Social–emotional Functioning of Children and Adolescents With Neurofibromatosis Type 1 and Plexiform Neurofibromas: Relationships With Cognitive, Disease, and Environmental Variables

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Objective This descriptive cross-sectional study aimed to determine how cognitive, disease, and environmental variables relate to social–emotional functioning in youth with NF1 and plexiform neurofibromas. **Methods** Psychological assessments were administered to 53 children (mean age 12.4 years); parents and teachers completed the Behavior Assessment System for Children—Second Edition (BASC-2). Disease severity was quantified by nurse–practitioner ratings and tumor burden, and parents completed a life events checklist to indicate environmental stressors. **Results** Notable proportions of children scored in the at-risk/clinically significant ranges on several parent and teacher BASC-2 subscales including Somatization, Attention Problems, Depression, and Withdrawal. Combinations of cognitive, disease, and environmental variables predicted scores on parent BASC-2 Internalizing Problems, Behavior Symptoms Index, and Adaptive Skills composites. **Conclusions** Cognitive, disease, and environmental variables relate to social–emotional outcomes in children with NF1. These youth may benefit from interventions targeting social skills, cognitive functioning, and adaptive ways of coping with NF1-related pain.

Key words chronic illness; psychosocial functioning; social skills and development.

Introduction

Neurofibromatosis type 1 (NF1) is a genetic disorder caused by a mutation on chromosome 17. The disease affects approximately 1 in 3,500 individuals, and can be inherited by an autosomal dominant transmission or come about through spontaneous mutation (Tonsgard, 2006). Common clinical manifestations include café-au-lait macules, skin-fold freckling, cutaneous and plexiform neurofibromas, scoliosis, and optic gliomas (Gutmann et al., 1997). Currently, there are no effective treatments other than surgical removal of the tumors, which is often complicated by the involvement of nearby nerve tissue, and tumor regrowth is common (Tonsgard, 2006). In addition, involvement of the central nervous system is frequent, with 30–65% of these children having cognitive impairments (North et al., 1997). Areas of deficits include visual-spatial skills (Levine, Materek, Abel, O'Donnell, & Cutting, 2006; Schrimsher, Billingsley, Slopis, & Moore, 2003) and executive functions such as planning and working memory (Payne, Hyman, Shores, & North, 2011; Roy et al., 2010). Furthermore, rates of attention-deficit hyperactivity disorder (ADHD) and learning disabilities (LDs) are higher in youth with NF1 compared to unaffected siblings and the general population (Koth, Cutting, & Denckla, 2000; Mautner, Kluwe, Thakker, & Leark, 2002).

Social-Emotional Functioning in Youth with NF1

The physical and neurocognitive symptoms of NF1 put children with this disorder at risk for a myriad of social–emotional problems, but very few studies have addressed

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this topic. Initial evidence indicates that children with NF1 experience more problems with social skills, anxiety, depression, and aggressive behavior compared to normative means and unaffected siblings on the Child Behavior Checklist (CBCL; Barton & North, 2004; Johnson, Saal, Lovell, & Schorry, 1999). In one of the first reports on this topic, Dilts and colleagues (1996) found that parents and teachers both rated children with NF1 as significantly worse than their unaffected siblings on the Social Problems subscale of the CBCL. Furthermore, parent and teacher ratings placed one-third or more of the children in the clinically significant range on this subscale. More recently, Barton and North (2004) found a difference between children with NF1 and their sibling pairs on the same CBCL subscale, but only on the parent form. In another study, children with NF1 and their parents both reported impairments in various domains of health-related quality of life (HR-QOL), including social, emotional, and cognitive functioning (Graf, Landolt, Mori, & Boltshauser, 2006). In contrast, a recent study reported no differences between preschool-aged children with NF1 and unaffected peers on any BASC scales other than Somatization, but the proportion of children scoring in the clinically significant range was not reported (Sangster, Shores, Watt, & North, 2010).

Factors contributing to social–emotional outcomes in children with NF1 can be considered within a systemic and social–ecological model. According to Kazak (1989), such an approach necessitates consideration of numerous variables that may influence psychological well-being in a child with chronic illness. Among these are internal variables, such as disease severity, and external variables, such as ''ongoing daily issues that the child and family face'' (Kazak, 1989, p. 25). This model has been applied to children with illnesses such as cancer (Shapiro, Perez, & Warden, 1998), diabetes (Naar-King et al., 2006), and HIV infection (Hosek et al., 2008). Given the central nervous system (CNS) involvement in NF1, cognitive functioning should be included as a potential influence also. Thus, we put forth a conceptual framework whereby cognitive functioning, disease severity, and environmental stressors may contribute to social–emotional wellbeing in children with NF1.

