Prospective, Longitudinal Study of Tic, Obsessive-Compulsive, and Attention-Deficit/Hyperactivity Disorders in an Epidemiological Sample

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ABSTRACT

Objective: Understanding the interrelatedness of tics, obsessive-compulsive disorder (OCD), and attention-deficit/hyperactivity disorder (ADHD) has been complicated by studying only cross-sectional samples of clinically referred subjects. The authors report the cross-sectional and longitudinal associations of these disorders in an epidemiological sample of children followed prospectively into early adulthood. **Method:** Structured diagnostic interview information was acquired on 976 children, aged 1 to 10 years, who were randomly selected from families living in upstate New York in 1975. Reassessments were acquired in 776 of these subjects 8, 10, and 15 years later. Diagnostic prevalences were estimated at each time point. The associations among tics, OCD, and ADHD were assessed within and across time points, as were their associations with comorbid illnesses and demographic risk factors. **Results:** In temporal cross-section, tics and ADHD symptoms were associated with OCD symptoms in late adolescence and early adulthood after demographic features and comorbid psychiatric symptoms were controlled. In prospective analyses, tics in childhood and early adolescence predicted an increase in OCD symptoms in late adolescence and early adulthood. ADHD symptoms in adolescence predicted more OCD symptoms in early adulthood, and OCD in adolescence predicted more ADHD symptoms in adulthood. The associations of tics with ADHD were unimpressive in temporal cross-section and were not significant in prospective analyses. Tics, OCD, and ADHD shared numerous complex associations with demographic and psychopathological risk factors. ADHD was associated with lower IQ and lower social status, whereas OCD was associated with higher IQ. **Conclusions:** Tics and OCD were significantly associated in this sample, as were OCD and ADHD. These findings are in general consistent with those from family studies, and they help to define the natural history, comorbid illnesses, and interrelatedness of these conditions. *J. Am. Acad. Child Adolesc. Psychiatry*, 2001, 40(6):685–695. **Key Words:** tics, obsessive-compulsive disorder, attention-deficit/hyperactivity disorder, epidemiology, risk factors.

In clinical samples, tics, obsessive-compulsive disorder (OCD), and attention-deficit/hyperactivity disorder (ADHD) commonly co-occur. Their overlap in clinical settings (Leonard et al., 1992; Pauls et al., 1991; Shapiro et al., 1988) has supported speculation that the conditions may share a common pathophysiology (Pauls et al., 1986b; Peterson and Klein, 1997). The strongest evidence for a shared etiology is from family studies of clinic patients. Those studies have shown that OCD is present in the families of probands with Tourette's syndrome (TS) more often than it is present in control families, whether or not the proband has comorbid OCD (Eapen et al., 1993; Pauls et al., 1986b). Conversely, tics are present in the family members of probands who have OCD more often than they are present in control families, whether or not the proband has a comorbid tic disorder (Leonard et al., 1992; Pauls et al., 1995). These findings suggest that a particular genetic vulnerability may be variably expressed as tics, OCD, or both disorders in combi-

Accepted January 25, 2001.

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This work was supported in part by NIMH grants MH01232 (Dr. Peterson), MH01391 (Dr. Pine), MH36971 (Dr. Cohen), K05-DA-00244 (Dr. Brook), MH-16432, and MH-43878, and NIDA grant DA-03188 (Dr. Brook). The authors are grateful to Drs. James F. Leckman and Donald J. Cohen for their helpful comments on this manuscript.

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nation. Although the familial transmission of ADHD in persons who have either tics or OCD is less clear (Pauls et al., 1986a, 1993), some investigators regard ADHD as an additional variable manifestation of putative TS vulnerability genes (Comings and Comings, 1987).

Aggregation of comorbid illnesses in families of clinically identified probands does not conclusively establish the existence of etiological relationships among these disorders because various biases may affect familial aggregation (Peterson et al., 1995; Shapiro and Shapiro, 1992). Shared environmental risk factors among family members could predispose to particular symptom constellations throughout the family, which could then produce an apparent association between disorders whose pathophysiologies are not intrinsically related. Alternatively, characteristics of parents in family studies may affect their tolerance and report of psychopathology in their children, which would increase the representation of these families in clinical samples and influence their tendency to participate in family studies. These possible confounds can be addressed by assessing associations among ADHD, OCD, and tic disorders in epidemiological samples. If the disorders are indeed etiologically related, then they should occur together in the general population in the absence of clinic referral bias (Berkson, 1946).

Available epidemiological studies inconsistently document associations among tics, OCD, and ADHD (Douglass et al., 1995; Flament et al., 1988). The studies that have suggested a relationship among these disorders examined relatively few cases ascertained by interviewers who were not blind to the hypothesized interrelatedness of these conditions (Apter et al., 1993; Zohar et al., 1997). Moreover, prior epidemiological studies have not included prospective, longitudinal assessments of these disorders. Cross-sectional studies of adults are likely to underestimate the lifetime prevalence of tics and ADHD because the prevalence of these symptoms declines with age. Conversely, cross-sectional studies of children are likely to underestimate the lifetime rates of OCD, which has a later window of maximum risk for new onset (Rasmussen and Tsuang, 1986). Prospective longitudinal assessments in epidemiological samples would provide more accurate lifetime diagnostic information and clarify the natural history of tics, OCD, and ADHD. Longitudinal assessments would also permit analyses of both the cross-sectional and prospective associations among these disorders.

