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Positive relations mediate the bidirectional connections between depression and anxiety symptoms

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ABSTRACT

Introduction: Major depressive disorder (MDD) and generalized anxiety disorder (GAD) co-occur at high rates, often preceding and predicting one another over long durations. Interpersonal theories propose that relationships with others may contribute to the longitudinal connections between MDD and GAD. Therefore, the current study examined the mediational effect of positive relations with others in these connections over 18 years.

Methods: Community-dwelling adults (n = 3294) participated in data collection at three time-points (Time 1 [T1], Time 2 [T2], and Time 3 [T3]) spaced about nine years apart. MDD and GAD symptoms were assessed using the Composite International Diagnostic Interview–Short Form. Positive relations was measured with the Psychological Well-Being Scale–Positive Relations with Others subscale. Structural equation mediation modeling was used for data analysis.

Results: Results indicated that lower T2 positive relations significantly mediated the relationship between higher T1 MDD severity predicting more severe T3 GAD symptoms (d = 0.375) and explained 10.7% of the variance. T2 positive relations also had a significant mediational effect in the association between T1 GAD symptoms positively predicting T3 MDD severity (d = 0.360), accounting for 12.2% of the variance of this connection. These mediational effects were significant after adjusting for age, gender, education, and T1 symptoms (d = 0.277–0.677).

Conclusions: Supporting interpersonal theories, lack of positive relations with others mediated the bidirectional connections between MDD and GAD symptoms across 18 years. Future research should continue to explore the influence of positive relations on mental health and whether treatments that enhance interpersonal functioning could improve treatment for depression and anxiety.

1. Introduction

Major depressive disorder (MDD) and generalized anxiety disorder (GAD) are highly prevalent and potentially debilitating mental health conditions that often co-occur (Kessler et al., 2008; Lamers et al., 2011). It is estimated that approximately 50–60% of individuals with depression will meet lifetime criteria for an anxiety disorder and vice versa (Brown et al., 2001; Kessler et al., 2005). Comorbid MDD and GAD, either at a single time point or across multiple time points, are associated with greater symptom severity, more significant impairment, and worse quality of life (Hofmeijer-Sevink et al., 2012; Norberg et al., 2008; Penninx et al., 2011). Given the poor outcomes associated with this common comorbidity, a clearer understanding of the association between MDD and GAD is imperative.

Causal models of comorbidity posit that the presence of one disorder can lead to the development of another disorder (Avenevoli et al., 2001; Cummings et al., 2014; Mathew et al., 2011; Rice et al., 2004). Supporting this notion, a meta-analysis by Jacobson and Newman (2017) indicated that depression and anxiety symptoms were bidirectional risk factors for each other. Indeed, studies have found reciprocal

Abbreviations: GAD, generalized anxiety disorder; MDD, major depressive disorder; T1, Time 1; T2, Time 2; T3, Time 3; MIDUS, Midlife Development in the United States project; CIDI-SF, Composite International Diagnostic Interview–Short Form; DSM–III–R, Diagnostic and Statistical Manual of Mental Disorders 3rd edition, revised; CFI, confirmatory fit index; RMSEA, root mean squared error of approximation; SRMR, standardized root mean squared residual; MLR, maximum likelihood with robust estimators.

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relationships between MDD and GAD across more than a decade (Fichter et al., 2010; Kessler et al., 2008; Moffitt et al., 2007). Experiencing MDD or GAD may trigger mechanisms that give rise to the onset of the other disorder over long periods (Kraemer et al., 2001). However, these factors remain unclear. Thus, more research is needed to understand processes that might underlie these long-term bidirectional connections.

Interpersonal relations may be one such factor that contributes to the temporal relationships between depression and anxiety. Interpersonal theories of psychopathology postulate that social and relational processes are critical components of MDD and GAD (Horowitz, 2004; Leary, 1957; Sullivan, 1953). Supporting this, research has consistently linked depression and anxiety with interpersonal dysfunction (McEvoy et al., 2013; Newman et al., 2013; Santini et al., 2015; Starr et al., 2014) and a lack of positive relations with others (Nierenberg et al., 2010; Paech et al., 2016; Segrin and Rynes, 2009). Moreover, comorbid depression and anxiety were associated with worse social impairment than either MDD or GAD alone (Hirschfeld, 2001; Saris et al., 2017). Taken together, these findings suggest that relations with others may play a role in the reciprocal connections between these disorders.

