Parent-Reported Social Skills in Children with Neurofibromatosis Type 1: Longitudinal Patterns and Relations with Attention and Cognitive Functioning

Danielle M. Glad, MS,* Christina L. Casnar, PhD,† Brianna D. Yund, MS,‡ Kristin Lee, MS,* Bonita P. Klein-Tasman, PhD*

ABSTRACT: ***Objective:*** **Social skills difficulties are commonly reported by parents and teachers of school age (SA) children with neurofibromatosis type 1 (NF1). Investigations of social skills of young children with NF1 are scarce. This study aimed to characterize the emergence of social skills challenges beginning in early childhood, examine social skills longitudinally into SA, and explore interrelations with attention-deficit hyperactivity disorder (ADHD) symptomatology and cognitive functioning among children with NF1 cross-sectionally and longitudinally.** ***Method:*** **Three samples of children with NF1 and their parents participated: (1) early childhood (n = 50; ages 3–6; mean [M] = 3.96, SD = 1.05), (2) SA (n = 40; ages 9–13; [M] = 10.90, SD = 1.59), and (3) both early childhood and SA (n = 25). Parent-reported social skills (Social Skills Rating System and Social Skills Improvement System), ADHD symptomatology (Conners Parent Rating Scales – Revised and Conners – Third Edition), and parent-reported cognitive abilities (Differential Ability Scales – Second Edition) were evaluated.** ***Results:*** **Parental ratings of social skills were relatively stable throughout childhood. Ratings of social skills at the end of early childhood significantly predicted school-age social skills. Parental ratings of ADHD symptomatology showed significant negative relations with social skills. Early childhood inattentive symptoms predicted school-age social skills ratings. Cognitive functioning was not significantly related to social skills.** ***Conclusion:*** **Parent-reported social skills difficulties are evident during early childhood. This work adds to the literature by describing the frequency and stability of social skills challenges in early childhood and in the school-age period in NF1. Research about interventions to support social skills when difficulties are present is needed.**

(*J Dev Behav Pediatr* 42:656–665, 2021) **Index terms:** neurofibromatosis type 1, NF1, social skills, longitudinal.

Social functioning difficulties are commonly reported for school-age children with neurofibromatosis type 1 (NF1) based on parent, teacher, and peer reports,[1–5] but little is known about these difficulties in young children with NF1 or about the trajectory of social functioning across development. NF1 is an autosomal dominant genetic disorder caused by a mutation of the *NF1*-gene on chromosome 17q11.2 responsible for encoding the tumor suppressor protein, neurofibromin.[6] Approximately half of cases are familial, and half represent de novo *NF1* mutations. NF1 has a prevalence rate of 1 in 3500 births[7] and includes medical, cognitive,[6] and psychosocial difficulties.[7] Using peer reports, children with NF1 are more sensitive and more socially isolated, show less leadership behavior, are chosen as a best friend less often, have fewer reciprocated friendships, and are less liked in comparison with classroom peers.[5] Most previous research about social functioning, using parent-rated questionnaire measures, demonstrates that school-age children with NF1 display poorer social skills compared with normative data[1] and unaffected controls,[2–4] display more social problems compared with unaffected controls[3,4,7–10] and normative data,[10,11] and have less social competence compared with unaffected controls.[10,12]

Relations of social functioning with attention problems have been explored in school-age children with NF1. Attention deficits are recognized as a central part of the cognitive phenotype of individuals with NF1 with a prevalence of 30% to 50% meeting DSM criteria for attention-deficit hyperactivity disorder (ADHD).[13] Significant correlations between attention problems and social skills have been found for school-age children with NF1.[1] Furthermore, children with NF1 and comorbid ADHD show poorer social skills than children with NF1 only and children with NF1 and comorbid learning deficits.[1,13] However, attention difficulties among young

From the *Department of Psychology, University of Wisconsin-Milwaukee, Milwaukee, WI; †Department of Neurology, Division of Neuropsychology, Medical College of Wisconsin, Wauwatosa, WI; ‡Division of Clinical Behavioral Neuroscience, Department of Pediatrics, University of Minnesota, Minneapolis, MN.

Received July 2020; accepted January 2021.

Supported by grants from NFMidwest, NFMidAtlantic, NFNortheast, University of Chicago Clinical and Translational Science Award (Grant Number UL1 RR024999), and the University of WI-Milwaukee Research Growth Initiative.

The authors declare no conflict of interest.

Address for reprints: Danielle M. Glad, MS, Department of Psychology, University of Wisconsin-Milwaukee, Milwaukee, WI; e-mail: dmglad@uwm.edu.

children are not consistently indicated in young children with NF1[14]; they may be subtle and difficult to detect.[15]

Investigations of associations between cognitive and social functioning in children with NF1 have yielded inconsistent findings. Most individuals with NF1 show overall intellectual functioning in the low average to average range,[16] with lowering in verbal and performance IQ relative to same-age peers.[4,9,17] Some studies of social skills, social problems, and social competence have not found significant correlations with intellectual functioning in children with NF1.[1,8,12] Other studies, however, have provided evidence for such relations.[11,18] A study of young children with NF1, whose sample overlaps with this study, observed a trend for stronger social skills in children with stronger intellectual functioning.[19]

In this study, parent-reported social skills of children with NF1 are examined in both early childhood and the school-age years separately and also among a subsample of children seen at both time points. To date, there have been limited studies about social skills among young children, and there has been no examination of social skills longitudinally in children with NF1. Studies of early childhood have found parental ratings of social skills to be comparable with contrast groups but used broad behavioral screening questionnaire measures rather than measures focused specifically on social skills.[14,18,19] This study primarily aims to examine the developmental trajectory of social skills in children with NF1 cross-sectionally and longitudinally. The emergence of social skills difficulties, the frequency of social skills difficulties, and the persistence of these difficulties over time are investigated using a measure focused on assessment of social skills. Given that social deficits are apparent for school-age children, teenagers,[20] and adults with NF1[21,22] and given the progressive nature of NF1,[23] social skills difficulties in NF1 may emerge over time, highlighting the importance of a longitudinal approach. Overall, it is hypothesized that parents of young children (early childhood [EC] Subsample) and school-age children (school-age [SA] Subsample) with NF1 will report poorer social skills in comparison with normative data. Using a subset of participants who were followed longitudinally into the school-age years (Longitudinal Subsample), it is expected that parent-reported school-age social skills will be poorer than in early childhood, there will be higher frequency of social skills difficulties in the school-age years than in early childhood, and social skills will be significantly correlated over time.