Relationship Between Social–Emotional Functioning and Neurocognitive Variables

Two recent studies highlighted the relationship between neurocognitive variables and psychological wellbeing in children with NF1. First, Huijbregts and de Sonneville (2010) found significant correlations between cognitive control (e.g., inhibitory control and working memory) and parent-reported emotional problems and social skills in a sample of 30 children with NF1. In the second study (Noll et al., 2007), neurological severity (based on variables such as the presence of absence of seizures, ADHD/LD, and behavior problems) was associated with multiple indices of social and emotional functioning, including parent-reported externalizing symptoms, child-reported depression, and peer-reported measures of popularity and isolation. The authors concluded that children with NF1 who have neurological involvement, particularly those with attention and learning problems, are most at risk for social and emotional problems.

Relationship Between Social–emotional Functioning and Disease Severity

Given the complicated symptom profiles in NF1, it is reasonable to conceive that disease severity could impact children's social–emotional functioning. Plexiform neurofibromas (PNs), present in 30–50% of patients with NF1 (Friedrich, Schmelzle, Hartmann, Funsterer, & Mautner, 2005; Gutmann et al., 1997), are benign tumors that can be disfiguring and limit physical functioning. Children with PNs report a high frequency (Kim et al., 2009) and severity (Burns et al., 2011) of pain, which can negatively impact quality of life (Page et al., 2006). Other NF1-related symptoms that can impact psychological well-being and/or quality of life include scoliosis (Reichel & Schanz, 2003), optic pathway gliomas (Wolkenstein et al., 2009), and visible or disfiguring manifestations of the disease (Page et al., 2006). Barton and North (2004) found no significant differences in parent- or teacher-rated social skills between kids with minimal/mild symptoms versus moderate/severe symptoms, although children in the moderate/severe group rated themselves as having significantly poorer social skills than children in the minimal/mild symptom group.

Relationship Between Social–Emotional Functioning and Stressful Life Events

In addition to the potential contributions of cognitive and disease variables, environmental factors may impact social–emotional functioning in children with NF1. Stressful life events have been shown to increase the risk of negative psychological outcomes, including internalizing and externalizing disorders, in community samples of children and adolescents (Tiet et al., 2001). Moreover, life events during adolescence increase the risk of depression in adulthood (Pine, Cohen, Johnson, & Brook, 2002). A few studies have explored this topic among youth with chronic illness. Elliott-Desorbo et al. (2009) found that school-related events in the last 6 months significantly predicted self-reported depression in children and adolescents with

HIV infection. The potential impact of stressful life events on the functioning of youth with NF1 has not been addressed in the literature to date.

Study Objectives

Initial studies indicate that problems exist in the social–emotional functioning of youth with NF1, and preliminary evidence suggests that cognitive and disease variables may play a role in these problems. The current study seeks to further explore the relationship of cognitive and disease variables to social–emotional functioning. Based on a systems/social–ecological framework, we incorporate an assessment of environmental stressors as a third potential influence on social–emotional wellbeing, thus allowing for a more broad exploration of the variables influencing social–emotional functioning in these children. Determining the potential relationship of these variables to social–emotional functioning can help guide the development of effective interventions. Also, by specifically examining a sample of children with PNs, we provide a thorough characterization of this subgroup of the pediatric NF1 population, which has not been done previously in the literature.

Our primary hypothesis was that more impaired cognitive functioning, worse disease severity, and more environmental stressors would be associated with worse parent-reported social and emotional problems in a sample of youth with pervasive NF1 and PNs. As a secondary objective, we sought to explore the ability of these variables to predict social–emotional problems using multiple regression analyses. Other secondary objectives were to identify specific problem areas within social–emotional functioning, to explore associations between social–emotional variables and demographic characteristics (i.e., child age and gender, parent education), and to examine differences between parent- and teacher-reported social–emotional functioning among our sample.

Methods

Eligibility Criteria

Eligible patients included children and adolescents aged 6–18 years with NF1 and PNs who were enrolled on a natural history (NH) protocol at the National Cancer Institute (NCI) and whose parent completed the BASC-2 during one of their psychological assessments on the NH protocol. All patients on the NH study must have had a diagnosis of NF1 according to the NIH Consensus Conference criteria (NF1 Cognitive Task Force, 1988) or have had a confirmed NF1 mutation with analysis performed in a CLIA-certified laboratory. Sixty of the patients on the NH protocol were within the current sub-study's age range. Of these, seven did not participate in the psychological assessment for the following reasons: Spanish-speaking ($n = 1$), autistic ($n = 1$), withdrew from NH protocol before testing was completed ($n = 1$), medical complications related to a malignant tumor prevented testing from being scheduled ($n = 1$), and declined due to no interest ($n = 3$). Thus, 53 patients participated in the psychological assessment.

