The Psychosocial Problems of Children With Narcolepsy and Those With Excessive Daytime Sleepiness of Uncertain Origin

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ABSTRACT

BACKGROUND. Narcolepsy is a predominantly rapid eye movement sleep disorder with onset usually in the second decade but often in earlier childhood. Classically it is characterized by combinations of excessive sleepiness especially sleep attacks, cataplexy, hypnagogic hallucinations, and sleep paralysis. The psychosocial effects of this lifelong condition are not well documented, especially in children. This study aims to describe the psychosocial profile of a large group of children with narcolepsy compared with other excessively sleepy children and controls.

METHODS. We used an international cross-sectional questionnaire survey of children aged from 4 to 18 years who had received from a physician a diagnosis of narcolepsy compared with age- and gender-matched controls. Assessments were made of behavior, mood, quality of life, and educational aspects.

RESULTS. Recruited children were separated into those who met conventional criteria for narcolepsy (n = 42) and those whose primary complaint was excessive daytime sleepiness without definite additional features of narcolepsy (excessive daytime sleepiness group; n = 18). Compared with controls, children with narcolepsy and also those with excessive daytime sleepiness alone showed significantly higher rates of behavioral problems and depression. Again, to a significant extent, their quality of life was poorer and they had more educational problems. The children with narcolepsy and the excessive daytime sleepiness group were indistinguishable from each other on these measures.

CONCLUSIONS. A range of psychosocial problems can be identified in children with narcolepsy. The origins of these problems are unclear. The similar profiles of difficulties in the narcolepsy and excessive daytime sleepiness groups suggest that excessive sleepiness is the main cause. Clinicians and others responsible for the care of such children need to be mindful of the importance of early detection, intervention, and, ideally, the prevention of these problems.
Narcolepsy is a chronic disorder closely associated with an abnormality of the neuropeptide hypocretin (orexin) system and the most common neurologic cause of excessive daytime sleepiness.1 It mainly causes intrusion into the awake state of the component parts of rapid eye movement (REM) sleep. The condition is not the rarity once supposed, its prevalence in western countries being 0.02% to 0.05%. Age of onset varies widely from early childhood to middle age but is usually before the age of 25, with a peak at 14 years. It has been reported that at least a third experience symptoms before 15 years of age, ~16% before 10 years, and 4.5% before 5 years of age. A major problem at any age is delay in diagnosis (often for several years) and possibly failure to correctly diagnose the condition at all. Narcolepsy can manifest itself in many ways, each liable to be misinterpreted, perhaps especially in children.3

The main feature of narcolepsy is excessive daytime sleepiness (EDS) with recurrent episodes of irresistible sleep (sleep attacks) occurring unpredictably, including during conversation and while eating, walking, driving, or in monotonous situations. The attacks usually last 10 to 20 minutes but may be longer. On waking, the patient feels refreshed. Disturbed nocturnal sleep with frequent awakenings is common and may contribute to general sleepiness during the day.

In young children, recognition of EDS can be complicated by the occurrence of daytime naps in normal children. However, these generally cease by the age of 3 to 4 years. An additional difficulty can be that, in young children, sleepiness may take the form of an increase rather than a reduction in activity with features of attention-deficit/hyperactivity disorder, which may be mistakenly diagnosed as a condition in its own right. Other misinterpretations of the excessive sleepiness in childhood narcolepsy include laziness, conduct or oppositional defiant disorder, epilepsy, other neurologic or medical disorders, and intellectual impairment.1

In its fully developed, classical form, the “narcolepsy syndrome,” in addition to EDS, includes cataplexy, sleep paralysis, and hypnagogic (sleep onset) and/or hypnopompic (waking) hallucinations. However, only ~50% of individuals develop all of these features, excessive sleepiness almost always being the initial symptom. The combination of excessive sleepiness and cataplexy is considered pathognomonic of narcolepsy.4 Narcoleptic sleepiness without cataplexy is described, but this may simply represent the first stage in the development of the condition, especially in children. The components of the narcolepsy syndrome other than EDS can be difficult to elicit or detect, particularly at a young age.

Cataplexy consists of sudden, brief, bilateral losses of muscle tone, from obvious to subtle, usually in response to emotions such as laughter, surprise, excitement, anger, or fright. In sleep paralysis, short-lived episodes occur of inability to move when falling asleep or when waking up, sometimes with a feeling of pressure on the chest and difficulty breathing. Hypnagogic and hypnopompic hallucinations in various modalities are dreamlike and often vivid. The combination of such experiences and sleep paralysis can be particularly alarming.

