Depressive Symptoms and Neurocardiogenic Syncope in Children: A 2-Year Prospective Study

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KEY WORDS: neurocardiogenic syncope, depression, children, adolescence

ABSTRACT

Dr. Hyphantis contributed to the conception and design of the study, supervised the acquisition of data, analyzed and interpreted the data, drafted the manuscript and approved its final version. Drs. Pappas and Vlahos contributed to the conception and design of the study, as well as to data acquisition, analysis, and interpretation; drafted the manuscript; and approved its final version. Dr. Carvalho and Levenson contributed to data analysis and interpretation, critically revised the manuscript for important intellectual content, and approved its final version. Dr. Kolettis contributed to the conception and design of the study, as well as to data acquisition, analysis, and interpretation; critically revised the manuscript for important intellectual content; and approved its final version.

WHAT’S KNOWN ON THIS SUBJECT: Adult patients with neurocardiogenic syncope have shown high rates of depression. Patients with more severe depressive symptoms have higher rates of syncope recurrence. Psychiatric interventions improve quality of life and decrease syncope recurrence rates.

WHAT THIS STUDY ADDS: Children with neurocardiogenic syncope presented a 2.8-fold higher rate of clinically significant depressive symptoms compared to healthy controls. No recurrent syncope was noted during follow-up which along with improvement in family functioning predicted depressive symptoms improvement.

OBJECTIVE: To evaluate prospectively the relationship between neurocardiogenic syncope (NCS) and depressive symptoms in pediatric patients.

METHODS: Forty-five patients (aged 12.3 ± 2.9 years) with NCS (diagnosed as ≥1 syncopal episodes with typical symptoms, reproduced by tilt-table testing, in the absence of structural or primary electrical heart disease) were compared with 45 age- and gender-matched control subjects. Assessment was performed at baseline and 2 years thereafter. Depressive symptoms and self-perception profile of participants were evaluated, along with their parents’ psychological distress, defensive profile and hostility. Family cohesion and adaptability, as well as the opinion of parents and teachers on children’s strengths and difficulties, were also examined.

RESULTS: At baseline, patients showed more (P = .008) depressive symptoms than controls, correlating with the number of syncopal episodes, impaired relationship with parents and poor family cohesion. A conservative management strategy of NCS was adopted and psychological counseling was offered, focusing on patients with clinically significant depressive symptoms and their families. During follow-up, depressive symptoms decreased in patients (P < .001), but remained stable in controls. Child-parent relationship, family cohesion and family adaptability improved at follow-up in patients. No recurrent syncope was noted during follow-up and this along with improvement in child-parent relationship were associated with depressive symptoms improvement.

CONCLUSIONS: Depressive symptomatology is common in pediatric patients with NCS. Our findings call for additional investigation in larger controlled clinical interventional studies that will enhance understanding of the possible pathophysiological association between depressive symptomatology and NCS in pediatric populations.
Neurocardiogenic syncope (NCS) is common in children and adolescents, with an incidence of ~15%. Although invariably benign, NCS can cause injury and is often a source of distress for parents, patients, teachers, and health care providers. NCS has long been linked to psychiatric morbidity. Indeed, several studies in adults have shown that patients with syncope exhibit high levels of psychological distress, including anxiety and depression. However, relevant information in children and adolescents with NCS is limited. Moreover, the interpretation of available data is difficult because of methodological limitations; to this end, no studies have evaluated depressive symptoms in pediatric NCS patients compared with healthy control subjects. Furthermore, it is not known whether improvement in psychosocial indices affects the clinical course of NCS.

The aims of the current study were (1) to assess depressive symptomatology, self-perception profile, and strengths and difficulties in children and adolescents with NCS, compared with an age- and gender-matched sample of healthy participants; (2) to examine the parents’ psychological profile, as well as family cohesion and adaptability (to account for limitations associated with parents’ reports of their children’s internalized disorders); (3) to examine the relationship between syncope recurrence and alterations in the psychological profile during a medium-term follow-up.

