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Is psychological flexibility a mediator between perceived stress and general anxiety or depression among suspected patients of the 2019 coronavirus disease (COVID-19)?

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ABSTRACT
This study is aimed to investigate the status of general anxiety and depression among suspected patients of COVID-19 and explore whether psychological flexibility can serve as a mediator between perceived stress and general anxiety or depression. Total of 180 participants completed the online questionnaire which comprised demographic information, the Perceived Stress Scale (PSS), the 7-item Generalized Anxiety Disorder scale (GAD-7), the 9-item Patients Health Questionnaire (PHQ-9), the Acceptance and Action Questionnaire-II (AAQ-II) and the Cognitive Fusion Questionnaire (CFQ). Statistical methods including correlation analysis, multiple linear regression analysis and structural equation model were used in this study. The scores of 23.9% (43/180) and 34.4% (62/180) of participants were higher than the cut points of GAD-7 and PHQ-9 respectively. Psychological flexibility was significantly correlated with perceived stress, general anxiety and depression. Multiple regression analyses showed the possible mediation effect of psychological flexibility between perceived stress and general anxiety or depression. The structural equation model confirmed that psychological flexibility partially mediated between perceived stress and general anxiety or depression. Our findings suggested the potential benefit of Acceptance and Commitment Therapy (ACT) as a psychological support approach in suspected patients of COVID-19 because ACT targets psychological flexibility.

1. Introduction
Since December 2019, a novel coronavirus initially called SARS-CoV-2 and later coronavirus disease (COVID-19) by the World Health Organization, has emerged and caused respiratory illness in Wuhan, China (World Health Organization, 2020a; Zhu et al., 2020). As the epidemic developed, number of fatalities and laboratory-confirmed cases has risen rapidly; scope of the infection has spread to 31 provinces in mainland China, Hong Kong, Macao and Taiwan, as well as over 200 countries and regions spanning Asia, Europe, Oceania, Americas and Africa. On 30 January 2020, the World Health Organization declared the outbreak a public health emergency of international concern (Mahase, 2020). As the epidemic continued to develop globally, the World Health Organization made an assessment that characterized the COVID-19 as a pandemic on 11 March 2020 (World Health Organization, 2020b). From the outbreak to the present (data updated to June 27 2021), 5535 people died and 118,871 had been infected throughout China, and 3,916,771 people died and 180,492,131 had been infected globally (World Health Organization, 2021). With such fast transmissibility and large affected scope, the COVID-19 pandemic now is a global health threat (Wang, Horby, Hayden, & Gao, 2020), and is by far the largest outbreak of atypical pneumonia since the severe acute respiratory syndrome (SARS) outbreak in 2003.

Because of the fear of infection, the uncertainty of treatment, concerns about the development of the illness, physical discomfort, loneliness from quarantine, social bias and stigma (Mental Health Center of Gansu Province, 2020; Xiang et al., 2020; Xiao, 2020), suspected patients usually suffer from tremendous perceived stress pressure in such epidemics. As we know, people who sustained lasting perceived stress are also more vulnerable to psychological problems such as anxiety and depression (Daudelin-Peltier, Forget, Blais, Deschenes, & Fiset, 2017; Hill, Hellemans, Verma, Gorzalka, & Weinberg, 2012; Klein et al., 2016).

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During the 2003 severe acute respiratory syndrome (SARS) outbreak, which was caused by another coronavirus that killed 916 of 8422 patients with confirmed infection globally (World Health Organization, 2003), a series of psychological problems were reported in suspected patients and the most common problems were anxiety and depression (Zhao, Yang, X, Peng, & Zhang, 2003). A study reported that positive rates of anxiety and depression were 56.1% and 38.7% among suspected SARS patients, respectively (Shen, 2003).

