Speech–Language Characteristics of Children With Neurofibromatosis Type 1

Heather L. Thompson, 1* David H. Viskochil, 2 David A. Stevenson, 2 and Kathy L. Chapman 1

1Department of Communication Sciences and Disorders, University of Utah, Salt Lake City, Utah
2Division of Medical Genetics, Department of Pediatrics, University of Utah, Salt Lake City, Utah

Received 26 June 2009; Accepted 18 November 2009

Delays in speech and articulation development have been found in school-aged children and adolescents with neurofibromatosis type 1 (NF1). This report examines speech and language skills of preschool children with NF1. Nineteen 3- to 5-year-old children diagnosed with NF1 were assessed using measures of articulation (GFTA-2), and receptive and expressive language (CELF-P2). Significant differences were observed between mean scores obtained by the group of children with NF1 compared to the validated controls from the speech and language instruments ($P < 0.009$). Sixty-eight percent of the children exhibited delays in speech and/or language. Thirty-two percent demonstrated delays in articulation, 37% percent demonstrated delays in receptive language, and 37% exhibited delays in expressive language. Sixteen percent of the children exhibited a voice disorder and 42% were judged to have a resonance problem. No significant differences were observed on any of the measures of speech and language for children with non-familial versus familial NF1. Results of this study support the need for early assessment of speech and language problems for children diagnosed with NF1 and implementation of appropriate timely intervention as needed. © 2010 Wiley-Liss, Inc.

Key words: speech; articulation; language; resonance; voice; neurofibromatosis type 1; NF1; preschool; children

INTRODUCTION

Learning disabilities including language deficits are well-known manifestations of neurofibromatosis type 1 (NF1); however, the problems associated with delays in other aspects of communication are lesser known. Communication disorders are characterized by problems in understanding, processing, or conveying verbal, non-verbal, or graphic messages [ASHA, 1993]. Communication disorders include problems in articulation, language, voice, and resonance. An articulation disorder is seen when an individual exhibits problems in producing speech sounds. It is characterized by omission, substitution, addition, or distortion errors, negatively impacting speech intelligibility [ASHA, 1993]. Fourteen percent of 3-year olds and 4% of 6-year olds exhibit an articulation disorder [Shriberg et al., 1999; Campbell et al., 2003]. A language disorder is referred to as an impairment in comprehending (receptive language) and/or using (expressive language) speech, writing and/or other symbol systems [ASHA, 1993]. A language disorder can include problems with the form, content or function of verbal or written communication. Approximately 7.4% of kindergarten children in the United States exhibit a language disorder [Tomblin et al., 1997].

Riccardi and Eichner [1986] alluded to problems with communication in the population of individuals with NF1. More specifically, Riccardi reported that approximately 52% of individuals with NF1 (primarily adults) exhibit delayed speech characterized by imprecise consonant production, hypernasality, breathiness, voice tremor, hoarseness, monopitch, and monoloudness [Riccardi and Eichner, 1986]. Wong [1994] found that 12% of 50 Chinese children with NF1 from 21 months to 18 years of age exhibited an articulation disorder.

Children with NF1 also exhibit language delays [Eldridge et al., 1989; North et al., 1994; Dilts et al., 1996; Hyman et al., 2005]. Eldridge et al. [1989] found that 2 of 13 (15%) patients with NF1 between 6 and 27 years of age had possible spoken language disorders when language was assessed using either the Clinical Evaluation of Language Fundamentals (CELF) [Semel-Mintz and

Grant sponsor: National Center for Research Resources; Grant Numbers: UL1-RR025764, C06-RR11234; Grant sponsor: Canadian Institutes of Health Research (CIHR) Doctoral Research Award Program; Grant sponsor: Ontario Barbershoppers’ Harmonize for Speech Fund; Grant sponsor: Doris Duke Charitable Foundation.

