ORIGINAL ARTICLE

Childhood and Adolescent Psychiatric Disorders as Predictors of Young Adult Disorders

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Context: Most adults with a psychiatric disorder first met diagnostic criteria during childhood and/or adolescence, yet specific homotypic and heterotypic patterns of prediction have not been firmly established.

Objective: To establish which childhood and adolescent psychiatric disorders predict particular young adult disorders when accounting for comorbidities, disaggregating similar disorders, and examining childhood and adolescent predictors separately.

Design: Eleven waves of data from the prospective population-based Great Smoky Mountains Study (N=1420) were used.

Setting: The Great Smoky Mountains Study is a longitudinal study of the development of psychiatric disorder and need for mental health services in rural and urban youth. A representative sample of children was recruited from 11 counties in western North Carolina.

Participants: Children in the community aged 9 to 16, 19, and 21 years.

Main Outcome Measures: Common psychiatric disorders were assessed in childhood (ages 9-12 years) and adolescence (ages 13-16 years) with the Child and Adolescent Psychiatric Assessment and in young adulthood (ages 19 and 21 years) with the Young Adult Psychiatric Assessment.

Results: Adolescent depression significantly predicted young adult depression in the bivariate analysis, but this effect was entirely accounted for by comorbidity of adolescent depression with adolescent oppositional defiant disorder, anxiety, and substance disorders in adjusted analyses. Generalized anxiety and depression cross-predicted each other, and oppositional defiant disorder (but not conduct disorder) predicted later anxiety disorders and depression. Evidence of homotypic prediction was supported for substance use disorders, antisocial personality disorder (from conduct disorder), and anxiety disorders, although this effect was primarily accounted for by *DSM-III-R* overanxious disorder.

Conclusions: Stringent tests of homotypic and heterotypic prediction patterns suggest a more developmentally and diagnostically nuanced picture in comparison with the previous literature. The putative link between adolescent and young adult depression was not supported. Oppositional defiant disorder was singular in being part of the developmental history of a wide range of young adult disorders.

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More than three-quarters of young adults with psychiatric disorders first had a diagnosis between the ages of 11 and 18 years,[1-8] indicating that we must consider childhood and adolescent mental illness as a key risk factor for later psychiatric problems. However, there remain important questions about diagnostic prediction from childhood and adolescence to adulthood. Herein, we present new evidence about which childhood and adolescent disorders reliably precede later disorders.

Homotypic prediction refers to a disorder predicting itself over time (eg, earlier depression predicting later depression). This supports the idea that a single disease process expresses itself robustly across developmental contexts. Homotypic prediction has been identified in most studies predicting from childhood to late adolescence[9-13] and from childhood and adolescence to young adulthood.[1,2,5,14-19] Indeed, prior disorder status is typically the strongest predictor of having that disorder later.

Heterotypic prediction refers to different disorders predicting one another over time (eg, earlier oppositional defiant disorder [ODD] predicting later depression). Such patterns may suggest that the different disorders reflect a general disease process that has specific phenotypic expressions in different developmental contexts. Although typically less common than homotypic prediction, 2 pat-

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terns of heterotypic prediction have received consistent support. First, anxiety and depression tend to cross-predict from childhood/adolescence to adulthood (anxiety predicting depression: full support[1,3,10,11,20]; partial support[9,13,16,19]; depression predicting anxiety: full support[1,3,10,11,20]; partial support[13,16]). Second, childhood/adolescent conduct/oppositional problems tend to precede adult anxiety and depression,[1,10,16,21-23] but not vice versa[1,11,13] (Hofstra et al[17] present an exception).

Taken together, homotypic prediction appears to be common across a range of disorders, whereas heterotypic prediction is limited to a few specific pathways, but a number of substantive and methodological issues complicate the interpretation of this work. First, many studies collapse childhood and adolescent disorders to predict adult disorders, despite the fact that important changes in the prevalence of some disorders, such as depression and conduct disorder (CD), occur between childhood and adolescence.[24-26] Such changes could indicate that disorders at different ages result from different etiologic pathways[27-30] and so combining across childhood and adolescence could obscure important differences between childhood and adolescent prediction. Also, little attention has been paid to the fact that these developmental pathways may be different for males and females. For example, the prevalence of depression changes at puberty for girls but not for boys.[31]

Second, most studies collapse multiple, potentially heterogeneous disorders into more general diagnostic groupings. For example, all anxiety disorders tend to be combined into one category, which could mask differences in prediction between individual anxiety disorders. Furthermore, ODD and CD are often combined, despite the fact that they are distinct in factor analytic studies,[32,33] in risk factors studies,[34] and when tested as predicting later problems.[35] Indeed, ODD may be as likely to be linked with emotional disorders as CD.[10]

Finally, studies of diagnostic predictors of later disorders have typically focused on pairwise associations: one earlier disorder predicting one later disorder. Yet, disorders tend to co-occur, and when comorbidity is not taken into account, pairwise associations may simply represent indirect effects rather than direct associations.[36,37] For example, bivariate analyses may suggest that childhood anxiety disorders predict adolescent depression, but this association could be accounted for by comorbidity between childhood anxiety and depression.

