JIMD Reports
DOI 10.1007/8904_2016_31

CASE REPORT

Cognitive Development in a Young Child with Mucolipidosis Type IV: A Case Report

Evelyn L. Fisher • Rose A. Sevcik • MaryAnn Romski

Received: 18 August 2016 / Revised: 11 November 2016 / Accepted: 28 November 2016 / Published online: 03 January 2017

Abstract Mucolipidosis Type IV (ML IV) is an autosomal recessive genetic disorder characterized by severe psychomotor impairments and ophthalmologic abnormalities. Reports on the cognitive development of people with ML IV are limited, but suggest that achievement of language and cognitive milestones varies between a 3- and 18-month level. There is also variability in reports of whether people with ML IV make developmental progress, regress, or remain static after infancy. This study examines the longitudinal development of a young child with ML IV who participated in an augmentative and alternative communication (AAC) intervention.

At 26 months, the child displayed significant developmental delays on direct assessment, with the exception of a possible relative strength in receptive language. An examination of adaptive behavior over time indicated improvements in raw scores but declines in standard scores across all domains. She learned to use 13 new words with a speech generating device (SGD) by the end of intervention.

These results add to literature on the clinical manifestations of ML IV and indicate that although children with this disorder have deficits in many domains, they may be most severely affected in gross motor or oral motor development and have a relative strength in receptive language. Moreover, this child made progress in all domains of adaptive functioning, but at a slower pace than typically developing children. She also gained expressive vocabulary in the AAC intervention, and this may have supported her development in other areas.

Communicated by: Maurizio Scarpa, M.D, Ph.D

E.L. Fisher (✉)
Psychology Department, Georgia State University, PO Box 5010, Atlanta, GA 30302, USA
e-mail: Efisher7@student.gsu.edu

R.A. Sevcik · MA. Romski
Georgia State University, PO Box 5010, Atlanta, GA 30302, USA

Introduction

Background

Mucolipidosis Type IV (ML IV) is a lysosomal storage disorder characterized by severe psychomotor impairments and ophthalmologic abnormalities (Amir et al. 1987). It was first described in 1974 by Berman and colleagues (Berman et al. 1974). ML IV affects approximately 1 in 40,000 Ashkenazi Jewish births and is very rare in other populations. The disorder is caused by a mutation in the MCOLN1 gene, which codes for the cation channel protein mucolipin 1(Wakabayashi et al. 2011). The exact mechanism by which the mutation results in the clinical presentation of MLIV is not fully understood, but the disruption in normal cell function due to an absence of mucolipin 1 is believed to cause damage and dysfunction in many systems of the body. As such, a variety of medical comorbidities are characteristic of ML IV. Common digestive complications observed in people with ML IV are achlorhydria and anemia (Geer et al. 2010). Ophthalmologic abnormalities often include corneal opacity and retinal degeneration. Vision in people with MLIV is thought to be close to normal early in life, but impairments are typically severe by the teenage years (Geer et al. 2010). Delayed motor development is often the first cause for concern among parents of children with ML IV. Muscular abnormalities initially present as hypotonia, and often gradually transform into spasticity. The majority of people with ML IV are not able to walk independently (Mucolipidosis type IV 2015). Neuroanatomical studies reveal that people with ML IV exhibit decreased white matter volume, especially in the cerebellum (Schiffmann et al. 2014).

Reports on the neurodevelopment of people with ML IV are limited in number, and consist predominantly of case studies, as well as a few studies of larger samples. They suggest that motor milestones achieved are usually between a 12- and 15-month level, whereas cognitive milestones achieved may vary between a 3- and 18-month level (Amir et al. 1987). Results of assessments of people with ML IV must be interpreted with great caution, however, due to the difficulty in making valid inferences about cognition from tasks that may be inaccessible to people with severe motor impairments (Martin et al. 2008). There is also variability in reports of whether people with ML IV make developmental progress, regress, or remain static after infancy (Amir et al. 1987; Schiffmann et al. 2014).

