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Research paper

Mapping post-traumatic stress disorder symptoms and quality of life among residents of Wuhan, China after the COVID-19 outbreak: A network perspective

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ABSTRACT

Objectives: The Coronavirus Disease 2019 (COVID-19) outbreak may have a long-term impact on mental health in the general population. This study examined inter-relationships between post-traumatic stress disorder symptoms (PTSS) and quality of life (QOL) in Wuhan residents after the COVID-19 outbreak using network approach.

Methods: A cross-sectional survey was conducted between May 25 and June 18, 2020. PTSS and QOL were measured using Chinese versions of the Post-Traumatic Stress Disorder Checklist - Civilian Version and the World Health Organization Quality of Life Questionnaire - brief version, respectively.

Results: A total of 2598 participants were included. A network analysis revealed “Avoiding reminders”, “Feeling emotionally numb”, “Avoiding thoughts”, “Hypervigilance”, and “Reliving experiences” as the most central (influential) nodes in PTSS network models both before and after controlling for covariates. The connection between “Avoiding thoughts” and “Avoiding reminders” had the strongest edge. Three symptom communities were detected and can be summarized as “re-experiencing and avoidance”, “negative changes in thinking and mood”, and “hyperarousal”. The bridge symptoms connecting PTSS and QOL were “Sleep disturbances”, “Irritability”, and “Loss of interest”.

Limitations: Limitations included the cross-sectional study design, self-report measures in data collection, and lack of follow-ups beyond the initial phase of the pandemic.

Conclusions: PTSS were common among Wuhan residents even after the initial COVID-19 outbreak had passed. Attention should be paid to lingering symptoms of avoiding reminders, emotional numbness, avoiding thoughts, hypervigilance, and reliving experiences in treating PTSS related to the COVID-19 outbreak.

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1. Introduction

The Coronavirus Disease 2019 (COVID-19) outbreak first emerged in Wuhan, China at the end of 2019 (Lu et al., 2020). Living in its epicenter, residents of Wuhan were the first population to confront this devastating bio-disaster directly. Fear of infection from a novel and unknown disease, lack of effective treatment and specific preventive measures, and potentially fatal consequences contributed to severe psychological stress among Wuhan residents. Furthermore, even though strict preventive measures, such as quarantine, isolation, and traffic restrictions (Xiao et al., 2020) efficiently reduce the spread of novel viruses (severe acute respiratory syndrome coronavirus-2; SARS-CoV-2), they also exacerbated psychological distress (Ammar et al., 2020; Barratt et al., 2011; González-Blanco et al., 2020), which persisted until outbound travel restrictions were lifted on April 8th, 2020 (Xinhuanet, 2020).

Even after the local outbreak was well controlled and strict preventive measures were terminated, people could experience persistent psychological problems (Ammar et al., 2020; Barratt et al., 2011; González-Blanco et al., 2020; Murphy et al., 2021; Nguyen-Fong et al., 2022). To date, several waves of the outbreak have occurred in China since 2020, and numerous studies have investigated psychological consequences of the COVID-19 outbreak within the general population and specific subpopulations. The common reported psychological problems in the general population included anxiety, depression, insomnia, stress, and distress (Alzahrai et al., 2022; Bello et al., 2022; Hernández-Díaz et al., 2022; Pappa et al., 2022; Zhang et al., 2022). Nevertheless, evidence has indicated that mental health such as depression is greatly influenced by sociocultural contexts (Kleinman, 2004; Roche et al., 2021; Zhao et al., 2021a), therefore, it is important to investigate psychological problems among populations encountering the COVID-19 outbreak, since this can benefit the development of psychological/psychiatric interventions for people suffering from psychiatric comorbidities following severe natural disaster.

When the Wuhan COVID-19 outbreak was under control in 2020, post-traumatic stress disorder (PTSD) and its related symptoms (PTSS) were among the most commonly reported mental health problems of health professionals (Huang et al., 2020; Yin et al., 2020), confirmed and suspected cases with COVID-19 (Bo et al., 2021), and the general population (González-Sanguino et al., 2020; Liang et al., 2020; Liu et al., 2020). The epidemiology of PTSS in Wuhan residents has been investigated during the early stage of the outbreak. For instance, the prevalence of PTSS as measured by PTSD Checklist for the DSM-5 (PCL-5) was 7.0% among 285 Wuhan residents (Liu et al., 2020). However, the prevalence of PTSS among Wuhan residents after the COVID-19 peak had passed is not clear. Furthermore, most studies on PTSS related to COVID-19 have been based on total scores of standard scales, yet PTSS comprise clusters of individual symptoms with different neuropsychological mechanisms. Consequently, it is not clear whether particular PTSS symptoms or symptom clusters are more salient than others for people affected by the pandemic.