Measures

Demographic Variables

Demographic information was obtained through a background information form completed by a parent or legal guardian. Parent education was used as an indicator of socioeconomic status.

Social–Emotional Functioning

The Behavioral Assessment Scale for Children—Second Edition (BASC-2; Reynolds & Kamphaus, 2004) is an inventory that assesses aspects of emotional and social functioning in terms of internalizing and externalizing symptoms and adaptive skills. On the Parent Report and Teacher Report forms, respondents rate the frequency of behaviors for children ages 2 to 18 years. Raw scores on both forms are converted to T-scores (mean = 50, standard deviation = 10). Scores between 60 and 69 fall in the ‘‘At Risk’’ range, and scores of 70 or higher fall in the ‘‘Clinically Significant’’ range.

Cognitive Functioning

The Wechsler Abbreviated Scale of Intelligence (WASI) reliably estimates cognitive functioning in children ages 6 and up (Wechsler, 1999). Verbal IQ (VIQ) and Performance IQ (PIQ) scores, each of which has a *M* of 100 and *SD* of 15, were included in analyses. Based on past research identifying areas of impairment in children with NF1, several other tests were chosen for analyses. The Benton Judgment of Line Orientation Test (JLO; Benton, Varney, & Hamsher, 1978) is a measure of visual-spatial perception administered to individuals 7 years and older. Raw scores were converted to *z*-scores for children ages 7–14 years and 18-year olds, since normative data were available for these age ranges. The Trails switching task from the Delis Kaplan Executive Function System (DKEFS; Delis, Kaplan, & Kramer, 2001) was administered to patients 8 years and older to assess mental flexibility. From the Wechsler Intelligence Scale for Children—Fourth Edition (WISC-IV; Wechsler, 2003), the Digits Backward (DB) scaled score was analyzed as a measure of working memory, as advocated in numerous past studies (e.g., Hale, Hoeppner, & Fiorello, 2002).

NF1 Disease Severity

To quantify disease severity, the nurse practitioner who conducts physical examinations with patients on the natural history study completed a rating form created by the authors. The form lists 17 diagnoses and physical complications related to NF1, including scoliosis, optic gliomas, pseudoarthrosis, and hearing or vision impairment. Based on retrospective chart reviews, the nurse practitioner rated each patient for the presence (1) or absence (0) of each diagnosis. Ratings were summed across the 17 diagnoses to yield an overall severity score. To assess the interrater reliability of the form, the research nurse who coordinated the study and who is very familiar with the patients rated a subset of 15 patients by conducting chart reviews. The resulting concordance correlation coefficient (Lin, 2000) was .81.

As a separate indicator of disease severity, the volume of PNs was examined. Specifically, the patients' total tumor burden (TTB) was calculated as the sum of all PN volumes derived from whole-body Short T1 Inversion Recovery Magnetic Resonance Imaging, expressed as a percentage of body weight (Solomon, Warren, Dombi, Patronas, & Widemann, 2004). Because the TTB variable was positively skewed, a log transformation was performed and the resulting variable approximated a normal distribution.

Environmental Stressors

The Life Events Checklist (LEC) consists of a list of 29 potentially stressful life events. The measure was modified from previously existing scales (Moss, Bose, Wolters, & Brouwers, 1998). Parents indicate which events their child experienced in the 6 months prior to the evaluation. Items fall into the categories of Family (e.g., marriage or divorce of parents, birth of a sibling; seven items), School (e.g., decline in school grades, moving to a new school; six items), Loss (e.g., death of a friend or immediate family member; four items), and Financial (e.g., parental job loss; three items) events in accordance with procedures described in a prior study (Elliott-Desorbo et al., 2009). Several items did not fall reliably into any category (e.g., being teased in school, substantial change in peer group) but are included in the sum of all life events. In several previously published studies, the total score and subdomains have demonstrated significant associations with various psychological and medical variables (Elliott-DeSorbo et al., 2009; Moss, Bose, Wolters, & Brouwers, 1998).