We report a longitudinal study of tics, OCD, ADHD, and other comorbid neuropsychiatric disorders in an epidemiological sample of children assessed prospectively at four time points from early childhood into young adulthood. We test the hypothesis that tics, OCD, and ADHD are associated with one another both within and across time points (Peterson et al., 1995). We also examine longitudinal patterns of comorbidity and demographic risk factors for each of these conditions.

METHOD

Sample

The original sample was selected in 1975 (time 1) from 976 households in two semirural upstate New York counties by means of a multistaged random sampling strategy with complete enumeration (Kogan et al., 1977). Families with children in the 1- to 10-year age range were selected in 1975, and one child was randomly selected from each household. This initial study wave obtained an 85% completion rate. In 1983 (time 2), 724 (74%) children in the original sample were located for reassessment. Those lost to follow-up were more often younger, more urban, and from lower social strata than those who were retained in the study (Bernstein et al., 1993). The sample was therefore supplemented at time 2 with 54 families selected randomly from areas of urban poverty by means of the same sampling procedures used at time 1. The time 2 sample, including this supplement, was representative of the original sample with regard to race, income, maternal education, and family structure (Cohen and Cohen, 1996). The number of families successfully reinterviewed was 776 in 1983 (time 2), 760 in 1985 (time 3), and 728 in 1992 (time 4) (Table 1) (Cohen and Cohen, 1996).

Assessments

At time 1, psychiatric symptoms in the child were assessed in a 1-hour interview with the child's mother. Symptom measures were derived from a principal components analysis of 15 individual symptom scales that yielded scores for four domains of psychopathology: conduct problems (Cronbach $\alpha = .79$), depressive symptoms ($\alpha = .50$), anxiety/fear ($\alpha = .62$), and immaturity ($\alpha = .62$). These measures have been shown to have considerable stability and predictive utility (Cohen and Brook, 1987).

Psychopathology was further assessed at times 2 and 3 in interviews of both mothers and subjects, and at time 4 with the subjects alone, by using the Diagnostic Interview Schedule for Children (DISC) (Costello et al., 1985). The DISC was administered by 1 of 15 trained lay interviewers in a highly structured interview format to elicit reports of psychiatric symptoms. Different interviewers were typically used across time to assess a given child. The DISC was modified at each time point to integrate changes that optimized the reliability and validity of epidemiological assessments. The time 2 DISC was adapted from the original DISC by adding items about functional impairment for each diagnosis, removing skips from the interview, and revising the major depression section to more precisely date the timing of symptom onset. The time 3 DISC was adapted from the time 2 DISC by integrating the then-proposed *DSM-III-R* criteria and by adding another three to five items for each diagnosis to document interference in school and social activities, subjective distress, and desire for help with symptoms. The DISC at time 4 was unchanged from time 3 except for modifications to reflect adult nosology. In addition, no parental report was obtained at time 4. Tics at time 1 were ascertained only by parental report and at time 4 only by interviewer observation. The questions concerning tic and obsessive-compulsive symptoms are available on request.

TABLE 1
Prevalence Estimates for Tics, OCD, and ADHD

	Time Point				
	1 (1975)	2 (1983)	3 (1985)	4 (1992)	Lifetime (1975–1992)
No. studied	976	776	760	728	1030
Mean age (SD)	6.1 (2.8)	13.7 (2.7)	16.3 (2.8)	22.1 (2.7)	
Age range	1–10	9–20	11–22	17–28	1–28
% White	93	90	91	91	91
% Male	51	50	51	51	51
Informant	Mother	Mother and subject	Mother and subject	Subject (interviewer observations of tics)	—
Motor tics[a]	172 (17.7 ± 1.22)	17 (2.2 ± 0.53)	16 (2.1 ± 0.51)	5 (0.64 ± 0.29)	189 (18.4 ± 1.2)
Males	92 (18.6 ± 1.7)	8 (2.1 ± 0.72)	12 (3.0 ± 0.85)	2 (0.51 ± 0.36)	104 (20.0 ± 1.8)
Females	80 (16.6 ± 1.7)	9 (2.3 ± 0.77)	4 (1.1 ± 0.53)	3 (0.79 ± 0.45)	85 (16.7 ± 1.7)
Vocal tics[a]	NA	2 (0.26 ± 0.26)	2 (0.26 ± 0.26)	NA	3 (0.39 ± 0.22)
Males		1 (0.26 ± 0.26)	0		1 (0.26 ± 0.26)
Females		1 (0.26 ± 0.26)	2 (0.52 ± 0.37)		2 (0.52 ± 0.37)
Tourette's syndrome[a]	NA	2 (0.26 ± 0.26)	2 (0.26 ± 0.26)	NA	3 (0.39 ± 0.22)
Males		1 (0.26 ± 0.26)	0		1 (0.26 ± 0.26)
Females		1 (0.26 ± 0.26)	2 (0.52 ± 0.37)		2 (0.52 ± 0.37)
OCD[a]	NA	43 (5.5 ± 0.82)	14 (1.9 ± 0.49)	24 (3.3 ± 0.67)	74 (9.1 ± 1.0)
Males		24 (6.2 ± 1.2)	6 (1.5 ± 0.61)	11 (3.1 ± 0.93)	36 (8.6 ± 1.4)
Females		19 (4.9 ± 1.1)	8 (2.1 ± 0.75)	13 (3.6 ± 1.0)	38 (9.5 ± 1.5)
ADHD[a]	NA	93 (12.0 ± 1.2)	59 (7.6 ± 0.95)	8 (1.1 ± 0.40)	124 (15.1 ± 1.2)
Males		61 (15.7 ± 1.8)***	38 (9.5 ± 1.5)*	5 (1.4 ± 0.64)	78 (18.7 ± 1.9)***
Females		32 (8.3 ± 1.4)***	21 (5.6 ± 1.2)*	3 (0.83 ± 0.48)	46 (11.4 ± 1.6)***