The prognosis for speech development is generally poor. Although a few more mildly affected individuals have been identified in the literature, most people with ML IV do not develop speech beyond a few single words, and many have no intelligible speech at all (Amir et al. 1987). Despite severe impairments in speech production, several studies have indicated a relative strength in receptive language, and a few people with ML IV have demonstrated success in learning to use up to 50 sign language words to communicate (Schiffmann et al. 1993). Together, these findings strongly suggest that augmentative and alternative communication, or AAC, is the ideal approach for meeting the communication needs of people with ML IV and supporting quality of life and inclusion for those affected by the disorder. Research suggests that people with severe intellectual disability and/or sensorimotor impairments can successfully learn to communicate using AAC (Romski and Sevcik 2005). AAC modalities include unaided symbols, such as sign language and gesture, as well as aided communication supported by external symbols, such a pictures on a speech generating device (SGD).

The purpose of this case study was to describe the development of a young child with ML IV who participated in a longitudinal parent-coached augmented language intervention study. This case study adds to the literature on clinical manifestations and course of ML IV and provides information on one child's outcome following a specific early intervention technique for addressing the characteristic neurodevelopmental deficits associated with the disorder. We examined her initial developmental profile, change in skills over time, and effect of AAC on her communication skills.

Case Report

Methods

Participant

The child was a Caucasian female. Parents first observed delayed motor development when she was 4 months of age. She was subsequently diagnosed with ML IV after a neurological evaluation and genetic testing. She was referred to the study by the state public early intervention program for infants and toddlers with developmental disabilities and began study participation at 26 months of age. Although the intervention was intended to supplement the clinical services that children received outside of the study, this child did not receive any additional speech-language therapy until after the post-intervention time point. At this point, she began receiving 90 min of speech-language therapy per week in a public co-taught preschool setting. Her hearing and vision were tested prior to study participation. Her hearing acuity was within normal limits and her visual acuity was possibly slightly impaired. In terms of motor skills, she was unable to walk or crawl throughout the duration of the study, and used a stroller for mobility. However, she had sufficient control of upper extremities to independently reach for and press large buttons on an SGD. The child's mother also participated in the study as the primary reporter for most measures and a communication partner. At the time of the study, she had completed a master's degree in special education and was a homemaker. English was the primary language spoken at home, and Hebrew was a secondary language. The household included the child's mother, father, and one brother (age 4 years).

Procedure

The mother–child dyad participated in a randomized controlled trial of parent-coached augmented language interventions for young children with significant developmental delays (Romski et al. 2016). The mother–child dyad was randomly assigned a waitlist period, followed by the Augmented-Input and Output Hybrid (AC-IO) condition. In this condition, children were encouraged to use an SGD to communicate using both adult modeling and prompting. The child received the Tech Talk by Advanced Multi-Media Devices Incorporated (AMDI) as the SGD. The intervention protocol included 24 sessions implemented over

Table 1 Measures administered to the participant

	Time Point	Age	MSEL	VABS	SICD	CDI	CALC	PPVT
T1	Three months pre-intervention	26	×	×	×	×	×	
T2	At start of intervention	29	×	×	×	×	×	
T3	Post-intervention	37			×	×	×	
T4	Three months post-intervention	41			×	[a]	×	
T5	Six months post-intervention	45			×	[a]	×	
T6	Twelve months post-intervention	50		×	×	×	×	×

[a] Measure was administered, but not returned by parent

20 weeks. Each session lasted 30 min, and consisted of three 10 min activities: play, book, and snack. The first 18 intervention sessions were conducted in the Toddler Language Intervention Project Lab at Georgia State University. The final six sessions were conducted in the child's home. Target vocabulary words for the child were chosen collaboratively by the parent and the project's speech-language pathologist. When the child mastered the use of their target vocabulary set, additional words were added to it.