To elaborate, traditional conceptualizations of the psychopathology of PTSS presume that the underlying psychiatric disorder causes the occurrence of clinical manifestations, such as symptoms related to re-experiencing and avoidance, negative changes in thinking and mood and hyperarousal, as measured by diagnostic instruments, such as the Diagnostic and Statistical Manual of Mental Disorders (DSM), Fifth Edition (DSM-5) (American Psychiatric Association, 2013) or standardized assessment scales, such as the Post-Traumatic Stress Disorder Checklist - Civilian Version (PCL-C). Based on this assumption, total scores of assessment instruments were used to measure PTSS in previous studies (González-Sanguino et al., 2020; Liang et al., 2020; Liu et al., 2020). However, this approach obscures potential differences in manifestations between different PTSS symptoms. In addition, the alternative, “causal systems perspective” (Borsboom, 2008) posits that the co-occurrence of a cluster of symptoms is due to their direct relationships with each other rather than an underlying psychiatric disorder. Merely considering total scores on assessment scales obscures information about inter-relationships between scale items (i.e., individual symptoms). Network analysis offers an approach that addresses these limitations, by directly testing the premise that PTSS items cohere as a syndrome, with inter-relationships between items (Borsboom and Cramer, 2013). Furthermore, network analysis provides an approach to understanding particular “bridging” PTSS that have the strongest and weakest associations with measures of health status including quality of life (QOL) which reflects general perceptions of one’s physical/mental health and social well-being and serves as an outcome measure in evaluating the effectiveness of treatments for PTSS (Katschnig, 2006).

Existing network studies have examined PTSS within healthy populations (Jiang et al., 2020), patients with psychotic disorders (Hardy et al., 2021), and healthcare workers (Hoorelbeke et al., 2021) during the COVID-19 pandemic. However, to date, network analysis studies on PTSS in Wuhan residents have not been published. Therefore, this study explored inter-relationships between individual PTSS items and their associations with quality of life (QOL) among Wuhan residents during the later stage of the COVID-19 pandemic.

2. Methods

2.1. Participants

This cross-sectional survey was based on a large-scale project conducted between May 25 and June 18, 2020 on mental health among Wuhan residents after the initial COVID-19 outbreak (Zhao et al., 2021b). A snowball sampling method was adopted in Wuhan, Hubei province, China, a large city of approximately 12.3 million of residents in 2020 (Wuhan Bureau of Statistics, 2021). The survey invitation was initially advertised online using WeChat by research team members who work and live in Wuhan. WeChat is the most popular smartphone-based social communication application in China, with >1.2 billion active users per month nationwide; all residents needed to report health information, via WeChat, when entering public service buildings (e.g., such as schools, hospitals, stores, libraries, airports and train stations) and workplace settings during the COVID-19 pandemic. Therefore, all residents were presumably WeChat users. In this study, a WeChat-imbedded QuestionnaireStar application was used to collect data. A quick response (QR) code and link to the online questionnaire were designed and provided in the survey invitation advertisement.

The inclusion criteria were: 1) aged 18 years or older; 2) never infected with COVID-19 based on self-report (Goldrick-Rab et al., 2022; Perlis et al., 2021); 3) able to understand the purpose and contents of the survey. All participants were required to provide electronic informed consent before the assessment. The study protocol was approved by the Ethics Committee of Beijing Anding Hospital, Capital Medical University.

