Differential Phonological Awareness Skills in Children with Classic Galactosemia: A Descriptive Study of Four Cases

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Received: 28 August 2012 / Revised: 16 October 2012 / Accepted: 12 November 2012 / Published online: 29 December 2012
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Abstract Educational achievement, which for individuals with the metabolic disorder classic galactosemia (GAL) is significantly lower than in the wider population, correlates with self-reported quality of life. Phonological awareness skills underpin the development of literacy, and although literacy is a key contributor to successful academic outcomes, no study to date has investigated phonological awareness skills in children with GAL. This study investigated phonological awareness (PA) in four school-aged children with the disorder, two of whom were siblings. Age range for the children was 7 years 7 months to 9 years 2 months. Each child was assessed with the Phonological Awareness criterion-referenced subtest from the Clinical Evaluation of Language Fundamentals-Fourth Edition. Included in the data for analysis was each child's performance measures obtained from their most recent assessment of cognitive and lexical development. A number of descriptive analyses were undertaken on the data. One child, who met her age criterion for PA,

had cognitive and lexical development skills in the average range. The remaining three children failed to meet their age criteria. Although these three children presented with clinically similar cognitive and lexical development skills, disparate PA skills were identified. The PA skills of one of the sibling pair were notably more advanced than his older sibling. The limitations of relying on behavioural test results in children with GAL to predict those most at risk of reduced skill development are discussed in terms future research directions.

Abbreviations

CELF-4	Clinical Evaluation of Language Fundamentals-Fourth Edition
EVT-2	Expressive Vocabulary Test-Second Edition
GAL	Galactosemia
PA	Phonological awareness
PPVT-4	Peabody Picture Vocabulary Test-Fourth Edition
SES	Socio-economic status
STM	Short-term memory

Communicated by: Alberto B Burlina

Competing interests: None declared

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Introduction

One of the most important skills that a child learns when they start school is how to read (McGeown et al. 2012). Literacy skills are a key contributor to successful academic outcomes (Snow and Beals 2006) and are important functional skills in today's technologically advanced society (Organization for Economic Cooperation and Development 2000). One skill critical to the development of literacy is phonological awareness (Gillon 2004; Ziegler and Goswami 2005; Neuman and Dickinson 2010; Apel et al. 2012), or

the awareness of the sound structure of a spoken word (Gillon 2004).

Phonological awareness (PA) is knowledge that a spoken word is composed of syllables and phonemes (Kovelman et al. 2012) and involves the explicit and deliberate manipulation of components of speech (Castles and Coltheart 2004). PA skills encompass auditory discrimination of familiar sounds, similar sounds, rhyming words, and sounds of letters (Morrow 2007), segmentation of words into individual phonemes, the blending of phonemes into words, and manipulation of the sound structure of words, such as deleting sounds from words and stating what remains (Apel et al. 2012). Growth in PA can be attributed to a number of factors, including age, lexical development, cognitive abilities, and socio-economic status (Lonigan et al. 1998; Nation and Snowling 2004; Lemons and Fuchs 2010).

Based on the recognition that PA precedes and predicts successful transition from language to literacy (Kovelman et al. 2012), investigations of PA skill development have been undertaken in a range of potentially-at-risk paediatric populations including cerebral palsy (Vandervelden and Siegel, 1999), vision impairment (Dodd and Conn 2000), Down syndrome (Hulme et al. 2012), hearing impairment (Briscoe et al. 2001), and following treatment for brain tumours (Docking et al. 2003). Further, proactive intervention programmes aimed at nurturing the maturation of PA (Morrow 2007) have been implemented with successful outcomes for at-risk populations such as children with Down syndrome (Lemons and Fuchs 2010), speech impairment (Al Otaiba et al. 2009), specific language impairment (Collet et al. 2012), minority language speakers (Vadasy and Sanders 2010), foetal alcohol spectrum disorders (Adnams et al. 2007), and emotionally disturbed children (Nelson et al. 2005).