Positive relations with others could plausibly mediate the long-term association between MDD and future GAD. Depressive symptoms are associated with suboptimal interpersonal tendencies, such as withdrawal and overdependence, which could burden existing relationships and create barriers to forming new positive connections (Girard et al., 2014; Hames et al., 2013; Sharabi et al., 2016). Individuals with MDD may also have a negatively biased view of social situations (Hindash and Amir, 2012), potentially discouraging future social interactions. Lending credence to these points, prior studies have found that experiencing depression symptoms predicted interpersonal dysfunction and fewer social relationships (Domenech-Abella et al., 2019; Rhebergen et al., 2010; Stice et al., 2004). Heightened MDD and a subsequent lack of positive relations with others could then lead to the development of GAD symptoms. For instance, having fewer positive relations might increase feelings of social rejection and trigger worry around social situations (Leary, 2015; Newman and Erickson, 2010; Newman et al., 2013). In line with this idea, past research showed that factors such as social disconnection and low feelings of belonging predicted later anxiety (de Moor et al., 2018; Santini et al., 2020). Thus, a lack of positive relations with others may contribute to the relationship between heightened MDD and future GAD.

Similarly, positive relations with others could mediate the connection between GAD and later MDD. GAD symptoms were linked to distinct interactional styles (e.g., intrusive, nonassertive, avoidant; Erickson and Newman, 2007; Przeworski et al., 2011; Shin and Newman, 2019), which can create distance in relationships and produce obstacles to connecting with others. Additionally, individuals with GAD may have a skewed perception of their impact on close others (Erickson and Newman, 2007; Newman and Erickson, 2010; Salzer et al., 2008). Further, past studies found that more severe GAD symptoms predicted interpersonal distress (Zaider et al., 2010) and future relationship problems (Erickson et al., 2016). It follows that a lack of positive relations with others from anxiety-related impairment could then trigger depressive symptoms. For example, having fewer positive relations limits the amount of social support available to help cope with life's challenges, and low interpersonal support is an established risk factor for the development of later depression (Metts et al., 2021; Wang et al., 2018). Therefore, positive relations with others could be a factor that mediates the longitudinal pathway between GAD and later MDD.

Considering the above theories and research, a lack of positive relations with others is a candidate mediator of the connection between depression and subsequent anxiety, and vice versa. Whereas prior research has explored the indirect effects of social factors in the link between anxiety and future depression (Jacobson et al., 2017; Jacobson and Newman, 2016; Starr and Davila, 2012), no studies have investigated positive interpersonal relations as a mechanism connecting the two. Moreover, although past studies tested social mediators of the association between anxiety and later depression, the role of interpersonal relations in the reverse pathway (i.e., depression predicting future anxiety) has not been examined. As MDD and GAD are bidirectional risk factors for one another (Jacobson and Newman, 2017), it is important to understand the factors that underlie both directions of the MDD-GAD relationship. Further, as these disorders are often chronic, examining potential mediators of the reciprocal pathways between MDD and GAD over long periods is similarly essential.

Clarifying interpersonal factors that contribute to the development and maintenance of MDD and GAD over time is valuable for several reasons. This basic science effort could guide treatment and prevention approaches, especially as emerging evidence shows modifiable factors such as social support positively affect treatment outcomes for MDD and GAD (Cui et al., 2016; Dour et al., 2014; Malivoire et al., 2020). Further, a more fine-grained understanding of how positive interpersonal relationships impact depression and anxiety symptoms over time could refine etiological conceptualizations of comorbidity and pinpoint areas for future translational research.

Thus, the present work examined positive relations with others as a mediator in the longitudinal bidirectional associations between MDD and GAD symptoms. Our study extended extant research by analyzing these relationships across almost two decades in a large sample of community-dwelling adults. Participants completed three waves of measurement (Time 1 [T1], Time 2 [T2], and Time 3 [T3]) spaced about nine years apart. Based on interpersonal theories of psychopathology and past research, we hypothesized that heightened T1 MDD severity would predict more severe T3 GAD symptoms via lower positive relations with others at T2 (Hypothesis 1). Likewise, we hypothesized that T2 positive relations would mediate higher T1 GAD symptoms predicting more severe T3 MDD symptoms (Hypothesis 2).

2. Methods

2.1. Participants

Data were drawn from the Midlife Development in the United States project (MIDUS; Brim et al., 2019; Ryff et al., 2017; Ryff et al., 2019). MIDUS includes three waves of data collection spaced approximately nine years apart: Time 1 (T1) was collected from 1995 to 1996, Time 2 (T2) from 2004 to 2006, and Time 3 (T3) from 2012 to 2013. The present sample included 3294 adults who participated in all data collection waves. Of these participants, 54.6% identified as female, 44.8% as male, and 0.6% did not identify their sex. The majority of the sample described their race as White Caucasian (89%; 3% African American; 0.7% Multiracial; 0.4% Asian or Pacific Islander; 0.3% Native American or Aleutian Islander/Eskimo), and 46.8% were college-educated. The average age at T1 was 45.6 ($SD = 11.4$, range = 20–74). Table 1 displays the demographic data and a correlation matrix of primary study variables.