Statistical Analyses

To test our primary hypothesis, Pearson correlations were used to assess bivariate relationships between BASC-2 parent scores and cognitive, environmental, and disease variables. Variables with significant bivariate correlations with a BASC-2 composite score were entered simultaneously into a multiple regression model. We chose not to use a stepwise entry method because of the exploratory nature of the analyses. Only parent BASC-2 scores (not teacher scores) were included in the correlation matrix to reduce the number of analyses. To assess secondary objectives, Pearson correlations were used to examine the relationship of BASC-2 parent scores with child age and parent education; *t*-tests were used to examine differences in BASC-2 parent and teacher scores between male and female patients. Finally, paired-sample *t*-tests were used to compare differences between parent and teacher ratings on the BASC-2 scales. Because so little is known about the social–emotional functioning of children and adolescents with NF1, analyses were considered exploratory and alpha was set at .05.

Procedures

Families of children with NF1 are referred by physicians to the NCI from around the country. The NF1 research team also is contacted directly by parents who locate information about ongoing studies at this center via the internet. The facility's Institutional Review Board approved the natural history study. Informed consent was obtained from the patient's parent or legal guardian prior to enrollment, and minor assent was obtained from all patients age 7 years and older. Data were collected between February 2008 and January 2011 during outpatient clinic visits. As part of the protocol, patients received a complete history and physical examination by a nurse-practitioner, during which NF1-related symptoms and disease severity were reviewed. Patients also were administered a baseline comprehensive psychological evaluation that included the above measures, and parents completed the questionnaires while their child was being tested. In addition, families were given the BASC-2 teacher form and asked to give it to the child's teacher. Teachers were provided with a self-addressed stamped envelope in which to return the form directly to the researchers.

Results

Demographic Variables

Fifty-three children (66% male) participated in the psychological assessment (mean age $= 12.4 \pm 3.4$ years, range 6.3–18.7 years). The mean level of parent education was 14.3 ± 2.0 years (range 11–20 years). By parent report, 32% had been diagnosed with ADHD, and 70% were receiving special education services. No significant relationships emerged between demographic variables (child age, gender, parent education) and any of the BASC-2 parent scales. However, on the teacher BASC-2, higher parent education was associated with better social skills ($r = .43$) and adaptive skills ($r = .40$) in the children ($ps < .05$).

Social–Emotional Functioning

The BASC-2 parent questionnaires were completed by mothers (75%), fathers (19%), and extended family members who were the child's legal guardians (6%). Twenty-seven BASC-2 teacher forms were received. Table I shows the mean scores on the parent and teacher BASC-2 forms, as well as the percentages of scores falling in the At-Risk or Clinically Significant (AR/CS) ranges. On the parent measure, all mean scores were within normal limits. Thirty-two percent of scores on the Internalizing Problems composite were in the AR/CS range, compared to only 11% of scores on the Externalizing Problems composite ($t = 3.06$, $p < .01$). Within the subscales, the highest percentages of patients falling in the AR/CS range were in Somatization (42%), Leadership (34%), Attention Problems (32%), and Depression (30%). Notably, only 8% of parent ratings yielded AR/CS scores on the Aggression and Conduct Problems subscales.

All composite and subscale scores on the Teacher BASC-2 were within normal limits. Like on the parent BASC-2, more AR/CS scores were obtained on the Internalizing Problems composite (22%) compared to the Externalizing Problems composite (15%), but this difference was not statistically significant ($t = 0.70$, $p > .05$). AR/CS scores were most prevalent on the Somatization (41%), Withdrawal (37%), and Attention Problems (30%) subscales. Problems with learning (25%) and study skills (26%) also were common. Similar to results of the parent BASC-2, relatively few of the children's scores were in the AR/CS range on the Aggression (15%) and Conduct Problems (7%) subscales.

A comparison of BASC-2 results across informants indicates that parent ratings were significantly lower (reflecting worse functioning) than teacher ratings on the Adaptive Skills composite ($t = 2.41$), and on the Social Skills ($t = 2.28$) and Leadership ($t = 2.17$) subscales (p's $< .05$). No other significant differences emerged between parent and teacher reports.

Table I. *Mean T-Scores on the BASC-2 Parent (n = 53) and Teacher (n = 27) Scales*

