Temporal associations among loneliness, anxiety, and depression during the COVID-19 pandemic period

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Abstract
Numerous studies have reported that individuals' loneliness, anxiety, and depression levels increased during the COVID-19 pandemic period. However, reciprocal associations among loneliness, anxiety, and depression, as well as gender differences in these associations, have not been investigated. Therefore, temporal associations among loneliness, anxiety, and depression and gender differences in these associations were examined in a longitudinal study during the COVID-19 pandemic period. The loneliness, anxiety, and depression levels of 458 university students were evaluated at three timepoints (T1, T2, and T3) during the COVID-19 pandemic period in China. The timepoints were separated by 1 month. Cross-lagged panel designs were used to examine reciprocal associations among loneliness, anxiety, and depression as well as the stability and gender differences of these associations. Cross-lagged panel analysis revealed that T1 depression positively predicted T2 anxiety and loneliness, T1 loneliness positively predicted T2 depression, T2 anxiety positively predicted T3 depression, T2 depression positively predicted T3 anxiety and loneliness, T2 loneliness positively predicted T3 depression, and T1 loneliness positively predicted T3 anxiety through the mediating role of T2 depression. No gender differences were observed in the cross-lagged associations. During the COVID-19 pandemic period, loneliness and depression predicted each other across time, and loneliness predicted anxiety across time, mediated by depression. No gender differences were observed in the cross-lagged associations among loneliness, anxiety, and depression.

KEYWORDS
anxiety, COVID-19 pandemic period, depression, loneliness, longitudinal design

1 | INTRODUCTION

On December 31, 2019, the new coronavirus disease (COVID-19) was identified in Wuhan, Hubei, China (Chen et al., 2020). Numerous studies have investigated the effects of COVID-19 on mental health problems such as anxiety and depression. Findings indicate that individuals’ anxiety and depression levels tended to increase (Pappaa, Ntella, Giannakas, Giannakoulsc, Papoutsi, & Katsaounou, 2020; Özdin & Ö zdin, 2020). Studies with longitudinal designs have suggested that anxiety and depression disorders are comorbid, with significant bidirectional associations (Brown, Lehman, Sills, Brown, & Grisham, 2001; Fichter, Quadflieg, Fischer, & Kohlboeck, 2010; Jacobson & Newman, 2017a and b; Kessler, Gruber, Hettema, Hwang, Sampson, & Yonkers, 2008). More specifically, many longitudinal studies have documented temporal associations between anxiety and depression, and vice versa, across varying time frames,
including days (Starr & Davila, 2012), weeks (Schindel-Allon, Aderka, Shahar, Stein, & Gilboa-Schechtman, 2010), months (Coelho, Murray, Royal-Lawson, & Cooper, 2011), and years (Jacobson & Newman, 2017a and b). However, studies have indicated that comorbid anxiety and depression is associated with numerous negative outcomes, such as decreased quality of life and increased psychiatric problems, including suicidal behaviour (Norberg, Diefenbach, & Tolin, 2008; Hunter & Schmidt, 2010). Therefore, investigation of the predictors of anxiety-depression comorbidity is also warranted.

Studies have determined that loneliness, defined as negative thoughts and feelings of being isolated and disconnected from others (Russell, Peplau, & Ferguson, 1978), is significantly associated with anxiety and depression (Domènech-Abella, Mundó, Haro, & Maria, 2019; Evren & Cikirikci, 2018; Heinrich, & Gullone, 2006; Hsueh, Chen, Hsiao, & Lin, 2019; Mahon, Yarcheski, Yarcheski, Cannella, & Hanks, 2006; Mushtaq, Shoib, Shah, & Mushtaq, 2014; West, Keller, & Moore-West, 1986; Richardson, Roberts, & Jansen, 2017; Pritchard & Yalch, 2009). These studies have suggested that individuals with loneliness generally have less social support (Adamczyk & Segrin, 2015; Shaw & Gant, 2002; Wang, Farhana, Brynmor, Ma, & Sonia, 2018), which increases the risk of anxious and depressive emotions when setbacks or difficulties are encountered (Jacobson et al., 2017; White & Roberson-Nay, 2009). Although these studies have indicated that loneliness is a principal predictor of anxiety-depression comorbidity, their findings were limited (Jaremka, Fagundes, Glaser, Bennett, & Klec Kot-Glaser, 2013; Shaw & Gant, 2002; Winkel et al., 2017). First, most studies were cross-sectional; thus, a causal relationship cannot be confirmed; longitudinal studies are needed to verify the results. Second, loneliness tended to be both the predictive and outcome variable of anxiety and depression. For example, existing studies determined that individuals with depressive symptoms reported a higher level of loneliness than did individuals without depressive symptoms (Hsueh et al., 2019; Fernandes, Davidson, & Guthrie, 2018; Holvast, Burger, de Waal, van Marwijk, Comijs, & Verhaak, 2015). Loneliness, anxiety, and depression can be defined as both predictive and outcome variables by using cross-lagged panel designs (CLPD; Rogosa, 1980). Therefore, we used CLPD to test the reciprocal association among loneliness, anxiety, and depression.