2.2. Measures

2.2.1. Major depressive disorder symptom severity

MDD symptom severity was assessed at each wave of data collection with the Composite International Diagnostic Interview–Short Form (CIDI-SF; Kessler et al., 1998; Wittchen et al., 1994), derived from criteria from the revised Diagnostic and Statistical Manual of Mental Disorders (3rd ed., rev.; DSM–III–R; American Psychiatric Association, 1987). Participants indicated how frequently they experienced depression symptoms over the past 12 months using a four-point Likert scale (1 = *never* to 4 = *on most days*). Sample items include "feel down on yourself, no good, or worthless" and "lose interest in most things." Comparisons of the brief and complete CIDI diagnostic tests indicate high specificity and sensitivity of the CIDI-SF for MDD (93.9% and 89.6%, respectively) (Kessler et al., 1998). The CIDI-SF for MDD had excellent internal consistency (Cronbach's $\alpha = 0.93$ at T1 and T3) herein.

Table 1
Correlation matrix of study variables.

	1	2	3	4	5	6	7	8
1. Age	–							
2. Gender (Female)	0.013	–						
3. Ethnicity	−0.021	0.075	–					
4. T1 MDD	−0.032***	0.176***	0.104	–				
5. T1 GAD	−0.095*	0.297***	0.053	0.565***	–			
6. T2 PRO	0.129***	0.135***	0.083**	−0.130***	−0.163***	–		
7. T3 MDD	−0.017***	0.145***	0.134**	0.370***	0.335***	−0.130***	–	
8. T3 GAD	−0.010	0.195***	0.132*	0.367***	0.499***	−0.196***	0.573***	–
M or n	45.62	1799	2932	0.28	21.8	41	0.25	22.2
SD or %	11.41	54.61	89.01	0.73	6.35	6.82	0.70	6.9
Min	20			0	10	14	0	10
Max	74			2.75	40	49	2.75	40
Skewness	0.24	4.29	5.26	2.40	0.70	−0.85	2.64	0.59
Kurtosis	−0.70	38.8	28.50	4.13	−0.11	0.13	5.40	−0.43

GAD = generalized anxiety disorder; MDD = major depressive disorder; PRO = positive relations with others; T1 = time 1; T2 = time 2 (9 years after T1) T3 = time 3 (9 years after T2 and 18 years after T1).
*** $p < .001$.
** $p < .01$.
* $p < .05$.

2.2.2. Generalized anxiety disorder symptom severity

GAD severity was measured at each time point using the CIDI-SF, which aligns with the DSM–III–R criteria for GAD (Kessler et al., 1998; Wittchen et al., 1994). Participants used a four-point Likert scale (1 = *never* to 4 = *on most days*) to answer ten items assessing how frequently they experienced anxiety-related symptoms over the previous 12 months. Examples of items include "were irritable because of your worry" and "were keyed up, on edge, or had a lot of nervous energy." Compared to the full-length CIDI, the CIDI-SF has high levels of specificity (99.8%) and sensitivity (96.6%) for GAD (Kessler et al., 1998). The CIDI-SF for GAD had high internal consistency in our study (α = 0.87 at T1 and 0.89 at T3).

2.2.3. Positive relations with others

Positive relations with others was measured at T2 using the seven-item self-report Psychological Well-Being Scale–Positive Relations with Others subscale (Ryff, 1989, 2014; Ryff and Keyes, 1995). Participants rated the extent to which they agreed with seven statements about the quality of their social relationships using a seven-point Likert scale (1 = *strongly agree* to 7 = *strongly disagree*). Example items include "maintaining close relationships has been difficult and frustrating for me" and "I have not experienced many warm and trusting relationships with others." This subscale had good internal consistency in the present study (α = 0.78 at T2). At T1, level of positive relations with others was assessed using three items from the Psychological Well-Being Scale–-Positive Relations with Others subscale (Ryff, 1989; Ryff and Keyes, 1995). In this sample, scores on the three-item T1 scale were moderately correlated with scores on the seven-item T2 scale ($r = 0.56$, $p < .001$). However, the three-item scale at T1 had unacceptable internal consistency (α = 0.60) (Nunnally and Bernstein, 1994) and thus was not included in the present analyses.