	Parent Version		Teacher version	
	Mean (*SD*)	AR/CS (%)	Mean (*SD*)	AR/CS (%)
Depression	55.3 (10.7)	30	52.6 (7.8)	26
Anxiety	53.5 (10.2)	23	51.7 (10.6)	15
Atypicality	52.5 (10.5)	23	53.1 (13.0)	19
Withdrawal	52.7 (10.3)	28	55.2 (10.8)	37
Hyperactivity	53.0 (13.0)	17	51.7 (10.7)	19
Aggression	48.2 (8.0)	8	49.2 (10.0)	15
Conduct Problems	49.9 (8.9)	8	47.8 (8.5)	7
Somatization	58.4 (15.2)	42	56.0 (11.3)	41
Attention Problems	54.5 (10.1)	32	52.3 (12.2)	30
Learning Problems	–	–	54.8 (11.8)	25
Social Skills[a]	50.6 (9.3)	13	54.3 (11.6)	11
Adaptability[a]	48.7 (9.4)	26	52.6 (9.8)	19
Leadership[a]	46.3 (8.9)	34	50.6 (10.5)	26
Activities of Daily Living[a]	45.3 (9.1)	26	–	–
Functional Communication[a]	45.3 (10.5)	26	47.7 (8.8)	19
Study Skills[a]	–	–	49.7 (10.3)	26
Behavior Symptoms Index	53.5 (10.2)	23	51.1 (11.4)	15
Externalizing Problems	50.5 (9.4)	11	49.9 (10.0)	15
Internalizing Problems	57.1 (12.7)	32	53.6 (10.0)	22
Adaptive Skills[a]	46.8 (9.0)	28	50.9 (10.2)	22
School Problems	–	–	53.6 (11.7)	26

Note. T-scores are compared to a mean of 50, *SD* of 10. AR/CS = At-Risk/Clinically Significant range (≥60 for clinical scales, ≤40 for adaptive scales).
[a]Adaptive scales; higher scores are better.

Cognitive Functioning

Table II shows the descriptive statistics for the cognitive measures, as well as the percentage of patients scoring more than one standard deviation below the mean for each test. The mean Verbal IQ (VIQ) and Performance IQ (PIQ) were both in the average range. On the JLO, the mean z-score was more than one standard deviation below the normative mean, with nearly half (47%) of the children scoring below average. Mean scaled scores were in the average range on the Trails switching and Digits Backward tasks.

Table II. *Mean Scores on Cognitive Measures*

Cognitive measure	Mean (*SD*)	Range	Below Average (%)
Verbal IQ	99.45 (15.4)	75 to 146	18
Performance IQ	92.19 (14.4)	65 to 124	29
Judgment of Line Orientation	−1.10 (1.69)	−5.29 to 1.37	47
Trailmaking Switching	8.53 (3.5)	1 to 14	19
Digits Backward	9.05 (2.8)	1 to 16	10

Note. IQ scores have a *M* of 100, SD of 15. The Judgment of Line Orientation scores ($n = 36$) are presented as z-scores ($M = 0$, $SD = 1$). Scores for the Trailmaking Switching ($n = 45$) and Digits Backward ($n = 42$) tests are scaled scores ($M = 10$, $SD = 3$).

NF1 Disease Severity

Disease severity ratings were completed by the nurse practitioner for 50 children. On the 0 to 17 scale, scores ranged from 0 to 8 ($M = 3.36$, $SD = 1.6$; median = 3). In addition to PNs, which were present in all children, the most common NF1-related diagnoses included spinal neurofibromas (75%), vision impairment (58%), and scoliosis (57%). The least common diagnoses were chiari malformation (4%), stroke (2%), precocious puberty (2%), and pseudoarthrosis (2%). The mean total tumor burden percentage (available for 43 children) was 3.5 ($SD = 4.6$), and ranged from less than 1% to 25.0%.

Stressful Life Events

The mean number of life events endorsed by parents was 2.21 ($SD = 1.9$), with a range of 0 to 8 events experienced in the past 6 months. The most commonly endorsed events were being teased in school (30%) and family experiencing financial hardship (28%).

Relationship Between Social–Emotional Functioning and Cognitive Functioning

As hypothesized, cognitive scores were associated with social–emotional scores. First, IQ scores were significantly correlated with several of the BASC-2 parent clinical and adaptive scores (Table III). Specifically, lower VIQ scores were related to worse scores on the Behavioral Symptoms Index composite and on the clinical subscales of Withdrawal, Attention Problems, and Conduct Problems ($p < .05$). In addition, children with lower VIQ and PIQ scores had more problems indicated on the Adaptive Skills composite ($p < .01$), and the Adaptive subscales of Functional Communication ($p < .01$), Leadership ($p < .01$), and Social Skills ($p < .05$). Scores on each of the other selected cognitive indices were related to several parent BASC-2 scores in the hypothesized direction.

Relationship Between Social–emotional Functioning and Disease Severity

Disease variables were related to social–emotional functioning, as hypothesized (Table III). Greater nurse–practitioner-rated disease severity was associated with worse scores on the parent BASC-2 Internalizing Problems composite ($p < .05$) and on the Somatization subscale ($p < .01$). Disease severity was not related to any other parent BASC-2 scores. Higher tumor burden percentages were related to higher scores on the Attention Problems subscale on the Parent BASC-2 ($p < .05$).

