

Research Article

DOES RELATIONAL DYSFUNCTION MEDIATE THE ASSOCIATION BETWEEN ANXIETY DISORDERS AND LATER DEPRESSION? TESTING AN INTERPERSONAL MODEL OF COMORBIDITY

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Background: *Anxiety disorders tend to precede onset of comorbid depression. Several researchers have suggested a causal role for anxiety in promoting depressive episodes, but few studies have identified specific mechanisms. The current study proposes an interpersonal model of comorbidity, where anxiety disorders disrupt interpersonal functioning, which in turn elevates risk for depression.* **Methods:** *At age 15 (T1), 815 adolescents oversampled for maternal depression completed diagnostic interviews, social chronic stress interviews, and self-report measures. At age 20 (T2), participants repeated all measures and reported on self-perceived interpersonal problems. At approximately age 23 (T3), a subset of participants (n = 475) completed a self-report depressive symptoms measure.* **Results:** *Consistent with other samples, anxiety disorders largely preceded depressive disorders. Low sociability and interpersonal oversensitivity mediated the association between T1 social anxiety disorder and later depression (including T2 depressive diagnosis and T3 depressive symptoms), controlling for baseline. Interpersonal oversensitivity and social chronic stress similarly mediated the association between generalized anxiety disorder before age 15 and later depression.* **Conclusions:** *Interpersonal dysfunction may be one mechanism through which anxiety disorders promote later depression, contributing to high comorbidity rates.* *Depression and Anxiety 00:1–10, 2013. © 2013 Wiley Periodicals, Inc.*

Key words: *social phobia; social anxiety disorder; generalized anxiety disorder; depressive disorder; interpersonal relations; comorbidity*

Depression and anxiety disorders show pronounced comorbidity, with 50–60% of depressed individuals

meeting lifetime criteria for an anxiety disorder.^[1] Understanding how and why comorbidity emerges is critical to understanding etiology; however, research has rarely attempted to identify specific psychosocial risk factors that may contribute. The current study examines the little-explored role of interpersonal dysfunction.

Several researchers have suggested that anxiety disorders act as a causal risk factor for later depression.^[2–7] This hypothesis is rooted in the widely supported finding that anxiety typically temporally precedes depression,^[1,5,6,8–12] for exception see.^[13] Similarly,

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anxiety predicts increases in later depression in what may be a dose–response relationship.^[3,14] Causal models of comorbidity parsimoniously explain not only why anxiety and depression co-occur, but why anxiety usually comes first. Mathews et al.^[15] recently supported the causality hypothesis, showing that among cases where anxiety preceded depression (i.e., most comorbid individuals), comorbidity was best explained using statistical models where anxiety directly predicted depression. In contrast, among the minority of cases where depression preceded anxiety, comorbidity was better explained by shared etiological factors, with no evidence for the reverse causality hypothesis that depression causes later anxiety.

Although this study provided support for the basic premise of the causal model, research specifying mechanisms explaining how anxiety impacts later depression risk remains limited.^[16,17] One promising category of possible mechanisms is interpersonal dysfunction. Depression has long been reciprocally linked to negative interpersonal behaviors, including poor social support, attachment disruptions, romantic distress, and chronic social stress.^[18–26] A smaller but growing literature also links anxiety to a range of problematic interpersonal behaviors.^[27–36] Interpersonal dysfunction may link anxiety disorders to later depression, as anxiety may provoke interpersonally destructive behaviors, and the resulting strain on relationships may trigger depressive episodes.

Although interpersonal mediators of comorbidity have rarely been explicitly tested, a few studies have tested similar hypotheses using various methodological approaches. Katz et al.^[37] showed that social impairment at age 15 mediated the prospective association between social withdrawal at age 5 and depression at age 20. Grant et al.^[38] found that avoidance of expressing emotion within relationships mediated the association between social anxiety and later depressive symptoms. In a daily diary study of generalized anxiety disorder (GAD), Starr and Davila^[39] found that daily anxious mood fluctuations predicted higher subsequent depressed mood on days when self-reported interpersonal hassles and rejection were elevated. Whittal and Dobson^[40] experimentally demonstrated that undergraduates with high need for social approval (associated with anxiety) responded to negative social feedback with greater depressive symptoms than controls. Finally, anxiety–depression comorbidity is associated with greater interpersonal impairment than noncomorbid anxiety or depression,^[27,41–43] consistent with the basic idea that interpersonal dysfunction contributes to co-occurrence. However, no previous studies have directly tested interpersonal mediators of diagnostic comorbidity in a longitudinal database.