2.3. Data analyses

Longitudinal structural equation mediation modeling was conducted with *R* (Version 4.1.0) and *RStudio* software (Version 1.4.1717) using the *lavaan R* package (Rosseel, 2012). Model fit indices were evaluated using the confirmatory fit index (CFI; Bentler, 1990), root mean squared error of approximation (RMSEA; Browne and Cudeck, 1993; Steiger, 1990), and standardized root mean squared residual (SRMR; Hu and Bentler, 1999). All models were conducted using maximum likelihood with robust estimators (MLR) to increase power and reduce bias in parameter estimates and standard errors since the manifest indicators of the latent variables of MDD, GAD, and positive relations were ordinal (Zhong and Yuan, 2011). Confirmatory factor analyses showed that the measurement models had a good fit for the following constructs of interest: MDD symptom severity at T1 ($\chi^2(df = 9) = 0.99$, $p = .99$, CFI = 1.00, RMSEA = 0.00, SRMR = 0.01) and T3 ($\chi^2(df = 9) = 0.64$, $p = 1.00$, CFI = 1.00, RMSEA = 0.00, SRMR = 0.01); GAD symptom severity at T1 ($\chi^2(df = 35) = 179.68$, $p < .001$, CFI = 0.98, RMSEA = 0.07, SRMR = 0.06) and T3 ($\chi^2(df = 35) = 149.87$, $p < .001$, CFI = 0.98, RMSEA = 0.06, SRMR = 0.06); positive relations with others at T2 ($\chi^2(df = 14) = 267.57$, $p < .001$, CFI = 0.95, RMSEA = 0.08, SRMR = 0.07). The individual items that comprise the constructs of MDD, GAD, and positive relations with others loaded onto unidimensional constructs for each respective variable of interest. The factor loadings (λ) were statistically significant (all *p*s < .001) for the indicators of latent T1 MDD (λ = 0.75–0.95), T3 MDD (λ = 0.76–0.96), T1 GAD (λ = 0.53–0.75), T3 GAD (λ = 0.53–0.78), and T2 positive relations with others (λ = 0.47–0.71). Figs. 1 and 2 depict the regression path coefficients, standard errors, factor loadings, item residual variances, and factor residual variances of the mediation models for Hypotheses 1 and 2, respectively.

We used a bootstrapped product-of-coefficients method (Leth-Steensen and Gallitto, 2016; Shrout and Bolger, 2002) to determine if higher T1 MDD severity predicted lower T2 positive relations with others (*a* path) and if reduced T2 positive relations predicted higher T3 GAD severity (*b* path). We evaluated if the *a* and *b* paths were statistically significant above and beyond the direct effect (*c'*) that signified longitudinal comorbidity between MDD and GAD. Unstandardized regression coefficients (β) and 95% confidence intervals (CIs) were reported, and bootstrapping was used with 10,000 resampling draws (Cheung and Lau, 2008). To assess effect sizes, we computed the percentage that the mediator accounted for in the associations between T1 MDD and T3 GAD severity. The mediation effect size was the ratio of the indirect effect (*a*b*) to the total effect ($c = a*b + c'$) (Preacher and Kelley, 2011; Wen and Fan, 2015). The same approach was used to test the mediational effect of T2 positive relations in the associations between T1 GAD and T3 MDD symptoms. To increase rigor in all mediation models, T1 MDD and GAD symptoms,[1] age, gender, and education level were included as covariates (D'Onofrio et al., 2020; Maxwell and Cole, 2007). In total, 35% of the observed data were missing, managed using full information maximum likelihood, a gold standard approach for data

[1] We did not adjust for T2 MDD and GAD symptoms because experts in causal analyses recommend against controlling for variables concomitant with mediators in prospective observational studies (D'Onofrio et al., 2020; Rosenbaum, 1984). Such controls can bias the direct and mediation effect estimation and would impede detecting part of the potential causal effect via the mediator.

