseline $P = 0.63$.

Patient Characteristics

Values are mean (SD) or N (%) unless otherwise indicated.

	MPS IH
N	8
Male	3 (37.5%)
Age (months) at Transplant	8.74 (1.96)
Median (range)	8.76 (5.03-11.93)
ERT delivery	
IV	8
IV + IT	4
Early IQ Score:	
Baseline	91.6 (7.35)
Year 1	87.9 (8.55)
Missing Year 1	1 (12.5%)
Year 2	93.4 (15.0)

- Five patients (62.5%) had a 2-year post-HCT IQ score **equal to or higher than** their baseline IQ score
  - Average change = 12.4 points
- Three patients (37.5%) had a 2-year post-HCT IQ score declined from baseline
  - Average loss = 12.7 points

DISCUSSION

- No evidence of loss in IQ points from time period prior to HCT to 2 years afterward.
- Likely cognitive benefit when transplant is conducted at younger than 12 months of life.
- Finding is different from the general literature which has a broader range of transplanted children and shows there is generally a loss of IQ points following HCT.
- Findings further support research that indicates earlier treatment leads to favorable outcomes.
- Important at the dawn of newborn screening.

FUTURE DIRECTIONS

- Longer-term analyses of a larger cohort transplanted at less than 12 months to determine if cognitive outcomes remain superior from those transplanted at older ages.
- Compare this group to children transplanted at 12 months and older while controlling for additional factors such as baseline IQ, transplant preparation, and ERT.