Note: Seven hundred seventy-six families were reinterviewed at times 2, 3, and 4, but complete information was not available at times 3 and 4, accounting for the smaller number of subjects at those time points. OCD = obsessive-compulsive disorder; ADHD = attention-deficit/hyperactivity disorder; NA = not available.

Significant sex differences, χ^2: * $p < .05$; *** $p < .005$.

[a] Values represent no. (%).

Categorical diagnoses for all DISC interviews were assigned in accordance with *DSM-III* criteria at time 2 and *DSM-III-R* criteria at times 3 and 4. Only diagnoses present during the previous year were considered. All disorders were diagnosed without exclusionary criteria, and diagnosis of all except tic symptoms required the presence of functional impairment. Continuous measures of symptom severity were constructed by summing the numbers of individual symptoms endorsed within a diagnostic domain.

Cross-informant agreement can be poor in structured diagnostic interviews. This is particularly true for diagnosing internalizing disorders (depression, anxiety, and OCD) (Jensen et al., 1995) and for documenting the presence of tics in nonreferred samples (Pauls et al., 1984). We therefore considered various methods for combining the information from parent and subject reports and interviewer observations that were available for times 2 and 3. We considered a categorical diagnosis to be present when two conditions were satisfied. First, the subject met *DSM* criteria on the basis of symptom endorsement from either the child or mother (or, in the case of tics, if they were observed by the interviewer). Second, the symptom impairment score for the relevant diagnostic domain (with the exception of that for tics) was at least 1 SD above the sample mean. These criteria have been shown to optimize the balance between sensitivity and specificity in the diagnosis of disorders (Cohen et al., 1993). Combining parent and child reports can provide diagnostic sensitivity that approaches 100% for tic disorders and 90% for OCD (Fisher et al., 1993).

Numerous studies have examined the reliability and validity of the DISC. The test-retest reliability at 2 to 4 weeks is comparable to the reliability of other instruments, although the reliability for anxiety, depressive, and obsessive-compulsive disorders tends to be poor across instruments (κ values range from 0.25 to 0.50) (Jensen et al., 1995; Schwab-Stone et al., 1994). The validity of the DISC in this particular sample is supported by the correlation of categorical diagnoses and continuous symptom scales with clinicians' ratings of psychopathology (Cohen et al., 1987) and with various external validators (Cohen and Brook, 1987; Cohen et al., 1989; Pine et al., 1998).

Additional subject characterization included age, ethnicity, socioeconomic status (SES), and estimated intelligence. SES was assessed with a composite measure of maternal and paternal years of education, paternal occupational status, and family income (Cohen and Brook, 1987). Intelligence was estimated with the Quick Test, a brief picture vocabulary neuropsychological test with a high test-retest reliability (0.91) and good correlation with more extended measures of intelligence in children ($r = 0.85$ with the full Binet) (Ammons and Ammons, 1962). Averages of this measure at times 2 and 3 were used in all statistical analyses.

Statistical Analyses

Our initial analyses examined the prevalence estimates of tics, OCD, and ADHD at each of the time points. We then used multiple

linear regression to examine the associations among scalar indices of symptom severity within and across time points. The scaled scores were constructed by summing the number of symptoms for each subject in each diagnostic category. Analogous regression procedures were conducted for categorical diagnostic variables by using multiple logistic regression. Although the results of these analyses were similar, we will report those that are based on scalar indices because they increased the power and stability of the analyses involving times of low prevalence for particular categorical diagnoses, such as ADHD in early adulthood. For each analysis, age, sex, SES, IQ, and minority status were forced into the regression equations. For all stepwise variable selection procedures, the probability of F to enter the regression equations was set at .05; and to remove, at .10. In all final models, linearity and homoscedasticity of the residuals were assured by examining plots of the studentized residuals against predicted values of the dependent variable (Hair et al., 1992). Probability values were two-tailed, with an $\alpha = .05$. P values were not corrected for multiple comparisons to minimize type II errors when testing our primary hypothesis concerning associations among tics, OCD, and ADHD within and across time points. All other analyses were considered to be exploratory.