The clinical picture of narcolepsy may be further complicated by various additional experiences or associated conditions. Episodes of automatic behavior may occur with increasing levels of sleepiness. In such episodes, lasting ≤30 minutes or so, inappropriate or poorly executed habitual behavior may be enacted, with amnesia for the events, which may be misinterpreted as epileptic or syncopal in nature. Other sleep disorders associated with narcolepsy are night terrors and nightmares, periodic limb movements, sleep apnea, and REM sleep behavior disorder. Details of this wide range and other clinical manifestations of narcolepsy are provided elsewhere.4

The symptoms of narcolepsy are highly likely to cause fear and embarrassment to many patients. Misinterpretation of the condition and the usual long delays in correct diagnosis add to the distress. In addition, the effect on patients’ home life and social activities can be profound, as well as quality of life in general. The uncertainties and possible adverse effects of medication may produce further difficulties. In view of this wealth of potentially harmful effects, it is not surprising that significant psychological problems have been consistently reported in many adults with narcolepsy.7

Although such difficulties seem likely to be similarly serious in children with narcolepsy, detailed information on this point has been lacking and confined to impressionistic accounts or reports of individual cases or small series.3 The present study aimed to document, by means of standardized or otherwise systematic measures, the psychosocial correlates of a large group of children diagnosed as having narcolepsy in a way that would indicate the care that such children require in addition to their medical management.

METHODS

Design

The study was a cross-sectional international survey of patients and healthy controls using questionnaire assessments.

Participants

Children up to the age of 18 years qualified for inclusion if they had been diagnosed by a physician as suffering from narcolepsy. Recruitment was achieved by contacting clinicians involved with narcoleptic children’s care via the British Pediatric Neurology Association; sleep clinics in the United Kingdom, Europe, United States and Australia; and scientific meetings of national sleep society meetings in the United Kingdom, Europe, and  

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the United States. In addition, through the United Kingdom Narcolepsy Association, by means of publicity about the study in national newspaper articles in the United Kingdom, and an Internet advertisement on the University of Oxford Department of Psychiatry Web site, families of children with a medical diagnosis of narcolepsy were notified of the study and invited to participate. The recruited children’s teachers provided local control subjects matched by age and gender where possible, augmented by best-friend controls or children of staff in the authors’ department.

Assessments
The following assessments were chosen for their relevance to the aim of the study and their satisfactory psychometric properties. The means of evaluating educational aspects was specially designed for the study. Assessments were translated into the appropriate language where necessary.

Narcolepsy
The Ullanlinna Narcolepsy Scale is an 11-item questionnaire, adapted for use in this study by deleting the item concerning sleep latency, which children might not be able to estimate accurately. The scale assesses the symptoms of the narcolepsy syndrome and reliably distinguishes between narcolepsy and sleep apnea and other causes of excessive sleepiness. This measure was completed by children with assistance from parents where necessary.

Table 1 shows the diagnostic criteria for narcolepsy according to the 1997 International Classification of Sleep Disorders (ICSD). For the purpose of this investigation, the information on each child from the Ullanlinna Narcolepsy Scale was assessed according to these diagnostic criteria. In addition, where polysomnography or human leukocyte antigen (HLA) typing had been performed, these results were incorporated.

Behavior
The Strengths and Difficulties Questionnaire is a well-established 25-item instrument. It provides quantifiable information on 5 subscales: prosocial behavior (positive attributes), peer problems, hyperactivity, conduct problems (misbehavior), and emotional disturbance. Behaviors are rated on a 3-point scale indicating the extent to which they apply to the child. A total difficulties score can also be calculated based on the subscales, as can a score measuring adverse impact on the family. Normal population values are provided.

Mood
Because depression is not particularly covered by the other assessments used, yet is a potentially important complication of narcolepsy, the Child Depression Inventory was included. It consists of 27 items answered by the child indicating on a 3-point scale the extent to which each item applies. A total score of 19 indicates a degree of depression encountered in children undergoing psychiatric care. General population norms are available.

Quality of Life (General Health, Social, and Family Effects)
The 50-item Child Health Questionnaire covers children’s physical, emotional, and social well being and some aspects of behavior and impact on the parents and family as judged by parents who rate the child’s behavior on a Likert scale. The parent report rather than the self-report version was chosen to allow consistency across the age groups, because some (younger) children may be less able to respond than others. Higher scores indicate better health. Normative data are available. The 3 summary subscales were used: mental health, physical health, and global health (an overall rating of quality of life).