Psychological flexibility is a fundamental aspect of psychological health (Kashdan & Rottenberg, 2010). Hayes defined psychological flexibility as the ability to fully notice experiences in the present moment without judgment and to remain flexible in persisting in or changing behaviours to serve valued ends, mainly reflecting in experiential avoidance and cognitive fusion (Hayes, Strosahl, & Wilson, 2011). Experiential avoidance refers to individuals trying to change the form, frequency, or sensitivity to the situation that their inner experiences appear in their minds, even if this leads to behaviours that are inconsistent with personal values or goals (Hayes, Wilson, Gifford, Follette, & Strosahl, 1996). Cognitive fusion is the tendency of one’s actions to be dictated by their internal content, which makes the individual's behaviour over-controlled by the cognitive evaluation and cannot use the experience of the present to guide behaviour (Hayes, Villatte, Levin, & Hildebrandt, 2011). Therefore, higher degrees of experiential avoidance and cognitive fusion signify lower psychological flexibility and vice versa.

Relevant studies have noted that psychological flexibility is closely associated with psychopathological indicators such as stress, anxiety and depression (Gloster, Klotzsche, Chaker, Hummel, & Hoyer, 2011; Kashdan & Rottenberg, 2010). Furthermore, Hussey and Barnes-Holmes (2012) have indicated the mediating role of psychological flexibility of anxiety and depression, which assessed on the Implicit Relational Assessment Procedure (IRAP) at baseline and again after an experimentally induced sad mood state. Moreover, subsequent researches have suggested that psychological flexibility is a mediator of anxiety or depression among populations with trauma exposure, chronic pain and work-related stress (Gentili et al., 2019; Kurz, Bethay, & Lader-Graham, 2014; Richardson & Jost, 2019). However, the relationship between perceived stress, anxiety, depression and psychological flexibility among suspected patients of COVID-19 is unreported, and whether psychological flexibility acts as a mediating variable among perceived stress and anxiety or depression has not been confirmed. Thus, it is meaningful to explore the above problems and provide timely guidance to apply effective psychological interventions such as Acceptance and Commitment Therapy (ACT) to promote psychological flexibility for suspected patients of COVID-19 in the current pandemic (Hayes & Strosahl, 2004).

Among suspected patients of COVID-19, We hypothesized that: 1) higher perceived stress and lower psychological flexibility will be statistically associated with higher general anxiety and depression; 2) psychological flexibility will mediate or partially mediate the effect of perceived stress on general anxiety or depression.

2. Material and methods

2.1. Design

This is an exploratory, cross-sectional and quantitative study conducted in The Third Xiangya Hospital of Central South University in Changsha city and Hainan General Hospital in Haikou city in China from 30 January to 6 April 2020, through an online survey. Both hospitals are local tertiary general hospitals.

2.2. Participants

We recruited participants who were; 1) diagnosed as suspected cases of COVID-19 according to the Diagnosis and Treatment of Coronavirus Disease (trial version 7) (2020) by doctors at outpatient clinics; 2) over 18 years old and 3) informed and consented to participate. We excluded participants; 1) with poor literacy, reading or comprehension problems which may have difficulty understanding and answering questionnaire; 2) with known severe medical or psychiatric problems; 3) with no access to the internet as the study was conducted through an online survey.

Non-probabilistic convenience sampling was adopted because of resource constraints. Sample size calculations (using G*Power version 3.1 ( Faul, Erdfelder, Buchner, & Lang, 2009 ) determined that 107 participants were needed to provide sufficient power (1-β = 0.95) to detect medium effect size ($\eta^2 = 0.15$) associations using multiple linear regression analyses with two presumed predictors (perceived stress and psychological flexibility), and an alpha level of 0.05. The addition of 15% of non-response rate resulted in the required sample size of 126.