Herein, we use Great Smoky Mountains Study (GSMS) data from middle childhood through young adulthood and stringent criteria to examine a broader range of patterns of homotypic and heterotypic prediction from middle childhood and adolescence to young adulthood.

METHODS

SAMPLE AND PROCEDURES

The GSMS is a longitudinal study of the development of psychiatric disorder and need for mental health services in rural and urban youth.[14-19] A representative sample of 3 cohorts of children, aged 9, 11, and 13 years at intake, was recruited from 11 counties in western North Carolina. Potential participants were selected from the population of some 20 000 children using a household equal probability, accelerated cohort design.[20] The accelerated cohort design means that over several years of data collection each cohort reaches a given age in a different year, thus controlling for cohort effects.[21] Youth with behavior problems were oversampled. A screening questionnaire was administered to a parent (usually the mother) of the first-stage sample (n=3896). The questionnaire consisted mainly of the Externalizing (Behavioral) Problems Scale of the Child Behavior Checklist[22] and was administered by telephone or in person. All children scoring higher than a predetermined cut point (the top 25% of the total scores), plus a 1-in-10 random sample of the rest (ie, the remaining 75% of the total scores), were recruited for detailed interviews. Ninety-five percent of families contacted completed the telephone screen.

About 8% of the area residents and the sample were African American, and fewer than 1% were Hispanic. American Indian individuals made up only about 3% of the population of the study area, which is overwhelmingly white, but were oversampled from school records to constitute 25% of the study sample. This was done by using the same screening procedure but recruiting everyone irrespective of screen score. Of the 456 American Indian children identified, 96% were screened, and 81% (n=350) participated in the study. All subjects were given a weight inversely proportional to their probability of selection so that the results presented are representative of the population from which the sample was drawn. Of all subjects recruited, 80% (n=1420) agreed to participate.

Table 1 presents the study design and participation rates at each wave. Data were collected on 1 cohort at ages 9 and 10 years, 2 cohorts at ages 11, 12, and 13 years, and all 3 cohorts at ages 14, 15, 16, 19, and 21 years. This article presents data on 8806 parent/child pairs of interviews carried out across the age range 9 through 21 years. Participants were interviewed as closely as possible to their birthday each year. Funding constraints prevented our interviewing the youngest cohort from January 1997 through June 1998.

Interviews were completed with the children and their primary caregiver at their home or a convenient location until age 16 years and with the young adults only thereafter. Before the interviews began, interviewees signed informed consent forms approved by the Duke institutional review board. Across waves, an average of 82% of all possible interviews were completed, ranging from 75% to 94% at individual waves.

MEASURES

Psychiatric disorders were assessed using (1) the Child and Adolescent Psychiatric Assessment (CAPA)[38-40] until age 16 years and (2) the upward extension of the CAPA, the Young Adult Psychiatric Assessment (YAPA)[40] at ages 19 and 21 years. Scoring programs for the CAPA and YAPA, written in SAS,[41] combined information about the date of onset, duration, and intensity of each symptom to create diagnoses according to the *DSM-IV*.[29] With the exception of attention-deficit/hyperactivity disorder (ADHD), for which only parental reports were counted, a symptom was counted as present if it was reported by either the parent or the child until age 16 years or by the young adult at ages 19 and 21 years, as is standard clinical practice. Two-week test-retest reliability of CAPA diagnoses in children aged 10 to 18 years is comparable with that of other highly structured interviews (κs for individual disorders range from 0.6-1.0).[39] To minimize recall bias, the time frame of both interviews for determining the presence of most psychiatric symptoms was the preceding 3 months. A previous publication suggested that there was little evidence of symptom attenuation (lower reported symptom levels in subsequent data waves), cohort differences, or differential dropout in this sample.[11]

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Table 1. Great Smoky Mountains Study: Data Collection by Cohort

	Cohort										
	A (n=508)		B (n=497)		C (n=415)						
Year	Age 9 y	Age 10 y	Age 11 y	Age 12 y	Age 13 y	Age 14 y	Age 15 y	Age 16 y	Age 19 y	Age 21 y	Participation, %
1993	A1[a]		B1[a]		C1[b]						94
1994		A2[a]		B2[a]		C1[b]					91
1995			A3[a]		B3[b]		C3[b]				87
1996				A4[a]		B4[b]		C4[b]			78
1997							B5[b]				80
1998						A5[b]		B6[b]			81
1999							A6[b]		C5[c]		74
2000								A7[b]			81
2001									B7[c]	C6[c]	81
2002											
2003									A8[c]	B8[c]	80
2004											
2005										A9[c]	76

[a] Childhood observations.
[b] Adolescent observations.
[c] Young adulthood observations.