*Correspondence to: Heather L. Thompson, Department of Communication Sciences and Disorders, University of Utah, 390 S. 1530 E. Rm 1201 BEH SCI, Salt Lake City, UT 84112-0252. E-mail: heather.thompson@utah.edu

Published online 22 January 2010 in Wiley InterScience (www.interscience.wiley.com)

DOI 10.1002/ajmg.a.33235

© 2010 Wiley-Liss, Inc.
Wiig, 1982], the Token Test [DiRenzi and Vignolo, 1962], or the Boston Naming Task (BNT) [Borod et al., 1980]. North et al. [1994] examined the language profile of children in a narrower age range (8–16 years) and reported that children with NF1 exhibited language skills in the low-average range, with many requiring special educational services. Hyman et al. [2005] reported that 13% and 2.5% of their group of 81 children (ages 8–16 years) had receptive and expressive language delays, respectively. Dilts et al. [1996] examined the expressive and receptive language in a group of 6- to 17-year-old children with NF1 and matched unaffected siblings. They found that 11 of 19 (58%) children with NF1 exhibited deficits in expressive language with or without receptive language deficits according to results of the CELF-screening [Semel et al., 1989] and CELF-revised [Semel et al., 2003] expressive language subtest. Twenty-six percent also exhibited deficits in receptive language according to the receptive language subtest of the CELF-revised. Although the participants in the study represented a large age-range, the assessment measures employed included standardized language assessment measures, making this study a valid contribution toward describing the behavioral phenotype of the NF1 population. In light of the current literature, school-aged children, adolescents, and adults with NF1 are at-risk for language delays, even though the variable prevalence of language delay reported in these studies may be related to the large age ranges studied or test instruments employed.

Previous studies of communication disorders in NF1 have limitations. Results of formal testing of both speech and language have not been reported in the same study. In a few of the studies, the diagnostic criteria for determining speech and language delays/deficits was either limited or information was omitted, such as the tests employed, or the means and standard scores of the group. Thus, a concise description of the global communication abilities is difficult to determine. Finally, while previous studies examined the speech and language profiles of older children and adults with NF1, a study has not yet described the communication profile of a larger group of young children with NF1 (refer to Table I).

To the best of our knowledge, there are no studies which document the speech and language profile of preschool children with NF1. This report used standardized speech and language assessment measures (Goldman–Fristoe Test of Articulation–2 (GFTA-2) and the Clinical Evaluation of Language Fundamentals—Preschool, 2nd edition) to assess speech and language in preschool children with NF1 and without a family history of the condition.

### METHODS

#### Participants

This study was approved by the Institutional Review Board at the University of Utah. Parents of all participants signed informed consent forms prior to enrollment in the study. Children with hearing impairment or other congenital anomalies were excluded from the study. Children between 3 and 5 years of age, who were monolingual English speakers, and who fulfilled the National Institutes of Health clinical NF1 diagnostic criteria [Stumpf et al., 1988] were recruited from the University of Utah NF1 clinic from September 2008 until April 2009. For inclusion, participants needed to pass a hearing screening at 500, 1,000, 2,000, and 4,000 Hz at 20 dB SPL. Because it might be argued that children who performed outside the normal range for cognitive skills might have a different underlying etiology for their speech and language delays, it was required that all children demonstrated cognitive abilities within normal limits according to results of the Nonverbal Cognitive Subtest of the Differential Abilities Scale [Elliot, 1979].

All children referred to the NF1 clinic, born between October 2002 and April 2006 who met the inclusion criteria, were eligible to participate in the study. Forty-six children were identified as candidates for the study. Of these children, 13 could not be contacted, 5 were not interested in participating, and 2 lived too far away. Additionally, seven children were assessed but later excluded from the study. Of the excluded children, two had nonverbal cognitive skills ≤70, one parent with two children wished to

### TABLE I. Studies Examining Speech and Language Outcomes of Individuals With NF1

<table>
<thead>
<tr>
<th>Author</th>
<th>Area assessed</th>
<th>Number with delays</th>
<th>Age of participants</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wong [1994]</td>
<td>Speech</td>
<td>12/50 (24%) definite speech problems</td>
<td>21 months–18 years</td>
</tr>
<tr>
<td>Riccardi and Eichner [1986]</td>
<td>Speech</td>
<td>57/219 (26%) suspected or had speech delays</td>
<td>18.5 ± 15.2 years*</td>
</tr>
<tr>
<td>Eldridge et al. [1989]</td>
<td>Language</td>
<td>2/13 (15%) possible SLD</td>
<td>6–27 years</td>
</tr>
<tr>
<td>North et al. [1994]</td>
<td>Language</td>
<td>Mean RL and EL scores in the low-average range (n = 40)</td>
<td>8–16 years</td>
</tr>
<tr>
<td>Dilts et al. [1996]</td>
<td>Language</td>
<td>45% of the group received special services</td>
<td>6–17 years</td>
</tr>
<tr>
<td>Hyman et al. [2005]</td>
<td>Language</td>
<td>Mean RL scores in the low-average range</td>
<td>8–16 years</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Mean EL scores in the high-average range</td>
<td></td>
</tr>
</tbody>
</table>

SLD, spoken language disorder; DLD, other learning disorder; EL, expressive language; RL, receptive language.