2.3. Measures

The main variables of the study were perceived stress, general anxiety, depression and psychological flexibility. For this study: perceived stress was defined as specific feelings of stress on unpredictable, uncontrollable and overloaded events, the level of perceived stress measured by Perceived Stress Scale was the independent variable; general anxiety was defined as persistent and excessive worry and fear feelings of possible adverse situations, the level of general anxiety measured by 7-item Generalized Anxiety Disorder scale was one of the dependent variables; depression was defined as a kind of negative emotions of persistent and obvious sadness, lack of interest and loss of pleasure, the level of depression measured by 9-item Patients Health Questionnaire was one of the dependent variables; psychological flexibility's definition has been previously described, the level of psychological flexibility measured by Acceptance and Action Questionnaire-II & Cognitive Fusion Questionnaire was the mediator.

2.3.1. Perceived Stress Scale

The version of Perceived Stress Scale (PSS) we used has 14 items (PSS-14) (Cohen, Kamarck, & Mermelstein, 1983), which is a 5-point Likert scale (total scores ranging from 0 to 56), with higher scores representing higher levels of perceived stress. A Chinese version of PSS-14 with satisfactory content validity and reliability (Leung, Lam, & Chan, 2010) was adopted. Cronbach’s alpha in this study was 0.796.

2.3.2. 7-item Generalized Anxiety Disorder scale

7-item Generalized Anxiety Disorder scale (GAD-7) (Spitzer, Kroenke, Williams, & Loewe, 2006) is a 4-point Likert scale (total scores ranging from 0 to 21) use to screen the presence of generalized anxiety disorder; and to measure the severity of general anxiety, with higher scores indicating severer general anxiety. Cut points of 5, 10, and 15 were interpreted as representing mild, moderate, and severe levels of general anxiety. A Chinese version of GAD-7 with satisfactory content validity and reliability (Tong, An, McGonigal, Park, & Zhou, 2016) was adopted. Cronbach’s alpha in this study was 0.939.

2.3.3. 9-item Patients Health Questionnaire

9-item Patients Health Questionnaire (PHQ-9) (Kroenke, Spitzer, & Williams, 2001) is a 4-point Likert scale (total scores ranging from 0 to 27) use to screen for the presence of depression and to measure the severity of depression, with higher scores indicating severer depression. Cut points of 5, 10, 15, and 20 were interpreted as representing mild, moderate, moderately severe, and severe levels of depression. A Chinese version of PHQ-9 with satisfactory content validity and reliability (Wang et al., 2014) was adopted. Cronbach’s alpha in this study was 0.899.

2.3.4. Acceptance and Action Questionnaire-II & Cognitive Fusion Questionnaire

Acceptance and Action Questionnaire-II (AAQ-II) (Fledderus, Voshaar, ten Klooster, & Bohlmeijer, 2012) is a seven-item Likert scale (total
scores ranging from 7 to 49) use to measure experiential avoidance. Higher scores indicate higher degrees of experiential avoidance. A Chinese version of AAQ-II with satisfactory content validity and reliability (Zhang, Chung, Si, & Liu, 2014) was adopted. Cognitive Fusion Questionnaire (CFQ) (Gillanders, Bolderston, Dempster, & Bond, 2010) is a 13-item Likert scale comprised of Cognitive Fusion Questionnaire-Fusion (CFQ-F) with 9 items and Cognitive Fusion Questionnaire-Defusion (CFQ-D) with 4 items. Reliability and validity of the Chinese version of CFQ showed that CFQ-D should be removed for not reaching the psychometric standard in item analysis. However, CFQ-F is a reliable and valid assessment of cognitive fusion (Zhang, Ji et al., 2014). Therefore, we used the Chinese version of CFQ-F to measure cognitive fusion (total scores ranging from 9 to 63), with higher scores reflecting higher degrees of cognitive fusion. The scores of AAQ-II and CFQ-F are added together to measure the level of psychological flexibility, with higher scores reflecting lower psychological flexibility and vice versa (Zhao et al., 2018). Cronbach’s alpha of AAQ-II and CFQ-F in this study was 0.930 and 0.950 respectively.