In the current study, disorder status was aggregated across childhood (ie, ages 9-12 years), adolescence (ie, ages 13-16 years), and young adulthood (ie, ages 19-21 years). Childhood and adolescent diagnostic groupings included depression (including major depressive disorder [MDD], dysthymia, and depressive disorder, not otherwise specified), separation anxiety disorder in childhood, generalized anxiety disorder (GAD), CD, ADHD, and ODD. *DSM-III-R* overanxious disorder (OAD) was also included because we had previously found that it predicted several adolescent disorders when diagnosed in childhood.[9] Disorders with a prevalence of less than 1% in a given developmental period were not included in analyses (eg, separation anxiety in adolescence, social phobia, posttraumatic stress disorder). Substance disorders (including those meeting abuse or dependence criteria) were only sufficiently common for inclusion beginning in adolescence. Young adult diagnostic groups included depression (same as childhood and adolescence groups), GAD, panic disorder without agoraphobia, agoraphobia without panic, and antisocial personality disorder (ASPD).

ANALYSES

Weighted logistic regression models were estimated using generalized estimating equations implemented by SAS PROC GENMOD. Sampling weights were inversely proportional to selection probability. Robust variance (sandwich-type) estimates were used to adjust the standard errors of the parameter estimates for the stratified design effects. Therefore, the resulting parameters are representative of the population from which the sample was drawn.

Ideally, all diagnoses from all developmental periods would be combined into a single path-type multivariate analysis. Because such complex models did not converge despite our reasonable sample size, we examined psychiatric status across 2 developmental periods at a time: from adolescence to young adulthood and from childhood to young adulthood. Homotypic and heterotypic patterns were determined by predicting each later disorder (eg, depression in young adulthood) from each earlier disorder in a series of 3 models. In the bivariate, unadjusted model, a prior disorder was the single predictor of the later diagnosis. The unadjusted odds ratios (ORs) resulting from model 1 are reported in **Table 2** and **Table 3**. In the sex differences model, model 2, the prior disorder, sex, and the sex × prior disorder interaction were included (full results are available on request). In the final comorbidity or adjusted model, the prior disorder that corresponded to the outcome variable and all other prior disorders were included. For example, childhood depression and all other childhood disorders were entered to predict young adult depression in the childhood/young adulthood model. The adjusted ORs resulting from the final model are reported in Table 2 and Table 3. Inclusion of comorbid disorders provides a stringent test of homotypic and heterotypic prediction patterns. Where evidence of a sex × disorder interaction was detected, separate results for adjusted models were provided for males and females. Analyses involving childhood were based on 2 GSMS cohorts (n=1008; <13 years at intake) and those involving adolescence were based on all 3 GSMS cohorts (N=1420).

As with any longitudinal study, not all assessments were completed at each data wave. Such missing assessments may affect prediction estimates if individuals with missing observations were more or less likely to have a psychiatric disorder than individuals with complete observations. To test for such effects, each individual's total number of missed assessments adjusted for the total number of expected assessments was predicted by the individual's psychiatric status at his or her first assessment (because all subjects had at least 1 assessment). Initial rates of psychiatric disorder did not predict the likelihood of missing assessments ($z=1.5$; $P=.23$), suggesting no effect of differential dropout. Therefore, observations missing within a given developmental period were excluded from analyses involving that development period. Because subjects were interviewed multiple times within each developmental period, subjects could miss 1 interview and still be included in analyses for that period.

RESULTS

HOMOTYPIC PREDICTORS

Table 2 and Table 3 display the results from unadjusted and adjusted models for each pair of developmental groups (adolescence to young adulthood, childhood to young adulthood). Separate adjusted results are provided for males and females where a significant sex × disorder interac-

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Table 2. Young Adult Diagnoses Predicted From Adolescent Diagnoses[a]