METHODS

Participants

The study population consisted of 45 consecutive children and adolescents with NCS, matched for age and gender with an equal number of healthy control subjects. All children agreed to participate, and signed informed consent was obtained from their parents. All procedures are in accordance with international ethical standards and were approved by the institutional ethics committee.

Patients were recruited from our syncope clinic. For purposes of this study, the diagnosis of NCS was based on a typical history and was confirmed with a positive head-up tilt test (HUTT). Despite the relatively low sensitivity of the HUTT, syncope patients with negative HUTT were excluded; this criterion aimed at enhancing the homogeneity of the patient population by eliminating other causes of syncope. The criteria used to classify typical NCS include short episode duration, presence of triggering factors or provocative situations, and symptoms and signs of autonomic dysfunction, such as pallor, nausea, or sweating. Physical examination, 12-lead electrocardiogram, 24-hour Holter monitoring, and echocardiographic studies were normal in all patients. EEG and MRI were normal, excluding neurologic causes of loss of consciousness.

The control group was formed from healthy age- and gender-matched children and adolescents, recruited randomly from parents’ classmates. Consent was obtained from participants, as well as from their parents and teachers. Exclusion criteria (for patients and controls) were inability to understand Greek, comorbid physical diseases, and mental retardation.

Tilt-Table Testing

All HUTTs were performed by a pediatric cardiologist (APV) and a cardiologist/electrophysiologist (TMK), both with broad experience in the management of syncope. The protocol used at our institution has been described previously. Briefly, after a 10-minute supine phase, the patients were tilted to a head-up position at 85° for 20 minutes; heart rhythm was monitored continuously, and blood pressure was recorded every 2 minutes or every 30 seconds in the presence of symptoms. If no symptoms occurred after 20 minutes, isoproterenol was administered intravenously in escalating doses (0.02–0.08 μg/kg) every 2 minutes, targeting at a heart rate of 150 beats per minute. If the patient developed presyncope or syncope, associated with a sudden fall in systolic blood pressure (of >40 mm Hg) and/or a sudden drop in heart rate (to <50 beats/minute), the test was considered positive, negative tests were defined as absence of these findings after 20 minutes of isoproterenol administration.

Psychological Assessment

Psychological data were collected via a semistructured interview with children, parents, and teachers by a single interviewer (A-IP). Data were obtained at baseline (T1), that is, after the diagnosis of NCS. Follow-up assessments (T2) were carried out by the same interviewer 2 years after the initial evaluation, using the same inventories. Depressive symptoms were assessed by using the standardized Greek version of the Children’s Depression Inventory (CDI), a 27-item self-report measure of cognitive, affective, and behavioral symptoms of childhood depression; higher scores indicate more severe symptoms. Although CDI is not a diagnostic instrument for the diagnosis of depression but only a measure of severity, high scores correlate well with the diagnosis of depression. Thus, CDI is widely used and has satisfactory reliability and validity. Although cutoffs ranging from 13 to 19 have been suggested in the original version, a cutoff point of 15 (corresponding to 90th percentile) has been used in the current study, indicating clinically significant levels of depressive symptoms, as previously suggested. Standardized Cronbach’s alphas (a measure of the internal consistency and reliability of psychometric tests) showed satisfactory
values, at 0.84 for the patient-sample and 0.81 for controls. Self-esteem was assessed by using the standardized Greek version of the Self-Perception Profile for Children (SPPC). The SPPC evaluates 5 domains: scholastic competence, social acceptance, athletic competence, physical appearance, and behavioral conduct. It comprises 36 items that are written in a structural alternative format designed to reduce the tendency to give socially desirable responses.

The emotional and behavioral problems were assessed with the standardized Greek version of the Strengths and Difficulties Questionnaire (SDQ), completed by the parents and the teachers. SDQ comprised 25 items, categorized into 5 scales: hyperactivity/inattention, emotional distress, conduct problems, peer problems, and prosocial behavior. The validity of the Greek SDQ has been confirmed in children and adolescents.