2.4. Procedure

Doctors in emergency, fever and respiratory outpatient clinics referred suspected patients of COVID-19 to researchers. Then researchers invited potential participants through telephone and sent an online questionnaire to eligible participants via the Wenjuanxing platform (a platform providing functions equivalent to SurveyMonkey platform) through a cell phone message. Informed and consented participants completed the questionnaire at their convenience. All items in the questionnaire were electronically set to be completely answered before it could be submitted successfully.

2.5. Analysis

We used SPSS version 22.0 (IBM Corporation, Armonk, NY, USA) for data analysis. $P < 0.05$ was considered to have statistical significance. Percentages, means and SDs were used to describe the study variables. The 1-way analysis of variance test or t-test was used to examine mean differences in general anxiety and depression among demographic characteristics. The correlations between perceived stress, general anxiety, depression and psychological flexibility were analysed by Pearson’s correlation coefficients.

Multiple linear regression was used to analyse whether and how perceived stress and psychological flexibility can significantly influence general anxiety or depression. First, significant demographic variables were put in Model 1 to control their influence on the dependent variable. Then, Model 2 was established based on Model 1 with the addition of perceived stress. And finally, Model 3 was built by adding psychological flexibility based on Model 2.

We employed the structural equation model (using AMOS version 23.0(IBM Corporation, Armonk, NY, USA)) with 5000 bootstrap samples for further mediation effect confirmation and path coefficient estimation (Baraff, McCormick, & Raftery, 2016). Four indices were employed to assess the goodness of fit of the model (Iacobucci, 2010): Chi-square statistic ($\chi^2$) and its p-value $>0.05$, $\chi^2/df$ of 3 or less, Comparative Fit Index (CFI) of 0.95 or more, and Standardized Root Mean Square Residual (SRMR) of 0.09 or less. The path coefficients were accepted as significant at the 0.05 level.

2.6. Ethical approval

The study was approved by the Institutional Research Review Board of The Third Xiangya Hospital of Central South University (approval number: I20002) and by the boards of executives of both two hospitals.

3. Results

We telephoned a total of 227 potential participants, 212 were eligible for the study and 180 submitted their questionnaires finally.

3.1. Preliminary analyses

Detailed demographic characteristics are reported in Table 1. The mean scores of measures are reported in Table 2. Of the total, 23.9% (43/180) fell at or above the cut points of GAD-7 and 34.4% (62/180) fell at or above the cut points of PHQ-9. Age had significant differences in depression ($P < 0.05$) in univariate analyses (Table 1).

3.2. Correlation analyses

As shown in Table 2, all variables were significantly correlated in the predicted directions ($P < 0.001$).

3.3. Multiple linear regression analyses

Taking general anxiety as the dependent variable, when psychological flexibility was added in Model 3, the influence of perceived stress on general anxiety decreased from 0.614 to 0.271 (decreased by 34.3%), and the multiple linear regression accounted for 59.9% variance of Table 1