Previous research has emphasized that attention and cognitive difficulties are present during early childhood for children with NF1.[14,24] The literature on children without NF1 points to links between attention[25] and cognitive[26] functioning with social functioning. The secondary aims of this study are to (1) replicate previous school-age findings of relations between parent-reported attention difficulties and parent-reported social skills with school-age children and extend the description of social skills to younger children with NF1, (2) examine relations between cognitive functioning and parent-reported social skills in NF1 during both developmental periods given inconsistent findings in the literature, and (3) examine the predictive value of early childhood ADHD symptomatology and cognitive functioning for later parent-reported social skills. Parent-reported ADHD symptomatology and cognitive functioning are expected to be significantly correlated with parent-reported social skills cross-sectionally during early childhood (EC Subsample), school age (SA Subsample), and longitudinally across time (Longitudinal Subsample).

METHODS

Participants

Participants were 65 children with a confirmed clinical diagnosis of neurofibromatosis type 1 (NF1) and their parents. This study has a mixed design with cross-sectional and longitudinal approaches. The sample consists of 3 somewhat overlapping subsamples: (1) children with NF1 seen between 1 and 4 times yearly beginning between ages 3 and 6 (we refer to this as the "early childhood" time point, although it does extend to the early school-age years [early childhood [EC]]; n = 50); this approach resulted in 22 participants assessed at 3 years old, 30 participants at 4 years old, 33 participants at 5 years old, and 28 participants at 6 years old; (2) children with NF1 seen once during school age (SA; ages 9–13; n = 40) with 14 participants at 9 years old, 10 participants at 10 years old, 4 participants at 11 years old, 6 participants at 12 years old, and 6 participants at 13 years old; and (3) a subset of children with NF1 who were seen during both early childhood (T1) and during school age (T2; n = 25), referred to as the longitudinal sample. The first assessment time point during early childhood (visit 1) was used as the T1 time point for longitudinal analyses. The mean time between T1 visit 1 and T2 for the longitudinal sample was 6.28 years (SD = 0.76). Table 1 describes the participant demographic information for each subsample.

Procedure

Recruitment took place at several midwestern neurofibromatosis clinics and through flier distribution through NF organizations. For the school-age study, previous research participants who had consented to be informed of future studies were mailed a study flier or called. Inclusion criteria included (1) a confirmed clinical diagnosis of NF1 by a physician, (2) age 3 to 8 years (for early childhood study) and/or 9 to 13 years (school-age study), and (3) first and main language spoken in the home is English. Early on in the study, enrollment of 7- and 8-year-olds was discontinued; because of the small sample size at these ages, participants at 7 and 8 years old were excluded from this investigation. Although no participants were excluded for

Table 1. Participant Demographic Data for the Early Childhood Sample, School-Age Sample, and a Subset of Longitudinal Participants Seen at Both Time Points

	Cross-Sectional		Longitudinal Subset	
	Early Childhood	School Age	T1	T2
Variable	**n = 50**	**n = 40**	**n = 25**	
Mean age (SD)	3.96 (1.05)	10.9 (1.59)	4.12 (1.09)	10.40 (1.35)
Sex (frequency, %)				
Female	19 (38)	18 (45)	11 (44)	—
Male	31 (62)	22 (55)	14 (56)	—
NF etiology (frequency, %)	Familial: 19 (38); de novo: 31 (62)	Familial: 13 (32.5); de novo: 27 (67.5)	Familial: 7 (28); de novo: 18 (72)	—
Race/ethnicity (frequency; %)				
White	37 (74)	33 (82.5)	20 (80)	—
African American	5 (10)	4 (10)	3 (12)	—
Latino	5 (10)	—	—	—
Asian	1 (2)	1 (2.5)	1 (4)	—
Mixed ethnicity	2 (4)	2 (5)	1 (4)	—
Hollingshead SES index mean (SD)	41.92 (14.86)	46.13 (12.43)	43.04 (14.26)	44.99 (10.82)

Cross-sectional refers to analyses of 1 time point. Longitudinal subset refers to analyses across early childhood and school age within the same participants. NF, neurofibromatosis; SES, socioeconomic status; T1, early childhood visit for the longitudinal subset; T2, school-age visit for the longitudinal subset.

the following reasons, exclusion criteria included (1) any comorbid conditions not commonly associated with NF1 and (2) a significant surgery within the past 6 months. Consent forms and questionnaire measures were mailed to participants for parental completion before the assessment appointment. Informed consent was obtained. Each participant was administered an age-appropriate neuropsychological battery. This study was conducted with approval by the University of Wisconsin-Milwaukee's Institutional Review Board.

Measures

The Social Skills Rating System (SSRS)[27] and the Social Skills Improvement System (SSIS)[28] are parent report questionnaires used to assess social skills during early childhood and school age, respectively. The SSIS is a revised version of the SSRS and has a moderate-to-strong correlation with the SSRS. Both measures demonstrate adequate reliability and validity. Internal consistency estimates are as follows: SSRS Preschool $\alpha = 0.90$, SSRS Elementary $\alpha = 0.87$, SSIS Elementary $\alpha = 0.95$, and SSIS Secondary $\alpha = 0.96$. The SSRS Parent Elementary form Social Skills scale is moderately correlated (0.58) with the Child Behavior Checklist Social Competence scale. The SSIS is moderately to strongly correlated (0.85 for preschool and 0.52 for elementary) with the Behavior Assessment System for Children-Second Edition and moderately with the Vineland-II (0.44). The SSRS Preschool form was used for children ages 3 to 5 years and the Elementary form for children in K–first grades. The SSIS Elementary form was used for children in K–sixth grades grades and the Secondary form for children in seventh and eighth grades. The Social Skills scale standard score (Mean [M] = 100, SD = 15) on each measure was used to assess the presence of positive social behaviors. Higher scores represent more positive social behaviors. Standard scores of <85 are classified as a difficulty, and ≥ 85 are classified as not a difficulty.

