LUND UNIVERSITY

A prospective study of anxiety disorders in children

Last, Cynthia; Perrin, Sean; Hersen, Michel; Kazdin, Alan

Link to publication

A Prospective Study of Childhood Anxiety Disorders

CYNTHIA G. LAST, Ph.D., SEAN PERRIN, Ph.D., MICHEL HERSEN, Ph.D., AND ALAN E. KAZDIN, Ph.D.

ABSTRACT

Objective: To evaluate course and outcome of *DSM-III-R* anxiety disorders prospectively in clinically referred children. **Method:** Children were blindly and repeatedly assessed with a structured diagnostic interview over a 3- to 4-year period to determine recovery from anxiety disorder and development of new psychiatric disorders. Both psychopathological (attention-deficit hyperactivity disorder, *n* = 50) and never psychiatrically ill (NPI, *n* = 83) controls served as comparison groups for children with anxiety disorders (*n* = 84). **Results:** The majority of children (82%) were free from their intake anxiety disorders by the end of the follow-up. Relapse of these anxiety disorders after remission was rare (8%). During follow-up, anxious children were more likely to develop new psychiatric disorders (30%), primarily new anxiety disorders (16%), than were NPI children (11% and 2%, respectively), but not psychopathological controls (42% and 10%, respectively). **Conclusions:** Overall, results suggest a favorable outcome with respect to diagnostic status for clinically referred children with anxiety disorders. However, these children may be at risk for new psychiatric disorders over time. *J. Am. Acad. Child Adolesc. Psychiatry*, 1996, 35(11):1502–1510. **Key Words:** anxiety disorders, children, prospective study, *DSM-III-R*.

Prior to 1980, anxiety disorders in children and adolescents had been relatively ignored in terms of scientific inquiry. One reason for this was the widely held notion that fears and worries during childhood were transitory in nature and thus did not constitute an important or compelling area for investigation. With the arrival of *DSM-III* (American Psychiatric Association, 1980), childhood anxiety disorders gained a prominent position in our diagnostic nomenclature. The improvements in the diagnostic criteria that accompanied this revision led to increased attention to childhood anxiety disorders from the research community. Anxiety disorders now are recognized to be among the most prevalent of childhood disorders (Bernstein and Borchardt, 1991), with anxious children manifesting levels of symptom severity and impairment akin to adult anxiety disorders (Last, 1993). Moreover, retrospective studies of children and adults suggest that childhood anxiety

disorders may persist for many years and lead to the development of other psychiatric disorders over time (Bland et al., 1988; Burke et al., 1990; Flament et al., 1988; Keller et al., 1992; Schneier et al., 1992).

Despite the apparent short- and long-term consequences of childhood anxiety disorders, our knowledge of their course and outcome is limited primarily to retrospective data. While prospective studies are considered to be the preferred approach to assessing course and outcome, since such data are not biased by retrospective recall and memory lapses, such studies are both time-consuming and costly. However, they are of paramount importance for understanding the phenomenology or natural history of childhood disorders, and they provide information that can be used to assist in the formulation of treatment and prevention efforts.

Of those studies that have used a prospective approach with this population, only five have included direct interview using systematic diagnostic assessments at study entry and follow-up (Berg et al., 1989; Cantwell and Baker, 1989; Flament et al., 1990; Leonard et al., 1993; Thomsen and Mikkelsen, 1995). One of these studies was conducted by Cantwell and Baker (1989), who examined the course and outcome of psychiatric disorders (including anxiety disorders) in a sample of linguistically impaired children referred to a speech disorder clinic. Diagnoses were based on

nonblind, structured diagnostic interviews conducted with both the child and parent at intake and again 4 to 5 years after study entry. Although only a few children received treatment during the follow-up period (10% to 15%), speech-impaired children with a "pure" anxiety disorder (i.e., no comorbidity with other psychiatric disorders) at intake (*n* = 31) showed high rates of recovery at follow-up, with more than three quarters remitting from their initial anxiety disorders. However, a number of these children developed additional psychiatric disorders during follow-up, particularly anxiety (29%) and behavior disorders (26%). By contrast, few children with behavior disorders developed anxiety disorders during follow-up (4.7%), although more than one quarter (28%) of these youngsters developed additional behavior disorders.

The other four prospective studies examined the course and outcome of children with obsessive-compulsive disorder (OCD). In the first study (Berg et al., 1989), a community sample of nonreferred adolescents with OCD were assessed with diagnostic interviews at study entry and again 2 years later. Of the 16 children with OCD at study entry, 31% still met criteria for the disorder at follow-up. Moreover, 56% received additional psychiatric diagnoses at that time (mostly anxiety and affective disorders). By contrast, only 3 (14.4%) of 21 children with no diagnosis at intake received diagnoses for psychiatric disorders at follow-up.

Less favorable results were obtained by Flament et al. (1990) from a 2- to 7-year follow-up of clinically referred adolescents with OCD evaluated at the National Institute of Mental Health (NIMH). Of the 25 youngsters reevaluated, 17 (68%) retained their OCD diagnosis. Of note, the overall rate of psychopathology at follow-up was much higher in the OCD youngsters than in psychiatric controls.