Cross-Sectional Associations. We examined the multivariate associations of tics, OCD, and ADHD with each other and with other psychiatric diagnoses within temporal cross-section. At time 1, diagnostic information was available only for tics. At each time point, tics, OCD, and ADHD were forced into the regression equations. The remaining diagnoses—depression, dysthymia, anxiety disorders, conduct disturbance, and oppositional defiant disorder—were allowed to compete for entry in forward stepwise variable selection procedures. The anxiety disorders in these analyses included simple phobia, social phobia, "fearful spells" (episodes of brief, spontaneous, crescendo anxiety), separation anxiety, and either overanxious or generalized anxiety disorders (depending on age and the *DSM* criteria invoked at that time point) (Pine et al., 1998). Multiple linear regression was used to examine the associations of the continuous variables, OCD and ADHD symptom severity; multiple logistic regression was used to examine the associations of tics at each time point because a continuous index of tic severity was not available.

Temporal Antecedents. We used multiple regression modeling procedures to examine which prior symptoms predicted current tics, OCD, and ADHD symptoms while controlling for demographic and prior diagnostic confounds. Tics, OCD, or ADHD symptoms (along with the demographic variables) were forced into the model that predicted the corresponding variable at the next time point. We allowed all symptoms at previous time points to compete with one another for entry into the regression equations in forward stepwise variable selection procedures. Because prior tic, OCD, or ADHD diagnoses were included as covariates, these analyses modeled predictors of change in symptom severity across time points (Cohen and Brook, 1987).

Future Comorbid Conditions. Similar modeling procedures were used to examine the associations of future symptoms with past tic, OCD, and ADHD symptoms. Each possible diagnosis at a single time point was entered as a dependent variable into a separate regression equation. The same diagnosis at the preceding time point was forced, along with the demographic variables, into the model (thus each model assessed the change in severity of that particular symptom across time points). All possible diagnoses at all preceding time points were allowed to compete for entry into the model. The diagnoses for which previous tic, OCD, or ADHD symptoms entered as significant predictors were then tabulated.

Subjects Lost to Follow-up. These subjects were included in the calculations of prevalence estimates and in cross-sectional associations for the time points at which they were assessed, but they were excluded from the analyses of associations across time points at which they were not assessed.

RESULTS

For the sake of clarity, only associations at a significance level of $p < .05$ are tabulated (Tables 1–4). Tables of the statistical models that include all final terms and covariates are available on request.

Prevalence Estimates

Tics and ADHD declined in prevalence across each time point, whereas the prevalence of OCD declined at time 3 (late adolescence) before increasing in early adulthood (Table 1). Significant sex differences were seen only for ADHD at times 2 and 3. Sex differences for motor tics reached only trend levels of significance ($p < .07$) at time 3. The modal age of onset for tics was 6 to 8 years and for OCD was age 12.

Cross-Sectional Associations

The use of categorical diagnoses and scaled symptom variables in the regression models produced very similar results. Only the results for scaled symptom variables will be presented (Table 2).

Demographic Risk Factors. Tics in early childhood were significantly associated with older age, minority status, and lower SES. IQ was positively associated with OCD symptoms and negatively associated with ADHD symptoms at times 2 to 4. Males and younger subjects had more ADHD symptoms at times 2 to 4.

Tics, OCD, and ADHD. Tics were significantly associated with OCD symptoms concurrently at times 3 and 4. OCD symptoms were also associated with ADHD symptoms at times 3 and 4. Tics were not significantly associated with ADHD symptoms at any time.

Other Comorbid Disorders. Conduct problems were associated with tics at times 1 and 2. ADHD and OCD were associated with depression and anxiety symptoms at times 2, 3, and 4. In addition, ADHD symptoms were more consistently associated with conduct disorder symptoms at all time points, and OCD symptoms were more consistently associated with separation anxiety symptoms and fearful spells at times 2 and 3.

Temporal Antecedents

Tics, OCD, and ADHD Predicting One Another. Tics at time 1 predicted OCD symptoms at time 3, and tics at

TABLE 2
Comorbid Disorders in Temporal Cross-Section

Tics at Time 1	OR	OCD at Time 1	β	ADHD at Time 1	β
Age	1.12**	—[a]		—	
Ethnicity	0.18†	—		—	
Social class	0.74*	—		—	
Conduct problems at time 1	1.10**	—		—	
Tics at Time 2	**OR**	**OCD at Time 2**	**β**	**ADHD at Time 2**	**β**
Conduct disorder at time 2	1.10*	Age	.18†	Age	–.10†
		IQ	.09*	Sex	.16†
		Depression at time 2	.19†	IQ	–.09***
		Simple phobia at time 2	.20†	Conduct disorder at time 2	.35†
		Fearful spells at time 2	.12†	Depression at time 2	.31†
		Overanxious disorder at time 2	.15†	Overanxious disorder at time 2	.10***
		Separation anxiety at time 2	.10*	Separation anxiety at time 2	.08*
Tics at Time 3	**OR**	**OCD at Time 3**	**β**	**ADHD at Time 3**	**β**
Sex	0.16*	IQ	.08*	Age	–.14†
OCD at time 3	**1.10***	Depression at time 3	.23†	Sex	.15†
Depression at time 3	1.03**	Simple phobia at time 3	.26†	IQ	–.11†
		Fearful spells at time 3	.12†	**OCD at time 3**	**.06***
		Separation anxiety at time 3	.13†	Conduct disorder at time 3	.38†
				Depression at time 3	.14†
				Overanxious disorder at time 3	.22†
				Simple phobia at time 3	.07*
Tics at Time 4	**OR**	**OCD at Time 4**	**β**	**ADHD at Time 4**	**β**
IQ	0.93*	IQ	.17†	Age	–.09*
OCD at time 4	**1.34***	**ADHD at time 4**	**.15†**	Sex	.09*
		Depression at time 4	.19†	IQ	–.11***
		Simple phobia at time 4	.25†	**OCD at time 4**	**.15†**
		Conduct disorder at time 4	.13†	Depression at time 4	.29†
				Social phobia at time 4	.13***
				Overanxious disorder at time 4	.10**
				Conduct disorder at time 4	.08*