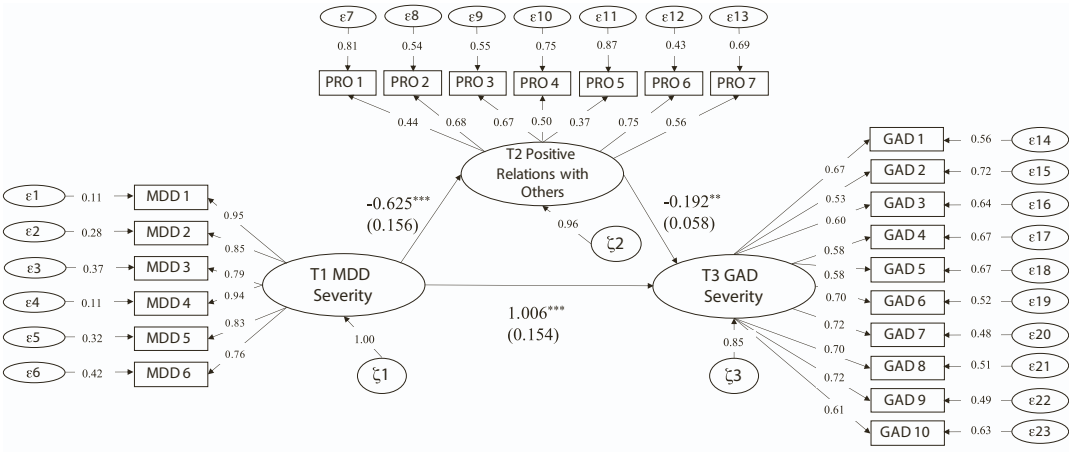

Fig. 1. T1 MDD predicting T3 GAD via T2 positive relations with others.
Note. ε = item residual variance; ζ = factor residual variance; GAD = generalized anxiety disorder; MDD = major depressive disorder; PRO = positive relations with others; T1 = time 1; T2 = time 2; T3 = time 3.
The meaning of the T3 GAD item indicators were as follows: GAD1 = restless due to worry; GAD2 = keyed up, on edge, or had a lot of nervous energy due to worry; GAD3 = irritable due to worry; GAD4 = trouble falling asleep due to worry; GAD5 = trouble staying asleep due to worry; GAD6 = trouble keeping your mind on what you were doing due to worry; GAD7 = have trouble remembering things due to worry; GAD8 = low on energy due to worry; GAD9 = tired easily due to worry; GAD10 = sore or arching muscles due to worry. The meaning of the T1 MDD item indicators were as follows: MDD1 = Feel more tired or low energy; MDD2 = Lose appetite or appetite increases; MDD3 = Trouble falling asleep; MDD4 = Trouble concentrating; MDD5 = Feel down or worthless; MDD6 = Think a lot about death. The meaning of the T2 PRO item indicators were as follows: PRO1 = Most people see me as loving and affectionate; PRO2 = Maintaining close relationships has been difficult and frustrating for me; PRO3 = I often feel lonely because I have few close friends with whom to share my concerns; PRO4 = I enjoy personal and mutual conversations with family members and friends; PRO5 = People would describe me as a giving person, willing to share my time with others; PRO6 = I have not experienced many warm and trusting relationships with others; PRO7 = I know that I can trust my friends, and they know they can trust me.