In another study (Leonard et al., 1993), 54 clinically referred children with OCD, who originally had participated in a clomipramine treatment study at the NIMH, were followed for 2 to 7 years after the end of the treatment trial. Although the majority were still receiving pharmacological treatment by the end of the follow-up period, 43% continued to meet criteria for OCD. Furthermore, almost all (96%) of the subjects had additional psychiatric disorders diagnosed at follow-up.

Finally, in a very recent study (Thomsen and Mikkelsen, 1995), 23 Danish children and adolescents with OCD were followed prospectively every 6 months for 1½ to 5 years after treatment. Results were compared with those of a psychiatric control group with anxiety disorders, but not OCD, who were age- and sex-matched to the OCD subjects. Results indicated that approximately one half of the OCD youngsters retained the diagnosis at follow-up and that these youngsters were likely to receive comorbid diagnoses of other anxiety disorders, depressive disorders, and/or tic disorders. None of the control subjects received the diagnosis of OCD at follow-up, but comorbid anxiety disorders were common. Unfortunately, statistical comparison of the OCD and control group was not conducted for comorbid disorder present at follow-up, making interpretation of findings difficult.

Overall, the above studies preliminarily suggest that anxiety disorders in both clinically referred (Cantwell and Baker, 1989; Flament et al., 1990; Leonard et al., 1993) and nonreferred children (Berg et al., 1989), and in both treated (Flament et al., 1990; Leonard et al., 1993) and untreated samples (Berg et al., 1989; Cantwell and Baker, 1989), show moderate to high rates of recovery from initial anxiety disorders, but these youngsters may be at increased risk for additional psychiatric disorders over time (Berg et al., 1989; Cantwell and Baker, 1989; Leonard et al., 1993). However, certain methodological limitations in each of the above studies, in addition to the relative dearth of research on this topic, limit the conclusions that can be drawn.

Four of the five studies did not conduct follow-up interviews blindly (Cantwell and Baker, 1989; Flament et al., 1990; Leonard et al., 1993; Thomsen and Mikkelsen, 1995). Thus, interviewers were aware of subjects' initial diagnoses, which may have biased results that were obtained. Only one of the five studies included repeated (more than one) follow-up assessments (Thomsen and Mikkelsen, 1995), which is important for obtaining detailed information on developing disorders as well as accurate "endpoints" for remitting disorders. None of the studies included *both* psychopathological and never psychiatrically ill (NPI) control groups. In evaluating rates of new disorders developing during follow-up, inclusion of two control groups is needed to control for the effects of psychopathology per se and to obtain community base rates of different psychiatric disorders. Finally, only one study indicated which disorders diagnosed at follow-up *first* developed

during the follow-up period (Cantwell and Baker, 1989). Such data are important for determining the sequence of development among disorders diagnosed over time.

In light of the above, it is clear that additional prospective studies of children with anxiety disorders are needed. Such studies are useful for determining whether childhood anxiety disorders are episodic or chronic in nature ("course"), and whether these disorders are related to the development of other particular psychiatric disorders over time ("outcome"). Therefore, the purpose of the present investigation was to prospectively examine the course and outcome of DSM-III-R anxiety disorders in clinically referred children in an empirically rigorous manner. This was accomplished by prospectively and blindly reassessing the children over a 3- to 4-year period after study entry and determining (1) recovery from anxiety disorders present at study entry, and (2) psychiatric disorders developing during the follow-up period. To determine whether children with anxiety disorders were at increased risk for the development of new disorders during follow-up, both psychopathological (attention-deficit hyperactivity disorder [ADHD]) and NPI control groups were included in the study design.

METHOD

Subjects

Subjects were recruited for a large-scale family and follow-up study of childhood anxiety disorders. Details of the family study are reported elsewhere (Last et al., 1991). The follow-up study is the subject of this report. The original sample included 102 children with an anxiety disorder (anxiety group), 58 children with ADHD, and 87 children who had never been psychiatrically ill (NPI). Children in the anxiety group were recruited from the Child and Adolescent Anxiety Disorder Clinic at Western Psychiatric Institute and Clinic during a 3-year period. ADHD youngsters were recruited during the same period from the general child outpatient clinic at the same facility. NPI children were recruited from the community via mailings using Cole's directory, and they were matched as closely as possible to the anxiety group for age, sex, and socioeconomic status. The socioeconomic status of the three groups was estimated using the Four Factor Index of Social Status (Hollingshead, 1975).

Diagnostic Procedures

Children and their parent(s) were interviewed separately with a modified version of the Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present Episode (K-SADS-P) (Last, 1986, unpublished manuscript) by a trained, clinical child psychologist. This modified version of the K-SADS-P includes comprehensive and detailed sections on all DSM-III-R anxiety disorders and allows evaluation of both current and past psychopathology. Previous studies have indicated that the modified interview schedule yields high rates of diagnostic reliability when administered by clinicians trained in its use (Last et al., 1991, 1992).