The Conners Parent Rating Scales – Revised (CPRS-R) Short Form[29] and Conners – Third Edition (Conners-3) – Parent Short Form[30] are parent report questionnaire measures that were used to assess attention difficulties in early childhood and school age, respectively. Both measures have demonstrated good reliability and validity. The CPRS-R Hyperactivity and Cognitive Problems/Inattention scales' T-scores (M = 50, SD = 10) were used to examine attention-deficit hyperactivity disorder (ADHD) symptomatology during early childhood. The Conners-3 Hyperactivity/Impulsivity and Inattention scales' T-scores were used during the school-age years. Higher scores on both measures represent more ADHD symptomatology.

The Differential Ability Scales – Second Edition (DAS-II)[31] was used to assess cognitive abilities. The DAS-II demonstrates excellent reliability and validity. The DAS-II Early Years version was used during early childhood, and the School-Age version was used during school age. Standard scores (M = 100, SD = 15) for an overall general conceptual ability (GCA) and verbal, nonverbal, and spatial reasoning were examined. The DAS-II GCA is highly correlated with the commonly administered Wechsler Preschool and Primary Scale of Intelligence-Third Edition Full Scale IQ (0.87) and the Wechsler Intelligence Scale for Children-Fourth Edition Full Scale IQ (0.84). Higher scores represent higher cognitive abilities.

The Four-Factor Index of Social Status (Hollingshead, unpublished data, 1975) was used as a measure of socioeconomic status (SES) for each participant at both

time points. Education and occupational levels of parents, marital status, and sex contribute to an overall SES index score. Educational levels are rated on a 7-point scale, with a score of 1 indicating less than seventh grade to a score of 7 indicating graduate or professional training. Occupational levels are rated on a 9-point scale, with a score of 1 indicating menial service workers to a score of 9 indicating higher executives and major professionals. Each educational code is multiplied by 3, and each occupational code is multiplied by 5 and then summed and averaged to compute a SES index score, ranging from 8 to 66. Higher SES index scores indicate higher overall SES. Criticisms have arisen related to this method of calculating SES[32]; however, many studies have used this method and demonstrated reliability and high correlation with other methods of SES calculations.[33]

Statistical Analysis

IBM SPSS for Windows, version 25, was used for data analysis. False discovery rate correction was used to control for multiple comparisons (q value of < 0.05 indicated significance). Analyses of 1 time point are referred to as cross-sectional examinations (i.e., EC Subsample and SA Subsample). Analyses across early childhood and school age within the same participants are referred to as longitudinal examinations (i.e., Longitudinal Subsample). Spearman's *rho* correlations were used where specified. Attrition analyses were conducted to compare early childhood children who returned for a visit at T2 and those who did not return for a visit at T2 and to illustrate the representativeness of the longitudinal sample and the validity of the longitudinal findings, using independent samples t test and χ^2 tests of independence. Attrition within early childhood was also examined comparing early childhood participants who had a visit at age 6 years and those who did not, using independent samples t test and χ^2 tests of independence. Group differences among the subsamples were examined using independent samples t test and correlations. One sample t test was used to compare social skills with the normative mean. One-way analysis of variance and Fisher's least significance difference post hoc tests were used to examine differences between ages during early childhood. Longitudinal examinations were explored using a paired samples t test, correlations, and exact McNemar's tests.

RESULTS

Attrition

When examining attrition from early childhood to school age, no significant differences were found for sex (χ^2[1, N = 50] = 0.76, q = 0.44), socioeconomic status (SES) (t[48] = 0.53, q = 0.59, d = 0.15), neurofibromatosis (NF) etiology classification (χ^2[1, N = 50] = 2.12, q = 0.35), or general conceptual ability (GCA) (t[48] = 0.92, q = 0.44, d = 0.26) among individuals with a visit at school-age (SA) (Longitudinal Subsample; n = 25) and those who did not have a visit at SA (n = 25). Notably, social skills were significantly higher for those who did return at SA (t[48] = −3.05, q = 0.014, d = 0.86). Conners Parent Rating Scales – Revised (CPRS-R) Short Form Hyperactivity during early childhood was significantly lower for those who did return at SA compared with those who did not return at SA (t[34.4] = 3.35, q = 0.014, d = 0.95), suggesting that those with more hyperactivity difficulties were more likely to drop out, and thus, this investigation could be examining a less impaired group of individuals with NF1. There was no significant difference for CPRS-R Cognitive Problems/Inattention (t[48] = 1.14, q = 0.44, d = 0.32). As a note, although there were no differences in the representation of familial and de novo NF etiology classification within the early childhood (EC) Subsample and SA Subsample, there was a significant difference in the Longitudinal Subsample with more participants with de novo NF etiology classification.

For analysis of stability during early childhood (within EC Subsample), 18 individuals with a visit at age 3 or 4 years and a visit at age 6 years were examined. When examining attrition within early childhood, no significant differences were found for sex (χ^2[1, N = 50] = 1.25, q = 0.38), SES (t[48] = −1.12, q = 0.38, d = 0.35), NF classification (χ^2[1, N = 50] = 1.25, q = 0.38), GCA (t[48] = 0.29, q = 0.81, d = 0.11), social skills (t[48] = 0.24, q = 0.81, d = 0.19), or attention-deficit hyperactivity disorder (ADHD) symptomatology (CPRS-R Hyperactivity: t[47.77] = 2.00, q = 0.20, d = 0.607 and Cognitive Problems/Inattention: t[48] = 1.95, q = 0.20, d = 0.604) among young children included in this analysis and those who were excluded because they did not have a visit at age 6 years.