Note: Cross-sectional associations at time 1 (childhood), time 2 (early adolescence), time 3 (late adolescence), and time 4 (early adulthood). Associations in which OCD or ADHD scaled symptom scores were entered as the dependent variable are provided as standardized regression coefficients (β values), and those for tics (coded as either absent or present) are presented as odds ratios (OR; 95% confidence intervals are available upon request). In the multivariate analyses, the diagnoses of tics, OCD, and ADHD at the preceding time point were forced into the regression equations along with demographic variables (age, sex, social class, ethnicity) and IQ. All other diagnoses at prior time points competed for entry in forward stepwise variable selection procedures. Only associations significant at $p < .05$ are shown. Boldface type represents significant associations between tic, OCD, or ADHD symptoms. OCD = obsessive-compulsive disorder; ADHD = attention-deficit/hyperactivity disorder.

[a] Not available.

* $p < .05$; ** $p < .01$; *** $p < .005$; † $p < .001$.

time 2 predicted OCD symptoms at time 4 (Table 3). ADHD symptoms at time 2 predicted tics at time 3 and OCD symptoms at time 4. OCD symptoms at time 3 predicted tics and ADHD symptoms at time 4 (Table 3). For purposes of comparison with these analyses of scaled scores, the odds ratios for the significant prospective associations in analyses of categorical diagnoses were calculated. Only one of the significant associations detected with symptom scores was not supported by analyses of categorical diagnoses (tics at time 1 predicting OCD symptoms at time 3) (Table 3).

Other Comorbid Disorders. Conduct problems at time 1 predicted OCD symptoms at time 2, whereas separation anxiety symptoms at time 2 predicted OCD symptoms at time 3. Depression, anxiety, and disruptive behaviors broadly predicted future ADHD symptoms at times 2 and 3.

TABLE 3
Temporal Antecedents of Tics, OCD, and ADHD Symptoms

Tics at Time 2	OR	OCD at Time 2	β	ADHD at Time 2	β
Tics at time 1	**3.63***	Age	.10**	Age	–.08*
		Conduct problems at time 1	.18†	Social class	–.10*
				Sex	.13†
				IQ	–.17†
				Conduct problems at time 1	.29†
				Immaturity at time 1	.14†
				Anxiety/fear at time 1	–.07*
Tics at Time 3	**OR**	**OCD at Time 3**	**β**	**ADHD at Time 3**	**β**
Sex	6.37*	**Tics at time 1**	**.09***	Age	–.07*
Tics at time 1	**9.58†**	**OCD at time 2**	**.21†**	Sex	.07*
Tics at time 2	**60.18†**	Separation anxiety at time 2	.21†	Depression at time 1	.06*
ADHD at time 2	**1.05***			**ADHD at time 2**	**.56†**
				Separation anxiety at time 2	.09***
				Oppositional defiance at time 2	.09*
Tics at Time 4	**OR**	**OCD at Time 4**	**β**	**ADHD at Time 4**	**β**
Social class	11.95*	Sex	–.11***	**ADHD at time 2**	**.26†**
IQ	0.84*	IQ	.15†	**ADHD at time 3**	**.22†**
OCD at time 3	**1.25***	**ADHD at time 2**	**.12*****	**OCD at time 3**	**.13†**
Simple phobia at time 3	1.19***	**Tics at time 2**	**.10***		
		OCD at time 3	**.21†**		