Despite the interest across a broad range of paediatric presentations, no research to date has investigated PA skills in children with metabolic disorders. Classic galactosemia [GAL] is one of a number of metabolic disorders tested through newborn screening, a mass screening programme widely undertaken throughout the world. GAL is the result of an inborn deficiency of the enzyme *galactose-1-phosphate uridylyltransferase* [GALT] (Bosch 2006). Approximately one child in 53,000 in the United States is born with the disorder (Ridel et al. 2005). Intervention for galactose toxicity is the implementation of a galactose-restricted diet (Hughes et al. 2009). Despite dietary restrictions, long-term complications, including developmental delays (Fridovich and Walter 2008), speech and language deficits (Waisbren et al. 1983; Waggoner et al. 1990; Nelson et al. 1991), and academic difficulties (Bosch et al. 2004) have been reported in children with GAL.

Heterogeneity of developmental abilities and attainment is evident across individuals with GAL (Doyle et al. 2010), but neither genetic nor biochemical measures predict or explain the heterogeneous outcomes for children (Ridel et al. 2005). Given the currently inexplicable outcomes for children with GAL, Bosch et al. (2004) have suggested that a focus of ongoing care should be aimed at supporting children to attain the best achievable quality of life (Bosch et al. 2004). Educational achievement, which for individuals with GAL is significantly lower than in the wider population, correlates with self-reported quality of life (Bosch et al. 2004). There are, thus, psychosocial benefits associated with facilitating academic achievement through the development of literacy skills to approximate as near to normal attainment as possible in children with GAL.

The purpose of this study was largely descriptive in order to provide preliminary data on PA skills in a small group of school-aged children with a diagnosis of GAL. Based on the heterogeneity of developmental achievement observed in children with GAL (Doyle et al. 2010), it was hypothesized that variable PA skill would be noted in the group of children.

Method

Participants

Recruitment of the participants was undertaken through a mass recruitment mail-out to all families with children monitored through the Metabolic Clinic at the Royal Children's Hospital, Brisbane, Australia, who met the study's inclusion criteria of school-aged children with a neonatal diagnosis of classic galactosemia as defined by GALT activity < 1.3 units/ml blood, the presence of two known pathogenic mutations in the GALT gene (Duarte variants of GAL were excluded from the study), and English as the language spoken in the family home. The parents of five children responded. One child withdrew from the research prior to assessment. Thus, four children with classic GAL participated in the research.

Child 1

WG, a female, was aged 7 years 7 months at the time of the assessment of PA skills. WG was born at term and breast feeding was initiated. WG presented during the neonatal period with decreasing levels of alertness, hepatic dysfunction, and coagulopathy. She was subsequently identified through newborn screening as having GAL. Dietary restrictions of galactose were initiated through the implementation

Table 1 Neonate's presentation and laboratory findings

Child ID	Gender	<i>GALT</i> genotype	Gal-1-P uridyltransferase activity reference range (0.26–0.52)	Age at diagnosis and clinical features at time of diagnosis	Initial treatment
WG	Fe	Q188R/Q188R	<0.01 U/g Hb	Day 5 from newborn screening Poor feeding, jaundice, coagulopathy	Intravenous fluids Fresh frozen plasma to correct coagulopathy Phototherapy Breast feeding ceases, soy formula introduced
BS	Fe	Q188R/Q188R	<0.01 U/g Hb	Day 5 from newborn screening Poor feeding, jaundice, coagulopathy	Intravenous fluids Fresh frozen plasma to correct coagulopathy Phototherapy Breast feeding ceases, soy formula introduced
FP	Fe	Q188R/Q188R	<0.01 U/g Hb	Day 5 from newborn screening Poor feeding, jaundice, coagulopathy	Intravenous fluids Fresh frozen plasma to correct coagulopathy Phototherapy Breast feeding ceases, soy formula introduced
MP	M	Q188R/Q188R	<0.01 U/g Hb	Day 5 from newborn screening	Soy formula introduced from birth as older sibling presented with GAL

GALT galactose-1-phosphate uridyltransferase, *GAL* galactosemia

Table 2 Biographical details of the children with GAL

Child ID	Occ Grp ^a	Age at assessment of phonological awareness	Most recent results from an assessment of cognitive development ^b			Most recent results from an assessment of lexical development ^b	
			VIQ (WPPSI-III)	PIQ	FSIQ	Rec Vocab (PPVT-4)	Exp Vocab (EVT-2)
WG	1	7; 7 years	119	112	118	111	107
MP	1	7; 8 years	77	59	67	75	80
FP	1	8; 5 years	61	61	60	67	71
BS	3	9; 2 years	72	78	73	70	70