In the current study, we examined interpersonal mediators of the association between early anxiety disorders and later depression in a longitudinal sample following community youth at elevated depression risk from mid-adolescence into young adulthood. Adolescence is an appropriate age to address this question, as anxiety disorders typically have onsets by early adolescence,^[44]

whereas depression rates grow steadily beginning in mid-adolescence^[45]; thus, mechanisms bridging early anxiety with later depression may emerge during this developmental period. Further, better understanding the processes connecting early-onset anxiety to depression in young adulthood may help improve early detection of at-risk youth. Based on their prevalence in this age group and preexisting evidence for associations with interpersonal distress, we selected two specific anxiety disorders to include in mediation models: social anxiety disorder (SAD) and GAD. Among anxiety disorders, SAD, being defined by social avoidance, has the widest support for linkages with interpersonal dysfunction.^[27,32,36,46–50] An emerging literature suggests that GAD also impairs interpersonal behaviors, with worry content often focusing on social relationships.^[31,51–53]

Although we have discussed interpersonal dysfunction as if it were a monolithic construct, social relationships are complex and draw upon multiple competencies, and likewise disruptions in interpersonal functioning take a variety of forms. While numerous aspects of interpersonal dysfunction may bridge anxiety disorders and later depression, as a starting point, we examined three aspects of self-perceived interpersonal functioning with conceptual ties to anxiety: low sociability (LS; difficulty socializing and interpersonal avoidance), interpersonal oversensitivity (IO; over-heightened sensitivity, worry, and guilt over interpersonal failures and negative social responses), and unassertiveness (UA; oversubmissive tendencies). As a preliminary step in the construction of mediation models, we conducted exploratory analyses examining associations between anxiety disorders and forms of interpersonal dysfunction. LS and UA are both closely linked to SAD,^[36,49,50] and although it has not been explicitly researched within the context of anxiety disorders, IO (reflecting excessive interpersonal worry and sensitivity to criticism and rejection) aligns with prior interpersonal conceptualizations of GAD.^[51] As we anticipated that these three factors would be correlated, we adopted a multiple mediation approach.

As a consequence of gravitating individuals toward specific maladaptive interpersonal behaviors, anxiety disorders may lead to objectively higher levels of chronic stress within relationships. Social chronic stress (SCS) encompasses a broad range of factors impacting day-to-day functioning within salient interpersonal relationships, constituting a general index of interpersonal distress. SCS predicts depression^[26] and in one study mediated the association between social withdrawal in early childhood and depression in young adulthood.^[37] Thus, in addition to self-perceptions of specific interpersonal problems, we tested interview-assessed SCS as another potential comorbidity mediator.

The current study examines several related hypotheses. First, we examined temporal sequencing of anxiety and depressive disorders within this dataset, expecting to replicate temporal antecedence of anxiety over depression as the modal pattern. Second, we conducted exploratory analyses examining how anxiety disorders

and depression related to specific forms of interpersonal dysfunction. Finally, we predicted that interpersonal dysfunction would mediate sequential comorbidity between anxiety disorders and later depression. Initial analyses, evaluating diagnostic outcomes, tested mediation models across two time points, collected at ages 15 and 20. To improve causal inference by temporally spacing all variables, supplemental analyses used as outcomes self-reported depressive symptoms assessed at age 23 in a third, smaller follow-up.

METHOD

PARTICIPANTS

Youth were drawn from a birth cohort study following 7,775 children born at the Mater Misericordiae Mothers' Hospital in Queensland, Australia, between 1981 and 1984. A subsample of 815 adolescents (403 female) was selected for follow-up at age 15. Participants were preferentially recruited on the basis of self-reported maternal depression, producing a sample with an overrepresentation of depressed mothers ranging in severity and chronicity. Participants were largely Caucasian (89%) and lower to lower-middle class (see^[54]).

Youth were invited for an additional follow-up at age 20 (T2), and 705 participated (363 female, 92% Caucasian). T2 participants did not differ from those lost to attrition by depression/anxiety status or ethnicity, but were more likely to be female, $P < .01$ (details in^[55]).