Inclusion criteria for the study were a current DSM-III-R diagnosis of an anxiety disorder and no history of ADHD. The ADHD group was required to have a current DSM-III-R diagnosis of ADHD and no history of an anxiety or affective disorder. Finally, the NPI group had no history of any psychiatric disorder or mental health contact of any kind at or prior to intake. Informed consent was obtained from at least one parent and the child/adolescent at intake.

Every 12 months, for 3 to 4 years after study entry, children and their parents were asked to complete follow-up interviews, which consisted of blind readministrations of the modified K-SADS-P to the child and at least one parent. Again, summary symptom ratings were combined from the two interviews and the child was diagnosed for current DSM-III-R disorders and disorders present during the interim period (i.e., the 12-month period following the previous interview). Follow-up interviews were administered by clinicians who were blind to the children's previous diagnoses.

Interrater diagnostic agreement was obtained by having a second interviewer (also blind to subjects' previous diagnoses) independently score audiotapes of both the parent and child interviews and assign DSM-III-R diagnoses to the child. Reliability was performed on 45% (n = 111) of the original interviews (n = 247) and revealed κ coefficients of 1.00, .98, and 1.00 for any anxiety disorder, ADHD, and no psychiatric disorder, respectively. The κ coefficients of agreement for the specific anxiety disorders at intake were as follows: separation anxiety disorder (SAD) = .94, overanxious disorder (OAD) = .93, avoidant disorder = .74, panic disorder = .88, social phobia = .94, simple phobia = .71, OCD = .78, and posttraumatic stress disorder (PTSD) = 1.0.

Interrater diagnostic agreement obtained for 41% (n = 160) of the 394 follow-up interviews conducted over the 4-year follow-up were .91, 1.00, and 1.00, for any anxiety disorder, ADHD, and no psychiatric disorder, respectively. At follow-up, κ coefficients of agreement for the specific anxiety disorders were as follows: SAD = .89, OAD = .87, avoidant disorder = .74, panic disorder = .89, social phobia = .79, simple phobia = .82, OCD = .86, and PTSD = .79. In the few instances in which the two interviewers disagreed about diagnosis(es), the diagnosis(es) of the "live" interviewer was (were) used.

The overall severity of a disorder was assessed by the interviewer, using a 5-point Likert scale (0 through 4), with higher scores indicating greater severity. Severity ratings reflected both symptoms and impairment. Agreement for severity ratings was conducted by having a second clinician rate 39 (38%) of the 102 intake interviews for severity of primary anxiety disorder. The Spearman rank correlation coefficient for interviewer and observer severity ratings was .64 (p < .001). In the event of disagreement, the severity rating of the live interviewer was used.

Attrition

Of the original sample, 82.4% (n = 84) of the anxiety group, 86.2% (n = 50) of the ADHD group, and 95.4% (n = 83) of the NPI group returned for follow-up interviews. To determine whether we had selective attrition, statistical comparisons of the attrition (n = 30) and nonattrition (n = 217) groups were performed for several sociodemographic variables, including age at intake, sex, race, parental marital status, and socioeconomic status of the child's

TABLE 1
Sociodemographic Characteristics

Sociodemographic Variable	Group			Anxiety vs.	
	Anxiety ($n = 84$)	ADHD ($n = 50$)	NPI ($n = 83$)	ADHD $p<$	NPI $p<$
Mean age in years[a]	12.1	8.8	10.8	.001	.02
(SD)	(3.6)	(2.6)	(3.4)		
Sex (% male)	46.4	86.0	42.2	.001	NS
Race (% white)	81.0	66.0	67.5	NS	NS
Parental marital status (% single/ divorced)	52.4	60.0	42.2	NS	NS
SES (% low)	39.3	52.0	30.1	NS	NS

Note: ADHD = attention-deficit hyperactivity disorder; NPI = never psychiatrically ill; SES = socioeconomic status; NS = not significant.

[a] Anxiety and NPI groups initially were matched for age, but after attrition show differences.

family. Subjects who did not return for follow-up tended to be older (12.4 versus 10.9 years old; $t = 2,12$, $df = 245$, $p < .05$) and from lower socioeconomic backgrounds (66.7% versus 38.7%; $\chi^2 = 7.34$, $df = 1$, $p < .007$) than subjects who returned for follow-up.

Sample Characteristics

The sociodemographic characteristics of the subjects who participated in the follow-up study are presented in Table 1. Ages of subjects in the anxiety group ranged from 5 to 18 years (mean = 12.1 years, SD = 3.5), the majority were white (81%), and there were roughly equal numbers of males and females and children from two-parent and one-parent homes. As expected, children in the anxiety group were more similar to those in the NPI group than the ADHD group, since the NPI subjects were matched at study entry to anxious subjects. The ADHD and NPI groups tended to be younger than the anxiety group ($F[2,214] = 15.7$, $p < .001$), and there were more males in the ADHD group than the anxiety group ($\chi^2[1] = 19.0$, $p < .001$).