The results of longitudinal studies on loneliness, anxiety, and depression have been inconsistent. For example, one study reported that anxiety and depression could not predict loneliness across time, and loneliness could predict anxiety and depression across time (Richardson et al., 2017). However, another study reported that loneliness and depression could predict each other across time (Hsueh et al., 2019). These inconsistent results may be attributable to the observation of dynamic associations among loneliness, anxiety, and depression, as reported in several daily diary studies (Doane & Thurston, 2014; Mor, 2010; Starr & Davila, 2012; Shrout, Herman, & Bolger, 2010); that is, variations at two time points may yield different associations. These associations are challenging to test (Lord, Jacobson, Suvak, & Newman, 2020; Gunnell et al., 2016) and require measurements at more than two time points.

Studies have noted positive associations among loneliness, anxiety, and depression, suggesting that their dynamic associations involve mediating mechanisms. For example, loneliness positively predicts anxiety through the mediating role of depression. Specifically, loneliness can positively predict anxiety in that lonely individuals tend to experience interpersonal problems and, in turn, negative emotions such as anxiety (James, Norman, Allie, & Paula, 2010). Furthermore, depression can positively predict anxiety; one study suggested anxiety and depression disorders are both associated with increased levels of corticotrophin-releasing factor, a hormone secreted during stress response (Boyer, 2000). The shared abnormalities in neural circuits may make depression a key predictor of anxiety. Loneliness may be associated with interpersonal relationships, with such problems causing negative emotions that are linked to depression (James et al., 2010). However, depression and anxiety are positively associated, and higher levels of depression, in turn, increase levels of anxiety (Fergusson & Woodward, 2002; Gallerani, 2008). On the basis of the literature, the present study explored the potential mediating mechanisms within the dynamic associations among loneliness, anxiety, and depression.

Studies have noted that university is a critical period in the development of anxiety and depression (Inam, Saqib, & Alam, 2003; Kurtovic, 2014). Although studies have observed that anxiety and depression were mutually predictive over time (Creamer et al., 1999; Jacobson et al., 2017; Domènech-Abella et al., 2019), few have examined the temporal associations among loneliness, anxiety, and depression in university students during the COVID-19 pandemic. A study on 7143 university students during the COVID-19 pandemic reported that 21.3% of students exhibited mild symptoms of anxiety, 2.7% displayed moderate symptoms, and 0.9% displayed severe symptoms (Cao et al., 2020). Therefore, investigating the longitudinal association between anxiety and depression in university students during the COVID-19 pandemic could provide intervention implications for treating mental health problems among university students.

1.1 | The COVID-19 pandemic period

Studies have reported that individuals’ anxiety and depression levels tend to increase when faced with the lack of definite answers to the following question: When will the pandemic end and how can we treat COVID-19? The lack of definitive answers may cause individuals’ to suffer from worries regarding death for the decreased level of security, which may then increase the level of anxiety and depression (OZdin & Ö zdin, 2020). Second, exposure to information regarding the pandemic and its effects may be a factor. Rumours may be spread on the Internet or through other channels that exaggerate the negative effects of COVID-19, which may also increase the level of individuals’ anxiety and depression (Tasnim, Hossain, & Mazumder, 2020). Studies have reported that individuals’ loneliness levels had increased during the pandemic (Msw & Voilcer, 2020), because recommendations and regulations regarding staying at home...
have been put in place to reduce individuals’ social interactions, which can increase the feeling of loneliness. However, the increased levels of loneliness, anxiety, and depression may be associated with different associations. For example, the association among loneliness, anxiety, and depression may be stronger than usual, and the loneliness–anxiety–depression comorbidity across time could be increased. Moreover, the present sample of university students have encountered a confluence of challenges, including the sudden switch to online learning, academic pressure, and even the pressure to find a job, which may trigger loneliness, anxiety, and depression. In the diathesis–stress model of psychopathology, environmental stress influences mental health (such as by causing loneliness, anxiety, and depression; Rende & Plomin, 1992). The challenges that students face may result in them perceiving numerous stressors, with the consequence of an increased number of experiences of loneliness, anxiety, and depression (ÖZdin & Ö zdin, 2020). Testing the reciprocal associations among loneliness, anxiety, and depression may reveal influential mechanisms, which could be valuable in improving individuals’, especially university students’, mental health during the COVID-19 pandemic period.

1.2 Gender differences in the association among loneliness, anxiety, and depression

Numerous studies have identified gender differences in loneliness, anxiety, and depression (Maes, Qualter, Vanhalst, Noortgate, & Goossens, 2016; Mclean, Asnaani, Litz, & Hofmann, 2011; Salk, Hyde, & Abramson, 2017). Mclean et al. (2011) determined that women had higher rates of lifetime diagnosis for all anxiety disorders than men. Salk and colleagues concluded that women also had a higher level of depression than men. Therefore, including gender as a moderator in analyses to investigate whether associations among loneliness, anxiety, and depression are invariant (or not) across gender is necessary. Study has that suggested that women are more sensitive to interpersonal relationships than men and have a higher desire to maintain relationships with others (Liu & Alloy, 2010). Higher interpersonal sensitivity is generally associated with more mental health problems (e.g., anxiety and depression) (Chang, 2018). Interpersonal relationships are negatively associated with loneliness. Therefore, women may also have a higher sensitivity to loneliness; thus, the effect of loneliness on anxiety and depression may differ based on gender. A study tested the effect of gender and loneliness on anxiety and depression (Chang, 2018). However, this study had two major limitations. First, the cross-sectional design prohibited investigation of the moderating effects of gender on the effects of loneliness on anxiety and depression across time. Therefore, longitudinal studies are needed to verify the study results. Second, interpersonal sensitivity is also significantly associated with anxiety and depression, and the association among loneliness, anxiety, and depression is generally reported to be bidirectional. Therefore, the effects of anxiety and depression on loneliness may also differ by gender. This hypothesis was investigated in the present study. Most studies have investigated the main effect of gender or the interaction effects between gender and other variables on anxiety and depression, with some considering gender to be a covariate (Yu, Yu, & Lin, 2019; Chang, 2018; Bjerkeset, Romundstad, & Gunnell, 2008). Overall, more studies are warranted to explore gender differences in the association between anxiety and depression. Therefore, the present study investigated these specific differences in this association over time.