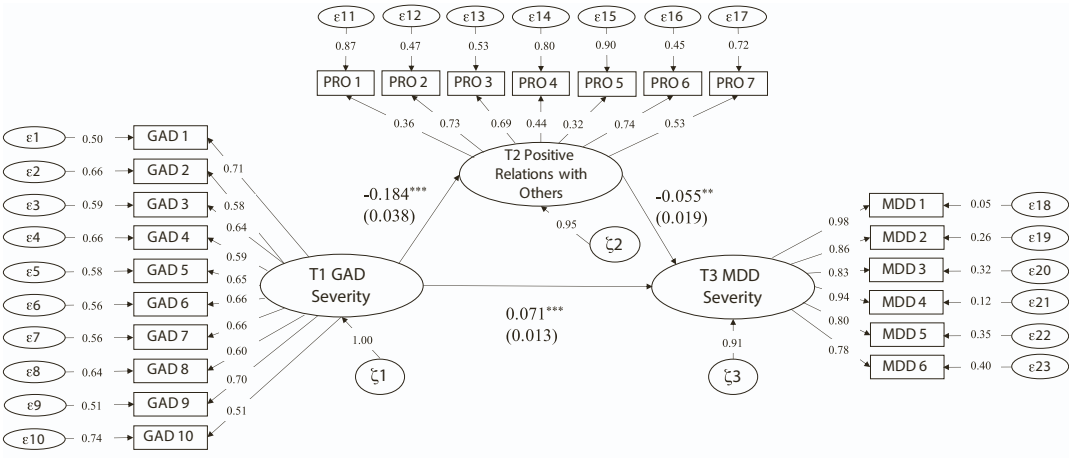

Fig. 2. T1 GAD predicting T3 MDD via T2 positive relations with others.
Note. ε = item residual variance; ζ = factor residual variance; GAD = generalized anxiety disorder; MDD = major depressive disorder; PRO = positive relations with others; T1 = time 1; T2 = time 2; T3 = time 3.
The meaning of the T1 GAD item indicators were as follows: GAD1 = restless due to worry; GAD2 = keyed up, on edge, or had a lot of nervous energy due to worry; GAD3 = irritable due to worry; GAD4 = trouble falling asleep due to worry; GAD5 = trouble staying asleep due to worry; GAD6 = trouble keeping your mind on what you were doing due to worry; GAD7 = have trouble remembering things due to worry; GAD8 = low on energy due to worry; GAD9 = tired easily due to worry; GAD10 = sore or arching muscles due to worry. The meaning of the T3 MDD item indicators were as follows: MDD1 = Feel more tired or low energy; MDD2 = Lose appetite or appetite increases; MDD3 = Trouble falling asleep; MDD4 = Trouble concentrating; MDD5 = Feel down or worthless; MDD6 = Think a lot about death. The meaning of the T2 PRO item indicators were as follows: PRO1 = Most people see me as loving and affectionate; PRO2 = Maintaining close relationships has been difficult and frustrating for me; PRO3 = I often feel lonely because I have few close friends with whom to share my concerns; PRO4 = I enjoy personal and mutual conversations with family members and friends; PRO5 = People would describe me as a giving person, willing to share my time with others; PRO6 = I have not experienced many warm and trusting relationships with others; PRO7 = I know that I can trust my friends, and they know they can trust me.

that was likely to be missing at random (Lee and Shi, 2021). Moreover, the Little's Missing Completely at Random test was not statistically significant ($\chi^2(df = 34) = 45.90$, $p = .084$).

3. Results

Hypothesis 1. T1 MDD predicting T3 GAD via T2 Positive Relations with Others.

The model testing T2 positive relations as a mediator in the pathway

between T1 MDD and T3 GAD symptom severity (Fig. 1) showed good fit ($\chi^2(df = 224) = 586.96$, $p < .001$, CFI = 0.96, RMSEA = 0.04, SRMR = 0.05). In this model, all individual items had significantly high factor loadings for T1 MDD (λ = 0.76–0.95), T2 positive relations with others (λ = 0.44–0.75), and T3 GAD (λ = 0.53–0.78) (all p values <.001), offering evidence for the unidimensionality of all constructs of interest. Direct effect results demonstrated that more severe MDD symptoms at T1 predicted higher T3 GAD symptoms (β = 1.006, $p < .001$, $d = 0.870$). Higher T1 MDD symptoms led to lower T2 positive relations with others nine years later (β = −0.625, $p < .001$, $d = -0.537$). Lower T2 positive relations subsequently predicted more severe T3 GAD symptoms (β = −0.192, $p = .001$, $d = -0.443$). T2 positive relations with others had a significant mediational effect in the relationship between T1 MDD symptoms and T3 GAD severity (β = 0.120, $p = .005$, $d = 0.375$), accounting for 10.7% of the variance. This indirect effect of T2 positive relations remained significant after adjusting for age, gender, education, and T1 GAD (d = 0.184–0.342). Collectively, the results were consistent with Hypothesis 1.

Hypothesis 2. T1 GAD predicting T3 MDD via T2 Positive Relations with Others.

The model testing T2 positive relations as a mediator between T1 GAD and T3 MDD (Fig. 2) showed good fit ($\chi^2(df = 225) = 691.48$, $p < .001$, CFI = 0.96, RMSEA = 0.04, SRMR = 0.05). All individual items loaded strongly onto their respective unidimensional constructs in this model (T1 GAD: λ = 0.51–0.71; T2 positive relations with others: λ = 0.32–0.74; T3 MDD: λ = 0.78–0.98) (all p values<.001). Higher T1 GAD severity was significantly linked to elevated T3 MDD symptoms (β = 0.071, $p < .001$, $d = 0.712$). Elevated T1 GAD severity also predicted lower T2 positive relations with others (β = −0.184, $p < .001$, $d = -0.648$). Decreased T2 positive relations significantly predicted greater T3 MDD severity (β = −0.055, $p = .004$, $d = -0.380$). The indirect effect was significant, indicating that T2 positive relations with others mediated the path between T1 GAD and T3 MDD severity (β = 0.010, $p = .007$, $d = 0.360$). T2 positive relations explained 12.2% of the variance of the T1 GAD–T3 MDD connection. Further, the mediational effect remained significant after controlling for age, gender, education, and T1 MDD (d = 0.277–0.368). Thus, Hypothesis 2 was supported.