GAL classic galactosemia; *Occ Grp* Jones' (2003) parental occupational grouping; *Fe* female; *M* male; age shown in years, months; *VIQ* verbal intelligence quotient; *PIQ* performance intelligence quotient; *FSIQ* full scale intelligence quotient; *WPPSI-III* Wechsler Preschool and Primary Scale of Intelligence-Third Edition; *Rec Vocab* receptive vocabulary; *PPVT-4* Peabody Picture Vocabulary Test-Fourth Edition; *Exp Vocab* expressive vocabulary; *EVT-2* Expressive Vocabulary Test-Second Edition

^a Jones' Occupational Group 1 = senior management in large business organization, government administration and defence, and qualified professionals; Jones' Occupational Group 3 = tradesperson, clerks, and skilled office, sales and service staff

^b Test mean = 100; test standard deviation = 15 for all test results provided

of a soy-based diet and neonatal symptoms subsided. Table 1 displays WG's neonatal experience and laboratory data. She remains on a galactose-restricted diet. Results from her most recent assessment of cognitive development [Wechsler Preschool and Primary Scale of Intelligence-Third Edition-Australian Standardised Edition] (Wechsler 2004)] and lexical development [Peabody Picture Vocabulary Test-Fourth Edition [PPVT-4] (Dunn and Dunn 2007); Expressive Vocabulary Test-Second Edition [EVT-2] (Williams 2007)] are shown in Table 2. Her performance scores indicate her

cognitive and lexical development was in the high average to above average range for her chronological age.

Child 2

BS, a female, was 9 years 2 months at the time of her involvement in the research. BS was born at term and breast feeding was commenced. Once home, she experienced weight loss and unexplained jaundice. BS was readmitted to hospital with liver disease and failure to thrive. She was

Table 3 Performance by the children with GAL on the CELF-4 Phonological Awareness subtest

Phonological skill assessed	Child ID			
	WG	MP	FP	BS
Syllable blending	5	4	4	5
Rhyme detection	5	2	0	4
Initial phoneme identification	5	5	4	5
Two syllable deletion	5	3	2	4
Rhyme production	5	1	0	1
Syllable segmentation	5	1	0	5
Final phoneme identification	5	5	0	4
Sentence segmentation	4	2	#	3
Three syllable deletion	3	3		2
Phoneme blending	5	4		4
Final syllable deletion	2	2		2
Medial phoneme identification	5	2		2
Initial phoneme substitution	5	1		3
Phoneme segmentation	2	3		1
Initial phoneme deletion	4	2		3
Medial phoneme substitution	4	2		0
Final phoneme substitution	4	0		0
TOTAL SCORE	73	42	10	48
Age-criterion score	≥ 46	≥ 46	≥ 58	≥ 61

GAL classic galactosemia; CELF-4 Clinical Evaluation of Language Fundamentals-Fourth Edition. Maximum score for each subtest = 5; maximum total score = 85

Test discontinuation rule = four incorrect responses on three consecutive item sets

in hospital when the results of newborn screening identified her as having GAL. Dietary restrictions were implemented, and she responded well both clinically and biochemically to the change in diet. BS's neonatal presentation and laboratory data are shown in Table 1. She continues on diet-implemented intervention. As shown in Table 2, BS's most recent assessment of cognitive (Wechsler 2005) and lexical development (Dunn and Dunn 2007; Williams 2007) indicated she had significant cognitive and lexical skill deficits.

Child 3

FP, a female, was 8 years 5 months at the time of her involvement in the study. She was born at term with a birth weight of 5470 grams. She was extremely sick in the neonatal period. Once identified as having GAL through newborn screening, dietary restrictions were implemented. Table 1 presents FP's neonatal experience and laboratory data. FP's diet continues to be galactose restricted. Recent assessment of FP's cognitive (Wechsler 2004) and lexical

(Dunn and Dunn 2007; Williams 2007) development, as displayed in Table 2, indicated she had significant deficits in cognitive and lexical development.