	Young Adult Disorders, OR (95% CI), %					
	GAD	**PAN**	**AGOR**	**DEP**	**ASPD**	**SUB**
	3.1 (1.3-4.8)	5.0 (2.8-7.1)	4.5 (2.4-6.6)	5.2 (3.1-7.2)	1.9 (0.6-3.2)	18.0 (14.2-21.9)
Adolescent dx						
OAD						
Dx absent, %	2.3	3.2	4.3	4.9	1.9	18.3
Dx present, %	17.6	40.7	8.6	11.0	1.6	13.3
Unadjusted	**8.9 (2.1-37.2)**	**20.9 (7.0-62.5)**	2.1 (0.5-9.9)	2.4 (0.6-10.6)	0.8 (0.2-4.2)	0.7 (0.2-2.4)
Adjusted[b]	F: 6.0 (0.4-88.5); **M: 51.7 (1.8-149.6)**[c]	**F: 13.2 (2.8-61.1);** **M: 77.0 (8.5-701.8)**[c]	1.3 (0.3-6.1)	F: 0.1 (0.1-0.7); **M: 37.1 (3.6-387.7)**[c]	0.6 (0.1-3.2)	0.4 (0.1-1.4)
GAD						
Dx absent, %	3.0	4.8	4.4	4.7	1.9	18.2
Dx present, %	4.2	11.3	5.4	26.5	1.5	11.1
Unadjusted	1.4 (0.4-5.6)	2.5 (0.9-7.3)	1.2 (0.3-4.5)	**7.4 (1.9-28.5)**[c]	1.0 (0.2-5.2)	0.6 (0.2-1.5)
Adjusted[b]	**F: 0.1 (0.1-0.7)**; M: 1.6 (0.2-16.2)	0.3 (0.1-1.8)	0.4 (0.1-2.9)	**4.6 (1.0-21.9)**	0.6 (0.1-4.4)	0.4 (0.1-1.5)
DEP						
Dx absent, %	2.4	3.9	4.0	4.5	2.1	17.6
Dx present, %	11.8	18.2	10.9	13.7	0.0	24.3
Unadjusted	**5.5 (1.4-21.6)**	**5.4 (1.9-15.9)**[c]	3.0 (0.8-10.7)	**3.3 (1.1-10.5)**	. . .	1.5 (0.7-3.5)
Adjusted[b]	F: 0.5 (0.1-3.0); M: 1.6 (0.4-7.0)	1.0 (0.2-4.4)	**4.3 (1.3-13.9)**	0.9 (0.2-4.5)	. . .	1.7 (0.6-4.7)
ADHD						
Dx absent, %	3.1	5.0	4.5	5.2	1.9	18.0
Dx present, %	0.0	4.2	4.2	8.5	0.0	22.0
Unadjusted	. . .	0.9 (0.1-6.6)	1.0 (0.1-7.4)	1.7 (0.4-7.7)	. . .	1.3 (0.5-3.4)
Adjusted[b]	. . .	0.5 (0.1-6.9)	0.9 (0.1-9.5)	0.8 (0.1-5.1)	. . .	1.1 (0.3-3.4)
CD						
Dx absent, %	2.8	4.6	4.3	4.3	1.5	17.6
Dx present, %	7.2	10.6	6.6	18.2	7.7	24.7
Unadjusted	2.7 (0.5-15.2)	2.5 (0.6-10.9)	1.6 (0.3-9.6)	**4.9 (1.5-16.4)**[c]	**5.4 (1.1-27.0)**	1.5 (0.7-3.4)
Adjusted[b]	0.8 (0.1-10.0)	1.1 (0.2-4.8)	1.8 (0.5-7.0)	2.1 (0.7-6.9)	**5.6 (1.0-29.2)**	1.1 (0.4-3.1)
ODD						
Dx absent, %	2.0	4.1	4.3	4.2	1.8	17.7
Dx present, %	15.9	16.0	6.3	17.4	3.2	22.8
Unadjusted	**9.2 (2.7-31.4)**[c]	**4.5 (1.5-13.5)**[c]	1.5 (0.3-7.0)	**4.8 (1.8-13.4)**[c]	1.8 (0.6-5.6)	1.4 (0.7-2.9)
Adjusted[b]	**6.3 (2.0-19.8)**[c]	F: 2.0 (0.3-13.5); **M: 5.3 (1.6-17.5)**[c]	0.8 (0.2-2.7)	**2.8 (1.0-8.3)**	1.1 (0.3-4.6)	1.2 (0.5-3.0)
SUB						
Dx absent, %	2.6	4.4	4.8	4.0	1.8	16.2
Dx present, %	7.5	9.9	1.1	15.5	2.7	34.6
Unadjusted	3.1 (0.8-12.2)	2.4 (0.7-7.7)	**0.2 (0.1-0.8)**	**4.4 (1.6-12.0)**[c]	1.5 (0.5-4.4)	**2.8 (1.4-5.4)**[c]
Adjusted[b]	1.5 (0.3-8.7)	1.2 (0.3-4.9)	**0.1 (0.0-0.7)**	**3.1 (1.0-9.6)**	0.9 (0.3-3.3)	**2.7 (1.3-5.5)**[c]

Abbreviations: ADHD, attention-deficit/hyperactivity disorder; AGOR, agoraphobia without panic; ASPD, antisocial personality disorder; CD, conduct disorder; CI, confidence interval; DEP, depression; dx, diagnosis; ellipses, no cases of the 2 disorders overlap; F, female; GAD, generalized anxiety disorder; M, male; OAD, overanxious disorder; ODD, oppositional defiant disorder; OR, odds ratio; PAN, panic disorder without agoraphobia; SUB, substance-related disorder.