Over the course of the 24 sessions, the parent was taught to implement the components of the intervention and gradually led the intervention sessions. For the first eight sessions, the project's interventionist implemented the intervention while the speech-language pathologist explained the techniques to the parent and answered his or her questions. For sessions 9–10, the parent implemented the intervention during the last 10 min, or snack. For sessions 11–12, the parent implemented the intervention during the last 20 min, or book and snack. Beginning in session 13, the parent led the entire 30 min session, including all three activities. The interventionist continued to coach the parent as needed throughout all of the sessions.

Measures

In order to characterize participants and evaluate the effectiveness of the intervention, the child was assessed at six time points: three months prior to intervention, at the start of intervention, post-intervention, three months post-intervention, six months post-intervention, and twelve months post-intervention. Table 1 lists the assessments and the time of their administration. Standardized assessment measures included the *Mullen Scales of Early Learning* (MSEL) (Mullen 1995), *Vineland Adaptive Behavior Scales, Second Edition* (VABS-II) (Sparrow et al. 2005), *Sequenced Inventory of Communication Development-Revised* (SICD-R) (Hedrick and Prather 1975), *MacArthur-Bates Communication Development Inventory* (CDI) *Words and Gestures* form (Fenson et al. 2006), *Clinical Assessment of Language Comprehension* (CALC) (Miller and Paul 1995), and *Peabody Picture Vocabulary Test, Fourth Edition* (PPVT-4) (Dunn and Dunn 2007). Tests were administered by the project's speech-language pathologist. Interventionists did not administer any assessments in order to avoid potential bias.

In addition to standardized assessment, transcripts of intervention sessions were created using the Systematic Analysis of Language Transcripts (SALT) program (Miller and Chapman 1985) in order to characterize parent and child communication over the course of the intervention (Romski et al. 2010). Trained, reliable transcribers used an event-based coding scheme to document each instance in which a child used a target vocabulary word and the mode in which he or she used it: spoken, augmented, or both spoken and augmented. Communication also was coded as prompted or unprompted.

Finally, parents completed the Parenting Stress Index (PSI) (Abidin 1995) and the Parent Perception of Language Development (PPOLD) (Romski et al. 2011) measures in order to allow the investigators to examine the experiences and views of parents participating in the study.

Results

Initial Developmental Profile

At 26 months, the child performed in the Very Low range ($T \leq 20$) on all domains of the MSEL, with the exception of Receptive Language, which was a relative strength ($T = 37$; AE = 22 months.). Her most severe delays were in Gross Motor ($T \leq 20$; AE = 7 months) and Expressive Language ($T \leq 20$; AE = 7 months), with Fine Motor somewhat less delayed ($T \leq 20$; AE = 13 months). Additionally, the VABS-II indicated Moderately Low abilities across Communication, Daily Living Skills, and Socialization, and Low abilities in Motor skills. At the subdomain level of the VABS-II, her most severe delays