Group Differences in Social Skills

No group differences in social skills were found by sex (EC: t[48] = −1.71, q = 0.26, d = 0.51; SA: t[38] = −1.84, q = 0.26, d = 0.59; T1 Social Skills Rating System [SSRS]" t[23] = −0.78, q = 0.53, d = 0.31; and T2 Social Skills Improvement System [SSIS]: t[23] = −2.70, q = 0.13, d = 1.12). No significant differences in social skills were evident for familial compared with de novo NF etiology classification (EC: t[48] = −1.52, q = 0.27, d = 0.43; SA: t[15.64] = −0.86, q = 0.53, d = 0.32; T1 SSRS: t[23] = 0.62, q = 0.54, d = 0.26; and T2 SSIS: t[23] = −0.93, q = 0.53, d = 0.37). Social skills were not significantly related to SES (EC: *rho*[50] = 0.29, q = 0.13; SA: *rho*[40] = −0.03, q = 0.53; T1 SSRS: *rho*[25] = 0.25, q = 0.26; and T2 SSIS: *rho*[25] = −0.006, q = 0.53).

Emergence and Stability of Social Skills Challenges During Early Childhood

Young children with NF1 had significantly lower social skills compared with the normative mean (Table 2; mean [M] = 100, SD = 15; t[49] = −4.41, q = 0.002,

Table 2. Descriptive Statistics of Study Measures for Children in Early Childhood (n = 50), School Age (n = 40), and Longitudinal Participants (n = 25)

	Early Childhood					School Age			
	Cross-Sectional		Longitudinal (T1)			Cross-Sectional		Longitudinal (T2)	
	n = 50		n = 25			n = 40		n = 25	
Scale	M	SD	M	SD	Scale	M	SD	M	SD
Social functioning (SSRS)					Social functioning (SSIS)				
Social SS	89.24	17.26	96.24	16.58	Social SS	91.85	15.25	92.76	13.51
ADHD symptomatology (CPRS-R)					ADHD symptomatology (Conners-3)				
Hyperactivity T	54.04	10.94	49.32	6.05	Hyperactivity/impulsivity T	61.33	13.98	59.00	11.81
Cognitive problems/inattention T	56.84	12.16	54.88	10.91	Inattention T	67.23	13.04	66.08	12.75
Cognitive functioning (DAS-II)					Cognitive functioning (DAS-II)				
GCA SS	93.02	11.87	94.56	9.87	GCA SS	93.90	13.24	94.60	15.09
Verbal SS	96.00	12.8	98.76	11.22	Verbal S	98.65	13.20	99.72	14.74
Nonverbal SS	93.54	12.59	93.88	11.99	Nonverbal SS	94.08	15.56	93.80	17.95
Spatial SS	92.5	12.59	94.10	9.91	Spatial SS	91.82	11.36	92.76	10.89

Cross-sectional refers to analyses of 1 time point. Longitudinal refers to analyses of the subset of participants seen both in early childhood and school age. ADHD, attention-deficit hyperactive disorder; CPRS-R, Conners Parent Rating Scales – Revised; DAS-II, Differential Ability Scales – Second Edition; GCA, general conceptual ability; M, mean; SS, standard score; SSIS, Social Skills Improvement System; SSRS, Social Skills Rating System; T, T score; T1, early childhood visit for the longitudinal subset; T2, school-age visit for the longitudinal subset.

d = 0.67), and children ages 3, 4, and 5 years had significantly lower social skills compared with the normative mean (M = 100, SD = 15; age 3: M = 81.73, SD = 13.46, $t(21) = -6.37$, $q = 0.002$, $d = 1.28$; age 4: M = 89.97, SD = 18.23, $t(29) = -3.01$, $q = 0.007$, $d = 0.60$; age 5: M = 90.67, SD = 18.22, $t(32) = -2.94$, $q = 0.007$, $d = 0.56$). Children age 6 years did not significantly differ from the normative mean (M = 96.96, SD = 17.42, $t(27) = -0.92$, $q = 0.37$, $d = 0.19$). Early childhood social skills were significantly correlated with age (rho = 0.44, $q = 0.002$). There was a statistically significant difference between age groups [$F(3, 109) = 3.23$, q = 0.028]. Post hoc tests revealed that the children with NF1 age 3 years had statistically significantly more impaired social skills compared with children with NF1 age 6 years ($q = 0.004$, $d = 0.98$). Social skills at ages 3 or 4 years were strongly significantly correlated with social skills at age 6 years [$rho(18) = 0.71$, $q = 0.002$].

Emergence and Stability of Social Skills Challenges During School Age and Longitudinally Across Time

School-age children with NF1 had significantly lower social skills compared with the normative mean (Table 2; M = 100, SD = 15; $t[39] = -3.38$, $q = 0.004$, $d = 0.54$). School-age social skills were not significantly correlated with age (rho = 0.049, $q = 0.38$).

EC social skills (M = 96.24, SD = 16.58) did not differ significantly from SA social skills for children with NF1 (M = 92.76, SD = 13.51, $Z[24] = -1.09$, $q = 0.35$, d = 0.23) and were not significantly correlated across time (using visit one data; $rho = 0.29$, $q = 0.17$) with a small to medium effect size. To further explore longitudinal relations, early childhood was grouped into 2 age groups using any visit number rather than visit 1 only: (1) 3- and 4-year-olds and (2) 5- and 6-year-olds. Sixteen participants were represented in both age groups. EC social skills for the 3- and 4-year-olds were not significantly correlated with SA social skills ($rho[17] = 0.32$, $q = 0.17$), with a small to medium effect size. EC social skills of the 5- and 6-year-olds were significantly correlated with SA social skills ($rho[24] = 0.56$, $q = 0.01$). Social skills difficulties were observed for 32% of young children and 24% of school-age children with NF1. Exact McNemar's test indicated no significant difference in the proportion of social skills difficulties over time ($q = 0.69$). Further examination of social skills difficulties revealed that 4% of young children and 8% of school-age children had social skills difficulties greater than 2 standard deviations below the mean.