[a] Analyses are based on 1149 cases. The following sex × disorder interactions were found: OAD predicting GAD, $z=2.3$; $P=.02$; OAD predicting AGOR, $z=2.2$; $P=.03$; OAD predicting DEP, $z=3.3$; $P=.001$; GAD predicting GAD, $z=2.3$; $P=.02$; DEP predicting GAD, $z=2.0$; $P=.05$; and ODD predicting PAN, $z=2.5$; $P=.01$. In these cases, results from adjusted models are presented separately for males and females. Odds ratios in bold are significant at the $P<.05$ level.

[b] Adjusted for other disorders from ages 13 to 16 years.

[c] $P<.01$.

tion was detected. Prediction between anxiety disorders, even if not the same disorder, is discussed as homotypic.

Adolescence to Young Adulthood

In unadjusted models, homotypic prediction was found for antisocial personality disorder (from adolescent CD), depression, and substance disorders (Table 2). Both generalized anxiety and panic disorders were predicted from OAD. The apparent association of adolescent depression with young adult depression was completely attenuated in adjusted models, whereas the homotypic prediction of ASPD, GAD, and substance and panic disorders was undiminished. Overanxious disorder predicted later GAD and panic disorders more strongly for males than females.

Because the attenuation of homotypic prediction of depression in the comorbidity-adjusted model was unexpected, possible informant effects were tested by running the adjusted models separately by parent and self-reports. The results were the same regardless of informant (parent report, OR, 0.6; 95% confidence interval [CI], 0.2-2.7; self-report, OR, 1.0; 95% CI, 0.4-3.1). To clarify whether homotypic prediction for CD predicting ASPD was an artifact of the diagnostic criterion for ASPD re-

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Table 3. Young Adult Diagnoses Predicted From Childhood Diagnoses[a]

	Young Adult Disorders, OR (95% CI), %					
	GAD	PAN	AGOR	DEP	ASPD	SUB
	2.6 (0.7-4.4)	5.7 (3.0-8.3)	5.0 (2.4-7.5)	5.1 (2.8-7.4)	1.5 (0.2-2.8)	17.9 (13.3-22.4)
Childhood dx						
OAD						
Dx absent, %	2.6	5.3	4.9	5.2	1.4	17.8
Dx present, %	3.0	29.2	6.6	3.2	3.2	19.8
Unadjusted	1.2 (0.1-10.8)	**7.4 (1.2-46.5)**	1.4 (0.3-7.3)	0.6 (0.1-5.3)	2.3 (0.2-23.4)	1.1 (0.3-3.9)
Adjusted[b]	0.6 (0.1-5.3)	**5.3 (1.33-22.1)**	1.7 (0.3-9.7)	0.6 (0.1-5.9)	1.9 (0.2-15.5)	0.8 (0.2-2.6)
SAD						
Dx absent, %	2.4	5.6	4.4	4.8	1.5	12.5
Dx present, %	7.6	5.8	17.7	11.4	1.4	16.1
Unadjusted	**3.4 (1.0-11.5)**	1.0 (0.3-3.3)	**4.7 (1.0-21.7)**	**2.5 (1.0-6.6)**	1.0 (0.1-8.9)	2.2 (0.7-6.8)
Adjusted[b]	2.6 (0.8-8.6)	1.1 (0.4-3.4)	**3.0 (1.1-8.0)**	2.0 (0.7-5.4)	0.8 (0.1-6.3)	1.7 (0.4-7.0)
GAD						
Dx absent, %	2.4	5.7	4.5	5.0	1.5	12.4
Dx present, %	11.6	1.0	30.3	12.2	0.0	18.1
Unadjusted	**5.3 (1.2-24.4)**	0.2 (0.0-1.5)	**9.3 (1.2-70.4)**[c]	2.6 (0.7-10.7)	. . .	3.1 (0.6-16.8)
Adjusted[b]	2.4 (0.6-10.2)	**0.1 (0.0-0.8)**	**10.7 (1.8-64.5)**[c]	2.0 (0.4-9.7)	. . .	1.8 (0.3-10.1)
DEP						
Dx absent, %	2.4	5.3	4.9	5.1	1.5	12.8
Dx present, %	8.2	18.9	4.1	4.4	0.0	6.0
Unadjusted	**3.7 (1.0-13.7)**	4.2 (0.8-22.0)	0.8 (0.2-4.0)	0.9 (0.2-3.6)	. . .	2.4 (0.7-8.3)
Adjusted[b]	**2.7 (1.0-7.5)**	**4.3 (1.2-15.5)**	0.2 (0.0-2.1)	0.5 (0.1-2.8)	. . .	1.8 (0.5-5.7)
ADHD						
Dx absent, %	2.6	5.3	4.9	5.1	1.5	12.4
Dx present, %	2.6	12.9	5.2	5.2	1.3	18.1
Unadjusted	1.0 (0.2-5.3)	2.6 (0.4-17.6)	1.1 (0.3-3.7)	1.0 (0.3-3.4)	0.8 (0.1-8.0)	1.4 (0.4-4.8)
Adjusted[b]	0.7 (0.2-3.4)	3.3 (0.3-27.4)	1.3 (0.4-4.5)	0.9 (0.3-2.6)	0.6 (0.1-4.9)	1.0 (0.2-4.5)
CD						
Dx absent, %	2.5	5.9	5.0	5.1	1.2	11.7
Dx present, %	2.9	1.3	3.0	5.3	5.2	28.8
Unadjusted	1.1 (0.3-4.6)	0.2 (0.0-1.2)	0.9 (0.3-2.7)	1.0 (0.4-2.9)	**4.3 (1.0-18.6)**	**2.5 (1.0-6.3)**
Adjusted[b]	0.9 (0.3-2.5)	0.1 (0.0-0.7)	0.4 (0.1-1.7)	0.7 (0.2-1.9)	**5.2 (1.1-23.8)**	2.3 (0.8-6.1)
ODD						
Dx absent, %	2.5	5.7	5.0	4.8	1.5	12.1
Dx present, %	4.1	3.9	4.4	10.1	1.5	21.7
Unadjusted	1.7 (0.5-5.9)	0.7 (0.2-2.1)	0.9 (0.3-2.7)	**2.2 (1.0-5.3)**	1.4 (0.3-7.9)	1.8 (0.8-4.2)
Adjusted[b]	1.2 (0.5-2.7)	0.6 (0.2-2.0)	0.7 (0.2-2.5)	**2.4 (1.0-5.6)**	0.6 (0.1-3.2)	1.0 (0.4-2.6)