*Mean age of total group, n, 238.
discontinue testing, one could not complete testing, and three children had some characteristics (such as the presence of café au lait macules) but did not fulfill the diagnostic criteria of NF1. Thus, not all eligible children participated in the study. It is possible that a recruitment bias may exist for the 13 children who could not be contacted. That is, perhaps parents did not provide most recent contact information to the NF clinic due to the fact that they felt their children did not require services. Additionally, it was known through a discussion with parents that three of the five children who chose not to participate had delays (i.e., were receiving speech services through the school district). Finally, all of the children who did not complete testing exhibited delays in the area(s) assessed.

Procedures

Parents of all participants provided information about birth and developmental history through a case history form modified for the purpose of the study. Children’s articulation was assessed through the GFTA-2 [Goldman and Fristoe, 2000]. The GFTA-2 is an assessment tool designed to assess children’s ability to articulate sounds in single-words. Children’s expressive and receptive language was assessed through the Clinical Evaluation of Language Fundamentals—Preschool 2 (CELF-P2) [Semel et al., 2004]. The CELF-P2 expressive subtest assessed children’s word structure, expressive vocabulary and sentence structure. The CELF-P2 receptive subtest assessed children’s understanding of sentence structure, comprehension of basic concepts, and sentence recall abilities [Semel et al., 2004]. Both the GFTA-2 and the CELF-P2 are reliable and valid measures commonly used in pediatric speech-language pathology clinics. Finally, the nonverbal subtest of the differential abilities scale (DAS) [Elliot, 1979] was used to assess children’s nonverbal cognitive development. Children were seen in one or two assessment sessions at the University of Utah Speech, Language and Hearing Clinic based on the convenience of the participating families.

Participant’s raw scores, standardized scores, and percentile ranks for the GFTA-2, DAS, and CELF-P2 were analyzed. Children’s tests were scored and results compared with test norms. Children who obtained a standard score of less than 85 (1 standard deviation below the mean) on the GFTA-2 or the CELF-P2 receptive or expressive language subtests were considered to have an articulation or language delay [Anderson et al., 2006; Rvachew, 2006]. Children who obtained a standard score of less than 80 (1 standard deviation plus one standard error of measure) on the DAS were considered to have a nonverbal cognitive delay.

Quality of voice and resonance was assessed by three speech–language pathologists employed at the University of Utah Speech–Language–Hearing Clinic (MF, KP, HS) with at least 5 years of experience working with children. Audio-taped conversational speech samples were evaluated. A rating of the presence or absence of a voice or resonance disorder was provided for each child.

A family history was obtained in order to assess the NF1 inheritance pattern, and children were categorized as cases without a parent affected with NF1 (non-familial) versus cases with a parent affected with NF1 (familial). In order to ensure that the two groups of children were not significantly different in terms of self-reported maternal level of education, chi-square analysis was employed. Results were not significant, suggesting that the two groups of children (non-familial vs. familial NF1) were not significantly different in terms of one of five levels of maternal educational level (high school graduate; some college; associate’s degree, college graduate, more than a college degree).

RESULTS

Nineteen children fulfilled the inclusion criteria and participated in the study. Participants were between the ages of 3 and 5 years, 9 months of age ($M_{age} = 4.5$ [years:months], $SD = 12$ months), and included 10 males ($M_{age} = 4.4$, $SD = 13$ months) and 9 females ($M_{age} = 4.7$, $SD = 12$ months). Nine children did not have a parent affected with NF1 (non-familial) while 10 children had familial NF1. Table II shows the demographic and diagnostic characteristics for the study participants.

Mean standard scores for the articulation, receptive and expressive language, and nonverbal cognitive assessments for 19 children are presented in Table III. Results of the GFTA-2 showed that 32% of preschool children with NF1 had an articulation delay. Receptive language delays were found in 37% of children. Expressive language delays were also found in 37% of children. Four children (21%) presented with delays in both receptive and expressive language. One child exhibited a delay in all three areas. Some children exhibited delays only in expressive language, while others exhibited delays only in receptive language. In total, approximately 68% of preschool children with NF1 exhibited either a delay in speech, a delay in language, or delays in all domains. Using a one-sample $t$-tests with a test value of 100, mean standard scores of the group of children with NF1 for the GFTA-2, and CELF-P2 expressive and receptive subtests were significantly lower for both GFTA-2 and CELF-P2 subtests. Results are presented in Table III. Finally, three (16%) and eight (42%) of the children were found to have a voice or resonance problem, respectively.