With regard to the clinical characteristics of the anxiety group at intake, 41 children (48.8%) presented with a single anxiety disorder only and 43 (51.2%) presented with two or more concurrent psychiatric disorders. A total of 149 psychiatric disorders (127 anxiety disorders) were assigned at intake to these 84 children. The frequencies of specific anxiety disorders at intake were as follows: simple phobia = 26, SAD = 24, social phobia = 23, OAD = 20, OCD = 12, panic disorder = 10, avoidant disorder = 6, PTSD = 5, and anxiety disorder not otherwise specified (NOS) = 1. There were six cases of major depression (7.1%), five cases of dysthymic disorder (5.9%), and four cases of oppositional defiant disorder (4.8%) at intake. Additional psychiatric disorders at intake included depressive disorder NOS ($n = 1$), cyclothymia ($n = 1$), enuresis ($n = 2$), adjustment disorder ($n = 2$), and sleep terror disorder ($n = 1$).

A distinction was made between "primary" and "secondary" disorders in children with more than one psychiatric disorder at study entry. The disorder with the highest severity rating (based on symptoms and impairment) was considered the "primary" disorder. Thus, all other disorders were termed "secondary." The temporal sequence of onset of disorders was not used to determine primary/secondary status. The 84 children with anxiety disorders at study entry had the following primary anxiety disorder diagnoses: SAD ($n = 18$), simple phobia ($n = 14$), social phobia ($n = 13$),

OAD ($n = 12$), OCD ($n = 10$), panic disorder ($n = 9$), PTSD ($n = 5$), avoidant disorder ($n = 2$), and anxiety disorder NOS ($n = 1$).

For all anxiety disorders at intake (primary and secondary), the mean severity rating was 2.6 (SD = 0.8), the mean age at onset was 9.2 years (SD = 3.9 years), and the mean duration was 3 years (SD = 2.9 years, range = 0.08 to 11.8). Regarding treatment during the follow-up period, of the two psychopathological groups, 72.6% ($n = 61$) of the anxiety group and 84.0% ($n = 42$) of the ADHD group received treatment after intake. A few children in the NPI group who developed a psychiatric disorder during the follow-up period also received treatment (15.7%). The percentages of treated subjects in the anxiety and ADHD groups receiving pharmacological versus psychosocial treatments were as follows: pharmacological only (anxiety = 4.9% and ADHD = 11.9%), psychosocial only (anxiety = 59% and ADHD = 35.7%), and pharmacological plus psychosocial treatment (anxiety = 36.4% and ADHD = 52.4%).

All of the children with anxiety disorders who participated in this study were offered treatment at the Child and Adolescent Anxiety Disorder Clinic following their intake evaluations. Those children who elected to participate in treatment were not randomly assigned to treatment condition (treatment was based on clinical judgment) and were most likely to receive treatment for their primary disorder.

Measures

Recovery. Recovery from anxiety disorder was defined as the absence of sufficient DSM-III-R criteria by the end of the follow-up period for diagnosis of the original disorder(s). Rates of recovery were calculated in the anxiety group for (1) primary anxiety disorders, (2) secondary anxiety disorders, and (3) all initial anxiety disorders (primary and secondary). Relapse was defined as the recurrence of an anxiety disorder after its remission during follow-up.

New Psychiatric Disorders during Follow-up. A new psychiatric disorder was defined as any DSM-III-R disorder that developed during follow-up that was not present at intake. Rates of new psychiatric disorders (any), anxiety disorders, behavior disorders (ADHD, oppositional defiant disorder, and conduct disorder), and depressive disorders (major depression, dysthymic disorder, and depressive disorder NOS) developed during follow-up were compared for the anxiety and two control groups.

Final Psychiatric Status. Children who met criteria for one or more *DSM-III-R* disorders at the end of the follow-up period were designated as psychiatrically ill. The specific disorders present at the end of follow-up were examined.

Factors Influencing Recovery and Outcome. Seven sociodemographic and clinical variables were chosen to examine their relationship to recovery and time to recovery from primary anxiety disorder and the development of new psychiatric disorders, based on previous literature suggesting their relationship to the development of anxiety disorders (Esser et al., 1990; Kovacs et al., 1984; Leonard et al., 1993; Offord et al., 1992; Stanger et al., 1992). These variables included age at intake, sex of the child, age at onset of earliest psychiatric disorder, severity of primary anxiety disorder, history of a depressive disorder, treatment during follow-up, and family history of an anxiety disorder in any first-degree family member.

Family history of anxiety disorder was obtained from blind, direct interviews of first-degree relatives by using either the Structured Clinical Interview for *DSM-III-R*–Non-Patient Version (adult relatives) (Spitzer, Williams, and Gibbons, 1986, unpublished manuscript) or K-SADS-P (child/adolescent relatives) as part of a larger family study of childhood anxiety (Last et al., 1991). Interrater diagnostic agreement for families of the probands was obtained by having a second interviewer independently score audiotapes from 95 (40%) complete families (1,178 individuals interviewed) and assign *DSM-III-R* diagnoses. The κ coefficient of agreement for any anxiety disorder in family members was .95.

Specific Anxiety Disorders. Recovery rates and rates of new psychiatric disorder are presented (sample size allowing) for several specific anxiety disorders: SAD (n = 24), social phobia (n = 23), simple phobia (n = 26), OAD (n = 20), OCD (n = 12), and panic disorder (n = 10).