Note: Predictors of future tic, OCD, and ADHD symptoms at time 2 (early adolescence), time 3 (late adolescence), and time 4 (early adulthood). Represented here is the strength of association of previous scaled symptom scores with changes in tic, OCD, and ADHD symptoms across time points. Previous symptom scores for the symptom being modeled were forced into the regression equations along with demographic variables (age, sex, social class, ethnicity) and IQ. Scaled scores for the predicted variables were available only for OCD and ADHD symptoms because tics were coded as dichotomous variables (present or absent). The predictions of future OCD and ADHD symptoms were therefore modeled with multiple linear regression (middle and right columns) and the prediction of future tics was modeled with multiple logistic regression (left column). Prior symptom scores for all comorbid conditions were selected for entry by means of forward stepwise variable selection procedures. The strengths of association for each variable are presented as adjusted odds ratios when predicting future tics and as standardized regression coefficients (β values) when predicting future OCD and ADHD symptom scores. Only associations significant at $p < .05$ are shown. Boldface type represents significant associations between tic, OCD, or ADHD symptoms. For purposes of comparison with these analyses of scaled scores, the odds ratios (OR) and 95% confidence intervals (CI) for the significant prospective associations in analyses of categorical diagnoses (reported as OR, CI, respectively) were as follows: tics at time 2 predicted OCD at time 4 (6.36, 1.23–32.76); ADHD at time 2 predicted OCD at time 4 (3.73, 1.22–11.35); OCD at time 3 predicted tics at time 4 (18.74, 1.68–209.45); and OCD at time 3 predicted ADHD at time 4 (13.28, 1.01–249.98). OCD = obsessive-compulsive disorder; ADHD = attention-deficit/hyperactivity disorder.

* $p < .05$; ** $p < .01$; *** $p < .005$; † $p < .001$.

Future Comorbid Conditions

Tics. Tics at time 1 predicted subsequent anxiety symptoms, whereas tics at time 2 predicted both conduct disorder and depressive symptoms at time 3 (Table 4).

OCD. At time 2, OCD predicted subsequent symptoms of depression, generalized anxiety, and phobias. OCD symptoms at time 3 predicted depressive symptoms at time 4.

ADHD. In adolescence, ADHD symptoms predicted future symptoms of conduct disorder, depression, and generalized anxiety.

DISCUSSION

As hypothesized, tics, OCD, and ADHD were significantly interrelated in this sample. Use of categorical diagnoses and scaled symptom scores produced similar findings. In temporal cross-section during late adolescence and early adulthood, tics and OCD were significantly associated with one another, as were OCD and ADHD. In prospective analyses, tics in childhood or early adolescence predicted OCD symptoms later in adolescence or in early adulthood. Conversely, OCD in late adolescence predicted tics in adulthood. ADHD in early

TABLE 4
Tics, OCD, and ADHD Predicting Future Symptoms

Tics at Time 1	β	OCD at Time 1		ADHD at Time 1	
Separation anxiety at time 2	.07*	—[a]		—	
Social phobia at time 3	.11†	—		—	
Overanxious disorder at time 3	.07*	—		—	
Tics at Time 2	**β**	**OCD at Time 2**	**β**	**ADHD at Time 2**	**β**
Conduct disorder at time 3	.07*	Depression at time 3	.08*	Conduct disorder at time 3	.22†
Depression at time 3	.09***	Simple phobia at time 3	.47†	Depression at time 4	.12***
		Overanxious disorder at time 3	.07*		
Tics at Time 3	**β**	**OCD at Time 3**	**β**	**ADHD at Time 3**	**β**
None		Depression at time 4	.11†	Conduct disorder at time 4	.15†
				Generalized anxiety at time 4	.10*

Note: Tics, OCD, and ADHD predicting future symptoms at time 1 (childhood), time 2 (early adolescence), and time 3 (late adolescence). Multivariate modeling was used to assess which symptoms predict future symptoms for each disorder at each time point. Regardless of which symptom was entered as the dependent variable, the same symptom at the preceding time point was forced into the regression equation along with demographic variables. The modeling procedures therefore were controlling for preceding symptom severity, and the symptoms at preceding time points that entered the equations in forward stepwise selection procedures were predicting the change in symptoms indexed by the dependent variable. Only the dependent variables that were predicted by prior tic, OCD, or ADHD symptoms with $p < .05$ are listed here. Those prospective associations indicated the future trajectory of symptoms for tic, OCD, ADHD, and comorbid illnesses. The associations between tic, OCD, or ADHD symptoms are not presented here because they were similar to those shown in Table 3. The full models for each of the significant associations presented above are available upon request. OCD = obsessive-compulsive disorder; ADHD = attention-deficit/hyperactivity disorder; β = standardized regression coefficient.

[a] Not available.

* $p < .05$; *** $p < .005$; † $p < .001$.

adolescence weakly predicted tics in late adolescence and more strongly predicted OCD in adulthood, whereas OCD in late adolescence predicted ADHD in adulthood. The most robust associations in these analyses were those of tics with OCD and OCD with ADHD; the associations of ADHD with tics were unimpressive.

These findings are consistent with the conclusions from family-genetic studies that tics and OCD share a common underlying etiology. The associations also support findings from prior immunological and neuroimaging studies that suggest an etiology common to some forms of OCD and ADHD (Peterson et al., 2000; Swedo et al., 1993). The frequent co-occurrence of tics and ADHD that has been noted in clinical samples was not observed in this epidemiological sample. Our findings suggest that the co-occurrence of tics and ADHD in clinic patients may result in part from a complex sharing across development of numerous psychopathological risk factors, including OCD, other anxiety disorders, conduct disturbances, and depression.

We will now comment on the prevalence estimates for tics, OCD, and ADHD in this sample. We will then discuss the implications of the correlation analyses for our understanding of risk factors, patterns of comorbidity, and the natural history of these disorders. We will conclude with a discussion of this study's limitations and its clinical implications.