4. Discussion

The current study examined positive relations with others as a mediator in the long-term pathway between MDD and GAD symptoms. Results indicated that more severe T1 MDD symptoms predicted higher T3 GAD severity almost two decades later, and T2 positive relations with others mediated this relationship (Hypothesis 1). Similarly, T2 positive relations mediated the association between T1 GAD symptom severity positively predicting T3 MDD symptoms (Hypothesis 2). The indirect effect of T2 positive relations in both mediation analyses remained significant after controlling for baseline symptoms, age, gender, and education level. All mediation models had a good fit, as reflected by the fit indices and high item loadings on all unidimensional latent factors examined in each SEM mediation model. Overall, these results supported our hypotheses and are in line with causal models of comorbidity (Cummings et al., 2014; Mathew et al., 2011; Rice et al., 2004) and interpersonal theories of psychopathology (Horowitz, 2004; Leary, 1957; Sullivan, 1953). Collectively, our findings suggest that having few positive relations with others may be a factor via which MDD and GAD lead to one another over long periods.

Our findings align with prior research suggesting that interpersonal processes may have a salient impact on the temporal associations between depression and anxiety. For example, deficits in positive relations with others coincided with trait anxiety and depressive symptoms among community adults (Andrews and Hicks, 2017; Paech et al., 2016). Further, close friendships mediated the pathway between anxiety and future depression severity in adolescents (Jacobson and Newman, 2016). Likewise, reduced sociability and heightened interpersonal sensitivity mediated the connection between anxiety during adolescence and depression in young adulthood (Starr et al., 2014). Interpersonal distress similarly had an indirect effect on the relationship between depression and future anxiety in adolescents (Hamilton et al., 2016). MDD and GAD symptoms also predicted dysfunctional interpersonal styles and issues in social relationships (Hames et al., 2013; Przeworski et al., 2011; Shin and Newman, 2019). Moreover, a meta-analysis of older adults found a bidirectional relationship between social disconnection and symptoms of depression and anxiety, similar to our findings of reciprocal associations between low positive relations and heightened MDD and GAD (Santini et al., 2020).

Why did positive relations mediate the pathway between higher T1 MDD symptoms and more severe GAD almost two decades later? One potential explanation for this finding may be that distinct social characteristics related to heightened MDD led to fewer positive relationships, which then triggered the onset of anxiety symptoms. Research consistently connects MDD with dysfunctional interpersonal tendencies and subsequent social difficulties. Even individuals in remission from depression experienced persistent interpersonal problems as a scar effect (Hames et al., 2013; Kupferberg et al., 2016; Petty et al., 2004; Rhebergen et al., 2010). Depression was also associated with cold and overdependent interactional styles that could have strained existing relationships and hindered one's ability to foster positive connections (Hames et al., 2013; Rohde et al., 1990; Shin and Newman, 2019). Supporting this idea, in a study of depression in romantic partnerships, participants reported that their depressed partners' overdependency and tendency to self-isolate negatively impacted their relationships (Sharabi et al., 2016). Further, since persons with MDD often perceive social situations as unfavorable and overreact to feeling excluded, these individuals might have withdrawn from relationships to avoid expected negative experiences (Downey and Feldman, 1996; Hindash and Amir, 2012). Taken together, interpersonal styles and social withdrawal could have made it difficult for individuals with MDD to form and sustain positive relationships.

For persons with heightened MDD, a lack of positive relations then could have increased the risk of developing future GAD, as indicated by our findings. Congruent with this, prior research suggested that low interpersonal support and having fewer social contacts were vulnerability factors for heightened anxiety (Bolger and Eckenrode, 1991; Metts et al., 2021; Santini et al., 2020). Having fewer positive relations also could have triggered feelings of social rejection and provoked worry related to interpersonal situations (Leary, 2015; Newman and Erickson, 2010; Newman et al., 2013). Indeed, increased social fears often precipitate worsened GAD symptoms, and high worriers reported interpersonal problems as a top concern (Roemer et al., 1997; Ryum et al., 2017). Supporting these notions, interpersonal distress had an indirect effect on the link between depression and later anxiety in adolescents (Hamilton et al., 2016). Thus, it is plausible that difficulties related to having few positive relationships after experiencing heightened MDD symptoms could have contributed to more severe anxiety in the future.

Moreover, we found that positive relations with others mediated the link between more severe T1 GAD symptoms predicting higher T3 MDD symptom severity. This aligns with past literature supporting a connection between anxiety and dysfunctional behavioral tendencies in social relationships (Erickson et al., 2016; Shin and Newman, 2019). Maladaptive interpersonal styles associated with anxiety (e.g., avoidant, intrusive, nonassertive) may cause relationship stress and negative social experiences (Eng and Heimberg, 2006; McEvoy et al., 2013; Przeworski et al., 2011; Salzer et al., 2008). Persons with GAD may also interpret social information negatively and have biased perceptions of their impact on close others (Erickson and Newman, 2007; Newman and Erickson, 2010; Salzer et al., 2008). These relational styles and biased cognitions could lead to relationship problems. Further, research suggests increased GAD symptoms can impede problem-solving in social contexts (Llera and Newman, 2020; Pawluk et al., 2017). Taken

together, these interactional styles and negatively skewed social cognitions for persons with GAD could have posed barriers to forming and maintaining positive relationships.