Participants were invited to participate in a third, smaller follow-up (T3) between ages 22 and 25, and 512 participated, of whom 475 provided complete relevant data (mean age = 23.75 years, 271 female). Participants lost to attrition did not differ by anxiety/depression history but were more likely to be male, $P < .001$.

PROCEDURE

Pregnant women were recruited into the birth cohort study during their first antenatal visit (see^[56]). When the child reached age 15, families selected for inclusion in the current study were telephoned and asked to participate in the T1 assessment. Interviewers conducted in-home interview sessions, including collection of consent/assent and interviews and questionnaire completion. When youths reached age 20, families were contacted and invited to participate in the T2 follow-up. Youth completed similar procedures as in T1. At T3, 2–5 years after the T2 follow-up (mean interval = 3.32 years), participants completed a depression self-report measure in conjunction with DNA samples submission (unrelated to current analyses).

MEASURES

Diagnostic Evaluations. The Schedule for Affective Disorders and Schizophrenia in School-Aged Children^[57] was administered at T1 to establish current and lifetime psychiatric diagnoses. Following standard procedures, trained clinicians administered interviews separately to adolescents and their mothers and assigned diagnoses using all available data. Weighted kappas ranged from .76 to .82 for current disorders and .73 to .79 for past disorders. At T2, youth diagnoses between ages 15 and 20 were established using the Structured Clinical Interview for DSM-IV (SCID-IV^[58]), administered by trained clinicians, to assess current and past psychopathology. Weighted kappas ranged from .83 to .94 for current and .89 for past disorders. Maternal depression was assessed at T1 using the SCID-IV (45% met criteria).

Self-Reported Depressive Symptoms. The Beck Depression Inventory (BDI^[59]) is a 21-item measure assessing depressive symptomatology, with widely supported reliability, validity, sensitivity, and specificity in community samples.^[60,61]

TABLE 1. Cross-sectional bivariate correlations among interpersonal variables, assessed at age 20

	1.	2.	3.	4.
1. Interpersonal oversensitivity	–			
2. Low sociability	0.67	–		
3. Unassertiveness	0.58	0.60	–	
4. Social chronic stress	0.33	0.37	0.17	–
<i>M</i>	14.90	14.70	16.26	10.03
<i>SD</i>	6.04	6.40	6.06	2.58

All correlations significant at $P < .0001$ level.

Interpersonal Problems. The Inventory for Interpersonal Problems (IIP^[62]) has been widely adopted in psychological research. The original measure contains 127 items, including behaviors “hard for you to do” and that “you do too much.” The IIP shows good test–retest reliability and external validity.^[49,63,64] Numerous shorter forms of the IIP have been developed;^[65] here, we used the IIP-48,^[66] which contains three bipolar (pathological at each extreme) subscales: interpersonal sensitivity, sociability, and assertiveness, with evidence for structural and external validity.^[66] As we had a priori interest in one particular pole of each subscale (high interpersonal sensitivity, low sociability, low assertiveness) and not in their opposite extremes (pathologically high sociability, etc.), we excluded items assessing low interpersonal sensitivity, high sociability, and high assertiveness, creating 8-item subscales assessing LS (e.g., “hard to socialize,” “avoid others too much,” Cronbach’s $\alpha = .91$), IO (“worry too much about disappointing others,” “too sensitive to criticism,” $\alpha = .88$), and UA (“hard to say ‘no,’” “hard to set limits,” $\alpha = .85$). The IIP-48 was administered at T2.

Social Chronic Stress. A semistructured interview for adolescents, adapted from the UCLA Life Stress Interview,^[67] was used to assess objective indicators of ongoing circumstances over the prior 6 months in four relationship categories: social group, close friends, romantic life, and family relationships. Ratings in each domain were averaged, creating a composite score of interpersonal functioning with higher scores reflecting greater chronic stress. For details, see^[68]. Inter-rater reliability = 0.70.

RESULTS

TEMPORAL SEQUENCING OF ANXIETY AND DEPRESSION

Among youth with a depressive ($n = 247$, including major depression or dysthymia) or anxiety ($n = 295$, including panic disorder, agoraphobia, obsessive-compulsive disorder, GAD, specific phobia, SAD, post-traumatic stress disorder, and separation anxiety disorder) disorder by age 20, 135 met criteria for both. Of these, most (72%) reported anxiety disorder onset at least 1 year prior to depression onset, $\chi^2(2, N = 135) = 91.24, P < .001$; 18% reported depressive onset first, and 10% reported same-year onset.