Abbreviations: ADHD, attention-deficit/hyperactivity disorder; AGOR, agoraphobia without panic; ASPD, antisocial personality disorder; CD, conduct disorder; CI, confidence interval; DEP, depression; dx, diagnosis; ellipses, indicates no cases of the 2 disorders overlap; GAD, generalized anxiety disorder; OAD, overanxious disorder; ODD, oppositional defiant disorder; OR, odds ratio; PAN, panic disorder without agoraphobia; SAD, separation anxiety disorder; SUB, substance-related disorder.

[a] Analyses are based on 838 cases. No significant sex × disorder interactions were found when predicting young adult disorders from childhood disorders. Odds ratios in bold are significant at the $P < .05$ level.

[b] Adjusted for other disorders from ages 9 to 12 years.

[c] $P < .01$.

quiring prior evidence of CD before age 15 years, the adjusted model was rerun using an ASPD diagnosis in which subjects were not required to have displayed prior evidence of CD before age 15 years. Again, CD alone predicted ASPD (OR, 5.2; 95% CI, 1.4-19.1).

Childhood to Young Adulthood

As in the adolescence/young adulthood models, the link between CD and ASPD was also found after adjusting for comorbidity (Table 3). This link remained if the alternative form of the ASPD diagnosis (requiring no prior CD symptoms) was used (OR, 3.2; 95% CI, 1.0-9.6).

There was evidence of prediction between various anxiety disorders in unadjusted models, although only 3 associations were significant after adjustment: OAD predicted panic disorder, separation anxiety disorder predicted agoraphobia without panic disorder, and GAD predicted agoraphobia without panic disorder.

HETEROTYPIC PREDICTORS

Adolescence to Young Adulthood

In adjusted models, heterotypic patterns were found for depression and all anxiety disorders. Specifically, GAD and OAD predicted depression (in males for the depression-OAD link). Adolescent depression also predicted agoraphobia without panic disorder. Adolescent ODD predicted later GAD, panic disorder without agoraphobia (in males only), and depression. Finally, adolescent substance disorders predicted later depression.

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Childhood to Young Adulthood

Compared with adolescent/young adulthood models, limited support for heterotypic prediction emerged in the childhood to young adulthood adjusted models: childhood ODD predicted young adult depression and childhood depression predicted panic disorder without agoraphobia and GAD.

COMMENT

A review of previous studies suggested the following conclusions with respect to the continuity of disorders from childhood and adolescence to young adulthood: (1) Homotypic prediction is the norm from childhood/adolescence to young adulthood. (2) Generalized anxiety and depression cross-predict. (3) Childhood/adolescent combined disruptive disorders (ODD and/or CD treated as a single entity) predict adult anxiety and depressive disorders in addition to ASPD. This study provided developmentally differentiated and stringent tests of these patterns by (1) separating childhood from adolescent diagnostic predictors, (2) disaggregating specific anxiety and disruptive disorders, and (3) adjusting for comorbid conditions. Our results indicate that prediction patterns are actually more developmentally and diagnostically nuanced than the previous literature suggests.

In summary, although homotypic patterns were common, the path from adolescent to young adult depression was entirely accounted for by other comorbidities. Of childhood and adolescent anxiety disorders, *DSM-III-R* OAD was most likely to predict later young adult anxiety disorders. Generalized anxiety and depression cross-predicted, although these effects were not uniform across childhood and adolescence. Finally, a single behavioral disorder, adolescent ODD, preceded anxiety and depressive disorders.