Data Analyses

Sociodemographic and clinical characteristics of the three groups at intake were compared by using 3×2 χ^2 tests and univariate analysis of variance with post hoc Tukey tests. The primary focus of this study was the comparisons between the anxiety and two control groups for recovery, development of new disorders, and final psychiatric status. As such, only the anxiety and ADHD groups and the anxiety and NPI groups were compared with regard to outcome variables by using 2×2 χ^2 tests with Yates' continuity correction. Because the anxiety group differed from the ADHD and NPI groups for age at intake, a subset of children with anxiety disorders who more closely resembled the ADHD and NPI groups were selected for comparison for rate of psychiatric disorders during follow-up. Also, because the ADHD group was primarily male (86.0%), the rates of psychiatric disorders in the anxiety and ADHD groups were reanalyzed for males only in the two groups.

Using an analytical strategy suggested by Hosmer and Lemeshow (1989), logistic regression was used to examine the relationship between the seven sociodemographic and clinical variables and the following: (1) recovery from primary anxiety disorder, and (2) development of new psychiatric disorders. First, each correlate was regressed separately on the two outcome variables, using the maximum likelihood method of logistic regression. Correlates that were moderately related to the outcome variable (i.e., log-likelihood ratio with associated p < .25) were then chosen for multivariate analysis. Second, a full model was fitted with these remaining correlates and then individual correlates were eliminated using a backward stepwise procedure (based on the probability of the likelihood-ratio statistic). During each phase of the stepwise logistic regression, estimated coefficients were examined to determine

whether eliminated variables served as confounders and should be reincluded in the model. The appropriateness of higher-order variables (interactions) in the model was evaluated after all noncontributing predictors were eliminated. Finally, a full model was fitted to the data and goodness of fit was examined.

RESULTS

Recovery from Childhood Anxiety Disorders

We examined recovery during follow-up for primary, secondary, and all anxiety disorders (primary and secondary combined). For primary anxiety disorders, 81.7% (68/84) remitted by the end of the follow-up period. A similar remission rate was obtained for secondary anxiety disorders (83.7%, 36/43) and all anxiety disorders (81.9%, 104/127).

Recurrence of remitted anxiety disorders also was examined. The overall rate of relapse for all initial anxiety disorders was very low, with only 10 (7.8%) of 127 recurring after remission (3 cases each of social phobia and SAD, and 2 cases each of OAD and panic disorder).

Development of New Psychiatric Disorders during Follow-up

Table 2 shows the percentage of children in the anxiety, ADHD, and NPI groups who developed a new anxiety, behavior, and/or depressive disorder during follow-up. Fewer than one third (29.8%) of the children with anxiety disorders developed new psychiatric disorders during the follow-up period; this rate differed from that of the NPI controls ($\chi^2[1]$ = 8.1, p < .005), but not ADHD controls. For specific types of new disorders, the anxiety group was more likely than the NPI group ($\chi^2[1]$ = 7.2, p < .008), but not the ADHD group, to develop new anxiety disorders during follow-up. For new behavior disorders, anxious children were more likely than NPI children ($\chi^2[1]$ = 6.3, p < .02), but less likely than ADHD children, to develop these disorders ($\chi^2[1]$ = 4.3, p < .04). There were no differences between the anxiety and two control groups for new depressive disorders at follow-up. No differences also emerged when examining major depression only (anxiety = 9.5%, ADHD = 4.0%, and NPI = 6.0%).

Twenty-five children with anxiety disorders developed a total of 39 new psychiatric disorders during follow-up (Table 2). Of the 25 children, 13 developed

TABLE 2
Development of New Psychiatric Disorders during Follow-up

| | Group | | | | | | Anxiety vs. | |
| | Anxiety (n = 84) | | ADHD (n = 50) | | NPI (n = 83) | | ADHD | NPI |
DSM-III-R Disorder	%	n	%	n	%	n	p<	p<
Any new psychiatric disorder	29.8	25	42.0	21	10.8	9	NS	.005
Any new anxiety disorder	15.5	13	10.0	5	2.4	2	NS	.008
Any new behavior disorder	7.1	6	24.0	12	0.0	0	.02	.04
Any new depressive disorder	13.1	11	8.0	4	7.2	6	NS	NS

Note: ADHD = attention-deficit hyperactivity disorder; NPI = never psychiatrically ill; NS = not significant.

16 new anxiety disorders (SAD = 5, simple phobia = 3, OCD = 3, social phobia = 2, OAD = 2, and avoidant disorder = 1). Six children developed six behavior disorders during follow-up, including five cases of oppositional defiant disorder and one case of conduct disorder. Eleven children developed 13 depressive disorders during follow-up (major depression = 8, dysthymic disorder = 3, and depressive disorder NOS = 2). Of these 13 depressive disorders, 8 were new disorders and 5 were second episodes of major depression, with the initial episode occurring prior to study entry. Finally, 4 children developed other disorders, including schizophrenia (n = 1), adjustment disorder (n = 2), and enuresis (n = 1).