2.2. Assessment tools

Basic demographic data included age, gender, marital status, and education level. The validated Chinese version of the PCL-C was used to assess PTSS (Weathers et al., 1993; Yang et al., 2007). The index event for PCL-C was the COVID-19 pandemic, which was presented in the instructions for participants. The PCL-C comprises 17 items assessing three clusters of PTSS: intrusion, avoidance/numbing, and hyperarousal. Each item was rated on a severity scale from 1 (not at all) to 5 (extremely). A total score of 38 to 49 indicates “having some degree of PTSS”, while a total score of ≥50 indicates “having significant PTSS” (Yang et al., 2007). In this study, participants with total scores ≥38 were defined as clinical cases, while those with a total score of <38 were nonclinical cases. Global QOL was assessed using the first two general items of the World Health Organization Quality of Life Questionnaire - brief version (WHOQOL-BREF) (Fang et al., 1999; The WHOQOL GROUP, 1998). These items (i.e., “How satisfied are you with your
“How would you rate your health?” and “How would you rate your quality of life?” have been found to be a valid representation of overall QOL (Yao et al., 2002). Each general item was scored from 1 (very poor/very dissatisfied) to 5 (very good/very satisfied). Total QOL scores were calculated by summing the two item scores; higher scores represented better QOL (Skevington and Tucker, 1999). Chinese versions of the PCL-C and WHOQOL-BREF have been validated previously and have adequate psychometric properties (Xia et al., 2012; Yang et al., 2007). Cronbach’s alpha values for PCL-C and the two-item WHOQOL were 0.94 and 0.63, respectively in the present sample.

2.3. Statistics

2.3.1. The original network of PTSS

The R packages “bootnet” (Epskamp et al., 2018) and “qgraph” (Epskamp et al., 2012) were used to estimate the original network of PTSS. In this network, all PCL-C items were displayed as nodes while partial correlation coefficients between each pair of items were displayed as edges. The network structure was estimated using a Gaussian graphical model, in which possible spurious edges were controlled using the technique of least absolute shrinkage and selection operator (LASSO) (Epskamp et al., 2018). The tuning parameter related to LASSO was selected with the extended Bayesian information criterion (EBIC). The network layout followed the Fruchterman-Reingold algorithm (Fruchterman and Reingold, 1991).

Local network properties of each node were tested using indices of strength and predictability, which were calculated using the R packages “qgraph” (Epskamp et al., 2012) and “mgm” (Haslbeck and Waldorp, 2018), respectively. The strength of a node refers to the summation of absolute edge weights connecting this node with all other nodes in the network. Predictability quantifies the extent to which a node can be predicted by all of its neighboring nodes.

Stability of strength was tested by the correlation stability coefficient (CS-coefficient) using the R package “bootnet” (Epskamp et al., 2018). Centrality was regarded as stable when the corresponding CS-coefficient was larger than 0.25, and preferably larger than 0.50 (Epskamp et al., 2018). Edge-weight accuracy was tested using a non-parametric bootstrap approach and visualized with a line diagram. Significant differences between edge weights and between node strengths were visualized using separate bootstrapped difference tests. In addition, Exploratory Graph Analyses (EGA) (Christensen and Golino, 2019) was used to detect the dimensionality of the PTSS with the R packages “EGAnet” (Golino et al., 2020).

Finally, PTSS networks of clinical and nonclinical samples were...
compared using Network Comparison Tests, including a network invariance test, global strength invariance test, and edge invariance test. All of these indices were calculated based on permutation tests using the R package “Network Comparison Test” (van Borkulo et al., 2017).

2.3.2. The network of PTSS after controlling for covariates

To estimate potentially confounding effects of basic demographic variables as covariates (i.e., age, gender, marital status, and education level) on the original PTSS network, a network of PTSS was also constructed after controlling for these demographic covariates. Since both categorical and continuous variables were included in this network, Mixed Graphical Models (MGM) were used to estimate the network with the R package “mgm” (Haslbeck and Waldorp, 2015). In this network model, LASSO was applied to avoid false positive edges, while the corresponding tuning parameter was selected with EBIC. Strength and predictability were calculated in this network after controlling for covariates to re-examine the significance of each PCL-C item. In addition, Spearman’s rank correlation coefficients were calculated to test the consistency of strengths and predictability generated from the original network of PTSS and the alternative PTSS network generated after controlling for covariates.

2.3.3. The association between PTSS and QOL

Associations between QOL and PTSS items were estimated by constructing a EBIC GLASSO network with the QOL total score and all PTSS items displayed as nodes and partial correlation coefficients between nodes displayed as edges. To investigate bridge symptoms between the PCL-C community and QOL, bridge expected influence 1-step (EI1) and 2-step (EI2) procedures were applied using the R package “network-tools” (Jones, 2017). EI1 represents the summation of weights of all edges for each PCL-C item with QOL as well as vice versa. In addition, EI2 includes the indirect effect a node has on its neighboring nodes based on EI1 results.