| Demographic variable          | n (%) | General anxiety | Depression |
|------------------------------|-------|-----------------|------------|
|                             | M (SD) | P               | M (SD)     | P          |
| Gender                       |       |                 |            |
| Male                         | 107 (59.4) | 2.79 (3.88) | 3.65 (4.55) |
| Female                       | 73 (40.6)  | 2.86 (4.18) | 3.82 (4.38) |
| Age                          |       |                 |            |
| 18–29                        | 57 (31.7)  | 2.54 (3.71) | 3.49 (4.28) |
| 30–39                        | 75 (41.7)  | 2.40 (3.92) | 3.05 (4.13) |
| 40–49                        | 19 (10.6)   | 3.89 (4.29) | 3.11 (4.37) |
| 50–59                        | 18 (10.0)   | 4.00 (5.36) | 6.33 (6.47) |
| ≥60                          | 11 (6.1)    | 3.36 (2.34) | 6.27 (3.00) |
| Marital status               |       |                 |            |
| Married                      | 121 (67.2) | 2.99 (4.29) | 4.10 (4.93) |
| Unmarried/divorced/widowed   | 59 (32.8)   | 2.47 (3.31) | 2.95 (3.24) |
| Education                    |       |                 |            |
| Junior high school or below  | 28 (15.6)   | 3.43 (4.59) | 5.00 (5.09) |
| Senior high school           | 28 (15.6)   | 3.19 (3.99) | 3.86 (3.94) |
| Three-year college           | 32 (17.8)   | 2.38 (4.15) | 2.56 (4.12) |
| Bachelor's degree            | 67 (37.2)   | 3.09 (4.23) | 4.00 (4.67) |
| Master's degree or above     | 25 (13.9)   | 2.68 (3.52) | 2.88 (4.00) |
| Monthly income (RMB)         |       |                 |            |
| <3000                        | 24 (13.3)   | 3.58 (4.55) | 5.54 (4.75) |
| 3000–5000                    | 49 (27.2)   | 2.35 (3.47) | 2.96 (3.99) |
| 5000–10,000                  | 63 (35.0)   | 3.03 (4.63) | 3.78 (5.15) |
| >10,000                      | 44 (24.4)   | 2.64 (3.20) | 3.50 (3.55) |

* $P < 0.05$.
outcomes. The standardized structural equation model analysis was explained after psychological flexibility was added (Table 3). Accounted for 50.7% variance of depression, a total of 16.0% of which was confirmed the direct, indirect, and total effects of mediation. The standardized indices of two models presented good model fits:

| Model | Variables                | 1     | 2     | 3     | 4     |
|-------|--------------------------|-------|-------|-------|-------|
|       |                          | M(SD) | M(SD) | M(SD) | M(SD) |
|       | 1. Perceived stress      | 20.28 | 7.71  | -     | -     |
|       | 2. General anxiety       | 2.82  | 3.99  | 0.614*** | -     |
|       | 3. Depression            | 3.72  | 4.47  | 0.568*** | 0.784*** | -     |
|       | 4. Psychological         | 42.50 | 5.84*** | 0.745*** | 0.681*** | -     |
|       | flexibility              | (19.77)|       |       |       |

Two-tailed tests. *** P < .001.

general anxiety, a total of 22.6% of which was explained after psychological flexibility was added (Table 3).

Taking depression as the dependent variable, when psychological flexibility was added in Model 3, age was no longer a significant predictor; the influence of perceived stress on depression decreased from 0.561 to 0.268 (decreased by 29.3%), and the multiple linear regression accounted for 50.7% variance of depression, a total of 16.0% of which was explained after psychological flexibility was added (Table 3).

3.4. Mediation analyses

The regression analyses indicated the possible mediation effect of psychological flexibility when general anxiety and depression were the outcomes. The standardized structural equation model analysis confirmed the direct, indirect, and total effects of mediation. The standardized indices of two models presented good model fits: $\chi^2 = 0.047(P = 0.828)$, $\chi^2/df = 0.047$, CFI = 1.000, SRMR = 0.002; $\chi^2 = 0.014(P = 0.907)$, $\chi^2/df = 0.014$, CFI = 1.000, SRMR = 0.001. The standardized path coefficients among the variables of the two models were all significant ($P < 0.01$), shown in Fig. 1.

The standardized total effects, direct effects and indirect effects for both mediation models of general anxiety and depression are reported in Table 4. The indirect effect of perceived stress on general anxiety through psychological flexibility accounted for 66.8% (0.410/0.614) of the total effect. The indirect effect of perceived stress on depression through psychological flexibility accounted for 65.5% (0.372/0.568) of the total effect. It means that psychological flexibility plays a partially mediating role and this role accounts for more than half of the total effect for both models.

4. Discussion

First and foremost, we found the positive rates of screening general anxiety and depression among suspected patients of COVID-19 were 23.9% and 34.4% respectively. Additionally, we found that perceived stress, general anxiety, depression and psychological flexibility in this population significantly correlated with each other. Lastly and most importantly, we found psychological flexibility was a mediator (as a partial mediator) between perceived stress and general anxiety or depression.