To control for age differences between anxiety and ADHD groups, rates of new disorders in the two groups were reanalyzed for subgroups of younger children matched as closely as possible for age. When reanalyzing the data in this matter, the anxiety (n = 45) and ADHD (n = 48) groups continued to show no differences on the rates of psychiatric disorders (any), anxiety disorder, and depressive disorder. However, anxious children and children with ADHD no longer differed for the rate of behavior disorder during follow-up (anxiety = 8.9% versus ADHD = 20.8%). Rates of disorders also were reanalyzed to account for age differences between the anxiety and NPI groups. When comparing age-matched groups of children in the anxiety (n = 62) and NPI (n = 71) groups, findings remained the same.

To control for the greater number of males in the ADHD group compared with the anxiety group, rates of disorders were reanalyzed for boys only. The anxiety

(n = 39) and ADHD (n = 43) groups did not significantly differ on any of the diagnostic categories.

Final Psychiatric Status of Children with Anxiety Disorders

A total of 30 children in the anxiety group (35.7%) were still psychiatrically ill at the end of the follow-up period. Of these 30, 16 (53.3%) retained their primary anxiety disorders. Six children (20%) retained one or more of their secondary anxiety disorders. None retained a secondary, nonanxiety disorder. Thirteen (43.3%) retained one or more new disorders. Finally, four children (13.3%) had a relapse during follow-up of an anxiety or depressive disorder that was present at intake.

Factors Related to Recovery and Outcome of Children with Anxiety Disorders

Logistic regressions were performed to evaluate the relationship of age at intake, sex, history of depression (at or before intake), treatment after intake ("yes," "no"), family history of an anxiety disorder (at intake), age at onset of the earliest psychiatric disorder, and severity of primary anxiety disorder, to (1) recovery from intake anxiety disorders, and (2) the development of new psychiatric disorders. None of the sociodemographic or clinical correlates emerged as reasonable predictors of recovery during the univariate screening procedure (i.e., had a log-likelihood ratio with associated $p < .25$). In the event that this screening procedure was too conservative, we attempted to fit a full model including all seven correlates and again found no relationship.

Treatment after intake emerged as the only significant predictor of new disorders during follow-up (log-likelihood ratio = 7.16. p = .0075). While being male and having a history of depression were marginally associated with the development of new disorders in the univariate logistic regression procedure (p < .20), only treatment status (estimated coefficient = 1.78, standard error = 0.79) and the constant (estimated coefficient = −2.35, standard error = 0.74) reached criteria for inclusion in the final model. Conversion of the log-odds (estimated coefficient) to an odds ratio indicated that treated children were 5.9 times more likely than their untreated counterparts to develop a new disorder(s) during follow-up (95% confidence interval for odds ratio = 1.26 to 27.89).

Specific Anxiety Disorders

Rates of recovery for specific *DSM-III-R* anxiety disorders were observed. As there were no differences between recovery rates for primary versus secondary anxiety disorders (rates available upon request), rates are presented for all anxiety disorders combined. SAD (95.7%, 22/24) and social phobia (86.4%, 19/23) had the highest rates of recovery of all the specific anxiety disorders examined, followed by OAD (80.0%, 16/20), OCD (75.0%, 9/12), and panic disorder (70.0%, 7/10), respectively. Simple phobia had the lowest rate of recovery during follow-up (69.2%, 18/26). However, no significant differences were found among the groups (χ^2 [5] = 6.2, p = .3).

Table 3 presents rates of new psychiatric disorders developing during follow-up for each specific anxiety disorder. As there were no differences between primary and secondary anxiety disorders (rates available upon

request), rates are presented for both primary and secondary anxiety disorders combined. OAD had the highest percentage of youngsters developing new psychiatric disorders during follow-up (35%), usually anxiety or depression, while simple phobia had the lowest (15.4%). However, comparison of the five diagnostic groups for rate of new disorder (any) was nonsignificant (χ^2 [4] = 2.6, p = .62). Specific types of anxiety and depressive disorders developed by OAD children included the following: major depression = 5, SAD = 3, OCD = 2, social phobia = 1, panic disorder = 1, and simple phobia = 1.

DISCUSSION

Overall, our findings suggest that anxiety disorders in clinically referred children have a generally favorable course and outcome. Most of the children in this study (81.7%) recovered from their anxiety disorders, both primary and secondary, during follow-up. For those who did recover, there were very few instances of relapse during follow-up (7.8%). Only one third of the children with anxiety disorders still had psychiatric diagnoses at the end of follow-up. Of these, most either retained their primary anxiety disorder or showed a new psychiatric disorder that had developed during the follow-up period.