Relationship Between Social–emotional Functioning and Stressful Life Events

In support of our primary hypothesis, a higher number of stressful life events was significantly related to higher

Table III. *Correlations of BASC-2 Parent Scores to Cognitive, Environmental, and Disease Variables*

BASC-2 Parent Scale	VIQ	PIQ	JLO	TS	DB	NFSEV	TTB	LEC
Depression	−.26	−.14	−.05	−.01	−.22	.15	.14	.40**
Anxiety	−.13	.01	−.19	.12	−.11	.25	.23	.36**
Atypicality	−.18	−.13	−.29	−.11	−.38*	−.01	−.01	.35**
Withdrawal	−.32*	−.12	−.39*	−.07	−.36*	−.09	−.03	.28*
Hyperactivity	−.06	−.06	−.19	−.15	−.16	−.02	−.20	.29*
Aggression	−.12	−.06	−.05	−.04	−.08	−.25	−.08	.21
Conduct Problems	−.30*	−.07	.02	−.07	−.06	−.16	−.07	.36**
Somatization	−.23	−.01	−.11	.09	.02	.37**	.18	.29*
Attention Problems	−.34*	−.24	−.40*	−.25	−.32*	−.03	−.31*	.43**
Social Skills[a]	.32*	.32*	.31	.35*	.31*	.15	.33	−.16
Adaptability[a]	.29*	.23	.18	.24	.23	−.06	−.05	−.40**
Leadership[a]	.53**	.42**	.36*	.39**	.29	−.03	.09	−.24
Activities of Daily Living[a]	.24	.29	.21	.36	.20	−.08	.28	−.25
Functional Communication[a]	.57**	.42**	.59**	.37*	.62**	−.01	.32	−.23
Behavior Symptoms Index	−.28*	−.16	−.29	−.14	−.34*	−.05	−.11	.44**
Externalizing Problems	−.18	−.07	−.07	−.12	−.13	−.15	−.15	.34*
Internalizing Problems	−.27	−.05	−.12	.09	−.09	.31*	.22	.39**
Adaptive Skills[a]	.48**	.42**	.44**	.43**	.42**	−.01	.24	−.32*

Note. VIQ = Verbal IQ; PIQ = Performance IQ; JLO = Judgment of Line Orientation test; TS = Trails Switching; DB = Digits Backwards; NFSEV = Disease Severity; TTB = Total Tumor Burden; LEC = Life Events Checklist.

[a]Higher scores are better.

*$p < .05$, **$p < .01$.

scores on the parent BASC-2 Internalizing Problems and Externalizing Problems composites ($ps < .05$), the Behavior Symptoms Index ($p < .001$), and most of the Clinical subscales (Table III). More stressful life events also were correlated with worse scores on the Adaptive Skills composite ($p < .05$) and the Adaptability subscale ($p < .01$). With respect to event categories, more school-related events were related to worse scores on the parent BASC-2 Internalizing Problems composite and Behavioral Symptoms Index and the Adaptive Skills composite ($p < .05$). School events also were positively correlated with the Depression, Anxiety, and Aggression subscales ($p < .05$), and negatively correlated with the Adaptability subscale ($p < .01$). More loss-related events were correlated with worse scores on the Attention Problems subscale ($p < .05$). Family and Financial events were not correlated with any of the parent BASC-2 scores (results for event categories not shown in table).

Multiple Regression Results

Based on a priori hypotheses and the pattern of results in the correlation matrix, three separate multiple regression analyses were conducted to determine the influence of cognitive, disease, and environmental variables on the BASC-2 parent (a) Internalizing Composite, (b) Behavior Symptoms Index, and (c) Adaptive Skills Composite. Results are presented in Table IV. First, the combination of Verbal IQ, disease severity, and total stressful life events significantly predicted Internalizing Composite scores ($F = 6.76$, $p < .001$; $Adj\ R^2 = .26$). Moreover, disease severity and life events each accounted for a significant amount of unique variance (12% and 19%, respectively; $p < .01$). Next, the combination of Verbal IQ, Digits Backward, and total stressful life events significantly predicted scores on the Behavior Symptoms Index ($F = 7.43$, $p < .001$; $Adj.\ R^2 = .32$). Digits Backward scores and total stressful life events each accounted for significant unique variance (12% and 24%, respectively; $ps < .01$). In predicting Adaptive Skills Composite scores, the combination of Verbal IQ, disease severity, and total stressful life events was statistically significant ($F = 6.73$, $p < .001$; $Adj.\ R^2 = .26$). Only Verbal IQ accounted for significant unique variance (19%, $p < .01$).