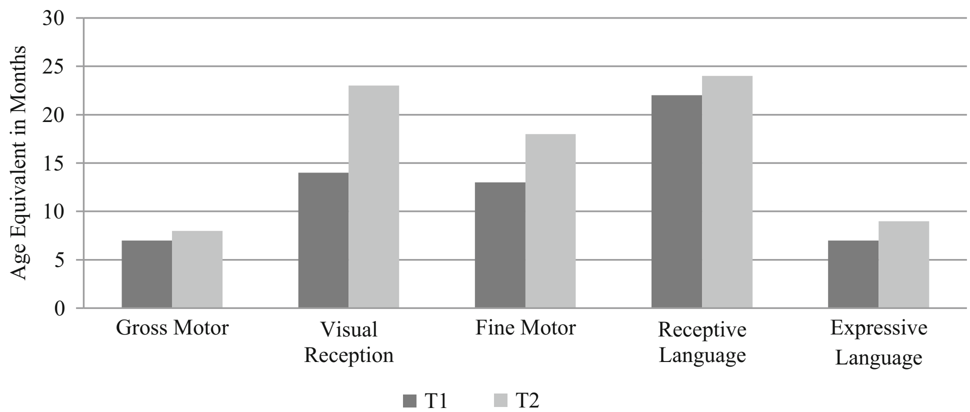

Fig. 1 MSEL at T1 and T2

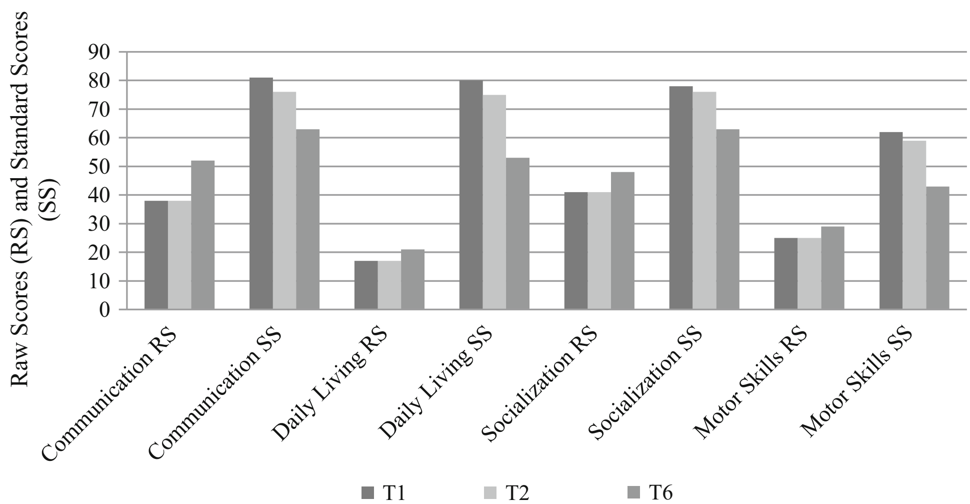

Fig. 2 VABS raw and standard scores at T1, T2, and T6

were again in Gross Motor (*v*-scale score = 6; AE = 5 months) and Expressive Communication (*v*-scale score = 10; AE = 13 months). Fine Motor was also at a similar level (*v*-scale score = 10; AE = 14 months). Her Receptive Communication was somewhat stronger (*v*-scale score = 13; AE = 18 months).

Her SICD performance supported a relative strength in receptive language, which was at the 20-month level, compared to expressive language, which was at the 12-month level. On the CDI, the child's mother reported that she understood 273 words, and was able to say one word (the animal sound baa baa). The Emerging Language Stage section of the CALC, an informal measure of early language comprehension that uses known objects and people, indicated that the child responded to joint attention bids and comprehended familiar object names at baseline.

Change in Skills Over Time

At 29 months, the child continued to exhibit Very Low performance in the Gross Motor, Fine Motor and Expressive Language domains of the MSEL. She demonstrated relative strengths in Receptive Language (T = 38; AE = 24 months) and Visual Reception (T = 34; AE = 23 months). A comparison of age equivalent MSEL scores at T1 and T2 was conducted in order to examine the child's progress in relation to gains that would be expected, given three months of maturation. This comparison revealed that the child made gains in all areas, though her progress in Gross Motor was minimal (see Fig. 1).

A comparison of the VABS profile at 26 and 29 months and 50 months revealed improvements in raw scores, but declines in Standard Scores across all domains (see Fig. 2).

Table 2 SICD and CDI scores across time points

	T1	T2	T3	T4	T5	T6
SICD						
Receptive	20	20	24	24	24	24
Expressive	12	12	12	12	12	12
CDI						
Words understood	275	282	290	N/A	N/A	290
Words spoken	1	3	16	N/A	N/A	5

Note: SICD scores represent estimated age equivalence in months, CDI scores represent total items endorsed by the parent from a total of 396 possible words

Between 26 and 29 months, Age-equivalent subdomain scores remained identical for Receptive Communication, Expressive Communication, and Fine Motor, and increased mildly in the Gross Motor domain, from 5 to 7 months AE. Age-equivalent score gains between 29 and 50 months were variable (Receptive Communication +12 months; Expressive Communication +4 months; Gross Motor +1 month; Fine Motor −4 months).