Mean GFTA-2, CELF-P2 receptive and expressive standard scores for each group (Group 1: non-familial NF1, $n = 9$; Group 2: familial NF1, $n = 10$) were compared through nonparametric Mann–Whitney $U$ tests. Due to the exploratory nature of this investigation, no Bonferroni corrections for multiple comparisons were made. Thus, the alpha for all tests was set at 0.05. Results of all Mann–Whitney $U$ tests were not significant between non-familial and familial NF1 groups (Table IV).

DISCUSSION

This study examined speech and language performance of preschool children with NF1. Examining the outcomes of preschool children with NF1 is relevant because rapid development takes place for children from 3 to 5 years of age, and delays warrant early speech and language assessments and intervention.

An examination of the error patterns of the results of the GFTA-2 showed that the articulation skills of children with NF1 were frequently delayed, characterized by the omission and substitution of sounds (e.g., “hous” for “house” or “tup” for “cup”) and cluster reduction (e.g., “fog” for “frog”). These articulation patterns are typical of what would be observed in children with developmental
Phonological disorders [Grunwell, 1997]. That is, these children were not using atypical productions, but were using patterns that are typically seen (and considered normal) for children who are younger than the children tested here. In terms of voice and resonance, approximately 16% (n=3) of children had a voice disorder, with the most salient feature being voice hoarseness. This number is considered high as the incidence of voice disorders in the general population of school aged children is approximately 6–9% [Andrews, 1986; Kahane and Mayo, 1989; McNamara and Perry, 1994].

Forty-two percent (n=8) of participants were judged to have problems with resonance. The incidence of resonance imbalance in school aged children is approximately 3–4% [Warr-Leeper et al., 1979]. Objective measures of velopharyngeal insufficiency (VPI; such as nasendoscopy or multiview videofluoroscopy) are not available from this group of preschool children due to the young age of the children studied. VPI was documented in seven children with hypernasality who also had a diagnosis of NF1 [Pollack and Shprintzen, 1981]. Other studies [Berman et al., 2009; Zhang et al., 2009] verified the association between NF1 and VPI using nasometry, perceptual evaluation, and multiview videofluoroscopy in older children with NF1. Although resonance concerns were identified through perceptual evaluation in the present study, it should be noted that objective measurement of VPI in the population of children with NF1 is an important part of a comprehensive evaluation.

The results of this investigation indicate that voice and resonance disorders occur frequently in the preschool population of children with NF1, with resonance disorders being more frequent than voice disorders. Children with NF1 have a higher incidence of problems in the areas of articulation, language, voice, and/or resonance, thus the diagnosis of NF1 places children at risk for communication disorders. As it is generally understood that the prevalence of speech delays decreases with age [Shriberg et al., 1999; Campbell et al.,

![Table III. Group Means and Standard Deviations of Nonverbal Cognitive, Speech, and Language Testing for 19 Children With NF1](image)

![Table II. Demographic Data for Participants (n=19)](image)
In terms of language, impairment was noted in all subtests of receptive and expressive language (e.g., sentence structure, concepts and following directions, basic concepts, word structure, expressive vocabulary, and recalling sentences) with much variability observed between participants. While the mean receptive and expressive language scores for these children fell in the low-average range, a large number of children with NF1 had delayed speech and/or language. Additionally, children with NF1 obtained test scores which were significantly lower than expected for their age. Differences were noted between this investigation and the study by Hyman et al. [2005], who examined language development in 8–16 years old children with NF1 (n = 81) and their unaffected siblings (n = 49). These differences can primarily be explained by the measures employed. While the present study used measures of receptive and expressive language that would capture potential deficits in understanding of morphosyntax, basic concepts, and sentence length (CELF-P2), the measures employed in the Hyman et al. [2005] study were heavily based on children’s understanding and use of vocabulary. Since language delays occur in many areas in addition to vocabulary skills (e.g., morphosyntax, mean length of utterance), we surmise that more children were identified as language-delayed in our study by use of the CELF-P2 measure.