Heightened GAD and having few positive relations with others then could have increased the risk of experiencing more severe depressive symptoms in the future. This finding is consistent with evidence that reduced social support and few close relationships were risk factors for the development of future psychopathology (Cohen, 2004; Santini et al., 2015; Scardera et al., 2020; Segrin and Rynes, 2009). Having fewer positive relations likely makes it more difficult to access social support when facing significant stressors and challenges. As relational support was shown to attenuate the adverse psychological impacts of stressful events, it follows that fewer positive relations could have increased vulnerability to depression (Forbes et al., 2020; Jacobson and Newman, 2017; McGuire et al., 2018). A lack of positive relations with others also could have fostered feelings of loneliness and social rejection, which are vulnerability factors implicated in the onset of depressive symptoms (Domenech-Abella et al., 2019; Heinrich and Gullone, 2006; Slavich et al., 2010; Wang et al., 2018). In sum, over long durations, fewer positive relations could have limited available social support and triggered negative emotions that increased susceptibility to MDD.

The limitations of this study deserve mention. First, positive relations with others was assessed using self-report, which introduces the possibility of response biases. Future research could utilize a multiple-informant approach to corroborate the validity of participants' perceptions of their interpersonal relations. Moreover, unlike the seven-item T2 positive relations measure, the three-item T1 positive relations measure had inadequate internal consistency reliability ($\alpha = 0.60$), rendering it inappropriate for inclusion in the analyses (Nunnally and Bernstein, 1994). Also, this measure was only moderately correlated with the T2 measure ($r = 0.56$). Future similar studies using measures with good psychometric properties could test if a moderated mediation effect exists. Additionally, the MIDUS dataset comprised mainly White American participants, which may have limited the generalizability of our results. Future studies should replicate these analyses in more diverse samples regarding ethnicity, race, gender identity, and sexual orientation. Lastly, MDD and GAD symptoms were assessed using the CIDI-SF, based on DSM-III-R diagnostic criteria. Therefore, replication using DSM-5 criteria is warranted. However, the present study has notable strengths, including the 18-year duration and large sample size. Our sample of middle-aged community adults extends previous research examining the effect of interpersonal factors on the links between MDD and GAD in adolescents (Jacobson and Newman, 2016; Starr et al., 2014), older adults (Domenech-Abella et al., 2019; Jacobson et al., 2017), and clinical samples (Mogi and Yoshino, 2017; Starr and Davila, 2012).

In summary, the present study tested the mediational role of positive relations in the connections between MDD and future GAD symptom severity and vice versa. In a large sample of community-dwelling adults, positive relations with others mediated the bidirectional associations between depression and anxiety across almost two decades based on a series of latent variable models with consistently good model fit. This study extends the existing literature on interpersonal factors that may influence the sequential relationships between depression and anxiety. Our results also could have implications for future clinical research. In light of these findings, along with past research suggesting that social support can positively affect treatment outcomes for depression and anxiety (Dour et al., 2014; Malivoire et al., 2020), future studies should investigate whether a focus on positive relations and interpersonal functioning might similarly improve treatment effects for MDD and GAD. Further, our findings highlight the importance of testing if interpersonally-focused psychotherapies could enhance treatment outcomes by improving positive relations with others (Erickson et al., 2015; Newman and Zainal, 2020).

Author contributions

My research team, Dr. Zainal, Dr. Newman, and I, conceived of the presented idea and performed the statistical analyses. Dr. Zainal verified the analytical methods and outputs. Dr. Newman encouraged Dr. Zainal and I to refine the analyses and supervised the findings of this work. We take full responsibility for the data, the accuracy of analyses and interpretation, as well as conduct of the research. All authors have (1) made substantial contributions to analysis and interpretation of the study and its findings; (2) drafted and revised the article for intellectual content; and (3) gave their final approval of the version to be submitted. The manuscript has been read and approved by all authors.

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Conflict of interest

None of the authors, Kathryn E. Barber, Nur Hani Zainal, and Michelle Gayle Newman, have any conflicts to disclose. We do not have any financial relationships (regardless of amount of compensation) with any entity, grants, personal fees, non-financial support, or royalties, and neither have any patents, whether planned, pending or issued, broadly relevant to the work. We confirm that there no relationships or activities that readers could perceive to have influenced, or that give the appearance of potentially influencing, what we wrote in the submitted work.

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