The positive rates of screening general anxiety and depression among suspected patients of COVID-19 were 23.9% and 34.4%, which were much higher than the normative data from general residents in China (7.8% and 13.4%) (Qi, 2014). Comparing data of this study to the previous study, 56.1% and 38.7% of suspected patients of SARS in a previous study had anxiety and depressive symptoms respectively. In contrast, the data from this study seems to show a more moderate status (Shen, 2003). This may be because participants in the previous study were under hospital quarantine. However, most of the participants in our study were under home quarantine due to the shortage of health equipment in the current outbreak, and the atmosphere at home is more relaxed and comfortable than that in the hospital. However, this comparison among these studies should be made with caution since these two studies used different measurements.

Our results suggested that perceived stress was positively and significantly associated with the severity of general anxiety and depression. In other words, the more perceived stress that one reported, the more symptoms they experienced. This is consistent with an abundance of prior research that linked perceived stress with anxiety and depression (Bergdahl & Bergdahl, 2002; de Rooij, Schene, Phillips, & Roseboom, 2010; Rusli, Edimansyah, & Naing, 2009). In addition to testing the effect of perceived stress on symptomatology, we tested the association between perceived stress and psychological flexibility. The results indicated that individuals who had experienced higher perceived stress reported lower levels of psychological flexibility. This is consistent with previous literature that reported more stress was associated with lower psychological flexibility (Wesese, Lieb, Meyer, Hofer, & Gloster, 2018). We also found that lower psychological flexibility was associated with higher levels of general anxiety and depression, which have echoed in previous studies in other populations suggesting lower psychological flexibility is associated with greater depressive symptoms, more anxiety-related symptoms, and greater overall psychological ill-health (Bond et al., 2011; Dalrymple & Herbert, 2007; Karekla & Panayiotou, 2011).

Most importantly, perceived stress indirectly affects anxiety and depression through psychological flexibility from regression analysis results. The structural equation model verified that psychological flexibility was a mediator (as a partial mediator) between perceived stress and general anxiety or depression. These results suggest that higher psychological flexibility plays a protective role in reducing the psychological impact of stress on individuals and it is a protective mediator between perceived stress and general anxiety or depression. Although other studies have reported a significant mediation of psychological flexibility on anxiety or depression among chronic-pain individuals, trauma-exposed individuals and individuals with workplace-related stress (Gentili et al., 2019; Kurz et al., 2014; Richardson & Jost, 2019). Nonetheless, to the best of our knowledge, this is the first study to date, which shows that when suspected patients of COVID-19 are facing...
the same pressures, individuals with higher levels of psychological flexibility are less likely to have general anxiety and depression. Consequently, relevant interventions such as ACT should be implemented to enhance psychological flexibility. Considering the particular circumstances of this pandemic, online ACT interventions or ACT self-help books could be used in suspected patients of COVID-19, which were proven to improve psychological flexibility in other populations (Pots et al., 2016; Wersebe et al., 2018).

The above findings supported our hypotheses and suggested that ACT is a promising psychological support approach for suspected patients of COVID-19. The positive rates of screening general anxiety and depression among suspected patients of COVID-19 were 23.9% and 34.4% and psychological flexibility was a mediator between perceived stress and general anxiety or depression. The findings of this study provided important implications of effective psychological interventions for suspected patients of COVID-19. Future studies should explore the potential effectiveness of ACT as a psychological support approach in this population because ACT targets psychological flexibility.

CRediT authorship contribution statement
Chi Huang: project development, data collection, data analysis and manuscript writing. Jiaying Xie: data collection, data analysis, and manuscript editing. Theressa Owusu: data collection and manuscript editing. Zhiheng Chen: project development. Jiangang Wang: manuscript editing. Chunxiang Qin: project development and manuscript editing. Qingnan He: project development and manuscript editing.

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