Family functioning dimensions of cohesion (emotional bonding) and adaptability (the ability of the family system to change) were assessed by using the Greek version of the Family Adaptability and Cohesion Scale-III (FACES-III). FACES-III comprises twenty 5-point Likert-type items and shows satisfactory internal consistency and good construct validity for both dimensions.

Assessment of Parents

Parents’ symptoms of psychological distress were assessed with the standardized Greek version of the 28-item General Health Questionnaire, a screening instrument that estimates the likelihood of mild, moderate, or severe psychological distress. Higher scores indicate more severe psychological distress. Hostility was assessed by using the standardized Greek version of the 51-item Hostility and Direction of Hostility Questionnaire, which reflects an attitudinal personality trait; it consists of 3 components measuring extrapunitive manifestations of hostility and 2 components measuring intrapunitive manifestations of hostility. Lastly, to assess the parents’ defensive profile, we used the standardized Greek version of the Defense Style Questionnaire, an 88-item rating scale, designed to estimate behavior indicating four defense styles, namely maladaptive action, image-distorting, self-sacrificing, or adaptive styles on a 0- to 9-point Likert-type scale. The Defense Style Questionnaire is the most widely used self-report method for assessing ego defense mechanisms, and its Greek version has shown adequate internal consistency and construct validity.

Follow-up and Treatment

A conservative management strategy of NCS has been adopted at our syncope clinic, consisting of reassurance of the patient and family, increased consumption of water and salt, tilt training, as well as detailed instructions of early prodromal-symptom recognition and posture maneuvers. Psychological counseling was offered to all patients and their families focusing on those children with CDI scores indicative of clinically significant depressive symptoms (CDI ≥15, n = 16). Healthy children with CDI ≥15 (n = 6) were referred to the outpatient Department of Psychiatry. Pharmacologic treatment is generally reserved only for resistant symptoms, but such cases were not encountered in our study group.

Statistical Analysis

All values are reported as mean ± SD. Differences in continuous variables were assessed with 2-tailed t test with Bonferroni’s correction for multiple comparisons and differences in categorical variables were compared by using $\chi^2$. The effect sizes were also estimated through calculation of Cohen’s $d$ statistic: a value >0.4 was considered clinically significant and a value of >0.8 representative of a large effect. Factors independently associated with depressive symptoms were assessed by using multiple linear regression analysis. The dependent variable was the CDI score, and independent variables were demographic variables, NCS parameters, and the statistically significant psychological variables derived from univariate analyses. Collinearity among independent variables was tested by using the variance inflation factors and tolerance for individual variables.

The time course of depressive and other psychological variables was assessed by using paired t tests. Multiple linear regression analysis was performed to assess factors independently associated with alterations in depressive symptomatology during follow-up; dependent variable was the improvement in CDI score between baseline and follow-up, whereas the selection of independent variables was based on univariate analyses. Hierarchical models were used to assess the unique contribution of each set of psychological variables to the variance in improvement of depressive symptoms. Statistical significance was defined at an $\alpha$ value of .05.

RESULTS

Patients’ Characteristics

The demographics of patients and healthy control subjects are presented in Table 1. Patients had 2.4 ± 1.2 episodes of syncope over a period of 12 ± 12 months before the index evaluation. All were medication-free, and none had any comorbid disease or had seen a mental health professional before the current study. No significant differences were observed between the 2 groups in the demographic variables of parents. Of the 45 patients, 36 (80%) completed the follow-up period, as did a similar
(P = .78) percentage (38/45, 84.4%) of healthy control subjects. Patients were lost to follow-up (n = 9) mainly because they moved to another town; compared with those who completed the study, they were similar in terms of gender, number of syncopal episodes, and psychological variables at baseline, but they were older (16.7 ± 0.5 vs 11.2 ± 2.1 years; P < .001).