Discussion

To our knowledge, this is the first study to explore social–emotional functioning among a sample of youth with NF1 and PNs. The pattern of significant correlations provides support for our primary hypothesis. That is, cognitive scores, disease variables, and environmental stressors all related to social–emotional scores. Specifically, each cognitive score was associated with one or more BASC-2 parent scores, providing further support for a previously reported (Huijbregts & de Sonneville, 2010) link between cognitive and social–emotional functioning in children with NF1. Notably, the Leadership and Functional Communication subscale scores each were associated with at least four of the five cognitive variables, indicating that these aspects of adaptive functioning are particularly at risk among children with NF1 and cognitive deficits. Consistent with this finding, Noll et al. (2007) found that children with NF1 had fewer reciprocated friendships and were less well liked than healthy peers, and that unpopularity was associated with more severe neurological symptoms. Research on nonverbal learning disabilities (Casey, Rourke, & Picard, 1991) suggest that the visual-perceptual impairments evidenced by the children in our study may relate to their weakness in social skills. In sum, neurocognitive deficits in children with NF1 may underlie their poor social skills, exemplified in our study by not taking leadership roles in peer groups and difficulty expressing themselves to others.

Cognitively, our sample performed similarly to other studies of children with NF1 in general. For example, a relative deficit in visual-spatial perception on the JLO test also has been reported by Krab et al. (2005) and Clements-Stephens, Rimrodt, Gaur, & Cutting (2008). However, in contrast to past studies of NF1 noting a relative impairment in working memory (Huijbregts, Swaab, & de Sonneville, 2010; Payne et al., 2011), our sample did not evidence such a deficit. Prior reports in the literature on the frequency of learning problems in NF1 and the notable percentage (25%) of teacher-reported learning problems in our study implicate the need for studies

Table IV. *Multiple Regression Analyses for Prediction of BASC-2 Composite Scores*

	β	*t*-value	*p*-value
Internalizing Composite			
Verbal IQ	−0.14	−1.08	.29
Disease severity	0.36	2.87	.006
Total life events	0.40	3.16	.003
Behavior Symptoms Index			
Verbal IQ	0.03	0.34	.74
Digits Backward	−1.41	−2.71	.01
Total life events	2.56	3.83	<.001
Adaptive Skills Composite			
Verbal IQ	0.46	3.60	<.001
Disease severity	−0.02	−0.17	.86
Total life events	−0.21	−1.68	.10

Note. β = standardized beta weights.

assessing cognitive interventions in this population. The fact that several cognitive test scores predicted social–emotional scores suggests that some of the cognitive deficits experienced by these children may negatively influence their emotional wellbeing, although the cross-sectional nature of our study limits causal implications. Future research should investigate whether interventions targeting cognitive deficits may ameliorate some of the social–emotional impairments in children with NF1. Early results on computerized training techniques such as Cogmed (McNab et al., 2009) are promising in other illness groups. However, more data are needed and the applicability of these techniques to NF1 has yet to be evaluated. Moreover, the field could benefit from exploration of the underlying biological mechanisms linking cognitive and social–emotional functioning in youth with NF1, as well as comparisons of children with and without learning disabilities.

Nurse-practitioner rated disease severity related to only one aspect of social–emotional functioning: parent-reported somatization symptoms. It is worth noting that the items on the Somatization subscale go beyond simply experiencing physical symptoms. Many items refer to the child complaining about and being concerned about their symptoms. Parental response to a child's physical complaints can influence the child's distress (Blount et al., 1997). Thus, the way that parents of children with NF1 react to their child's pain and complaints may mediate the relationship between physical symptoms and social–emotional outcomes. Interventions targeting chronic pain and other physical symptoms may help patients cope with their disease more effectively.

Higher tumor burden percentages were related to more parent-reported attention problems in our sample. While this specific relationship has not been reported previously, some evidence has in fact indicated the presence of a shared neural pathway that causes both PNs and cognitive problems (Weiss, Bollag, & Shannon, 1999; Wolters et al., 2011). However, our finding should be considered with appreciation of the complexity of PNs. In addition to the volume of these tumors, their location is of central importance; a small spinal or orbital tumor can cause more severe problems than an extensive PN in a different location. Results of these exploratory analyses are presented tentatively.

Stressful school events were associated with multiple aspects of social–emotional functioning, including depression, anxiety, aggression, and attention problems, providing the first account of the relationship between these variables within the NF1 population. Social problems (e.g., being teased by peers) and behavior difficulties in school were common in this study. It is well-established that children with learning disabilities (Wiener & Schneider, 2002) and ADHD (Murray-Close et al., 2010) are prone to peer rejection and behavior problems. These diagnoses may serve to elicit the stressful school events experienced in our sample. Conversely, repeated occurrence of stressful school events may lead to greater internalizing and/or externalizing problems in the child. Healthcare professionals should be pro-active by referring children with NF1 for psychological assessments to identify potential learning problems if they are struggling in school. In addition, studies are needed to assess the efficacy of social skills training with these children.