INTERPERSONAL PROBLEMS AS CORRELATES OF DEPRESSION AND ANXIETY DISORDERS

As displayed in Table 1, all proposed interpersonal mediators were significantly correlated with each other.

TABLE 2. Standardized coefficients for associations between interpersonal functioning variables and anxiety disorders and depression

	%/M(SD)	IO	LS	UA	T1 social CS	T2 SCS
Model I						
T1 any anxiety disorder	12.3%	0.13**	0.18***	0.06	0.07	0.16***
T1 GAD	1.6%	0.17***	0.09*	0.09*	0.04	0.15***
T1 SAD	3.7%	0.11**	0.18***	0.03	0.06	0.10**
T1 depressive disorder	13.5%	0.13**	0.16***	0.11**	0.10*	0.17***
T1 BDI	6.01 (6.76)	0.29***	0.28***	0.22***	0.07*	0.14***
T2 any anxiety disorder	24.5%	0.22***	0.19***	0.15***	0.07	0.18***
T2 GAD	6.5%	0.32***	0.23***	0.16***	0.04	0.18***
T2 SAD	17.4%	0.16***	0.18***	0.12**	0.05	0.17***
T2 depressive disorder	26.5%	0.35***	0.30***	0.22***	0.07	0.30***
T2 BDI	7.05 (8.40)	0.61***	0.48***	0.34***	0.05	0.39***
T3 BDI	7.64 (8.52)	0.46***	0.39***	0.27***	-0.05	0.26***
Model II						
T1 any anxiety disorder		0.10**	0.16***	0.04	0.06	0.13***
T1 GAD		0.16***	0.07	0.08*	0.03	0.14***
T1 SAD		0.09*	0.16***	0.01	0.05	0.08*
T2 any anxiety disorder		0.16***	0.14***	0.12***	0.05	0.13**
T2 GAD		0.26***	0.17***	0.12***	0.02	0.12**
T2 SAD		0.13***	0.16***	0.10***	0.05	0.14***

* $P < .05$, ** $P < .01$, *** $P < .001$.

Notes: Model I: controlling for gender and maternal depression status. Model II: controlling for gender, maternal depression status, and depression diagnosis at equivalent time point. BDI, Beck Depression Inventory; GAD, generalized anxiety disorder; SAD, social anxiety disorder; IO, interpersonal oversensitivity; LS, low sociability; UA, unassertiveness; SCS, social chronic stress. $N = 815$ at T1, $N = 705$ at T2, $N = 475$ at T3.

Table 2 presents associations between interpersonal variables and GAD, SAD, and depression diagnosis at T1 and T2, with gender and maternal depression status entered as covariates. Anxiety and depressive diagnoses were associated with broad interpersonal impairment. Of note, T1 GAD predicted higher IO, LS, and UA, and SAD predicted higher LS and IO. Interestingly, at T1 SCS showed no associations with anxiety disorders, but at T2 it was associated with all disorders. To ensure that associations between interpersonal problems and anxiety disorders were not explained by comorbid depression, associations were recomputed controlling for depression at corresponding time points. T1 GAD no longer predicted LS; otherwise, the significance pattern was unchanged (Table 2).

INTERPERSONAL PROBLEMS AS MEDIATORS OF ASSOCIATION BETWEEN T1 ANXIETY DISORDERS AND T2 DEPRESSION

Multiple mediation models were tested using bootstrapping methods (5,000 resamples), using the SPSS PROCESS macro provided by Hayes.^[69] This software conducts regression analyses to provide the magnitude and significance of the a (independent variable [IV] to mediator), b (mediator to dependent variable [DV]), c (IV to DV), and c' (IV to DV, controlling for mediators) paths, and generates bias-corrected confidence intervals for indirect effects (ab). The PROCESS macro applies linear regression when outcomes are continuous (e.g., a paths predicting mediator variables from anxiety status) and logistic regression when outcomes are dichotomous (depression diagnosis).

T1 depression, gender, and maternal depression status were entered as covariates in pathways predicting depression. Mediators were selected based on associations with disorders reported above (LS and IO for T1 SAD predicting T2 depression, and IO and UA for T1 GAD predicting T2 depression, illustrated in Fig. 1), but including all three IIP-48 subscales in all models produced similar results.