Relations of Attention-Deficit Hyperactivity Disorder Symptomatology and Cognitive Functioning with Social Skills

Table 3 includes the correlations of social skills with ADHD symptomatology and cognitive functioning during early childhood, school age, and across time. ADHD symptomatology within the longitudinal sample increased from early childhood to school age (Inattention: $Z[24] = -2.89$, $q = 0.008$, $d = 0.94$ and Hyperactivity: Z [24] = −3.37, $q = 0.004$, $d = 1.03$). EC CPRS-R Hyperactivity and Cognitive Problems/Inattention had significant negative correlations, ranging from weak to moderate strength, with EC SSRS social skills. T1 CPRS-R Cognitive Problems/Inattention was significantly negatively correlated with T2 SSIS social skills with a medium effect size. SA Conners-3 Hyperactivity/Impulsivity and Inattention were significantly negatively correlated with SA SSIS social skills, with strength in the moderate range. Cognitive functioning was not significantly correlated with social skills.

Table 3. Spearman's *rho* Correlations Between Social Functioning Standard Scores and ADHD Symptomatology and Cognitive Functioning by Sample

	Social Functioning			
	Early Childhood		School Age	
	SSRS		SSIS	
Scale	*rho*	*q*	*rho*	*q*
	n = 50		n = 25	
Early childhood				
ADHD symptomatology (CPRS-R)				
Hyperactivity	−0.46	0.004**	−0.05	0.42
Cognitive problems/inattention	−0.25	0.046*	−0.39	0.034*
Cognitive functioning (DAS-II)				
GCA	0.26	0.03*	−0.06	0.39
Verbal	0.15	0.14	−0.19	0.18
Nonverbal	0.21	0.07	0.15	0.24
Spatial	0.22	0.097	0.15	0.26
			n = 40	
School age				
ADHD symptomatology (Conners-3)				
Hyperactivity/impulsivity	—		−0.35	0.021*
Inattention	—		−0.42	0.008*
Cognitive functioning (DAS-II)				
GCA	—		0.025	0.44
Verbal	—		−0.05	0.37
Nonverbal	—		0.01	0.48
Spatial	—		0.09	0.29

Significant Spearman's rho correlations with false discovery rate (FDR) correction: *$q < 0.05$; **$q < 0.01$. ADHD, attention-deficit hyperactive disorder; Conners-3, Conners – Third Edition – Parent Short Form; CPRS-R, Conners Parent Rating Scales – Revised; DAS-II, Differential Ability Scales – Second Edition; GCA, general conceptual ability; SSIS, Social Skills Improvement System; SSRS, Social Skills Rating System.

DISCUSSION

The emergence and stability of parent-reported social skills challenges in children with neurofibromatosis type 1 (NF1) were characterized in the early childhood and school-age periods in this investigation. As hypothesized, parents of young and school-age children with NF1 reported poorer social skills compared with the normative mean. Rates of social skills difficulty were relatively stable throughout early childhood and school age. Approximately one-third of young children and one-fourth of school-age children with NF1 displayed social skills difficulties with no significant difference in the proportion of social skills difficulties at each time point. Children with NF1 ages 3, 4, and 5 years (but not age 6) had significantly lower social skills compared with the normative mean, which provides partial support for our hypothesis. Longitudinally, social skills ratings did not differ from early childhood to school age, although they were not significantly correlated. However, when multiple time points within early childhood were considered as predictors of social skills in school age, social skills at the end of early childhood (5- and 6-year-olds, which could also be termed early school age) were indeed predictive of social skills during school age.

This study, together with the available literature, provides evidence that social skills difficulties in children with NF1 are variable. In fact, Behavior Assessment System for Children and Behavior Assessment System for Children 2nd Edition have been used as a measure of social skills and have generally indicated that young children with NF1 do not have poorer social skills compared with normative data[19] or unaffected controls,[14,19] which is distinct from the current findings with a more comprehensive measure of social skills. There is a need for continued research to determine which social functioning measure is most sensitive to identifying social deficits in children with NF1. Here, parent-reported social skills difficulties occurred in 24% to 32% of the sample of children with NF1 (rates that are comparable with another study[1]), which illustrates that many children with NF1 (at least two-thirds) do not have significant social skills difficulties. Distinctions between terminology used to describe social skills and functions have been made and suggest that social functioning measures likely tap different social constructs, and these constructs should be evaluated independently.[34] An exploratory examination of the social skills items most frequently endorsed by parents during early childhood

and school-age years for children with NF1 was conducted and revealed that the specific social skills that were problematic varied across children. Few social skills evaluated on the Social Skills Rating System (SSRS) and Social Skills Improvement System (SSIS) emerged as consistent weaknesses—*compromising in conflict situations* and *introducing themselves to other people* are the only items to emerge as problematic for a substantial subset of the children with NF1 across time. However, it should be noted that without a control group in the current investigation, areas of strengths and weaknesses identified are strictly relative for children with NF1 rather than normative.

There has been suggestion within the NF1 literature of an increased vulnerability for autism spectrum disorders (ASD) with 13% to 33% of children with NF1 meeting criteria for ASD and frequently reported subthreshold ASD symptoms (social communication impairment and restricted and repetitive behaviors).[35,36] A recent multisite study identified a strong correlation between a measure often used to examine ASD symptomatology (Social Responsiveness Scale-2) and the central social skills measure used in this investigation (SSIS).[37] Overlap with the autism spectrum remains somewhat controversial. There is evidence to suggest that associations with ASD may be confounded by attention-deficit hyperactivity disorder (ADHD) symptomatology, emotional functioning, and communication challenges.[38,39] At least one study has found that children with NF1 had significantly milder social deficits compared with individuals with ASD.[40] Most studies that have examined social skills using the SSRS and SSIS in children and adolescents with ASD have reported social skills in the below average range,[41] whereas the current investigation found mean social skills in the average range for children with NF1. Some children with NF1 may indeed also show sociocommunicative and repetitive behaviors that are consistent with comorbid ASD diagnosis. ASD symptomatology was not addressed in the current investigation and may warrant additional attention in future social skills investigations. Furthermore, studies of the relatively new diagnostic category of Social Communication Disorder among children with NF1 are needed.