Approximately 30% of the anxious children developed new psychiatric disorders during follow-up, usually new anxiety disorders. However, when comparing the groups for rates of any new psychiatric disorder and new anxiety disorder, anxious children significantly differed from NPI controls, *but not* psychopathological controls. Thus, children with anxiety disorders do not

TABLE 3
Development of New Psychiatric Disorders for Specific Anxiety Disorders

	Disorder							
	Any		Anxiety		Behavior		Depressive	
Specific Anxiety Disorder	%	n	%	n	%	n	%	n
Separation anxiety (n = 24)	25.0	6	8.3	2	8.3	2	16.7	4
Social phobia (n = 23)	21.7	5	8.7	2	0.0	0	13.0	3
Simple phobia (n = 26)	15.4	4	7.7	2	3.8	1	7.7	2
Overanxious (n = 20)	35.0	7	25.0	5	0.0	0	25.0	5
Obsessive-compulsive (n = 12)	25.0	3	8.3	1	8.3	1	8.3	1
Panic (n = 10)	30.0	3	10.0	1	10.0	1	10.0	1

Note: The number of children with specific disorders exceeds the number of children with any new disorder because some subjects had more than one disorder.

appear to be at greater risk for the development of other psychiatric disorders in general, or anxiety disorders in particular, than children with other types of psychiatric illness, or at least ADHD.

Given the paucity of prospective data available on the natural history of anxiety disorders during childhood, it was a logical first step to lump the anxiety disorders together for analysis. However, as a second step, where sample size allowed, course and outcome were examined for individual disorders. Consistent with Cantwell and Baker's findings (1989), both SAD (96%) and OAD (80%) showed high rates of recovery. Although the majority of children with OAD recovered, this specific anxiety disorder had the highest rate of new disorders during follow-up (35%). We also note that our recovery rate for OCD (75%) is comparable with that previously reported by Berg et al. (1989) (69%), but higher than that reported for the clinically referred samples of Leonard et al. (1993) and Thomsen and Mikkelsen (1995).

Several sociodemographic and clinical variables were evaluated as potential prognostic indicators of recovery and/or the development of new disorders. Contrary to expectation, treatment after intake did not emerge as a significant predictor of recovery from primary anxiety disorder. Univariate analyses revealed untreated (n = 23) and treated children (n = 61) to be comparable with respect to recovery rates at follow-up (82.6% versus 80.3%, respectively). In addition, treated children were *more* likely to develop new disorders during follow-up than untreated children.

Post hoc comparisons of treated and untreated children showed that the primary anxiety disorders of untreated children were rated at intake as less severe by clinicians than were those of treated children (2.4 versus 2.8, respectively) ($t = -2.1$, $df = 82$, $p < .04$). While logistic regression analyses did not support a general relationship between primary anxiety disorder severity at intake and the development of new disorders during follow-up, it may be that there is a particular subgroup of clinically referred children whose disorders are less severe and more likely to remit spontaneously, and who thus never enter treatment. In fact, close inspection of the 12-month follow-up data revealed that the majority of untreated children who got better did so within a few weeks of study entry, providing preliminary support for this hypothesis.

The absence of findings for a treatment effect on recovery also should be considered in light of the generally favorable outcome for the sample overall ("ceiling effect"), the lack of random assignment to treatment, and the very small number of untreated children followed (n = 23). Had there been additional untreated children in the anxiety group, comparisons between treated and untreated children may have yielded a pattern of results different from that found here. While it would have been methodologically preferable to randomly assign children to treatment and no-treatment conditions during the study, to rigorously examine the effects of treatment, such a design was not possible with this clinic population.

Another finding contrary to expectation was the increased risk for new disorders observed among treated versus untreated children (odds ratio = 5.9). Again, these findings must be considered in light of the small number of untreated children under study. However, it may be that our findings reflect the heightened risk of new disorders, particularly anxiety disorders, among more seriously disturbed treatment-seeking children. Alternatively, treated children simply may be better at identifying symptoms of clinically significant anxiety than their untreated counterparts.

Depression was not among the disorders frequently observed to develop during follow-up in the anxiety group. This finding runs contrary to previous studies that have suggested that anxiety disorder increases the child's risk for depression (Brier et al., 1984; Kovacs et al., 1994). There are several possible explanations for this finding. First, it may be that treatment for anxiety disorder reduces the risk of developing depression. However, in the present study untreated children (n = 23) were no more likely than treated children (n = 61) to develop depressive disorders during follow-up (4.3% versus 9.8%, respectively). Second, given the relatively young age of the children in the anxiety group at the end of the follow-up (mean = 15.1 years), extended follow-up might reveal a different pattern of results, as more of these children enter late adolescence and early adulthood. Third, our findings may suggest that children with anxiety disorders simply are not at risk for developing depressive disorders.

How do the current findings impact our knowledge of the diagnosis and treatment of childhood anxiety disorders? From our analyses of diagnostic subtypes, preliminary findings suggest that youngsters with OAD

are at risk for developing additional psychiatric disorders over time, particularly new anxiety disorders and depression. Such findings may be viewed as supporting a psychosocial approach to treatment, where specific coping skills are taught to the child to ameliorate risk of new illness over time, as well as alleviate current symptomatology.

With the recent publication of *DSM-IV*, it is unclear how children previously diagnosed as overanxious according to *DSM-III-R* will fare, as OAD per se has been eliminated from the manual. While it is assumed that most of these youngsters now will meet *DSM-IV* criteria for generalized anxiety disorder, such assumptions await empirical investigation.