Table 3 displays mediation results. LS and IO both emerged as significant mediators of the association between SAD and later depression, as demonstrated by 95% CIs for indirect effects exclusive of zero. In addition, IO, but not UA, mediated the association between T1 GAD and T2 depression. In both models, c paths were significant but c' paths were not, indicating full mediation.

INTERPERSONAL PROBLEMS AS MEDIATORS OF ASSOCIATION BETWEEN T1 ANXIETY DISORDERS AND T3 DEPRESSIVE SYMPTOMS

Mediation models ideally include temporally lagged variables (IV preceding mediator, mediator preceding DV) to exclude reverse causality.^[70] Although not possible in previous analyses because the IIP-48 was only administered at T2, we conducted supplemental analyses using self-reported depressive symptoms at T3 as the DV ($N = 475$). Because youths varied in age at T3, we included T3 age as a covariate, along with maternal depression, gender, and T1 depressive symptoms. All analyses applied linear regression.

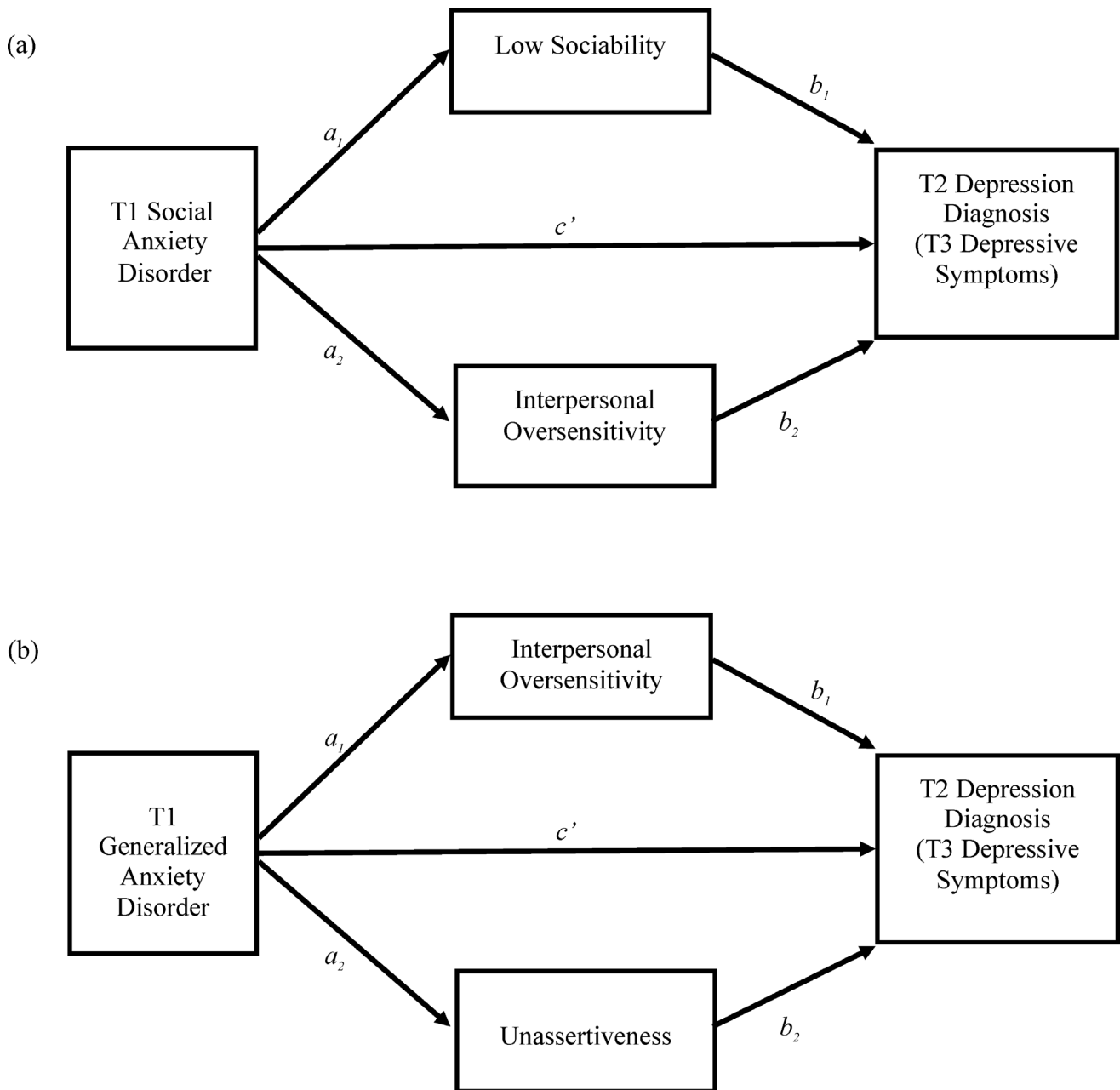


Figure 1. Models for mediation of associations between T1 anxiety diagnoses and later depression by interpersonal problems. See Tables 2 and 3 for path coefficients and estimates of indirect effects. T2 depression diagnosis and T3 depressive symptoms were separately evaluated as outcomes. T1 depression (or T1 depressive symptoms), maternal depression, and gender were entered as covariates in b and c paths. In models predicting T3 depressive symptoms, T3 age was also included as a covariate.

Table 4 displays results. For T1 SAD as a predictor of increased T3 depressive symptoms, IO was a significant mediator, but LS was not. However, when LS was examined in a single mediator model, it yielded a significant indirect effect, $ab = 2.68$, $SE = 0.97$, 95% CI [1.11, 5.03]. When T1 GAD was included as the IV, IO produced a significant direct effect but UA did not, mirroring previous results.

SCS AS MEDIATOR OF ASSOCIATION BETWEEN ANXIETY AND LATER DEPRESSION

We planned to test a model where T1 SCS mediated the association between T1 anxiety diagnosis and T2 depressive diagnosis (allowing mediators to precede DVs), but we did not conduct these analyses because GAD and SAD were not associated with T1 SCS ($ps > .05$). Note that models testing T2 SCS as a mediator of the