Child 4

MP, a male, is a younger sibling of FP. He was aged 7 years 8 months at the time of his involvement in the study. He and his dizygotic twin brother were born at 33 weeks. MP's birth weight was 2300 grams. Due to the family history of GAL, intake was galactose restricted from birth for both infants. MP, but not his twin, was identified with GAL through newborn screening. Restrictions in MP's diet continued upon confirmation and he remains on diet-implemented treatment for GAL. MP's neonatal presentation and subsequent laboratory data is shown in Table 1. His most recent assessment of cognitive (Wechsler 2004) and lexical development (Dunn and Dunn 2007; Williams 2007) indicated he was performing in the low range cognitively and experiencing delays in receptive and expressive vocabulary skill development (refer to Table 2).

Measures

The Phonological Awareness criterion-referenced subtest from the Clinical Evaluation of Language Fundamentals-Fourth Edition [CELF-4] (Semel et al. 2003) was administered to the children. Criterion-referenced scores allow comparison of the child's performance to an objective and absolute standard (criterion) of performance. Criterion-referenced scores indicate the cut-off point considered typical performance for the child's chronological age. Raw scores obtained from measurement of skills not dependent upon learning but rather upon developmental maturity, such as PA, tend to deviate greatly from the normal distribution. Criterion-referenced scores, however, are not dependent upon an approximately normal distribution of raw scores (Semel et al. 2003). The child either meets the age-based criterion score or does not meet the criterion-based score.

Procedure

The research was given institutional and ethical approval from the Behavioural and Social Sciences Ethical Review Committee at the University of Queensland and the Royal Children's Hospital and Health Services District Ethics Committee. Each child provided a signed informed assent and the child's parent provided a signed informed consent prior to acceptance into this study. Each child was individually assessed at the University of Queensland or in their home.

Descriptive Analyses

A number of descriptive approaches were used to examine the performance of the four children. Firstly, to investigate PA skill development in the children with GAL, the age-criterion score as provided by the CELF-4 test manual (Semel et al. 2003) was used to determine which of the four children met their age criterion. For any child failing the age criterion for PA skill development, a percentage correct of the total required to meet the criterion was calculated. For example, if a child's Total Score on the CELF-4 Phonological Awareness subtest (Semel et al. 2003) was 26 and the age criterion for the child was 42, the child's percentage would be 62 %. A subjective figure of ≥ 90 % of the score required to meet an age criterion was chosen as indicative of a notable performance despite not meeting the age criterion. Secondly, to investigate the performance by the siblings MC and FC, a subjective figure of ≥ 25 % was chosen as indicative of a notable distinction between the siblings' Total Scores from the CELF-4 Phonological Awareness subtest. Thirdly, to investigate factors that may have influenced the children's performance on the CELF-4 Phonological Awareness subtest, the children's age-corrected standard scores on the assessments of cognitive (Wechsler 2004, 2005) and lexical development (Dunn and Dunn 2007; Williams 2007), as displayed in Table 1, were examined. A score difference > 1.5 *SD* of the test mean was chosen to indicate a clinically significant difference between the individual children on each performance score provided by the tests.

Results

As shown in Table 3, one of the four children with GAL (Child WG) met the age criterion for PA skill. Of the three children failing their age criterion on PA skill development, MC's total score was 91 % of the score required to meet his age criterion, indicating a notable performance despite not meeting his age criterion (≥ 90 % of the score required to meet an age criterion). FC's total score of 17 % of the score required to meet her age criterion and BS's total score of 79 % of the score required for her to meet her age criterion were not identified as notable performances (< 90 % of the score required to meet an age criterion). In regard to the performance by the siblings, there was a notable distinction between the two siblings' PA skills, with MC outperforming his older sister FC (≥ 25 % difference in total scores).

Based on a score difference of > 1.5 *SD* of the test mean, there was a clinically significant difference between Child WG's performance scores reflecting cognitive and lexical development and the three other children with GAL, with Child WG outperforming the remaining three children

on each test outcome measure. There were no clinically significant differences between the performance scores reflecting the cognitive and lexical development of MP, FP, or BS (all scores between the three children within 1.5 *SD* of each other).