CAVEATS

Before considering these findings in more detail, the following methodological considerations should be kept in mind. First, the GSMS participants lived in a rural area, and the study oversampled American Indian children, with very few African American (8%) and no Latino or Asian American children. Thus, the sample is not representative of the US population. However, comparison of the GSMS with other studies indicates that there are similar rates of cumulative childhood disorders in representative samples from other counties, other regions of the United States, and samples involving higher levels of Hispanic and African American youth.[42,43] While the subjects were followed up to 12 years (age 9-21 years), cases will have been missed because subjects may have met criteria for disorders prior to our study, between assessments, or after their last assessment.

Second, some associations of moderate to large magnitude were nonsignificant because of the limited number of youth with the particular disorder. However, studies of homotypic and heterotypic predictors from child to adult psychiatric disorder that deal with a range of disorders are rare because they depend on large, longitudinal community-based samples carefully characterized over many years. We are unaware of any currently existing studies with greater power to address these questions. Finally, our research aim was to determine which childhood and adolescent disorders reliably precede young adult disorders. This did not allow us to examine the chronological order of disorders within a developmental period. For the current analysis, the order of the disorders within a developmental period, however, had no effect on the strength of the association with the young adult outcome.

A terminological note is also in order. We have referred herein to homotypic and heterotypic *prediction* rather than *continuity*, despite the latter term's common usage. We believe that typical measurement schedules in prospective studies cannot adequately capture (dis) continuity, because observations of disorders tend to be intermittent (rather than continuous).

HOMOTYPIC PREDICTION

Although homotypic patterns were identified (eg, CD to ASPD and substance-related disorders), homotypic patterns were less common than previously reported by other studies when accounting for comorbidity between disorders. There was no evidence of homotypic prediction for depression and homotypic prediction of young adult anxiety disorders was primarily accounted for by *DSM-III-R* OAD, rather than by *DSM-IV* GAD.

In preparation for *DSM-IV*, Klein and colleagues[44] reviewed taxonomic issues related to the *DSM-III-R* anxiety disorders. Overanxious disorder was the focus of particular attention because it included a group of heterogeneous worries (eg, about the future, academic performance, self-consciousness) and was highly comorbid with other anxiety disorders (particularly GAD). Despite these concerns, it was recommended that it be retained as a childhood anxiety disorder, but with modified criteria to reduce overlap with other disorders. Instead, it was eliminated with the rationale that these children would likely receive a diagnosis of *DSM-IV* GAD. In a prior study, our group compared the relative predictive validity of childhood OAD as compared with *DSM-IV* GAD in predicting adolescent disorders. Overanxious disorder not only predicted later anxiety disorders but also predicted adolescent depression and CD. In contrast, *DSM-IV* GAD only predicted later CD. In this study predicting young adult disorder status, OAD again predicted both anxiety disorders and depression. This is in line with findings from the New York Child Longitudinal Study in which OAD predicted young adult depression, social phobia, and generalized anxiety.[3] Together, these findings suggest that the *DSM-IV* GAD criteria are insufficient for assessing the full range of "generalized anxiety" in children and adolescents and fail to identify anxious children at risk for a range of later disorders. It seems that Klein and colleagues were right to suggest that OAD should have been retained in the *DSM-IV*. We recommend its rehabilitation in the *DSM-V*.

The example of depression illustrates the importance of separating childhood from adolescent predictors and controlling for comorbidities. The significant bivariate prediction from adolescent to young adult

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depression (OR, 3.3) was entirely accounted for by comorbidity of adolescent depression with adolescent ODD, GAD, OAD, and substance disorders (OR for depression reduced to 0.8), whereas there was no direct prediction from childhood depression to young adult depression even in the bivariate models. This suggests that the apparent association between adolescent depression and young adult depression is epiphenomenal, resulting from the direct associations between comorbid adolescent disorders and later depression.

This may appear to be a clear departure from the consensus of previous research,[45] but actually it is not. Many studies looking at the adolescence–young adult depression link have used highly selected or clinical samples and/or failed to account for common comorbid disorders.[46-50] While these studies can demonstrate that adolescent depression precedes young adult depression, they are insufficient, on their own, to provide evidence of direct prediction. Such evidence can only come from community samples that assess for a range of disorders, in addition to depression, at multiple points in both adolescence and young adulthood.

To date, 3 such studies have been published. The first, a community sample of adolescents followed up into young adulthood by Lewinsohn and colleagues, concludes that their results "clearly illustrate a strong pattern of continuity for depression."[5(p61)] Their initial analyses demonstrate higher risk of later depression for a group of adolescents with MDD as compared with groups with either no depression or a nonaffective disorder. In this comparison, however, adolescent MDD cases were allowed to have other Axis I nonaffective disorders (and 51.0% did). A more stringent test compared risk for depression between a group with "pure" adolescent depression and a group with comorbid depression and found no difference. This might seem to suggest that even after controlling for comorbidity there is a link from adolescent to young adult depression, but rates of young adult depression are not provided for either of these 2 groups. It is entirely plausible then that the "pure" MDD group could both only be marginally associated (or not associated) with later MDD and, at the same time, not be statistically different from the comorbid MDD group. Without knowledge of the rates of young adult depression in these 2 groups, one cannot draw any conclusions about the role of comorbidity in the adolescent–young adult MDD link.