In line with previous reports (e.g., Barton & North, 2004), mean scores on the Parent and Teacher BASC-2 scales were all within normal limits, which initially suggests healthy functioning. Interestingly, mean scores within normal limits were also reported in the BASC-2 manual for the normative sample of children with ADHD as well as in studies of social–emotional functioning in children with cancer and HIV that used the BASC-2 (Malee et al., 2011; Wolfe-Christensen et al., 2009). However, closer inspection of our data reveals that the percentages of children in our sample falling in the At-Risk and Clinically Significant ranges are substantial, ranging from 11% to 32% on the Composite scales. Thus, while our overall sample of youth with NF1 and PNs may be functioning well, a notable subgroup is dealing with a variety of social–emotional problems. Malee et al. (2011) utilized the parent BASC-II to compare behavior problems in HIV perinatally exposed children and HIV-positive children. Results were similar to our study, with mean scores within normal limits but substantial proportions of children in both groups with scores in the at-risk or clinically significant ranges. In their conclusions, the authors emphasize the prevalence of mental health problems in their samples, thus underscoring the importance of looking beyond mean scores that may mask the problems that exist in subgroups of children. Percentages of children scoring in clinical ranges were not reported in the BASC-2 manual or in the study of children with cancer noted above. Inclusion of such information would be helpful in future studies on social–emotional functioning in pediatric illness groups. Furthermore, the need to focus subsequent research on the subgroups scoring in the at-risk and clinically significant ranges as well as on what variables contribute to their significant scores is implicated.

Parents and teachers consistently indicated that somatization, attention problems, depression, and withdrawal are among the most significant problems in our sample. Importantly, internalizing problems (i.e., scores in the

AR/CS range) were more common than externalizing problems. Similarly, in Barton & North's (2004) study, the mean CBCL Internalizing Problems score was slightly higher (57.1) than the mean Externalizing Problems score (53.0). Comparisons between our study and Barton and North's must be tempered since different measures were used (BASC-2 vs. CBCL), and all children in our sample had PNs, which may be associated with a different psychological profile (Wolters et al., 2011). The presence or absence of PNs in Barton and North's sample was not reported.

Limitations and Future Directions

While the descriptive, cross-sectional nature of this study and our lack of a comparison group limit their implications, our results nonetheless can be used for planning future studies. Descriptive research is important in new areas of scientific inquiry, and is particularly useful for gathering information and generating further hypotheses (Marincola, 2007). Our results should be interpreted in this context. The next steps will be to explore social–emotional functioning and related variables using a comparison group, such as unaffected siblings. Comparisons of children with NF1 with and without PNs will be important as well, since PNs are an important aspect of disease severity. The generalizability of our results to children without PNs is limited.

Results of the multiple regression analyses suggest that combinations of cognitive functioning, disease severity, and environmental stressors may influence social–emotional outcomes in children with NF1, although a longitudinal design would lend support to a possible causal relationship. The conceptual framework underlying our hypotheses was guided by a systems and social-ecological model, which has been applied to other pediatric illness groups. This is the first time such a model has been adapted and applied to NF1. Working from this model can help develop a more definitive and elaborate framework that can be tested for its applicability to NF1. However, given our relatively small sample size and the fact that some of the cognitive measures did not span the entire age range of the sample, findings must be interpreted with caution.

Inclusion of additional variables from the systems and social-ecological model, such as coping and family functioning, would be useful in future studies. Also, systems models typically include longitudinal assessments to capture developmental changes over time. Thus, research incorporating multiple timepoints will be important as well.

Conclusions

In our sample of children and adolescents with NF1 and PNs, poorer cognitive functioning, more severe disease, and more environmental stressors all related to social–emotional impairments. Also, while mean social–emotional scores are within normal limits, a substantial subgroup of children is scoring in the At-risk or Clinically Significant range. This descriptive study provides a basis for further research questions regarding children and adolescents with NF1, including (a) what physiological etiologies contribute to their cognitive and social–emotional functioning; (b) what are the potential mediators of the relationship between cognitive, disease, and environmental variables and social–emotional wellbeing (e.g., parental responses to child's complaints of pain); and (c) what interventions will be effective in addressing the social–emotional difficulties in these youth? Well-designed studies with comparison groups and the development of interventions will help to answer these questions.

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