3. Results

3.1. Characteristics of the study sample

A total of 2598 participants met the study entry criteria and were included in the analyses. Sociodemographic data for the sample are summarized in Table 1. The mean age of participants was 35.5 years (standard deviation (SD) = 10.9 years) and 25.7% (n = 668) were men. Total mean scores for PTSS and QOL were 23.7 (SD = 8.4) and 6.5 (SD = 1.3), respectively. Mean PTSS item scores ranged from 1.15 (SD = 0.45) (‘Flashbacks’, PCL2) to 1.66 (SD = 0.84) (‘Irritability’, PCL14) (Table 2). The prevalence of “having some degree of or significant PTSS” (i.e., total score of PCL-C ≥ 38) and “having significant PTSS” (total score of PCL-C ≥ 50) were 5.89% (95% CI = 4.98% to 6.80%) and 2.00% (95%CI = 1.46% to 2.54%), respectively.

3.2. The original network of PTSS

The original network model of PTSS is displayed in Fig. 1a, while brief node labels are presented in Table 1. A total of 101 (74.3%) non-zero edges emerged out of the 136 possible edges. In relation to strength, the most central node was “Avoiding reminders” (PCL7) followed by “Feeling emotionally numb” (PCL11), “Avoiding thoughts” (PCL6), “Hypervigilance” (PCL16), “Reliving experiences” (PCL3), and “Loss of interest” (PCL9). The bootstrapped difference test for strength revealed that strengths of these nodes were significantly larger than other nodes in the network (Fig. 2a and Supplementary Fig. 1). The strength index was reliable since the CS-
The coefficient value for strength was 0.75 when 70% of the sample was dropped (Epskamp et al., 2018).

The predictability index of each node ranged from 0.40 (‘Memory difficulties’, PCL8) to 0.73 (‘Avoiding reminders’, PCL7). On average, 56% of each node’s variance could be explained by neighboring nodes (mean predictability = 0.56 (SD = 0.09); hence, less than half of the variance (i.e., 44%) in the network was unexplained. In addition, node strength and predictability were not related to mean item scores (r_s = 0.14, P = 0.59 and r_s = 0.16, P = 0.54, respectively).

As displayed in Supplementary Fig. 2, the relatively narrow bootstrapped CIs indicated that the estimated edge-weights were precise. The bootstrapped difference test for edge-weights revealed that the connection between “Avoiding thoughts” (PCL6) and “Avoiding reminders” (PCL7) was the strongest edge and was significantly different from all other edges (Supplementary Fig. 3).

The Network Comparison Test did not find significant differences in terms of the network invariance test (M = 0.14, P = 0.99) or global strength invariance test (S = 0.02, P = 0.95) between networks of clinical and nonclinical samples (Supplementary Fig. 4). The edge invariance test was not examined since the network structure was invariant (van Borkulo et al., 2017).

3.3. The impact of covariates on the network of PTSS

The network of PTSS, after controlling for covariates, is displayed in Fig. 1b. Similar to initial network model results (Fig. 2b), the most central PTSS item in this network based on index strength was “Avoiding reminders” (PCL7), followed by “Feeling emotionally numb” (PCL11), “Hypervigilance” (PCL16), “Reliving experiences” (PCL3), “Concentration difficulties” (PCL15), and “Avoiding thoughts” (PCL6). Predictability indexes of nodes ranged from 0.40 (‘Memory difficulties’, PCL8) to 0.73 (‘Avoiding reminders’, PCL7). Also replicating initial results, on average, 56% of each node’s variance could be explained by neighboring nodes (mean predictability = 0.56 (SD = 0.09)).

Strengths generated from the original PTSS network model and the PTSS network model after controlling for covariates were highly correlated (r_s = 0.97, P < 0.01). Similarly, predictability generated from the two network models was also highly correlated (r_s = 0.99, P < 0.01).

3.4. Community detection

A total of three symptom communities were detected in the original PTSS network, with the nodes closely related with each other within each of the communities. The nodes in community 1 (PCL1 - PCL7) were symptoms related to re-experiencing and avoidance, while the nodes in community 2 (PCL8 - PCL12) and 3 (PCL13 - PCL17) were symptoms related to negative changes in thinking and mood and hyper-arousal, respectively (Supplementary Fig. 5).