TABLE 3. Results of mediation models examining interpersonal mediators of the association between T1 anxiety disorders and changes in depressive symptoms at T2

Independent variable	Mediators(s)	<i>a</i> Path (IV to M)		<i>b</i> Path (M to DV)		<i>c</i> Path (total effect)		<i>c'</i> Path (direct effect)		<i>ab</i> (indirect effect)		
		<i>B</i>	<i>SE</i>	<i>B</i>	<i>SE</i>	<i>B</i>	<i>SE</i>	<i>B</i>	<i>SE</i>	<i>ab</i>	<i>SE</i>	95% CI
SAD	Full model					0.86*	0.43	0.41	0.48	0.55	0.20	[0.18, 0.97]
	LS	6.07***	1.34	0.04*	0.02					0.24	0.15	[0.01, 0.60]
	IO	3.35*	1.27	0.09***	0.02					0.32	0.15	[0.08, 0.68]
GAD	Full model					2.06**	0.70	0.84	0.32	1.00	0.31	[0.44, 1.68]
	IO	8.33***	1.89	0.11***	0.02					0.92	0.31	[0.39, 1.60]
	UA	4.34*	1.92	0.02	0.02					0.08	0.11	[-0.06, 0.45]

* $P < .05$, ** $P < .01$, *** $P < .001$. Bolded confidence intervals do not include zero, suggesting significant indirect effect.

Notes. Dependent variable = T2 depression diagnosis. T1 depression status, maternal depression, and gender entered as covariates in steps predicting DV. LS, low sociability; IO, interpersonal oversensitivity; social CS, social chronic stress.

association between T1 anxiety diagnosis and T2 depression met criteria for mediation for both disorders.

Next, we examined a fully temporally staggered model, with T2 SCS as a mediator of the association between T1 anxiety disorder and T3 depressive symptoms, with T1 depressive symptoms, gender, maternal depression, and age at T3 entered as covariates (see Fig. 2). Results (Table 4) supported mediation for GAD, but not SAD.

DISCUSSION

The current study tested an interpersonal model of anxiety–depression comorbidity. First, we replicated the frequently reported temporal antecedence of anxiety over depressive disorders,^[7–11] as in most comorbid cases, anxiety onset preceded depression. This result is highly consistent with prior research (in fact, distribution of temporal patterns was remarkably similar to those reported elsewhere^[11,15,71]), adding to mounting evidence of the temporal precedence of anxiety over depression. As this finding motivated the development of causal comorbidity models,^[3,15] frequent replication is critical.

The current dataset, as a large, longitudinal, high-risk, community-recruited, adolescent sample assessed using empirically valid clinical interviews, is particularly well suited to do so.