**Depressive Symptoms at T1 and Associated Factors**

Compared with controls, NCS patients had higher CDI scores (P < .008; Table 1). In addition, more patients (16, 35.6%) had CDI scores ≥15 (χ² = 6.02, df = 1, P = .014), indicative of clinically important depression, compared with controls (6, 13.3%). NCS patients reported worse (P = .05) relationships with their parents, compared with controls (Table 1). The psychological profile of parents was similar in the 2 groups, as was their opinion of their children's strengths and difficulties (data not shown). In contrast, the teachers' opinions indicated that NCS patients had more difficulties than controls on most SDQ components (Table 1).

Univariate analyses revealed that diagnosis of NCS (P = .005), the number of syncopal episodes (P = .011), worse child-parent relationship (P = .041), poor family cohesion (P = .002), and adoption of a self-sacrificing defense style by the parents (P = .011) were significantly associated with the severity of the children's depressive symptoms; with the exception of parents' self-sacrificing defense style, these variables were associated with depressive symptomatology in multiple regression analysis (Supplemental Table 4). All individual tolerance values were >0.2 and all variance inflation factors were <2, indicating that colinearity was not biasing the regression model.

Figure 1 shows the relationship between depressive symptomatology and number of syncopal episodes across three age groups. As shown in this figure, in all age groups the higher the CDI score the higher the number of syncopal episodes.

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**TABLE 1 Demographic Profile, Severity of Depressive Symptoms (CDI), and Scores on the SPPC, FACES-III, and SDQ of Patients With NCS and Healthy Controls**

<table>
<thead>
<tr>
<th>Variables</th>
<th>Patients (N = 45)</th>
<th>Healthy Controls (N = 45)</th>
<th>df</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean ± SD or n (%)</td>
<td>Mean ± SD or n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>12.3±2.9</td>
<td>12.5±2.6</td>
<td>-.072</td>
<td>.678</td>
</tr>
<tr>
<td>Gender: female</td>
<td>23 (51.1%)</td>
<td>23 (51.1%)</td>
<td>.000</td>
<td>1.000</td>
</tr>
<tr>
<td>School grades</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Elementary (4th–8th grades)</td>
<td>16 (35.6%)</td>
<td>16 (35.6%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gymnasium (7th–8th grades)</td>
<td>17 (37.8%)</td>
<td>17 (37.8%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lyceum (10th–12th grades)</td>
<td>12 (26.7%)</td>
<td>12 (26.7%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CDI Total Depression score</td>
<td>11.9±7.7</td>
<td>7.9±5.9</td>
<td>.583</td>
<td>0.008</td>
</tr>
<tr>
<td>Scholastic competence</td>
<td>3.0±0.8</td>
<td>3.1±0.7</td>
<td>-.133</td>
<td>.802</td>
</tr>
<tr>
<td>Relationships with peers</td>
<td>3.4±0.6</td>
<td>3.2±0.6</td>
<td>.333</td>
<td>.115</td>
</tr>
<tr>
<td>Relationships with parents</td>
<td>2.4±0.7</td>
<td>2.8±0.6</td>
<td>-.614</td>
<td>.050</td>
</tr>
<tr>
<td>Athletic competence</td>
<td>3.3±0.5</td>
<td>3.1±0.7</td>
<td>.329</td>
<td>.078</td>
</tr>
<tr>
<td>Physical appearance</td>
<td>3.2±0.7</td>
<td>2.8±0.6</td>
<td>.614</td>
<td>.009</td>
</tr>
<tr>
<td>Behavioral conduct</td>
<td>3.1±0.7</td>
<td>3.0±0.5</td>
<td>.164</td>
<td>.637</td>
</tr>
<tr>
<td>Family cohesion</td>
<td>4.6±2.3</td>
<td>5.0±2.0</td>
<td>-.185</td>
<td>.361</td>
</tr>
<tr>
<td>Family adaptability</td>
<td>4.0±2.0</td>
<td>4.3±1.8</td>
<td>-.158</td>
<td>.514</td>
</tr>
<tr>
<td>Teacher's opinion</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total difficulties</td>
<td>10.2±6.1</td>
<td>6.1±4.5</td>
<td>.765</td>
<td>.001</td>
</tr>
<tr>
<td>Emotional symptoms</td>
<td>3.5±2.6</td>
<td>1.9±1.7</td>
<td>.728</td>
<td>.001</td>
</tr>
<tr>
<td>Conduct problems</td>
<td>2.8±2.2</td>
<td>1.4±1.2</td>
<td>.790</td>
<td>.001</td>
</tr>
<tr>
<td>Hyperactivity/inattention</td>
<td>2.1±1.9</td>
<td>1.9±2.2</td>
<td>.097</td>
<td>.648</td>
</tr>
<tr>
<td>Peer problems</td>
<td>1.8±1.6</td>
<td>0.9±1.1</td>
<td>.855</td>
<td>.002</td>
</tr>
<tr>
<td>Prosocial behavior</td>
<td>9.9±0.4</td>
<td>8.4±1.7</td>
<td>1.134</td>
<td>.001</td>
</tr>
</tbody>
</table>