1.3 The present study

The study objectives were to investigate the temporal associations among loneliness, anxiety, and depression and its potential mediating mechanisms within these associations during the COVID-19 pandemic and to determine the gender differences in these temporal associations. A latent cross-lagged panel model design was used to investigate these associations and differences in a Chinese sample. Based on the literature review, we hypothesized that (i) loneliness and anxiety could predict each other across time; (ii) loneliness and depression could predict each other across time; (iii) anxiety and depression could predict each other across time; and (iv) mediating mechanisms were present in the temporal associations among loneliness, anxiety, and depression. Furthermore, the self-reported scores for loneliness, anxiety, depression, and cross-lagged associations were tested for gender differences.

2 METHODS

2.1 Participants

All participants in this study were recruited from one university located in northeast China. The first survey was conducted three months after the outbreak of COVID-19 (T1) (Chen et al., 2020), and 734 students (male = 390, account for 53.13%) completed the questionnaires. After 1 month (T2), the second survey was administered, and 656 students (male = 345, account for 52.59%) completed the questionnaires. After two months (T3), the final survey was administered, and 599 students (male = 304, account for 50.75%) completed the questionnaires. Of the 458 students who completed all three surveys (of whom 240 were male, accounting for 52.40% of the total), 195 and 263 had urban and rural registration statuses, respectively. The data of only these students were subjected to further analysis (Tian, Bian, Han, Gao, & Wang, 2017; Yao & Zhong, 2014). The mean age of participants included in the analysis was 20.35 years (standard deviation [SD] = 1.65). Students who did not complete the survey may have not done so because of illness or not receiving the message. A series of independent-sample t tests revealed no differences between participating and nonparticipating students in loneliness, anxiety, and depression across time (Tian et al., 2017).
All the variables were surveyed online (with the online survey tool Wenjuanxing used for data collection) for the prohibitions/recommendations of staying at home. All the students were required to complete the survey within one day during each assessment. Data collection was performed in three steps. First, teachers were asked to inform their students that the survey would be administered three times, at intervals of approximately 1 month. Teachers further informed their students that small gifts (two signature pens, worth $0.5) would be given as compensation for participation and that the survey results would remain anonymous and would not affect the final performance for the term. Second, after an online class, teachers asked students to complete the survey within a limited time. Students who had questions regarding the survey could ask their teacher for instructions. Third, students were then told regarding the purpose of the study and assured of the absolute anonymity of their responses. The present study was conducted in accordance with the principles of the Helsinki Declaration and its revisions or with similar ethical standards and approved by the Human Research Ethics Committee of ×× University. Written informed consent was obtained from all participants.

2.3 | Measures

The Chinese version of the Loneliness Scale (Wang, 1995) was used to measure individuals’ loneliness. This scale was adapted from the Cheek and Russell Loneliness Scale (Russell et al., 1978). The Loneliness Scale consisted of 20 items (e.g., ”Do you often feel isolated from others?”) associated with experiences concerning interpersonal relationships, emotions, and life satisfaction over the past week. A four-point Likert (1 = never to 4 = often) was used to estimate each individual’s perception of the applicability of each item. The total score of the scale was used as individuals’ loneliness scores (higher scores indicate higher levels of loneliness). The Loneliness Scale had good reliability and validity ($\chi^2 (148) = 546.70, p < 0.001, \text{RMSEA} = 0.05, \text{TLI} = 0.98, \text{CFI} = 0.99$) (the data of the first time point measurement was used and the same below). Cronbach’s $\alpha$ values for the Loneliness Scale at the three timepoints were 0.89, 0.89, and 0.90, respectively.

The Chinese version of the Anxiety Scale (Duan & Sheng, 2012) was used to measure individuals’ anxiety, which was adapted from the Self-rating Anxiety Scale (SAS; William, 1971). The Anxiety Scale consisted of 20 items (e.g., ”Anxious mood” and ”Fear”), associated with physical symptoms, negative emotions, and sleep disorders. As with the Anxiety Scale, respondents rate the applicability of the items to their experiences over the past week. A five-point Likert (1 = never, 5 = often) was used to estimate each individual’s perception of the applicability of each item, and the total score of the scale was used as each participants’ anxiety score (higher scores indicated higher levels of anxiety). Anxiety Scale had good reliability and validity ($\chi^2 (152) = 573.45, p < 0.001, \text{RMSEA} = 0.06, \text{TLI} = 0.98, \text{CFI} = 0.98$). Cronbach’s $\alpha$ values for the Anxiety Scale at the three timepoints were 0.90, 0.96, and 0.97, respectively.