3.5. The association between PTSS and QOL

As displayed in the PTSS-QOL network (Fig. 3), QOL was connected to all PTSS items except for “Reliving experiences” (PCL3), “Psychological reactions” (PCL4), “Avoiding thoughts” (PCL6), and “Hypervigilance” (PCL16). Of all the connections between QOL and PTSS items, the most influential bridge symptoms were “Sleep disturbances” (PCL13), “Irritability” (PCL14), and “Loss of interest” (PCL9) (Supplementary Fig. 6).

4. Discussion

This is the first study to examine inter-relationships between PTSS symptoms and their association with QOL after the initial COVID-19 outbreak among residents at its initial epicenter using a network...
In this study, “Avoiding reminders”, “Feeling emotionally numb”, “Avoiding thoughts”, “Hypervigilance”, and “Reliving experiences” were the most central (influential) nodes based on index strength in the original PTSS network model and an alternate model that first controlled for age, gender, marital status, and education level. The strongest connection was the edge between “Avoiding thoughts” and “Avoiding reminders”. Three PTSS communities were detected and can be summarized as “re-experiencing and avoidance”, “negative changes in thinking and mood”, and “hyperarousal”. Key bridge symptoms connecting the PTSS cluster and QOL were “Sleep disturbances”, “Irritability”, and “Loss of interest”. The identification of central PTSS could indicate particular symptoms that are most influential in triggering and/ or maintaining a broader range of PTSS symptoms (Epskamp et al., 2012). Conversely, the identification of the most influential bridging symptoms connecting the PTSS community and QOL could indicate particular PTSS that have the strongest impact on QOL. Information about central symptoms and bridge symptoms connecting PTSS and QOL provides useful information about symptoms that are potentially those most critical as intervention targets. Furthermore, the identified key interactions between individual PTSS symptoms should be considered specifically when developing intervention strategy for PTSS.

Previous network analysis studies examining the structure of PTSS in different subpopulations following various traumatic events have produced mixed results. This study found that “Avoiding reminders” (PCL7) was the most influential PTSS symptom, in line with some (An et al., 2021; Hooorelbeke et al., 2021) but not all previous findings (Hardy et al., 2021; Jiang et al., 2020). To elaborate, avoidance of reminders was the most central item in a PTSS network model based on PCL-C items in Chinese healthcare workers assessed during the COVID-19 pandemic (Hooorelbeke et al., 2021), as well as a PTSS network measured by the Child PTSD Symptom Scale in a sample of Chinese youth earthquake survivors at a 1.5 year post-earthquake assessment (An et al., 2021). In contrast, self-destructive/reckless behaviors related to the COVID-19 pandemic as assessed by the PCL-5 were the most central symptom within a healthy sample from the general population (Jiang et al., 2020). Different central symptoms in other studies included negative beliefs about the self or other negative beliefs (Hardy et al., 2021), flashbacks (Lazarov et al., 2020), and psychophysiological reactivity (Fried et al., 2018; McNally et al., 2017). Inconsistent network structures between studies may be partly due to different PTSS measures, traumatic events (Benfer et al., 2018), follow-up durations (An et al., 2021; Bryant et al., 2017), sample demographics and psychiatric conditions under study. Nonetheless, our findings for the most prominent edge between “Avoiding reminders” and “Avoiding thoughts” dovetail with results of other China-based studies conducted during the COVID-19 pandemic (Hooorelbeke et al., 2021; Jiang et al., 2020) and underscore avoidance as a key facet of PTSS in this context.

Three symptom communities were detected in the PTSS network: a re-experiencing and avoidance community, a negative change in thinking and mood community, and a hyper-arousal community. According to PTSD diagnostic criteria in the DSM-5, symptoms of PTSD can be sorted into four groups, including intrusive symptoms, avoidance symptoms, negative alterations in cognitions and mood, and alterations in arousal and reactivity. PTSS items (PCL1 - PCL7) in the re-experiencing and avoidance community are similar to intrusive and avoidance symptoms in this DSM-5 formulation. PTSS items that comprise the negative changes in thinking and mood community (PCL8 - PCL12) align with the DSM-5 cluster reflecting negative alterations in cognitions and mood. And finally, PTSS items in the hyper-arousal community (PCL13 - PCL17) are similar to symptoms in the DSM-5 cluster reflecting alterations in arousal and reactivity. As such, these findings provided empirical support for the PTSS symptom clusters widely adopted in diagnostic instruments such as DSM-5 (American Psychiatric Association, 2013).