a Cohen’s d as effect size.

b Two-tailed t test.

c χ² test.

d Based on SPPC.

e Based on FACES-III.

f Based on teachers’ responses to SDQ.

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(P = .78) percentage (38/45, 84.4%) of healthy control subjects. Patients were lost to follow-up (n = 9) mainly because they moved to another town; compared with those who completed the study, they were similar in terms of gender, number of syncopal episodes, and psychological variables at baseline, but they were older (16.7 ± 0.5 vs 11.2 ± 2.1 years; P < .001).

**Depressive Symptoms at T1 and Associated Factors**

Compared with controls, NCS patients had higher CDI scores (P < .008; Table 1). In addition, more patients (16, 35.6%) had CDI scores ≥15 (χ² = 6.02, df = 1, P = .014), indicative of clinically important depression, compared with controls (6, 13.3%). NCS patients reported worse (P = .05) relationships with their parents, compared with controls (Table 1). The psychological profile of parents was similar in the 2 groups, as was their opinion of their children's strengths and difficulties (data not shown). In contrast, the teachers' opinions indicated that NCS patients had more difficulties than controls on most SDQ components (Table 1).

Univariate analyses revealed that diagnosis of NCS (P = .005), the number of syncopal episodes (P = .011), worse child-parent relationship (P = .041), poor family cohesion (P = .002), and adoption of a self-sacrificing defense style by the parents (P = .011) were significantly associated with the severity of the children's depressive symptoms; with the exception of parents' self-sacrificing defense style, these variables were associated with depressive symptomatology in multiple regression analysis (Supplemental Table 4). All individual tolerance values were >0.2 and all variance inflation factors were <2, indicating that colinearity was not biasing the regression model.

Figure 1 shows the relationship between depressive symptomatology and number of syncopal episodes across three age groups. As shown in this figure, in all age groups the higher the CDI score the higher the number of syncopal episodes.
Syncope, Depression, and Psychosocial Variables in Patients at T₂

No recurrent syncope was observed in any NCS patient during the 2-year follow-up period. Depressive symptomatology remained stable in control subjects but decreased (P < .001) in the NCS group (Table 2). Similarly, the number of NCS patients with CDI scores ≥15 decreased (χ² = 12.96, df = 1, P < .001) from 16 of 45 (35.6%) to 1 of 36 (2.8%), being comparable (χ² = 0.41, df = 1, P = .525) to controls (13.3% at T₁ vs 18.4% at T₂).

Child-parent relationship (P = .011), family cohesion (P = .032), and adaptability (P < .001) improved in patients between T₁ and T₂ (Table 2). The opinions of parents regarding their children’s strengths and difficulties remained stable between T₁ and T₂. Similarly, no significant changes were observed in parents’ psychological distress, hostility, and defensive profiles between T₁ and T₂. In contrast, the teachers thought that the difficulties of patients decreased over time for most SDQ components (Table 2).

The factors associated with improvement in depressive symptoms in the multivariate analysis (Table 3) were the improvement in syncopal episodes (P = .048) and child-parent relationship (P = .019). However, addition of the CDI score at T₁ rendered the previously significant associations nonsignificant, indicating that the initial rates of depression were the most significant predictor of improvement in depressive symptoms.