Discussion

This study investigated PA skills in four children with the metabolic disorder GAL. Three of the four children failed to meet the age criterion for PA skill development. As predicted, there was marked heterogeneity noted between the individual children, a finding which offers further support for the variations in individual outcomes previously reported across a range of neurocognitive and academic measures in children with GAL (Doyle et al. 2010). Further, and in support of previous findings (Hughes et al. 2009), despite a similar profile on a number of pertinent indices, considerable variation in PA skill between the sibling pair was noted.

Child WG, with cognitive and lexical development skills in the average range, presented with age-appropriate PA skills. The three remaining children (Child MP, Child FP, and Child BS) all presented with cognitive and lexical development skills in the low range and all failed to meet the criterion expected for their age. Nonetheless, the skill of these three children differed considerably. Child MP's phonological awareness skills approximated his age criterion (91 % of score required), Child BS's performance placed her within 79 % of the score required for age appropriateness, while Child FP's performance indicated severely restricted PA skill.

Although growth in PA is influenced by age, lexical development, and cognitive abilities (Lonigan et al. 1998; Nation and Snowling 2004; Lemons and Fuchs 2010), no clear profile of PA skill associated with GAL was evident in the data from the three children failing to meet their respective age criteria. MP, who notably outperformed FP and BS, was the youngest of the three children. Lexical development of the three children was clinically similar as were their measures of cognitive skill. Socio-economic status (SES) likewise influences the growth of PA (Lonigan et al. 1998), and Jones' (2003) parental occupational codings were used in this study as an indicator of SES, and again there was no clear profile to predict performance. Child BS's parental occupational coding was lower than Child FP, yet BS was notably more skilled than FP on the PA tasks.

The inclusion in the study of the sibling pair with similar IQs and performance scores on measures of lexical development effectively controlled a number of the variables discussed above that are known to influence the

development of PA. Although FP's status as the older sibling would suggest her PA skills would be more developed than her sibling MP, MP's skills were notably more advanced than his older sister. The finding of vastly contrasting PA skills between siblings with GAL is consistent with previous research findings where intra-family variability has been reported (Lambert and Boneh 2004; Hughes et al. 2009; Coman et al. 2010, Doyle et al. 2010; Bosch 2011).

Siblings FP and MP experienced contrasting neonatal histories. Galactose was introduced to FP in the neonatal period. She subsequently presented with features of galactose intoxication including poor feeding lethargy and hepatic dysfunction and was eventually identified with GAL through newborn screening. In contrast, galactose restriction was implemented at birth for MP, thus avoiding the diverse system failure associated with the accumulation of galactose and its by-products in the blood and tissues (Fridovich and Walter 2008). Research to date suggests that differential developmental outcomes observed in the disorder are not related to conditions during the neonatal (e.g., age at diagnosis and restriction of galactose intake or severity of neonatal crisis) or postnatal period [e.g., adherence to diet] (Cleary et al. 1995; Bosch 2011). Rather, developmental outcome may be influenced by prenatal conditions (Fridovich and Walter 2008, Potter et al. 2008; Berry and Elsas 2011) such as harmful intrauterine levels of galactitol causing early but static neural injury (Ridel et al. 2005). Exposure to galactose in the neonatal period may magnify the galactose toxicity in individual children (Berry and Elsas 2011).

Harmful intrauterine conditions for both siblings, compounded by FP's galactose neurotoxicity in the neonatal period may account for the differential outcome for the siblings, but not the intact developmental outcomes for Child WG, who also experienced serious galactose toxicity in the neonatal period. Another theory of poor ongoing development in children with GAL, despite neonatal changes to diet, is a complication of dietary compliance itself. An over-restriction of galactose can potentially interfere with myelin development by secondary impairments in N-glycosylation (Hughes et al. 2009; Coman et al. 2010; Coss et al. 2010, 2012). Epigenetic effects may subsequently determine the variable developmental outcomes (Coman et al. 2010), such as those observed in this study.

Proactive interventions designed to facilitate the maturation of PA in at-risk children have shown to be efficacious with at-risk groups of children (Nelson et al. 2005; Adnams et al. 2007; Vadasy and Sanders 2010; Collet et al. 2012). With 75 % of the children with GAL investigated in this study presenting with diminished PA skills, a means of identifying which children with GAL require proactive

support would be beneficial. The preliminary findings of this study failed to identify behavioural factors supporting the differential performance scores of the children with GAL. PA, however, can be viewed as a subset of implicit phonological processing skills such as verbal short-term memory (STM) and rapid automatized naming (Alloway et al. 2004; Melby-Lervåg et al. 2012). STM deficits have been described in individuals with GAL (Kaufman et al. 1995; Manis et al. 1997; Antshel et al. 2004) and individual STM skill may account for the performance outcomes observed in the three children with similar cognitive measures but with discrepant PA skills.