Children with a family history of NF1 did not have poorer articulation or decreased receptive or expressive language skills compared to children with sporadic NF1. However, mean scaled scores were lower on language subtests for the familial group compared to the non-familial group. Further research examining the relationship between speech and language outcomes and family history of NF1 is warranted.

Speech and language delays put children at-risk for later academic problems, particularly in the area of literacy [e.g., Bishop and Adams, 1990; Menyuk et al., 1991; Catts, 1993; Bird et al., 1995; Snowling et al., 2001; Catts et al., 2002]. More specifically, language delays contribute to later difficulties in learning to read [Bishop and Adams, 1990; Catts, 1993; Naunilé and Magnusson, 1998; Catts et al., 2002], and delays in articulation often result in persistent academic problems (e.g., requiring exceptional educational services) [Shriberg and Kwiatkowski, 1988]. In addition to academic consequences [Bashir and Scavuzzo, 1992; van Agt et al., 2007], speech and language delays have a negative impact on social development [Aram et al., 1984; Bashir and Scavuzzo, 1992; US Preventive Services Task Force, 2006]. Although variables other than poor articulation and language contribute to later poor academic achievement (e.g., socioeconomic status, history of speech, and language concerns) [Hart and Risley, 1995; Segebart Dethorne et al., 2006], participation in early speech–language intervention can reduce the likelihood of a child developing reading problems [Catts, 1993]. As intervention has been found to ameliorate lifetime outcomes, early intervention for communication disorders in children with NF1 is needed.

Language delays tend to disproportionally occur in families with a history of language disorders [Tomblin, 1989]. Studies have shown that adults with NF1 have language learning disabilities [Lorch et al., 1999]. It is possible that factors related to the family unit or the language learning environment may play a role in language development in children with NF1.

This study found that speech and language delays frequently occur in the population of preschool children with NF1. A limitation of this study is the small sample size, which may be biased due to recruitment through an NF clinic located at a children’s hospital. It is possible that children who were most mildly affected with NF1 would not have a diagnosis and therefore would not have participated in the study. The referral pattern for our NF Clinic for children in this age group includes NF1 assessments primarily due to café-au-lait spots with and without family history of NF1. Referrals for optic pathway glioma and tibial dysplasia in the context of NF1 also occur, but primary reasons for referrals to the NF clinic typically, do not include developmental delay, speech abnormalities, or behavior problems. Another limitation is that a typically developing group of children from the same geographical location with which to compare results of standardized tests was not included. We rely on the normalized scores from the respective instruments themselves to identify speech and language abnormalities in the NF1 cohort. However, as test scores in conjunction with sound clinical judgment are used to classify children as having a speech or language delay, these results are clinically valid.

The findings of this study have important implications for the management of children with NF1. First, all preschool children with NF1 should have a speech and language assessment with follow-up speech–language intervention as needed. Second, a speech–language pathologist should be part of a multi-discipline team.
providing care for children with NF1. Third, a typical assessment battery should include an assessment of articulation in single words and in a conversational context, a standardized assessment of receptive and expressive language, and a screening for voice and resonance concerns. Following identification, children with voice and resonance disorders should be referred to an otolaryngologist for a formal evaluation. Future research should examine the prevalence of VPI in children with NF1 as well as outcomes of speech and language intervention for children with NF1 and speech–language delays.

ACKNOWLEDGMENTS

We wish to thank the families and children with NF1 who participated in this investigation. We also thank Dr. Sean Redmond for his helpful suggestions in the study design, and Dr. Alan Rope, Dr. John Carey, and Dr. Susan Lewin for their assistance with participant recruitment. Finally, we wish to thank the graduate students (Lindsay Downs, Melissa Whitchurch) and speech–language pathologists (Julia Lidgard, Karen Pardyjak, Hilary Silberman, and Mary Foye) who assisted with this study. This investigation was supported by the Clinical Genetics Research Program at the University of Utah, the Public Health Services research grant numbers UL1-RR025764 and C06-RR11234 from the National Center for Research Resources. Heather Thompson is funded through the Canadian Institutes of Health Research (CIHR) Doctoral Research Award Program and the Ontario Barbershoppers’ Harmonize for Speech Fund. Dr. David Stevenson is a recipient of a Doris Duke Clinical Scientist Development Award and work is supported by the Doris Duke Charitable Foundation.

REFERENCES