The Centre for Epidemiologic Studies Depression Scale (Radloff, 1977) was used to measure individuals’ depression. The Depression Scale consisted of 20 items (e.g., ”I was bothered by things that usually don’t bother me.”). A four-point Likert scale (1 = none of the time or rarely to 4 = most or all of the time) was used to estimate each individual’s perception of the applicability of each item, and the total score on the scale was used as participants’ depression scores (higher scores are associated with higher levels of depression). Respondents rate the applicability of the items to their experiences over the past week. The Depression Scale had good reliability and validity ($\chi^2 (150) = 562.78, p < 0.001, \text{RMSEA} = 0.05, \text{TLI} = 0.98, \text{CFI} = 0.98$). Cronbach’s $\alpha$ values for the Depression Scale at the three timepoints were 0.93, 0.93, and 0.95, respectively.

2.4 | Data analysis

Correlation analyses and factorial ANOVA were performed using SPSS 20.0 to determine the association among the studied variables, gender differences, and changes in the studied variables over time. Cross-lagged panel analysis was performed using the Mplus 7.0 software package to investigate reciprocal associations between the studied variables, and multigroup comparisons were used to investigate gender differences in these associations. Furthermore, the total scores of loneliness, anxiety, and depression were used as observed variables within each of the structural equation modelling (SEM). In the cross-lagged model, the associations between time-adjacent measurements (autoregressive effect) were used to investigate the stability of each variable across time (e.g., T1 anxiety predicts T2 anxiety, and T2 anxiety predicts T3 anxiety). The unidirectional effects between the two variables were determined to be causal associations (e.g., T1 anxiety predicts T2 depression, and T2 anxiety predicts T3 depression), and bidirectional effects between the two variables were determined to be cross-lagged associations (e.g., T1 anxiety predicts T2 depression, and T1 depression predicts T2 anxiety). According to a suggestion by Guo et al (2015), multigroup comparisons with SEM were used to test for gender difference in the associations among loneliness, anxiety, and depression.

A series of model fit indices of root-mean-square error of approximation (RMSEA), chi-squared ($\chi^2$) statistic, degree of freedom (df), comparative fit index (CFI), and Tucker–Lewis Index (TLI) were used to assess each of the SEM. Studies have indicated that smaller $\chi^2/\text{df}$ and RMSEA values reflect better models, while larger CFI and TLI values reflect better models (Brown, 2015; Hu and Bentler, 1999). The models of the present study were generally nested models. Therefore, $\Delta\chi^2/\Delta\text{df}$ could be used to determine which model is more accurate. A significant $\Delta\chi^2/\Delta\text{df}$ indicates that the less constrained model should be retained.
3 | RESULTS

3.1 | Descriptive statistics and difference test

All variables of interest were highly correlated at each time point, respectively, which is to be expected (see Table 1). The clinical cutoff of anxiety score was 40; 10 (2.18%) students’ anxiety scores were higher than 40 at T1, 29 (6.33%) had scores higher than 40 at T2, and 27 (5.90%) had scores higher than 40 at T3. The clinical cutoff of depression score was 56; 6 (1.31%) students’ depression scores were higher than 56 at T1, 6 (1.31%) had scores higher than 56 at T2, and 11 (2.40%) had scores higher than 56 at T3.

A significant main effect of gender on loneliness was observed, $F(1, 456) = 12.80, p < 0.01, \eta^2_p = 0.03$. Female students ($M = 41.40, SD = 9.04$) had a higher level of loneliness than did male students ($M = 38.40, SD = 9.19$). The main effect of time was nonsignificant, $F(1, 456) = 0.05, p = 0.82, \eta^2_p = 0.00$; the interaction effect of gender and time was also nonsignificant, $F(1, 456) = 2.52, p = 0.11, \eta^2_p = 0.01$.

The main effect of gender was not significant, $F(1, 456) = 1.60, p = 0.21, \eta^2_p = 0.00$; that of time was also nonsignificant, $F(1, 456) = 1.50, p = 0.22, \eta^2_p = 0.00$. The gender $\times$ time interaction exerted a significant main effect on anxiety, $F(1, 456) = 4.35, p < 0.05, \eta^2_p = 0.01$. Simple effect analysis demonstrated that female students ($M = 25.67, SD = 9.98$) had a higher level of anxiety than did male students ($M = 24.12, SD = 6.66$) at T2, $F(1, 456) = 3.88, p < 0.05, \eta^2_p = 0.01$.

Gender exerted a significant main effect on depression, $F(1, 456) = 9.89, p < 0.01, \eta^2_p = 0.02$; female students ($M = 40.32, SD = 11.08$) had a higher level of depression than did male students ($M = 37.59, SD = 10.24$). The main effect of time on depression was also significant, $F(1, 456) = 7.00, p < 0.01, \eta^2_p = 0.02$; simple effect analysis indicated that levels of depression were higher at T3 ($M = 39.50, SD = 11.39$) than at T2 ($M = 38.31, SD = 10.34$), $F(1, 456) = 7.05, p < 0.01, \eta^2_p = 0.02$. The main effect of the gender $\times$ time interaction was nonsignificant, $F(1, 456) = 0.01, p = 0.92, \eta^2_p = 0.00$.