According to the distress/protection model, QOL is determined by the interaction between risk factors and protective factors (Voruganti et al., 1998). In this study, “Sleep disturbances” (PCL3), “Irritability” (PCL4), and “Loss of interest” (PCL9) were the most influential “risk factors” of poorer QOL. Sleep disturbances may lead to daily time fatigue, general emotional malaise and impairments in cognitive functioning, work performance and social functioning (Fortier-Brochu et al., 2012), and poor physical health (Khan et al., 2020), all of which could lower QOL. Loss of interest, a common associated feature of PTSD and a core symptom of depressed mood, has been identified as a risk factor of lower QOL (Eren et al., 2006; Gudmundsson et al., 2006; Ruo et al., 2003; Sainsbury et al., 2013) due to its links with impairments in cognitive functioning (Kulpers et al., 2016; Wei et al., 2019), physical health (Holvast et al., 2017; Roy-Byrne et al., 2008), and social functioning (Prina et al., 2011). Finally, irritability has been linked to hyper-arousal and sleep disturbances both more generally (Bandypadhyay and Sigua, 2019) and during the COVID-19 pandemic (De Los Santos et al., 2022). Irritability can contribute to problems in social relationships, losses of social support and increased conflict with others, possibly worsening emotional distress and lowering QOL. In light of the emergence of sleep disturbances, irritability, and loss of interest as key bridge symptoms linking PTSS with poorer quality of life, disturbances in sleep hygiene and depressed mood symptoms should be considered as a focus of assessments and interventions for Wuhan residents with PTSS elevations during the COVID-19 pandemic.
Concerning the continuity of clinical versus nonclinical experiences of PTSS, a broad phenotype of PTSS may exist in the general population (Waller et al., 2022). Therefore, this study examined PTSS networks in both clinical and nonclinical samples. Network comparison tests revealed network structures of PTSS did not differ between cohorts who reported clinically significant PTSS and those who did not. This finding suggests that central PTSS symptoms, strong connections between symptoms, and symptoms bridging PTSS to QOL are shared between these two groups and should be addressed, regardless of clinical status.

Strengths of this study included a large sample size and utilization of a rigorous network analysis approach to identify key central and bridge symptoms of PTSD in a group at the initial epicenter of the COVID-19 pandemic. However, several methodological limitations should also be noted. First, due to the cross-sectional study design, causal relations cannot be inferred. Second, although there is value in recruiting and following samples at history of COVID-19. Unfortunately, self-report measures are susceptible to participant biases related to recall and/or social desirability. Third, although there is value in recruiting and following samples at initial epicenters of pandemics, it is not clear how well our findings may generalize beyond Wuhan residents recruited in early stage of the COVID-19 outbreak in China. Finally, the alpha for the QOL measure was slightly lower than the preferred threshold of α = 0.70 or higher.

In conclusion, central PTSS symptoms identified in this network model (e.g., avoiding reminders, feeling emotionally numb, avoiding thoughts, hypervigilance, and reliving experiences) reflected avoidance and intrusiveness should be prioritized as targets in both psychological assessment and intervention for PTSS among Wuhan residents after the COVID-19 outbreak. In addition, the emergence of sleep disturbances, irritability, and loss of interest as key bridge symptoms linking PTSS with poorer QOL suggests interventions to improve sleep hygiene, stress management, and depressed mood also warrant consideration among at-risk Wuhan residents.

CRediT authorship contribution statement

Study design: Shu-Fang Zhang, Bingxiang Yang, Sha Sha, Yu-Tao Xiang.

Data collection, analysis and interpretation: Wen Li, Yan-Jie Zhao, Shu-Fang Zhang, Bingxiang Yang.

Drafting of the manuscript: Wen Li, Teris Cheung, Yu-Tao Xiang.

Critical revision of the manuscript: Todd Jackson.

Approval of the final version for publication: all co-authors.

Conflict of Interest

The authors have no conflicts of interest to declare.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jad.2022.08.074.

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