Results also showed that, like depression, anxiety disorders are associated with broad interpersonal impairment, including specific maladaptive interpersonal styles as well as general SCS, which in turn mediates sequential comorbidity between anxiety and later depression. Specifically, IO and LS mediated the association between SAD and later depression, and IO and SCS mediated the relationship between GAD and later depression. IO reflects hypervigilance over negative interpersonal experiences, such as perceived interpersonal failures or rejecting behavior by others. IO linked both GAD and SAD to depression, but may relate to each anxiety disorder for different reasons. The excessive worry that defines GAD frequently extends into the interpersonal sphere,^[53] likely often translating into extreme concern over social behaviors and other people's opinions. Social phobics, for their part, may view the prospect of rejection and other negative interpersonal events as intensely aversive, and may become excessively concerned about

TABLE 4. Results of mediation models examining interpersonal mediators of the association between T1 anxiety disorders and changes in depressive symptoms at T3

Independent variable	Mediators(s)	<i>a</i> Path (IV to M)		<i>b</i> Path (M to DV)		<i>c</i> Path (total effect)		<i>c'</i> Path (direct effect)		<i>ab</i> (indirect effect)		
		<i>B</i>	<i>SE</i>	<i>B</i>	<i>SE</i>	<i>B</i>	<i>SE</i>	<i>B</i>	<i>SE</i>	<i>ab</i>	<i>SE</i>	95% CI
SAD	Full model					5.37**	1.94	3.53	1.83	3.00	1.15	[1.03, 5.64]
	LS	5.77***	1.52	0.16*	0.08					0.95	0.67	[-0.05, 2.74]
	IO	4.32**	1.51	0.48***	0.08					2.06	0.93	[0.60, 4.35]
GAD	Full model					5.64 ^a	2.91	1.27	2.81	5.35	1.72	[2.50, 9.41]
	IO	9.00***	2.23	0.59***	0.08					5.28	1.77	[2.41, 9.48]
	UA	2.11	2.16	0.03	0.07					0.07	0.29	[-0.28, 1.08]
SAD	SCS	0.88	0.59	0.79***	0.15	5.37**	1.94	4.85*	1.89	0.70	0.48	[-0.06, 1.92]
GAD	SCS	2.78***	0.87	0.79***	0.16	5.64 ^a	2.91	4.03	2.85	2.19	0.98	[0.56, 4.47]

* $P < .05$, ** $P < .01$, *** $P < .001$, ^a $P = .053$. Bolded confidence intervals do not include zero, suggesting significant indirect effect.

Notes. Dependent variable = T3 depressive symptoms. T1 depressive symptoms, maternal depression, gender, and age at T3 entered as covariates in steps predicting DV. LS, low sociability; IO, interpersonal oversensitivity; SCS, social chronic stress.

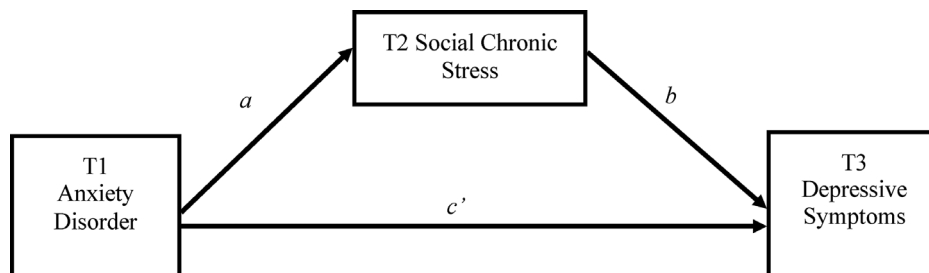


Figure 2. Model for mediation of association between T1 anxiety diagnosis and increases in depressive symptoms at T3 by T2 social chronic stress. T1 social anxiety disorder and T1 generalized anxiety disorder were tested as predictors in separate models. T1 depressive symptoms, maternal depression, gender, and age at T3 were entered as covariates in *b* and *c* paths. See Table 3 for estimates of path coefficients and indirect effects.

avoiding these experiences. Once anxious individuals develop IO, it may serve as a common pathway to depression. Oversensitivity to negative interpersonal experiences such as rejection can become a self-fulfilling prophecy, where rejection-sensitive individuals enact relationship-eroding behaviors that ultimately provoke actual rejection,^[72,73] in response to which oversensitive individuals may be especially prone to developing depression.^[74]