A theoretical framework of PA skill assessment has been proposed, whereby assessment should include not only detection, isolation, and manipulation of sub-word phonological segments at the syllabic, onset-rime, and/or phonemic level, as undertaken with the Phonological Awareness criterion-referenced subtest from the CELF-4 (Semel et al. 2003), but also conversion or the ability to use PA skills, such as, for instance, grapheme-phoneme conversion rules required for processing non-words (Dodd et al. 1996). The use of a more comprehensive PA assessment tool, such as the Queensland University Inventory of Literacy (Dodd et al. 1996), which provides a broad base of quantitative and qualitative data, may clarify the differential outcomes observed in this study.

The pathophysiology of neurodevelopmental impairments in GAL, including the PA deficits identified in the children in this study, remains unknown, but abnormalities associated with the disorder detected through brain imaging include cerebral atrophy, abnormal white matter signal, diffuse white matter abnormalities, and delayed myelination (Nelson et al. 1992; Kaufman et al. 1995; Wang et al. 2001). Kovelman et al. (2012), through functional magnetic resonance imaging (fMRI) during an auditory word rhyming task, identified the left dorsolateral prefrontal cortex as the neural correlate of PA and suggested that the site may play a critical role in the development of PA for spoken language. Advanced neurophysiological (e.g., electroencephalography) and imaging (fMRI, diffusion tensor imaging) studies that investigate neural activity related to cognitive function (see Timmers et al. 2011) are required to further elucidate the current unpredictable long-term complications of the disorder, for, as shown in this study, behavioural testing alone offers limited predictive value for identifying which children with GAL need proactive support.

Clinical Implications and Conclusion

This descriptive study of the PA skills of four children with GAL revealed widely disparate performance scores. Three of the four children presented with clinically similar cognitive and lexical development skills, but displayed

dissimilar PA skill. In the current absence of therapeutic strategies to prevent *GALT* deficiency (Bosch 2006) and the current restricted understanding of the cognitive pathophysiological processes associated with GAL (Timmers et al. 2011), the focus of ongoing care should be aimed at supporting children with GAL to attain the best achievable quality of life (Bosch et al. 2004). Due to marked variability noted in PA skills in the four children investigated in this study, specific individualized testing and support for skill development should be implemented for all children with the disorder (Kaufman et al. 1995) in order to optimize their literacy development.

Acknowledgement The authors wish to thank the four children who participated in the research. This study was supported by funding from Apex Foundation for Research into Intellectual Disability (Australia).