Finally, the present findings must be interpreted within the context of certain study limitations. First, our findings for course and outcome are based on a sample of clinically referred youths and may not be representative of nonreferred children with anxiety disorders. Second, our analyses of course and outcome for individual anxiety disorders were hampered by the small number of children in several of the specific groups. Third, there were significant sociodemographic differences between subjects who returned for follow-up and those who did not. Fourth, symptom status and adjustment were not assessed in this study. It is possible that some children were still experiencing significant symptoms of anxiety at follow-up, although they were free of their initial anxiety disorders. While the absence of a diagnosable disorder is evidence of a favorable outcome from a clinical perspective, future studies should explore the course of symptoms in this population and their relationship to adjustment and risk for relapse over time.

In summary, results from this 4-year prospective investigation suggest that clinically referred children with anxiety disorders show a generally favorable outcome. Continued follow-up of this sample will provide additional, much needed information on how these youngsters do as they enter adulthood.

REFERENCES

American Psychiatric Association (1980), *Diagnostic and Statistical Manual of Mental Disorders, 3rd edition (DSM-III)*. Washington, DC: American Psychiatric Association

Berg CZ, Rapoport JL, Whitaker A et al. (1989), Childhood obsessive compulsive disorder: a two-year prospective study of a community sample. *J Am Acad Child Adolesc Psychiatry* 28:528–533

Bernstein GA, Borchardt CM (1991), Anxiety disorders of childhood and adolescence: a critical review. *J Am Acad Child Adolesc Psychiatry* 30:519–532

Bland RC, Newman SC, Orn H (1988), Age at onset of psychiatric disorders. *Acta Psychiatr Scand* 77(suppl 338):43–49

Brier A, Charney DS, Heninger GR (1984), Major depression in patients with agoraphobia and panic disorder. *Arch Gen Psychiatry* 41:1129–1135

Burke KC, Burke J, Regier DA, Rae DS (1990), Age at onset of selected mental health disorders in five community populations. *Arch Gen Psychiatry* 47:511–518

Cantwell DP, Baker L (1989), Stability and natural history of *DSM-III* childhood diagnoses. *J Am Acad Child Adolesc Psychiatry* 28:691–700

Esser G, Schmidt H, Woerner W (1990), Epidemiology and course of psychiatric disorders in school-age children: results of a longitudinal study. *J Child Psychol Psychiatry* 31:243–263

Flament M, Whitaker A, Rapoport J et al. (1988), Obsessive compulsive disorder in adolescence: an epidemiological study. *J Am Acad Child Adolesc Psychiatry* 27:764–771

Flament MF, Koby E, Rapoport JL et al. (1990), Childhood obsessive-compulsive disorder: a prospective follow-up study. *J Child Psychol Psychiatry* 31:363–380

Hollingshead AB (1975), *Four Factor Index of Social Status*. New Haven, CT: Yale University Department of Sociology

Hosmer DW, Lemeshow S (1989), *Applied Logistic Regression*. New York: Wiley

Keller MB, Lavori PW, Wunder BA, Beardslee WR, Schwartz CE, Roth J (1992), Chronic course of anxiety disorders in children and adolescents. *J Am Acad Child Adolesc Psychiatry* 31:595–599

Kovacs M, Akiskal H, Gatsonis C, Parrone P (1994), Childhood-onset dysthymic disorder: clinical features and prospective naturalistic outcome. *Arch Gen Psychiatry* 51:365–374

Kovacs M, Feinberg T, Crouse-Novak M, Pauluaskas S, Finkelstein R (1984), Depressive disorders in childhood: I. A longitudinal prospective study of characteristics and recovery. *Arch Gen Psychiatry* 41:229–237

Last CG (1993), Introduction. In: *Anxiety across the Lifespan: A Developmental Perspective*, Last CG, ed. New York: Springer, pp 1–7

Last CG, Hersen M, Kazdin AE, Orvaschel H, Perrin S (1991), Anxiety disorders in children and their families. *Arch Gen Psychiatry* 48:928–934

Last CG, Perrin S, Hersen M, Kazdin AE (1992), *DSM-III-R* anxiety disorders in children: sociodemographic and clinical characteristics. *J Am Acad Child Adolesc Psychiatry* 28:1070–1076

Leonard HL, Swedo SE, Lenane MC et al. (1993), A two to seven year follow-up study of 54 obsessive compulsive children and adolescents. *Arch Gen Psychiatry* 50:429–439

Offord D, Boyle M, Racine Y et al. (1992), Outcome, prognosis, and risk in a longitudinal follow-up study. *J Am Acad Child Adolesc Psychiatry* 31:916–923

Schneier FR, Johnson J, Hornig CD, Liebowitz MR, Weissman MM (1992), Social phobia: comorbidity and morbidity in an epidemiologic sample. *Arch Gen Psychiatry* 49:282–288

Stanger C, McConaughy SM, Achenbach TM (1992), Three-year course of behavioral/emotional problems in a national sample of 4- to 16-year-olds: II. Predictors of syndromes. *J Am Acad Child Adolesc Psychiatry* 31:941–950

Thomsen PH, Mikkelsen HU (1995), Course of obsessive-compulsive disorder in children and adolescents: a prospective follow-up study of 23 Danish cases. *J Am Acad Child Adolesc Psychiatry* 34:1432–1440