Expressive communication scores on the SICD-R remained at the 12-month level throughout the duration of the study. It is important to note that the SICD-R Expressive items specifically focus on vocalizations and speech, and thus progress in the use of an SGD would not be represented on this test. Receptive communication scores shifted from the 20- to the 24-month level at the post intervention time point, and remained at that level for all follow-up assessments. On the CDI, the number of words that the child's mother reported she understood increased gradually from the three months prior to intervention to post intervention time points, and remained stable at the 12-month follow-up. Words spoken also increased from the three months prior to intervention to post intervention time points, but had declined at the 12-month follow-up (see Table 2). In terms of the CALC, at the post intervention time point, two additional skills appeared in the child repertoire: comprehension of action words and comprehension of words for absent person and objects. At the 12-month follow-up, the child correctly identified 23 words by touching pictures, and received a standard score of 63 and an age equivalent score of 26 months on the PPVT-4, consistent with other measures.

Effect of Language Intervention

The observational coding scheme indicated that the child independently produced one manual sign (eat) in the baseline intervention session. In session 24, she independently produced one manual sign (eat) and 13 different augmented words (applesauce, baby, bar, bee, bucket, cheese, cup, out, play, potty, sing, the end, turn page) spontaneously using the SGD. She did not produce any spoken words during either session. The proportion of her utterances that were intelligible increased from 0.43 to 0.85 between session 1 and 24 due to the use of the augmented words. Her type token ratio, an indication of the diversity in the words she produced, decreased slightly, from 0.16 in session 1 to 0.13 in session 24. Finally, the total number of turns she took in communicative exchanges increased from 48 in session 1, to 120 in session 24.

At follow-up appointments, the child was no longer using the SGD in the home environment because the family had chosen to use a combination of manual signs, facial expressions, and vocalizations as a means of communication instead of the SGD. Parents reported to study staff that they found the SGD too cumbersome for their daily lives, but they were interested in exploring iPad apps as a communication system in the future. However, in her preschool environment, the child continued to use an SGD similar to the one used in the study in order to participate in classroom activities.

Parent Questionnaires

The mother's responses on the PSI indicated average to below average levels of parenting stress throughout the entire durations of the study. Changes over time were marginal. The mother's responses to the POLD were similar to other parents in the sample. A comparison of pre and post intervention PPOLD ratings indicated increased perceptions of child success in communicating, but no change in perceptions of the degree of difficulty the child faces when attempting to communicate.

Discussion

These results add to literature on the clinical manifestations of ML IV and indicate that although children with this disorder have deficits across many domains, they may be most severely affected in gross motor and expressive language development. The child reported on in this study displayed significant developmental delays in these areas, but more mild delays relative to peers in receptive language and visual reception at 29 months. The age equivalence scores observed for this child were also somewhat more advanced than those reported in other studies of people with ML IV (Amir et al. 1987; Schiffmann et al. 2014). Possible explanations for this difference include the individual variation in disorder severity and course, the reporting style of the mother, the content of the direct assessment measures, or the effect of early intervention for the child.

Observations regarding the course of development for the child over the time span of 26–50 months generally suggest progress, though at a slower pace than peers. Consistent increases in skills were apparent on both the MSEL and VABS. Improvements also were observed on the SICD, CDI, and CALC, though not consistently, and no further progress was apparent on these measures after the post-intervention time point. It is difficult to determine whether this suggests a slowing of development, or reflects insufficiency in the measure's ability to capture small changes in the skills of children with developmental disabilities.