References

- Adnams CM, Sorour P, Kalberg WO et al (2007) Language and literacy outcomes from a pilot intervention study for children with fetal alcohol spectrum disorders in South Africa. *Alcohol* 41:403–414
- Al Otaiba S, Puranik CS, Ziolkowski RA, Montgomery TM (2009) Effectiveness of early phonological awareness interventions for students with speech or language impairments. *J Spec Educ* 43:107–128
- Alloway TP, Gathercole SE, Willis C, Adams AM (2004) A structural analysis of working memory and related cognitive skills in young children. *J Exp Child Psychol* 87:85–106
- Antshel KM, Epstein IO, Waisbren SE (2004) Cognitive strengths and weaknesses in children and adolescents homozygous for the galactosemia Q188R mutation: a descriptive study. *Neuropsychology* 18:658–664
- Apel K, Wilson-Fowler EB, Brimo D, Perrin NA (2012) Metalinguistic contributions to reading and spelling in second and third grade students. *Read Writ* 25:1283–1305
- Berry GT, Elsas LJ (2011) Introduction to the Maastricht workshop: lessons from the past and new directions in galactosemia. *J Inherit Metab Dis* 34:249–255
- Bosch AM (2006) Classical galactosaemia revisited. *J Inherit Metab Dis* 29:516–525
- Bosch AM (2011) Classic galactosemia: dietary dilemmas. *J Inherit Metab Dis* 34:257–260
- Bosch AM, Grootenhuys MA, Bakker HD, Heijmans HS, Wijburg FA, Last BF (2004) Living with classical galactosemia: health-related quality of life consequences. *Pediatrics* 113:e423–e428
- Briscoe J, Bishop DVM, Norbury CF (2001) Phonological processing, language, and literacy: a comparison of children with mild-to-moderate sensorineural hearing loss and those with specific language impairment. *J Child Psychol Psychiatry* 42:329–340
- Castles A, Coltheart M (2004) Is there a causal link from phonological awareness to success in learning to read? *Cognition* 91:77–111
- Cleary MA, Heptinstall LE, Wraith JE, Walter JH (1995) Galactosemia: relationship of IQ to biochemical control and genotype. *J Inherit Metab Dis* 18:151–152
- Collet G, Colin C, Serniclaes W et al (2012) Effect of phonological training in French children with SLI: perspectives on voicing identification, discrimination and categorical perception. *Res Dev Disabil* 33:1805–1818
- Coman DJ, Murray DW, Byrne JC et al (2010) Galactosemia, a single gene disorder with epigenetic consequences. *Pediatr Res* 67:286–292
- Coss K, Coman D, Brown A et al (2010) Biochemical and glycomic effects of diet relaxation in classical galactosaemia. *J Inherit Metab Dis* 33:S69–S69
- Coss KP, Byrne JC, Coman DJ et al (2012) IgG N-glycans as potential biomarkers for determining galactose tolerance in classical galactosaemia. *Mol Genet Metab* 105:212–220
- Docking KM, Murdoch BE, Ward EC (2003) High-level language and phonological awareness abilities of children following management for supratentorial tumour: part II. *Acta Neuropsychologica* 1:367–381
- Dodd B, Conn NL (2000) The effect of Braille's orthography on blind children's phonological awareness. *J Res Read* 23:1–11
- Dodd B, Holm A, Oerlemans M, McCormick M (1996) Queensland University Inventory of Literacy, Brisbane, Australia. Department of Speech Pathology and Audiology, University of Queensland
- Doyle CM, Channon S, Orlowska D, Lee PJ (2010) The neuropsychological profile of galactosaemia. *J Inherit Metab Dis* 33:603–609
- Dunn LM, Dunn DM (2007) Peabody Picture Vocabulary Test. Harcourt Assessment Inc., San Antonio, TX
- Fridovich JL, Walter JH (2008) Galactosemia, Chapter 72. In: Valle D, Beaudet A, Vogelstein B, Kinzler KW, Antonarakis SE, Ballabio A, Scriver CR, Sly WS, Childs B, Bunz F, Gibson KM, Mitchell G (eds) *The online metabolic and molecular bases of inherited D*, 9th edn. McGraw-Hill, New York
- Gillon GT (2004) Phonological awareness: from research to practice. The Guilford Press, New York
- Hughes J, Ryan S, Lambert D et al (2009) Outcomes of siblings with classical galactosemia. *J Pediatr* 154:721–726
- Hulme C, Goetz K, Brigstocke S et al (2012) The growth of reading skills in children with Down syndrome. *Dev Sci* 15:320–329
- Jones RG (2003) Parental occupation coding. Department of Education Science and Training, Canberra, Australia
- Kaufman FR, McBride-Chang C, Manis FR, Wolff JA, Nelson MD (1995) Cognitive functioning, neurologic status and brain imaging in classical galactosemia. *Eur J Pediatr* 154:S2–S5
- Kovelman I, Norton ES, Christodoulou JA et al (2012) Brain basis of phonological awareness for spoken language in children and its disruption in dyslexia. *Cereb Cortex* 22:754–764
- Lambert C, Boneh A (2004) The impact of galactosaemia on quality of life - A pilot study. *J Inherit Metab Dis* 27:601–608
- Lemons CJ, Fuchs D (2010) Phonological awareness of children with Down syndrome: its role in learning to read and the effectiveness of related interventions. *Res Dev Disabil* 31:316–330
- Lonigan CJ, Burgess SR, Anthony JL, Barker TA (1998) Development of phonological sensitivity in 2- to 5-year-old children. *J Educ Psychol* 90:294–311
- Manis FR, Cohn LB, McBride-Chang C, Wolff JA, Kaufman FR (1997) A longitudinal study of cognitive functioning in patients with classical galactosaemia, including a cohort treated with oral uridine. *J Inherit Metab Dis* 20:549–555
- McGeown SP, Johnston RS, Medford E (2012) Reading instruction affects the cognitive skills supporting early reading development. *Learn Individ Differ* 22:360–364
- Melby-Lervåg M, Lyster SAH, Hulme C (2012) Phonological skills and their role in learning to read: a meta-analytic review. *Psychol Bull* 138:322–352
- Morrow LM (2007) Developing literacy in preschool. Guilford Press, New York