Educational Assessment
This consisted of information provided by teachers concerning days absent from school in the previous term and their impressions about stated key aspects of the child in the teaching situation. To assess these qualities statistically, items were recoded into a continuous variable by combining values for teacher ratings of problems with learning, not reaching academic potential, not working hard enough, and being difficult to teach. Each item was scored 0 to 1 (a value of 1 indicating a problem), providing a composite educational difficulties score ranging from 0 to 4. Examination of the children’s school records (eg, attainment test results) was not considered feasible because of limitations on teachers’ time.
In addition, such assessments would have been difficult to compare across different countries.

**Demographics**

Data concerning the occupations of the primary carers (parents and step-parents where appropriate) were compiled, and each family’s socioeconomic status was assigned according to the highest scoring occupation, using United Kingdom Registrar General criteria based on father’s occupation or that of mother in the absence of a father. It was appreciated that there are potential differences in applicability of this approach among various countries and cultures, but it seemed unlikely that this would be a serious source of error in the series of families involved in the study.

**Procedure**

After referral from whichever source, parents of the children were sent information sheets and consent forms for themselves and the child. The parent consent form requested details of the child’s clinician who was then contacted if not already known to the researchers. Clinicians were asked to give consent and to provide as much diagnostic detail as possible about the child’s condition. This information was supplemented by the Ullalaninna Narcolepsy Scale as a check on the original diagnosis. Consenting families were sent a questionnaire package and asked to provide the child’s teacher and school contact details. Teachers were then sent a questionnaire and asked to randomly suggest another child, of the same gender, and approximate age, in the index child’s school year to act as a control subject. Where this was not possible, families recruited best-friend controls, otherwise, controls were recruited from the families of staff in the authors’ place of work.

**Analysis**

Because the children considered to have narcolepsy were, in fact, diagnostically heterogeneous, 2 clinical groups were derived, that is, narcolepsy and EDS of uncertain origin (see “Diagnostic Classification” under “Results”). Analyses of variance (ANOVs) were performed to investigate differences between the clinical and control groups on the measures of behavior, mood, and quality of life. Post hoc contrasts of the scores of the 3 groups were performed with Bonferroni corrections for multiple comparisons. Pearson correlation coefficients were calculated to explore factors associated with psychosocial disadvantage. Where population norms were available, these were compared with clinical group scores.

**Ethical Approval**

Approval was granted by the local research ethics committee.

**RESULTS**

**Recruitment**

Forty children with a diagnosis of narcolepsy as made by a physician were eventually recruited from United Kingdom sources and an additional 30 from centers in the United States, Europe, and Australia.

**Diagnostic Classification**

As described above, the ICSD criteria (see Table 1) were applied using the information derived from the Ullalaninna Narcolepsy Scale. Neither polysomnography nor HLA typing had been performed routinely and, therefore, could not be used to evaluate every case, but results were considered where these data were available (N = 15). Using these ICSD criteria, the following groups of children were compiled: (1) those meeting criteria A/B/G/H (the main significant feature being the combination of EDS and cataplexy) ± D + E were the narcolepsy group (N = 42); (2) those meeting criteria A + B + G + H (ie, EDS without cataplexy) were the EDS group (N = 18); this group might have included some with narcolepsy but without the development at the time of the study of other features, notably cataplexy; and (3) the control group (N = 23) in which none of the children met any of the ICSD criteria.

**Demographic Characteristics of the Groups**

As shown in Table 2, there were no obvious differences between the narcolepsy group and controls nor the EDS group and controls regarding age, gender ratio, and socioeconomic status.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Narcolepsy (N = 42)</th>
<th>EDS (N = 18)</th>
<th>Controls (N = 23)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender ratio, male/female</td>
<td>24/18</td>
<td>14/4</td>
<td>12/11</td>
</tr>
<tr>
<td>Age, mean (SD; range), y</td>
<td>12.46 (2.83; 7.3–17.9)</td>
<td>14.26 (3.84; 5.1–18.8)</td>
<td>11.30 (3.39; 6.0–16.8)</td>
</tr>
<tr>
<td>Socioeconomic level</td>
<td></td>
<td></td>
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<tr>
<td>Professional/management</td>
<td>17</td>
<td>11</td>
<td>11</td>
</tr>
<tr>
<td>Skilled manual/nonmanual</td>
<td>16</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Partly skilled/unskilled</td>
<td>6</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Missing data</td>
<td>3</td>
<td>1</td>
<td>4</td>
</tr>
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</table>
Referral Sources
Twenty-one members of the narcolepsy group were re-
cruited from United Kingdom centers, the same number 
from outside the United Kingdom. The 18 children in
the EDS group were equally divided between United 
Kingdom and non-United Kingdom sources. Five con-
trol children were from the United Kingdom, the re-
maining 18 from abroad.