She also gained expressive vocabulary via the use of an SGD. This finding is consistent with other studies showing that children with developmental disabilities, including those with complex medical conditions, benefit from language intervention with SGDs (Romski et al. 2008, 2010, 2015). The child's experience expanded her ability to successfully communicate with her family and may have supported her development in other areas. Given the significant motor impairments exhibited in ML IV, the use of an SGD may provide a viable communication approach at a very early age. Optimizing the ability of the individual to participate in social contexts by supporting communication is critical to quality of life among people with developmental disabilities (Sevcik and Romski 2016).

In light of the family's concerns about the SGD being cumbersome, future research in this area might further explore maximizing the convenience and transportability of SGDs. Many improvements have been made in technology in recent years, with the rapidly increasing availability of tablet computer apps for AAC. The child continued to use an SGD at preschool, suggesting that perhaps SGDs are especially valuable in educational environments. This could relate to increased demands on the child or the fact that preschool staff members are less familiar with her compared to her parents, and thus likely to have more difficulty anticipating her needs and interpreting other forms of communication.

Limitations of this report include that it involved only one child with ML IV, and thus the results may not be generalizable to all children with this disorder. It is also important to keep in mind that many issues influence cognitive and linguistic development in children with rare disorders, including both intrinsic and extrinsic factors. Also, our intervention was intensive and focused on parent-implemented intervention so that the child and parent could communicate at home. It may not be feasible for all families. At the same time, Romski et al. 2007 showed that parents were capable of implementing similar intervention with high fidelity to the standardized instructions. Additionally, the very low attrition rate observed in our study (5.6%) indicates that the majority of families were able to complete the intervention program. In conclusion, early language intervention using SGDs that focuses on parent coaching may provide a route for developing communication for children with ML IV.

Acknowledgments We would like to thank the participant and her family. This research was funded by Institute of Education Sciences Grant Number #R324A070122 to MaryAnn Romski.

Synopsis

This longitudinal case study of a child with ML IV suggests that people with this disorder (1) make slowed but measurable developmental progress in early childhood and (2) benefit from augmentative and alternative communication (AAC) interventions.

Author Notes

Contributions of Individual Authors

Evelyn Fisher completed data analysis and drafted the manuscript. Drs. MaryAnn Romski and Rose Sevcik were integrally involved in the conception, design, and implementation of the larger study. They also edited the manuscript and added specific information about the original study and data.

Guarantor Author

Evelyn Fisher serves as the guarantor and accepts responsibility for this work.

Competing Interests

The authors have no competing interests to declare.

Funding

This project was funded by the Institute of Education Sciences, Grant R324A070122 to MaryAnn Romski. The authors confirm independence from the sponsors; the content of this manuscript was not influenced by the sponsors.

Ethics Approval

The study was approved by the Georgia State University Institutional Review Board (IRB), and all procedures were performed in accordance with the ethical standards of the IRB.

Consent Statement

Informed consent was obtained from a parent of each child included in the study.

References

Abidin RR (1995) Parenting stress index: professional manual, 3rd edn. Pediatric Psychology, Charlottesville

Amir N, Zlotogora J, Bach G (1987) Mucolipidosis type IV: clinical spectrum and natural history. Pediatrics 79(6):953–959

Berman ER, Livni N, Shapira E, Merin S, Levij IS (1974) Congenital corneal clouding with abnormal systemic storage bodies: a new variant of mucolipidosis. J Pediatr 84(4):519–526. doi:10.1016/S0022-3476(74)80671-2

Dunn LM, Dunn DM (2007) Peabody picture vocabulary test, 4th edn. PsycTESTS, San Antonio. doi:10.1037/t15144-000

Fenson L, Marchman VA, Thal DJ, Dale PS, Reznick JS, Bates E (2006) MacArthur-bates communicative development inventories, 2nd edn. PsycTESTS, San Antonio. doi:10.1037/t11538-000

Geer JS, Skinner SA, Goldin E, Holden KR (2010) Mucolipidosis type IV: a subtle pediatric neurodegenerative disorder. Pediatr Neurol 42(3):223–226. doi:10.1016/j.pediatrneurol.2009.10.002