3.2 | Cross-lagged associations and their mediating mechanisms

Cross-lagged panel analysis was used to test reciprocal associations among loneliness, anxiety, and depression (Figure 1). The model yielded suitable model fit indices, $\chi^2 (7) = 44.70, p < 0.001$, RMSEA = 0.05, TLI = 0.92, CFI = 0.99. Loneliness and depression

<table>
<thead>
<tr>
<th>Variables</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
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</thead>
<tbody>
<tr>
<td>1. T1 loneliness</td>
<td>1</td>
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<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>2. T2 loneliness</td>
<td>0.69**</td>
<td>1</td>
<td></td>
<td></td>
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<tr>
<td>3. T3 loneliness</td>
<td>0.63**</td>
<td>0.74**</td>
<td>1</td>
<td></td>
<td></td>
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<tr>
<td>4. T1 anxiety</td>
<td>0.31**</td>
<td>0.25**</td>
<td>0.25**</td>
<td>1</td>
<td></td>
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<tr>
<td>5. T2 anxiety</td>
<td>0.32**</td>
<td>0.38**</td>
<td>0.33**</td>
<td>0.39**</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6. T3 anxiety</td>
<td>0.32**</td>
<td>0.31**</td>
<td>0.33**</td>
<td>0.39**</td>
<td>0.61**</td>
<td>1</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>7. T1 depression</td>
<td>0.73**</td>
<td>0.60**</td>
<td>0.61**</td>
<td>0.38**</td>
<td>0.36**</td>
<td>0.34**</td>
<td>1</td>
<td></td>
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<tr>
<td>8. T2 depression</td>
<td>0.56**</td>
<td>0.75**</td>
<td>0.66**</td>
<td>0.30**</td>
<td>0.43**</td>
<td>0.37**</td>
<td>0.63**</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>9. T3 depression</td>
<td>0.52**</td>
<td>0.63**</td>
<td>0.79**</td>
<td>0.29**</td>
<td>0.38**</td>
<td>0.39**</td>
<td>0.62**</td>
<td>0.70**</td>
<td>1</td>
</tr>
</tbody>
</table>

*p < 0.05, **p < 0.01.
predicted each other over time, depression predicted anxiety over time, and anxiety at T2 predicted depression at T3 (see Table 2). The significance of the mediational paths among loneliness, anxiety, and depression were tested through bootstrapping. According to Shrout and Bolger (2002), "a mediational effect is significant at the 0.05 level if the 95% confidence level does not include zero." The results indicated that loneliness at T1 was mediated by depression at T2 in its effect on anxiety at T3 (95% CI: 0.00–0.06).

### 3.3 | Gender difference in cross-lagged associations among loneliness, anxiety, and depression

Multiple group comparisons were used to investigate gender differences (with gender coded as a categorical variable) in cross-lagged associations among loneliness, anxiety, and depression within aforementioned model. Only the cross-lagged paths between the selected variables were tested. In the constrained model, the paths were considered one by one, and each was constrained to be equal across male and female students. The models were then compared with the fully unconstrained model, and the significant $\Delta \chi^2/\Delta df$ suggested a significant gender difference. The results of multiple group comparisons revealed no gender differences in cross-lagged associations among loneliness, anxiety, and depression: T1 anxiety $\rightarrow$ T2 loneliness ($\chi^2 = 0.03$, $\Delta df = 1$, $p = 0.87$), T1 depression $\rightarrow$ T2 loneliness ($\chi^2 = 0.32$, $\Delta df = 1$, $p = 0.57$), T2 anxiety $\rightarrow$ T3 loneliness ($\chi^2 = 0.32$, $\Delta df = 1$, $p = 0.57$), T2 depression $\rightarrow$ T3 loneliness ($\chi^2 = 0.01$, $\Delta df = 1$, $p = 0.91$); T1 loneliness $\rightarrow$ T2 anxiety ($\chi^2 = 1.19$, $\Delta df = 1$, $p = 0.28$), T1 loneliness $\rightarrow$ T2 depression ($\chi^2 = 0.58$, $\Delta df = 1$, $p = 0.45$), T2 loneliness $\rightarrow$ T3 anxiety ($\chi^2 = 0.49$, $\Delta df = 1$, $p = 0.49$), T2 loneliness $\rightarrow$ T3 depression ($\chi^2 = 0.28$, $\Delta df = 1$, $p = 0.60$); T1 anxiety $\rightarrow$ T2 depression ($\chi^2 = 2.41$, $\Delta df = 1$, $p = 0.12$), T2 anxiety $\rightarrow$ T3 depression ($\chi^2 = 1.47$, $\Delta df = 1$, $p = 0.23$), T1 depression $\rightarrow$ T2 anxiety ($\chi^2 = 0.09$, $\Delta df = 1$, $p = 0.76$), T2 depression $\rightarrow$ T3 anxiety ($\chi^2 = 0.03$, $\Delta df = 1$, $p = 0.86$). Furthermore, the model yielded suitable model fit indices for both male students ($\chi^2 = 16.98$, $df = 7$, $p < 0.01$, TLI = 0.97, CFI = 0.99, RMSEA = 0.04) and female students ($\chi^2 = 31.72$, $df = 7$, $p < 0.01$, TLI = 0.88, CFI = 0.98, RMSEA = 0.05).