Age-Specific Prevalence Estimates

The prevalence of tics in the children of this population at time 1 was 17.7%, compared with a prevalence of 4% to 18% reported in previous epidemiological studies (Achenbach and Edelbrock, 1981; Costello et al., 1996; Nomoto and Machiyama, 1990; Verhulst et al., 1985). Those prior studies, however, all sampled children over 10 years of age, and many studied only adolescents. Those that included younger children reported higher prevalence estimates of 10% to 18%; these rates would likely have been higher had they excluded adolescents. Our rates of 2% to 3% in the same children followed into adolescence, using a virtually identical probe, indicate that the majority of the tics reported at time 1 remitted by adolescence. The values agree well with rates found in other ado-

lescent samples (Costello et al., 1996; Verhulst et al., 1997; Zohar et al., 1992).

The 0.39% (± 0.22%) lifetime prevalence of TS found here agrees with the 0.1% to 0.5% values reported in prior epidemiological studies (Costello et al., 1996; Nomoto and Machiyama, 1990; Verhulst et al., 1997). Studies of older adolescents or adults tend to report the lowest values of TS (Apter et al., 1993), presumably because of the age-related decline in tic symptoms throughout later adolescence (Leckman et al., 1998).

The estimated prevalences for OCD of 1.8% to 5.5% in adolescents and 3.3% in young adults approximated those found in other community samples (Hollander et al., 1996/1997; Valleni-Basile et al., 1994; Zohar et al., 1992). They were especially close to the 4% to 5% rates found in studies that used the same or similar diagnostic instruments (Douglass et al., 1995; Leaf et al., 1991). The 1.9% weighted lifetime prevalence estimates for *DSM-III* OCD in a previous two-stage epidemiological study of adolescents (Flament et al., 1988) would have nearly doubled under the current *DSM* impairment criterion (time spent each day performing the compulsions); and, in fact, many met full diagnostic criteria at follow-up 2 years later (Berg et al., 1989). Nevertheless, the DISC used in this study can inflate OCD prevalence estimates because of an overrepresentation of false positive responses to stem questions in the structured lay interview (Breslau, 1987; Helzer et al., 1985). The noted decline in prevalence of OCD during adolescence is similar to findings reported in prior community studies (Berg et al., 1989; Valleni-Basile et al., 1996). The decline was unlikely to have resulted from changes in the diagnostic instrument because the OCD section of the DISC was virtually identical across time points.

The point prevalence of 7.6% to 12.0% for ADHD in adolescence was somewhat higher than the values of 6% to 9% reported in other recent epidemiological studies (Bird et al., 1988; Szatmari et al., 1989; Taylor et al., 1991). Most nonreferred samples have the same male predominance seen in this study (Costello et al., 1996; Schachar et al., 1981; Simonoff et al., 1997; Szatmari et al., 1989). The prevalence of ADHD decreased dramatically in the present sample as the children matured, consistent with findings from previous studies (Hill and Schoener, 1996).

Risk Factors, Comorbid Disorders, and Natural History

Tics. Predicting the future course of tics and comorbid illness seems to depend on the age and current comorbid illnesses of the child who has tics. In this study, for example, young children with tics were more likely to have lower IQ, lower SES, and more anxiety and conduct disturbances (Table 2). They were also likely to develop OCD and numerous other anxiety symptoms in adolescence (Table 4). Young adolescents with tics, however, were more likely to have (Table 2) or soon develop (Table 4) OCD, conduct disorder, and depressive symptoms. In young adolescents who had tics, comorbid ADHD symptoms predicted the persistence of their tics into later adolescence, whereas comorbid OCD and simple phobias predicted persistence of their tics into early adulthood (Table 3).

The overall similarity in patterns of comorbidity and natural history that tics in this epidemiological sample share with TS in clinical samples suggests an etiological continuity between TS and tics. The age of onset and overall trajectory of symptom prevalence of the tics ascertained in this study were similar to those reported in natural history studies of TS (Leckman et al., 1998). Family-genetic and twin studies have suggested that TS and chronic tic disorders are genetically related (Pauls and Leckman, 1986; Price et al., 1985). Patterns of comorbidity are similar, in that the aggressive behaviors, poor socialization, and anxiety disorders associated with tics in this study have been documented in clinic settings (Caine et al., 1988; Stokes et al., 1991). In fact, little or no evidence exists to support the nosological distinction between transient tics, chronic tics, and TS. The only difference between tic disorders seems to be their respective duration and number of symptoms, which is established by definition of the syndromes. The chronicity specified in the criteria for TS likely contributes (along with referral bias) to the higher rates of comorbidity seen in clinical studies of TS, as rates of comorbid disorders in chronic syndromes are inevitably higher than are rates in less chronic conditions (Cohen and Cohen, 1984).

OCD. The positive association of OCD symptoms with IQ increased steadily throughout adolescence (Table 2), and higher IQ predicted an increase in OCD symptoms from late adolescence to early adulthood. These findings are consistent with early case studies (Freud, 1913) and with some (Douglass et al., 1995; Rasmussen and Tsuang, 1984) but not all (Zohar et al., 1992) controlled studies of the association of IQ with OCD. The prevalence of OCD decreased significantly from early to late adolescence and then increased into early adulthood (Table 1).