Hedrick D, Prather EM (1975) Sequenced inventory of communication development, Revised edn. Western Psychological Services, Torrence

Martin, H. R., Poe, M. D., Reinhartsen, D., Pretzel, R. E., Roush, J., Rosenberg, A., Escolar, M. L. (2008). Methods for assessing neurodevelopment in lysosomal storage diseases and related disorders: a multidisciplinary perspective. Acta Paediatr 97(457), 69–75. 10.1111/j.1651-2227.2008.00651.x

Miller J, Chapman R (1985) Systematic analysis of language transcripts [computer software]. University of Wisconsin, Madison

Miller JF, Paul R (1995) The clinical assessment of language comprehension. Paul H Brookes Pub Co., Baltimore

Mucolipidosis type IV. (2015) Retrieved August 18, 2015 from http://ghr.nlm.nih.gov/condition/mucolipidosis-type-iv

Mullen EM (1995) Mullen scales of early learning manual (AGS ed). American Guidance Service, Circle Pines

Romski M, Sevcik R (2005) Augmentative communication and early intervention: myths and realities. Infants Young Child Interdiscip J Spec Care Pract 18(3):174–185

Romski M, Sevcik RA, Adamson LB, Cheslock M, Smith A (2007) Parents can implement AAC interventions: ratings of treatment implementation across early language interventions. Early Child Serv Interdiscip J Eff 1(4):249–259

Romski MA, Krupa JH, Cheslock M, Sevcik RA, Adamson LB (2008) Language and communication changes in a child with holoprosecephaly: a case report. Med J Speech Lang Pathol 14:10–19

Romski M, Sevcik RA, Adamson LB, Cheslock M, Smith A, Barker RM, Bakeman R (2010) Randomized comparison of augmented and nonaugmented language interventions for toddlers with developmental delays and their parents. J Speech Lang Hear Res 53(2):350–364

Romski M, Sevcik RA, Adamson LB, Smith A, Cheslock M, Bakemana R (2011) Parent perceptions of the language development of toddlers with developmental delays before and after participation in parent-coached language interventions. Am J Speech Lang Pathol 20(2):111–118. doi:10.1044/1058-0360(2011/09-0087)

Romski M, Sevcik RA, Barton-Hulsey A, Whitmore AS (2015) Early intervention and AAC: what a difference 30 years makes. AAC Augmentative Altern Commun 31(3):181–202. doi:10.3109/07434618.2015.1064163

Romski M, Sevcik R, Adamson L, Barton-Hulsey A, Barker RM, Bakeman R, Whitmore A, Smith A (2016). Parent-implemented language intervention for young children with developmental disabilities, manuscript in preparation

Schiffmann R, Grishchuk Y, Goldin E (1993) Mucolipidosis IV. In: Pagon RA, Adam MP, Ardinger HH, Wallace SE, Amemiya A, Bean LJ, Stephens K (eds) GeneReviews. University of Washington, Seattle Retrieved from http://www.ncbi.nlm.nih.gov/books/NBK1214/

Schiffmann R, Mayfield J, Swift C, Nestrasil I (2014) Quantitative neuroimaging in mucolipidosis type IV. Mol Genet Metabol 111(2):147–151. doi:10.1016/j.ymgme.2013.11.007

Sevcik RA (2016) Romski MA (2016) Examining the science and practice of communication interventions for individuals with severe disabilities. Am J Intellect Dev Disabil 121(2):121–138

Sparrow S, Cicchetti D, Balla D (2005) Vineland adaptive behavior scales: survey form manual, 2nd edn. American Guidance Services, Circle Pines

Wakabayashi K, Gustafson AM, Sidransky E, Goldin E (2011) Minireview: Mucolipidosis type IV: an update. Mol Genet Metabol 104:206–213. doi:10.1016/j.ymgme.2011.06.006