### 4 | DISCUSSION

#### 4.1 | Bidirectional associations between loneliness and depression

The present study determined that loneliness and depression predicted each other across time, which is consistent with the findings of previous studies (Hsueh et al., 2019; Fernandes et al., 2018; Holvast et al., 2015). Although both loneliness and depression are linked to negative emotions, large number studies have defined loneliness and depression as two independent variables (Isik et al., 2020; Shaw & Gant, 2002). For example, loneliness is caused by negative thoughts and feelings of being isolated and disconnected from others, which tend to stem from problems in interpersonal relationships (Russell et al., 1978). By contrast, depression involves feelings of helplessness and hopelessness, psychomotor retardation, loss of appetite, and sleep disturbance, which are typically considered general psychiatric problems (Radloff, 1977). Therefore, loneliness and depression were defined as two different variables in the present study. Studies have suggested that loneliness is positively associated with social isolation, which engenders further mental health problems, such as depression (Richardson, Elliott, Roberts, & Jansen, 2016). Moreover, Richardson et al. suggested that university time was a critical period in the development of depression among individuals with loneliness, because university students generally leave their family home and have to form new friendships. Loneliness in students is associated with poor interpersonal relationships, which causes negative emotions and depression. Therefore, loneliness can increase individuals’ depression. Furthermore, depression can increase individuals’ loneliness by reducing individuals’ interpersonal functioning (e.g., social skills) (Shaw & Gant, 2002), which may reduce their desire to be involved in social interactions. The decrease in social interactions could reduce social support from others, causing further loneliness.

<table>
<thead>
<tr>
<th>Items Paths</th>
<th>T1→T2 $\beta$</th>
<th>SE</th>
<th>P</th>
<th>T2→T3 $\beta$</th>
<th>SE</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Autoregressive effect of anxiety</td>
<td>0.36</td>
<td>0.04</td>
<td>&lt;0.001</td>
<td>0.58</td>
<td>0.03</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Autoregressive effect of depression</td>
<td>0.53</td>
<td>0.03</td>
<td>&lt;0.001</td>
<td>0.58</td>
<td>0.03</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Autoregressive effect of loneliness</td>
<td>0.61</td>
<td>0.03</td>
<td>&lt;0.001</td>
<td>0.65</td>
<td>0.03</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Anxiety $\rightarrow$ loneliness</td>
<td>0.01</td>
<td>0.06</td>
<td>0.866</td>
<td>0.03</td>
<td>0.04</td>
<td>0.460</td>
</tr>
<tr>
<td>Depression $\rightarrow$ loneliness</td>
<td>0.18</td>
<td>0.05</td>
<td>&lt;0.001</td>
<td>0.21</td>
<td>0.04</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Loneliness $\rightarrow$ anxiety</td>
<td>0.10</td>
<td>0.06</td>
<td>0.081</td>
<td>0.01</td>
<td>0.06</td>
<td>0.871</td>
</tr>
<tr>
<td>Loneliness $\rightarrow$ depression</td>
<td>0.24</td>
<td>0.06</td>
<td>&lt;0.001</td>
<td>0.31</td>
<td>0.06</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Anxiety $\rightarrow$ depression</td>
<td>0.12</td>
<td>0.07</td>
<td>0.069</td>
<td>0.12</td>
<td>0.05</td>
<td>0.013</td>
</tr>
<tr>
<td>Depression $\rightarrow$ anxiety</td>
<td>0.14</td>
<td>0.05</td>
<td>&lt;0.001</td>
<td>0.12</td>
<td>0.05</td>
<td>0.024</td>
</tr>
</tbody>
</table>

**Table 2**: Regression coefficients of cross-lagged associations among loneliness, anxiety, and depression.
Therefore, the association between loneliness and depression is bidirectional. The present study is the first to investigate the cross-legged association between loneliness and depression among university students during the COVID-19 pandemic. The temporal cross-legged associations were significantly stronger and more robust than those during other periods. For example, $\beta$ values between loneliness and depression ranged from 0.18 to 0.31 in the present study, whereas $\beta$ values in the study by Hsueh et al. ranged from 0.03 to 0.14. The associations may be stronger and more robust because of the increased level of loneliness and depression. For example, students were recommended to stay at home; thus, face-to-face interactions with friends were limited. However, the reduction in face-to-face interactions could hinder sufficient social support, which may engender loneliness (Msw & Volicer, 2020). Students usually have many ways to overcome loneliness, such as exercise (Page & Hammermeister, 1995) or shopping outside (Kim, Kang, & Kim, 2005), and the limited traveling may cause negative emotions and depression.