As hypothesized and consistent with previous research with older children,[1,8] ADHD symptomatology was negatively correlated with social skills cross-sectionally, with weak to moderate strength depending on the scale, for young children and school-age children with NF1. In addition, inattention in early childhood predicted school-age social skills, whereas hyperactivity/impulsivity did not show such relations over time. By contrast, social skills were not related to cognitive functioning, consistent with some previous investigations.[1,8,12] It is evident that children with NF1 who present with attention problems are at risk for social difficulties[1,42] and that this relation is seen even when attention problems are assessed in young children. Providers should supply social skills training resources and recommendations to aid in supporting social skills for children with NF1 who present with ADHD symptomatology in early childhood.

The findings of this investigation correspond to the socio-cognitive integrations of abilities (SOCIAL) model (Fig. 1).[34] This model suggests that multiple dimensions, such as biological functioning, cognitive functions, and internal and external factors, interact to determine an individual's social function. Any component of this model could be altered during development to influence social function directly or indirectly as well as positively and negatively. Consistent with the SOCIAL model, this study shows that internal factors, such as NF1, have the capacity to shape the emergence of social function. In addition, ADHD symptomatology is directly influencing the social skills of children with NF1. The SOCIAL model also includes physical attributes as a mediator of social function, which have been discussed in relation to the physical manifestations of NF1 as important for future research. For example, impairments in social functioning have been found to be associated with physical manifestations of NF1 for adults[22]; however, studies in children have not found relations with appearance[5] but rather clinical severity broadly.[1] Previous research in older children has also indicated that greater NF1 neurological severity (which includes headaches, brain tumors, seizures, vision impairments, and cognitive, learning, attention, and behavior difficulties) has been found to be associated with poorer social, emotional, and behavioral functioning.[5] It is important to note that research describes the progressive nature of NF1 physical symptomatology[23]; relations of social functioning with NF1 physical manifestations and visibility may become more pronounced within adolescence and adulthood when visible symptoms of NF1 are more likely to be present.

This study is, to our knowledge, the first to report on social skills longitudinally in children with NF1 and the first to report on relations with social skills over time. However, the study design has several limitations that indicate future directions. First, although previous longitudinal research in NF1 has used sample sizes smaller than or similar to the current longitudinal sample size,[43,44] the sample size is nevertheless relatively small, and there is a higher than expected frequency of de novo cases in the longitudinal sample, which detracts from its representativeness of the NF1 population. Second, the current investigation relies on parent report of social skills and attention difficulties, which introduces a possible response bias and common methods bias. These measures might not capture the full range of skills necessary to engage socially or the extent of ADHD symptomatology that occurs in a variety of contexts including real-world behavior. Parent report of children's social functioning may not correspond to a child's acceptance and status among peers, so peer nominations and peer

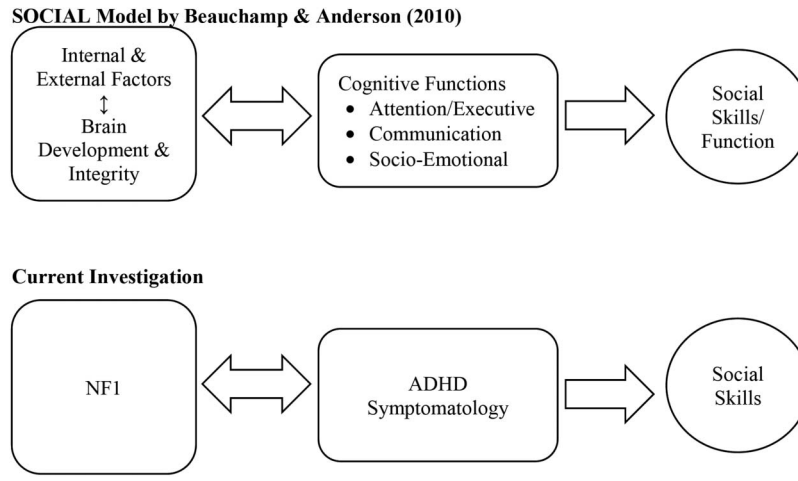

Figure 1. Graphic representation of the SOCIAL Model (Beauchamp and Anderson[34]) and a comparison with the current investigation. A unidirectional arrow illustrates the factor's impact on an outcome. The bidirectional arrows represent factors that influence each other. ADHD symptomatology, attention-deficit/hyperactivity disorder symptoms including inattention, hyperactivity, and impulsivity; NF1, neurofibromatosis type 1; SOCIAL, socio-cognitive integrations of abilities.

report of social abilities may be a more useful measure of social functioning.[45,46] Although concerns about low correspondence between parent report on the SSRS and peer report of social abilities have been raised,[45] studies examining the effectiveness of the Program for the Education and Enrichment of Relational Skills (PEERS) intervention on social functioning in children with ASD and ADHD have found improvements in both real-world behavior, such as increased social knowledge and increased frequency of hosted and invited get-togethers, and increased parent ratings on the SSIS.[47–49] No such studies are available in the early childhood period. There has been only one published study of social functioning using peer reports in children with NF1,[5] suggesting that such an approach may be less feasible in a rare population than are parental questionnaires. Although behavior rating scales do have limitations, they have a number of advantages, including quantifiable information with strong reliability, assessment of a broad range of social behaviors, and available normative data to compare individual performance with a representative sample.[50] Indeed, the Response Evaluation in Neurofibromatosis and Schwannomatosis group, a collective of experts about neurocognitive functioning in NF1, has developed expert consensus about the measurement of social functioning in NF1 as an endpoint in clinical trials and has pointed to the SSIS as a core recommended measure (Janusz et al., under review). Nevertheless, future research examining relations between parental ratings of social functioning and real-world social behavior is needed. Third, this study is limited by a lack of a comparison group, which would have been useful in determining the presence of social skills difficulties, the persistence of difficulties over time, and social strengths and weaknesses in comparison with unaffected controls.