- Nation K, Snowling MJ (2004) Beyond phonological skills: broader language skills contribute to the development of reading. *J Res Read* 27:342–356
- Nelson CD, Waggoner DD, Donnell GN, Tuerck JM, Buist NRM (1991) Verbal dyspraxia in treated galactosemia. *Pediatrics* 88:346–350
- Nelson JR, Benner GJ, Gonzalez J (2005) An investigation of the effects of a prereading intervention on the early literacy skills of children at risk of emotional disturbance and reading problems. *J Emot Behav Disord* 13:3–12
- Nelson MD, Wolff JA, Cross CA, Donnell GN, Kaufman FR (1992) Galactosemia: evaluation with MR imaging. *Radiology* 184:255–261
- Neuman SB, Dickinson DK (2010) Handbook of early literacy research. Guilford Press, New York
- Organization for Economic Cooperation and Development (2000) Literacy in the Information Age: final report of the International Adult Literacy Survey. Organization for Economic Cooperation and Development, Paris, France
- Potter NL, Lazarus J-AC, Johnson JM, Steiner RD, Shriberg LD (2008) Correlates of language impairment in children with galactosaemia. *J Inherit Metab Dis* 31:524–532
- Ridel KR, Leslie ND, Gilbert DL (2005) An updated review of the long-term neurological effects of galactosemia. *Pediatr Neurol* 33:153–161
- Semel E, Wiig EH, Secord WA (2003) Clinical Evaluation of Language Fundamentals. Harcourt Assessment Inc, San Antonio, TX
- Snow CE, Beals DE (2006) Mealtime talk that supports literacy development. *New Dir Child Adolesc Dev* 111:51–66
- Timmers I, Van Den Hurk J, Di Salle F, Rubio-Gozalbo ME, Jansma BM (2011) Language production and working memory in classic galactosemia from a cognitive neuroscience perspective: future research directions. *J Inherit Metab Dis* 34:367–376
- Vadasy PF, Sanders EA (2010) Efficacy of supplemental phonics-based instruction for low-skilled kindergarteners in the context of language minority status and classroom phonics instruction. *J Educ Psychol* 102:786–803
- Vandervelden M, Siegel S (1999) Phonological processing and literacy in AAC users and students with motor speech impairments. *Augment Altern Commun* 15:191–209
- Waggoner DD, Buist NRM, Donnell GN (1990) Long-term prognosis in galactosaemia: results of a survey of 350 cases. *J Inherit Metab Dis* 13:802–818
- Waisbren SE, Norman TR, Schnell RR, Levy HL (1983) Speech and language deficits in early-treated children with galactosemia. *J Pediatr* 102:75–77
- Wang ZI, Berry GT, Dreha SF, Zhao H, Segal S, Zimmerman RA (2001) Proton magnetic resonance spectroscopy of brain metabolites in galactosemia. *Ann Neurol* 50:266–269
- Wechsler D (2004) Wechsler Preschool and Primary Scale of Intelligence-Australian Standardised Edition. Harcourt Assessment Inc., Marrickville, Australia
- Wechsler D (2005) Wechsler Intelligence Scale for Children. Harcourt Assessment Inc., Marrickville, Australia
- Williams KT (2007) Expressive Vocabulary Test. Pearson Assessments, Minneapolis, MN
- Ziegler JC, Goswami U (2005) Reading acquisition, developmental dyslexia, and skilled reading across languages: a psycholinguistic grain size theory. *Psychol Bull* 131:3–29