Comorbidity and Current Medication
Information from parents about children’s comorbid 
conditions and medications at the time of the study are
included in Table 3. Some children had >1 problem or
type of medication

Comparisons of the Narcolepsy, EDS, and Control Groups on
Behavior, Mood, and Quality-of-Life Measures
ANOVAs were performed to investigate possible differ-
ences between the children with narcolepsy, those with 
EDS, and controls for each of the 7 scores derived from
the Strengths and Difficulties Questionnaire, the Child 
Depression Inventory, and the 3 summary scales of the
Child Health Questionnaire.

Behavior
As can be seen from Table 4, significant group differ-
ences were found for peer problems, conduct problems,
emotional symptoms, and total problems. In all of these 
domains there were no significant differences between
the narcolepsy and EDS groups, but both the narcolepsy
and EDS groups scored higher than the controls to a
highly significant extent. The clinical groups were very
similar to each other regarding adverse impact on the
family, but, in comparison with the control group, only
the scores from the narcolepsy group were significantly
worse. In general, the average scores of the narcolepsy
and EDS children were above the published reference
range. In contrast, their average scores for prosocial be-
havior and hyperactivity were not statistically signifi-
cantly different from controls and fell within the refer-
ence range.

Mood
On the Child Depression Inventory, both the narcolepsy
and EDS groups scored significantly higher than controls
(Table 4), with no significant difference between these 2
clinical groups. The scores of the narcolepsy and EDS
groups were above the published mean for children in
the general population.

Quality of Life
No group differences were found for the physical and
global health subscale scores as shown in Table 4. How-
ever, a significant group difference for the mental health
subscale score was seen; posthoc tests indicated that
there were no significant differences between the nar-
colepsy and EDS group scores, but both of these groups
of children scored higher than controls. The control
group scores were generally close to the published
norms.

Educational Aspects
School absence records and composite educational diffi-
culties scores as rated by teachers are shown in Table 5.
Although absence rates showed no significant group
differences, the composite educational difficulties score
was significantly higher in children with narcolepsy and
in those in the EDS group compared with control chil-
dren.

Factors Associated With Psychosocial Disadvantage in the
Narcolepsy Group
There was no significant correlation (Pearson) between
the severity of each child’s narcolepsy (as judged by the
total score on the Ullanlinna Narcolepsy Scale) and the
global health item on the Child Health Questionnaire
(Pearson correlation coefficient = 0.036; P = .835). Sim-
ilarly, duration of narcolepsy and delays in diagnosis
(according to parents) failed to show any significant
associations with global health (Pearson correlation co-
efficients = 0.274 and 0.142 [P = .096 and .410], re-
spectively).

DISCUSSION
This project, exploring the psychosocial consequences of
childhood narcolepsy, is characterized by the relatively
large size of the sample in comparison with earlier re-
ports, precise assessments of the symptoms of children
previously given the diagnosis of narcolepsy, the use
of standardized or otherwise systematic assessment meth-
ods, and comparisons with controls. Review of the chil-
dren said to have narcolepsy suggested possibly impor-
tant diagnostic distinctions.

Comparisons of the children with narcolepsy and

<table>
<thead>
<tr>
<th>Table 3</th>
<th>Comorbid Conditions and Current Medication</th>
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<tbody>
<tr>
<td></td>
<td>Group (N = 42)</td>
</tr>
<tr>
<td>Narcolepsy</td>
<td>Asthma (4), gastrointestinal problems (2), mood disorder (2), sleep apnea (1), tinnitus (1)</td>
</tr>
<tr>
<td>EDS (N = 18)</td>
<td>Asthma (2), headaches (1)</td>
</tr>
<tr>
<td>Controls (N = 23)</td>
<td>Asthma (4), thyroid problems (1)</td>
</tr>
</tbody>
</table>
control children demonstrated differences between them that were consistently statistically significant, with the worse scores of the narcolepsy group covering many aspects of behavior, emotional state, quality of life, educational progress, and impact on the children’s families.