Future research should include a multisite approach to help to ensure a large sample that has adequate representation of all ages and NF etiologies, greater power to detect significant findings, and the opportunity for a comparison group. A multisituational and multiinformant approach[45] would be beneficial, including exploration of relations among informants and with observational or peer report approaches. In addition, research about early indicators and trajectories of these challenges may help identify areas of support at key developmental periods for optimal social development. Finally, research should focus on identification and implementation of evidence-based social skills interventions for children with NF1 who experience social difficulties because there is no currently available literature of the efficacy of such interventions with children with NF1. In addition to social skills group interventions (e.g., PEERS[47–49]), peer-based interventions may also be a promising avenue to improve status among peers.[51]

Overall, this research contributes to a better understanding of when social skills difficulties emerge, the frequency at which social skills challenges occur for young children and school-age children, and the persistence of social skills difficulties over time in NF1 using parent report. It is important given the reduction in quality of life related to social functioning reported for children with NF1[8,52] and the variety of negative outcomes associated with social difficulties.[53] This research is important given the reduction in quality of life related to social functioning reported for children with NF1 and supports the importance of identification and implementation of early and effective intervention related to social skills challenges.

ACKNOWLEDGMENTS

The authors would like to thank the participants and their families. The authors are grateful to James Tonsgard, Scott Hunter, Pamela Trapane, Donald Basel, Robert Listernick, Dawn Siegel, and Heather Radtke for assistance with participant identification and recruitment. The authors also acknowledge our research laboratory team for their work and collaboration.