4.2 Dynamic associations between anxiety and depression

The present results indicate that the cross-lagged associations between anxiety and depression are dynamic, in line with the reports of relevant daily diary studies (Doane & Thurston, 2014; Mor, 2010; Starr & Davila, 2012; Shrout et al., 2010). Moreover, the present results confirm those of longitudinal studies. The dynamic associations between anxiety and depression could be explained by the tripartite model. The model indicated that both anxiety and depression could be caused by negative emotions despite their independent unique characteristics (Clark & Watson, 1991). According to this model, the shared negative emotions could cause anxiety and depression to predict each other across time. Furthermore, anxiety and depression are generally associated with the same abnormalities in neural circuits (Ressler & Mayberg, 2007). Kehne and Cain (2010) reported that both anxiety and depression are associated with the hypothalamic-pituitary-adrenal (HPA) system, which has a critical effect on hormonal systems. For example, anxiety and depression disorders are both associated with increased levels of the corticotropin-releasing factor, which is a hormone secreted during stress response (Boyer, 2000). The shared abnormalities in neural circuits may be another factor leading to anxiety and depression predicting each other across time.

In the present study, anxiety and depression were mutually predictive across time, partially consistent with the findings of relevant studies suggesting that initial anxiety predicts subsequent depression and that initial depression does not predict subsequent anxiety (Fichter et al., 2010; Kessler et al., 2008; Lord et al., 2020). These inconsistent results may be related to several factors. First, different samples were used. Most studies used social group samples, whereas university students were investigated in the present study. University students with higher levels of depression may have a higher risk of anxiety disorder because of the lack of social experience, which may be a moderating factor in the association between loneliness and depression. Second, the association between anxiety and depression may be stronger during the COVID-19 pandemic period. For example, university students with depression may overcome feelings of anxiety by exercising (Page & Hammermeister, 1995) or shopping outside (Kim et al., 2005) under normal conditions. However, students had to stay at home during the COVID-19 pandemic period, which might have increased the effects of depression on anxiety. Third, a meta-analysis revealed that the strength of the sequential relationships between anxiety and depression degraded as the intervals between assessments increased (Jacobson & Newman, 2017a and b). In the present study, the temporal associations between anxiety and depression were assessed within 3 months; this period was considerably shorter than those in the studies by Fichter et al. (2010), Kessler et al. (2008), and Lord et al. (2020) of 25, 11, and 10 years, respectively. The shorter study period may correspond to stronger associations between anxiety and depression. Additionally, the present study yielded unanticipated findings; for instance, T1 anxiety could not predict T2 depression across time, and T2 anxiety could not predict T3 depression across time. These findings may be due to the temporal association between anxiety and depression being examined in the context of the COVID-19 pandemic, which resulted in the association between anxiety and depression being dynamic. To verify this hypothesis, studies comparing the associations between anxiety and depression during and after the pandemic are needed.

4.3 Reciprocal associations among loneliness, anxiety, and depression

A critical finding of this study was that loneliness predicted both anxiety and depression, depression mediated the predictive effect of loneliness on anxiety over time. The mediating role of depression may be ascribable to the fact that loneliness is associated with poor interpersonal relationships, causing negative emotions that are linked to depression (James et al., 2010). However, in this study, depression and anxiety were positively associated, and higher levels of depression increase levels of anxiety (Fichter et al., 2010; Kessler et al., 2008), and this result was consistent with the illustrations in the introduction section. Furthermore, the results of the present study further verify the results of a cross-sectional study (Chang, 2018). Most studies have regarded anxiety and depression as two outcome variables, and few studies have tested the association among anxiety, depression, and other variables within one model (Schönberger, Ponsford, Gould, & Johnston, 2011; Innstrand, Langballe, & Falkum, 2012; Chang, 2018). We tested the association among loneliness, anxiety, depression, and simultaneous anxiety and depression, and the result indicated that depression was both the outcome variable and antecedent variable of loneliness, whereas anxiety tended to be the outcome variable of loneliness.
Although large number of cross sectional studies have found a significant association between loneliness and anxiety (e.g., Eric, Roth, Coles, Heimberg, Bravata, & Moser, 2004; Nkyi & Ninnoni, 2020; Odaci & Kalkan, 2010; which was consistent with the present study), these studies have not tested the cross-legged associations between them, especially with the context of COVID-19. The present study determined the association between loneliness and depression was stronger than that between loneliness and anxiety. The different associations may be caused by similar characteristics. For example, anxiety is significantly associated with physiological arousal, such as tension, shakiness, and nervousness, whereas depression is associated with reduced positive emotions, such as pleasure and interest (Compas et al., 1993). Loneliness was defined as negative thoughts and feelings of being isolated and disconnected from others (Russell et al., 1978), which was more closely related to reduced positive emotions than increased physiological arousal. Therefore, loneliness and depression share more similar characteristics, and the association between the two was determined to be stronger than the association between loneliness and anxiety. Physiological studies have revealed that anxiety is positively associated with glucocorticoid levels, whereas depression is negatively associated with glucocorticoid levels, which is consistent with loneliness (Boyer, 2000; Hawkley, Cole, Capitanio, Norman, & Cacioppo, 2012). The results of these studies indicated that depression and loneliness have more similar physiological bases than loneliness and anxiety, which further explains the stronger association.

4.4 Gender differences in the studied variables and their cross-legged associations

Gender differences were observed in loneliness and depression. Women reported higher levels of loneliness and depression than did men, which is in accordance with the result of previous studies (Moghanibashi-Mansourieh, 2020; Gorrochategi, Munitis, Santamaria, & Etkebarria, 2020; Özdin & Ö zdin, 2020) that reported that female students were more sensitive to negative emotions. Loneliness and depression are all positively associated with negative emotions (Cambron, Acitelli, & Pettit, 2009; Liu & Alloy, 2010). Moreover, studies have suggested that women are more likely than men to pay attention to their own depressive mood, and that this difference in response styles could stem from socialization processes that contribute to gender stereotypes (Martin & Davies, 2001; Piko, 2001). From this perspective, although the use of emotion-focused coping strategies increased among the participants during the COVID-19 pandemic overall, regardless of gender, the male students tended to select coping strategies involving emotional distraction, which may have contributed to greater disengagement from feelings of loneliness and depression.