DISCUSSION

We report an incidence of 35% in clinically significant depressive symptoms in children and adolescents with NCS, a 2.6-fold higher rate compared with healthy control subjects. Family functioning, as indicated by child-parent relationships and family cohesion, was associated with depressive symptomatology. Moreover, improvement in patients’ depressive symptoms was associated with improvement in child-parent relationship, underlining the association between family functioning and children’s emotional health.

Although the parents’ descriptions of their children’s strengths and difficulties were similar in the 2 groups, the teachers reported that children with NCS faced more difficulties in most areas. Such divergent ratings are frequently observed, mainly because parents tend to underreport their children’s internalized disorders. Thus, our data, along with previous reports, emphasize the need for health care providers to include the teachers’ opinion in their assessments.

Psychiatric Morbidity and NCS in Adults and Children

In addition to peripheral autonomic dysfunction, central serotonergic mechanisms have emerged as important mediators of vasovagal reflexes. The participation of serotonin in the provocation of vasovagal syncope suggests possible common pathophysiologic features between NCS and depression. Recurrent syncope has been unequivocally shown to impair quality of life, resulting in depressive symptomatology. However, a relationship between depression and NCS was suggested as early as in 1992 and was supported by subsequent reports in adults. These studies showed a high prevalence of psychiatric morbidity among syncope patients, with rates up to 80%; for example, it was recently shown that 45% of adult patients with depressive or anxiety disorders had a history of syncope. Similarly, higher prevalence of anxiety, depression, and somatization disorders have been reported among adult patients with recurrent syncope and positive HUTT.

In contrast to adults, relevant data in children and adolescents are scarce. Byars et al studied 44 children and adolescents with a history of recurrent syncope and reported adjustment difficulties, including symptoms of anxiety and social withdrawal. In contrast, Blount et al reported no significant differences in depressive symptomatology in 36 children with

### TABLE 2 Changes in Psychosocial Variables Studied Between T₁ and T₂ in NCS Patients.**

<table>
<thead>
<tr>
<th>Variables</th>
<th>Patients (n = 56) (Mean ± SD)</th>
<th>T₁</th>
<th>T₂</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Depressive symptoms</td>
<td>11.8 ± 7.5</td>
<td>5.4 ± 3.9</td>
<td>.001</td>
<td></td>
</tr>
<tr>
<td>Scholastic competence</td>
<td>3.1 ± 0.8</td>
<td>3.2 ± 0.8</td>
<td>.908</td>
<td></td>
</tr>
<tr>
<td>Relationships with peers</td>
<td>3.4 ± 0.6</td>
<td>3.4 ± 0.6</td>
<td>.987</td>
<td></td>
</tr>
<tr>
<td>Relationships with parents</td>
<td>2.2 ± 0.7</td>
<td>2.5 ± 0.9</td>
<td>.011</td>
<td></td>
</tr>
<tr>
<td>Behavioral conduct</td>
<td>3.0 ± 0.7</td>
<td>3.2 ± 0.6</td>
<td>.153</td>
<td></td>
</tr>
<tr>
<td>Family cohesion</td>
<td>4.4 ± 2.2</td>
<td>5.0 ± 1.4</td>
<td>.032</td>
<td></td>
</tr>
<tr>
<td>Family adaptability</td>
<td>3.8 ± 2.0</td>
<td>4.8 ± 1.1</td>
<td>.001</td>
<td></td>
</tr>
<tr>
<td>Desirable family cohesion</td>
<td>5.2 ± 1.7</td>
<td>6.2 ± 1.3</td>
<td>.001</td>
<td></td>
</tr>
<tr>
<td>Desirable family adaptability</td>
<td>4.6 ± 1.6</td>
<td>5.7 ± 1.0</td>
<td>.001</td>
<td></td>
</tr>
<tr>
<td>Teachers’ opinion</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total difficulties</td>
<td>10.5 ± 6.3</td>
<td>8.5 ± 5.7</td>
<td>.001</td>
<td></td>
</tr>
<tr>
<td>Emotional symptoms</td>
<td>3.6 ± 2.5</td>
<td>2.8 ± 2.4</td>
<td>.023</td>
<td></td>
</tr>
<tr>
<td>Conduct problems</td>
<td>2.8 ± 2.3</td>
<td>1.9 ± 1.5</td>
<td>.004</td>
<td></td>
</tr>
<tr>
<td>Hyperactivity/inattention</td>
<td>2.2 ± 1.9</td>
<td>2.5 ± 2.5</td>
<td>.378</td>
<td></td>
</tr>
<tr>
<td>Peer problems</td>
<td>1.8 ± 1.5</td>
<td>1.3 ± 1.7</td>
<td>.042</td>
<td></td>
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<tr>
<td>Prosocial behavior</td>
<td>9.0 ± 0.4</td>
<td>8.9 ± 1.6</td>
<td>.002</td>
<td></td>
</tr>
</tbody>
</table>