There have been several essentially anecdotal or impressionistic accounts suggesting that children with narcolepsy are particularly subject to psychosocial problems. However, apparently the only published investigation comparable to the present study, in using standardized measures (although narrower in scope), was confined to 18 cases of children with onset of narcolepsy symptoms before 14 years of age.14 The study was published in abstract form, and details of these children were not stated apart from the fact that 7 of them were “at least 16 years old.” No control group was used, but comparisons were made with normative data available for the several psychosocial assessment scales used. The children with narcolepsy were reported to be more moody than average, to have more adjustment problems, and to be more often engaged in delinquent behavior. When interviewed, most parents of the children with narcolepsy expressed concern about their child’s academic performance and their emotional lability. The findings in the present study are in broad agreement with these conclusions, although, in the absence of detail about the sample in the account by Kashden et al.,14 precise comparisons between the 2 sets of findings are not possible.

The 18 children with excessive sleepiness but no reported cataplexy (the EDS group) might well have included some who had not yet developed cataplexy (which would have confirmed the diagnosis of narcolepsy) or exhibited it in such a subtle form that it was not reported on enquiry. In clinical practice it is important to repeat assessments in such children to see whether more definitive diagnostic features emerge with time. At the time of the study, there was no convincing evidence that the children in the EDS group had another sleep disorder to account for their abnormal sleepiness. Their psychosocial problem profile was found to be closely similar to that of the narcolepsy group. This might suggest that the main disadvantage for children with narcolepsy is the excessive sleepiness that they share with the EDS group rather than something more specific to narcolepsy, such as exposure to the distressing experiences described earlier as part of the narcolepsy syndrome. In view of the low rate of comorbid conditions and current medication use in the clinical groups (and that both groups showed similar patterns), it seems unlikely that these biased the comparisons regarding the children’s psychosocial disadvantages.

The present investigation was subject to certain limitations, which need to be considered in the design of further studies. The low yield of recuits to the study from United Kingdom sources, despite the various efforts described earlier, is open to a variety of interpretations, including the worrying possibility that only a small proportion of children with narcolepsy are known to
medical services. The explanation may well be partly the result of misinterpretation of the symptoms of narcolepsy and, therefore, misdiagnosis. Although the clinical sample came from mixed sources, there is little reason to believe that it was particularly unrepresentative of affected children coming to medical attention. Attempts to study narcolepsy in general (ie, including undiagnosed or misdiagnosed cases) from any point of view would have to involve intensive, prospective population screening and assessment.

The grouping of the narcolepsy referrals was based on strict ICSD clinical criteria rather than uniformly the results of overnight polysomnography, multiple sleep latency test (MSLT) findings, or HLA typing (still less hypocretin estimations). Facilities for polysomnography including MSLT are not readily available in the United Kingdom. In any event, it can be practically difficult to perform and interpret MSLT in young children for whom adequate norms are not yet established. The use of laboratory measures was significantly greater for that part of the sample recruited from outside of the United Kingdom.

Ideally, an entirely matched case-control design would have been used for the study, but this proved to be unfeasible. Children were recruited to the control group from several countries, and it was not possible to ensure that each child in the clinical groups had an appropriate age- and gender-matched control. Sibling controls were considered but would not have provided comparable gender and age ratios. The socioeconomic status of each family was judged in terms of criteria used in the United Kingdom, which might not be entirely applicable in all other countries. As it was, despite the ways in which the control group might have been better compiled, the comparisons that were possible between the clinical groups and normative data closely reflected those between the clinical groups and control children, suggesting that the latter comparisons were legitimate.

In general, the required assessments were obtained satisfactorily, but that for educational aspects was affected (despite energetic attempts) by the limited response from teachers. Telephone conversations with nonresponding teachers suggested that the problem was the result of other pressures on their time rather than particular child characteristics.

Attempts to identify factors associated with poor psychosocial outcome in the children with narcolepsy (eg, delay in diagnosis and misdiagnosis, possible adverse medication effects, and inappropriate reactions to the child’s symptoms of peers, parents, teachers, and others) were frustrated by a lack of reliable retrospective information on these points. Prospective, comprehensive studies are needed to investigate these important aspects.

The present findings lend weight to the belief that children with narcolepsy are at particularly high risk for a range of psychosocial difficulties, but there are indications that this may be the result of their excessive sleepiness rather than factors more specific to narcolepsy. There is a need to refine these findings by additional more intensive research to identify how the psychosocial disadvantages of children with narcolepsy arise, including the comparative relevance of the different aspects of the condition. The findings would indicate how such disadvantages might be prevented or minimized to avoid such serious difficulties existing in adult life.

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The online version of this article, along with updated information and services, is located on the World Wide Web at: http://pediatrics.aappublications.org/content/118/4/e1116.full.html