REFERENCES

1. Barton B, North K. Social skills of children with neurofibromatosis type 1. *Dev Med Child Neurol*. 2004;46:553–563.
2. Huijbregts SCJ, de Sonneville LMJ. Does cognitive impairment explain behavioral and social problems of children with neurofibromatosis type 1? *Behav Genet*. 2011;41:430–436.
3. Huijbregts SC, Loitfelder M, Rombouts SA, et al. Cerebral volumetric abnormalities in neurofibromatosis type 1: associations with parent ratings of social and attention problems, executive dysfunction, and autistic mannerisms. *J Neurodevelop Disord*. 2015;7:1–9.
4. Loitfelder M, Huijbregts SC, Veer IM, et al. Functional connectivity changes and executive and social problems in neurofibromatosis type I. *Brain Connect*. 2015;5:312–320.
5. Noll RB, Reiter-Purtill J, Moore BD, et al. Social, emotional, and behavioral functioning of children with NF1. *Am J Med Genet A*. 2007;143A:2261–2273.
6. Miller DT, Freedenberg D, Schorry E, et al. Health supervision for children with neurofibromatosis type 1. *Pediatrics*. 2019;143:e20190660.
7. Cipolletta S, Spina G, Spoto A. Psychosocial functioning, self-image, and quality of life in children and adolescents with neurofibromatosis type 1. *Child Care Health Dev*. 2018;44:260–268.
8. Allen T, Willard VW, Anderson LM, et al. Social functioning and facial expression recognition in children with neurofibromatosis type 1. *J Intellect Disabil Res*. 2016;60:282–293.
9. Dilts CV, Carey JC, Kircher JC, et al. Children and adolescents with neurofibromatosis 1: a behavioral phenotype. *J Dev Behav Pediatr*. 1996;17:229–239.
10. Johnson NS, Saal HM, Lovell AM, et al. Social and emotional problems in children with neurofibromatosis type 1: evidence and proposed interventions. *J Pediatr*. 1999;134:767–772.
11. van der Vaart T, Rietman AB, Plasschaert E, et al. Behavioral and cognitive outcomes for clinical trials in children with neurofibromatosis type 1. *Neurology*. 2016;86:154–160.
12. K Lewis A, Porter A. Social competence in children with neurofibromatosis type 1: relationships with psychopathology and cognitive ability. *J Child Dev Disord*. 2016;2:1–12.
13. Mautner V-F, Kluwe L, Thakker SD, et al. Treatment of ADHD in neurofibromatosis type 1. *Dev Med Child Neurol*. 2007;44:164–170.
14. Sangster J, Shores EA, Watt S, et al. The cognitive profile of preschool-aged children with neurofibromatosis type 1. *Child Neuropsychol*. 2010;17:1–16.
15. Mahone EM. Measurement of attention and related functions in the preschool child. *Ment Retard Dev Disabil Res Rev*. 2005;11:216–225.
16. Cutting L, Clements A, Lightman A, et al. Cognitive profile of neurofibromatosis type 1: rethinking nonverbal learning disabilities. *Learn Disabil Res Pract*. 2004;19:155–165.
17. Hyman SL, Shores A, North KN. The nature and frequency of cognitive deficits in children with neurofibromatosis type 1. *Neurology*. 2005;65:1037–1044.
18. Martin S, Wolters P, Baldwin A, et al. Social-emotional functioning of children and adolescents with neurofibromatosis type 1 and plexiform neurofibromas: relationships with cognitive, disease, and environmental variables. *J Pediatr Psychol*. 2012;37:713–724.
19. Klein-Tasman BP, Janke KM, Luo W, et al. Cognitive and psychosocial phenotype of young children with neurofibromatosis-1. *J Int Neuropsychol Soc*. 2014;20:88–98.
20. Ejerskov C, Lasgaard M, Østergaard JR. Teenagers and young adults with neurofibromatosis type 1 are more likely to experience loneliness than siblings without the illness. *Acta Paediatr*. 2015;104:604–609.
21. Pride NA, Crawford H, Payne JM, et al. Social functioning in adults with neurofibromatosis type 1. *Res Dev Disabil*. 2013;34:3393–3399.
22. Hummelvoll G, Antonsen KM. Young adults' experience of living with neurofibromatosis type 1. *J Genet Counsel*. 2013;22:188–199.
23. DeBella K, Szudek J, Friedman JM. Use of the National Institutes of Health criteria for diagnosis of neurofibromatosis 1 in children. *Pediatrics*. 2000;105:608–614.
24. Casnar CL, Klein-Tasman BP. Parent and teacher perspectives on emerging executive functioning in preschoolers with neurofibromatosis type 1: comparison to unaffected children and lab-based measures. *J Pediatr Psychol*. 2017;42:198–207.
25. Nijmeijer JS, Minderaa RB, Buitelaar JK, et al. Attention-deficit/hyperactivity disorder and social dysfunctioning. *Clin Psychol Rev*. 2008;28:692–708.
26. Tipton LA, Christensen L, Blacher J. Friendship quality in adolescents with and without an intellectual disability. *J Appl Res Intellect Disabil*. 26:522–532.
27. Gresham FM, Elliott SN. *Manual for Social Skills Rating System*. Minneapolis, MN: NCS Pearson; 1990.
28. Gresham FM, Elliott SN. *Manual for Social Skills Improvement System*. Bloomington, MN: NCS Pearson; 2008.
29. Conners CK. *Conners Parent Rating Scale Revised*. Toronto, Ontario: Multi-Health Systems; 1997.
30. Conners CK. *Conners*. 3rd ed. Toronto, Ontario: Multi-Health Systems; 2008.
31. Elliott CD. *Manual for the Differential Abilities Scales*. 2nd ed. San Antonio, TX: The Psychological Corporation; 2007.
32. Duncan GJ, Magnuson KA. Off with Hollingshead: socioeconomic resources, parenting, and child development. In: Bornstein MH, Bradley RH, eds. *Socioeconomic Status, Parenting, and Child Development*. Mahwah, NJ: Lawrence Erlbaum Associates Publishers; 2003:83–106.
33. Cirino PT, Chin CE, Sevcik RA, et al. Measuring socioeconomic status. *Assessment*. 2002;9:145–155.
34. Beauchamp MH, Anderson V. SOCIAL: an integrative framework for the development of social skills. *Psychol Bull*. 2010;136:39–64.
35. Garg S, Lehtonen A, Huson SM, et al. Autism and other psychiatric comorbidity in neurofibromatosis type 1: evidence from a population-based study. *Dev Med Child Neurol*. 2013;55:139–145.
36. Walsh KS, Vélez JI, Kardel PG, et al. Symptomatology of autism spectrum disorder in a population with neurofibromatosis type 1: ASD in neurofibromatosis type 1. *Dev Med Child Neurol*. 2013;55:131–138.
37. Payne JM, Walsh KS, Pride NA, et al. Social skills and autism spectrum disorder symptoms in children with neurofibromatosis type 1: evidence for clinical trial outcomes. *Dev Med Child Neurol*. 2020;62:813–819.
38. Klein-Tasman BP. Are the autism symptoms in neurofibromatosis type 1 actually autism? *Dev Med Child Neurol*. 2021;63:132.
39. Morotti H, Mastel S, Keller K, et al. The association of neurofibromatosis and autism symptomatology is confounded by behavioral problems. *Dev Med Child Neurol*. 2021;63:226–232.
40. Adviento B, Corbin IL, Widjaja F, et al. Autism traits in the RASopathies. *J Med Genet*. 2014;51:10–20.
41. Laugeson EA, Gantman A, Kapp SK, et al. A randomized controlled trial to improve social skills in young adults with autism spectrum disorder: the UCLA PEERS® program. *J Autism Dev Disord*. 2015;45:3978–3989.
42. Lidzba K, Granström S, Lindenau J, et al. The adverse influence of attention-deficit disorder with or without hyperactivity on cognition in neurofibromatosis type 1: neurofibromatosis type 1 and AD(H)D. *Dev Med Child Neurol*. 2012;54:892–897.
43. Cutting L, Huang G, Zeger S, et al. Growth curve analyses of neuropsychological profiles in children with neurofibromatosis type 1: specific cognitive tests remain "spared" and "impaired" over time. *J Int Neuropsychol Soc*. 2002;8:838–846.
44. Payne JM, Pickering T, Porter M, et al. Longitudinal assessment of cognition and T2-hyperintensities in NF1: an 18-year study. *Am J Med Genet*. 2014;164:661–665.
45. Hoza B, Gerdes A, Mrug S, et al. Peer-assessed outcomes in the multimodal treatment study of children with attention deficit hyperactivity disorder. *J Clin Child Adol Psychol*. 2005;34:74–86.
46. Noll RB, Bukowski WB. Commentary: social competence in children with chronic illness: the devil is in the details. *J Pediatr Psychol*. 2012;37:959–971.

47. Laugeson EA, Frankel F, Gantman A, et al. Evidence-based social skills training for adolescents with autism spectrum disorders: the UCLA PEERS Program. *J Autism Dev Disord*. 2012;42:1025–1036.
48. Gardner DM, Gerdes AC, Weinberger K. Examination of a parent-assisted, friendship-building Program for adolescents with ADHD. *J Atten Disord*. 2015;23:363–373.
49. Schohl KA, Van Hecke AV, Carson AM, et al. A replication and extension of the PEERS intervention: examining effects on social skills and social anxiety in adolescents with autism spectrum disorders. *J Autism Dev Disord*. 2014;44:532–545.
50. Gresham FM, Elliott SN, Cook CR, et al. Cross-informant agreement for ratings for social skill and problem behavior ratings: an investigation of the Social Skills Improvement System—Rating Scales. *Psychol Assess*. 2010;22:157–166.
51. Kasari C, Rotheram-Fuller E, Locke J, et al. Making the connection: randomized controlled trial of social skills at school for children with autism spectrum disorders. *J Child Psychol Psychiatry*. 2012; 53:431–439.
52. Graf A, Landolt MA, Mori AC, et al. Quality of life and psychological adjustment in children and adolescents with neurofibromatosis type 1. *J Pediatr*. 2006;149:348–353.
53. Woodward LJ, Fergusson DM. Childhood peer relationship problems and later risks of educational under-achievement and unemployment. *J Child Psychol Psychiat*. 2000;41:191–201.