* Based on teachers’ responses to SDQ.

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**ARTICLE**

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TABLE 3 Factors Associated With CDI Total Depressive Symptoms at T1 and With Improvement of Depressive Symptoms Between T1 and T2 Within the NCS Patient Sample (n = 36)

<table>
<thead>
<tr>
<th>Variables</th>
<th>Univariate Associations With Depressive Symptoms at T1</th>
<th>Univariate Associations With Improvement in Depressive Symptoms Between T1 and T2</th>
<th>Hierarchical Multiple Regression Analysis With Dependent Variable the Improvement in Depressive Symptoms Between T1 and T2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>r² = — .078, p = .612</td>
<td>r² = .234, p = .169</td>
<td>—</td>
</tr>
<tr>
<td>Gender</td>
<td>r² = — .195, p = .198</td>
<td>r² = .091, p = .599</td>
<td>—</td>
</tr>
<tr>
<td>Number of syncopal episodes at T1</td>
<td>r² = .214, p = .043</td>
<td>r² = — .214, p = .043</td>
<td>—</td>
</tr>
<tr>
<td>Change in syncopal episodes between T1 and T2</td>
<td>r² = — .385, p = .046</td>
<td>r² = .176, p = .457</td>
<td>0.335 (P = .048) 0.117 (P = .445)</td>
</tr>
<tr>
<td>Relationships with parents at T1, d</td>
<td>r² = — .288, p = .055</td>
<td>r² = .534, p = .015</td>
<td>0.247 (P = .240) 0.085 (P = .528)</td>
</tr>
<tr>
<td>Improvement in relationships with parents, d</td>
<td>r² = — .251, p = .097</td>
<td>r² = .125, p = .468</td>
<td>0.543 (P = .019) 0.264 (P = .248)</td>
</tr>
<tr>
<td>Family cohesion at T1, e</td>
<td>r² = — .288, p = .055</td>
<td>r² = .176, p = .131</td>
<td>—</td>
</tr>
<tr>
<td>Family adaptability at T1, e</td>
<td>r² = — .251, p = .097</td>
<td>r² = — .125, p = .468</td>
<td>—</td>
</tr>
<tr>
<td>Increase in family cohesion between T1 and T2, e</td>
<td>r² = — .288, p = .055</td>
<td>r² = .534, p = .015</td>
<td>—</td>
</tr>
<tr>
<td>Parent’s self-sacrificing defense style</td>
<td>r² = .240, p = .112</td>
<td>r² = .255, p = .134</td>
<td>—</td>
</tr>
<tr>
<td>Depressive symptoms at T1</td>
<td>r² = — .214, p = .043</td>
<td>r² = — .214, p = .043</td>
<td>—</td>
</tr>
</tbody>
</table>

—, not applicable.

a Values shown are standardized β coefficients.
b Bivariate Pearson or Spearman’s correlations, as appropriate.
c Correlation based on Student’s t tests.
d Based on the SPPC.
e Based on the FACES-III.
f Based on the NCS.