The second study tested this link in a birth cohort of 1265 children and concluded that there was a "direct and specific" link from adolescent depression to later depression.[51] The study design provides a rather stringent test for the outcomes of adolescent depression by accounting for the effects of anxiety disorders, early cigarette smoking, CDs, alcohol abuse, and a range of other putative risk factors. At the same time, the negative outcomes (including depression) are assessed for ages 16 to 21 years and thus overlap both with late adolescence and young adulthood. If there were a rather punctuated shift in depression between adolescence and young adulthood, it would not be detected by this design. But is this likely? In fact, such a striking shift occurs in depression a few years earlier in the pubertal transition from childhood to adolescence,[52] so this possibility cannot be rejected a priori. While the pubertal shift is associated with significant biochemical changes, the shift to young adulthood and the associated transition to independent living may be similarly substantial in the social domain.

The final study by Pine and colleagues[3] found that the best-fitting multivariable prediction model of young adult depression did not include adolescent depression, after accounting for comorbidities. As with our findings, there was evidence of significant prediction from adolescent to adult depression in bivariate analyses. This significant effect was primarily attenuated by inclusion of CD in the best-fitting adjusted model; ODD was not included in their analysis.

We suggest, therefore, that the early conclusions about the link between adolescent and young adult depression may have been premature. This putative link may be attenuated by comorbid adolescent disorders, particularly anxiety and behavioral disorders. It may also be the case that there is a rather punctuated shift in the natural course of depression around age 17 or 18 years. This hypothesized shift is consistent with an emerging literature that suggests heterogeneity in childhood/adolescent and adult depressions with respect to biological correlates and psychosocial predictors.[30,53]

HETEROTYPIC PREDICTION

Each heterotypic pattern identified from previous research was extended by the current study. An emerging body of literature has suggested that generalized anxiety not only reliably precedes depression,[3,54-56] but vice versa.[3] By disaggregating childhood and adolescent diagnoses, the current study found that this pattern was developmentally nuanced: only childhood depression predicted young adult GAD and only adolescent GAD predicted later depression. In addition, adolescent OAD was a stronger predictor of later depression in males than GAD. Furthermore, the cross-prediction was stronger than homotypic prediction for these 2 disorders (a finding also previously reported by Pine and colleagues[3]).

Together with evidence that GAD and depression cooccur more often with one another than with other disorders[20,57] and have shared genetic etiology,[58,59] this lends support to the notion of grouping these disorders more closely than is currently reflected in the *DSM-IV*. Cross-prediction (or sequential comorbidity) is not, however, very strong evidence of diagnostic unity. Childhood and adolescent GAD and MDD predicted different adult disorders and young adult GAD and MDD were predicted by different childhood and adolescent disorders. Our findings, together with those of other longitudinal epidemiologic samples,[3,20] suggest that GAD and MDD, while closely related, are distinct both in terms of their natural courses and developmental histories.

A recent study by Kim-Cohen and colleagues found that CD/ODD "was a part of the developmental history of every adult disorder."[1(p713)] Because CD and ODD were combined in that study, it was unclear, for any given outcome disorder, whether it was preceded by ODD, CD, or both. We found that young adult depression and anxiety disorders were preceded by adolescent ODD, but not CD. This finding is at odds with the traditional "failure

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model,"[22,60] which suggests that depression results from the social and educational failures that often follow CD. As with homotypic patterns of depression, the bivariate link between adolescent CD and young adult depression in our study was entirely accounted for by comorbid disorders (here, adolescent GAD, ODD, and substance disorders). If it is indeed ODD, rather than CD, that predicts later depression, then this might suggest an amended failure model that emphasizes the social and emotional consequences of irritability and interpersonal difficultness rather than the legal and social sequelae of delinquency and overt aggression.

As part of the research agenda for *DSM-V*, questions have been raised about the diagnostic and predictive validity of ODD after accounting for comorbid disorders (eg, ADHD, CD).[61] Our findings suggest that ODD is a singular disorder in being part of the developmental history of many young adult affective and anxiety disorders. No other childhood or adolescent disorder demonstrated such pleiotropic effects. In *DSM-IV*, ODD is ruled out if criteria for CD are met. In *International Statistical Classification of Diseases, 10th Revision*, ODD is a mere subtype of CD. Our data suggest that this subordination of ODD may be misguided. One accepted measure of the utility of a psychiatric diagnosis is the extent to which it predicts future psychiatric functioning.[62,63] On this measure, ODD may be in a class by itself.

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