No gender differences were observed in the cross-legged associations among anxiety, loneliness, and depression, which contrasts with the result of a study by Chang (2018), who reported that associations among loneliness, anxiety, and depression were stronger in women than men. These inconsistent results might have been caused by two factors. First, cultural differences might have affected the results. Chang indicated that African American women were subjected to more stressors (e.g., sexual discrimination and racial discrimination) for being a double minority (i.e., Black and female), which could increase the association among loneliness, anxiety, and depression. However, all university students in the present study were Chinese and were thus not exposed to the same stressors as those reported in Chang's study. No gender differences were observed in the studied variables. Second, Chang's study was cross-sectional, whereas the present study was longitudinal. Therefore, gender differences in the association among loneliness, anxiety, and depression may be correlational inferences rather than a causal inference. However, these two possibilities require further research to verify.

4.5 Implications for prevention of loneliness–anxiety–depression comorbidity

These results indicate that loneliness, anxiety, and depression are closely associated during the COVID-19 pandemic period, which may cause loneliness–anxiety–depression comorbidity. However, the effects of loneliness on anxiety and depression are larger than the effects of anxiety and depression on loneliness, which suggests that interventions should target loneliness to disrupt the loneliness–anxiety–depression comorbidity cycle. Studies have suggested that encouraging lonely individuals to enhance social contacts (e.g., make new friends or increase their communication frequency with old friends) and attend social activities (e.g., playing cards, joining a club, or playing ball games) could reduce perceived loneliness (Isaac, Stewart, Artero, Ancelin, & Ritchie, 2009). However, with regard to safety considerations in the COVID-19 pandemic, students can opt for virtual or otherwise socially distanced alternatives. Furthermore, depression plays a critical role in the effects of loneliness on anxiety, which indicates that interventions targeting individuals' depression also could break the loneliness–anxiety–depression comorbidity cycle. Collective activities and periodi collective counselling may help reduce individuals' depression. University students could help each other and encourage each other during activities, which could increase positive emotions and reduce depressive emotions. Finally, female students had higher levels of loneliness, anxiety, and depression during the COVID-19 pandemic period, which suggested that teachers and parents should pay closer attention to female students than male students. Support from teachers and parents could reduce individuals’ negative emotions (Mcdowell & Parke, 2000; Tao, Zhou, & Wang, 2010) and reduce loneliness, anxiety, and depression.

4.6 Limitations and future directions

The present study is the first to investigate the temporal association among loneliness, anxiety, and depression during the COVID-19
pandemic period. This study has some limitations that must be addressed. First, all the data were collected from Chinese university students, which may limit the generalizability of findings to other groups and countries. Therefore, the temporal associations among loneliness, anxiety, and depression during the COVID-19 pandemic period warrant verification in other groups and countries. Second, questionnaires were administered to measure individuals’ loneliness, anxiety, and depression levels instead of experimental manipulations. Experimental studies are needed to further test the association among loneliness, anxiety, and depression. For example, a study determined that individuals with anxiety or depression disorders have higher judgemental biases (Mineka & Sutton, 1992). Future studies can use judgemental biases to identify individuals with high and low levels of anxiety or depression and test the effects of anxiety or depression on their loneliness. Third, the observed variables were used instead of latent variables of loneliness, anxiety, and depression. Therefore, testing the measurement invariance of each variable with the same measurement tools is difficult. A study suggested that the predictive power of each item may be different even though the same items were used to measure the same variables across time, which may introduce measurement errors in the analysis (Schuurman, Ferrer, De, & Hamaker, 2016). Therefore, studies with the latent variables of loneliness, anxiety, and depression are needed to test the measurement invariance of each variable and further verify the results of the present study. Fourth, the temporal associations among loneliness, anxiety, and depression were examined in the context of the COVID-19 pandemic. Therefore, different associations may be observed after the end of the pandemic, and the present findings require confirmation through studies not conducted in the same context. Fifth, because the data were collected after the start of the pandemic, no baseline comparison could be made to support the premise that the present findings constitute unique contributions in this context. Therefore, future studies can compare baseline levels of loneliness, anxiety, and depression with their corresponding levels during the COVID-19 pandemic. Finally, the withdrawal of some of the participants during the study may be associated with higher levels of loneliness, anxiety, and depression. As mentioned, no differences between participating and nonparticipating students were observed. Nevertheless, more studies with lower attrition rates are warranted to confirm the present findings.

5 | CONCLUSION

During the COVID-19 pandemic period, loneliness and depression predicted each other over time, and loneliness predicted anxiety over time, mediated by depression. No gender differences were observed in the cross-lagged associations among loneliness, anxiety, and depression during the COVID-19 pandemic period.

DATA AVAILABILITY STATEMENT
The data used to support the findings of this study are available from the corresponding author upon request.

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REFERENCES