LS may be more specific as a mediator to SAD. The positive link between LS and SAD is not surprising,^[32,36,75] as avoidance of feared social stimuli, including general social situations, is a cardinal symptom of SAD.^[76] However, the notion that socialization difficulties help explain the link between social anxiety and later depression has never to our knowledge been tested, although one study^[77] supported the role of behavioral avoidance (conceptually related to LS). Poor sociability likely impedes the development of close relationships, reduces available social support, limits engagement in enjoyable social experiences, and elevates loneliness and alienation, all of which may ultimately provoke depressive symptoms.^[27,78,79]

We did not test the reverse causal model, where depression leads to increased anxiety via interpersonal mechanisms, as testing both directions of effect would have required an excessive number of tests. Given the choice, temporal sequencing data (both in this sample and elsewhere) and prior conceptualizations in the literature (e.g.,^[3]) strongly supported treating anxiety as the IV rather than depression. Further, Mathews et al.^[15] found no evidence supporting the hypothesis that depression causes anxiety, even in cases where depression preceded anxiety diagnosis. Further, we lacked anxiety data at T3. Nonetheless, the idea that depression exacerbates interpersonal functioning, in turn elevating risk for anxiety, is conceptually plausible and not mutually exclusive with the current study's results, as there may be reciprocal, longitudinal associations between symptoms and disorders, perhaps bidirectionally linked by interpersonal disturbances. The current model may be oversimplified, and more research is likely needed to fully appreciate the intricacies of anxiety–depression comorbidity.

Our results support an interpersonal model of comorbidity, but interpersonal dysfunction undoubtedly does not exclusively explain anxiety–depression co-occurrence. Abundant research suggests that anxiety and depression share a common underlying substrate that contributes to comorbidity.^[80–83] In addition, anxiety disorders and depression share an extensive range of biological and psychosocial etiological factors (e.g., genetic^[84]) that presumably also promote comorbidity. Noninterpersonal causal mechanisms may link anxiety with later depression (e.g., cognitive factors^[17]). Even within the realm of interpersonal mechanisms, the interpersonal variables examined here do not represent all potential mediators (see^[38]). Far more work is needed to fully understand why anxiety and depression co-occur at such dramatic rates.

Our study boasts several strengths, including longitudinal design and use of bootstrapping and multiple mediation. However, several study limitations should also be noted. First, our primary interpersonal dysfunction scale assessed self-perceptions only, although this was supplemented by the chronic stress interview. Future research investigating interpersonal mediators of anxiety–depression co-occurrence should utilize alternative sources of information (peer report, behavioral observations) when possible. Second, the IIP-48 was only administered at T2, and diagnoses were only collected at T1 and T2, so in some models, the mediator was assessed concurrently with the outcome. However, additional analyses examining self-reported depression at T3 as outcomes showed very consistent findings. Third, T1 interviewers did not discriminate between subtypes of SAD. Generalized social anxiety is more strongly linked both depression and interpersonal problems than situational social anxiety^[48,85]; thus, results may have been stronger if we were able to examine this subgroup in isolation. We also did not distinguish between common and specific elements of anxiety and depression. Shared symptoms (negative affectivity^[80]) could more strongly predict interpersonal problems, perhaps partially explaining findings. Finally, although we have been referencing causality, mediation analyses and temporal antecedence offer only preliminary support for causality, not firm evidence. Although one cannot randomly

assign participants to anxiety disorders, we encourage researchers to creatively examine analogous processes using experimental methods (e.g., randomly assignment into anxiety treatments or mood induction conditions) to draw stronger causal inferences about pathways from anxiety to depression.

Our results may have important implications for prevention and treatment. Causal models of comorbidity broadly imply that early intervention for anxiety disorders may be an effective and cost-effective method of reducing long-term risk for a variety of internalizing disorders. Although an intuitive conclusion, more research is needed to verify that treating anxiety early improves long-term depression prognosis. Results specifically support interpersonal problems as important targets for intervention for anxiety disorders. Future research should examine whether treatments that emphasize recognition and reduction of IO, encourage socialization, and promote relationship harmony improve not only anxiety, but also subsequent depression risk. Overall, our findings stress the importance of maintaining an interpersonal perspective when exploring the origins, nature, and treatment of internalizing disorders.

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