Syncope and a positive HUTT, when compared with 20 children with syncope but negative HUTT. However, a major limitation of this study is the lack of appropriate controls; in fact, it is well established that a negative HUTT does not exclude the diagnosis of NCS, given the relatively low sensitivity of this test. Moreover, the identification of psychosocial difficulties is complex in pediatric populations and requires input from family and school sources, as discussed earlier. Our present findings extend previous conclusions in adults and indicate that psychological assessment should be considered also in pediatric patients presenting with NCS.

Improvement in Psychological Profile in NCS Patients During Follow-up

We report substantial improvement in depressive symptoms in patients with NCS during a 2-year-follow-up, correlating with strengthening of the child-parent relationship. This finding is in line with previous reports, implicating distressed family bonds and unstable parent-child relationship as important factors for NCS in children and adolescents. In addition, it has been reported that family cohesion and adaptability are significant factors in the adolescents’ feeling in control over their own health. Although we cannot establish whether depression decreased in our study because the family functioned better or vice versa, our results nonetheless underscore the importance of family functioning in pediatric patients with NCS.

Syncope Recurrence and Improvement in Depressive Symptoms

In our patient population, we observed no syncope recurrences. Although this improvement in the clinical course of NCS predicted improvement in depressive symptoms, the establishment of a causal association is difficult. This view is based on the nature of NCS symptoms (especially in pediatric patients with moderately symptomatic NCS, as in our study population), characterized by occasional episodes with long intermediate periods of spontaneous remissions. Despite these considerations, previous studies tried to explore the therapeutic potential of psychiatric interventions in adult NCS patients. A prospective study indicated improvement of both syncopal and depressive symptoms after psychiatric treatment, whereas psychiatric morbidity was predictive of syncopal recurrence during 1-year follow-up. Similarly, adult patients with NCS who did not respond to treatment after a 3-month follow-up period had higher baseline levels of psychosocial impairment and psychological distress. These findings indicate that psychological interventions may have a therapeutic potential in adult NCS patients.
The findings of the current study extend these observations to pediatric patients. Here, we demonstrated the complex association between depressive symptomatology, family functioning, and syncope in children and adolescents. However, the therapeutic value of psychological counseling in children with syncope is still uncertain; because we did not include a treatment control group, the decrease in depression observed in our study could have merely reflected the absence of syncopal episodes during the follow-up period. Nonetheless, we feel that our findings provide a rationale for designing interventional studies, targeting at decreasing depressive symptomatology in pediatric populations with NCS.

Strengths and Limitations

The in-depth psychological evaluation (including variables derived from the family and school environment), the use of well-recognized standardized instruments, and the inclusion of healthy participants as a control group, represent major strengths of this work. However, 3 limitations should be acknowledged: First, our sample size is relatively small, and this could explain the minor preponderance of female patients, as opposed to clear-cut female prevalence in NCS pediatric populations described in larger series.\textsuperscript{1,2} Furthermore, our patients were recruited from a dedicated syncope-clinic in a tertiary hospital, thereby introducing potential bias. Second, we used only self-report measures, and studies using structured interviews are needed to confirm our results. Third and foremost, the therapeutic value of psychological counseling on syncope recurrence cannot be formally assessed because of the lack of an NCS control group, as noted earlier; thus, our findings should be viewed only as hypotheses generating.

CONCLUSIONS

At the time of diagnosis, 45 children and adolescents with NCS had a 2.6-fold higher rate of clinically significant depressive symptoms, compared with an equal sample of age- and gender-matched healthy control subjects. During a medium-term follow-up, no syncope recurrences were observed; this was associated with depressive symptoms improvement, along with marked improvement in family functioning, based on information from patients, as well as from the family and school environment. Our findings call for additional investigation on the possible pathophysiologic association between depressive symptomatology and NCS and for clinical studies evaluating psychological counseling in pediatric patients.

REFERENCES


Depressive Symptoms and Neurocardiogenic Syncope in Children: A 2-Year Prospective Study
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