In cross-section, OCD was significantly associated at all time points with a broad range of anxiety and depres-

sive symptoms. This pattern of concurrent comorbid illnesses is similar to those described previously for OCD (Hollander et al., 1996/1997; Robins and Price, 1991; Swedo et al., 1989; Valleni-Basile et al., 1996). In prospective analyses, both younger and older adolescents were more likely to develop depressive and ADHD symptoms. Early adolescents with OCD, however, were especially likely to develop more anxiety and simple phobias in later adolescence (Table 4). Older adolescents with OCD and tics, in contrast, were likely to have persistent tics in early adulthood.

In contrast, childhood conduct disturbances predicted OCD symptoms in early adolescence (Table 3). Childhood tics and early adolescent separation anxiety predicted the development of OCD symptoms in late adolescence. Tics and ADHD in late adolescence predicted more OCD symptoms in adulthood. These associations of OCD symptoms with conduct disorder and separation anxiety have been noted previously (Hollander et al., 1996/1997; Ingram, 1961; Lipsitz et al., 1994; Lo, 1967; Pollitt, 1957; Robins and Price, 1991; Swedo et al., 1989).

ADHD. Lower IQ, younger age, and male sex were associated with ADHD symptoms at all time points, consistent with previous reports (Lambert et al., 1987; Taylor et al., 1991). In temporal cross-section, ADHD was associated with conduct disorder, depression, overanxious disorder, and phobias (Table 2), as reported in prior clinical, epidemiological, and family-genetic studies (Biederman et al., 1991, 1992; Mannuza et al., 1991, 1993; McArdle et al., 1995). In prospective analyses, ADHD was again significantly associated with many and varied anxiety, depressive, and externalizing symptoms (Tables 3 and 4).

Limitations

This study should be interpreted in light of the limited test-retest reliability and the imperfect sensitivity and specificity of the DISC. The stem questions for tics in the DISC seem especially likely to produce false positive responses, particularly in infants and toddlers (such as those included in the time 1 sample). Furthermore, the assessment of psychopathology, particularly tics, varied across time points (at time 4, only tics observed by the interviewer were recorded) (Table 1). Despite these limitations, tics, OCD, and ADHD consistently predicted themselves at subsequent time points (Tables 3 and 4), supporting the consistency of the diagnoses through time.

Prevalence estimates for all three diagnoses tended to be higher than in previous reports, and they may have been a result of more frequent false positive reporting of symptoms in this interview format, especially for younger children. Nevertheless, limitations in instrument reliability were more likely to reduce the statistical power to detect hypothesized associations (increase type II error) than to produce spurious associations (increase type I error) among these conditions. Validated clinician-based interviews that target these disorders in large multistage screenings would address these limitations. Spurious associations are more likely to have resulted from the number of statistical comparisons performed, particularly for the exploratory correlation analyses of tic, OCD, and ADHD symptoms with other psychiatric symptoms. Another difficulty is that misclassification errors could have been correlated with one another (for instance, if individuals misdiagnosed with tics were also more likely to be misdiagnosed with OCD), which would have biased the estimated associations away from the null value and inflated type I error.

Selective attrition and the addition of supplemental families at time 2 reduced the statistical power of correlation analyses involving time 1 assessments and could have systematically influenced the findings across later time points. In addition, OCD and ADHD symptoms were not assessed systematically with modern diagnostic criteria until time 2, when the mean age of the sample was 13.7 years. If these disorders were present at a younger age and remitted by time 2, their lifetime prevalences would have been underestimated. Moreover, the age range of the cohort was sufficiently large to produce substantial overlap in the ages across assessment time points, particularly at times 2 and 3. This limited the conclusions that could be drawn with regard to the specificity of changes in psychiatric symptoms across developmental stages.

Finally, the small number of adolescents and adults who reported tics (times 3 and 4) and the few young adults with ADHD (time 4) undoubtedly diminished the power and stability of these analyses. The small numbers also limited our ability to generalize the findings at those time points to other populations. Our use of continuous symptom scores in multivariate modeling procedures for all individuals in the sample, however, helped to address those limitations.

Clinical Implications

Findings from prospective, longitudinal studies will inform the design of experiments that will test not only models of developmental psychopathology but also models for disease prevention and early intervention. Testing these models of etiology and intervention will

prove mutually informative. The findings for OCD in the present study, for instance, suggest that treating separation anxiety in children who have an earlier history of tics, ADHD, or conduct disturbance could reduce the burden of later OCD symptoms. Likewise, the ADHD findings suggest that for children who have ADHD symptoms in early childhood, behavioral, educational, and pharmacological intervention could reduce ADHD and conduct disorder symptoms in later adolescence (Klein et al., 1997). In addition to their therapeutic import, the success or failure of these prevention and early intervention strategies will support or refute our models of pathogenesis. Controlled experimental interventions will therefore move us from the study of prospective associations to the investigation of causal mechanisms as we struggle to improve and refine our developmental theories.

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